When is Health Innovation Worth it?

Essays on new Approaches to value Creation in Health

Starr, Laila

COPENHAGEN BUSINESS SCHOOL
SOLBJERG PLADS 3
DK-2000 FREDERIKSBERG
DANMARK

WWW.CBS.DK

ISSN 0906-6934

Print ISBN: 978-87-7568-061-0
Online ISBN: 978-87-7568-062-7

WHEN IS HEALTH INNOVATION WORTH IT?

PhD Series 04.2022

LAILA STARR

WHEN IS HEALTH INNOVATION WORTH IT?

ESSAYS ON NEW APPROACHES TO VALUE CREATION IN HEALTH

CBS PhD School | **PhD Series 04.2022**

CBS COPENHAGEN BUSINESS SCHOOL
HANDELSHØJSKOLEN

WHEN IS HEALTH INNOVATION WORTH IT?

ESSAYS ON NEW APPROACHES TO VALUE CREATION IN HEALTH

LAILA STARR

Department of Economics
Copenhagen Business School

Market Access
Novo Nordisk A/S

Section of Health Service Research, Department of Public Health
University of Copenhagen

Supervisor: Professor Peter Bogetoft
Co-supervisor: Jens Gundgaard

CBS PhD School
Copenhagen Business School

LAILA STARR
WHEN IS HEALTH INNOVATION WORTH IT?
ESSAYS ON NEW APPROACHES TO VALUE CREATION IN HEALTH

1st edition 2022
PhD Series 04.2022

ISSN 0906-6934

Print ISBN: 978-87-7568-061-0
Online ISBN: 978-87-7568-062-7

The CBS PhD School is an active and international research environment at Copenhagen Business School for PhD students working on theoretical and empirical research projects, including interdisciplinary ones, related to economics and the organisation and management of private businesses, as well as public and voluntary institutions, at business, industry and country level.

Foreword

This doctoral dissertation presents the work that I have conducted in collaboration with the Depart of Market Access at Novo Nordisk A/S and the Department of Economics at Copenhagen Business School from 2013–2021 and with the Section of Health Service Research, Department of Public Health at University of Copenhagen from 2019–2021. I am thankful to the many people who have contributed directly or indirectly to this PhD dissertation through formal collaborative efforts, inspiration, casual dialogues, and cheering support, or simply by encouraging me to finish. This dissertation has only been made possible with the help of several people who I would like to take the opportunity to thank.

I was privileged to share my time between academia and industry, and I would like to express my appreciation to the good and knowledgeable colleagues, and the inspiring and very pleasant work environment, at all institutions. Especially, I would like to express my appreciation for my supervisor Professor Peter Bogetoft for your motivation, support, and rich academic knowledge during this dissertation's long gestation period. Thank you to my colleague at Novo Nordisk A/S, health economist Jens Gundgaard, who, for a period, stepped in as co-supervisor. Thanks to Theodor Stewart from the University of Cape Town and William Greene from New York University's Stern School of Business, for your inspiration and for making my research stays possible. A special recognition to Professor Karsten Vrangbæk, University of Copenhagen, and former colleague at Novo Nordisk A/S health economist Uffe Ploug for reaching out, sharing your knowledge and providing your encouragement and support when I needed it the most. Thanks to Professor Lars Peter Østerdal and Assistant Professor Kristian Schultz Hansen for providing constructive feedback and valuable suggestions for improvements towards the

end. Thanks go to my longtime friend Sara Kofoed Heiberg for your continuous enthusiasm, persistent encouragement, and interest into this PhD.

And to the most important people in my life: Theodor, Nora, and Siri Augusta: You are my everything and have taught me so much about life not least about decision-making, preferences, prioritization, and how maximizing utility works in real life. Zachary, thanks for your endless and unconditional love, for being my rock and for your inspiration and support. Thanks for dreaming with me and for living out our dreams. I am forever grateful for your positive and optimistic worldview and for believing that hope is a great strategy.

Although I am tremendously thankful to many others, this work is my own, and I am to be held solely accountable for the content of this dissertation.

Laila Starr

Funding Acknowledgements:

I am grateful for the generous economic support from Innovation Fund Denmark, Novo Nordisk A/S, the European Institute of Innovation and Technology (EIT) (the European Union's Horizon 2020 Research and Innovation program), and the Copenhagen Business School. I am also very thankful for the additional travel support that I received from Otto Mønsted Fonden, Augustinus Fonden, Vera and Carl Johan Michaelsens Legat, and Oticon Fonden. Thank you for believing in me and supporting me so liberally.

Summary (English)

Many countries are challenged with issues on how to allocate limited resources across a range of healthcare services at a time when the demand for healthcare continues to grow faster than healthcare budgets. For decision-makers, it has therefore become increasingly important to adopt robust processes for priority setting so that limited health resources are allocated effectively (i.e., doing the right things), efficiently (i.e., doing things right), and transparently. In my dissertation, I use different frameworks to shed light on this issue. This thesis comprises an introduction chapter, five self-contained papers, and a conclusion.

In the first paper, “Benchmarking and Predicting the Demand for New Diabetes Drug” (Bogetoft & Starr, 2021)”, we used benchmarking analysis and linear programming to evaluate existing diabetes drugs and to estimate the demand for a new drug. In this effort, we estimated the revealed/observed preferences for diabetes products and used this information proactively to identify the ideal target product profile (TPP) for new molecules as well as to identify target sales uptake and target price for future products. We benchmarked the existing drugs in 2019 using data envelopment analysis (DEA) and a multi-criteria decision analysis (MCDA) approach which examined the inevitable trade-offs among different product attributes. The results showed that some of the drugs were only marginally efficient, suggesting that they should be in limited demand. Using existing sales data, we next made partial inferences about the preferences that different patient groups have for the different drug attributes. Using this information, we determined how the attributes of a new drug are likely to affect demand for this drug. Likewise, we were able to estimate which share of the present users of the existing drugs are likely to switch to a new drug. This is a novel

and valuable tool when identifying new promising molecules expected to meet the unmet medical needs of the patients and identify the ideal sales prices to comply with the budget constraints that payers are subject to and, thus, minimize the development risk to manufacturers. This tool can be important in relation to having the most optimal product portfolio with the ideal price, and at the same time, it is a useful tool for communicating the value of the products.

The second paper, “Are Danish National Reimbursement Priorities Worthwhile for Patients? An Investigation Using the Discrete Choice Experiment” (Starr et al., 2021) documents a case study of national priority setting on the Danish market for insulin treatment. The aim of the study was to elicit patients’ benefit–risk preference for injectable diabetes treatment and to identify segments with differences in preference for treatment based on their socioeconomic position and individual health indicators. Further, another goal was to find out whether national recommendations for pharmacologically glucose-lowering treatment compared with Danish diabetes patients’ stated preferences for treatment. We found that different groups of insulin users may be stratified by their preference for diabetes treatment, and that these groups reflect the priorities for treatment set nationally. In general, type 2 diabetes patients with a strong preference for avoiding hypoglycemic events are prescribed treatment corresponding to their stated preferences. The significance of this study can be assessed via the comprehensive empirical data structure underpinning the analysis. The unique combination of self-reported and health registry data enabled the evaluation of segments with possible differences in preference for the benefit and risk characteristics of treatment. The results of this study should assist health organizations in deciding if the same treatment fits all patients or if segments of the type 2 diabetes population benefit more from particular characteristics of treatment than others.

Furthermore, it is one of few experiments eliciting preference for treatments modifying cardiovascular (CV) risk in diabetes, and so the potential for use in benefit–risk assessment is significant. This paper will inform such decisions by providing quantitative preference evidence for the trade-offs made between side effects and treatment efficacy by insulin users.

In order to ensure fast access to new possibly valuable health technologies, to obtain best value for money, and to ensure affordability, payers within healthcare have started to adopt new innovative reimbursement approaches, for example, value-based healthcare (VBHC). The effort to move towards VBHC should be seen in the context of a decade of experience with the introduction of performance measurement systems in which the reimbursement is linked to volume of activities, that is, a traditional fee-for-service or capitated approach. However, the traditional type of reimbursement has not provided much information or attention to the quality of service or the outcomes of treatment and care, which the VBHC seeks to do. The following three articles cover areas of VBHC.

In the paper, “Value-Based Healthcare Classification and Experiences in Denmark” (Starr & Vrangbæk, 2021), we aimed to provide a theoretical discussion of how VBHC may affect the public–private relationship in the Danish healthcare systems and to develop a typology of VBHC projects. The typology was used in our descriptive mapping of projects from Denmark involving public and private actors and VBHC concepts. We found that, despite a push for VBHC and suitable infrastructure in Denmark such as good national health registers, the concept is not used extensively within the Danish healthcare system. The high degree of definitional inconsistency and the lack of comprehensive evaluations made it difficult to compare VBHC payment models and draw conclusions about their

relative efficacy. In the identified examples, often times the projects involved only specific departments and patient groups and while this approach makes sense as a starting point, it does not fundamentally change the modus operandi, or indeed, adhere to the full set of VBHC principles.

In the paper, “Assessment of Roche Diabetes Care/Odsherred Municipality Value-Based Healthcare Diabetes Project 2017-2019 – Feasibility and Transferability Lessons” (Starr, 2021a), I evaluated one of the first public–private value-based healthcare projects in Denmark. My assessment was built on an exploratory analysis using semi-structured interviews. In this project, the payment was governed by an outcome-based agreement between the pharmaceutical company Roche Diabetes Care and Odsherred municipality. The aim of the project was to ensure that the diabetics received the necessary support, counseling, and tools, while the municipality’s reimbursement depended on the value achieved by the patients. The company and the municipality had hoped and expected a high number of participants, but after the initial two-year period, they had to conclude that very few patients had participated. I concluded that there is a significant potential for increasing patient value of the health services offered and to develop the private–public collaboration in Denmark; however, the experiences from Odsherred showed that design and implementation require significant and ongoing efforts – possibly greater efforts than most local municipalities are capable of.

In the paper “Designing a Value-based Healthcare Contract – Lessons from a Public-Private Pay-for-Performance Healthcare Collaboration” (Starr, 2021b) I evaluated the design of a VBHC contract using contract theory. I used one of the first Danish public–private VBHC contracts to discuss the different priority goals of

contract design. Designing a contract involves trading-off different goals of contract design while aiming at explicitly incorporating different stakeholders' engagement. It became clear that there is a complex set of principal–agent problems within healthcare which might give rise to conflict of interests and problems of control. It is essential that the findings of the principal–agent theory and the solution options are implemented in practice, so that the existing information asymmetries can be reduced and the objectives of the parties harmonized.

In line with this, motivation issues will arise among parties as contract theory assumes that people act opportunistically, that is, individuals are depicted as selfish and are presumed to exploit the situation for their own benefit, and thus will only act in self-interest and reveal private information and coordination. Likewise, coordination challenges are likely to be present when seeking an alignment between the patient preferences and the providers' deliverables and other stakeholders' interests. Transaction costs will arise during the course of negotiation and implementation of contracts. In order to limit monopoly situations, I recommended that individual contracts should be completed in a competitive procurement process, in which potentially relevant providers are invited to tender.

Thus, despite VBHC being intrinsically appealing, a number of major barriers were identified for implementing this at a larger scale, including: 1) the associated transaction and administration resources, time, and commitment, or some combination thereof, are constrained as is the case in many municipalities; 2) challenges in tracking performance and combining the data from different sources; 3) developing and agreeing on the contract; 4) involving and motivating all

stakeholders, for example, general practitioners, and collaboration across regions and sectors; and 5) ensuring trust among the different stakeholders aided by the design of the contract.

Thus, in summary, different approaches exist to achieve a more efficient, effective, and transparent allocation of the limited healthcare resources available which, at the same time, include the preferences of the stakeholders of the healthcare system; however, there are still many unsolved issues in respect to successful and more widespread implementation.

Keywords: health economics, health economic evaluation, health innovation, pharmaceutical forecasting, medical pricing, competitive analysis, multi-criteria decision analysis (MCDA), decision modeling, revealed preference, stated preference, value-based healthcare (VBHC), pay-for-performance, private–public partnership, innovative contracting, contract theory.

Abstract (Danish)

Efterspørgslen efter sundhedsydelser fortsætter i mange lande med at stige hurtigere end sundhedsvæsenets budgetter, og spørgsmålet om, hvordan man fordeler de begrænsede ressourcer på tværs af en række sundhedsydelser er derfor presserende. For beslutningstagere er det derfor blevet stadigt vigtigere at processerne til prioritering er transparente og robuste, så de begrænsede sundhedsressourcer fordeles *effektivt* (dvs. gør de rigtige ting) og *efficient* (dvs. gør tingene rigtigt) og transparent. I denne afhandling bruger jeg forskellige rammer til at belyse dette emne: Denne afhandling består af et introduktionskapitel, fem selvstændige artikler og en konklusion.

I den første artikel, "Benchmarking and Predicting the Demand for New Diabetes Drug" *(Benchmarking og forudsigelse af efterspørgslen efter et nyt diabetesmiddel)* bruger vi benchmarkinganalyse og lineær programmering til at evaluere eksisterende diabeteslægemidler og til at estimere den forventede efterspørgsel efter et nyt lægemiddel. I dette studie benytter vi de observerede præferencer for diabetesprodukter og bruger disse oplysninger proaktivt til at identificere den mest ideelle produktprofil for nye molekyler, samt identificerer det optimale markedsoptag såvel som pris for fremtidige produkter. Vi benchmarker de eksisterende lægemidler (i 2019) ved hjælp af en data envelopment analysis (DEA) og multikriterie beslutningsanalyse (MCDA) tilgang, hvor de uundgåelige trade-offs mellem forskellige produktattributter konfronteres. Vores resultaterne viser, at nogle af produkterne kun er marginalt efficiente. Dette antyder, at der burde være begrænset efterspørgsel efter disse produkter. Ved brug af eksisterende salgsdata har det været muligt at estimere de præferencer, som forskellige patientgrupper har for de forskellige lægemiddelattributter, dvs. fordele og ulemper ved at

benytte produktet, og bestemme, hvordan egenskaberne for et nyt lægemiddel sandsynligvis vil påvirke efterspørgslen efter dette lægemiddel. På samme måde kan vi estimere, hvilken andel af de nuværende brugere af de eksisterende lægemidler, der sandsynligvis vil skifte til et nyt lægemiddel. Dette redskab er vigtigt i forhold til at have den mest optimale produkt portfolio med den mest optimale pris, og er samtidig et nyttigt redskab til at kommunikere værdien af produkterne.

Inddragelse af patient præferencer indenfor sundhedsvæsenet og udviklingen af medicin er en oplagt mulighed, som benyttes i stigende grad. Den anden artikel i denne afhandling, "Are Danish National Reimbursement Priorities Worthwhile for Patients? An Investigation Using the Discrete Choice Experiment" *("Er danske nationale tilskudsprioriteringer umagen værd for patienter? En undersøgelse lavet med et diskret valgeksperiment"),* er et casestudie af danske prioriteringer og patientpræferencer indenfor insulinbehandling. Formålet med studiet er at estimere patienternes præferencerne for injicerbar diabetesbehandling, og identificere forskellige segmenter af population i forhold til forskelle i præferencer for behandling. I artiklen diskuterer vi desuden, om de nationale anbefalinger til farmakologisk glukosesænkende behandling er sammenlignelige med patienternes præferencer for behandling. Vi finder, at forskellige grupper af insulinbrugere kan stratificeres efter deres præference for diabetesbehandling, og at disse grupper afspejler de prioriteter for behandling, der er sat nationalt. På gruppe niveau kan vi konkludere, at diabetespatienter med en stærk præference for at undgå hypoglykæmiske hændelser generelt gives behandling svarende til deres angivne præferencer. Den unikke kombination af selvrapporterede data og data fra sundhedsregistre muliggjorde en evaluering af forskellene i præferencer i diabetesbehandlingen. Resultaterne af dette studie kan forhåbentlig hjælpe

sundhedsorganisationer med at beslutte, om den samme behandling passer til alle, eller om segmenter af type 2-diabetespopulationen har større fordel af en ofte dyrere behandling end andre.

For at sikre hurtig adgang til nye og muligvis værdifulde medikamenter, opnå den største værdi af de begrænsede ressourcer, samt sikre overkommelige priser, er betalere inden for sundhedsvæsenet begyndt at anvende nye innovative refusionsmetoder, fx værdibaseret styring (VBHC). VBHC er en strategi for udvikling af sundhedsvæsnet, som sigter mod at opnå de bedst mulige resultater for patienten med et effektivt ressourceforbrug. Ideen om, at sundhedsvæsenet skal levere behandling med værdi for patienten er selvsagt ikke ny, men VBHC indebærer, at de traditionelle, organisatoriske grænseflader udviskes, og sundhedsindsatsen i stedet organiseres med udgangspunkt i patients behov. VBHC er en styringsmodel, hvor udbydere betales baseret på patientens resultater i stedet for en traditionel gebyr-for-service tilgang, hvor udbyderen betales baseret på mængden af sundhedsydelser, de leverer. De næste tre artikler dækker områder med værdibaseret styring:

I artiklen "Value-Based Healthcare Classification and Experiences in Denmark" (Klassifikationer og erfaringer med værdibaseret styring indenfor sundhed i Danmark) (Starr & Vrangbæk, 2021) tilstræber vi, at give en teoretisk diskussion af, hvordan VBHC kan påvirke det offentligt-private samarbejde indenfor det danske sundhedsvæsen, samt desuden at udvikle en typologi af VBHC-projekter. Typologien bruges i vores beskrivende kortlægning af projekter fra Danmark, der involverer offentlige og private aktører og VBHC-koncepter. Vi fandt, at på trods af forskellige incitamenter til at forsøge med VBHC, og at infrastrukturen i Danmark er egnet til VBHC, grundet fx gode nationale sundhedsregistre, anvendes

konceptet ikke i vid udstrækning inden for det danske sundhedssystem. Opfattelsen af, hvad der kan defineres som VBHC er noget varierende og manglen på omfattende evalueringer gør det vanskeligt at sammenligne VBHC-betalingsmodeller og drage konklusioner om deres relative effektivitet. I de projekter som identificerede sig selv som VBHC omfattede projekterne ofte kun specifikke afdelinger og/eller patientgrupper, og selvom denne tilgang som udgangspunkt giver mening, ændrer den ikke fundamentalt modus operandi eller overholder det fulde sæt af VBHC-principper.

I artiklen "Assessment of Roche Diabetes Care/Odsherred Municipality Value-Based Healthcare Diabetes Project 2017-2019 – Feasibility and Transferability Lessons" (*Evaluering af Roche Diabetes Care/Odsherred Kommunes værdibaserede diabetes projekt 2017-2019 – feasibilitet og transferabilitet*) (Starr, 2021a), evaluerede jeg et af de første offentlige-private værdibaserede sundhedsprojekter i Danmark ved brug af semistrukturerede interviews med forskellige interessenter. I dette projekt var betalingen styret af en resultatbaseret aftale mellem medicinalfirmaet Roche Diabetes Care og Odsherred Kommune. Formålet med projektet var at sikre, at diabetikerne fik den nødvendige støtte, rådgivning og værktøjer til at håndtere deres sygdom, mens kommunens udbetaling var afhængig af patientens resultater – med andre ord værdien af behandlingen. Den primære intervention var udstyr til blodsukker samt digital adgang til diætister og trænere. Konklusionen af min evaluering var, at der er et betydeligt potentiale for at øge patientværdien af de tilbudte sundhedsydelser og at VBHC kan udvikle sig i det private-offentlige samarbejde i Danmark, men erfaringerne fra Odsherred viser samtidig, at design og implementering kræver en betydelig og løbende indsats og ressourcer som mange kommuner ikke har til rådighed.

I artiklen "Designing a Value-Based Healthcare Contract – Lessons from a Public-Private Pay-for-Performance Healthcare Collaboration" (Design af en værdibaseret sundhedskontrakt – lektioner fra en et offentligt-privat pay-for-performance samarbejde) (Starr, 2021) vurderer jeg ved hjælp af kontraktteori kontrakten indgået i den ovenfornævnte værdibaserede styringsmodel mellem Odsherred Kommune og Roche Diabetes Care. At designe en kontrakt indebærer at afveje forskellige mål for kontraktdesign, mens det samtidig sigter mod at inkorporere forskellige interessenters interesser. Der er et komplekst sæt af *principal-agent* problemer inden for sundhedsvæsenet, der kan give anledning til interessekonflikt og kontrolproblemer. Det er vigtigt, at *principal-agent* teoriens løsningsmuligheder implementeres i praksis, så de eksisterende informationsasymmetrier kan reduceres og parternes mål harmoniseres.

I tråd med dette vil der opstå motivationsspørgsmål mellem parterne, idet kontraktteori antager at folk handler opportunistisk, dvs. enkeltpersoner er egoistiske og formodes at udnytte situationen til deres egen fordel og således kun vil handle i egeninteresse og afsløre privat information og koordinering. Ligeledes vil der sandsynligvis være koordinationsudfordringer, når man søger en tilpasning mellem patientens præferencer og udbydernes leverancer og andre interessenters interesser. Transaktionsomkostninger vil opstå i løbet af forhandlingen og implementeringen af kontrakterne. Den nuværende kontrakt i Odsherred er i risiko for at skabe en uheldig monopolsituation, som gør det vanskelligt for patienterne at skifte eller benytte konkurrerende produkter. For at begrænse monopoleffekterne anbefaler jeg, at individuelle kontrakter etableres via en konkurrencedygtig indkøbsproces, hvor potentielt relevante udbydere opfordres til at byde.

På trods af at VBHC kan synes tiltrækkende identificerede vi en række barrierer, som vanskeliggør implementering i større skala, herunder: 1) i mange kommuner er de tilknyttede transaktions- og administrationsressourcer, tid, engagement eller en kombination deraf begrænsede, 2) der er betydelige udfordringer ved at spore ydelsernes effekter og kombinere data fra forskellige kilder, 3) det er vanskelligt at udvikle og blive enige om kontrakten, 4) det er vanskelligt at involvere og motivere alle interessenter, f.eks. praktiserende læger og samarbejde på tværs af regioner og sektorer og 5) det er vanskelligt at sikre den nødvendige tillid mellem de forskellige interessenter i forbindelse med udformningen af kontrakten.

Nøgleord: sundhedsøkonomi, sundhedsøkonomiskevaluering, sundhedsinnovation, medicinsk regulering, multikriteriebeslutningsanalyse (MCDA), beslutningsmodellering, observerede præferencer, afslørede præferencer, værdibaseret styring, pay-for-performance, privat-offentligt samarbejde, kontraktteori

List of the articles in the dissertation

The dissertation consists of an introduction and the following articles:

i. Bogetoft, P., & Starr, L. (2021) Benchmarking and Predicting the Demand for New Diabetes Drug, Submitted to *European Journal of Operational Research*, May 2021

ii. Starr, L., von Arx, L. B., & Kjær, T. (2021) Are Danish National Reimbursement Priorities Worthwhile for Patients? An Investigation Using the Discrete Choice Experiment, modified and shortened version submitted to *International Journal of Technology Assessment in Health Care,* June 2021

iii. Starr, L., & Vrangbæk, K. (2021) Value-Based Healthcare Classification and Experiences in Denmark, EIT Health and University of Copenhagen, ISBN: 978-87-92356-01-7

iv. Starr, L. (2021a). Assessment of Roche Diabetes Care/Odsherred Municipality Value-Based Healthcare Diabetes Project 2017-2019 – Feasibility and Transferability Lessons, Working Paper, EIT Health and University of Copenhagen.

v. Starr, L. (2021b). A design Perspective on Value-Based Healthcare Contracts – Lessons from a Danish Public/Private Pay-for-Performance Based Contract, Working Paper, EIT Health Working Paper.

Other Relevant Publications

During my PhD studies, I co-authored or contributed to other publications, which although relevant to the work presented here, did not directly contribute to the empirical work of the chapters included:

- Snyman, J., Molokoane, T., Gjesing, R. P., Starr, L., & Wing, J. (2018). Barriers to intensification of insulin treatment in patients with type 2 diabetes in South Africa. *African Journal of Clinical and Outcomes Research*, *2*(1), A612.

- Jones, A., Bardram, J. E., Bækgaard, P., Cramer-Petersen, C. L., Skinner. T., Vrangbæk. K., Starr, L., Nørgaard, K., Lind, N., Christensen, M. B., Glümer, C., Wang-Sattler, R., Laxy, M., Brander. E., Heinemann, L., Heise, T., Schliess, F., Ladewig, K., & Kownatka, D. (2020). Integrated personalized diabetes management goes Europe: A multi-disciplinary approach to innovating type 2 diabetes care in Europe*. Primary Care Diabetes*, *15*(2), 360–364.

- The Economist Intelligence Unit. (2020). Digital diabetes index – Enhancing diabetes care through digital tools and services.

- Hansen, P.E., Vrangbæk, K. & Starr, L. (2022). 210997-D01 – Implementation of outcomes-based payment models based on iPDM in a Danish community setting, EIT Health. ISBN: 978-87-92356-04-8

Course work

The following courses have been completed:

2013:

- Industrial PhD course hosted by the Innovation Fund (7.5 ECT)
- Productivity and Efficiency Analysis Summer School, EWEPA & Aalto University, School of Business (4 ECTS)
- 11th Summer School on Multi-criteria Decision Aiding and Multiple Criteria Decision-Making 2013, Helmut Schmidt Universität, Hamburg (7.5 ECTS)
- Choice Modeling, Benchmarking Theories and MCDM, 2013 (2.5 ECTS)

2014:

- Microeconometrics Evaluation Methods, University of Copenhagen (1.5 ETCS)
- Using Discrete Choice Experiments in Health Economics: Theoretical and Practical Issues, University of Aberdeen (2 ECTS)

2015:

- ISPOR Short Course: Conjoint Analysis – Theory & Methods, ISPOR (0.5 ECTS)
- ISPOR Short Course: Using Multi-criteria Decision Analysis in Healthcare Decision-Making: Approaches and Applications, ISPOR (0.5 ETS)

2017:

- Benchmarking and Productivity Analyses within Economic Applications, Copenhagen Business School (5 ECTS)

List of Abbreviations

AE	Adverse Events
BIA	Budget Impact Analysis
CBA	Cost Benefit Analysis
CEA	Cost-Effectiveness Analysis
CRS	Constant Return to Scale
CUA	Cost Utility Analysis
DCE	Discrete Choice Experiments
DDP-4	Dipeptidyl peptidase-4
DEA	Data Envelopment Analysis
EMA	European Medicines Agency
EUnetHTA	European Network for HTA
FDH	Free Disposal Hull
GLP-1	Glucagon-like peptide-1
HbA1c	Haemoglobin, Type A1C
HCP	Health Care Professional
HRQoL	Health-Related Quality of Life
HTA	Health Technology Assessment
ICER	Incremental Cost-Effectiveness Ratio
INAHTA	International Network for Agencies for HTA

ISPOR	International Society for Pharmacoeconomics
MAUT/MAVT	Multi-attribute Utility/Value Theory
MCDA/MCDM	Multi-Criteria Decision Analysis/Making
NICE	The National Institute for Health and Care Excellence
NPH	Neutral Protamine Hagedorn
PRO/PROM	Patient Reported Outcomes/Measures
QALY	Quality-Adjusted Life Years
SARP	Strong Axiom of Revealed Preference
SGLT-2	Sodium glucose co-transporter-2
SU	Sulphonylureas
TTP	Target Product Profile
TZD	Thiazolidinediones
VBHC	Value-Based Healthcare
VBP	Value-Based Pricing
VRS	Variable Return to Scale
WARP	Weak Axiom of Revealed Preference
WHO	World Health Organization
WTP	Willingness-to-Pay

Table of Contents

1. Introduction

Denmark, like most other countries, is challenged with how to allocate limited health resources across healthcare at a time when demand for healthcare continues to grow faster than health budgets. The introduction of new and costly health technologies has in recent years sparked a debate about the allocation of the limited resources either between different competing services (i.e., priority setting) or across different patients (i.e., rationing). Consequently, this has also fostered discussions on how value should be assessed and which evaluation criteria should be used to inform decisions (Cohen, 2017; Linley & Hughes, 2013).

At the same time, in order for a healthcare company to stay competitive, it requires that its products are innovative and constantly reflect the evolution of technology and knowledge as well as the preferences and demands expressed by a myriad of stakeholders. For Novo Nordisk A/S, a pharmaceutical company specializing in diabetes care, the process from product conception to market access is complex, and time-consuming, and it is subject to significant risk and opportunity costs. If a product gets a low market share, it will often be considered that the product has failed. Thus, knowing the development risk and likelihood of market uptake is critical for success.

While being employed in the market access department at a pharmaceutical company, I learned first-hand that market research and launch strategy does not necessarily rely on validated instruments. Thus, developing a more accurate method to predict a molecule or product's likelihood for success could be a valuable tool to deploy for decision milestones in the development and life cycle of a new drug. Accurate crystal balls are hard to come by, but based on the works contributing to this dissertation, we offer our humble suggestion for the next best

thing: By using benchmarking analysis and linear programming and historical data, we were able to estimate the demand for new products. In this novel approach, we provide useful insight into the competitive landscape and are able to forecast the likelihood for success for a new product or a hypothetical target product profile (TPP),[1] as we are able to determine how the attributes of a new pharmaceutical product are likely to affect demand for the next product. Further, we are able to estimate the share of the present users of the existing pharmaceutical products within the portfolio who are likely to switch to the new pharmaceutical product. This tool can thereby be important when building a portfolio strategy.

Pharmaceuticals play a central role in the healthcare system, but the combination of advancements in technology as well as longer life expectancy worldwide, higher patient expectations, and increased prevalence of chronic diseases have led to an increased consumption of pharmaceuticals (Organisation for Economic Co-operation and Development [OECD], 2017). For diabetes drugs in particular, the use of anti-diabetic drugs has almost doubled in OECD countries in the period from 2000 to 2015 (OECD 2017), and the increased use of anti-diabetic drugs as well as other drugs has had a substantial budgetary impact, placing a significant pressure on the healthcare budgets – of which governments are paying the vast majority. Therefore, regulatory agencies and payers need to balance access for

[1] TPPs state intended use, target populations. and other desired attributes of products, including safety and efficacy-related characteristics.

new medicines but at the same time provide the right incentives to industry to innovate and recognize that healthcare budgets are limited.

Access to medicine in publicly funded healthcare systems is often a controversial issue (Villesen & Hildebrandt, 2013), and national health priorities are often criticized for being detached from patient preference for treatment (MacLeod et al., 2016). Furthermore, empirical research on the concordance between national pharmaceutical reimbursement strategies and patient and public preferences for funding of high-cost medicines is scarce (MacLeod et al., 2016; Muhlbacher & Juhnke, 2013; Rogge & Kittel, 2016).

Given the resources governments and health systems can dedicate to healthcare, the pathway to optimal resource allocation passes through cost containment and efficiency improvement policies. However, the methodological approach to allocation of resources in an efficient and fair way that gives legitimacy to the decision outcomes is not straightforward, due to the complexity and importance of the decisions, and ethical and social responsibilities related to those decisions. Many healthcare decisions require a careful assessment of the underlying options and the criteria used to judge these options which can be challenging given the trade-offs between multiple value criteria. With scarce healthcare resources, trade-offs are needed at multiple levels: At the national level, healthcare's appropriation of the overall budget must be decided; within the healthcare system, budgetary decisions related to policy and treatment must be made (for example prevention versus treatment, or prioritization of one treatment over another); and within each treatment area, reimbursement and return of investment must be considered (to adopt, for example, a newer more effective and expensive treatment versus a current more affordable one). While often

difficult decisions, trade-offs can lead to better efficacy, convenience, safety, and higher-value care.

It has been argued (Porter, 2010) that maximizing value for patients, defined as maximized health outcomes achieved per unit of cost spent, should be the overarching goal of healthcare. Thus, healthcare should strive to deliver outcomes that truly matter to patients, yet often this aim is challenged. There is also a lack of clarity as to how value in healthcare should be defined as some use the value to convey the humanistic principles underpinning health systems (European Commission, 2019) while others define value as cost reduction and overall process efficiency (Hurst et al., 2019).

Maximizing value should involve uniting the interests of all the stakeholders, but often the stakeholders – such as patients, society, government regulatory agencies, and medical professionals – have conflicting goals concerning such factors as profitability, access to the product, safety, quality, and convenience. The conflicting interests among stakeholders often arise in resource allocation decisions, attributable, at least in part, to existing evaluation practices not sufficiently capturing different notions of value (Drummond et al., 2013).

Assessing the value of new medical technologies may require new approaches that take into account other parameters than the current value frameworks. It has, for example, been debated whether the concept of value in healthcare needs to be extended beyond the current value framework, by systematically incorporating patients' preferences (Muhlbacher & Juhnke, 2013). At the same time, the increased use of medical health records, medical wearables, mobile devices, etc. has opened up possibilities for collecting a large amount of data on how products are actually performing in real life. Harnessing the power of the real-world data

(RWD) can change how value is demonstrated as well as rewarded, for example, in terms of value-based healthcare (VBHC).

VBHC is a healthcare delivery model in which providers are paid based on the value created to the patient. Porter and Teisberg introduced the field of VBHC to define patient value as patient-relevant outcomes divided by the costs per patient across the full cycle of care in order to achieve these outcomes (Porter, 2010; Porter & Teisberg, 2006). VBHC focuses on maximizing the value of care for patients and reducing the cost of healthcare. Porter (2010) described the transformation of the care to VBHC based on six interrelated elements: 1) Organize into integrated practice units, 2) measure outcomes and costs for every patient, 3) move to bundled payments for care cycles, 4) integrate care delivery across separate facilities, 5) expand excellent services across geography, 6) build an enabling information technology platform. Thus, providers are rewarded for the value patients experience, which is in contrast to the fee-for-service approach in which providers are paid based on the amount of activity they deliver.

In recent years, a number of initiatives have been introduced in the Danish healthcare system, piloting the use of VBHC to improve quality and management in the healthcare sector. Since value is defined as outcomes relative to costs, it embraces efficiency (Porter, 2010). However, diabetes products are, to a higher extent today than in the past, characterized as not only delivering on primary outcomes (efficacy), but also having a complex product profile often with multiple secondary outcomes. For example, the primary outcome for diabetes products is to obtain glycemic control, but some patients are at risk of hypoglycemia and lipodystrophy which hinders their compliance. This has prompted the search for easier and safer medical products with an additional secondary protective effect

other than glucose control e.g., weight reduction, reduction in major cardiovascular events, and improvements in convenience, for example, mode of action (oral versus injectable) or frequency (once weekly versus once daily) (Bogetoft & Starr, 2021). At the same time, digital solutions, which aim at improving outcomes for people with diabetes, have been introduced (The Economist Intelligence Unit, 2020). It is therefore essential for a pharmaceutical company, to be able to differentiate its products beyond that of its primary efficacy. Furthermore, it is essential to ensure that the patients are experiencing the expected primary and secondary outcomes.

Although insulin was capable of controlling glucose levels, it lacked the protective effects that scientists strived to achieve. Moreover, patients on insulin are at risk of hypoglycemia and lipodystrophy which hinders their compliance. This has prompted the search for easier and safer medical products with an additional protective effect other than glucose control.

Consequently, payers are, to an increasing extent, using multiple criteria when assessing the value of new medicines, and therefore, there is a growing need for an improved decision-making tool, which can evaluate new pharmaceutical products and take multi-dimensional criteria into account to and thus support health technology assessment (HTA) agencies in setting healthcare priorities (Marsh, 2014; Marsh et al., 2016; Thokala et al., 2016; Thokala et al., 2014).

As a response to some of the concerns raised above, decision analysis methods and specifically quantitative modeling approaches, such as multiple criteria decision analysis (MCDA), have emerged as a potential alternative or supplementary approach to traditional economic evaluation approaches (Devlin & Sussex, 2011; Marsh et al., 2016; Thokala et al., 2016). MCDA is based on the

premise that any good or service can be described by its characteristics (criteria), and the extent to which a health good or service is valued depends on the preferences for those characteristics (Ryan et al., 2001). Thus, methods of MCDA allow the assessment and balancing of benefits and risks, under consideration of preferences, that is, the real or imagined choice between at least two options that can be ranked without necessarily knowing the utility function. MCDA can aid in medical decision-making to explicitly integrate objective measurement with value judgement while transparently managing subjectivity. In an evaluation of medical products, this is advantageous; despite that the effect of a medical product is objective, the interpretation of its value is subjective.

In healthcare, the preferences and demands expressed by patients, society, government regulatory agencies, and the medical professionals regarding various benefits, risks, or application aspects of a health technology (i.e., devices, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of life) (Johnson & Zhou, 2016) can be taken into account in the decision-making process. Weighing the benefit and risks of a health technology enable a comparison of individual alternatives on the basis of the overall benefit. Different criteria are thereby assigned values, which are converted into a total measure of the benefit to enable the direct comparison of the different alternatives. MCDA can be a great tool for value-based assessment, and could influence the current pharmaceutical business model. However, there are a series of unsolved issues that need to be addressed for MCDA to be a robust methodology.

1.1. Hypothesis and Thesis Objectives

The assessment of value over the course of the clinical development and regulation of new medical products is complex and involves different decision problems. It is my hypothesis that a number of implicit and explicit decision criteria and preferences are involved in the value assessment of pharmaceutical products. However, it is not always clear which preferences or criteria decision-makers choose to pursue or which weight they give to each.

The aim of this project is to find out how MCDA can be used as a benchmarking tool – from identifying new promising molecules expected to meet the unmet needs and preferences of the patients, physicians, and payers to proactively identifying target sales pricing of its products.

A second aim of this dissertation is to explore whether the priorities of the Danish diabetes guidelines are in alignment with the preferences of the patients, and the patient's value preferences for diabetes treatment will therefore be assessed and analyzed.

Lastly, it is my hypothesis that the current structure, reimbursement, and measurement of healthcare can be improved to be better aligned with the preferences, and hence optimizing the created value. The third objective is to discuss the feasibility of VBHC in Denmark and develop a framework for analyzing core dimensions of VBHC projects as well as pointing to design principles for future innovative contract designs. This leads me to the following main research question:

1.2. Question of Interest

By knowing the stated and revealed preferences of stakeholders within the healthcare system, how can modern benchmarking – where multiple criteria simultaneously are taken into account – be used in the development of pharmaceutical products and innovative contract design to decide which pharmaceutical product candidates will meet the unmet medical needs of the patient, consider the budget constraints that payers are subject to, and minimize the development risk to manufacturers and payers? In short: When is health innovation worth it?

2. Diabetes

As this dissertation focuses on diabetes care, I will start by providing a brief introduction to the epidemiology, pathophysiology, and clinical manifestations as well as the societal and economic impact of type 2 diabetes mellitus (T2DM) to define the scope of diabetes.

Once thought of as a disease of the West, the prevalence of T2DM is increasing at alarming rates in many other areas of the world. Due to the ageing population and an increasing prevalence of obesity, combined with decreasing levels of physical activity, diabetes mellitus has reached global epidemic proportions (International Diabetes Federation [IDF], 2013). The IDF estimates that more than 400 million people have diabetes (World Health Organization [WHO], 2016b). Every 20 years since 1945, the incidence of diabetes has more or less doubled (Barnett, 1998) and is set to rise to almost 600 million by 2030 equaling close to one in ten adults worldwide (IDF, 2013).

In Denmark, more than 250,000 people are diagnosed with T2DM and an additional 70,000 are expected to have diabetes without knowing it (Carstensen et al., 2020). The Danish health authorities estimate that the annual incidence of all diabetes types is roughly 30,000 cases, with most cases occurring in the 55–74 age group, and more frequently among men than women (Carstensen et al., 2020). It is estimated that diabetes costs the Danish society DKK 31.8 billion a year (equaling roughly 4 billion euros), with the biggest expense attributed to lost productivity (41 %), caregiving (20 %), and treatment by the general practitioner and at the hospitals (17 %), while the expenses for medicine are at about 3%, and cost for society for patients with complications was more than double compared with the cost for patients with no complications (Sortsø, 2016). To reduce the risk of

diabetes-related complications and thus the economic burden of diabetes, it is therefore essential that patients achieve appropriate treatment targets of diabetes management care (Zhuo, 2013).

2.1. Pathophysiology and Clinical Manifestations

A full description of the pathology of diabetes is not important for the main objective for this project; however, some basis knowledge of the disease is beneficial for understanding the complexity of the issue.

Diabetes is a chronic metabolic disorder that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar, and the disease is therefore characterized by elevated levels of blood glucose (hyperglycemia) (American Diabetes Association, 2009). Diabetes often persists over a patient's lifetime, and it is associated with increased morbidity and mortality (Bertoni et al, 2002).

The disease is usually classified into two types:

Type 1 diabetes mellitus (T1DM) is characterized by deficient insulin production and requires daily administration of insulin. Type 1 diabetes can occur at any age, the cause of is not yet known, and as far as it is currently known, the disease is not preventable (American Diabetes Association, 2009).

Type 2 diabetes mellitus (T2DM) – which comprises more than 80% of people with diabetes around the world (IDF, 2013) – is a progressive disease characterized by insulin resistance (decreased tissue response to insulin) and a progressive loss of pancreatic β-cell function resulting in insulin deficiency (Mashitisho, 2016).

The onset of sustained hyperglycemia occurs when insulin production can no longer compensate for insulin resistance. Deficiency in insulin production can be directly linked to declining β-cell function. In order to preserve remaining β-cell function, it is important to use therapies that optimize and maintain glycemic control (American Diabetes Association, 2009).

T2DM is caused by an interaction of genetic and environmental factors including excess body weight, physical inactivity, and increase in age while predisposition and family history can also play a role (IDF, 2013).

2.2. Type 2 Diabetes Morbidity and Mortality

Hyperglycemia, that is, raised blood sugar level, is a common effect of uncontrolled diabetes and over time can lead to serious damage to many of the body's systems, especially the nerves and blood vessels (American Diabetes Association, 2009). Prolonged, suboptimal glycemic control leads to microvascular complications including diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy. Macrovascular complications include hypertension, cardiovascular diseases, ischemic health disease, congestive heart failure, cerebrovascular disease, and peripheral vascular disease – complications which can be expected to have a negative impact on the patient health-related quality of life (HRQoL) (WHO, 2020).

2.3. Treatment

There is no cure for diabetes yet. During the nineteenth century, the discovery of insulin constituted the landmark of the era in terms of glucose control. Although insulin was capable of controlling glucose levels, it lacked the protective effects that scientists strived to achieve. Moreover, patients on insulin are at risk of hypoglycemia and lipodystrophy which hinders their compliance. This has

prompted the search for easier and safer medical products with an additional protective effect other than glucose control.

Most commonly, newly diagnosed diabetes patients are recommended to start with lifestyle changes (i.e., diet and exercise) (WHO, 2020). Patients with type 2 diabetes (T2D) typically use several drug treatments during their lifetime.
The preferred and most cost-effective first-line agent for patients with T2DM, if tolerated and not contraindicated, is metformin (Kwon et al., 2018). However, due to the progressive nature of the disease, many patients will over time require treatment intensification to maintain adequate HbA1c levels (Fonseca, 2008). There is a debate about the best second-line therapy after metformin monotherapy failure due to the increasing number of available antidiabetic drugs and the lack of comparative clinical trials of secondary treatment regimens (Kwon et al., 2018). Traditional therapies available to patients with T2DM after metformin failure (sulphonylureas [SUs], thiazolidinediones [TZDs]) are often associated with drawbacks such as weight gain, hypoglycemia, or poor long-term efficacy (Kwon et al, 2018). Different medical products have been introduced to the market to cater for patients who require an intensified treatment regimen, such as glucagon-like peptide-1 (GLP-1) agonists since 2005, dipeptidyl peptidase-4 (DPP-4) inhibitors since 2006, and sodium glucose co-transporter-2 (SGLT2) inhibitors since 2013 (Bogetoft & Starr, 2021). DPP-4, SGLT-2 and GLP-1 work in different ways, however all of these were found to improve glycemic control with a low risk of hypoglycemia and have beneficial secondary effects, such as avoidance of weight gain, reduced blood pressure, and improvements in β-cell function and cardiovascular risk biomarkers (Bogetoft & Starr, 2021).

The nature of the unmet medical needs for T2DM is explained in the guidelines of the European Medicines Agency (EMA) (European Medicines Agency, 2012) which address the clinical investigation of medicinal products in the treatment or prevention of diabetes. Glucose control in T2DM deteriorates progressively over time, and, after failure of diet and exercise alone, requires on average a new intervention with glucose-lowering agents every 3–4 years in order to obtain/retain good control.

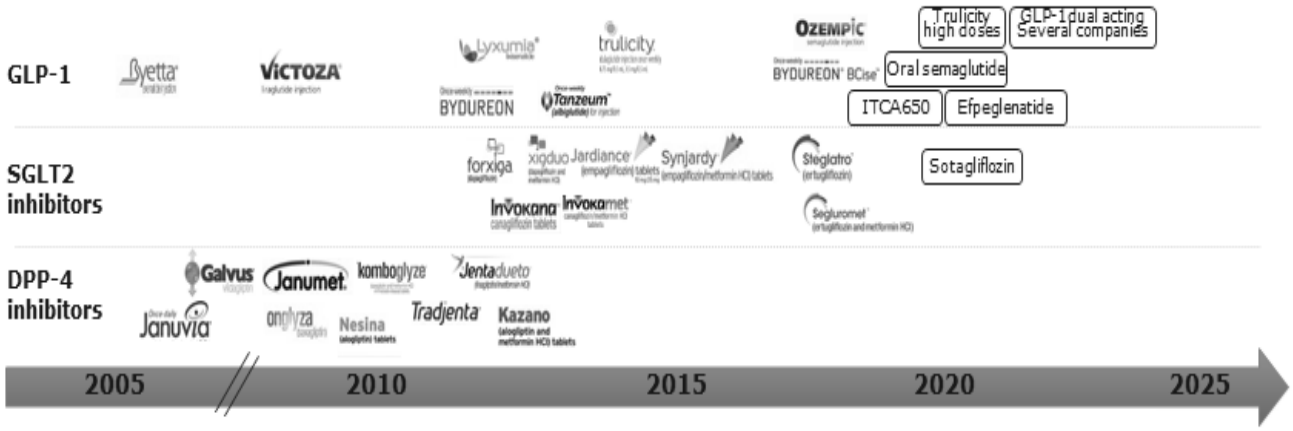
Clinicians must define a target for glucose control and prescribe a corresponding treatment regimen balancing medical and patient needs. However, despite the availability of a wide range of effective glucose-lowering therapies for diabetes, one of the main challenges faced by diabetes patients continue to be the control of blood sugar levels (Ross, 2013). Achieving good glycemic control is a clearly defined clinical goal in the treatment of diabetes; however, it remains suboptimal in a considerable proportion of patients (Ross, 2013), with an estimated half of patients not achieving the blood glucose targets (Ross, 2013). The benefits of intensive glycemic control for preventing or delaying the development and progression of long-term problems, such as complications related to microvascular complications, and reducing cardiovascular and all-cause mortality have been clearly shown (Ross, 2013; WHO, 2020). Low compliance to treatment has been mentioned as a reason for the high proportion of patients not achieving their glycemic targets (Ross, 2013).

The management of T2DM is burdensome to the patient, and some diabetes treatments increase the risk of hypoglycemia (which occurs when the plasma glucose level becomes too low) and weight gain, both of which are associated with reduced patient satisfaction with treatment (American Diabetes Association, 2020).

2.4. Crowded Diabetes Market

The T2DM market embodies a crowded treatment landscape. The product classes GLP-1, SGLT-2, and DPP-4 have over 20 approved medical products for the treatment of T2DM.

Continually, new diabetes medications are being developed by pharmaceutical manufacturers to address the unmet needs of the patients, and the clinical and preclinical pipeline is rich (Figure 1); however, not all new launches by the pharmaceutical company are considered to be innovative and fulfilling an unmet need.



Timing indicates first launch or expected launch

Figure 1. Crowded diabetes market: Many new products has been launched in the GLP-1, SGLT-2, and DPP-4 segment in recent years

However, despite the availability of multiple therapeutic intervention strategies, many patients still fail to achieve their treatment targets (Currie et al., 2010; Khunti et al., 2013; Stone et al., 2013). This is at least in part due to clinical inertia, that is, the ineffectiveness of treatment intensification to improve clinical outcomes

among patients who do not achieve their treatment goals despite the availability of guideline compliant healthcare services (Khunti, Gomes et al., 2018; Khunti, Davies et al., 2018). Other barriers that undoubtedly also limit treatment success include insufficient therapy adherence and lack of patient empowerment, both of which are dependent on the applied approaches and therapies (Iglay et al., 2015; McGovern et al., 2018). Together, these barriers point towards a need for the provision of evidence-based, patient-centered approaches to T2DM care if we want to improve outcomes for persons living with T2DM.

Thus, healthcare can be improved and made more efficient not solely through improvements in health technologies, but also through improvements in the care pathways and the ways consumers buy and use healthcare, and by generating new business models, particularly those that involve the horizontal or vertical integration of separate healthcare organizations or activities. Hence, health innovation remains an imperative for improving health.

2.5. Health Innovation

In the debate on how to maintain strong economic growth in an era that is increasingly being defined by the globalization of competition, as well as major fiscal and demographic challenges innovation has found to be key (Tidd, 2006). Innovation in health care can made in different context for example by patient organizations as an instrument for improving their services or for reducing their costs, by healthcare professionals for improving care of their patients, by patients and their informal caregivers who often innovate as a way to cope with their health condition (Barlow, 2017; DeMonaco et al., 2019; Oliveira et al., 2015), and by pharmaceutical companies to commercialize medical products and to bring new

innovative products to market as measured both by the number of patents and the number of new products. Simultaneously, technology is advancing, and artificial intelligence, robotics and big data have made an impact across all industries but perhaps in particular within healthcare. All of these different context innovations are formed by economic factors influencing the way they are conceived, developed, implemented or accepted by their markets and its users.

However, often, innovation is not to be considered a linear process and the different actors and contexts influence one another with a combination of a "technology push" where the development of a product or technology is pushed to the market and a "need pull" in which the development of a new product is oriented to fill a given market need (Tidd, 2006). Innovation, thus, is a coupling and matching process, where interaction is the critical element, where sometimes "push" will dominate, sometime "pull" (Tidd, 2006).

Innovation have been defined in many different way and with different focus, e.g., Joseph Schumpeter described innovation "as the practical implementation of ideas that result in the introduction of new goods or services or improvement in offering goods or services" (Schumpeter, 1983), Drucker described innovation as "Knowledge applied to tasks that are new and different" (Drucker, 1992), in 2004 after a yearlong study of invention and inventiness Lemelson-MIT described innovation as "the complex process of introducing novel ideas into use or practice"(Lemelson-MIT, 2004), and the former R&D director at 3M Geoffrey Nicholson described as "Research is the transformation of money into knwldge; Innovation is the transformation of knowledge into money".

Hence, *innovation* denotes novel, better, and more effective ways of solving problems. The term has been used to describe policies, systems, technologies,

ideas, services, and products that provide solutions to existing healthcare problems; yet, the word “innovative” has been a commonly used buzzword in the field of healthcare (Kimble, 2017). However, there seems to be a lack of clarity as to what defines a health innovation.

The WHO (2016a) explained that “health innovation” improves the efficiency, effectiveness, quality, sustainability, safety, and/or affordability of healthcare. This definition includes “new or improved” health policies, practices, systems, products and technologies, services, and delivery methods that result in improved healthcare. Thus, to describe a product as innovative entails that it has properties that are valuable and, hence, worthy of a reward, as the value of pharmaceutical products lies in the health outcomes it generates. A medical product may be considered a pharmaceutical innovation only if it meets otherwise unmet or inadequately met healthcare needs, which depends on its efficacy, safety, and convenience compared with the alternatives available at the time of launch.

Länsisalmi et al. (2006) suggested that the three components of innovation are i) a novelty, ii) an application component, and iii) an intended benefit. An “intended benefit” should be centered around the receiver of care, the patient, although stakeholder considerations must also be taken into account. Stakeholder considerations are particularly important in regard to the adaption and adoption of innovation. With these components in mind, the “innovation process” can be understood by analyzing the needs, wants, and expectations of stakeholder groups. However, even if the criteria are met, barriers remain for the recognition and uptake of innovations in healthcare.

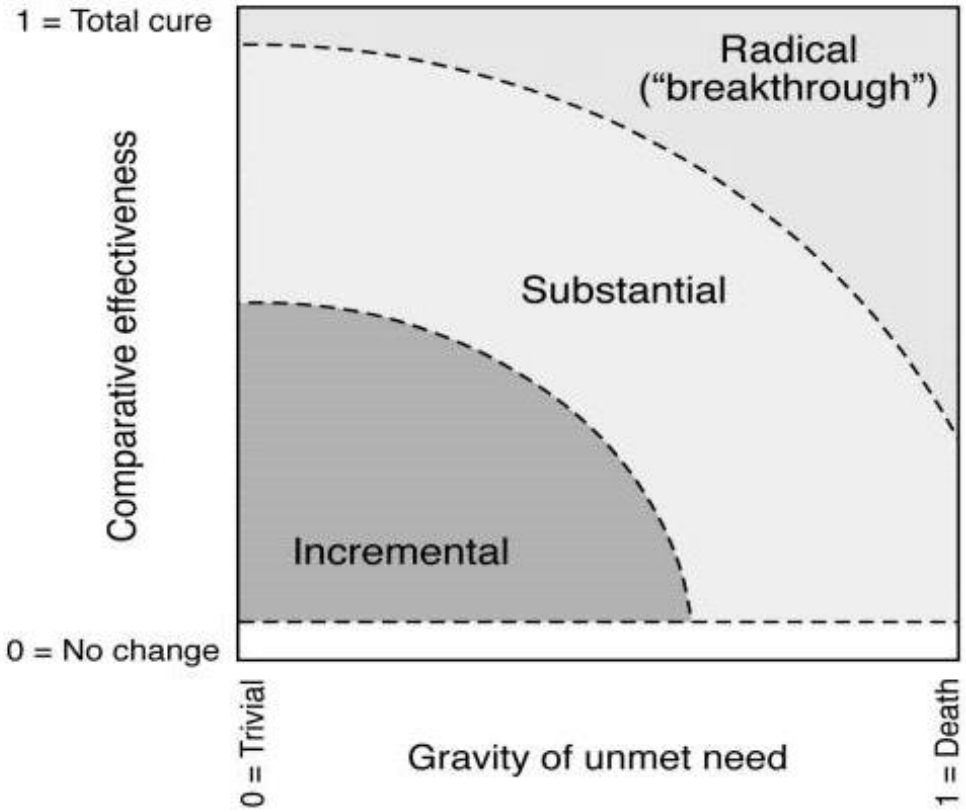
However, there is little consistency between stakeholders about what defines innovation and consequently how to reward it. A general perception in the

pharmaceutical industry is that innovation is not recognized by payers, and therefore, it is not rewarded (PwC, 2011; Barlow, 2017). Payers, on the other hand, have claimed that industry for the most part is not inventing true innovative products or that its innovation does not lead to improvement in health outcomes (increased effectiveness). Hence, payers are claiming that the pharmaceutical industry is trying to claim a reward for a “me-too” product with little or no added value (Morgan et al., 2008).

In the early 2000s, the pharmaceutical industry was generally held to be facing an unprecedented set of challenges to its business model (PwC, 2011), as a consequence of a combination of a growing technical risk (over time it is growing harder to develop drugs for complex diseases) and a commercial risk (drugs were reaching their patent expiration and payers were more unwilling to cover the cost of innovative products) (Barlow, 2017).

The effects have been described in terms of an innovation productivity crisis (PwC, 2011; Barlow, 2017), echoed in a declining number of new drugs developed and approved, coupled with increasing R&D costs. Success in the earlier stages of the pharmaceutical life cycle was becoming less likely to predict success in the later stages, hence, a scientific success could still be followed by a commercial failure, rejection by regulatory authorities or payers (Barlow, 2017). A reason for the declined productivity was that many major pharmaceutical companies went for similar blockbuster drug targets resulting in duplicated and wasted efforts and leading to decreasing returns (Berlow, 2017). However, another reason might be the growing complexity of the underlying science of discovery and the more complex disease profile of the patients with many comorbidities, for example (Barlow, 2017).

A pharmaceutical innovation may be thought of as incremental, substantial, or radical depending on the unmet healthcare need it addresses (gravity of unmet need) and the extent to which it improves net health outcomes related to that need (comparative effectiveness) (Figure 2) (Morgan et al., 2008).



Source: Figure from Morgan et al., 2008

Figure 2. A model of pharmacological innovation

To determine the level of innovativeness that a medical product actually achieves, one must also examine its comparative effectiveness in terms of net improvements in health outcomes, taking into account the negative effects of the medical product, that is, side effects and adverse events (Morgan et al., 2008). Within diabetes treatment, there is a limited scope for pharmaceutical innovation with

respect to hard clinical endpoints, as the current treatment regime already offers relatively good outcomes, but there is still potential for improvement in secondary endpoints.

National regulatory bodies use different assessments of innovative medicines in their pricing and reimbursement decisions. Thus, although there is a common expectation of therapeutic and clinical progress, the benefits that are considered as added value vary between agencies (European Comission, 2018).

In practice, very few new medicines are derived from a chemical structure which is not already in use, and very few have added health/therapeutic benefits, whereas the majority of medicines have a similar effectiveness to current alternatives. Among medicines with a health benefit, it is estimated that only approximately 10% are truly innovative or have a significant added health benefit (Sermet et al., 2010).

The key determinants of the costs of R&D can be summed up as the *scientific innovation*, i.e., discovery and early clinical development, and the business of *innovation adoption*, i.e., creating the information that regulators and customers need and communicating it to them (Barlow, 2017). For example, when insulin was first discovered and brought to market by Frederick Banting and Charles Best in the 1920s, it was argued to be the first lifesaving medical product in the world (Novo Nordisk, 2018), but compared with today's diabetes treatment, the first insulin preparations were not user-friendly and had major side effects. The first insulin was purified from the pancreas of pigs, but in the 1950s, the next breakthrough came when scientists were able to convert pork insulin to human insulin (Novo Nordisk, 2018). Through innovation and advanced technology, the insulin molecule has evolved in terms of safety, efficacy, and effectiveness

improvements. For example, treatment options have improved by offering new ways of administrating it to patients; for example, longer-lasting types of insulin have been introduced to reduce the number of daily injections. The most common diabetes treatment is insulin; however, new treatments include medical products that stimulate β-cells in the pancreas to release more insulin, decrease glucose production in the liver, or make muscles more responsive to insulin, and this innovation can be considered incremental. But, at the same time, each product advancement comes with an increased price compared with the product it replaces, so *when is the innovation worth it*?

3. Economic Evaluation

Overall, economic evaluation provides a framework to make the best use of clinical evidence through an organized consideration of the effects of all available alternatives on health, healthcare costs, and other valuable effects, where the overall aim is to maximize benefits given the available resources (Drummond et al., 2015), and a range of methods has been utilized to establish an explicit priority-setting framework within healthcare.

Different types of economic evaluations are applicable for answering different decision questions. While each approach measures costs in monetary terms, they differ in the way consequences are measured. The most common forms of health economic evaluations are cost-benefit analysis (CBA), cost-effectiveness analysis (CEA), and cost-utility analysis (CUA):

In mainstream economics, CBA is often used. In CBA, both cost and benefits are measured in monetary terms, which makes this analysis fitting for allocation decisions and for comparing interventions across different sectors.

CEA is an analysis in which costs are related to a single, common effect that may differ in magnitude among the alternative programs. The results can be stated in terms of an incremental cost-effectiveness ratio (ICER) or in terms of effect per unit of cost (Drummond et al., 2015).

In the healthcare sector, the extra-welfarist CUA approach is a more commonly used approach. In CEA as well as CUA, the decision-maker aims to find out how to best allocate the existing budget. CUA is essentially a variant of CEA; however, the consequence's generic measures of health gain, such as quality adjusted life years (QALYs), are used, which makes it possible to compare effects across disease areas

(Drummond et al., 2015). *Utility* is used in a general sense and indicates the preferences that individuals or society have for a determined set of health outcomes (Drummond et al., 2015). The estimation of preferences allows for differences in the valuation of the treatment (HRQoL adjustments) while also providing a generic outcome measure that can be used for comparing costs and outcomes across different programs – also among different sectors of public provision if needed (Drummond et al., 2015). The strength of a CUA is that, by using a relevant generic measure, it aids the decision-maker in assessing the opportunity costs of health forgone in other programs competing within the same budget (Drummond et al., 2015).

However, given the limited consideration of overall value in traditional economic evaluations, additional parameters have been included in value assessments; however, these are often *ad hoc* and non-systematic, which in the end might impact the transparency of the decision-making process and lead to inconsistencies in, for example, reimbursement decisions (Angelis et al, 2018).

3.1. Valuing Value

The aim of valuing something is to estimate how desirable or undesirable something is, and therefore, the concept of value plays an important role in economic evaluation. The debate of the theory of value reaches back to at least Aristotle in the fourth century BC who claimed that the source of value was based on need (Fogarty, 1996). Over the years the proposed concept of value has developed, but the theory of value is still of primary importance today.

Overall, the *value theory* state, that the alternative, *a* is preferred over alternative *b*, if and only if $V(a) > V(b)$, and is judged to be indifferent if and only if $V(a) = V(b)$,

where *V* is a real number reflecting the value associated with the performance of the alternatives based on which preference orderings are produced (von Winterfeldt & Edwards, 1968).

Within healthcare, the valuation of healthcare interventions is relevant to a number of decisions and decision-makers, from the investments made in research and development over the authorization, reimbursement, and resource allocation to the clinician and patient's choices.

Often, utility is used rather than value to emphasize value's subjective nature and hence, in classic utility theory, values are not measured, but rather inferred from preferences.

3.2. Preference Theory

Preferences can be identified through either stated or revealed preference methods. In stated preference methods, the preferences of key stakeholders are directly revealed by the decisions they make in a contrived framework. In revealed preference methods, individual preferences are revealed indirectly though the choices they make in markets (Samuelson, 1938; Samuelson, 1948). Thus, by observing an individual's actual market behavior, for example, the actual spending of money, time, or other resources, the importance of attributes affecting a decision can be ascertained. Therefore, the estimated preferences using revealed preference methods are likely to be more accurate than the preferences obtained using stated preference methods where choices are contrived and the resources are not actually spent.

In preference theory, as illustrated in Figure 3, preferences materialize into utility functions. The utility functions are maximized by consumers subject to restraints,

such as budgets or other restraints. Identifying the revealed preferences, we assume we can deduce the utility function from behavior. Analyzing these choices leads us to a set of preferences that influences the choices made. It therefore allows for studying behavior empirically. As illustrated, preference theory postulates a link between the latent/unobserved utility function and the observed/stated choice. From the systematic variation of product characteristics via an experimental design, the mapping between the choice behavior and the utility function is parametrized.

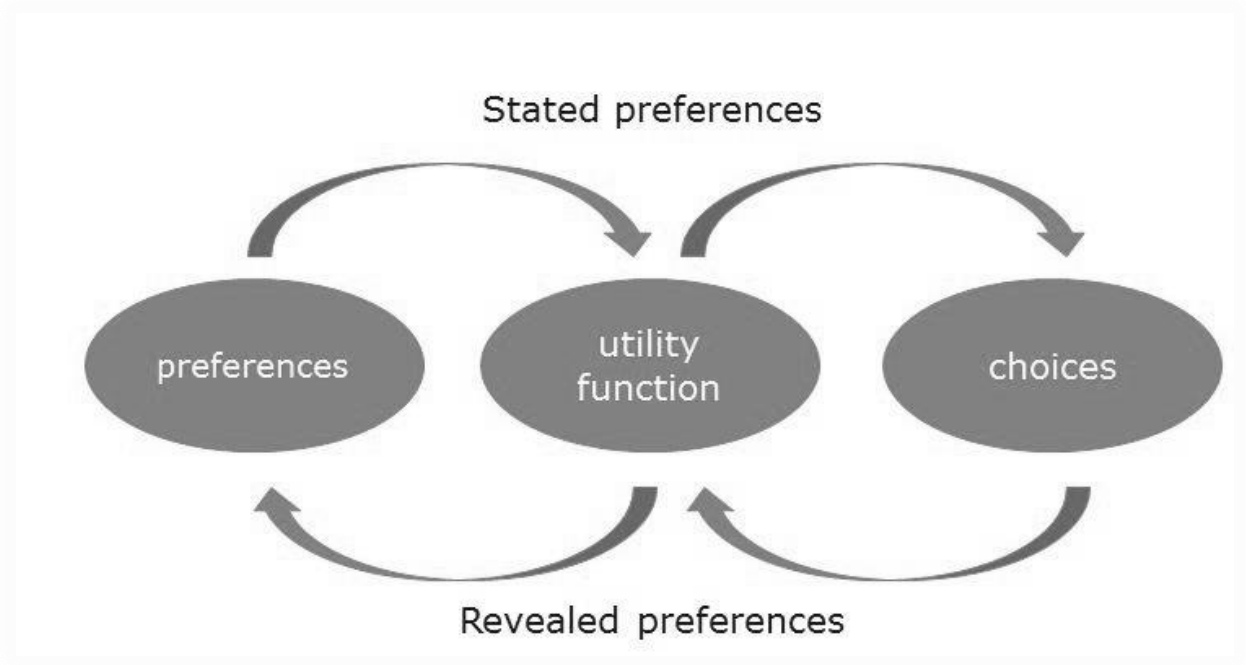


Figure 3. Revealed and stated preferences

However, healthcare services are often not traded in regular free markets in the same way as other goods, and thus, the revealed preference estimates might still show inaccuracy. For example, many health services have little or no out-of-pocket payment due to reimbursement, and the prices the individuals pay for health services might not reflect an accurate willingness-to-pay. Additionally, due to

asymmetric information, as when health professionals often have more information than the patient, the decisions made by the patient may not be based on their actual preferences.

In section 5 and 6, the concepts of stated and revealed preferences are described in more detail and in relation to the studies carried out as part of this dissertation.

3.3. Decision Making

Decision analysis has been defined as “a logical procedure for the balancing of the factors that influence a decision” achieved by incorporating “uncertainties, values, and preferences in a basic structure that models the decision” (Howard, 1966).

Thus, in an area like healthcare, where uncertainties and multiple conflicting objectives are contemporaneous, decision analysis seems fundamental. The physician has to determine what is wrong with the patient and recommend a treatment, the patient has to decide whether to seek medical care and, thereafter, whether to comply with the recommendations, health policymakers and regulators have to decide what to promote, what to discourage, and what to reimburse. Each of these decisions influences the quality of the healthcare that is provided and often the cost associated with it.

In the decision-making process, the aim is to find the best way to transform input into output by weighing the positives and negatives of each option, forecast the outcome of each option, and consider all the alternatives.

The main outcome of decision analysis theoretical axioms is that first the utility of an alternative is the indication of its desirability, and second, that an alternative A

with higher utility U(A) should be preferred to an alternative B with lower utility U(B), expressing the utility maximization as:

$$A > B \Leftrightarrow U(A) > U(B)$$

In decision analysis, there is a conceptual difference between value functions, which assess the value of a specific outcome, and utility functions, which assess the value of specific outcomes as well as risk attitudes and are thus suitable for choices under uncertainty. Expectation mainly relates to the concept of probability theory, with *expected* value being a weighted average of the value of specific outcomes and its respective probability of actually occurring (von Winterfeldt & Edwards, 1968).

Within a health technology assessment, the evaluation of new medical technologies predominantly relates to the evidence-based assessment of their value by measuring their marginal benefits, with the expected value (EV) of an event written as:

$$EV = p_1v_1 + p_1v_2 + p_3v_3 + \cdots + p_nv_n ,$$

where p_i is the probability that event *i* will take place, and v_i is the value or pay-off associated with the event.

The perspective of the analysis relates to the perspective of the decision-makers. Decision-makers are based in different settings, and their decisions can be expected to be formed from their own perspective of responsibility, and hence, decision-making is inherently subjective as it depends on individual utility and preferences which differ among individuals. Preference is the umbrella term, which describes the overall concept of utilities and values (Drummond et al., 2015). Given that a consumer chooses one alternative out of a set of alternatives, this

alternative must be the preferred alternative, thereby defining the utility functions. Therefore, the product that the consumer chooses can be referred to as the preferred choice, according to Samuelson (1948), whose consumption theory in terms of revealed preferences is further explained in section 6. Uncertainties can, in decision analysis, be traded off against some value aspects of the outcomes, formally through the incorporation of probabilities. Similarly, trade-offs can be made among different objectives and their associated values. Therefore, the trade-offs are judgements, depending on the decision-maker's assessment of the relative desirability of the different available alternatives across their dimensions together with the relative importance of these dimensions. However, trade-offs are personal and, thus, subjective by nature. This embodies the notion of rationality with the goal of making rational inferences and decisions. Possibly the most prominent of such criteria rules would be the maximization of (expected) utility or value (Savage, 1954).

Decision research has in particular explored three different research questions: the normative (how should decisions best be made?), the descriptive (how are decisions actually made?), and the prescriptive (how can decision theory be used to improve decision making?) (Chapman & Sonnenberg, 2003).

However, decisions are not always made in a logical, rational manner as the models describe them. Instead, decisions do not begin with the analysis of the problem and then the systematic analysis of alternatives, followed by implementation of solution; instead, the decision processes are often characterized by conflict, coalition building, trial and error, speed, and mistakes (Daft, 1998). Thus, decision analysis seems to be particularly useful for coping with the complexities arising from uncertainty and multiple conflicting objectives

(Raiffa, 1968). Daft explained that, since individuals make decisions, but organizational decisions are not made by individuals, decision-making will practically be done in collaboration (Daft, 1998).

In line with the notion of collaboration, Rogers and Blenko (2006) described critical roles that different stakeholders play in the decision-making process classifying the process as: *recommend, agree, input, decide, perform.* Thus, people who *recommend* a course of action are responsible for making a proposal or offering alternatives using data and analysis to support their recommendations, but also for using common sense in terms of what is reasonable, practical, and effective. People who *agree* to a recommendation are those who need to sign off on it before it can move forward. People with *input* responsibilities are consulted about the recommendation. They provide input by providing the relevant facts that lay the groundwork for a good decision. Eventually, one person will *decide* and, thus, bring the decision to closure and commit to act on it. In order to be strong and effective, the decision-maker needs good business judgement and understanding of the trade-offs. Finally, there are ones who will *perform* the decision and oversee that the decision is implemented promptly and effectively.

In a healthcare setting, that can translate into a formal approval and recommendation process by the health authorities in which it is agreed whether a medical product can be recommended or not after the pharmaceutical firm submitting a formal application. For example, after an HTA and receiving inputs from experts, the final clinical decision on whether to prescribe a medication to a patient ideally happens as a shared decision-making process between the patient and the general practitioner.

Stakeholders of the healthcare system have to make decisions on which health technologies to use, ideally assessing the underlying alternative options. This can be challenging given the trade-offs among multiple value criteria of the different options. In other cases, the decision-making is done on a more *ad hoc* basic. Decision-makers might have difficulties processing and systematically weighting all relevant information and making the trade-offs among the options under consideration. In order to increase the transparency and legitimacy of decisions, a structured, explicit approach involving multiple criteria can improve the quality of decision-making.

For assessment of healthcare interventions, the evaluation is primarily based on existing evidence, that is, clinical trials, and not expected evidence, and thus, it can be argued that expectations can be detached from the equation. On the other hand, it can also be argued that, in various cases, absence of (satisfactory or adequate) evidence essentially introduces an expectation variable given the attached probabilities of the respective outcomes to take place (e.g., clinical outcome or improved quality of life), especially when early in the life cycle of the pharmaceutical product.

4. Prioritization Traditions

One of the biggest challenges healthcare systems are facing is the scarcity of resources in combination with rising demand for services. As a result, decisions relating to the allocation of health care resources have been inevitable, either between different competing services and interventions (i.e. priority setting) or across different patients (i.e. rationing) (Angelis et al., 2017). However, the allocation of limited resources is a complex and difficult decision process and has been far from obvious (Angelis et al., 2017). The decisions are both very complex where many factors, objectives and stakeholders' needs need to be balanced, the decision outcomes are very important, and lastly, there are large ethical and social responsibilities behind the provision (Angelis et al., 2017).

Traditionally, an implicit approach to healthcare prioritization in publicly funded health systems has been adopted whereby decisions to a large extent are based on historic resource allocations and the rationale for these decisions is not necessarily made clear (Logan et al., 2004; Seixas et al., 2021). Since the late 1980s, though, the desirability for explicit prioritizations, where specific processes and criteria designed for priority-setting are made publicly available, has increased as the pressure on the healthcare budgets has increased (Baltussen et al, 2007; Logan et al., 2004; Seixas et al., 2021).

Internationally, countries have approached the prioritization challenge in different ways (Seixas et al., 2021). In the Netherlands, and Sweden, for example, the principles that ought to be included in the prioritization process have been mostly defined, while in New Zealand, the United Kingdom, and the US state of Oregon and Norway, they have been more explicit in their priority setting approaches by

defining the health services that will be publicly funded and/or establishing clinical guidelines (Sabik & Lie, 2008).

For example, in 1992, the Swedish Parliamentary Priorities Commission was appointed to explore priority setting in healthcare. They explicitly rejected defining health services that should or should not be funded and instead outlined three hierarchical principles for priority setting: human dignity (everyone is equally valuable), need and solidarity (people with the greatest need should be treated first), and cost-efficiency (to be used solely when considering treatments for the same condition) (Logan et al., 2004; Sabik & Lie, 2008). Further, the Commission defined five priority groups, based on the type of disease or treatment, to be used as a general guide by decision-makers at the clinical, management, and political levels (Calltorp, 1999).

In Norway, the severity of illness, the efficacy of interventions and their cost-effectiveness have been key criteria for priority setting in the Norwegian health services since the government commission on priorities in health care (the Lønning II Commission) submitted its recommendations in 1997.
Most recently, priority setting in the Norwegian health sector was in 2017 described by the third Norwegian Committee on Priority Setting in the Health Sector (Norwegian Ministry of Health and Care Services, 2017). The framework posits that priority setting in the Norwegian healthcare sector should pursue the goal of "the greatest number of healthy life years for all, fairly distributed" and centres on three criteria: 1) The health-benefit criterion: The priority of an intervention increases with the expected health benefit (and other relevant welfare benefits) from the intervention; 2) The resource criterion: The priority of an intervention increases, the less resources it requires; and 3) The health-loss

criterion: The priority of an intervention increases with the expected lifetime health loss of the beneficiary in the absence of such an intervention. Cost-effectiveness plays a central role in this framework, but only alongside the health-loss criterion which incorporates a special concern for the worse off and promotes fairness. In line with this, cost-effectiveness thresholds are differentiated according to health loss. Concrete implementation tools and open processes with user participation complement the three criteria.

The US state of Oregon was first to attempt to formulate a list of prioritized health services (Logan et al., 2004). To face rising medical costs and an increasing number of people who were unable to afford healthcare as either uninsured or not qualifying for federal assistance (Medicaid), Oregon attempted to develop a transparent process for prioritizing state-funded medical services in the late 80s. They aimed to increase coverage of Medicaid from 58% of Oregonians below the federal poverty line to *all* Oregonians below the federal poverty line by limiting coverage to a basic bundle of healthcare services (Sabik & Lie, 2008). Some guiding principles were developed, including that access to a basic level of care must be universal, society is responsible for financing care for poor people, and a basic level of care must be defined through a public process (Crawshaw et al., 1990). The public was consulted by way of public hearings, town meetings, and a telephone survey. The process of establishing the prioritized list was contentious with the first list being rejected by the public. Nevertheless, the list of prioritized services was revised and has continued to be modified over the years as circumstances have changed (Ham, 1997).

Thus, Sweden – as well as, for example, Norway, Denmark and the Netherlands – has an institutional approach whereby principles are used to guide priority-setting. Oregon, on the other hand, – as well as, for example, the United Kingdom and New Zealand – uses a more technical approach where prioritization is made explicit which can be argued to allow for more consistency in decision-making.

4.1. Health Technology Assessment and Regulation of Pharmaceuticals

In an attempt to evaluate new health technologies before they become part of clinical practice, many countries have established separate health evaluation or regulatory agencies to conduct HTAs. A HTA has by World Health Organization been described as "the systematic evaluation of the properties, effects, and/or impacts of health technology. It is a multidisciplinary process to evaluate the social, economic, organizational and ethical issues of a health intervention or health technology" (WHO, 2021). The HTA provides clinicians, managers, and policymakers with information relating to a new technology to assist them in their decision-making.

Traditionally, when payers are to make decisions about authorization, reimbursement, and resource allocation, they are looking at evidence and cost, at times formalized in an HTA, possibly with economic evaluation. The evidence will often draw on the results from clinical evaluations, for example, randomized clinical trials (RCTs), and it has been perceived to be essential that the clinical results are obtained in a "systematic way, interpreted appropriately (including an

assessment of its relevance and potential for bias) and then, when appropriate, synthesized to provide estimates of key parameter" (Drummond et al., 2015).

For example, in Denmark, medicines must be authorized by the Danish Medicines Agency or the European Commission before they can be sold in Denmark (Lægemiddelstyrelsen, 2017). An application for authorization of a medicine must contain documentation for the medicine's efficacy, safety, and quality (Lægemiddelstyrelsen, 2016).

The Medicinal Products Committee is responsible for advising the Danish Medicines Agency on issues such as granting, variation, suspension, or revocation of marketing authorizations for medicinal products, monitoring of adverse reactions and other risks involving medicinal products, evaluation of the risk–benefit balance of the medicinal products, and clinical trials with medicinal products. The Medicinal Products Committee consists of maximum 15 members of which two directly represent patient and consumer interests (Lægemiddelstyrelsen, 2017). If the product is authorized, the company will be granted a marketing authorization (Lægemiddelstyrelsen, 2017).

The Reimbursement Committee advises the Danish Medicines Agency in cases regarding reimbursement for prescription medicines from the Danish Regions in terms of the general reimbursement, conditional reimbursement, and individual reimbursement for medicines (Lægemiddelstyrelsen, 2017). The basic rules are as follows:

- When a medicine has general reimbursement, all citizens receive reimbursement from the Danish Regions. Reimbursement is automatically deducted from the price charged at the pharmacy

- When a medicine is granted conditional reimbursement, it is only granted in certain cases. In order to obtain reimbursement if the medicine is listed as conditional, it may be a condition that the medicine is prescribed to certain patient groups or for the treatment of specific diseases.
- If the medicine is used for other purposes, no reimbursement is awarded unless the party has been given a single reimbursement grant (Lægemiddelstyrelsen, 2017).

By using evidence-based medicine, the aim of HTA is to determine the value of a technology by appraising its (clinical) benefits and often its costs compared with existing alternatives of care, in order to inform coverage and pricing decision-making for clinicians, managers, and policymakers (WHO, 2014). Thus, current HTA approaches examine the clinical efficacy of new medicines in combination with or without their cost-effectiveness, while increasingly incorporating real-world post-marketing authorization evidence, to incorporate comparative effectiveness and efficiency (Kanavos & Angelis, 2013).

In practice, the pharmaceutical company submits its value dossier to the regulatory agency in which the company outlines the characteristics of the pharmaceutical product and then lists the benefits, such as the health technology's beneficial effects for the target population, and risks, that is, the health technology's detrimental effects on the patient's health (European Medicines Agency, 2010) found during (pre-) clinical studies as well as information about the target population. Based on this information, the regulatory agency evaluates the benefit–risk profile of the pharmaceutical and decides whether the available evidence is adequate to authorize a marketing authorization, in other words, whether it has found that the benefits outweigh the risk, or if further evidence is

required. Most European countries use HTA as a tool to determine the new health technologies' value. HTA is used to both assess access and pricing of a new medical product, but this can be far from consistent as to how and when HTA is used (*ex post* or *ex ante*), and the criteria for the assessment can vary from country to country (Wilsdon & Serota, 2010). The pharmaceutical life cycle is illustrated in Figure 4.

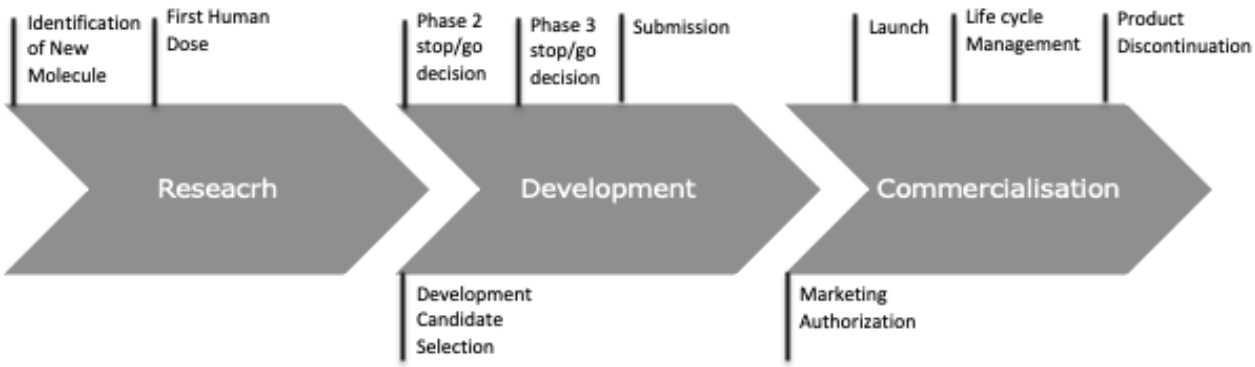


Figure 4. The pharmaceutical life cycle with decision points

Once a product has reached the market, prescribers may choose products from a pharmaceutical product list for their patients, subject to any conditions or patient criteria. Therefore, although patients are the end users of new health technologies, payers are very important decision-makers in the demand and, therefore, in the uptake of new health technologies.

Also, it has been shown that the pharmaceutical and health product industry spends large sums on lobbying and campaign contributions in some countries, such as the US. This might temper the influence of industry on health policy (Wouters, 2020). Lobbying is not perceived to be a large issue for generating demand in Denmark, but in other countries, contributions to influence legislative and election outcomes could be a factor in generating demand. Also, there are other forms of

errors, biases, and heuristics that affect individuals' judgements when confronted with complex decision problems.

As part of the current HTA practices, a number of value assessment approaches are used: 1) assessment of clinical benefits, b) economic evaluation, and c) risk sharing and managed entry agreements. It has however been questioned whether these methods fully capture the value of pharmaceutical products and aid the decision process, and it has been critiqued that the value judgement is not transparent and explicit; for example, it is not clear what the decision-makers' relative importance is or the trade-offs made. This gives rise to an arbitrariness in the criteria used to judge the alternatives, resulting in a non-transparent process and a lack of "accountability for reasonableness" (Daniels, 1999; Devlin & Parkin, 2004). However, MCDA has been suggested as a means to address these issues (Angelis et al, 2018; Baltussen & Niessen, 2006; Devlin & Sussex, 2011). MCDA will be described further in section

There is a definite impetus to have a greater understanding of what generates value, and data from clinical trials might no longer be sufficient (Garrison et al., 2007). Therefore, RWD – which shows the actual use and impact on health outcome for patients – and an understanding of the influence of other parameters than the clinical endpoints have recently been shown to have more importance in decision-making (Dreyer, 2018; Garrison et al., 2007), which has fostered a shift towards value-based healthcare.

4.1.1. Quality-Adjusted Life Years

In the HTA, QALYs are frequently used as a generic measure of the value of health outcomes. Assuming health is a function of length of life and QoL, the concept of QALY was developed as an attempt to combine the value of these attributes into a single index number: QALY = years of life x utility value.

QALY is a measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the QoL. One QALY is equal to one year of life in perfect health. QALYs are calculated by estimating the years of life remaining for a patient following a particular treatment or intervention and weighting each year with a quality-of-life score (on a 0 to 1 scale). It is often measured in terms of the person's ability to carry out the activities of daily life and freedom from pain and mental disturbance (The National Institute for Health and Care Excellence, 2020).

A common application of CUA is to use QALYs as a "currency" by which one health treatment can be compared with another in terms of the cost per QALY, or cost per QALY can be compared against a given threshold; for instance, the value of a cancer treatment can be compared with the value of an asthma medication. In the United Kingdom, for example, the National Institute for Care and Health Excellence (NICE) in its health prioritization often uses four steps: calculate the QALYs per treatment; compare the cost per QALY with a set threshold (i.e., the ICER can be comperes to the threshold); if the cost per QALY is below the threshold, the treatment is considered to be cost-effective; and if the cost per QALY is above the threshold, a treatment will only be provided if the additional cost can be justified.

Although widely used in economic evaluations, the use of QALYs and a cost per QALY threshold has its limitations (Bryan et al., 2002; Dolan et al., 2005): The QALY algorithm, as it is commonly used, assumes that the average cost and health effects (i.e., the number of QALYS gained) are independent of the number of patients treated, and it often assumes that costs are divisible. Another issue raised with QALYs is the challenges with intermethod variation in measuring utility, unwillingness to trade life expectancy to be relieved of health problems, fairness, and the *ex-ante* value of health states versus the value of interpretations for people with illness as challenges for conventional QALYs (Nord, 2009). However, although intermethod variation has been discussed as a problem when measuring utilities using different methods (Nord, 2009), empirical studies have shown that the time trade-off and standard gable methods are nearly equivalent in their results and thus comparable (Weinstein et al., 2009).

QALY has also been criticized for not adequately capturing additional considerations that may be important to society, such as equity in health or equal access to health (Devlin & Sussex, 2011; Dolan, 1998), and might not reflect societal values, based on being aggregated from individual preferences, and treated as equally valuable regardless of who gains from them (Drummond et al., 2015). A further limitation is that for some new health technologies' information might be limited in terms of, for example, efficacy, effectiveness, or cost, making it difficult to compare these new treatments with other treatments where QALYs are available (Raftery, 2001).

Furthermore, the threshold which is used to compare the cost per QALY for different treatments is often somewhat arbitrarily assigned (Detsky, 2007) and the overall budget implication is not always considered (Devlin & Sussex, 2011). Taking

into account additional considerations when evaluating health treatments is often based on qualitative judgements, which, given the complex nature of decision-making, can lead to inconsistencies in the way decisions are made (Devlin & Sussex, 2011). Devlin and Sussex (2011) argued that a more consistent and systematic approach is required to ensure accountability and transparency. They also noted that MCDA has been proposed as an alternative or addition to QALY to address some of the limitations of QALY. MCDA will be presented and discussed in section 7.

In Denmark, QALY has, until recently, not been used as a standard measure when new health technologies have been evaluated. From January 2021, the Danish Medicines Agency has implemented QALY in its process and method for recommendations. QALY will not be a stand-alone measure, as the Medical Council must continue to apply the Parliament's seven principles for prioritizing hospital medicine when the Council decides whether the new hospital medicine is to be recommended. The seven prioritization principles outlined by the Danish Parliament regard the process of deciding on which medicine the regions shall use for standard treatment of patients under the seven main terms: professionalism, independence, geographical equality, transparency, fast use of new effective medicine, more health for money, and access to treatment (Medicinrådet, 2021). In addition to the seven principles of the Parliament, the principle of severity and the precautionary principle can also be included in the assessment of new medicines (Medicinrådet, 2020).

5. Stated Preferences

A patient-centered approach to diabetes care of patients with T2DM is now widely accepted (Inzucchi et al., 2012). Patient preferences for diabetes medication are increasingly acknowledged as an influence on adherence and patient-centered care, which in turn can alter efficacy of treatment and burden of disease. Patient preferences for T2DM patients are particularly complex because of the variety of medication alternatives; medication-related benefits, harms, and burden; and the likelihood, uncertainty, and time horizons of these treatment-related outcomes. A distinct set of methodologies employing subjective evaluation of medical treatment are stated preference (SP) methods. SP methods are valuation-based techniques which try determine the strength of individuals' SPs by measuring trade-offs in utility (Bateman et al, 2002).

Various methods have been proposed for eliciting SPs and assessing criteria weights. Criteria weights can be determined directly or indirectly. In the direct rating the criteria weights are explicitly defined. In the indirect rating methods, decision-makers are presented with hypothetical options consisting of a number of criteria that vary over a range of levels, and they are asked to choose, rank, or rate the options, after which the particular algorithm determines the weights corresponding to the choices, ranking, or ratings.

The stated elicitation methods consist of *discrete choice-based elicitation methods* which examine the relative importance of trade-offs between attributes and their alternatives through a series of hypothetical choices (Whichello et al., 2020), including *indifference elicitation methods* which use techniques that examine a participant's preferences for one attribute or alternative over another, until the participant is indifferent or has no preference (Whichell, et al., 2020); *rating*

elicitation methods which use comparative rating approaches (Liberatore & Nydick, 2006), and lastly, *ranking elicitation methods* which use ranking exercises (Flynn et al., 2007; Ryan, 2001).

The weighting methods are rooted in different theoretical traditions: choice-based, matching, and trade-off methods, and direct rating methods such as SMART (Simple Multi Attribute Rating Technique) are based on multi-attribute utility theory (MAUT) or MAVT based on the work of Keeney and Raiffa (1976) and von Neumann and Morgenstern (1947), whereas the analytical hierarchal process (AHP) was developed from a different theoretical basis by Saaty (1980).

In the choice modelling techniques criteria, weights are determined indirectly: hypothetical alternatives with a number of criteria with varying levels are presented for decision-makers who are then asked to either rank, rate, or choose among the alternatives, and certain algorithms then determine the weights corresponding to ranking, ratings, or choices. Methods that use choice modelling to determine criteria weights include discrete choice experiments (DCEs) and AHP. See, for example, Belton and Stewart (2002) for a more thorough description of the different methods.

Examples of the different methods are illustrated in Figure 3:

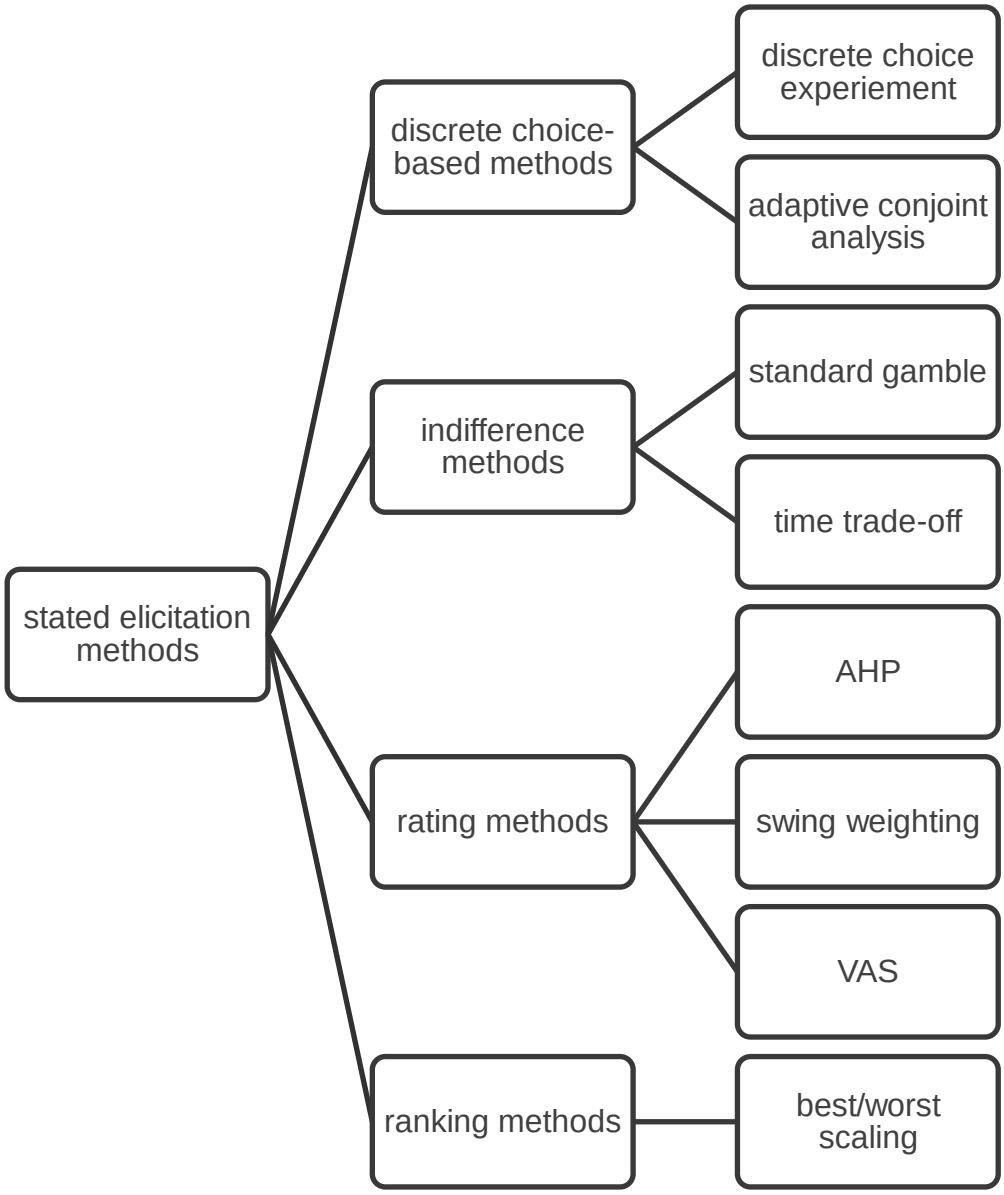


Figure 3. Examples of stated preference methods

DCEs have received particular attention in healthcare evaluations and health economic literature because they allow the influence of several treatment aspects to be considered (Bridges et al., 2011; von Arx & Kjær, 2014). DCEs are based on

the premise that treatments can be described by their characteristics, or attributes, and that the extent to which an individual values the treatment depends upon the nature and levels of these characteristics (Ryan, 2001). Thus, the respondent is asked to choose from a finite set of competing (hypothetical) products described by attributes (or characteristics), the levels of which are systematically varied. The choice data, the relative importance of different characteristics, and the values respondents attach to them (i.e., willingness-to-pay [WTP], time trade-off [TTO]) are estimated via probabilistic choice models. Thus, this provides information about the attributes' relative weight, allowing for an estimation of trade-offs among attributes (Bateman et al, 2002). DCEs are based on the economic theory that people maximize their utility in their choice behavior; thus, it is assumed that respondents will choose the treatment option which provides the highest utility.

5.1. Calculation of Aggregate Scores

The decision problem as well as the decision-makers' preferences should justify the aggregation method chosen and should be consistent with the scoring and weighting method adopted. In most of the indirect methods, the regression model is used to estimate each alternative's value (or utility) or its probability of being the preferred alternative.

Suppose that a given problem is defined by m alternatives and n criteria. Assume all the criteria are benefit criteria. Further, suppose that w_j denotes the relative weight of importance of the criterion C_j and a_{ij} is the performance value of alternative A_i when it is evaluated in terms of criterion C_j. Then, the total (i.e., when all the criteria are considered simultaneously) importance of alternative A_i, denoted as $A_i^{\text{WSM-score}}$, is defined as follows:

$$A_i^{WSM-score} = \sum_{j=1}^{n} w_j \, a_{ij} \text{ , for } I = 1,2,3, \ldots\ldots, m.$$

The most attractive alternative is the one that yields the highest utility (or the maximum total performance value) (Triantaphyllou, 2000) (Belton & Stewart, 2002).

The most appropriate method to choose depends on a number of factors, such as the objective of the analysis, the time available to undertake the analysis, and the stakeholders involved. The importance of which method to choose will in part depend on the objective of the analysis. If the object is to produce a precise estimate of the value of an option, for example, when informing pricing decisions or designing an HTA methodology, the decision is of utmost importance. However, if the objective is to rank options, it is possible to imagine a lower level of theoretical relevance being acceptable.

The cognitive burden for participants of the different methods varies as certain data is easier for participants to understand. Ordinal data, such as that required by ranking techniques or DCE, might be perceived as easier to understand than cardinal data. Pairwise comparison of criteria, such that as used by AHP, is easier than the simultaneous comparison of multiple criteria which is required by DCE.

In a choice modelling exercise, the decision-makers are forced to make trade-offs among criteria: “The advantage of choice-based methods is that choosing [ordinal], unlike scaling [cardinal], is a human task at which we all have considerable experience, and furthermore it is observable and verifiable” (Drummond et al., 2015, p. 145). Therefore, choosing among a few alternatives should be a cognitively less demanding task than having to rate or rank alternatives. Furthermore, it has been argued that “eliciting preference

information in ordinal form instead of cardinal form will result in more stable and reliable responses" (Moshkovich et al., 2002).

On the other hand, if the number of attributes to consider at one time becomes large, the choice sets get complex and make it difficult for the decision-maker to make a choice. The decision-maker might (unconsciously) simplify the decision process by focusing on only a few attributes, which will result in the estimated criteria weights to become inaccurate (Sampietro-Colom & Martin, 2008). In the AHP method, the decision-maker is required to make a relative judgement between two considerations, thus having to make pairwise comparisons of the criteria and/or alternatives at every hierarchical level. Making relative judgements is cognitively more difficult than making absolute ordinal judgements. The relative importance of each criteria and the willingness of a decision-maker to trade one criterion for another (marginal rate of substitution) is represented by the weight estimate. In the outranking and swing/SMART, the points (weights) are directly assigned. In the AHP, the weight is generated for each individual, but can only be directly compared if decision-makers have used the same factors and/or hierarchies (Bolloju, 2001).

All elicitation techniques are subject to potential bias. One risk is that participants may not read or understand the exercise and simply choose one alternative without making a true consideration of the weight they would give to each parameter, or that participants allocate similar weights to all criteria. Other possible sources of bias could, for example, be that participants often prefer sure things to gambles with similar utility.

For this dissertation, a DCE was conducted in order to elicit the patient preferences. This is documented in the article entitled "Are Danish National

Reimbursement Priorities Worthwhile for Patients? An Investigation Using the Discrete Choice Experiment" by Starr, von Arx, & Kjær (2021).

The DCEs involved the following steps:

(1) Relevant attributes of diabetes treatment were identified, and ways were found to measure them.
(2) Relevant levels (ranges) were identified for the attributes aiming at reflecting clinical practice.
(3) Associated levels and choice sets were then chosen using statistical design techniques.
(4) Respondents were shown a number of choice sets and asked to select an alternative for each choice set.

Below follows a description of how the DCE used to elicit the patient preferences of a Danish diabetes cohort was constructed. The description of the work going on prior to the construction of the DCE is described in more detail in the article by von Arx et al. (2017).

5.2. Method

The DCE was included in a 27-item survey distributed to insulin users with T2DM (*N* = 3,160) in the county of Funen, Denmark, in September 2014. The questionnaire is attached in *Appendix 1: Diabetes Survey*. The DCE formed part of a large-scale, registry-enabled study combining self-reported information on health status and socioeconomic position with objective health measures transferred from routine clinical practice to the registry (von Arx et al., 2017).

5.2.1. Selection of Attributes

The attributes and levels were developed on the basis of information gathered from qualitative research according to good practice guidelines (Bridges et al., 2011; von Arx & Kjær, 2014).

The definition of attribute levels was based on clinical and epidemiological data. The descriptive levels were based on treatment guidelines for the use of insulin, and insights were gained from seven one-to-one patient and specialist interviews and four focus group interviews with insulin users. Participants in the focus groups were recruited through a diabetes clinic at Hillerød Hospital, Denmark (von Arx et al., 2017).

The DCEs differed in their description of treatment effectiveness and side effects but were designed to ensure consistency concerning the differences patients would experience clinically based on epidemiological data and responses from interviews, for example, information from patients on which terminology to use (Johnson et al., 2013).

The information gained from the focus group interviews also guided the inclusion of certain attributes which were found to be of relevance by the patients, such as weight loss which was included as an attribute to represent a clinical benefit. Risk attributes included side effects in terms of severe and non-severe hypoglycemic events determined by the support required to manage the event. Incremental heart attack risk was included as a possible treatment-inherent risk.

Table 1 provides an overview of the final attributes and levels, including a priori expectations regarding the signs of each of the coefficients.

Table 1 – Attributes and levels in the discrete choice experiments.

HbA_{1c}*	HbA_{1c} + ordinal scale	LTS	
Arm 1	Arm 2	Arm 4	Parameter Expected sign
6.0 %	6.0 % (very good)	9 of 10 without LTS	+
7.5 %	7.5 % (good)	7 of 10 without LTS	+
8.5 %	8.5 % (moderate)	5 of 10 without LTS	Ref
Attributes identical for all versions of the discrete choice experiments			
1-year weight change		None	Ref
		–4 kg	+
		–10 kg	+
Risk increase of HA due to treatment, per year		Yes (3 additional people of 1000)	÷
		No (no risk increase)	
Low BS requiring assistance others, per year†		None	Ref
		1 per year	÷
		2 per year	÷
Self-managed low BS, per month‡		1 event per month	Ref
		4 events per month	÷
		8 events per month	÷

BS, blood sugar; HA, heart attack; LTS, long-term sequela; Pts, patients; Ref, reference level.
* An additional discrete choice experiment, arm 3, informed respondents of the LTS risk associated with each level of HbA_{1c} before the choice task but was otherwise identical to arm 1.
† Severe hypoglycemic events.
‡ Nonsevere hypoglycemic events.

Source: von Arx et al., 2017.

A full factorial design that uses all the combinations of the attributes would give rise to too many scenarios. In order to reduce the number of choice sets to a workable size, a balanced and orthogonal, fractional, factorial design was generated using the SAS macro %MktEx program (Kuhfeld, 2005). The orthogonal design ensured that the resulting parameter estimates were uncorrelated and could be determined independently of the other attributes. A balanced design ensured that the attribute levels occurred with equal frequency within each attribute, yielding equally robust results for all levels. To keep the questionnaire at a reasonable length, a set of choice "scenarios" were selected, each presenting attributes and levels for two different hypothetical diabetes treatments. The resulting experimental design consisted of 12 questions with two alterative choice answers. Respondents were asked to select the preferred treatment option within each scenario, providing a hypothetical trade-off which formed the basis of the analysis.

While the respondents were asked to complete the choice task, they read the following text:

“In the next part, there are different situations that you must choose between. What you have to do is consider advantages and disadvantages with diabetes treatment. Some of the situations will be different than your current treatment. They show what the future’s diabetes treatment can look like. The number of times that you take the medicine—and how you take it—is as you do with your current treatment.”

This was followed by a brief description of each of the attributes presented in the choice task.

Two different hypothetical diabetes medications, labelled treatment A and treatment B, were included in each choice scenario, and respondents were asked to indicate their preferred option (hypothetical trade-off questions). These choice scenarios were designed to elicit the patients’ trade-off for different attribute levels, and the trade-offs yielded the weight of each.

Example of a choice question is shown in Figure 4:

Choice question 1 of 12	Treatment A	Treatment B
People in treatment who avoid related illnesses	7 of 10 without related illnesses	5 of 10 without related illnesses
Possible weight loss in a year	No weight change	4 kg
Increased risk of heart attack through treatment, per year	No (no added risk)	Yes (3 more people of 1000)
Low blood sugar that requires help from others, per year	None	2 events
Low blood sugar that you can deal with yourself, per month	8 events	1 event
Which treatment do you prefer?	☐	☐

Source: von Arx et al., 2017

Figure 4. Examples of a choice question

The software Ngene was used to construct an unlabeled, Bayesian *D*-efficient design in accordance with good practice guidelines (Johnson et al., 2013).

5.2.2. Model and Analytical Strategy

For data management, randomization schedules, and descriptive statistics the SAS software (version 9.3 for Windows; SAS Institute Inc., Cary, NC, USA) was used. BIerlaire's Optimization Package for GEV Models Estimation software version 2.3 (Biogeme, Lausanne, Switzerland) was used for all other analyses (von Arx et al., 2017).

Separate models were estimated for each survey arm using an error component logit specification. The estimated utility function *U* for individual *n* of alternative *i* and choice set *t* resulted in the following specification:

$$U_{nit} = \frac{\beta o}{\sigma} + \frac{\beta 1}{\sigma} GC + \frac{\beta 2}{\sigma} WL + \frac{\beta 3}{\sigma} HA + \frac{\beta 4}{\sigma} nonSHE + \frac{\beta 5}{\sigma} SHE + \varepsilon_{nit} + \mu_n E_{nit},$$

where βo is the alternative specific constant, $\beta 1 - 5$ are the parameters for each of the treatment attributes; *GC* is glycemic control, presented as either A_{1c} or long-term sequela (LTS) mitigation; *WL* is weight loss; *HA* is incremental heart attack risk; *nonSHE* is non-severe hypoglycemic events; and *SHE* is severe hypoglycemic events. All attributes were tested for linearity. If linearity was rejected, the attributes entered the model as categorical variables. σ denotes a scale parameter confounded with the taste parameters and inversely related to variance (normalized at 1). ε is an error term assumed to be independent and identically distributed with type I extreme value distribution, and μ is a random term with zero mean. Lastly, ε denotes the alternative-specific individual random effects. In all models, individual-level heterogeneity was controlled for through the use of a panel specification capturing the repeated choice nature of the data. The models were estimated with simulated maximum likelihood using Halton draws with 300 replications (von Arx et al., 2017).

Swait and Louviere log-likelihood ratio (LLR) tests were performed to establish whether general preference patterns were the same across the four elicitation formats. The test was carried out for the full sample (joint model of all four arms) and for all pairwise comparisons. The LLR test statistic is chi-square distributed with *k*-1 degrees of freedom (*df*), using standard levels of statistical significance (von Arx et al., 2017).

5.2.3. Analysis

Data were validated and checked for consistency and error before conducting the statistical analyses with the SAS analytical software package (version 9.3; SAS Institute Inc., Cary, NC, USA). WTP for the different attributes was determined using a standard mixed multinomial logit model approach. The probability of

choosing one option *j* from n_i in a choice scenario (where there are n_i = 2 possible options in each scenario choice set C_i) is defined by the equation (Bogelund et al., 2011; Wooldridge, 2010):

$$P(j) = \frac{\exp\,(\chi'_{ij}\beta)}{\sum_{k\epsilon Ci}\exp\,(\chi'_{ik}\beta)}.$$

The estimated parameters β, will express preference weights for each attribute level. The WTP values for the attribute levels were calculated by dividing the estimated coefficients, β, for each attribute, by the coefficient of payment. The rationale underlying this approach was derived from the economic theory of demand, in which these calculated ratios are known as marginal rates of substitution.

The linearity of the relevant attributes was then tested using a standard likelihood ratio test. This was the case for weight loss, minor hypoglycemia events, and number of daily insulin injections. All these attributes exhibited linearity, and so the linear function was introduced into the basic model. Interaction effects were tested according to a predefined statistical analysis plan.

Initially, it was the intention to assess the respondent's WTP for several treatment attributes related to injectable insulin therapy in order to assess the relative importance of each attribute. WTP is a preference estimate of the patients' WTP to obtain certain benefits or to avoid certain side effects of treatments and by the value patients place on changing these attributes. However, in the pilot study, it was found that it was too difficult for the subject to put a money value on treatment, and consequently, the decision was made to not attempt to calculate the WTP in the study. Patients who are not usually paying out-of-pocket for treatment might not be able to make a realistic estimate, and the range of WTP

estimates might be very wide and possibly more predictive of an ability to pay. The use of DCE and conditional logit methods is the recommended approach to determine WTP in subjects choosing between two hypothetical packages. Although DCEs ensure that it is difficult for respondents to answer strategically (Louviere et al., 1990), there is a risk that respondents might have given different preferences in this study to those they would give in a real-life situation (Ryan et al., 2009). Another critique is that the price might have such a high impact for the respondent that it devalues the other attributes. A good understanding of how much people is willing to pay for different disease attributes within a given country may assist in tailoring diabetes management to meet those needs, and for a pharmaceutical company, it can therefore be used as a negotiation tool in the reimbursement discussion with payers.

6. Revealed preferences

The revealed theory is attributable to economist Paul Samuelson. He first described the concept in 1938 (Samuelson, 1938) writing that ". . . if an individual selects batch one over batch two, he does not at the same time select two over one." The revealed preference theory is concerned with the actual observed behavior in the market, and it works on the assumption that consumers (e.g., payers, prescribers, or patients) are rational. In other words, they will have considered a set of alternatives before making a purchasing decision that is best for them. Thus, the theory entails that if a consumer purchases a specific bundle of goods, then that bundle is "revealed preferred," given constant income and prices, to any other bundle that the consumer could afford. Thus, given that a consumer chooses one option out of the set, this option must be the preferred option. By varying income or prices or both, an observer can infer a representative model of the consumer's preferences.

The revealed preference theory assumes we can deduce the utility functions from consumer behavior. Analyzing these choices leads us backwards to a set of preferences that influences the choices they make which allows us to study consumer behavior empirically.

The theory of revealed preference developed three primary axioms of revealed preference which were identified as the weak axiom, the strong axiom, and the generalized axiom:

Weak Axiom of Revealed Preference (WARP): This axiom states that, given budget constraints, if one product or service is purchased instead of another, then, as consumers, we will always make the same choice. Further, the weak axiom states

that, if we buy a certain product, then we will never buy a different product or brand unless it is cheaper, offers increased convenience (e.g., oral instead of injectable), or is of better quality (i.e., unless it provides more benefits such as better control, fewer side effects, and/or higher weight loss). As consumers, we will buy what we prefer and our choices will be consistent, so this suggests the weak axiom. In other words, if A is revealed preferred to B (A RP B), then it must be so in every case. That is, if a consumer ever chooses B, then we must assume that A was previously chosen and that the budget constraint had enough "left over" to allow a consumer to choose B as well (as illustrated by the dark grey line in Figure 5).

This proof was for two goods only, and Samuelson recognized that a general proof for multiple goods was necessary. Houthakker (1950) provided the missing proof, and Samuelson (1950) recognized it stating, "He has given us the long-sought test for integrability that can be formed in finite index-number terms, without need to estimate partial derivatives." Houthakker's definition recognized the need for an indirect revealed preference relation by adding the Strong Axiom of Revealed Preference:

Strong Axiom of Revealed Preference (SARP): This axiom states that in a world where there are only two goods from which to choose, a two-dimensional world, the strong and weak actions are shown to be equivalent. Thus, if there are only two goods, then it is clear that WARP already defines a consumer's choice: A over B. However, the SARP adds the idea of indirectly revealing preferences: if A is chosen over B and B over C, SARP and transitivity dictate that A is also preferred to C, so A is indirectly revealed to be preferable to C.

Generalized Axiom of Revealed Preference (GARP): This axiom covers the case when, for a given level of income, budget, and/or price, we get the same level of benefit from more than one consumption bundle. In other words, this axiom accounts for when no unique bundle that maximizes utility exists.

RP is illustrated in Figure 5: If a bundle *b* is revealed preferred over bundle *a* in a budget set *B*, then the WARP says that bundle *a* cannot be strictly revealed preferred over bundle *b* in any budget set *B'*. This would also hold true if *a* had been located anywhere else in the scattered area. Bundle *c* will not violate WARP even if it chosen in budget set *B'* because it is not in the scattered area.

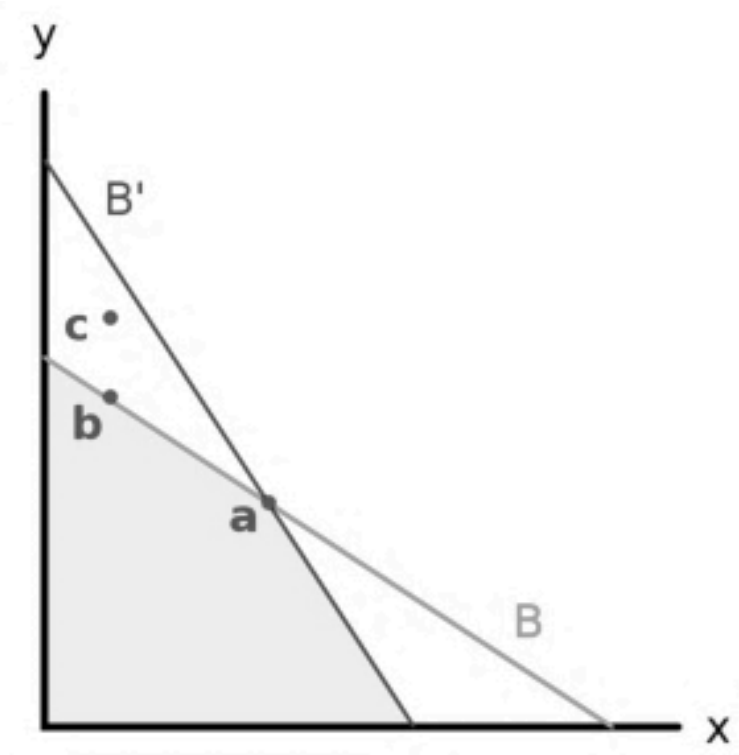


Figure 5. Revealed preferences

If we think of *a, b,* and *c* as infinitely complex bundles of goods, we can map out the consumer's choices. In this dissertation, I was able to combine data on market uptake (as represented by prescription to alternative diabetes products), pharmaceutical performance on selected criteria, and price information and track this backwards to build utility functions, thereby revealing the population's preferences.

Decision-makers can qualitatively rank the alternatives by determining whether any alternative dominates. A dominating alternative will occur if one option performs at least as well as another on all criteria and strictly better than the other on at least one criterion (Baltussen & Niessen, 2006). However, in practice, this is a rare situation, and thus, the method's assistance to choose among many options in real life is limited (Baltussen & Niessen, 2006).

It is also likely that the options have equal importance in terms of the options' overall performance and as this – to a large extent – is based on subjective reasoning, decisions are unlikely to be inconsistent and, thus, could result in an undesirable ranking of alternatives in particular when no alternatives dominate.

In this work, revealed preferences were used for a benchmarking analysis and linear programming to evaluate existing diabetes products and to estimate the demand for a new pharmaceutical product in the article: "Predicting the Demand for New Diabetes Drug" by Bogetoft and Starr (2021).

7. Multi-Criteria Decision Analysis

As described previously, priority setting in healthcare involves making trade-offs among multiple conflicting considerations or *criteria*. Thus, there is a need to develop methods which can assist decision-makers to weigh up evidence on multiple factors and, hence, make economic evaluations to go beyond solely generating evidence. MCDA is based on the premise that any good or service – in this case, new health technologies – can be described by characteristics or criteria, and the extent to which an individual values the good depends on the individual's preferences for those characteristics (Bogetoft & Pruzan, 1997).

MCDA is an analytical quantitative method aimed at supporting decision-makers faced with evaluating, comparing, and/or prioritizing among alternative strategies or products, taking into account multiple and often conflicting criteria (Belton & Stewart, 2002). Hence, MCDA is an approach as well as a set of techniques, with the goal of providing an overall ordering of options, by looking at the extent to which a set of objectives is achieved (Kanavos & Angelis, 2013). MCDA is a way of analyzing complex situations characterized by a mix of objectives and does so by disaggregating a complex problem into simpler components, measuring the extent to which certain options achieve the objectives, weighting these objectives, and reassembling the components to show a comprehensible overall picture (Bogetoft & Pruzan, 1997).

In multi-criteria decision-making (MCDM), a decision-maker uses several conflicting criteria to assess the desirability of different decision alternatives, which are choices or courses of action (Belton & Stewart, 2002). The elements of value can, in MCDA be measured and scored in their natural units or through

constructed scales, quantitatively or quantitatively, and weights are assigned to reflect criteria's importance (Kanavos & Angelis, 2013).

7.1. Definition of MCDA

Two often used and commonly accepted definitions of MCDA have been given by Keeney and Raiffa (1976), where MCDA is defined as "an extension of decision theory that covers any decision with multiple objectives. A methodology for appraising options on individual, often conflicting criteria, and combining them into one overall appraisal (. . . .)". An alternative definition was given by Belton and Stewart (2002), where MCDA was described as "an umbrella term to describe a collection of formal approaches, which seek to take explicit account of multiple criteria in helping individuals or groups explore decisions that matter."

7.2. MCDA in Healthcare Decision-Making

MCDA has been suggested as a methodology which could address the limitations of economic evaluations in healthcare decision-making (Devlin & Sussex, 2011; Kanavos & Angelis, 2013; Marsh et al., 2014; Marsh et al., 2016; Thokala et al., 2014; Thokala et al., 2016; Hansen & Devlin, 2019).

In other scientific disciplines and sectors, it is however, a more well-developed methodology that has gained widespread acceptance and is routinely used in decision-making within agriculture, energy, environment, finance, marketing, sustainability, and telecommunications (Thokala et al., 2014). The healthcare sector has been relatively slow in adapting MCDA, but there has been a sharp increase in articles discussing the potential of MCDA and use of MCDA within healthcare, in recent years (Diaby & Goeree, 2014). In a review of MCDA

applications in healthcare it was found, that the first application was published in 1990. Since then and up until 2018 data revealed that MCDA was primarily used in public health services and diagnosis and only a few applications in treatment (Glaize et al., 2019). Reviews on the application of MCDA in healthcare showed that most of the MCDAs were undertaken to support healthcare investment decisions, such as HTA as well as national and local coverage decisions. However, MCDA was also identified to support authorization and prescription decisions (Marsh et al., 2014) (Glaize et al., 2019). An early historic overview of the developments in MCDA was provided by Köksalan et al. (2013).
Below a few of the examples where MCDA is used to support healthcare decisions and setting priorities for HTAs are mentioned:

Several HTA bodies have piloted the use of MCDA, including the Swedish Dental and Pharmaceutical Benefits Agency (Angelis, 2018) and on e.g., an experimental basis to assess the (clinical) benefit–risk profile of new medicines for the purpose of regulatory approval during marketing authorization stage by the EMA (2010).

In the UK, the National Institute for Health and Clinical Excellence (NICE), considered the use of “structured decision-making” (i.e., MCDA) in its formal methods review (NICE, 2012; NICE 2020), eventually rejecting MCDA as not representing a clear improvement on existing deliberative processes.

The recent initiation of “value assessment frameworks” in the United States has also amplified the interest in MCDA’s potential to help weigh up the competing aspects of value being considered (Norman, Chalkidou, & Culyer, 2018). The U.S. value frameworks aim to support decision-making regarding new technologies in the U.S. health system and are envisioned to measure and to communicate the

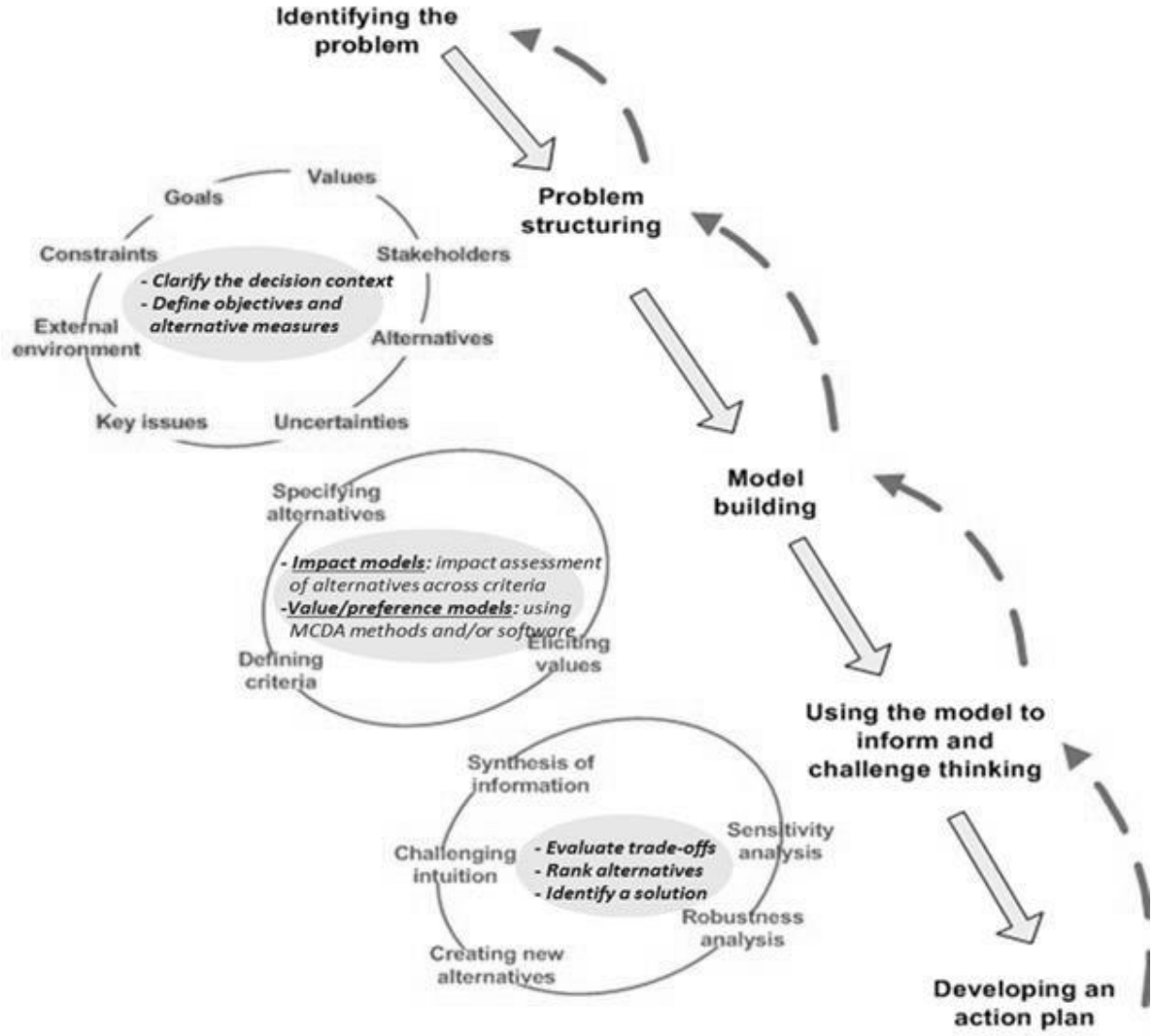
value of pharmaceuticals and other healthcare technologies for decision-making, using multiple attributes of value (Neumann, Willke, & Garrison, 2018).

In addition to HTA, other examples of health MCDA applications include for example: prioritizing R&D portfolios in pharmaceutical companies (Phillips & Bana E Costa, 2007); disease classification and diagnosis (Johnson et al., 2014); prioritizing antibiotic-resistant diseases for R&D (Tacconelli et al., 2018); supporting patients and clinicians in selecting treatments (Dolan, 2008); and weighing up the benefits and risks of new medicines to support licensing decisions (Phillips, Fasolo, Zafiropoulos, & Beyer, 2011). These examples have a wide range of applications, despite this, they all include the four key elements common to all MCDA applications in general: alternatives, criteria, weights, and decision makers, and hence involve ranking or selecting alternatives based on the application of criteria and weights (representing the relative importance of the criteria) according to the preferences of decision makers (and, potentially, other stakeholders).

Furthermore, in 2016 The Professional Society for Health Economics and Outcomes Research (ISPOR) published two reports on MCDA applications in healthcare. The first report (Thokala et al., 2016) provided an overview of the main MCDA methods with examples of applications in different healthcare areas. The second Task Force report (Marsh et al., 2016) offered an “MCDA Good Practice Guidelines Checklist” with recommendations on how to implement these key steps in healthcare decision-making situations.

7.3. Steps in Conducting an MCDA

During this PhD project, the main principles from standard works within MCDA were used, drawing on the work from other sciences as well as work published on MCDA in pharmaceutical product development and approval (Mussen, 2007). However, no comprehensive guideline has yet been developed in the field of the appraisals of medical products. Although there are many different ways to use and apply MCDA methods, there are several common elements of an MCDA process (Baltussen & Niessen, 2006). As illustrated in Figure 8, MCDA consists of a number of steps; however, the MCDA process has to be considered as iterative, rather than comprising a strictly sequential set of steps:



Modified from Belton and Stewart (2002).

Figure 6. The MCDA process

1. **Identification of the problem and problem structuring**: Identifying the decision problem and the corresponding decision goal. Establishing the decision context by defining the aims of the MCDA, identifying the decision-makers and other key stakeholders, and categorizing the relevant options and criteria that reflect the value associated with the consequences of each option.

2. **Model building**: “Scoring” the value associated with the performance of each option against the criteria and “weighting” each of the criteria to reflect their relative importance to the decision, combining the scores and weights for each option to derive the overall value, and finally examining the results.
3. **Using the model to inform and challenge thinking**: Perform uncertainty analysis to understand the robustness of the MDCA results; conduct a sensitivity analysis of the results to test the influence of changes in scores or weights; and finally, interpret the MCDA outputs to aid in the decision-making.
4. **Develop an action plan:** An action plan is ultimately developed and implemented.

In this work, MCDA is used as a modern benchmarking technique to evaluate the existing pharmaceutical products in the GLP-1, SGLT-2, and DPP-4 portfolio in Denmark by 2019 using data envelopment analysis (DEA) and to identify which preferences different patient groups have for the different pharmaceutical product attributes (Bogetoft & Otto, 2011). With this information, it is possible to determine how the attributes of a new pharmaceutical product are likely to affect demand for this pharmaceutical product, and it can be used in reimbursement discussion and value communication with payers.

7.4. Method

7.4.1. Identification of the Problem and Problem Structuring

The initial phase of any MCDA is to identify the decision problem, developing a clear description of the decision problem and identifying the corresponding decision goal in terms of the appropriate decision-makers and other stakeholders, and the decision-makers' objectives, as well as defining the alternatives under consideration. The objectives of decision-makers will determine which MCDA is the most appropriate.

The market for health services and technologies is distinct from that of most other markets as the demand for health services and products is largely decoupled from prices and customer preferences and the demand is, to a large extent, dependent on factors such as reimbursement decisions.

Usually, the weighting of criteria is done by stakeholders. In some instances, it is evident which preferences and priorities to take into account. In other applications, it is less clear. In HTA, for example, it is often undertaken by multi-disciplinary committees consisting of representatives from government, insurance funds, healthcare providers, academics, health professionals, patients, and the general public (Stafinski, 2011).

Within healthcare, as in any field, improving performance and accountability depends on having a shared goal that unites the interests and activities of all stakeholders (Porter, 2010). The choice about whose preferences are relevant to a given decision problem is a normative one. However, the outcome from the decision-making process may be sensitive to which and whose weights are used. The heterogeneous viewpoints of participating stakeholders are rarely

systematically addressed in health economic evaluations. In the healthcare system, there are many different stakeholders who can be expected to have many and, at times, conflicting goals and different perceptions of what creates value. For example, while patients and physicians might value treatments that help patients obtain optimal health, healthcare systems and policy decision-makers might value healthcare in regard to health benefits' relative to costs, while pharmaceutical companies might value profit and shareholder satisfaction, and society might place the highest value on treatments with health and social benefits relative to other public funds.

Identify Alternatives and Selecting the Relevant Criteria

The decision alternatives can be a finite set of alternatives, for example, treatment alternatives for patients, or a binary outcome which would either approve or deny recommendations for new health technologies (Thokala et al., 2016).

To carry out an MCDA, the decision criteria, by which alternative new pharmaceutical products and therapeutic biological products will be prioritized, need to be determined. The criteria need to be relevant to the decision-maker and can be identified and defined from several sources, such as the mission statements of the decision-making organization, documents describing previous decisions, evaluations to support related decisions, treatment guidelines, and stakeholder and expert consultation (Marsh et al., 2016).

A long list of potential criteria will usually be identified in the above sources. However, the criteria need to be relevant to the decision being made and independent of each other, and the alternatives being considered need to be accurately described in the criteria as otherwise the overall ranking of alternatives may not be accurate. There is no set rule as to how many criteria should be

included in an analysis, but the number of criteria should be as few as is consistent with making a well-founded decision (Marsh et al., 2016). Including too many criteria in an MCDA might have practical implications in terms of time and the cognitive burden. The selected criteria need to fulfill the following requirements:

- Completeness: The criteria should capture all factors important to measuring stakeholders' objectives.
- Non-redundancy: Criteria should be removed if they are unnecessary or judged unimportant.
- Non-overlap: Criteria should be defined to avoid double counting, which can give too much weight to a value dimension.
- Preferential independence: The weight for a criterion should be independent of the score on other criteria.

One of the objectives of this work is to develop a prioritization framework that helps to inform decision-making in early pharmaceutical product development. Therefore, the decision criteria, by which alternative new pharmaceutical products and therapeutic biological products will be prioritized, need to be determined.

Establishing Criteria for the Decision Survey

In order to identify which criteria to include, a literature review was carried out. The systematic identification of potentially relevant studies (papers, research reports, policy documents) concerned with decision-making in health was conducted in the period from July 2013 to September 2013. Potentially relevant papers were identified through systematic electronic databases, other online resources, contacting content experts within the field, and prior knowledge supplementing the process. The search was limited to: (i) literature published after

the year 2000, (ii) studies in English, (iii) grey literature,[2] and (iv) topics related to humans.

The search for literature was adapted to the timeframe of the review, and information sources that broadly covered different subjects were selected. Electronic databases were used to search for peer-reviewed literature, general search engines, and website searches for both peer-reviewed and grey literature. Reference lists from primary studies were checked for new leads.

The electronic database search was performed in healthcare-related and economic databases, each of which covered particular topics. Specifically, the following databases, catalogues, and bibliographies were used: Medline, Embase, Cochrane, NHS-eed, Scopus, and EconLit: Economic.

In addition, a comprehensive search in Google Scholar was performed, as well as searches in identified relevant research or content specific databases.

With regard to grey literature, additional searches for relevant studies and useful leads were made by means of the Google search engine and Google Scholar. Copies or links to relevant documents were made and the URL and date of access for relevant documents were recorded.

[2] Grey literature is the common name for academic or scientific publications that are not published via a traditional publisher or journal. Grey literature can be working papers or reports as well as articles and dissertations that are not ultimately published.

In addition, the following websites were searched for relevant studies, ongoing or unpublished research projects, and other useful leads: The National Institute for Health and Care Excellence (NICE) (nice.org), International Society for Pharmacoeconomics (ISPOR) (ispor.org), EMA (ema.europa.eu), International Network of Agencies for Health Technology Assessment (INAHTA) (Inahta.org), and European Network for HTA: EUnetHTA.

In order to make sure that none of the used words would be too limiting in a search, a search with each of the words found to be of relevance was performed and the number of corresponding hits recorded (for details, please see *Appendix 2: Literature Search Strategy*).

Search strategy

The search strategy consisted of a number of search sets (1–xx) which described various combinations of free text words in the title (TI), abstract (AB), and subjects (SU) and specific controlled descriptors (DE).

Screening

Through screening of titles and abstracts, it was assessed whether the study was of relevance to the topic. Those studies that passed or those where screening of title and abstract could not provide the required information were retrieved in full text and screened in more detail.

Coding

Articles included after second-level screening were coded according to a range of characteristics concerning study methodology, intervention characteristics,

structure and content, study design, sample, data collection and analytical procedure, results, and a range of factors related to quality assessment.

Initially, this project had two components: one attempting to make a tool to determine priorities across disease areas and another within diabetes only. The literature review was carried out with this in mind. A framework was developed for data analysis and identification of key themes, such as: severity of disease/burden of illness; number of potential beneficiaries (patients); benefits to others (family or society); age; health benefits to the patient (i.e., length and/or QoL); safety/side effects; cost effectiveness; budget impact; unmet medical needs; innovation; and others.

Value Tree

After mapping the various studies, it was found that the following value concerns influence the evaluation of new diabetes medications. The value tree (Figure 7) was decomposed into five value criteria clusters relating to: 1) therapeutic impact, 2) safety profile, 3) socioeconomic impact, and 4) innovation level:

Value = f(therapeutic impact + safety profile + socioeconomic impact + innovation).

These value clusters were intended to comprise the critical aspects of value concerns to decision-makers for evaluating the value of a new medicine within the GLP-1, SGLT-2, and DPP-4 segments.

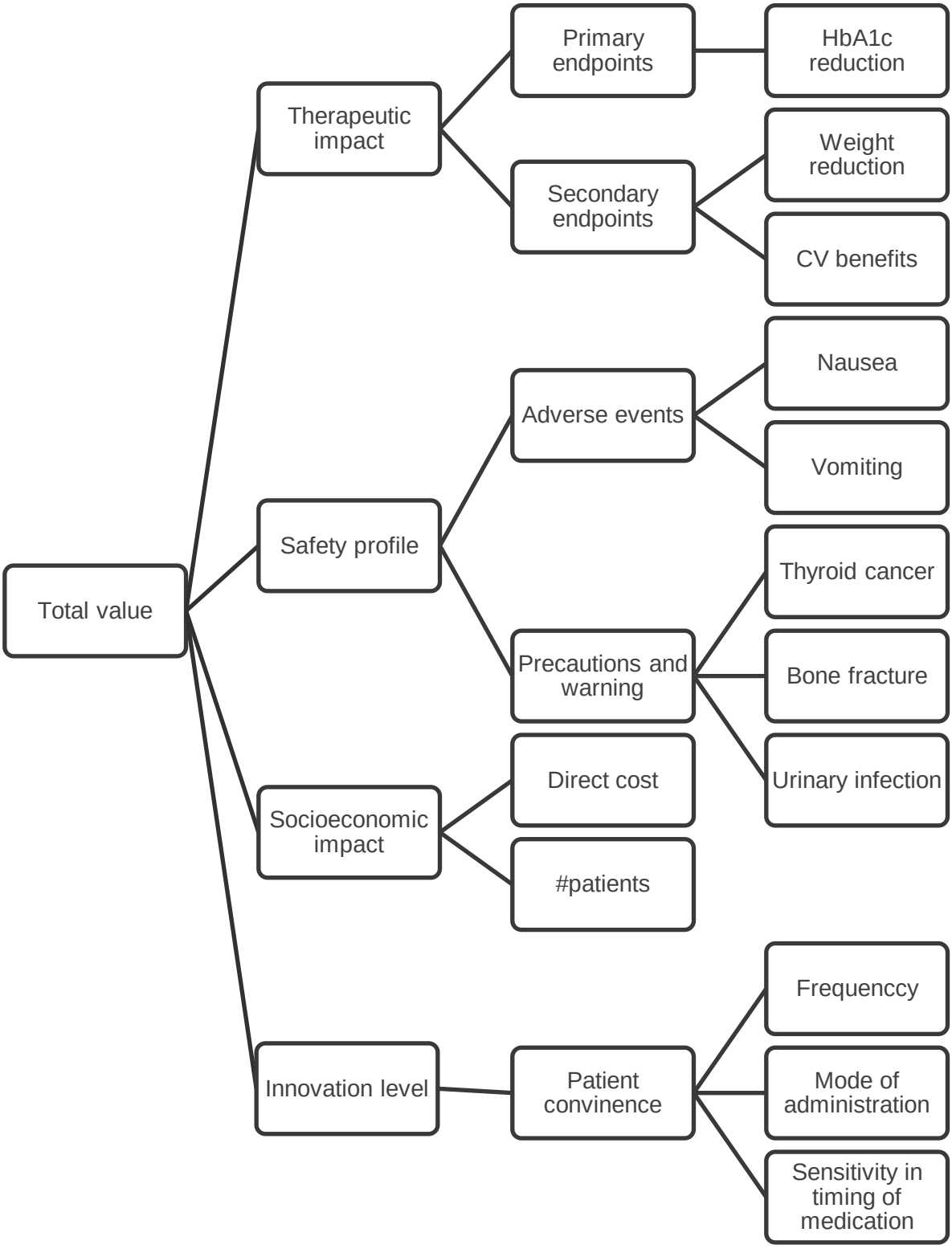


Figure 7. Value tree for T2DM for GLP-1, SGLT-2, and DPP-4 treatments

For diabetes patients, it is of primary importance that a product can assist the patient in achieving an HbA1c within the target. This is a quality or characteristic

patients and physicians expect of any product when considering the use of it. This primary clinical endpoint is currently – although with some variety – delivered by the products in the GLP-1, SGLT-2, and DPP-4 product portfolio, and it can be considered an expectation of a product in this space. Other secondary endpoints, such as weight loss or cardiovascular benefits, are competitive advantages only featured by some products in the group. There might also be opportunities in unmet category needs, which could become drivers if effectively developed and leveraged, for example, improved convenience.

Lastly, there are product features such as safety issues which are of advantage for the competitor's brands, including black box warnings or a high percentage of patients experiencing side effects, which may be brand liabilities for the current brand.

7.4.2. Model Building

When the criteria have been established, the stakeholder's preferences or priorities, in terms of the scoring associated with the performance of each criterion and the weight reflecting their relative importance to the decision, need to be established. The scoring and weighting are intrinsically linked and can be done sequentially, simultaneously, or iteratively, depending on the methods used (Thokala et al., 2016), but should result in combining the scores and weights for each option to derive the overall value and finally examining the results.

MCDA is flexible with a range of approaches which vary in complexity, and it can consider a broad range of aspects, for example, monetary, non-monetary, and equity efficiency as well as local data and explicit definitions of costs and benefits.

As such, most MCDA methods are capable of combining quantitative data, either on objective (e.g., probability of experiencing an adverse event) or subjective (e.g., Patient Reported Outcomes (PROs), subjective well-being) criteria, alongside qualitative data (e.g., expert opinion on the portability of an inhaler).

In order to capture stakeholders' preferences and priorities, different weighting and scoring techniques are employed. Weights capture preferences or priorities *among* criteria. Scores capture priorities or preferences *within* a criterion (Marsh et al., 2016). By combining weights and scores, we can assess the relative importance of any change in performance within any of the criteria (Marsh et al., 2016).

Data Envelope Analysis

Data Envelopment Analaysis (DEA) is a non-parametric mathematical programming method used to empirically measure production efficiency of a set of peer entities called Decision-Making Units (DMUs), which convert multiple inputs into multiple outputs. DEA have had a variety of application with many different kinds of entities engaged in many different activities, however DEA is mainly being used within production theory in economics and for benchmarking purposes within operational research for the estimation of production frontier[3] and there has been a great variety of the applications of DEA (Cooper et al., 2001).

[3] A production frontier is a curve, which shows various combinations of the amount of two goods which can be produced within the given resources, and a graphical representation showing all the possible options of output for two products that can be produced using all factors of production, where the given resources are fully and efficiently utilized per unit time.

Some of the advantages of DEA is, that is requires very few assumptions, and hence, DEA has been used in situation of complex nature (Cooper et al., 2001).

Parametric approaches require ex-ante specification of a production- or cost function, whereas non-parametric methods in contrast compare possible input and output combinations based on the available data only (Cooper et al., 2007). DEA has its name from its enveloping property of the dataset's efficient DMUs, where the empirically observed, most efficient DMUs constitute the production frontier against which all DMUs are compared.

In a traditional DEA study, we assume that the evaluated entities are described by the inputs used and products being produced. If there are *D* entities and if entity *d* used $x^d \in R_0^C$ inputs to produce $y^d \in R_0^A$ outputs, we can model the technology as the smallest set in an input-output space R_0^{C+A} that contains the actual observations and satisfies standard production economic properties, such as free disposability of inputs and outputs (we can always produce fewer outputs with more inputs) and convexity. This leads to the so-called variable return to scale (VRS)-DEA model. We might also assume that it is possible to operate at different scales, for example, by assuming constant returns to scale (CRS). Technically, the underlying technology *T* is estimated by T^* using linear constraint, for example in the VRS case as:

$$T^* = \left\{(x,y) \in R_0^{C+F} | \exists \lambda \in R_0^n : x \geq \sum_{d \in D} \lambda^d x^d , y \leq \sum_{d \in D} \lambda^d y^d , \sum_{d \in D} \lambda^d = 1\right\}.$$

The estimated technology is the smallest convex set that contains the actual pharmaceutical products and satisfy free disposability of outputs and inputs.

The efficiency of a given entity *d* can now be measured relative to this technology using a so-called Farrell approach, that is, as the maximal proportional expansion of all outputs *F* or the maximal proportional contraction *E* of all inputs, that is, as:

$F^d = \max\{ F \in R_0 \mid (x^d, Fy^d) \in T^* \}$ or $E^d = \min\{ E \in R_0 \mid (Ex^d, y^d) \in T^* \}$.

In the applications described in the paper by Bogetoft and Starr (2021), the different entities are the pharmaceutical products $d \in D$. The outputs are the attractive outcomes of using the pharmaceutical products, and the inputs are the negative aspect of using the drugs. Of course, there was some freedom in the ways we specified the features. Nausea, for example, can be handled as an input since it is unattractive, or it can be handled as an output using, for example, of the share of users experiencing no nausea. We have generally used the latter approach and think of the input side as only being costs – or even be entirely ignored when we think of a system with substantial governmental co-payments, as shown in the following calculations.

Formally, to find the efficiency scores, we need to solve linear programming problems. The output efficiency of decision-making unit zero 0, for example, can be determined as the solution to:

$$\max_{\lambda, F} \quad F$$

$$s.t. \quad x^0 \geq \sum_{d \in D} \lambda^d x^d$$

$$Fy^0 \leq \sum_{d \in D} \lambda^d \, y^d$$

$$\sum_{d \in D} \lambda^d = 1.$$

That is, we seek to find the largest proportion of increase (*F*) in all outputs that is feasible without spending more of any of the inputs than the decision-making unit zero.

Sensitivity, Robustness, and Uncertainty

The aggregate scores can be interpreted and used in a variety of ways, such as ranking the alternatives in order of importance or providing a relative value compared with the other alternatives, thus allowing for benchmarking analysis in respect to portfolio optimization and efficiency frontiers. However, the meaning of scores and weights might vary with the techniques employed and will need careful explanation to the stakeholders. The interpretation should also include discussion on the impact of uncertainty.

Uncertainty is usually carefully dealt with in health economic evaluations. In order to understand the robustness of the MCDA results, an uncertainty analysis needs to be performed and a sensitivity analysis of the results conducted to test the influence of changes in scores or weights. Sensitivity analysis thus reflects the extent and impact of the uncertainty in the decision, and it can therefore define the strength of validity (quality) of the economic evaluation and its related decision (Briggs, 2011). For the decision-maker, a sensitivity analysis can hence be an aid in the decision-making process. Such an analysis can indicate the existence of low uncertainty or whether further research is needed and thus aid in a more stable decision-making process to reach a secure conclusion. Who the stakeholders are, which criteria are chosen, performance against those criteria, and other choices can all impact the analysis, and the results should be considered in light of this. Uncertainty may affect both the design and evidence feeding into the assessment which will be explained in the section below.

To account for uncertainty in MCDA, three separate steps are proposed: 1) the sources of uncertainty need to be identified, 2) an assessment of the magnitude of the uncertainty needs to be conducted, and 3) an evaluation of whether the uncertainty would eventually lead to a different decision has to be made. An overview of some of the most likely types and sources of uncertainty in the context of MCDA-supported decision-making is presented in Table 2.

In a review by Broekhuizen et al. (2015), they reviewed how uncertainty explicitly was taken into account in MCDA. In the 569 identified studies, it was found that five approaches were used in MCDA: fuzzy set theory (45 % of studies), deterministic sensitivity analysis (31 %), probabilistic sensitivity analysis (15 %), Bayesian framework (6 %), and grey theory (3 %). A large number of papers considered the AHP in combination with fuzzy set theory (31%). However, only a few (3%) of the studies were published in healthcare-related journals. They concluded that a simple approach which is most likely sufficient for most decisions in healthcare is deterministic sensitivity analysis, although, when multiple sources of uncertainty have to be considered simultaneously, more complex approaches may be necessary.

Table 2. Examples of types and sources of uncertainty within MCDA

Type of uncertainty	Definition	Type of uncertainty	MCDA specific uncertainty
Stochastic uncertainty	Random variability in outcomes between identical patients	First-order uncertainty	Random variability in criteria weights or performance scores as assigned by identical persons
Parameter uncertainty	The uncertainty in estimation of the parameter of interest	Second-order uncertainty	The uncertainty in estimation of the parameter of interest
Heterogeneity	The variability among patients that can be attributed to characteristics of those patients	Variability Observed heterogeneity	Variability in criteria weights or performance scores that can be attributed to a person's characteristics
Structural uncertainty	The assumptions inherent in the decision model		Uncertainty about whether all relevant criteria are included, if they are properly structured and which transformations are used

Sources: Briggs et al. (2012) and Broekhuizen et al. (2015).

7.4.3. Implementation: Developing an Action Plan

Initially, it was our hope that this project would lead to the development of a generalizable tool that could be used in multiple markets and possibly in other disease or business areas; however, this does not seem suitable. The use over multiple decisions will require that global (or fixed) scales are employed, anchored by their endpoints at the best and worst performance that could realistically occur.

RP theory has been critiqued for making too many assumptions, for example, that consumer's preferences remain constant over time and that an action at a specific

point in time possibly reveals part of a consumer's preference scale just at that time. There is no proof to back up the assumption that a preference remains unchanged from one point in time to another. In the real world, there are lots of alternative choices. It is impossible to determine what product or set of products or behavioral options was turned down in preference to buying something else.

MCDA as Part of HTA

The potential for MCDA to support HTA has been much discussed (Castro et al., 2017) because it offers the means to consider a more comprehensive set of benefits compared with conventional HTA methods such as the QALY, while MCDA still summarizes these benefits in a single number.

Various HTA agencies have considered, are piloting or are applying MCDA (NICE, 2012; NICE, 2020; Endrei et al., 2014; Institute for Quality and Efficiency in Health Care [IQWIG], 2015; Youngkong et al., 2012), and as mentioned, in 2016 ISPOR convened the MCDA Emerging Good Practices Task Force "charged with establishing a common definition for MCDA in healthcare decision-making and developing good practice guidelines for conducting MCDA to aid health care decision-making" (Thokala et al., 2016, p. 2; Marsh et al., 2016).

Nevertheless, although MCDA can be well suited to support healthcare decision-making, including HTA, there are still skepticism towards the use of MCDA in healthcare decision-making, and flaws that undermine the usefulness, and further methodologic developments are required if MCDA is to achieve its potential to support HTA (Garau & Devlin, 2017). Furthermore, further research is required to evaluate the effectiveness of MCDA in healthcare decision-making.

8. Value-Based Healthcare

In order to address how to allocate the limited resources within healthcare, a shift in focus from volume of care to value of care, known as value-based healthcare (VBHC), has been suggested. VBHC has gained significant international attention since Porter and Teisberg (2006) introduced the concept in their article, "Redefining Health Care: Creating Value-Based Competition on Results." VBHC makes the delivery of improved health outcomes for the same or at lower costs the primary objective of the healthcare system. In this sense, VBHC is clearly aligned with traditional health economics. Yet, perspectives on value chains and measuring points go beyond most health economic frameworks and open up a range of questions in regard to the interpretation and practical implementation in specific health system contexts (Starr & Vrangbæk, 2021).

In Porter and Teisberg's terminology, it is important to assess the value from a patient standpoint and to evaluate costs and gains in a long-term perspective, including prevention, intervention, and follow-up. This assessment of costs and benefits of the entire treatment trajectory for each individual patient should be supported by an incentive structure where payments are linked to results in terms of value for patients.

A VBHC contract is an innovative payment model in which two parties, typically the healthcare payer and the pharmaceutical company or health service provider, agree to make payments for services depending on performance/value creation (Starr, 2021b). In principle, VBHC contracts reduce the payer's risk of a sub-optimal purchase, facilitate earlier access to new health technologies for patients or consumers because the risk is shared between payer and provider, provide higher value care for the patient since their feedback can be incorporated into the

performance measures, offer more efficient pricing mechanisms, and can serve as a catalyst for generating enhanced real-world medical evidence (Starr & Vrangbæk, 2021).

Despite the obvious potential benefits, the use of VBHC contracts is still limited (Starr & Vrangbæk, 2021). One reason for this is that the design and implementation of value-based contracts are complicated and come with inherent risks for both parties (Starr, 2021a; Starr, 2021b). Agreeing on the terms of a contract can be challenging, especially under conditions of uncertainty and asymmetric information which is common within healthcare. Economic transactions between self-interested economic agents, such as a healthcare provider and a payer, can give rise to conflicts of interest; thus, designing a utility regulation involves tradeoffs (Starr, 2021b).

In this dissertation, I use the three chapters to discuss the use of and issues with value-based healthcare:

- Starr, L., & Vrangbæk, K. (2021) Value-Based Healthcare Classification and Experiences in Denmark, EIT health and University of Copenhagen, ISBN: 978-87-92356-01-7
- Starr, L. (2021a). Assessment of Roche Diabetes Care/Odsherred Municipality Value-Based Healthcare Diabetes Project 2017-2019 – Feasibility and Transferability Lessons, Working Paper, EIT Health and University of Copenhagen
- Starr, L. (2021b). Design of Value-Based Healthcare Contract – Lessons from a Public-Private Pay-for-Performance Healthcare Collaboration, Working Paper, EIT Health Working Paper

From the work, I identified key issues and principles that must be considered when introducing outcomes-based payment models, which will be presented in the sections below.

8.1. Implementation of Value-Based Healthcare

For successful implementation, it is essential to understand the value from a patient perspective and to assess costs and gains using a long-term perspective. Therefore, a pilot study can be used to create a risk-sharing agreement to align the stakeholders' incentives around value created for each stakeholder involved. Suggestions for the steps of the co-creation process are shown and described in Figure 8.

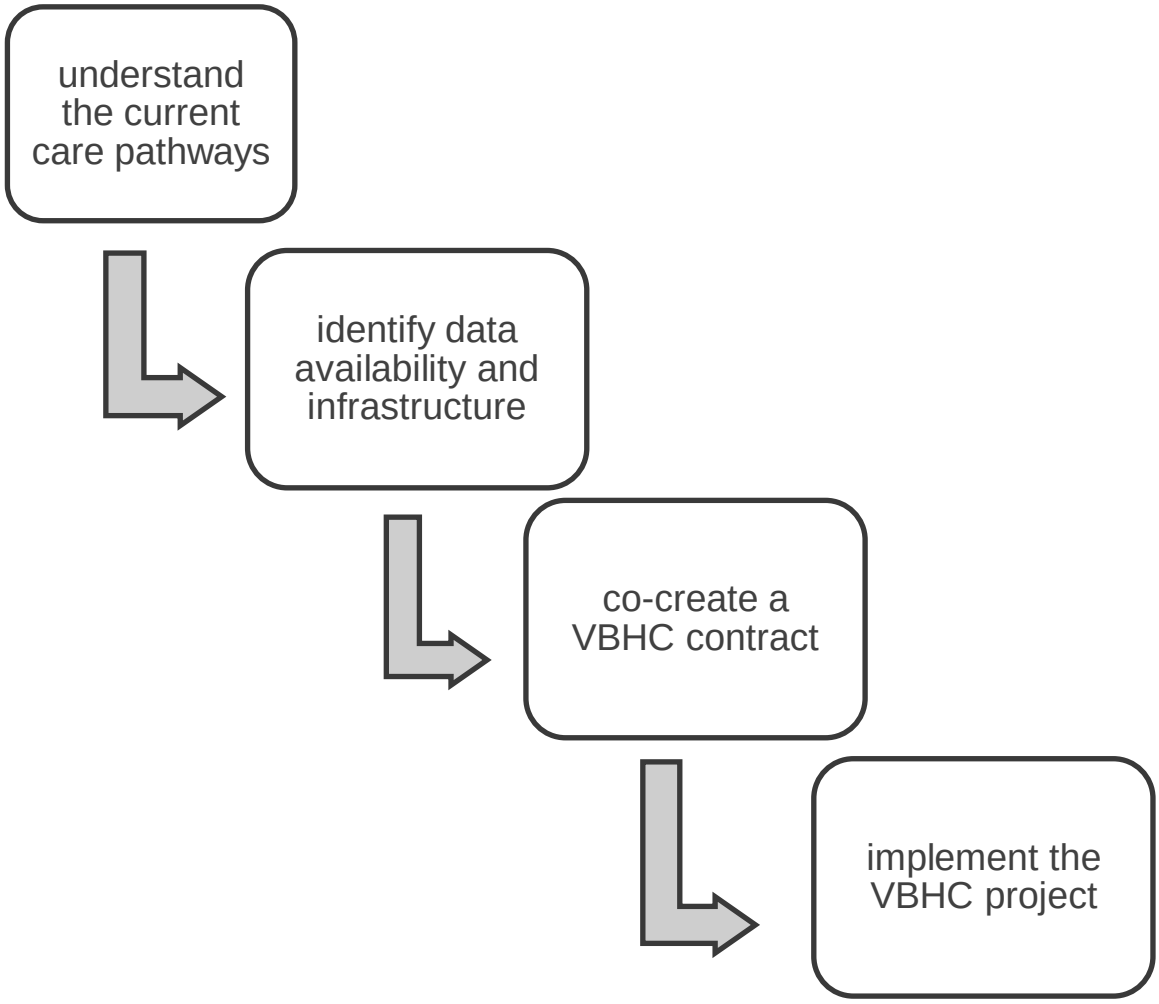


Figure 8. Implementing value-based healthcare in practice

The first step is to perform an analysis of the patient journey. Understanding the patient journey and mapping it with the healthcare professional point of view enables the identification of “pain points” in the local ecosystem and an overview of the challenges that patients and health care professionals (HCPs) face during the cycle of care. The second step is to develop a data-infrastructure and analysis approach. This illustrates a general principle of involving all relevant actors in the co-creation processes of determining goals, measurement points, data, and feasibility. The assessment of costs and benefits of the entire treatment trajectory for each individual patient is to be supported by an incentive structure where

payments are linked to the achievement of results in terms of value for patients (Starr, 2021b). Once the first phases have been finalized, the next step is to identify pain points and enrich them with respective digital solutions to address the latter. Here, it is important to explore the opportunities and potential improvements in the current pathway in the specific organizational context (i.e., Danish Region/municipality) with a focus on value creation for patients and healthcare professionals. The aim is to formulate a hypothesis for the payer to understand his WTP depending on the provider's ability to address the identified "pain points" and provide value that matters to patients and improved clinical outcomes.

8.1.1. Contracting in VBHC

The next step is to co-create the value-based healthcare contract with the payer, healthcare professional, and patients in a collaborative way. Thus, the parties need to agree on the risk-sharing terms within a contract. Designing a contract involves trade-offs among several different goals of contract design: coordinating (ensuring that the products are offered at the right time and place), motivation (ensuring that the contract parties have individual incentives to take socially desirable decisions), and transaction costs (ensuring that coordination and motivation are provided at the lowest possible cost), as outlined in the framework for contract theory outlined by Bogetoft and Olesen (2004) shown in Figure 9.

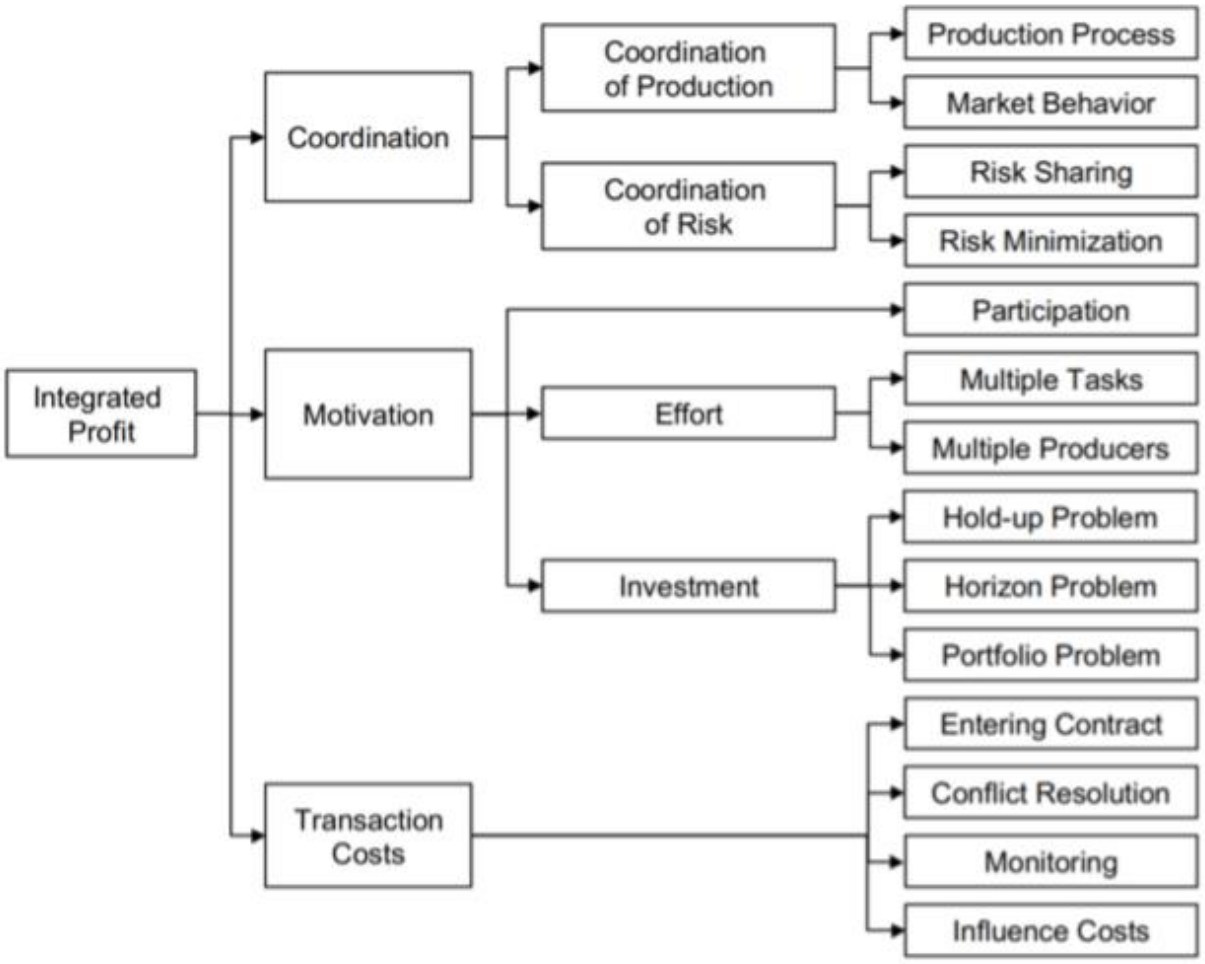


Figure 9. Hierarchy of goals for contract design

Oftentimes, the resulting contracts will include:

a) Physical products such as blood glucose monitoring devices as well as the required test strips and lancets
b) Digital tools
c) Supportive services such as coaching and/or lifestyle support.

This includes trading-off different goals from diverse stakeholders and distributing risks in a fair manner.

8.1.2. VBHC Requirements

The implementation of VBHC requires the availability of detailed patient-level data, ideally a digital infrastructure to support the assessment of costs and outcomes.

The following framework (Table 3) will be considered to characterize the translation and implementation of the pilot and to provide a shared perspective for co-creation of contracts (Starr & Vrangbæk, 2021).

Table 3. Dimensions of Value-Based Healthcare

Dimensions of Value-Based Healthcare	
Scope	Single diagnosis group, including multimorbidity? Population perspective (all citizens in a given area or affiliated with a given organizational entity)
Public/private	Public-private purchasing/contracting or public-public steering mechanism
Patient care trajectory	Single activity, treatment episode or full trajectory from prevention to recovery
Technology	Narrow/single technology, such as a drug or holistic technology and care package
Economic incentives	Strength and design of economic incentives
Performance measure	Activity, output, outcome (health and quality of life, patient reported or clinical, patient experience)
Organizational development perspective	Organizational quality development with or without performance related economic incentives

A key challenge for widespread implementation is that VBHC requires detailed patient-level data and a digital infrastructure to support the assessment of costs and value. The Nordic countries should, in principle, be in a favorable position to deal with this challenge due to a high level of digitalization and extensive health

registries that can be linked to a range of administrative and social data via personal ID numbers. It is therefore not surprising that the idea has been promoted by consultants and policymakers in Denmark and that several VBHC initiatives have been piloted in the Nordic region. The comprehensive data infrastructure and high level of policy interest in VBHC makes the Nordic countries particularly informative cases for studying VBHC implementation. Whereas some academic interest about VBHC in the Nordic region has been demonstrated, most contributions have focused on individual projects, such as the evaluation by McKinsey & Company (2019a) of the Danish Regions' cross-regional VBHC projects (McKinsey & Company, 2019a & 2019b) or general discussions about the phenomenon (Pedersen, 2017).

Common challenges emerging from the reviewed cases include the following:

1) Defining the necessary linkage in payment models across sectors or provider levels
2) Developing measurement systems for tracking health outcomes and costs and building the advanced analytics platform necessary both to feed data to providers and to use it as a basis for value-based payments
3) Creating systems to manage risk, both in terms of patient mix and providers' financial exposure.

Other potential barriers include the following: focusing on price rather than long-term value creation; and the lack of time, resources, and competencies to engage in contracting negotiations, which tend to be highly complicated in regard to determination of performance targets, risk sharing, models, and contractual obligations. Tough risk-sharing demands can create uncertainty and discourage

some private sector suppliers from engaging in the project. Uncertainty about economic gains can be a hindrance for smaller firms with limited financial buffers. Furthermore, health personnel may dislike the increased transparency on their own performance (Starr & Vrangbæk, 2021).

For VBHC to drive change in clinical practice, the payment models must be introduced in an environment of trust among providers and payers. As there are often conflicting interests among the different stakeholders, such as misalignment of incentives for fee-for-service reimbursement models between payers and providers, this can be challenging. To overcome this challenge, it is therefore important to emphasize and reflect that the focus for the incentive is not solely cost containment but also outcome improvement. Providers, on the other hand, should be involved in the design, implementation, and refinement of payment models, including defining outcomes and reviewing performance bonus criteria (Starr & Vrangbæk, 2021).

In an ideal implementation, the scope would be expanded to the full cycle of care across (economic) responsibilities by the regions and municipalities (i.e., diagnostics, surgery, and physical therapy), which would give the providers an incentive to share information, cooperate to redesign care pathways, and provide the highest quality care in the most cost-effective manner. For patients, inconsistent and uncoordinated healthcare is one of the biggest challenges in the healthcare system, and efforts to improve collaboration and integrated care across sectors has been attempted numerous times (Antunes & Moreira, 2011; Sandberg Buch & Petersen, 2012; Sandberg Buch, 2017; Sundhedsstyrelsen, 2011).

Whereas Porter's theory indicates that a healthcare provider must organize and implement the entire process to be responsible for all parts of the process, Denmark has several administrative actors with their own budgets. The multitude of stakeholders responsible for various components of treatment and rehabilitation distorts the incentive structure in value-based governance (Starr & Vrangbæk, 2021). It must pay off for doctors to discourage readmissions and to consider patients' ability to function. Often, components of the VBHC universe that make sense from the operational logic within the current institutional boundaries were used, and the schemes were implemented as limited pilot projects involving specific departments and patient groups. This approach makes sense as a starting point but does not fundamentally change the modus operandi or adhere to the full set of VBHC principles. Thus, value-based management is far from being a fully developed concept for managing the healthcare system in Denmark. To fulfil its promise, it is necessary to consider how clinical staff and patients can be involved and how the models can be developed to include collaboration across regions and sectors.

The identification of challenges and barriers in the Danish and Swedish cases and the experiences from the pilot project collaboration in Denmark led to the summary checklist shown in Table 4 for co-creation and implementation of VBHC projects for chronic care.

Table 4. Critical steps of co-creating value-based healthcare for chronic care

1. Map stakeholders and their interests to identify potential challenges
2. Invite key stakeholders to participate in design and development
3. Use the contracting framework to identify and discuss goals for participating stakeholders
4. Carefully investigate patient pathways and "pain points" in the existing context
5. Use the mapping of patient pathways and "pain points" to identify desired changes for payers and patients
6. Investigate data availability and creation of infrastructure for ongoing data collection to support the value-based contract
7. Use the descriptive framework for VBHC projects as a tool for co-creation of pilot projects with relevant stakeholders
8. Use the contracting framework to clarify and balance goals for participating stakeholders
9. Determine indicators and data infrastructure
10. Consider potential challenges and barriers for implementation in the specific context, and discuss options for overcoming such challenges if/when they arise
11. Implement and assess pilot projects
12. Use the assessment of pilot projects and additional considerations of potential implementation barriers to scale efforts
13. Evaluate and renegotiate at regular intervals, maintain flexibility, and acknowledge that co-creation of VBHC is an evolving process.

8.1.3. EIT Europe Health Project

Mobile health interventions targeting diabetics include, for example, insulin management applications, wearable blood glucose meters, automated text messages, health diaries, and virtual health coaching (The Economist Intelligence

Unit, 2020). In my work for this dissertation, I have collaborated on an EIT European Health project, “Integrated Personalized Diabetes Management Goes Europe: A multi-Disciplinary Approach to Innovating Type 2 Diabetes Care in Europe” (Jones et al., 2020).

The project strives to advance integrated personalized diabetes management (iPDM) adoption by (1) implementing the concept in a VBHC setting for the treatment of persons with T2DM, (2) providing tools to assess the patient’s physical and mental health status, and (3) exploring new avenues to take advantage of emerging big data resources.

In the realization that T2DM is a multi-dimensional challenge, a disease management process that leverages feedback loops and utilizes commodity digital tools was created to improve the standard of care for people living with diabetes in a sustainable way**.** The approach, therefore, leverages therapy-relevant data to inform treatment decisions while facilitating both shared decision-making and patient empowerment, all of which are important components of patient-centric care.

Specifically, the consortium aims to enhance the iPDM process by co-creating a novel digital, smartphone-based patient assessment tool that captures unique health and disease traits of people with T2DM, and therefrom deriving an in-depth understanding of their individual needs, barriers, and circumstances. This allows healthcare providers to strictly adapt a person-centric viewpoint and integrate diverse dimensions of the patients’ individual life situations. In parallel, the consortium strives for a further enhancement of iPDM by developing novel algorithms for early prediction of individual disease traits and chances of treatment success (Huang et al., 2020). Robust health economic modelling will be

an essential component of this endeavor in order to measure the impact iPDM enhancement has on some of the main drivers of diabetes-related costs, including hospitalization and the occurrence of co-morbidities (Kahm et al., 2018). Importantly, the novel tools developed in the iPDM project will be co-created with continuous and iterative input from all relevant stakeholder groups aiming to add real value for persons with T2DM, healthcare professionals, and healthcare providers alike.

One possible way for non-pharmaceutical improvement in diabetes healthcare is through better use of digital health solutions. Digital health solutions can be used across all aspects of health and disease management, and they use information and communication technologies to support and promote health (EU, 2020; WHO, 2019). Despite their potential to improve outcomes in diabetes care, as was particularly evident during the COVID-19 outbreak that disproportionally affected people with diabetes (Alromaihi et al., 2020; Nørgaard, 2020), there remain several barriers still limiting the effective use of digital tools in diabetes care.

Digital health solutions can refer to all technologies involving the collection, exchange, and analysis of information remotely, including managing patient records online through electronic health records (EHRs), decision-support tools for health professionals, wearable devices that transmit data for analysis, virtual consultations between people with diabetes and healthcare professionals, etc. (EU, 2020). Digital health solutions therefore provide an opportunity for better generation, storage, and leverage of data, thus ultimately improving healthcare.

Diabetes management relies greatly on monitoring and is therefore well suited for digital solutions as diabetics are accustomed to regularly collecting data on blood glucose levels, calculating insulin doses, etc. (EPHA, 2017). The ability to record and

analyze these data using digital tools, as well as to provide insulin dosing recommendations and reminders to measure blood glucose and take medication, can empower people with diabetes to manage their condition more effectively, enhance healthcare professionals' input, and potentially improve health as well as increase the convenience of reducing the number of face-to-face appointments.

Digitalization

Digital utilization and access to digital solutions, for example, are heavily dependent on age, socioeconomic status, and the respective healthcare system. Even if access to the respective technology is achieved, long-term engagement and health literacy are among the challenges which are difficult to overcome (Karnoe et al., 2018; Poduval et al., 2018). User-centered design represents a promising approach to address some of these barriers by identifying the users' preferences early on and tailoring solutions accordingly. To be most effective, however, co-creation should involve all relevant target groups, including elderly patients with their unique needs in managing T2DM (Quinn et al., 2015). Furthermore, clinical evidence of sufficient quality is needed to assess the real-world effectiveness of any novel digital solution. Such broader investigations will be required to evaluate the viability of the digital, smartphone-based patient assessment tool beyond the iPDM project phase, preferably in different cultural scenarios. Complementary approaches to assess potential users' health technology readiness and enablement may also help identify the patient segments that will benefit most from a given healthcare intervention such as the one developed in iPDM (Kayser et al., 2019).

There is substantial evidence indicating that digital tools and telemedicine approaches can improve outcomes for patients living with chronic diseases. Hu et al. (2109), for instance, analyzed the impact of telemedicine on hypoglycemia in

diabetes across 14 randomized controlled trials published between 2006 and 2017. While the authors did not observe an effect on patients' body mass index (BMI), they did observe improvements in HbA1c and a reduced occurrence of moderate hypoglycemia.

The WHO (2019), the European Commission (2019), and Danish Health Authorities (Healthcare Denmark, 2018) and other national bodies have recommended the use of digital technology and have launched digital strategies in efforts to promote digital solutions and/or highlight the potential for digital health to facilitate improved healthcare.

In the Danish national diabetes plan, which provides overarching guidance on direction and strategy for all stakeholders involved in diabetes care, Denmark has explicitly included its digital diabetes strategy (Healthcare Denmark, 2018). The Danish engagement is reflective of its strong engagement with digital healthcare more broadly in recent years. Specially for diabetes, many digital health initiatives have been pilot tested. In an internet search I did in May 2021 in an attempt to identify digital diabetes projects in Denmark, I found that 34 digital diabetes initiatives had been launched since 2005. For most of the projects, the aim has been to better the treatment quality and reduce the number of visits to the hospital, with the mean to get there ranging from follow-up on blood glucose, 24/7 guidance for optimal diabetes treatment to digital screening for diabetic retinopathy. Half of the projects has been discontinued after the pilot phase.

To support an effective roll-out of iPDM in Europe, I have explored concepts for value-based business creation in different European healthcare systems, starting in a Danish community setting. In this regard, I believe that a concerted effort by academic, administrative, and industry partners to co-create impactful new

business models holds great potential for changing the way healthcare is delivered and moving from volume to value. These efforts will be informed by economic modelling approaches and an analysis of existing programs and best practices compiled from a policy and operational perspective and supported by multiple international experts in European healthcare (EiT Health, 2020).

9. Conclusion

The allocation of scarce healthcare resources across alternative and, at times, competing health technologies is a complicated and difficult process. Assessing and appraising the value of new and often more expensive medicines and healthcare interventions is a challenge for the healthcare system. The implications of the valuation can be great, and the decisions will affect many directly and indirectly. New methodological approaches which can improve efficiency in resource allocation and, thereby, create better value for the money spent is urgent. For decision-makers, it has therefore become increasingly important to adopt robust processes for priority setting so that limited health resources are allocated effectively, efficiently, and transparently.

When I started this work, I developed an essential guiding research question:

By knowing the stated and revealed preferences of stakeholders within the healthcare system, how can modern benchmarking – where multiple criteria simultaneously are taken into account – be used in pharmaceutical product development and innovative contract design to decide which pharmaceutical product candidates will meet the unmet medical needs of the patients and the budget constraints that payers are subject to and minimize the development risk to manufacturers and payers, in short: When is health innovation worth it?

I have answered this overarching question through an introductory chapter and five self-contained papers.

Pharmaceutical expenditure accounts for a great and growing portion of healthcare expenditure. The clinical uncertainty of new pharmaceuticals in combination with their high costs have therefore led to an evaluation of their

benefits and costs by payers in order to estimate the value, reimbursement, and coverage status, and possible price. This work proposes that evaluation procedures aiming to rank alternative treatment options should be characterized by comprehensiveness and transparency, enabling a more rational decision-making process with acceptable outcomes. In the first article, the modern benchmarking methodology of MCDA was used. MCDA can aid decision-makers in their decision-making process by allowing them to explicitly take multiple criteria into account simultaneously. MCDA can be applied at many different stages of the value chain of a pharmaceutical product, from early identification of new molecules, to market access strategies and optimization of product launches, to gaining a better understanding of the patient's unmet needs and preferences, to priority decisions for payers.

Eventually, the MCDA could enable decision-makers to understand and construct their value perceptions and preferences for the purpose of assessing, ranking, and identifying the best decision alternatives. Applying MCDA earlier in the life cycle of the pharmaceutical product and, thus, making it part of the clinical development could enable the communication of value to decision-makers. Therefore, MCDA could aid in reforming the approval and reimbursement processes by identifying the evidence requirements and support clinicians and patient in their understanding of the benefits and risk of new treatments and thus aid them in their decision-making process.

Within this work, we were able to identify that some of the diabetes products in the GLP-1, SGLT-2, and DPP-4 classes were only marginally efficient. This suggests that they should be in limited demand. Using existing sales data, we next made partial inference about the preferences different patient groups have for the

different pharmaceutical attributes. Using this information, we were able determine how the attributes of a new pharmaceutical product are likely to affect demand for this product. Likewise, we estimated which share of the current users of the existing pharmaceutical products are likely to switch to a product.

In the second article, we likewise aimed at eliciting patient's benefit–risk preference for diabetes treatment and identifying segments with differences in preference for treatment based on their socioeconomic position and individual health indicators as well as determining how national recommendations for pharmacologically glucose-lowering treatment compare with Danish diabetes patients' stated preferences for treatment. We found that different groups of insulin users may be stratified by their preference for diabetes treatment, and that these groups reflect the priorities for treatment set nationally. In general, T2DM patients with a strong preference for avoiding hypoglycemic events are prescribed treatment corresponding to their stated preferences. The significance of this study can be assessed via the comprehensive empirical data structure underpinning the analysis. The unique combination of self-reported and health registry data enabled the evaluation of segments with possible differences in preference for the benefit and risk characteristics of treatment. The results of this study should assist health organizations in deciding if the same treatment fits all or if segments of the T2DM population benefit more from particular characteristics of treatment than others. Furthermore, it is one of few experiments eliciting preference for treatments modifying cardiovascular (CV) risk in diabetes, and so the potential for use in benefit–risk assessment is significant. This paper will inform such decisions by providing quantitative preference evidence for the trade-offs made between side effects and treatment efficacy by insulin users.

The rewarding mechanism for innovative pharmaceuticals has to consider the current value to patients while also encouraging future societal gains with the emergence of value-based healthcare being suggested as a way to improving patient's access while ensuring that prices reflect value to a variety of stakeholders. Thus, there are still unexplored opportunities for a better incorporation of patient preferences within healthcare, such as in the regulatory approval, pharmaceutical product development, and treatment. Today, despite patient representatives being present in the regulatory processes, and that pharmaceutical developers use patient inputs in their product development, and more value-focused reimbursement options are being tested, there is still much to explore, methods to develop, and strategies to facilitate in the use of patient preferences as evidence in stakeholder engagement, insight generation, and patient involvement.

In order to ensure fast access to new possibly valuable health technologies, obtain best value for money, and ensure affordability, payers within healthcare systems have started to adopt new innovative reimbursement approaches, such as VBHC. The effort to move towards VBHC should be seen in the context of a decade of experience with introduction of performance measurement systems in which the reimbursement is linked to activities, that is, a traditional fee-for-service or capitated approach. However, the traditional type of reimbursement has not provided much information or attention to the quality of service or the outcomes of treatment and care, which the VBHC seeks to do. In this paper, I have provided theoretical adaptions and empirical studies to lay the groundwork for further implementation of value-based healthcare by carrying out a comprehensive review of value-based healthcare and offering a reflection on the feasibility of further developing this innovative reimbursement model.

Despite a push for VBHC and suitable infrastructure such as good national health registers, the VBHC concept is not used extensively within the Danish and Swedish healthcare systems. The high degree of definitional inconsistency and the lack of comprehensive evaluations make it difficult to compare VBHC payment models and draw conclusions about their relative efficacy. There is a significant potential for increasing patient value of the health services offered and to develop the private/public collaboration in Denmark; however, the experiences involving this show that design and implementation require significant and ongoing efforts. In the identified examples, oftentimes, the projects involved only specific departments and patient groups, and while this approach makes sense as a starting point, it does not fundamentally change the modus operandi, or indeed, adhere to the full set of VBHC principles.

Another key input to the design of implementation contracts is a theoretically informed report that builds on recent developments in contracting theory to provide lessons for designing contracts that specify risk-sharing options to create value for all stakeholders involved. This document seeks to identify a set of key issues and principles – for example, goals, contract design, and outcome measures – that must be considered when introducing outcome-based payment models in Danish municipalities and/or regions.

Designing a value-based healthcare contract involves trading off different goals of contract design while aiming at explicitly incorporating different stakeholders' engagement. It became clear that there is a complex set of principal-agent problems within healthcare which might give rise to conflicts of interest and problems of control. It is essential that the findings of the principal-agent theory and the solution options are implemented in practice, so that the existing

information asymmetries can be reduced and the objectives of the parties harmonized.

In line with this, motivation issues will arise among the involved parties as contract theory assumes that people act opportunistically, that is, individuals are depicted as selfish and are presumed to exploit the situation for their own benefit and, thus, will only act in self-interest. Likewise, coordination challenges are likely to be present when seeking an alignment between the patient preferences and the providers' deliverables and other stakeholders' interests. Transaction costs will arise during the course of negotiation and implementation of contracts. In order to limit monopolistic situations, I recommend that individual contracts should be completed in a competitive procurement process, in which only potentially relevant providers are invited to tender.

Thus, despite VBHC being intrinsically appealing, a number of major barriers were identified for implementing this at a larger scale including: 1) the associated transaction and administration resources, time, and commitment, or some combination thereof are constrained as they are in many municipalities, 2) challenges in tracking performance and combining the data from different sources, 3) developing and agreeing on the contract, 4) involving and motivating all stakeholders, for example, general practitioners, and collaboration across regions and sectors, and 5) ensuring trust among the different stakeholders aided by the design of the contract.

After realizing how the financing of VBHC was poorly integrated in the VBHC pilots identified, I have, post this dissertation, started working on creating a framework for a description of different financing models that support multi-payer value-

based management, taking the theoretical and empirical knowledge of the advantages and disadvantages of different financing models in to account, and also focusing on the challenges that are sought to be solved within different treatment areas and types.

I am also attempting to apply the theory of contract design within VBHC in a multi-payer contract involving the innovative research project PreCare, whose purpose is to develop and test preventive and integrated services for chronically ill and elderly with both a Region, a municipality and possibly an external private company as partners.

In conclusion, health innovation denotes new, better, or more effective ways of solving healthcare problems by improving policies, systems, or products that provide solutions to existing healthcare problems. A health innovation provides a benefit to the field with patients at the center, but also other stakeholders of the healthcare systems' needs and demands can be addressed. Thus, health innovation is worth it when it improves our ability to meet the unmet healthcare needs and demands by optimizing the performance of the healthcare system. By identifying the preferences of the stakeholders, we will be better able to conceptualize what is needed in the field to increase efficiency and effectiveness in healthcare and, hence, bring more value.

9.1. Epilogue

The first part of this project was carried out with financial support from the Innovation Fund Denmark and the pharmaceutical company Novo Nordisk A/S. Working in the space between academia and the private sector has at times been challenging. While, to me, in theory, it sounded like a great opportunity to engage in relevant and applicable research, in real life, it was somewhat of a disconcerting position: being placed in between the open nature of in-depth academic science and the company's need to protect "confidential" or "market sensitive information,". Further, the company's many reorganizations and a general lack of management support was not ideal.

Despite the obvious confidential nature of some of the information gathered from a pharmaceutical company, which I completely understand and respect, there still needs to be a more externally aware attitude for these industrial–academic collaborations to be beneficial. To get more out of these collaborations, the diverse perspectives on how to do business should, to a greater extent, be used to inspire, and there should be a more open and welcoming approach as to new possibilities and how they can be explored, instead of perceiving anything new as a threat. A calculated risk taking is required, where the degree of disclosure needs to be evaluated for these kinds of industrial–academic collaborations to be worthwhile and more than just an academic exercise – or the company should not enter these types of academic collaborations in the first place.

Despite this, being placed at the headquarters of a large pharmaceutical company helped me gain a solid knowledge and understanding of health and pharmaco-economics, expanded my insight into the market access challenges and strategies,

identified key stakeholders and their influence on the life cycle of a pharmaceutical product, and provided an understanding of different stakeholders' perspectives and the benefits and challenges of how these can be incorporated in the pharmaceutical product development. It is my perception that this paper's combination of reviewing the literature, conducting semi-structured interviews, consulting experts, attempting to conceptualize and approach the challenges with critical thinking, and exploring the feasibility of new reimbursement models which are impacting market access has contributed conceptual, theoretical, methodological, and empirical insights into the area of health economics and market access within healthcare.

10. References

Alromaihi, D., Alamuddin, N., & George, S. (2020). Sustainable diabetes care services during COVID-19 pandemic. *Diabetes Research and Clinical Practice, 166*, 108298.

American Diabetes Association. (2009). Diagnosis and classification of diabetes mellitus. *Diabetes Care*, S62–S67.

American Diabetes Association. (2020). 6. Glycemic Targets: Standards of Medical Care in Diabetes—2020. *Diabetes Care*, 66–76.

Angelis, A. (2018). Evaluating the benefits of new drugs in health technology assessment using multiple criteria decision analysis: A case study on metastatic prostate cancer with the dental and pharmaceuticals benefits agency (TLV) in Sweden. Medical Decision Making: Policy and Practice, 3 (2), 1-17.

Angelis, A., Kanavos, P., Montibeller, G. (2017). REssource Allocation and Priority Setting in Health Care: A Multi-criteria Decision Analysis Problem of Value? Global Policy, *8*(S2), 76-83

Angelis, A., Lange, A., & Kanavos, P. (2018). Using health technology assessment to assess the value of new medicines: Results of a systematic review and expert consultation across eight European countries. *European Journal of Health Economics, 19*(1), 123–152.

Antunes, V., & Moreira, J. P. (2011). Approaches to developing integrated care in Europe: A systematic literature review. *Journal of Management & Marketing in Healthcare, 4*(2), 129–135.

Baltussen, R., & Niessen, L. (2006). Priority setting of health interventions: The need for multi-criteria decision analysis. *Cost Effectiveness and Resource Allocation, 4*(1), 14.

Baltussen, R. M. P. M., Ten Asbroek, A. H. A., Koolman, X., Shrestha, N., Bhattarai, P., & Niessen, L. W. (2007). Priority setting using multiple criteria: Should a lung health programme be implemented in Nepal? *Health Policy and Planning, 22*(3).

Barlow, J. (2017). Managing innovation in healthcare" World Scientific, Chapter 4

Barnett, T. (1998). The insulin treatment of diabetes: A practical guide. In T. Barnett (Ed.), *Epidemiology, complications and costs of diabetes mellitus* (pp. 6–9). EMAP Healthcare.

Bateman, I. J., Carson, R. T., Day, B., Hanemann, M., Hanley, N., Hett, T., Jones-Lee, M., Loomes, G., Mourato, S., Özdemirog¯lu, E., Pearce, D. W., Sugden, R., & Swanson, J. (2002). *Economic valuation with stated preference techniques: A manual.* Edward Elgar Publishing Ltd.

Belton, V., & Stewart, T. (2002). *Multiple criteria decision analysis: An integrated approach.* Kluwer Academic Publishers.

Bertoni, A. G., Krop, J. S., Anderson, G. F., Brancati F. L. (2002). Diabetes-related mobidity and mortality in a national sample of U.S. elders. *Diabetes Care, 25*(3), 471–475.

Bogelund, M., Vilsbøll, T., Faber, J., Henriksen, J. E., Gjesing, R. P., & Lammert, M. (2011). Patient preferences for diabetes management among people with

type 2 diabetes in Denmark - A discrete choice experiment. *Current Medical Research and Opinion, 27*(11), 2175–2183.

Bogetoft, P., & Olesen H. B. (2004). *Design of production contracts.* Copenhagen Business School Press.

Bogetoft, P., & Otto, L. (2011). *Benchmarking with DEA, SA and R.* International Series in Operations Research & Management Science. Springer Science & Business Media.

Bogetoft, P., & Pruzan, P. (1997). *Planning with multiple criteria: Investigation, communication and choice* (2nd ed.). Copenhagen Business School Press.

Bogetoft, P., & Starr, L. (2021). Benchmarking and predicting the demand for new diabetes drug. Submitted.

Bolloju, M. (2001). Aggregation of analytic hierarchy process models based on similarities in decision-makers' preferences. Eur J Operational Res. 128(3), 499-508

Bridges, J. F., Hauber, A. B., Marshall, D., Lloyd, A., Prosser, L. A., Regier, D. A., Johnson, F. R., & Mauskopf, J. (2011). Conjoint analysis applications in health—a checklist: A report of the ISPOR Good Research Practices for Conjoint Analysis Task Force. *Value in Health, 14*, 403–13.

Briggs, A. H. (2011). The use of probabilistic decision models in technology assessment: The case of total hip replacement. *Applied Health Economics and Health Policy, 3*, 79–89.

Briggs, A. H., Weinstein, M. C., Fenwick, E. A., Karnon, J., Sculpher, M. J., Paltiel, A. D. (2012). Model parameter estimation and uncertainty: A report of the

ISPOR-SMDM Modeling Good Research Practice Task Force-6. *Value in Health, 15*(6), 835–842.

Broekhuizen, H., Groothuis-Oudshoorn, C. G., van Til, J. A., Hummel, J. M., & IJzerman, M. J. (2015). A review and classification of approaches for dealing with uncertainty in multi-crieria decision analysis for health care decisions. *Pharmacoeconomics, 33*(5), 445–455. A conceptual framework and review of the literature. *Epidemiologic Reviews, 26*(1), 6377.

Bryan, S., Roberts, T., Heginbotham, C., & McCallum, A. (2002). QALY-maximisation and public preferences: Results from a general population survey. *Health Economics, 11*(8), 679–693.

Calltorp, J. (1999). Priority setting in health policy in Sweden and a comparison with Norway. *Health Policy, 50*, 1–22.

Carstensen, B., Rønn, P. F., & Jørgensen, M. E. (2020). Prevalence, incidence and mortality of type 1 and type 2 diabetes in Denmark 1996-2016. *BMJ Open Diabetes Research & Care*, *8*(1), e001071.

Castro, H., Tringali, M., Cleemput, I., Devriese, S., Leoni, O., & Lettieri, E. (2017). Advancing MCDA and HTA into civerage decision-making. In K. Marsh, M. Goetghebeur, P. Thokala, & R. Baltussen (Eds.), *Multi-criteria decision analysis to support healthcare decisions.* Springer International Publishing .

Chapman, G. B., & Sonnenberg, F. A. (2003). *Decision making in health care: Theory, psychology, and applications (Cambridge Series on Judgment and Decision Making).* Cambridge University Press.

Cohen, D. (2017). Cancer drugs: High price, uncertain value. *BMJ,* 359.

Cooper, W. W., Seiford, L. M., Zhu, J., eds. (2001). Handbook on Data Envelopment Analysis. International Series in Operations Research & Management Science (2 ed.). Springer US. ISBN 978-1-4419-6150-1

Cooper, W. W., Seiford L. M., Tone, K. (2007). Data Envelopment Analysis: a Comparative Text with Models. Applications, references and DEA-Solver Software. 2nd ed. Springer US. ISBN 978-0-387-45281-4.

Cooper, W. W., Seiford L. M., Zhu, J. (2007). Data Envelopment Analysis: History, Models, and Interpretations, Chapter 1. DOI:10.1007/978-1-4419-6151-8_1

Crawshaw, R., Garland, M., Hines, B., & Anderson, B. (1990). Developing principles for prudent health care allocation. The continuing Oregon experiment. *Western Journal of Medicine, 152*(4), 441.

Currie, C. J., Gale, E. A., & Poole, C. D. (2010). Estimation of primary care treatment costs and treatment efficacy for people with Type 1 and Type 2 diabetes in the United Kingdom from 1997 to 2007. *Diabetic Medicine: A Journal of the British Diabetic Association, 27*, 938–948.

Daft, R. L. (1998). *Essentials of organization theory and design.* South Western Educational Publishing.

De Monaco, H. , Oliveira, P., Torrance, A., von Hippel, C., von Hippel, E. (2019). When Patients Become Innovators", Sloan Management Review, 60 (3):81-88

Daniels, N. (1999). Decisions about access to health care and accountability for reasonableness. *Journal of Urban Health,* (76), 176–191.

Davies, M. J., D'Alessio, D. A., Fradkin, J., Kernan, W. N., Mathieu, C., Mingrone, G., Rossing, P., Tsapas, A., Wexler, D. J., & Buse, J. B. (2018). Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia, 61*(1), 2461–2498.

Detsky, A. S. (2007). Relevance of cost-effectiveness analysis to clinicians and policy makers. *JAMA, 298*(2), 221–224.

Devlin, N., & Parkin, D. (2004). Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. *Health Economics, 13*(5), 437–452.

Devlin, N., & Sussex, J. (2011). *Incorporating multiple criteria in HTA: Methods and processes.* London: Office of Health Economics.

Diaby, V., & Goeree, R. (2014). How to use multi-criteria decision analysis methods for reimbursement decision-making in healthcare: A step-by-step guide. *Expert Review of Pharmacoeconomics & Outcomes Research, 14*(1), 81–99.

Dolan, P. (1998). The measurement of individual utility and social welfare. *Journal of Health Economics, 17*, 39–52.

Dolan, J. (2008). Shared decision-making - Transferring research into practice: The analytic hierachy process (AHP). *Patient Education and Counseling*, 73 (3), 418-425

Dolan, P., Shaw, R., Tsuchiya, A., & Williams, A. (2005). QALY maximisation and people's preferences: A methodological review of the literature. *Health Economics, 14*(2), 197–208.

Dreyer, N. A. (2018). Advancing a framework for regulatory use of real-world evidence: When real is reliable. *Therapeutic Innovation & Regulatory Science, 52*(3), 362–368.

Drucker, P. (1992). Managing for the Future: The 1990s and Beyond, Butterworth Heinemann, Oxford

Drummond, M., Tarricone, R., & Torbica, A. (2013). Assessing the added value of health technologies: Reconciling different perspectives. *Value in Health, 16*, 7–13.

Drummond, M. F., Sculpher, M. J., Claxton, K., Stoddart, G. L., & Torrance, G. W. (2015). *Methods for the economic evaluation of health care programmes* (4th Edition). Oxford University Press.

EiT Health. (2020). *Implementing value-based health care in Europe: Handbook for pioneers (Director: Gregory Katz).* EiT Health.

Endrei, D., Molics, B., & Agoston, I. (2014). Multicriteria decision analysis in the reimbursement of new medical technologies: Real-world experiences from Hungary. *Value in Health, 17*, 487–489.

EPHA. (2017). *Digital solutions for health and disease management: Digital health discussion paper*. European Public Health Alliance.

EU. (2020). *eHealth: Digital health and care*. (B. E. Commission, Producer). https://ec.europa.eu/health/ehealth/overview_en

European Comission. (2018). *Assessing pricing*. http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/pricing_assessing_en.pdf

European Commission. (2019). *Defining value in "value-based healthcare" - Opinion by the expert panel on effective ways of investing in health.* https://ec.europa.eu/health/sites/health/files/expert_panel/docs/024_defining-value-vbhc_en.pdf

European Medicines Agency. (2010). *Benefit-risk methodology project Work package 2 report: Applicability of current tools and processes for regulatory benefit-risk assessment.* EMA.

European Medicines Agency. (2012). *Guideline on clinical investigation of medicinal products in the treatment or prevention of diabetes mellitus.* EMA.

Flynn, T. N., Louviere, J. J., Peters, T. J., & Coast, J. (2007). Best–worst scaling: What it can do for health care research and how to do it. *Journal of Health Econonomics, 26*(1), 171–189.

Fogarty, M. (1996). *A history of value theory*. https://www.tcd.ie/Economics/assets/pdf/SER/1996/Martin_Fogarty.html

Fonseca, V.A., Kulkarni, K. D. (2008). Management of type 2 diabetes: Oral agents, insulin, and injecatables. *Journal of American Dietetic Association, 108*(4), S29–S33.

Garau, M., & Devlin, N. J. (2017). Using MCDA as a decision aid in health technology appraisal for coverage decisions: Opportunities, challenges and

unresolved questions. In K. Marsh, M. Goetghebeur, P. Thokala, & R. Baltussen (Eds.), *Multi-criteria decision analysis to support healthcare decisions.* Springer International Publishing.

Garrison, L. P., Neumann, P. J., Erickson, P., Marshall, D., & Mullins, C. D. (2007). Using real-world data for coverage and payment decisions: The ISPOR Real-World Data Task Force Report. *Value in Health, 10*(5), 326–335.

Glaize, A., Duenas, A., Mrtinelly, C.D., Fagnot, I. (2019). Healthcare decision-making applications using multicriteria decision analysis: A scoping review. *Journal of Multi-Criteria Decision Analysis*, *26*(1-2), 62-83.

Ham, C. (1997). Priority setting in health care: Learning from international experience. *Health Policy, 42*(1), 49–66.

Hansen, P. & Devlin, N. (2019). Multi-Criteria Decision Analysis (MCDA) in Healthcare Decision-Making, *Oxford Research Encyclopedias,* https://doi.org/10.1093/acrefore/9780190625979.013.98

Hansen, P., Hendry, A., Naden, R., Ombler, F., & Stewart, R. (2012). A new process for creating points systems for prioritising patients for elective health services. *Clinical Governance: An International Journal*, *17*(3), 200–209

Healthcare Denmark. (2018). *Denmark - a telehealth nation*. https://www.healthcaredenmark.dk/media/r2rptq5a/telehealth-v1.pdf

Ho, M., Gonzalez, J. M., Lerner, H. P., Neuland, C. Y., Whang, J. M., McMurry-Heath, M., Hauber, A. B., & Irony, T. (2015). Incorporating patient-

preference evidence into regulatory decision making. *Surgical Endoscopy, 29*(10), 2984–2993.

Houthakker, H. S. (1950). Revealed preference and the utility function. *Economica, 17*(66), 159–174.

Howard, R. (1966). *Decision analysis: Applied decision theory.* Stanford Research Institute.

Hu, Y., Wen, X., Wang, F., Yang, D., Liu, S., Li, P., & Xu, J. (2019). Effect of telemedicine intervention on hypoglycaemia in diabetes patients: A systematic review and meta-analysis of randomised controlled trials. *Journal of Telemedicine and Telecare, 25*, 402–413.

Huang, J., Huth, C., Covic, M., Troll, M., Adam, J., Zukunft, S., Prehn, C., Wang, L., Nano, J., Scheerer, M. F., Neschen, S., Kastenmüller, G., Suhre, K., Laxy, M., Schliess, F., Gieger, C., Adamski, J., de Angelis, M. H., Peters, A., & Wang-Sattler, R. (2020). Machine learning approaches revealed metabolic signatures of incident chronic kidney disease in persons with pre-and type 2 diabetes. *Diabetes*, *69*(12), 2756–2765.

Hurst, L., Mahtani, K., Pluddemann, A., Lewis, S., Harvey, K., Briggs, A., Boylan A. M., Bajwa, R., Haire. K., Entwistle, A., Handa, A., & Heneghan, C. (2019). *Defining value-based healthcare in the NHS.* CEBM.

Husereau, D. B., Boucher, M., & Noorani, H. (2010). Priority setting for health technology assessment at CADTH. *International Journal of Technology Assessment in Health Care, 26*(3), 341.

IDF. (2013). *IDF Diabetes Atlas 6th Edition.* IDF.

Iglay, K., Cartier, S. E., Rosen, V. M., Zarotsky, V., Rajpathak, S. N., Radican, L., & Tunceli, K. (2015). Meta-analysis of studies examining medication adherence, persistence, and discontinuation of oral antihyperglycemic agents in type 2 diabetes. *Current Medical Research and Opinion, 31*(7), 1283–1296.

Institute for Quality and Efficiency in Health Care. (2015). *General methods.* IQWIG.

Inzucchi, S. E., Bergenstal, R. M., Buse J. B., Diamant M., Ferrannini e., Nauck, M., Peters A.L., Tsapas A., Wender, r., Matthews D.R., American Diabetes Association (ADA), European Association for the Study of Diabetes (EASD). Management of hyperglycemia in type 2 diabetes: A patient-centered approach: Position statement of the American Diabetes Association (ADA) and the European Association for the Study of diabetes (EASD). *Diabetes Care, 35*, 1364–1379.

Johnson, F. R., Lancsar, E., Marshall, D., Kilambi, V., Mühlbacher, A., Regier, D. A., Bresnahan. B. W., Kanninen, B., & Bridges, J. F. (2013). Constructing experimental designs for discrete-choice experiments: Report of the ISPOR Conjoint Analysis Experimental Design Good Research Practices Task Force. *Value in Health, 16*, 3–13.

Johnson, S., Naden, R., Fransen, J., Van Den Hoogen, F., Pope, J., Baron, M., . . . Gabrielli, A. (2014). Multicriteria decision analysis methods with 1000Minds for developing systemic sclerosis classification criteria. *Journal of Clinical Epidemiology*, *67*(6), 706–714.

Johnson, F. R., & Zhou, M. (2016). Patient preferences in regulatory benefit-risk assessments: A US perspective. *Value in Health, 19*(6), 741–745.

Jones, A., Bardram, J. E., Bækgaard, P., Cramer-Petersen, C. L., Skinner, T., Vrangbæk, K., Starr, L., Nørgaard, K., Lind, N., Christensen, M. B., Glümer, C., Wang-Sattler, R., Laxy, M. Brander, E. Heinemann, L., Heise, T., Schliess, F., Ladewig, K., & Kownatka, D. (2020). Integrated personalized diabetes management goes Europe: A multi-disciplinary approach to innovating type 2 diabetes care in Europe. *Primary Care Diabetes*, 1751.

Kahm, K., Laxy, M., Schneider, U., Rogowski, W. H., Lhachimi, S. K., & Holle, R. (2018). Health care costs associated with incident complications in patients with type 2 diabetes in Germany. *Diabetes Care, 41*(5), 971–978.

Kanavos, P., & Angelis, A. (2013). *Multiple criteria decision analysis for value based assessment of new medical technologies: A conceptual framework.* LSE Health.

Karnoe, A., Furstrand, D., Christensen, K. B., Norgaard, O., & Kayser, L. (2018). Assessing competencies needed to engage with digital health services: Development of the ehealth literacy assessment toolkit. *Journal of Medical Internet Research, 20*(5), e178.

Kayser, L., Rossen, S., Karnoe, A., Elsworth, G., Vibe-Petersen, J., Christensen, J. F., Ried-Larsen, M., & Osborne, R. H. (2019). Development of the Multidimensional Readiness and Enablement Index for Health Technology (READHY) Tool to measure individuals' health technology readiness: Initial testing in a cancer rehabilitation setting. *Journal of Medical Internet Research, 21*(2), e10377.

Keeney, R. L., & Raiffa, H. (1976). *Decisions with multiple objectives: Performances and value trade-offs.* John Wiley & Sons, Inc.

Khunti, K., & Davies, M. J. (2018). Clinical inertia versus overtreatment in glycaemic management. *The Lancet Diabetes & Endocrinology*, *6*(4), 266–268.

Khunti, K., Gomes, M. B., Pocock, S., Shestakova, M. V., Pintat, S., Fenici, P., Hammar, N., & Medina, J. (2018). Therapeutic inertia in the treatment of hyperglycaemia in patients with type 2 diabetes: A systematic review. *Diabetes Obesity and Metabolism, 20*(2), 427–437.

Khunti, K., Wolden, M. L., Wolden, M. L., Thorsted, B. L., Andersen, M., & Davies, M. J. (2013). Clinical inertia in people with type 2 diabetes: A retrospective cohort study of more than 80,000 people. *Diabetes Care, 36*(11), 3411–3417.

Kimble, L., & Massoud, M. R. (2017). What we mean by innovation in health care? *European Medical Journal, 1*(1), 89–91.

Köksalan, M., Wallenius, J., & Zionts, S. (2013). An early history of multiple criteria decision making. *Journal of Multi-Crieria Decision Analysis, 20*(1–2), 87–94.

Kuhfeld, W. F. (2005). *Marketing research methods in SAS: Experimental design, choice conjoint and graphical techniques.* SAS Institute.

Länsisalmi, H., Kivimäki, M., Aalto, P., & Ruoranen, R. (2006). Innovation in healthcare: A systematic review of recent research. *Nursing Science Quarterly 19*(1), 66–72.

Lemelson-MIT program (2004). Invention - Enhancing inventiveness for quality of life, competitiveness and sustainability. report of the Committee for Study of Invention, MIT Press.

Liberatore, M. J., & Nydick, R. L. (2006). The analytic hierarchy process in medical and health care decision-making: A literature review. *European Journal of Operational Research, 189*(1), 194–207.

Linley, W. G., & Hughes, D. A. (2013). Societal views on NICE, cancer drugs fund and value-based pricing criteria for prioritising medicines: A cross-sectoral survey of 4118 adults in Great Britain. *Health Economics, 22*, 948–964.

Logan, R., Fougere, G., Hague, K., Haretuku, R., Holloway, L., Moore, A., Page-Carruth, A., Pearce, N., Stewart, L., Sullivan, L., Talemaitoga, A., Tepania-Palmer, G., & The National Advisory Committee on Health and Disability in New Zealand (2004). *Prioritising health services. A background paper for the National Health Committee.* https://www.moh.govt.nz/notebook/nbbooks.nsf/0/386E76C777C9733CCC2579E3006D761F/$file/prioritisation-backgroundpapers.pdf

Louviere, J. J., & Timmermans, H. (1990). Stated preference and choice models applied to recreation research: A review. *Leisure Science, 12*(1), 9–32.

Lægemiddelstyrelsen. (2016). *Marketing authorisation for a medicine*. https://laegemiddelstyrelsen.dk/en/licensing/licensing-of-medicines/marketing-authorisation/#

Lægemiddelstyrelsen. (2017). *Lægemiddelstyrelsen*. https://laegemiddelstyrelsen.dk/en/

MacLeod, T. E., Harris, A. H., & Mahal, A. (2016). Stated and revealed preferences for funding new high-cost cancer drugs: A critical review of the evidence from patients, the public and payers. *Patient, 9*(3), 201–222.

Makady, A., & Van Veelen, A., De Boer, A., Hillege, H., Klungel, O. H., & Goettsch, W. (2019). Implementing managed entry agreements in practice: The Dutch reality check. *Health Policy, 123*(3), 267–274.

Marsh, K., Jzerman, M., Thokala, P., Baltussen, R., Boysen, M., Kaló, Z., Lönngren, T., Mussen, F., Peacock, S., Watkins, J., & Devlin, N. (2016). Multiple criteria decision analysis for health care decision making–emerging good practices: Report 2 of the ISPOR MCDA Emerging Good Practices Task Force. *Value in Health, 19*(2), 125–137.

Marsh K., Lanitis, T., Neasham, D., Orfanos, P., & Caro, J. (2014). Assessing the value of healthcare interventions using multi-criteria decision analysis: A review of the literature. *Pharmacoeconomics, 32*(4), 345–365.

Mashitisho, M. L. I., & Mashitisho, B. G. (2016). Early insulin therapy in patients with type 2 diabetes mellitus. *Journal of Endocrinology, Metabolism and Diabetes in South Africa*, 2(1), 50–54.

McGovern, A., Tippu, A., Tippu, Z., Hinton, W., Munro, N., Whyte, M., & de Lusignan, S. (2018). Comparison of medication adherence and persistence in type 2 diabetes: A systematic review and meta-analysis. *Diabetes, Obesity & Metabolism, 20*(4), 1040–1043.

McKinsey & Company. (2019a). *20190114 Det tværregionale projekt om værdibaseret sundhed.* https://www.regioner.dk/media/11405/20190114-det-tvaerregionale-projekt-om-vaerdibaseret-sundhed-pdf.pdf

McKinsey&Company. (2019b). *Bilag C- Oversigt over delprojekter.* [Appendix C - Overview of sub-projects] https://www.regioner.dk/media/11349/bilag-c-oversigt-over-hvert-delprojekt.pdf

Medicinrådet. (2021). *The Danish Medicines Council methods for assessing new pharmaceuticals*.

Medicinrådet. (2020). *QALY*. https://medicinraadet.dk/om-os/medicinradets-arbejde/qaly

Morgan, S., Lopert, R., & Greyson, D. (2008). Toward a definition of pharmaceutical innovation. *Open Medicine, 2*(1), e4–e7.

Moshkovich, H. M., Mechitov, A. I., & Olson, D. L. (2002, Mar). Ordinal judgments in multiattribute decision analysis. *European Journal of Operational Research, 137*(3), 625–641.

Muhlbacher, A. C., & Juhnke, C. (2013). Patient preferences versus physicians' judgement: Does it make a difference in healthcare decision making? *Applied Health Economics and Health Policy, 11*(3), 163–180.

Mussen, F. S. (2007). A quantitative approach to benefit-risk assessment of medicines - part 1: The development of a new model using multi-criteria decision analysis. *Pharmacoepidemiol Drug Safety*, 2–15.

National Institute for Health and Clinical Excellence (NICE). (2020). Briefing Paper for methods review workshop on structured decision making.

https://nicedsu.org.uk, pp274-354 in the collated document relating to the NICE Methods Review.

National Institute for Health and Clinical Excellence (NICE). (2020). CHTE methods review. Decision Making. Task and Finish Group Report.

Neumann, P., Wilke, R., & Garrison, L. (2018). A health economics approach to US value assessment frameworks - Introduction: an ISPOR Special Task Force Report. *Value in Health,* 21(2), 119-123

Nord, E., Daniels, N., & Kamlet, M. (2009). QALYs: Some challenges. *Value in Health, 12,* S10–S15.

Nørgaard, K. (2020). Telemedicine consultations and diabetes technology during COVID-19. *Journal of Diabetes Science and Technology, 14*, 767–768.

Norman, R., Chalkidou, C., & Culyer, A.J. (2018). A health economics approach to US value frameworks: Serving the needs of decision making. *Value in Health,* 21(2), 117-118.

Novo Nordisk. (2018). *The founders*. https://www.novonordisk.ca/about-novo-nordisk/novo-nordisk-history/the-founders.html

Oliveira, P., Zejnilovic, L., Canhão, H., von Hippel, E. (2015). Innovation by patients with rare diseases and chronic needs. *Orphanet Journal of Rare Diseases*, 10(1):41

Organization for Economic Co-operation and Development (OECD) (2017). *Health at a Glance 2017 - OECD Indicators*. OECD. https://doi.org/10.1787/health_glance-2017-68-en

Pedersen, K. M. (2017). *Værdibaseret styring. Er det smitsomt?* [Value-based management. Is it contagious?]. Odense, Denmark: COHERE discussion paper, no. 3.

Phillips, L., & Bana e Costa, C. A. (2007). Transparent prioritisation, budgeting and resource allocation with multi-criteria decision analysis and decision conferencing. *Annals of Operations Research*, *154*(1), 51–61.

Phillips, L. D., Fasolo, B., Zafiropoulos, N., & Beyer, A. (2011). Is quantitative benefit–risk modelling of drugs desirable or possible? *Drug Discovery Today*, *8*(1), e3–e10.

Poduval, S., Ahmed, S., Marston, L., Hamilton, F., & Murray, E. (2018). Crossing the digital divide in online self-management support: Analysis of usage data from HeLP-Diabetes. *JMIR Diabetes, 3*, e10925.

Porter, M. E. (2010). What is value in health care? *New England Journal of Medicine, 363*(26), 2477–2481.

Porter, M. E., & Teisberg, E. O. (2006). *Redefining health care: Creating value-based competition on results.* Harvard Business Press.

PwC. (2011). Medical Technology Innovation Scorecard - The race for global leadership.

Quinn, C. C., Khokhar, B., Weed, K., Barr, E., & Gruber-Baldini, A. L. (2015). Older adult self-efficacy study of mobile phone diabetes management. *Diabetes Technology & Therapeutics, 17*(7), 455–461.

Raftery, J. (2001). NICE: faster access to modern treatments? Analysis of guidance on health technologies. *BMJ, 323*(7324), 1300–1303.

Raiffa, H. (1968). *Decision analysis: Introductory lectures on choices under uncertainty.* Addison-Wesley.

Ricardo, D. (1817). *On the principles of political economy and taxation.* John Murray.

Rogers, P., & Blenko, M. (2006). Who has the D? *Harvard Business Review, 84*(1), 52–61.

Rogge, J., & Kittel, B. (2016). Who shall not be treated: Public attitudes on setting health care priorities by person-based criteria in 28 nations. *PloS One, 11*(6).

Ross, S. A. (2013). Breaking down patient and physician barriers to optimize glycemic control in type 2 diabetes. *American Journal of Medicine, 26*, 38–40.

Ryan, M., Scott, D. A., Reeves, C., Bate, A., Van Teijlingen, E. R., Russell, E. M., Napper, M., & Robb, C. M. (2001). Eliciting public preferences for healthcare: A systematic review of techniques. *Health Technology Assessment, 5*(5), 1–186.

Ryan, M., Watson, V. (2009). Comparing welfare estimates from payment card contingent valuation and discrete choice experiments. *Health Economics, 18*, 389–401.

Ryan, M. B. (2001). Use of discrete choice experiments to elicit preferences. *BMJ Quality & Safety, 10*(*Suppl 1)*, i55–i60.

Saaty, T. L. (1980). *The analytic hierarchy process.* McGraw-Hill.

Sabik, L. M., Lie, R. K. (2008). Priority setting in health care: Lessons from the experiences of eight countries. *International Journal for Equity Health, 7*(1), 1–13.

Samuelson, P. A. (1938). A note on the pure theory of consumer's behaviour. *Economica, 5*(17), 61–71.

Samuelson, P. A. (1948). Consumption theory in terms of revealed preferences. *Economica, 15*(60), 243–253.

Samuelson, P. A. (1950). The problem of integrability in utility. *Economica, 17*(68), 355–385.

Sampietro-Colom, L. & Martin, J. (ed.) (2017). Hospital-Based Health Technology Asessment: The Next Frontier for Health Technology Assessment

Sandberg Buch, M. &. Petersen, A. (2017). *Model for koordinerende indsatsplaner og tilhørende koordinatorfunktioner - Evaluering af et samarbejdsprojekt mellem Region Hovedstadens psykiatri og Københavns Kommune.* København: KORA.

Sandberg Buch, M. (2012). *Forløbskoordination for patienter med kronisk sygdom. Erfaringer fra Region Syddanmarks modelprojekt om udvikling af forløbskoordination på kronikerområdet.* [Course coordination for patients with chronic disease. Experiences from the Region of Southern Denmark's model project on the development of course coordination in the chronicler area]. København: DSI.

Savage, L. (1954). *The foundations of statistics.* Wiley.

Schumpeter, J.A., Opie, R., Elliott, J.E. (1983). The theory of Economic development: an inquiry into profits, capital, credit, interest, and the business cycle, New Brunswick, New Jersey: Transaction Publishers

Seixas, B., Reigier, D.A., Bryan, S., Mitton, C. (2021). Describing practives of priority setting and resource allocation in publicly funded health care systems of high-income countries. *BMC Health Services Research*, *21*(90)

Sermet, C., Andrieu, V., Godman, B., Van Ganse, E., Haycox, A., & Reynier, J. P. (2010). Ongoing pharmaceutical reforms in France: Implications for key stakeholder groups. *Applied Health Economics and Health Policy, 8*(1), 7–24.

Sortsø, C. G. (2016). Societal costs of diabetes mellitus in Denmark. *Diabetic Medicine, 33*, 877–885.

Stafinski, T. M. (2011). To fund or not to fund: Development of a decision-making framework for the coverage of new health technologies. *Pharmacoeconomics, 29* (9), 771–780.

Starr, L. (2021a). *Assessment of Roche diabetes care / Odsherred Municipality Value-based Health Care Diabetes Project 2017-2019 – Feasibility and transferability lessons.* University of Copenhagen.

Starr, L. (2021b). *Designing a value-based health care contract – Lessons from a public-private pay-for-performance health care collaboration.* University of Copenhagen.

Starr, L., von Arx, L. B., & Kjær, T. (2021). Are Danish national reimbursement priorities worthwhile for patients? An investigation using the discrete choice experiment. Submitted.

Starr, L., & Vrangbæk, K. (2021). *Value-based health care classifications and experiences in Denmark.* University of Copenhagen.

Stone, M. A., Charpentier, G., Charpentier, G., Doggen, K., Kuss, O., Lindblad, U., Kellner, C., Nolan, J., Pazderska, A., Rutten, G., Trento, M., & Khunti, K. (2013). Quality of care of people with type 2 diabetes in eight European countries: Findings from the Guideline Adherence to Enhance Care (GUIDANCE) study. *Diabetes Care, 36*, 2628–2638.

Sundhedsstyrelsen. (2011). *Forløbskoordinering i regioner og kommuner. Indsamling af erfaringer. [Cource coordination in Regions and municipalities. Collection of experiences].* Hørsholm: Sundhedsstyrelsen.

Tacconelli, E., Carrara, E., Savoldi, A., Harbarth, S., Mendelson, M., Monnet, D., . . . WHO Pathogens Priority List working group. (2018). Discovery, research, and development of new antibiotics: The WHO priority list of antibiotic-resistant bacteria and tuberculosis. *Lancet Infectious Diseases*, *18*(3), 318–327.

Tidd, J. (2006). A review of innovation models (discussion paper, Imperial College London

The Economist Intelligence Unit. (2020). *Digital Diabetes Index – Enhancing diabetes care through digital tools and services.* The Economist Intelligence Unit Limited 2020.

Thokala, P., Devlin, N., Marsh, K., Baltussen, R., Boysen, M., Kalo, Z., Longrenn, T., Mussen, F., Peacock, S., Watkins, J., & Ijzerman, M. (2016). Multiple criteria decision analysis for health care decision making—an introduction: Report 1 of the ISPOR MCDA Emerging Good Practices Task Force. *Value in Health, 19*, 1–13.

Thokala, P., Marsh, K., Devlin, N., van Til, J., Reddy, B., Baltussen, R., & IJzerman, M. J. (2014). Multi criteria decision analysis methods in health care: Current status, good practice and future recommendations. *Value in Health, 17*(3), A34.

Triantaphyllou, E. (2000). *Multi-Criteria decision making methods: A comparative study.* Kluwer Academic Publisher.

Villesen, K., & Hildebrandt, S. (2013). Staten spilder millioner på diabetesmedicin. [The State wastes millions on diabetes medicine]. *Information*.

von Arx, L. B., Johnson, F. R., Mørkbak, M. R., & Kjær, T. (2017). Be careful what you ask for: Effects of benefit descriptions on diabetes patients' benefit-risk tradeoff preferences. *Value in Health, 20*, 670–678.

von Arx, L. B., & Kjær, T. (2014). The patient perspective of diabetes care: Asystematic review of stated preference research. *Patient, 7*, 283–300.

von Neumann, J., & Morgenstern, O. (1947). *Theory of games and economic behavior* (2nd ed.). Princeton University Press.

von Winterfeldt, D., & Edwards, W. (1968). *Decision analysis: Introductiory lectures on choices under uncertainty.* Addison-Wesley.

Weinstein, M. C., Torrance, G., & McQuire, A. (2009). QALYs: The basics. In *Methods for economic evaluation of health care programmes* (4th ed). Oxford University Press.

Whichello, C., Levitan, B., Juhaeri, J., Patadia, V., DiSantostefano, R., Pinto, C. A., & de Bekker-Grob, E. W. (2020). Appraising patient preference methods for decision-making in the medical product lifecycle: An empirical comparison. *BMC Medical Informatics and Decision Making, 20*(1), 1–15.

WHO. (2014). *Global health expenditure database*. http://apps.who.int/nha/database

WHO. (2016a). *Innovation*. http://www.who.int/ topics/innovation/en/

WHO. (2016b). *Global report on diabetes.* https://www.who.int/publications/i/item/9789241565257

WHO. (2019). *WHO guideline: Recommendations on digital interventions for health system strengthening.* https://apps.who.int/iris/bitstream/handle/10665/311941/9789241550505-eng.pdf?ua=1

WHO. (2020). *WHO Diabetes Programme*. https://www.who.int/diabetes/action_online/basics/en/index3.html

WHO. (2021). *Health Technology Assessment.* https://www.who.int/medical_devices/

Wilsdon, T., & Serota, A. (2010). *A comparative analysis of the role and impact of health technology assessment.* EFPIA.

Wooldridge, J. M. (2010). *Econometric analysis of cross section and panel data.* The MIT Press.

Wouters, O. (2020). Lobbying expenditures and campaign contributions by the pharmaceutical and health product industry in the United States, 1999-2018. *JAMA Internal Medicine*, *180*(5), 688–697.

Youngkong, S., Baltussen, R., & Tantivess, S., Tantivess, S., Mohara, A., & Teerawattananon, Y. (2012). Multicriteria decision analysis for including health interventions in the universal health coverage benefit package in Thailand. *Value in Health, 15*(6), 961–970.

Appendixes

Appendix 1: Diabetes Survey

Questionnaire

The Future's Diabetes Treatment – What is important for you?

Region Syddanmark

SYDDANSK UNIVERSITET

novo nordisk®

«Løbenummer»

Thank you for your help in answering the questionnaire. Your knowledge is important to us!

It takes approximately 20 minutes to complete the questionnaire. We ask you to return the questionnaire at the latest 14 days after receipt in the postage-paid answer envelope. By your completing the questionnaire, we know that you understand and accept:

- the purpose of the study.
- use of your answers.
- use of the information in your medical journal.

You can read more in the letter from Funen's Diabetes Committee that is enclosed with this questionnaire. If you are in doubt about something, you are very welcome to contact the project leader, Lill-Brith von Arx, at lbwr@sam.sdu.dk or telephone 30 79 42 77.

The first part of the questionnaire is about your diabetes

1) If you think about the last week. How often did you measure your blood sugar? (put *one* X)

0 times last week	☐
1-7 times	☐
8-14 times	☐
15-21 times	☐
More than 21 times	☐
Don't know	☐

2) Have you ever had low blood sugar through using insulin? It can be indicated by paleness, shaking, rapid heartbeat, hunger, and visual difficulties (put *one* X)

Yes	☐
No – go to question 6	☐
Don't know – go to question 6	☐

3) **Think about the last month. How often have you had non-severe incidents? (That is, low blood sugar that you <u>could manage yourself</u> by drinking or eating something containing sugar) (put *one* X)**

None in the last month	
1-5 times	
6-10 times	
More than 10 times	
Don't know	

4) **Have you ever had an insulin shock? (That is, low blood sugar that required help from others <u>or</u> where you were unconscious) (put *one* X)**

Never	
1 time	
2 times	
3 times	
More than 3 times	
Don't know	

5) **Have you ever had low blood sugar at night? (put *one* X)**

Yes	
No	
Don't know	

6) **Your long-term tests (HbA_{1c}) are measured at diabetes checkups at the doctor's or at the hospital. Have you heard about the long-term test (HbA_{1c}) before? (put *one* X)**

Yes	
No – go to question 8	
Don't know	

7) What sounds right for you? (put *one* X)

A long-term test (HbA_{1c}) of 9 % means that my blood sugar, measured the same morning, was 9 mmol/L	
A long-term test (HbA_{1c}) of 9 % says something about how my blood sugar has been in the past 3 months	
A long-term test (HbA_{1c}) of 9 % means that my blood sugar on average has been 9 mmol/L in the past 3 months	

8) To what extent do you think that you follow your diabetes treatment? (put *one* X)

Not at all	
To some extent	
To a great extent	
Completely	

9) To what extent do you agree or disagree with the following statements? (put *one* X for each line)

	Completely disagree	Disagree	Neutral	Agree	Strongly agree
I think it is very difficult to follow the treatment					
I don't think that the treatment helps very much with my diabetes					
Once in a while I choose not to follow the treatment because I can't afford it					
I am well even though I don't always follow my treatment					
I think it is very time-consuming to take my medicine					

10) Which of the following places do you believe that there is a risk for related illnesses, if your blood sugar is too high over a longer period? (put *one* X for each line)

	Yes	No	Don't know
Hands			
Feet			
Heart			
Kidneys			
Eyes			
Teeth/Gums			

The next questions are about your wishes for treatment

11) Which long-term test (HbA_{1c}) would you be satisfied to be at? (put *one* X)

5.5 %	
6 %	
6.5 %	
7 %	
7.5 %	
8 %	
8.5 %	
9 %	
9.5 %	
10 %	
Don't know	

In the next part, there are different situations that you must choose between. What you have to do is consider advantages and disadvantages with diabetes treatment. Some of the situations will be different than your current treatment. They show what the future's diabetes treatment can look like. The number of times that you take the medicine – and how you take it – are completely as you usually do with your current treatment.

Here we describe for you what the choice questions in the next section are about

Disadvantages	Advantages
Increased risk for heart attack from the treatment Out of 1000 people, 3 people per year risk a heart attack with some treatments. With other treatments, you do not increase the risk that you already have for a heart attack.	**Prevention of related illnesses** Better blood sugar control. Better prevention of related illnesses over time. Depending on the treatment, up to 9 out of 10 people can avoid related illnesses.
Low blood sugar that requires others help, per year Insulin incidents can occur up to twice a year, depending on the treatment.	**Prevention of related illnesses with the treatment** **9 out of 10** avoid related illnesses | **7 out of 10** avoid related illnesses | **5 out of 10** avoid related illnesses Very good | Good | Moderate **Blood sugar control**
Low blood sugar you handle yourself, per month Non-severe incidents can occur 8 times per month, depending on the treatment.	The most common related illnesses are reduced vision and pain in the legs, feet, or hands. In severe cases blindness, amputation, or kidney failure.
	Possible weight loss in a year A weight loss of up to 10 kg is possible, depending on the treatment.

In total, 12 choice questions are shown. For each choice question, you must put an X for *one* treatment (A or B). A and B are always different. You can therefore of course choose A one time and B the next time.

We show here how you put an X

Choice question 5 of 12	Treatment A	Treatment B
People in treatment who avoid related illnesses	7 of 10 without related illnesses	5 of 10 without related illnesses
Possible weight loss in a year	4 kg	10 kg
Increased risk of heart attack through treatment, per year	Yes (3 people out of 1000)	No (no increased risk)
Low blood sugar that requires help from others, per year	1 incidents	2 incidents
Low blood sugar that you can deal with yourself, per month	1 non-severe incident	8 non-severe incidents
Which treatment do you prefer?		X

12) Put an X for the treatment you prefer for each of the 12 choice questions

Choice question 1 of 12	**Treatment A**	**Treatment B**
People in treatment who avoid related illnesses	7 out of 10 without related illnesses	5 out of 10 without related illnesses
Possible weight loss in a year	Unchanged weight	4 kg
Increased risk of heart attack through treatment, per year	No (no increased risk)	Yes (3 people out of 1000)
Low blood sugar that requires help from others, per year	No incidents	2 incidents
Low blood sugar that you can deal with yourself, per month	8 non-severe incidents	1 non-severe incident
Which treatment do you prefer?	☐	☐

Choice question 2 of 12	**Treatment A**	**Treatment B**
People in treatment who avoid related illnesses	9 of 10 without related illnesses	5 of 10 without related illnesses
Possible weight loss in a year	4 kg	Unchanged weight
Increased risk of heart attack through treatment, per year	Yes (3 people out of 1000)	Yes (3 people out of 1000)
Low blood sugar that requires help from others, per year	2 incidents	No incidents
Low blood sugar that you can deal with yourself, per month	4 non-severe incidents	1 non-severe incident
Which treatment do you prefer?	☐	☐

Choice question 3 of 12	**Treatment A**	**Treatment B**
People in treatment who avoid related illnesses	5 of 10 without related illnesses	9 of 10 without related illnesses
Possible weight loss in a year	10 kg	Unchanged weight
Increased risk of heart attack through treatment, per year	Yes (3 people out of 1000)	No (no increased risk)
Low blood sugar that requires help from others, per year	No incidents	1 incidents
Low blood sugar that you can deal with yourself, per month	4 non-severe incidents	1 non-severe incident
Which treatment do you prefer?	☐	☐

Choice question 4 of 12	Treatment A	Treatment B
People in treatment who avoid related illnesses	7 of 10 without related illnesses	9 of 10 without related illnesses
Possible weight loss in a year	10 kg	4 kg
Increased risk of heart attack through treatment, per year	Yes (3 people out of 1000)	No (no increased risk)
Low blood sugar that requires help from others, per year	1 incidents	2 incidents
Low blood sugar that you can deal with yourself, per month	4 non-severe incidents	8 non-severe incidents
Which treatment do you prefer?		

Choice question 5 of 12	Treatment A	Treatment B
People in treatment who avoid related illnesses	7 of 10 without related illnesses	5 of 10 without related illnesses
Possible weight loss in a year	4 kg	10 kg
Increased risk of heart attack through treatment, per year	Yes (3 people out of 1000)	No (no increased risk)
Low blood sugar that requires help from others, per year	1 incidents	2 incidents
Low blood sugar that you can deal with yourself, per month	1 non-severe incident	8 non-severe incidents
Which treatment do you prefer?		

Choice question 6 of 12	Treatment A	Treatment B
People in treatment who avoid related illnesses	9 of 10 without related illnesses	7 of 10 without related illnesses
Possible weight loss in a year	10 kg	4 kg
Increased risk of heart attack through treatment, per year	Yes (3 people out of 1000)	No (no increased risk)
Low blood sugar that requires help from others, per year	1 incidents	No incidents
Low blood sugar that you can deal with yourself, per month	1 non-severe incident	4 non-severe incidents
Which treatment do you prefer?		

Choice question 7 of 12	Treatment A	Treatment B
People in treatment who avoid related illnesses	5 of 10 without related illnesses	9 of 10 without related illnesses
Possible weight loss in a year	Unchanged weight	10 kg
Increased risk of heart attack through treatment, per year	No (no increased risk)	Yes (3 people out of 1000)
Low blood sugar that requires help from others, per year	2 incidents	No incidents
Low blood sugar that you can deal with yourself, per month	1 non-severe incident	8 non-severe incidents
Which treatment do you prefer?		

Choice question 8 of 12	Treatment A	Treatment B
People in treatment who avoid related illnesses	9 of 10 without related illnesses	5 of 10 without related illnesses
Possible weight loss in a year	Unchanged weight	10 kg
Increased risk of heart attack through treatment, per year	Yes (3 people out of 1000)	No (no increased risk)
Low blood sugar that requires help from others, per year	No incidents	1 incidents
Low blood sugar that you can deal with yourself, per month	8 non-severe incidents	4 non-severe incidents
Which treatment do you prefer?		

Choice question 9 of 12	Treatment A	Treatment B
People in treatment who avoid related illnesses	7 of 10 without related illnesses	9 of 10 without related illnesses
Possible weight loss in a year	10 kg	Unchanged weight
Increased risk of heart attack through treatment, per year	No (no increased risk)	Yes (3 people out of 1000)
Low blood sugar that requires help from others, per year	2 incidents	No incidents
Low blood sugar that you can deal with yourself, per month	8 non-severe incidents	4 non-severe incidents
Which treatment do you prefer?		

Choice question 10 of 12	Treatment A	Treatment B
People in treatment who avoid related illnesses	9 of 10 without related illnesses	7 of 10 without related illnesses
Possible weight loss in a year	Unchanged weight	4 kg
Increased risk of heart attack through treatment, per year	No (no increased risk)	Yes (3 people out of 1000)
Low blood sugar that requires help from others, per year	2 incidents	1 incidents
Low blood sugar that you can deal with yourself, per month	4 non-severe incidents	8 non-severe incidents
Which treatment do you prefer?	☐	☐

Choice question 11 of 12	Treatment A	Treatment B
People in treatment who avoid related illnesses	5 of 10 without related illnesses	7 of 10 without related illnesses
Possible weight loss in a year	4 kg	10 kg
Increased risk of heart attack through treatment, per year	No (no increased risk)	Yes (3 people out of 1000)
Low blood sugar that requires help from others, per year	1 incidents	2 incidents
Low blood sugar that you can deal with yourself, per month	8 non-severe incidents	1 non-severe incidents
Which treatment do you prefer?	☐	☐

Choice question 12 of 12	Treatment A	Treatment B
People in treatment who avoid related illnesses	5 of 10 without related illnesses	7 of 10 without related illnesses
Possible weight loss in a year	4 kg	Unchanged weight
Increased risk of heart attack through treatment, per year	No (no increased risk)	No (no increased risk)
Low blood sugar that requires help from others, per year	No incidents	1 incidents
Low blood sugar that you can deal with yourself,	1 non-severe incident	4 non-severe incidents
Which treatment do you prefer?	☐	☐

13) In the choice questions that you have just answered. How certain were you? (put *one* X on the scale)

Very uncertain	1	2	3	4	5	6	7	8	9	10	Very certain
	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	

The next questions are about your health

14) Think about the last month. What best describes your physical activity? (put *one* X)

I have regularly trained hard and several times a week (e.g. football or handball)	☐
I have exercised or carried out strenuous gardening at least 4 times a week	☐
I have walked or cycled at least 4 hours a week (include also Sunday walks and cycling/walking to and from work)	☐
I have read, watched TV, or carried out another activity sitting still	☐

15) What fits you best? (put *one* X)

I can carry out ordinary tasks with becoming short of breath, tired, or having increased heart rate (stairs to 2nd floor, mowing the lawn, vacuuming, carrying heavy shopping)	☐
I become short of breath, tired, or have increased heart rate with ordinary tasks (stairs to 2nd floor, mowing the lawn, vacuuming, carrying heavy shopping)	☐
I become short of breath, tired, or have increased heart rate with easy tasks (walking on a flat street, getting dressed/undressed, stairs to 1st floor)	☐
I cannot do much with becoming short of breath, tired, or having increased heart rate. I feel short of breath, even when I am resting.	☐

16) Do you smoke? (put *one* X)

No, I have never smoked	
No, I have stopped	
Yes, less and less every week	
Yes, at least once a week	
Yes, every day	

17) How would you evaluate your heart health? (put *one* X on the scale)

Worst possible health	1	2	3	4	5	6	7	8	9	10	Best possible health

18) Imagine your health as it normally is (ignore short-term periods of illness)

a) How is your ability to move around? (put *one* X)

I don't have any problems moving around	
I have some problems moving around	
I am stuck in bed	

b) How is your ability to carry out your own personal hygiene? (put *one* X)

I don't have any problems with my personal hygiene	
I have some problems washing myself or getting dressed myself	
I cannot wash myself or get dressed myself	

c) How is your ability to carry out usual activities? (put *one* X)

I don't have any problems carrying out my usual activities	
I have some problems carrying out my usual activities	
I cannot carry out my usual activities	

d) Do you have pain or discomfort? (put *one* X)

I don't have any pain or discomfort	
I have moderate pain or discomfort	
I have extreme pain or discomfort	

e) Are you anxious or depressed? (put *one* X)

I am not anxious or depressed	
I am moderately anxious or depressed	
I am extremely anxious or depressed	

19) How good/bad are you at doing, what you think is best for you? (put one X for each line)

	Very bad									Very good	Don't know
	1	2	3	4	5	6	7	8	9	10	
When it applies to your eating habits?											
When it applies to daily exercise?											
When it applies to visiting your dentist?											
When it applies to visiting your doctor?											
When in applies to taking your medicine?											
When it applies to following your doctor's recommendations?											

20) How satisfied are you with your life in general (put *one* X on the scale)

Very unsatisfied	1	2	3	4	5	6	7	8	9	10	Very satisfied

Now it is about you and your life

21) What is your current occupation? (you are welcome to put several Xs)

No occupation (pensioner, staying at home, seeking employment, etc.)	
Apprentice/student	
Employed, non-professional	
Employed, professional	
Civil servant	
Self-employed	
Other	

22) What is your highest education? (put *one* X)

High school/Secondary School	
College/Sixth Form	
Vocational education	
Higher education with a short duration (under 3 years)	
Higher education with a middle duration (3-4 years)	
Higher education with a long duration (5 years or more)	
Other	

23) How much was <u>your</u> gross income in 2013 (<u>before tax</u> and other deductions)? (put *one* X)

0-149,000 kr.	
150,000-249,000 kr.	
250,000-374,000 kr.	
375,000-524,000 kr.	
525,000-699,000 kr.	
700,000-849,000 kr.	
850,000 kr. or greater	

24) How much was your household's gross income in 2013 (before tax and other deductions)? (put *one* X)

0-149,000 kr.	
150,000-249,000 kr.	
250,000-374,000 kr.	
375,000-524,000 kr.	
525,000-699,000 kr.	
700,000-849,000 kr.	
850,000 kr. or greater	

25) Are you a member of "Health Insurance Denmark"? (put *one* X)

Yes, I am an active member (group 1-5)	
Yes, I am a passive member (group 8)	
No	
No. I would like to, but I can't become a member because of chronic illness	

26) Finally, we would like to hear what your home measurement was while you answered the questionnaire? You should only answer this, if you will in any case measure your blood sugar now (put *one* X)

Less than 5 mmol/L	
5-6 mmol/L	
7-8 mmol/L	
9-10 mmol/L	
11-12 mmol/L	
13-14 mmol/L	
15-16 mmol/L	
17-18 mmol	
Over 18 mmol/L	

The last 3 questions are about something completely different than diabetes

We are now interested in understanding how you would act in a couple of imaginary situations about money. We hope that you will also take time to answer the last three questions.

27) Imagine that you unexpectedly inherit 2,500 kr. from a distant relative. Afterwards, you get the possibility of taking part in a lottery with equal chances of either doubling the money to 5,000 kr. or losing the money. In other words, there is a 50 % chance that you win 5,000 kr. and a 50 % chance that you lose the 2,500 kr. What do you choose?

I choose to take part in the lottery	☐
I choose to not take part in the lottery and keep the 2,500 kr.	☐

28) Now imagine that you have won the 5,000 kr. in the lottery. You can choose to have the money paid out to you today or wait and get 6,000 kr. later. What is the maximum number of months you would accept to wait?

I wouldn't wait, but would choose to get the 5,000 kr. paid out today	☐
1 month	☐
2 months	☐
3 months	☐
6 months	☐
8 months	☐
10 months	☐
12 months	☐
More than 12 months	☐

29) Now imagine a new situation. You can now get the 5,000 kr. paid out in 12 months or wait and instead get 6,000 kr. later. What is the maximum number of months you would accept to wait?

I wouldn't wait, but would choose to get the 5,000 kr. paid out in 12 months	☐
13 months	☐
14 months	☐
15 months	☐
17 months	☐
19 months	☐
21 months	☐
23 months	☐
More than 23 months	☐

There aren't any more questions! Thank you for your help in answering the questionnaire.

Are you brave enough for more, have access to the Internet, and are interested in a lottery for **5 gift vouchers worth 1,000 kr. each**? Then visit www.sam.sdu.dk/skema in the next 3 weeks.

There are 13 more questions to be used for research. Your answers are anonymous. To take part you must enter the 5-digit number at the bottom of the page (for example, 1439A).

Appendix 2: Literature Search Strategy

In order to identify which criteria to include, a literature review was carried out.

The systematic identification of potentially relevant studies (papers, research reports, policy documents) concerned with decision-making in health was conducted in the period from July 2013 to September 2013. Potentially relevant papers were identified through systematic electronic databases, other online resources, through contacting content experts within the field and prior knowledge supplementing the process. The searched was limited to: (i) literature published after the year 2000, (ii) studies in English, (iii) grey literature,[4] and (iv) topics related humans.

The search for literature was adapted to the timeframe of the review and information sources that broadly covered different subjects were selected. Electronic databases were used to search for peer-reviewed literature, and general search engines and website searches were used for both peer-reviewed and grey literature. Reference lists from primary studies were checked for new leads.

The electronic database search was performed in healthcare-related and economic databases each of which covers particular topics. Specifically, the following

[4] Grey literature is the common name for academic or scientific publications that are not published via a traditional publisher or journal. Grey literature can be working papers or reports as well as articles and dissertations that are ultimately not published.

databases, catalogues, and bibliographies were used: Medline, Embase, Cochrane, NHS-eed, Scopus, EconLit: Economic.

In addition, a comprehensive search in Google Scholar was performed, as well as searches in identified relevant research or content-specific databases.

With regard to grey literature, additional searches for relevant studies and useful leads were made by means of the Google search engine and Google Scholar. Copies or links to relevant documents were made and the URL and date of access for relevant document was recorded.

In addition, the following websites were searched for relevant studies, ongoing or unpublished research projects, and other useful leads: National Institute for Health and Care Excellence (nice.org), International Society for Pharmacoeconomics (ISPOR) (ispor.org), European Medicines Agency (ema.europa.eu), International Network of Agencies for Health Technology Assessment (Inahta.org), and European Network for HTA: EUnetETA.

In order to make sure that none of the used words would be too limiting in a search, a search with each of the words found to be of relevance was performed and the number of corresponding hits recorded (Table 5).

Table 5. Search strategies: Identifying if search words or MeSH terms would be too limiting.

#	Key words	Results
1	health	245,6134
2	new drug development	77,517
3	pharmacol	1,950
4	decision-making	117,126
5	priority-setting	1,246
6	decision support models	26
7	prioritization	2,948
8	resource allocation	10,688
9	criteria	335,108
10	benchmarking	11,484
11	ethics	126,978
12	needs	226,066
13	conjoint analysis	363
14	criteria-based scoring system	408
15	multi criteria objective programming	309
16	multi-criteria priority	160
17	multiple decision	72
18	MCDA	130
19	MCDM	49

20	multi-criteria decision	771
21	multi criteria objective programming	17
22	multi criteria decision making	88
23	Analytic Hierarchy Process	62
24	evolutionary multi-objective	80
25	multi-objective	384
26	genetic multi-objective	107
27	preference based ranking	31
28	comprehensive review	6,103
29	comprehensive assessment	3,277
30	reimbursement	29,561

#	**MesH words**	**Search results**
1	Cost-Benefit Analysis	56,078
2	Models, Economic	9,259
3	Technology Assessment, Biomedical/economics	1,101
4	Technology Assessment, Biomedical/methods*	957
5	diabetes mellitus	294,024
6	health priorities	8,376
7	Choice behavior	35,437
8	Decision Making	111,201

9	Decision Support Techniques*	54,910
10	Health Care Rationing/economics	1,623
11	Health Care Rationing/standards*	763
12	Health Priorities/economics	527
13	Legislation as topic	131,728
14	Logistic Models	79,491
15	Needs Assessment	20,744
16	Policy Making	17,709
17	Quality-Adjusted Life Years	6,111
18	Outcome and Process Assessment (Health Care)	648,040
19	Pharmaceutical Preparations/standards*	4,995
20	Risk Assessment/methods*	17,658
21	Stochastic Processes	18,122
22	Decision Support Techniques	54,910
23	Health	244,847

PhD Papers 1-5

The dissertation includes the following articles which can be find in the next sections:

i. Bogetoft, P., & Starr, L. (2021) Benchmarking and Predicting the Demand for New Diabetes Drug, Submitted to *European Journal of Operational Research,* May 2021

ii. Starr, L., von Arx, L. B., & Kjær, T. (2021) Are Danish National Reimbursement Priorities Worthwhile for Patients? An Investigation Using the Discrete Choice Experiment, modified and shortened version submitted to *International Journal of Technology Assessment in Health Care,* June 2021

iii. Starr, L., & Vrangbæk, K. (2021) Value-Based Healthcare Classification and Experiences in Denmark, EIT Health and University of Copenhagen, ISBN: 978-87-92356-01-7

iv. Starr, L. (2021a). Assessment of Roche Diabetes Care/Odsherred Municipality Value-Based Healthcare Diabetes Project 2017-2019 – Feasibility and Transferability Lessons, Working Paper, EIT Health and University of Copenhagen

v. Starr, L. (2021b). A design Perspective on Value-Based Healthcare Contracts – Lessons from a Danish Public/Private Pay-for-Performance Based Contract, Working Paper, EIT Health Working Paper

Benchmarking and predicting the demand for a new diabetes drug

Peter Bogetoft[1] and Laila Starr[2]

Abstract

In this paper, we use benchmarking analysis and linear programming to evaluate existing diabetes drugs and to estimate the demand for a new drug. We benchmark the existing drugs in 2019 using data envelopment analysis (DEA) and show that some of the drugs are only marginally efficient. This finding suggest that they should be in limited demand. Using existing sales data, we next make partial inferences about the preferences that different patient groups have for the different drug attributes. Using this information, we can determine how the attributes of a new drug are likely to affect the demand for this drug. Likewise, we can estimate the share of the present users of the existing drugs that are likely to switch to a new drug.

1. Introduction

In many industries, and in the pharmaceutical industry in particular, the process from product conception to market access is complex, time consuming, and subject to significant risk and opportunity costs. The potential value of a product relative to alternative products naturally plays a central role. For a pharmaceutical company to remain competitive, its products must reflect the preferences and demands expressed by end users, as well as by a myriad of stakeholders, including patients, doctors, health authorities, reimbursement agencies, etc.

Diabetes products are, to a greater extent today than in the past, characterized by not only delivering primary outcomes (efficacy) but also by having complex product profiles with multiple secondary outcomes. For a pharmaceutical company, it is therefore essential to be able to differentiate its products beyond the primary efficacy.

The complex product profiles have led customers to use multiple criteria when assessing the value of new medicines. For example, Angelis (2017), Marsh (2014), and Marsh (2016) proposed the use of multicriteria decision making (MCDM) as an attractive way to capture those different criteria (Baltussen R N. L., 2006). MCDM is a set of analytical techniques that can be used to aid in comparing, prioritizing and selecting between different alternatives, e.g., products, characterized by multiple

[1] Professor, Copenhagen Business School, CBS, pb@cbs.dk. Address: Department of Economics, Porcelaenshaven 16A, 2000 Frederiksberg, Denmark
[2] Research Assistant, Department of Public Health, University of Copenhagen and PhD candidate, Copenhagen Business School.

features, see, e.g., Bogetoft and Pruzan (1991) for an early textbook. Weighting the benefits and risks of a pharmaceutical product enables a comparison of individual alternatives based on the overall benefit.

In this paper, we also used multiple criteria to evaluate diabetes drugs. We do not assume, however, that there is one best compromise between the different drug attributes. Rather, we allow for different patient groups to have different preferred attribute profiles. We make partial inferences about the preferences of the different patient segments using existing demand data, and we use this to predict the demand for a new drug and to study which drugs a new drug is likely to cannibalize.

Our approach is based on a simple model of revealed preferences. Revealed preference theory is concerned with the actual observed behavior in the market and works on the assumption that consumers have considered a set of alternatives before making a purchasing decision. Thus, given that a consumer chooses one alternative out of a set of alternatives, this alternative must be the preferred alternative for this consumer (Samuelson, 1948). If we have enough price-choice data, we may approximate the consumer's preferences with great detail.

When we only have limited choice information, the inference will have to be partial. Assume, for example, that the patients have linear preferences, i.e., the relative utility of a drug can be measured as a weighted sum of the drug attributes. In this case, patient segments can be delineated as cones of possible weights, namely, the weights that can be used to rationalize the choice between the different drug products. Although the preference information is partial, it is sufficient to predict how the introduction of a new drug – or the variation of prices of an existing drug – is likely to impact the sales of the different competing drugs. For certain weights, the new drug is preferable to the old drugs. We can therefore also construct a preference cone for the new drug, and by investigating which of the old cones the new cone overlaps with, we can predict which of the old drugs will be cannibalized by the new drug and to what extent. We flesh out the details of this approach in the paper, and we use the approach on a data set of diabetes drugs.

The paper is organized as follows. In Section 2, we provide a brief background on traditional marketing approaches to brand positioning, as well as traditional economic approaches to product differentiation and spatial competition. In Section 3, we introduce our new approach. Section 4 provides a brief introduction to benchmarking and the relation to preferences. Section 5 presents our data about the usage of diabetes drugs in Denmark. Section 6 provides an initial benchmarking of these diabetes drugs, while Section 7 illustrates the use of our sales prediction approach. Final remarks are provided in Section 8.

2. Background and related literature

The problem of finding an optimal price and positioning of a new product is discussed in great detail in the marketing literature. Brand positioning describes how a brand is

different from its competitors and where or how it sits in customers' minds and influences how consumers interpret the product. (Kotler 2002). There is a large body of literature on different approaches, which range from purely theoretical approaches to more applied approaches.

A simple way to think of this is by describing products or brands in terms of their multiple attributes, including price. If there are A relevant attributes to consider, different products correspond to different vectors in R^A. Pricing and brand positioning, therefore, become a question of selecting a new vector in product attributes space R^A.

Now, the standard approach in psychology, economics, and marketing is to assume that consumers evaluate products by integrating information about their attributes in a linear additive fashion (e.g., Combris, Lecocq, & Visser, 2000; Feenstra, 1995; Green & Wind, 1973; Shocker & Srinivasan, 1979). That is, the available attribute information is multiplied by its importance and then additively integrated to form an overall judgment (e.g., Keeney & Raiffa, 1993; Shocker & Srinivasan, 1979). The value of product $y = (y_a, a \in A) \in R^A$ is described as follows:

$$Value(y) = \sum_{a \in A} v_a y_a$$

where y_a is the value of the a attribute for product y and v_a is the weight that the consumer assigns to the a attribute. Although very simple, attribute-based models have been shown to accurately predict the observable outcomes of many judgment and decision tasks ranging from personnel evaluation (e.g., Rotundo & Sackett, 2002) to medical decisions (e.g., Agha, Arora, & Sevdalis, 2011); they naturally lend themselves to estimations of continuous criteria, such as price. This approach will also be the starting point in this paper.

The idea that the market price of a product can be described by a linear function of the product's attributes has also gained popularity as the price hedonic model in the economic literature (e.g., Feenstra, 1995; Thrane, 2004). These weighted-additive strategies are similar to linear regression approaches, and they have been labeled attribute-based, piecemeal, rule-based, feature-based, or cue abstraction approaches (Juslin, Olsson, & Olsson, 2003; Lynch, 1985; Sujan, 1985; Troutman & Shanteau, 1976; for a review on consumer inference processes, see Kardes, Posavac, & Cronley, 2004). Hedonic models are most commonly estimated using regression analysis, although more generalized models exist, such as sales adjustment grids. Like generalized multi-attribute utility theory, hedonic models can accommodate nonlinearity, variable interaction, or other complex valuation situations.

There are, of course, many other ways to integrate the attribute information. We can, for example, use more advanced multi-attribute utility models that transform the different features and use nonlinear aggregations. One can, for example, use various versions of the lexicographic model, introduced by Tverski (1972), conjunctive and disjunctive models, e.g., Einhorn (1970), Kororita and Tosen (1972), or an exponential discrepancy model, Einhorn and Gonedes (1971). In the more applied decision theory, a popular approach is to define an ideal product y^* and to evaluat the value of product y by its closeness to y^*, e.g. as:

$$Value(y) = \frac{1}{d(y, y^*)}$$

where $d(y, y^*)$ is some distance measure.

One can also depart more radically from such classical approaches and assume that preferences have little meaning in a vacuum. One can then use more iterative methods where the decision making process is assumed to involve a series of iterations where the decision maker gradually learns about the available alternatives and forms his preferences, see e.g., Bogetoft and Pruzan (1991). In the marketing literature, a prominent alternative is the so-called exemplar or instance-based models, which predict that consumers evaluate products in comparison to similar options they encountered in the past (Cohen & Basu, 1987; Smith & Medin, 1981; Sujan, 1985). A mathematical formulation of an exemplar-based strategy is found in Juslin et al. (2008).

Real product positioning and pricing problems are, of course, much more complicated. This is especially the case when more novel or radical products are introduced. In such cases, there may be considerable uncertainty about the product attributes, and beliefs and preferences will change dynamically. The design of a successful product launch can, therefore, be extremely complicated. The modeling in Roberts and Urban (1988) illustrates this. Their model development starts by considering the effect of uncertainty on multi-attribute preference models using a decision analysis framework. In common with recent economics and marketing models, the transformation of preference to probability of choice is then considered. The diffusion effect is modeled by suggesting that as consumers gain more information about the brand, their beliefs about mean attribute levels and uncertainty change. Bayesian updating provides the framework used to incorporate the effect of new information on a potential consumer's prior beliefs and information uncertainty. The amount of word of mouth per period circulating about the brand is related to cumulative sales, a proxy for how many owners there are early in the diffusion process. Changes in beliefs about the expected attribute levels and uncertainty, in turn, influence the probability of brand choice. Therefore, it is important to acknowledge that our deterministic model abstracts away many complications.

A simple way to understand our approach and point to some of its limitations is also to think of horizontal product differentiation and spatial competition, as in the famous Hotelling model of a linear city, see Hotelling (1929) and Tirole (1990, Ch7). Hotelling introduced the notions of locational equilibrium in a duopoly in which two firms have to choose their locations while taking into consideration the distribution of consumer and transportation costs. The model was developed as a game in which firms first chose a location and then a selling price for their products. To set their business in the best location to maximize profits, the firms will have to evaluate the following three key variables: competitors' location, customers' distribution and transportation costs. As in Hotelling's model, we have a set of consumers; only now, they are not located on a single-dimensional line but are located in A-dimensional space. Each consumer type corresponds to a given weight vector v in R_+^A. Additionally, in contrast to the Hotelling model, we do not know ex ante that the consumers are uniformly distributed in the type space. Rather, we use the observed demand to approximate the distribution of

consumers in the weight space. A limitation of the results in this paper is that we do not solve for a subgame perfect equilibrium. When we predict the demand for a new product, we allow for the products to compete, but it is only passive competition we consider, i.e., one in which the competition does not react to our moves by modifying product specifications or changing prices. We therefore do not identify subgame perfect Nash equilibria as in the traditional analysis of the linear city. We simply develop a residual demand function for a new product.

3. Predicting the demand for a new drug

In this section, we propose an approach to predict the demand for a new drug. We first introduce the idea and provide an illustrative example and then discuss some implementation issues.

3.1 Setting

Consider a market with D drugs. Each drug $d \in D$ is described by a vector of A attribute values, i.e., as follows:

$$y^d \in R^A$$

We assume that the attributes are defined such that larger values of each of the attributes are desirable to all users.

We can also think of price as being part of the attribute description, but since a low price is desirable, we shall in such cases include minus-the-price as an attractive output attribute. In many countries, the price is not paid directly by the users, and in such cases, it may be relevant to simply ignore prices and focus only on the benefits derived from the drugs.

We also assume that the drugs constitute (imperfect) substitutes. A user can change his drug, but he cannot combine the drugs.

We assume that the demand for the different drugs is known in the form of the present numbers of users of the different drugs, $N(d), d = 1, \dots, D$. Hence, total demand is as follows:

$$N = \sum_{d \in D} N(d)$$

where N is the total number of drug users in our market.

Assume now that a pharmaceutical company considers launching a new product with the following attributes:

$$y^0 \in R^A$$

Our basic aim is determine how many of the N existing users of the old drugs are likely to substitute the new drug – and from which of the old drugs they will substitute.

In terms of preferences, we will initially assume that each patient $p \in P$ uses a linear aggregation of the product attributes. The weights or values assigned to the individual attributes by patient p are $v^p \in R_+^A$.

Hence, patient p prefers drug d if and only if the following is true:

$$v^p \, y^d \geq v^p \, y^{d'} \text{ for all } d' \in D$$

For patient p who prefers drug d, we can therefore make partial inferences about his attribute values. We know that this patient has values in the (polyhedral) convex cone defined by the above constraints. Note also that the preference rankings are unaffected by a positive linear transformation of the weights. Hence, without loss of generality, we may restrict the weight to be below the unit simplex. In summary, therefore, we can assume that a patient choosing drug d^* has preference values in the following:

$$V(d) = \{v \in R_+^A : v \, y^d \geq v \, y^{d'} \text{ for all } d' \in D, v_1 + \cdots + v_A \leq 1\}$$

Given the observed users of the different drugs, we know that $N(d)$ patients have weights in $V(d)$. Given the discrete set of D existing drugs the patients can choose from, we cannot make more specific inferences. In the following, we will therefore assume that the $N(d)$ patients have preference weight vectors that are uniformly distributed in $V(d)$.[3]

3.2 Predicting the demand of the new product

When a new drug d^0 is introduced, we obtain new sets of weights or new sets of patients preferring the different drugs. Let the new set of patient types preferring drug d have weights in:

$$V^{NEW}(d) = \{v \in R_+^A : v \, y^d \geq v \, y^{d'} \text{ for all } d' \in D \cup \{0\}, v_1 + \cdots + v_A \leq 1\}$$

for all $d \in D \cup \{0\}$.

Since we have added an extra constraint to all sets, the new sets are subsets of the old:

$$V^{NEW}(d) \subseteq V(d)$$

[3] Note that we assume the sum of weights to be less than or equal to 1. This is, however, only one way to restrict the weight space. It implies that we shall find volumes of polyhedral, cone-like sets in in R^A. We could alternatively – and more like the DEA-vrs model introduce below, have assumed that the sum of weights shall be exactly 1. This would make the volumes equal to the areas of the polyhedral subsets of the A-1 dimensional unit-simplex in R^A. The relative volumes would not be affected by such a change.

for all $d \in D$. This simply reflects that all the original drugs now potentially have to also compete with the new drug d^0.

By making use of the assumption that the patients $N(d)$ are uniformly distributed on the original weight sets $V(d)$, we can predict the new demands for the old products as follows:

$$N^{NEW}(d) = N(d)\frac{Volume\left(V^{NEW}(d)\right)}{Volume\left(V(d)\right)} \text{ for all} d \in D$$

and the demand for the new product as follows:

$$N^{NEW}(d^0) = N - \sum_{d \in D} N^{NEW}(d)$$

Although this approach is conceptually sound, it may be associated with numerical challenges in the implementation. We will return to this issue below. First, let us consider a small illustrative example.

3.3 Illustrative example

To illustrate our approach, consider a simple example with two original products with features $y^1 = (1,0)$ and $y^2 = (0,1)$ and with a corresponding number of consumers $N(1) = 100, N(2) = 200$. A new drug $y^0 = (\alpha, \alpha)$ is now introduced. We will examine how the demand for the products changes for values of $\alpha \in [0,1]$. The situation is illustrated in Figure 1 below, where the red line corresponds to the possible configuration of the new drug.

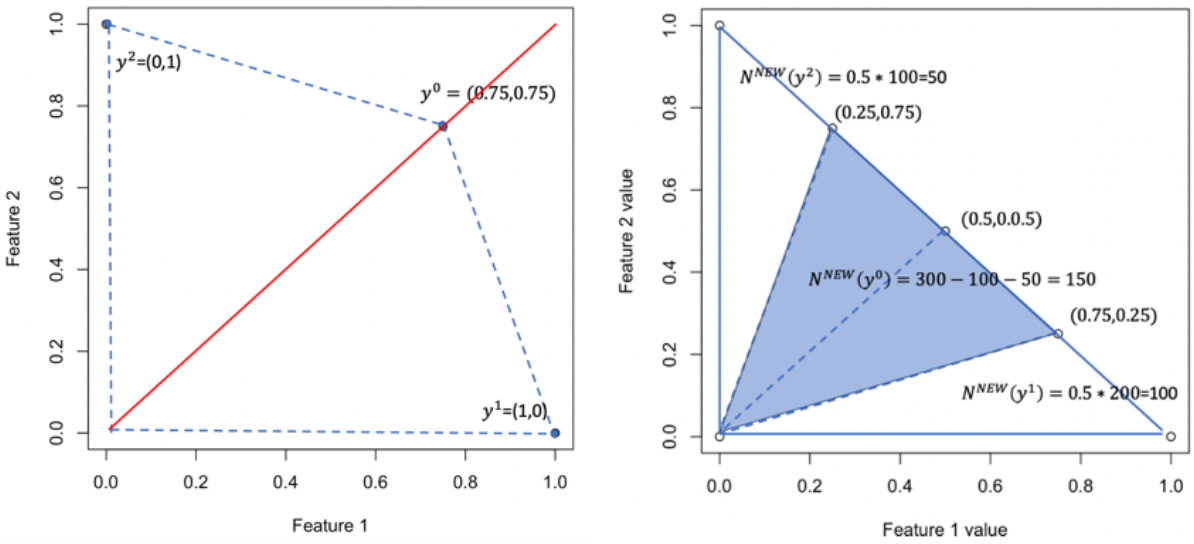


Figure 1 Illustrative example with new product$y^0 = (0.75, 0.75)$

It is clear that for a value of α less than 0.5, there are no possible patients who would prefer the new product. As α increases above 0.5, an increasing number of patients that

value the two features more or less equally will prefer the new product, and when $\alpha \geq 1$, all demand will be directed towards the new drug.

In the right panel of Figure 1, we illustrate the inference we can make about the types of patients preferring the different drugs when $\alpha = 0.75$. We can observe that half of the patients previously using drug y^1 and y^2 switch to the new drug in this case.

In Figure 2, we illustrate how the demand for the 3 products changes as a function of α.

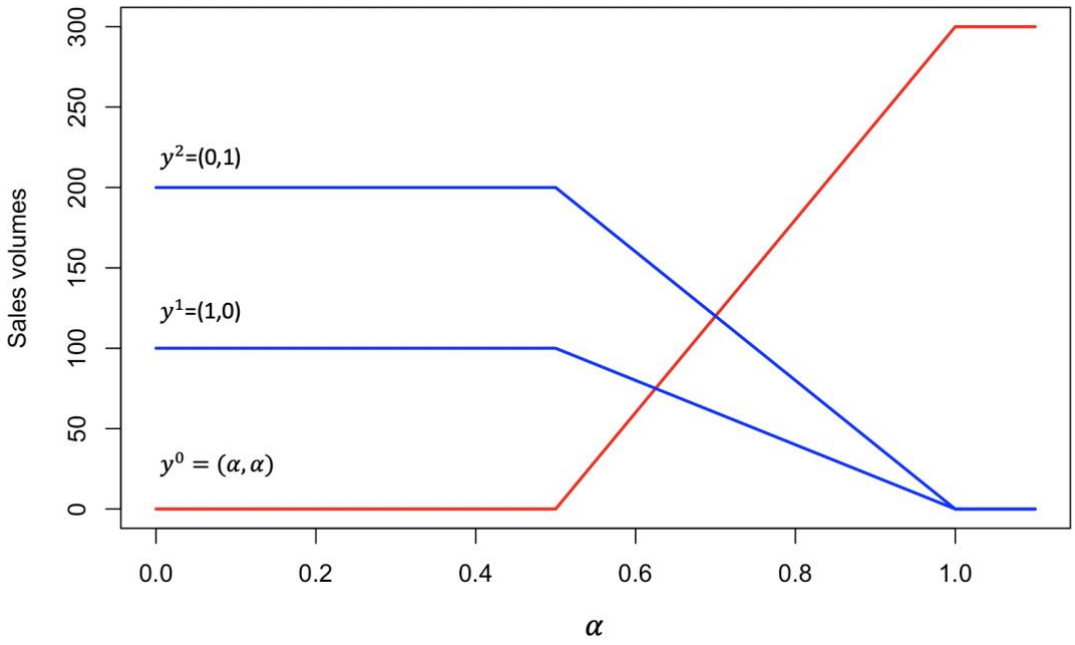


Figure 2 Sales volumes in the illustrative example

3.4 Practical implementation

To implement the above procedures, we need to find the volumes of $V(d)$ and $V^{NEW}(d)$ for all $d \in D$ and $d \in D \cup \{y^0\}$, respectively.

The set of weights leading to the choice of d is:

$$V(d) = \{v \in R_+^A : v\, y^d \geq v\, y^{d'} \text{ for all } d' \in D, v_1 + \cdots + v_A \leq 1\}$$

We can flesh this out using the following linear constraints:

$$\begin{aligned} & v\left(y^{d^1} - y^d\right) \leq 0 \\ & . \\ & . \\ & v\left(y^{d^D} - y^d\right) \leq 0 \\ & v_1 + \cdots + v_A \ \leq 1 \end{aligned}$$

$$v_1 \geq 0, \ldots, v_A \geq 0$$

Using matrix notation, we can formulate this as follows:

$$\begin{aligned} Ev &\leq f \\ v &\geq 0 \end{aligned}$$

We can describe the structure of matrix E and right hand side f as follows: First let Y be an $D \times A$ dimensional matrix with $Y_{d,a} = y_a^d$, i.e., with the alternative drugs in the rows and the features in the columns. Now let $Y[-d,.]$ be Y except that we have eliminated row d. Additionally, let B be a $(D-1) \times A$ matrix with y^d in each row. We can now construct the matrix E as follows:

$$E = \begin{bmatrix} Y[-d,.] \\ 1_A \\ -\text{Diag} \end{bmatrix} - B$$

and the right-hand side constraint f as follows:

$$f = \begin{bmatrix} 0_{D-1} \\ 1 \\ 0_A \end{bmatrix}$$

where 1_A is a row with A 1 s, Diag is a $A \times A$ dimensional diagonal matrix with values 1 in the diagonal, and 0_{D-1} and 0_A are two vectors of 0 s with lengths $D-1$ and A, respectively.

We can estimate the volume of the set $\{v | Ev \leq f, v \geq 0\}$ by first identifying the extreme points and then calculating the volume of the convex hull of these extreme points. There are several ways to do so using the R programming language. In our calculations, we used the "scdd" procedure from the "rcdd" package to move from a hyperplane formulation as above to a vertex representation. Next, we used the "convhulln" procedure from the "geometry" package to calculate the volume of the convex hull of the vertexes. The "convhulln" procedure interfaces with the Qhull library available from http://www.qhull.org.

3.5 Numerical challenges and biased estimates

In practice, the calculation of volumes may be numerically challenging. This happens when the vertexes are almost colinear and the volumes are, therefore, very small. In such cases, we may wrongly estimate small positive volumes as zero volumes.

Since we estimate the demand for the new drug as a residual, as follows,

$$N^{NEW}(d^0) = N - \sum_{d \in D} N^{NEW}(d),$$

such cases with numerical difficulties may result in somewhat optimistic estimates of the demand for a new drug.

3.6 Allocating nonrationalizable demand to existing drugs

A similar but more profound problem occurs if there are inconsistencies in the sense that some drugs have been subject to positive demands in our data even though the original volumes are estimated as 0:

$$N(d) > 0 \text{ and } Volume\big(V(d)\big) = 0$$

This happens when one or more consumers choose a drug d from the set of drugs D that cannot be an optimal choice with a linear aggregation of the attributes, i.e. when

$$\forall v \in R_+^A \;\; \exists d' \in D: vy^{d'} > vy^d$$

In this case, our procedure does not work since the new and old volumes are 0. Moreover, and more profoundly, the original data contradict the assumptions of our model. There can be many reasons for this, the most obvious being that our description of the features is too limited. We will return to this in the applications. For now, let us search for other ways to remedy this problem

One remedy in this case is to make an initial reallocation of the inconsistent demand such that only drugs that can be rationalized have a positive demand. After the initial reallocation, we can then calculate the demand for a new product and determine which drugs lose using the procedure above.

There are many ways to make the initial reallocation. In the example below, we use an approach based on the idea of super-efficiency from the benchmarking literature. A drug whose demand cannot be rationalized with linear indifference curves is weakly dominated by a convex combination of other drugs. We can therefore allocate its demand to the dominating drugs in proportion to the weights they have in the convex combination. A difficulty is of course that there may be many convex combinations dominating a given drug with irrational demand. In such cases, we shall use the convex combination that leads to the largest proportional expansion of all attributes. This corresponds to the use of the weights of these drugs in the super-efficiency calculations using output-based Farrell efficiency, as shown below.

To illustrate the idea of inconsistencies, the reallocations, and some alternative approaches, consider
Figure 3 below.

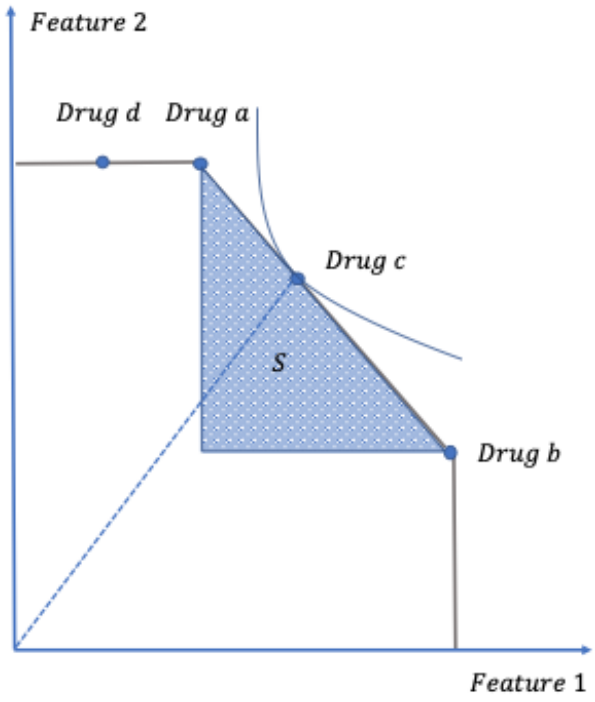


Figure 3 Rationalizable demand and curved indifference curves

Initially, we observe that no drugs to the southwest of the frontier can be rationalized with linear preferences.

We also observe that drugs d and c can be rationalized but only barely. Drug d is a rational choice for a consumer only if he assigns zero weight to Feature 1. Drug d is only rational if the consumer assigns exactly the same weights to the two features. Any deviation will lead to a consumer preferring Drug a or Drug b to Drug c. This also means that the volumes of the weight sets supporting Drug d and Drug c will be 0 and that our procedure above does not work properly.

A natural approach in this case is to initially reallocate the demand for Drug d to Drug a and to allocate the demand for Drug c to Drug a and Drug b. In the latter case, we can write the Drug c profile, y^c, as a convex combination of the Drug a and Drug b profiles,

$$y^c = \lambda y^a + (1 - \lambda) y^b$$

We can therefore naturally add $\lambda N(y^c)$ to the demand for Drug a and $(1 - \lambda)N(y^c)$ to the demand for Drug b. In this way, we allocate the demand for Drug c in proportion to the closeness of y^c to y^a and y^b, respectively.

We can generalize this approach to reallocate the demands for drugs that are located to the southwest of the frontier using the output-based super-efficiency approach. This means that any drug with a positive demand that is located on the line from the origin to Drug c will be allocated in the same way as the Drug c demand.

3.7 Alternative rationalization

An alternative approach to inconsistent initial demand is to relax the assumption of linear preferences. If we have nonlinear indifference curves, it is possible to strictly prefer some drugs even when they are weakly inefficient compared to a linear combination of other drugs. An example of this is illustrated in *Figure 3*. Drug c is located on the hyperplane spanned by Drugs a and b; however, with a curved indifference curve, it can still be strictly preferred to all the other drugs.

If we assume, for example, that preferences are given by Cobb-Douglas utility functions:

$$U(y) = y_1^{v_1} \cdot \ldots \cdot y_A^{v_A}$$

where the sum of the v_a values is one, we can rationalize more drugs. Technically, it would also be easy to implement since we could just log-transform all the features and then use a linear utility on the log-transformed features.

An alternative and more flexible idea along these lines is to assume a CES (constant elasticity of substitution) utility function, as follows:

$$U(y) = \left[\sum_{a \in A} v_a (y_a)^{-\rho}\right]^{-1/\rho}$$

where the elasticity of substitution is $s = \frac{1}{1+\rho}$. When the elasticity of substitution s approaches infinity, i.e., ρ approaches -1, we get linear indifference curves. When ρ goes to infinity, the elasticity of substitution s goes to 0, and we obtain Leontief-like indifference curves. Using such functions, we can rationalize not only Drug c but also any drug in area S in *Figure 3*. The difficulty with this approach is, of course, that we need to decide on the elasticity of substitution. In the example below, we will illustrate the use of $\rho = 3$, i.e., $s = 0.25$.

It should be noted that while curved indifference curves may create a strict preference for some of the drugs with a super-efficiency of 1 , such as Drug c above, they will not work in all cases. In *Figure 3* above, an example of such a drug is Drug d. It is weakly dominated by Drug a, and any utility function supporting Drug d will also support Drug a, and it must assign no value to a unilateral increase in feature 1.

Instead of introducing nonlinear preferences to accommodate linear inconsistencies, one can, of course, introduce more radical changes to our setup.

One change is to acknowledge that consumers may have incomplete information about the prices and features of the different drugs. This is very likely since such information

can typically only be extracted from several databases. It may, therefore, be more relevant to use a stochastic modeling framework.

Another possible explanation is switching costs and the resulting inertia or stickiness in the drug usage of a patient. If a patient has been using a drug, he knows how it works and may be reluctant to change his choice of drug. This means that older drugs may have a demand that cannot be justified by simply examining their attributes. One possible extension of our framework would be to introduce thresholds to reflect inertia. We might assume that one drug must outperform another drug with a least a certain threshold for a possible switch to take place.

While interesting extensions, the ideas of introducing stochastic models or threshold-based models shall not be explored further in this paper.

4. Benchmarking and preferences

The demand prediction approach developed above has links to nonparametric performance evaluations using socalled Data Envelopment Analysis (DEA). We explain the link here and suggest also that it may be interesting to simply benchmark drugs against each other. In this section, we provide a short introduction to DEA and its relationship to linear preference models.

4.1 DEA

DEA is a mathematical programming approach to multi-dimensional performance evaluations of so-called decision-making units (DMUs), i.e., firms, organizations, processes, etc. DEA was firm proposed by Charnes, Cooper and Rhodes (1978,79). It was later further developed and applied in 10,000+ studies, and several textbooks are available about DEA and related methods, see e.g., Bogetoft (2012) and Bogetoft and Otto (2011).

DEA is grounded in production economic theory. In a traditional DEA study, we assume that the evaluated entities are described by the inputs used and products being produced. If there are D entities and if entity d used $x^d \in R_0^C$ inputs to produce $y^d \in R_0^A$ outputs, we can model the technology as the smallest set in input-output space R_0^{C+A} that contains the actual observations and satisfies standard production economic properties, such as free disposability of inputs and outputs (we can always produce less outputs with more inputs) and convexity. This leads to the so-called variable returns to scale vrs-DEA model. We might also assume that it is possible to operate at different scales, e.g., by assuming constant returns to scale (crs). Technically, the underlying technology T is estimated by T^* using linear constraints, e.g., in the vrs case, as follows:

$$T^* = \left\{(x,y) \in R_0^{C+F} | \exists \lambda \in R_0^n : x \geq \sum_{d\in D} \lambda^d x^d, y \leq \sum_{d\in D} \lambda^d y^d, \sum_{d\in D} \lambda^d = 1\right\}$$

The estimated technology is the smallest convex set that contains the observations $\{(x^d, y^d), d \in D\}$ and satisfies the free disposability of outputs and inputs.

The efficiency of a given entity d can now be measured relative to this technology using a so-called Farrell approach, i.e., as the maximal proportional expansion of all outputs F or the maximal proportional contraction E of all inputs, i.e., as follows:

$$F^d = \max\{F \in R_0 \mid (x^d, Fy^d) \in T^*\} \text{ or } E^d = \min\{E \in R_0 \mid (Ex^d, y^d) \in T^*\}$$

Formally, to find the efficiency scores, we simply need to solve linear programming problems. The output efficiency of drug d, for example, can be determined as the solution to the following:

$$\begin{aligned} \max_{\lambda,F} \quad & F \\ s.t. \quad & x^d \geq \sum_{d' \in D} \lambda^{d'} x^{d'} \\ & Fy^d \leq \sum_{d\hat{}' \in D} \lambda^{d'} y^{d'} \\ & \sum_{d' \in D} \lambda^{d'} = 1 \end{aligned}$$

Below, we will not only calculate the usual input- and output-oriented Farrell efficiencies E and F, we will also calculate so-called super-efficiencies. These are the efficiencies of the enties when they are evaluated against a technology spanned by all the other entities. Technically, when evaluating d, we simply remove it from the set D, i.e., we use $D - \{d\}$ instead of D. Super-efficiency allows us to obtain more detailed information about the efficient entities. If the super-efficiency is 1.1 on the input side, it suggests that the inputs could be increased by 10% before the entity becomes inefficient. Likewise, if the super-efficiency is 0.9 on the output side, it suggests that the entity's outputs could all be decreased by 10% before the drugs become inefficient.

4.2 Drugs as production units

In this paper, we view drugs as production entities. Although DEA has been used to benchmark the performance of a very large number of different entities, we are not aware of papers that benchmark drugs. When benchmarking drugs, the outputs are the attractive outcomes of using the drugs, and the inputs are the negative aspect of using the drugs. Of course, there is some freedom in the ways we specify the features. Nausea, for example, can be handled as an input since it is unattractive, or it can be handled as an output using, for example, the share of users experiencing no nausea. We will generally use the latter approach and think of the input side as only being costs – or even be entirely ignored when we think of a system with substantial governmental copayments, as shown below.

We will also calculate super-efficiencies. This leads to insights that are clearly related to the demand for alternative drugs. If the super-efficiency of a drug is 1.1 on the input side, it suggests that the drug price could be increased by 10% before the drugs become

inefficient. Likewise, if the super-efficiency of a drug is 0.9 on the output side, it suggests that all the attractive drug features could be decreased by 10% before the drug becomes inefficient.

4.3 Dual prices and preferences

We introduced our estimate of the technology, T^*, in production economic terms above. There is, however, also an alternative dual interpretation that is directly related to preferences and to our approach to demand estimation introduced in Section 3.

Consider a user and assume that he has linear preferences, i.e., there exists relative importance weights $(u, v) \geq 0$, such that:

$$(x, y) \succcurlyeq (x', y') \Leftrightarrow -ux + vy \geq -ux' + vy'$$

If the user is fully rational, he will then only choose points that are at the frontier of T^*. This follows directly from the fact that the convex hull of a set of points can also be described as an intersection of half-spaces[4]. We can therefore say that if all users are rational and have linear preferences, there will only be a demand for drugs that are fully efficient, i.e., for which $F^d = 1$ or $E^d = 1$. If, for example, F^d=1.2, it means that all features of drug d should be increased by 20% to make it attractive to any user. Likewise, if $E^d = 0.9$, it means that the costs should be reduced by 10% before a rational user may possibly consider it.

It is worthwhile to note that the dual preference interpretations can also be supported formally by the dual versions of the *E* and *F* linear programs commonly used in the DEA literature. Taking program E as an example, let *u* be the dual prices associated with the input constraints, let *v* be the dual prices associated with the output constraints, and let *k* be the dual prices associated with the equality constraint. Now, it is easy to show, see e.g., Bogetoft and Otto (2011), that *E* can alternatively be calculated as the solution to the following:

$$\begin{aligned} \max_{u,v,k} \quad & vy^d + k \\ s.t. \quad & ux^d \leq 1 \\ & -ux^{d'} + vy^{d'} + k \leq 0 \ \text{ for all } d' \in D \\ & u \geq 0, v \geq 0, k \in R \end{aligned}$$

This corresponds to a classic pricing problem. We choose shadow prices or implicit values to make the value of using drug d appear as attractive as possible subject to a norming constraint $ux^d \leq 1$ and the constraints stating that no drug should have a positive net benefit, i.e., the priced outputs minus priced inputs shall not exceed 0.

[4] The result can be generalized to cover other DEA models like the FDH model which does not invoke convexity by extending the set of preference functions to the set of all functions that are weakly increasing in y and weakly decreasing in x, cf, e.g., Bogetoft and Pruzan (1991) Theorem 1

Let us finally note that we do not need to work with both the inputs and outputs above. Instead of distinguishing between inputs and outputs, we can also think of the inputs as negative outputs. Hence, we can redefine the feature vector as follows:

$$y = (-x, y^{old})$$

This simplifies the notation in regard to the revealed preferences analysis. Taking this approach, the DEA framework is directly aligned with our revealed preference framework from Section 3 above.

5. Health care and diabetes drugs in Denmark

In a modern health care system, many different decision-makers (organizations, institutions and individual health care providers) interact to care for patients and manage the health care system.

5.1 Danish players

In Denmark, the general practitioner is the primary gatekeeper to the health care system, and the general practitioner is responsible for the majority of drug prescriptions in Denmark. Until recent years, medical decisions were made by the general practitioner, with patients advised but rarely consulted about the alternatives. In recent years, patients have been given an increasing role in the medical decision process.

Payers are in the position of determining which drugs to pay for, for whom, and at what level to offer coverage (i.e., formulary coverage decisions), as well as how much to pay for each drug (i.e., reimbursement decisions). Coverage and reimbursement decision making is increasingly complex, and the decision-making process involves committees reviewing the traditional clinical and economic evidence of a drug and its alternatives.

In Denmark, the National Board of Health reviews new drugs based on information on the new drug's effect, side effects and price compared to relevant alternatives. The advice and information are targeted at doctors in general practice. The purpose is to promote rational use of medicines - both when choosing between different medicines and when opting out is the best choice. The recommendations are made by the Department of Efforts for Rational Pharmacotherapy (Indsatser for Rationel Farmakoterapi (IRF)) at the National Board of Health (Sundhedsstyrelsen, 2019).

5.2 Diabetes drugs

Diabetes drugs are located in a crowded space. Most new products are incremental innovations, i.e., upgraded versions or adaptions of already existing products. Only rarely does a radical innovative or breakthrough diabetes product enter the market.

This makes historical or existing sales data particularly useful. We illustrate our approach using data on pharmaceutical products within the so-called GLP-1, SGLT-2 and DPP-4 diabetes portfolios in Denmark.

For diabetes patients, it is of primary importance that a product can assist the patient in achieving well-controlled blood sugar, i.e., an HbA1c measure within the target. This is a quality that physicians expect any product to meet when considering its use. This endpoint is currently – although with some variety – delivered by the products in the GLP-1, SGLT-2 and DPP-4 product portfolios. In regard to brand positioning, this product feature should be maintained (or improved), as it is a necessity for being the choice of medication. Other product benefits, such as weight loss or cardiovascular benefits, are competitive advantages featured only by some products in the group. There might also be opportunities in unmet category needs, which could become drivers if effectively developed and leveraged, e.g., improved convenience. Finally, there are product features, e.g., safety issues, that are advantageous for competitor brands, e.g., black box warnings or a high percentage of patients experiencing nausea, which may be brand liabilities for the current brand.

In *Figure 4,* a value tree offering an overview of the various value concerns when evaluating new diabetes medications in the GLP-1, SGLT-2 and DPP-IV segments is shown.

The value tree is decomposed into five value criteria clusters relating to 1) the therapeutic impact, 2) the safety profile, 3) socioeconomic impact, 4) patient convenience and 5) the innovation level.

These value clusters are intended to comprise the critical aspects of value concerns to decision makers for evaluating the value of a new medicine within the GLP-1, SGLT-2 and DPP-IV segments.

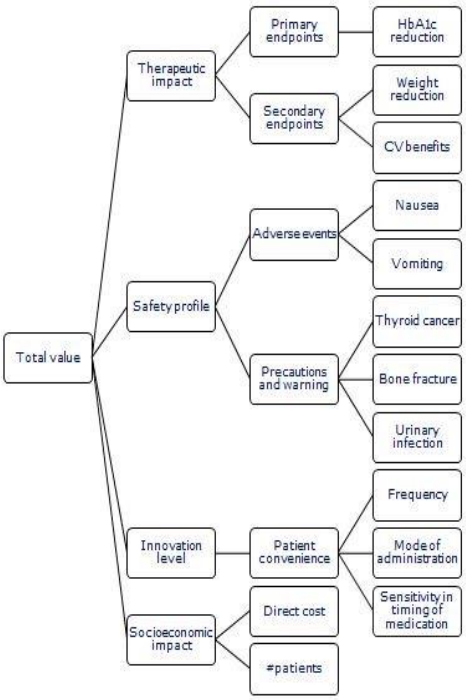


Figure 4 Value tree for diabetes type 2 for GLP-1, SGLT-2 and DPP-IV treatments

5.3 Data

The data used for this paper were collected from the observed market behavior of all marketed GLP-1 (seven products in the class), DPP-IV (five products in the class), and SGLT-2 (three products in the class) products in Denmark in the period from 2012-2019. To measure the market uptake of the products, the number of patients prescribed was recorded from www.medstat.dk. List price information for the products was obtained from www.medicinpriser.dk.

The benefits and safety profiles of the key product attributes of the GLP-1, DPP-IV and SGLT-2 products were obtained from the literature and from published results on double-blinded randomized control trials in phases III and IV. To identify relevant studies, a literature search was conducted. Citations were identified by searching the following databases: Medline, EMBASE, and the Cochrane Central Register of Controlled Trials. Data relating to the results for the criteria included in the study were extracted.

The PICOS (population, interventions, comparators, outcomes, study design criteria) summarizing the scope of the relevant studies used to map out the product attributes is presented in Table 1

Criteria	Definition
Population	Patients with diagnosed Type 2 diabetes on GLP-1, SGLT-2 and DPP-IV

Interventions	• GLP-1 • SGLT-2 • DPP-IV
Comparative products	Any of the above-listed interventions or placebo
Outcomes	At least one of the following outcomes is reported: Primary Outcome Measures: • Change in glycosylated hemoglobin (HbA1c) Secondary Outcome Measures: • Change in Body weight (kg) • Percentage experiencing nausea • Percentage experiencing vomiting • Thyroid cancer warning • Bone fracture warning • Urinary infections warning
Study Design	Double-blinded randomized controlled trials, phase III or phase IV
Other	English language only

Table 1: Scope of the literature review

Data were extracted on study characteristics, interventions, patient characteristics at the baseline, and outcomes for the study populations of interest. Data were extracted from the following 14 published drug studies, where the intervention is provided in parentheses: PIONEER (oral semaglutide), SUSTAIN (semaglutide), LEADER (liraglutide), DURATION (exenatide), REWIND (dulaglutide), ELIXA (alogliptin), CARMELIA (Linagliptin/tradjenta), EXAMINE (alogliptin/vipidia), SAVOR-TIME 53 (saxagliptinønglyza), VERIFY (Galvus/Vildagliptin), TECOS (Januvia/Sitagliptin), DECLARE TIMI 58 (Forxiga/Dapagliflozin), CANVAS (Invokana/Canagliflozin), and EMPA-REG (Jardiance/Empagliflozin).

The main data about the drug outcomes (features) are shown in Table 1 below. We have, in all cases, ordered the outcomes such that large numbers are attractive.

Drug	ATC code	Brand name	Name	HbA1c reduction pct	Weight loss kg	Non Nausea pct	Non Vomiting pct	Thyroid cancer warning 0=Yes, 1=No	Bone fracture warning 0=Yes, 1=No	Urinary infections warning 0=Yes, 1=No	Device 1 is oral 0=No, 1=Yes	Admin. days between
1	A10BJ06	Rybelsus	Semaglutide_oral_0,5mg	1.7	6.1	76	89	0	1	1	1	1
2	A10BJ06	Ozempic	Semaglutide_1mg	1.6	4.5	65	90	0	1	1	0	7
3	A10BJ02	Victozia	Liraglutide_1.2_mg	1.2	2.9	79	93	0	1	1	0	1
4	A10BJ01	Bydureon	Exenatide_LAR_2mg	1.3	2.7	91	96	0	1	1	0	7
6	A10BJ05	Trulicity	Dulaglutide_1.5mg	1.4	2.9	80	93	0	1	1	0	7
7	A10BJ03	Lyxumia	Lixisenatide_20mg	0.6	2	75	91	0	1	1	0	1
8	A10BH05	Trajenta	Linagliptin_5mg	0.7	0	99	97	1	0	0	1	1
9	A10BH04	Vipidia	Alogliptin_25mg	0.5	0	99	99	1	0	0	1	1
10	A10BH03	Onglyza	Saxagliptin_5mg	0.5	0	95	98	1	0	0	1	1
11	A10BH02	Galvus	Vildagliptin_50mg	1	0	96	93	1	0	0	1	0.5
12	A10BH01	Januvia	Sitagliptin_100mg	0.7	0	99	100	1	0	0	1	1
13	A10BK01	Forxiga	Dapagliflozin_5mg	1	1.6	97.7	100	1	0	0	1	0.5
14	A10BK02	Invokana	Canagliflozin_300 mg	0.9	3.6	98	100	1	0	0	1	1
15	A10BK03	Jardiance	Empagliflozin_25mg	0.8	2.5	98.9	100	1	0	0	1	1

Table 1 Drug features – therapeutic impact and safety files, where large numbers are attractive

Information about the number of patients using the different drugs is shown in Table 2 below, where we also provide information about the year when a drug was approved and the monthly price in 2019 for the different drugs.

Drug	ATC code	Brand name	Name	Year approval	Patients 2019	Patients 2018	Patients 2017	Patients 2016	Patients 2015	Patients 2014	Patients 2013	Patients 2012	DKK price per month 2019
1	A10BJ06	Rybelsus	Semaglutide_oral_0,5mg	2019	0	0	0	0	0	0	0	0	0
2	A10BJ06	Ozempic	Semaglutide_1mg	2018	21910	5745	0	0	0	0	0	0	1330.95
3	A10BJ02	Victozia	Liraglutide_1.2_mg	2009	23425	27275	25305	23420	21271	19384	19084	17807	992.11
4	A10BJ01	Bydureon	Exenatide_LAR_2mg	2011	185	250	285	380	439	420	536	609	985.13
6	A10BJ05	Trulicity	Dulaglutide_1.5mg	2015	1615	1965	1580	755	62	0	0	0	973.31
7	A10BJ03	Lyxumia	Lixisenatide_20mg	2013	30	45	55	85	118	143	36	0	966.6
8	A10BH05	Trajenta	Linagliptin_5mg	2011	6735	6565	6080	5190	4015	2775	1698	425	435.07
9	A10BH04	Vipidia	Alogliptin_25mg	2013	780	770	760	685	552	245	5	0	336.77
10	A10BH03	Onglyza	Saxagliptin_5mg	2009	595	700	830	960	1109	1209	1344	1487	375.06
11	A10BH02	Galvus	Vildagliptin_50mg	2008	2260	2430	2475	2530	2636	2456	2101	1687	366.53
12	A10BH01	Januvia	Sitagliptin_100mg	2006	14690	14795	14005	13065	12097	11022	10212	9714	425.82
13	A10BK01	Forxiga	Dapagliflozin_5mg	2012	11965	10260	8740	7345	6106	4077	1966	20	482.01
14	A10BK02	Invokana	Canagliflozin_300 mg	2013	1300	690	420	425	370	115	0	0	452.95
15	A10BK03	Jardiance	Empagliflozin_25mg	2014	23350	17755	11275	5710	1595	205	0	0	462.92

Table 2 Drug features – innovation level and socioeconomic impact

6. Benchmarking diabetes drugs

Let us first make a traditional DEA-based efficiency analysis of the diabetes drugs available on the Danish market.

To do so, we must decide on the model specification, i.e., what the inputs and outputs that we consider should be. We have analyzed different alternatives, as explained in *Table 3* below.

Model	**Base:** **Base model**	**Multi:** **Multi-feature model with payment**	**Multi-no-pay:** **Multi-feature model without payments**

Inputs	Price per month 2019	Price per month 2019	
Outputs	HbA1c reduction pct	HbA1c reduction pct points Weight loss kg Non-Nausea pct Non-Vomiting pct Thyroid cancer warning Bone fracture warning Urinary infections warning Device 1 is oral Administration days between	HbA1c reduction pct points Weight loss kg Non-Nausea pct Non-Vomiting pct Thyroid cancer warning Bone fracture warning Urinary infections warning Device 1 is oral Administration days between

Table 3 Models

The base model focuses on the cost side and the primary therapeutic outcome, i.e., HbA1c reduction. In the multi-feature model with payment, we extend the outcome description to include secondary outcomes as well. In the multi-feature model with no payment, we ignore the payment side since, for several patients, the out-of-pocket payment amounts are approximately the same for all drugs due to governmental copayments. In addition to these models, we have also examined other models, most notably models where the warnings have been ignored in the calculations. We have done this primarily to make the volume calculations easier and to test the quality of our numerical procedures.

In Table 4 and Table 5 below, we show the input and output efficiencies of the drugs in the different models. We also show the super-efficiencies of the drugs in the different models (last three columns starting with S).

In all cases, we have used a DEA model with variable returns to scale, i.e., assuming that the (composite) reference drug must be a weighted average of the available drugs as reflected by the $\sum_{d' \in D} \lambda^{d'} = 1$ constraint. When we include the warning variables that are 0 (active warning) and 1 (no warning) in the analysis, this effectively means that a drug without a given warning can only be compared to other drugs without the warning. A drug that has a warning can, however, be compared to drugs both with and without the warning. A similar logic is present in the case of the oral variable. Oral drugs will only be compared to other drugs that are oral, but non-oral drugs can be compared to oral and non-oral drugs.

Examining the base model first, we see that only four drugs are fully efficient, namely, Drugs 2, 6, 9, and 11. If we are only interested in the price and the HbA1c reduction pct, a drug such as Drug 3, Victozia, should lower its price by 32% (since the input efficiency is 68%) to become competitive. Alternatively, it should increase its HbA1c reduction pct by 18% (since its output efficiency is 1.18. Note that it is an 18% increase from its present HbA1c reduction pct points of 1.2, i.e., it should go from 1.2 to 1.4 pct point. A third alternative is to use some combination of lowering its price and increasing its benefits.

Now, in reality, all drugs are actually sold on the market. There can be several reasons for this, as discussed earlier.

One reason may be that the base model is too simple. As soon as we increase the number of attributes that are included in the model, almost all drugs become fully efficient. Only Drugs 3, 8 and 10 are still modestly inefficient in the input-based model, i.e., a modest price reduction of between 2% and 10% would suffice to make them competitive. If we ignore the price aspects, all drugs are efficient, i.e., there may be rational consumers with linear preferences that choose them. Hence, the fact that these products are in demand is understandable and rationalizable when we look at the normal efficiencies of the multi-feature without payments model.

Drug	ATC code	Brand name	Name	Base	Multi	Multi-no-pay	S Base	S Multi	S Multi-no-pay
2	A10BJ06	Ozempic	Semaglutide_1mg	1.00	1.00	1.00	Inf	Inf	Inf
3	A10BJ02	Victozia	Liraglutide_1.2_mg	0.68	0.98	1.00	0.68	0.98	1.00
4	A10BJ01	Bydureon	Exenatide_LAR_2mg	0.83	1.00	1.00	0.83	Inf	Inf
6	A10BJ05	Trulicity	Dulaglutide_1.5mg	1.00	1.00	1.00	1.04	1.13	1.00
7	A10BJ03	Lyxumia	Lixisenatide_20mg	0.35	1.00	1.00	0.35	1.01	1.00
8	A10BH05	Trajenta	Linagliptin_5mg	0.80	0.98	1.00	0.80	0.98	1.00
9	A10BH04	Vipidia	Alogliptin_25mg	1.00	1.00	1.00	1.09	1.26	1.00
10	A10BH03	Onglyza	Saxagliptin_5mg	0.90	0.90	1.00	0.90	0.90	1.00
11	A10BH02	Galvus	Vildagliptin_50mg	1.00	1.00	1.00	1.32	1.32	1.00
12	A10BH01	Januvia	Sitagliptin_100mg	0.82	1.00	1.00	0.82	Inf	Inf
13	A10BK01	Forxiga	Dapagliflozin_5mg	0.76	1.00	1.00	0.76	Inf	Inf
14	A10BK02	Invokana	Canagliflozin_300 mg	0.80	1.00	1.00	0.80	Inf	Inf
15	A10BK03	Jardiance	Empagliflozin_25mg	0.77	1.00	1.00	0.77	Inf	Inf

Table 4 Input efficiencies

Drug	ATC code	Brand name	Name	Base	Multi	Multi-no-pay	S Base	S Multi	S Multi-no-pay
2	A10BJ06	Ozempic	Semaglutide_1mg	1.00	1.00	1.00	0.87	0.69	0.69
3	A10BJ02	Victozia	Liraglutide_1.2_mg	1.18	1.00	1.00	1.18	1.00	1.00
4	A10BJ01	Bydureon	Exenatide_LAR_2mg	1.08	1.00	1.00	1.08	0.90	0.90
6	A10BJ05	Trulicity	Dulaglutide_1.5mg	1.00	1.00	1.00	0.98	0.93	1.00
7	A10BJ03	Lyxumia	Lixisenatide_20mg	2.33	1.00	1.00	2.33	0.99	1.00
8	A10BH05	Trajenta	Linagliptin_5mg	1.49	1.00	1.00	1.49	1.00	1.00
9	A10BH04	Vipidia	Alogliptin_25mg	1.00	1.00	1.00	-Inf	-Inf	1.00
10	A10BH03	Onglyza	Saxagliptin_5mg	2.01	1.00	1.00	2.01	1.00	1.00
11	A10BH02	Galvus	Vildagliptin_50mg	1.00	1.00	1.00	0.60	0.60	1.00
12	A10BH01	Januvia	Sitagliptin_100mg	1.48	1.00	1.00	1.48	1.00	1.00
13	A10BK01	Forxiga	Dapagliflozin_5mg	1.08	1.00	1.00	1.08	0.97	0.97
14	A10BK02	Invokana	Canagliflozin_300 mg	1.17	1.00	1.00	1.17	0.64	0.80
15	A10BK03	Jardiance	Empagliflozin_25mg	1.33	1.00	1.00	1.33	0.99	0.99

Table 5 Output efficiencies

Examining the super-efficiencies of the multi-feature model without payments, however, suggests that this model may still be too simplistic. We observe that all drugs except for Drugs 2, 4, 12, 13, 14 and 15 have super-efficiencies of 1. This means that they are efficient, but only barely so. They are weakly dominated by a combination of other drugs. By examining the lambda values in the linear program for F, we observe, for example, that Drug 3 Victozia is almost equivalent to a weighted sum of Drug 2, Drug 4 and Drug 7, see also Table 6 below

Lambdas	Drug 2 0.280702	Drug 4 0.45614	Drug 7 0.263158	Weighted sum	Drug 3
HbA1c reduction pct	1.6	1.3	0.6	1.2	1.2
Weight loss kg	4.5	2.7	2	3.0	2.9
Non Nausea pct	65	91	75	79.5	79.0
Non Vomiting pct	90	96	91	93.0	93.0
Thyroid cancer warning 0=Yes, 1=No	0	0	0	0	0
Bone fracture warning 0=Yes, 1=No	1	1	1	1	1
Urinary infections warning 0=Yes, 1=No	1	1	1	1	1
Device 1 is oral 0=Yes, 1=No	0	0	0	0	0
Admin. days between	7	7	1	5.4	1

Table 6 Linear combination weakly dominating Drug 3

We observe that there is a point, the weighted sum point, that is entirely spanned by other drugs and that are performing strictly better in terms of weight loss, non-nausea and administration frequency. For Victozia to be an attractive drug, it therefore, requires rather specific weights. In particular, 0 weights must be assigned to weight loss, non-nausea and admin frequency. In addition, the relative weights of the other features must be such that no other combination of the other drugs would make it attractive. In fact, as we will observe below, the volume of the set of weights making Drug 3 nondominated is effectively zero. This will lead to complications when we seek to analyze the changes in the volumes.

By extending the base model to the multi-attribute model, we succeeded in making the choice of all the drugs potentially rational, i.e., there exists linear preference structures that would make each of the drugs attractive compared to the other drugs. However, for several of the drugs, the set of fully rational consumer types they attract is likely very small. We have already discussed three alternative modifications of our model for use in such cases.

One alternative is to assume that consumers have incomplete information about the prices and features of the different drugs and to introduce stochasticity in the framework. Incomplete information is very likely in the case of diabetes drugs. In fact, the systematic comparison in Table 1 and Table 2 has been established by extracting information from several databases, as well as the detailed product descriptions, and it is not entirely realistic to assume that consumers perform similar data collection procedures. Price is also not fixed in reality. In Denmark, new prices are announced twice every month based on drug auctions. Although prices do not vary much and over time, it seems likely that general practitioners advising patients would tend to avoid dominant drugs.

A more likely explanation is switching costs. This implies that older drugs may have a demand that cannot be justified by simply considering their attributes. Drug 3, which we examined above, is, for example, a relatively old drug from 2009 compared to the other drugs in the comparison, i.e., Drugs 2, 4 and 7, which are from 2018, 2011 and 2013.

Remaining with the idea of rationality, we could also relax the assumption of linear preferences, as suggested previously. It should be noted that while curved indifference curves may create a strict preference for some of the drugs with a super-efficiency of 1,

this approach will not work in all cases. In the dataset, there are drugs that are weakly dominated by specific other drugs. This is the case for Drug 5, which is weakly dominated by Drug 2. The same is true for Drugs 7 and 8. They are both weakly dominated by Drug 10. This means that with preferences that are increasing in all attributes, there will be no preference function that creates a strict preference for Drugs 5, 7 and 8.

7. Sales predictions

In this section, we will illustrate our sales prediction approach. We first consider no-pay situations and later investigate the demand for a new drug as a function of a contemplated price.

7.1 No-pay cases

In Denmark, the yearly out-of-pocket user payment for prescription drugs is limited. Drug expenses above certain thresholds are partially or fully covered by governmental copayments. The exact rules involve several thresholds, but as an approximation, we may assume that the direct costs of all diabetes drugs exceed the threshold for full reimbursements and, therefore, that the user costs are effectively the same irrespective of the drug being prescribed. Thus, an analysis where we ignore the prices of the individual drugs, i.e., an analysis using the multi-feature no-pay model from Table 3 above, is relevant.

The data of the existing drugs Drug 2 to Drug 15 are as described in Table 1 and Table 2 above. As a new drug, we will examine Drug 1, Rybelsus, which is an oral version of the highly popular Drug 2, Ozempic. Instead of simply analyzing Drug 1, we will also analyze more or less efficient versions of Drug 1. Specifically, we will analyze the demand for a drug with the following attributes:

$$y^{NEW} = \alpha y^1 \text{ for values of } \alpha \in [0,2]$$

i.e., new drugs with features proportional to y^1 but ranging from an entirely useless drug to a drug with features twice as good as y^1.

In Figure 5, we show the estimated demands with the assumption of linear preferences. We first ignored initial reallocations. In this case, all non-rationalizable demand is allocated to the new drug as a default solution, and we do not show drugs with estimated volumes and, therefore, demand equal to 0. This explains the high starting value of the demand for αy^1. The starting value is equal to the present (irrational) demand for drugs 3, 6, 7, 8, 9, 10 and 11, namely, 35440 patients. We observe that the demand for the new drug starts to reduce the demand for the other drugs when α is approximately 0.7. One of the first drugs to suffer is Drug 2.

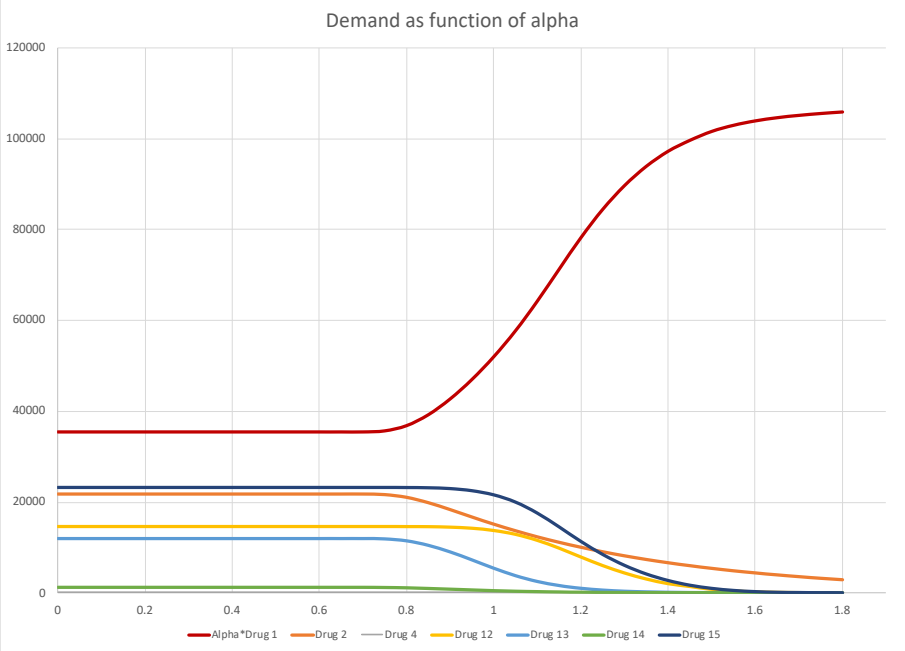


Figure 5 Demand as a function of alpha without an initial reallocation of non-rationalizable demand

As an alternative, we also calculated the demand if we initially reallocated the non-rationalizable demand to the super-efficient drugs according to their weights (λs) in the super-efficiency calculations. In Table 7, we show how the existing demand has initially been reallocated. We observe that in partular Drugs 4 and 12 gains from this reallocation.

Drug	Sales before reallocation	Sales after reallocation
2	21910	25051
3	23425	0
4	185	22114
6	1615	0
7	30	0
8	6735	0
9	780	0
10	595	0
11	2260	0
12	14690	22800
13	11965	14225
14	1300	1300
15	23350	23350

Table 7 Sales before and after the initial reallocation of nonrationalizable sales

This reflects that Drugs 4 and 12 play important roles in spanning several of the hyperplanes used to dominate some of the drugs with non-rationalizable demand. The spanning matrix is shown in Table 8 below. Each row shows the relative importance of the spanning drugs, shown in the columns, in the dominance of the row drug. We see for example that that Drug 12 directly dominates Drugs 8, 9 and 10.

Drug	2	4	12	13	14	15
3	0.111	0.889	0	0	0	0
6	0.333	0.667	0	0	0	0
7	0	1	0	0	0	0
8	0	0	1	0	0	0
9	0	0	1	0	0	0
10	0	0	1	0	0	0
11	0	0	0	1	0	0

Table 8 Reallocation of row demand to column demand (lambdas)

In Figure 6 below, we show how the demands are expected to depend on α when the existing demand has been initially reallocated. We see that the demand for the new drug starts at 0 and that it is Drugs 4 and 12, in particular, that gain from the reallocation.

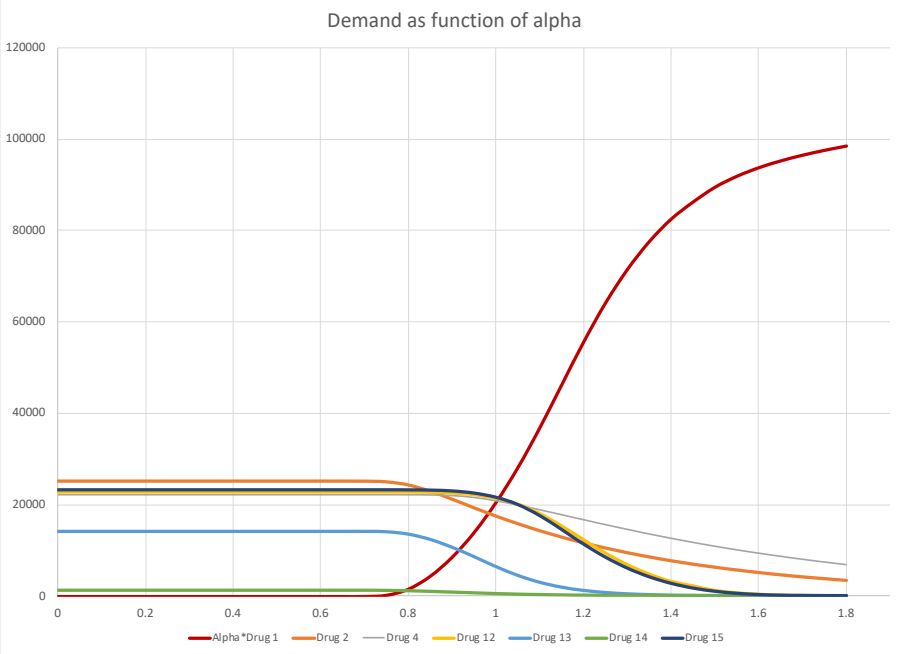


Figure 6 Demand as a function of alpha with the initial reallocation of non-rationalizable demand

We performed a similar analysis assuming a preference function of the Cobb Douglas class instead. Technically, this is performed by log-transforming the attribute values.

We observe in *Figure 7* that the main effect of doing so is that the demand responses become more sensitive to the changes in α. The changes in demand are now restricted to a narrower interval of α values. In addition, the initial reallocation is different. With log linear preferences, Drug 2 obtains much more and Drug 4 much less of the non-rationalizable reallocations. We also note that moving to log-linear preferences was not enough to make all realized demand rational.

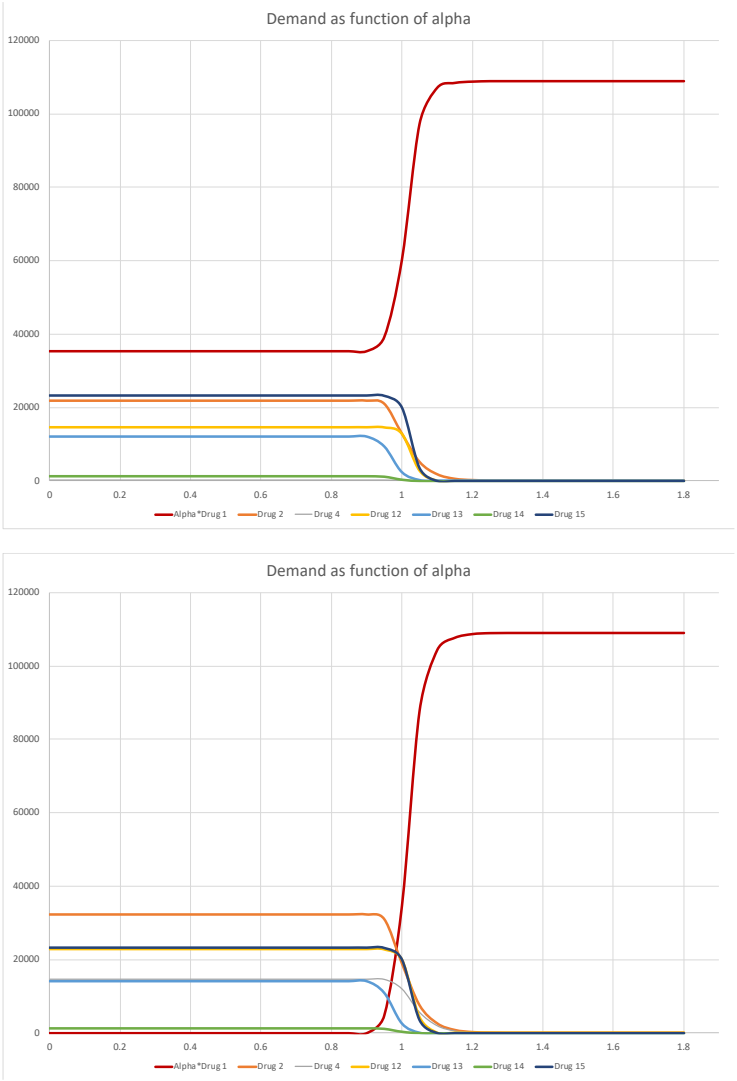


Figure 7 Demand as a function of alpha with Cobb-Douglas preferences: without initial reallocation (top) and with initial reallocation (bottom)

Finally, we performed similar analyses using CES (constant elasticity of substitution) functions, as illustrated in *Figure 8*. We restrict ourselves to cases with initial reallocations and instead investigate the role of the ex ante presumed elasticity of substitution s by varying it from 1.1 to 2. Recall that the larger the value of s, the less curved the indifference curves. This explains why the $s = 2$ case appears more like the linear case than the $s = 1.1$ case.

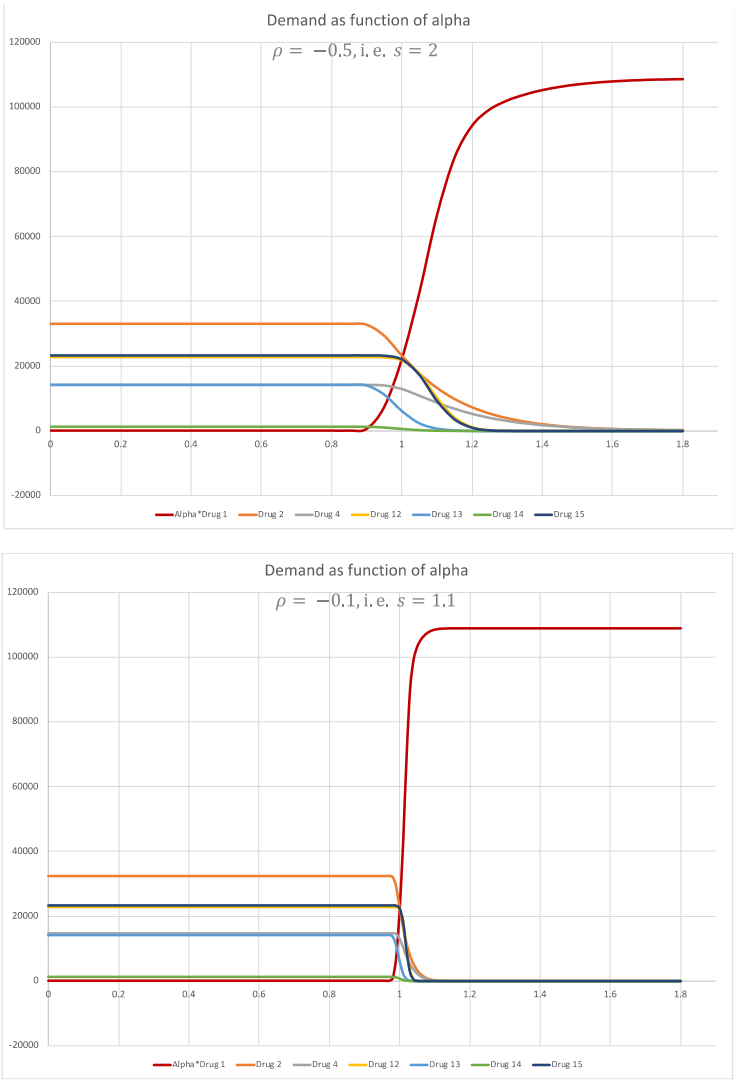


Figure 8 Demand as a function of alpha with CES preferences and initial reallocations

7.2 Pay cases

In addition to the above simulations, we analyzed the multi-attribute model with payments and estimated how demand for the different drugs is likely to develop as a function of the prize of Drug 1. As explained, this is technically easy since we can consider the drug price as an extra negative feature.

Some results are shown in Figure 9. As before, we have initially reallocated the demand that cannot be rationalized, and we have assumed a linear preference function. We observe that as the price for Drug 1 increases from 500 to 1900 DKK per month, the demand for Drug 1 declines. As the demand for Drug 1 decreases, the demand for other drugs, such as Drugs 2 and 6, very clearly increases. Other drugs, most notably Drugs 12 and 15, are unaffected by the changes in the Drug 1 price. We have also performed these simulations in a model without the warning attributes, and we observe similar patterns here.

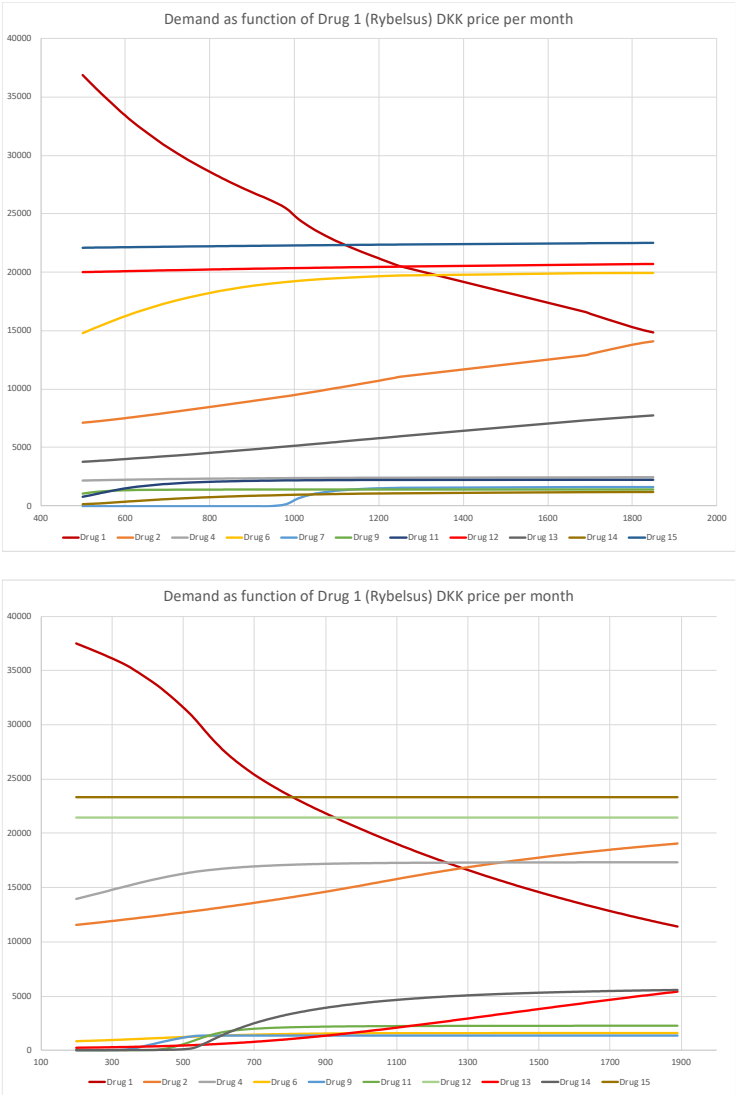


Figure 9 Demand as a function of possible Drug 1 prices in models with initial reallocations: multi-attribute model with payments (top) and multi-attribute model without warnings and with payments (bottom)

8. Conclusions

In this paper, we use benchmarking analysis and linear programming to evaluate how the introduction of a new product is likely to affect the demand for existing products. We assume that consumers evaluate the products by using linear (or log-linear) aggregations of the products' attributes. A consumer type can, therefore, be represented by its weight vector, i.e., by how much weight it places on the different attributes. When a user chooses a particular product, its preferences are partially revealed since they must be such that the chosen product is at least as favorable as all other products. We can in this way delineate the types of consumers that will prefer the different products. Linking this with the actual number of consumers buying a given product, we obtain

information about the density of consumer types in the weight space. We use this to investigate how the attributes of a new drug are likely to affect the demand for this drug and to determine which products will have their demand reduced. We illustrated our approach using information about diabetes drugs in Denmark.

Intuitively, a new drug is likely to be successful if it resembles already existing drugs with large demands, such that it can cannibalize on the large consumer bases of these drugs. At the same time, it is preferable if a new drug is placed in the "holes" between successful drugs since it can hereby limit competition and attract demand from several "neighboring" drugs at the same time.

There are several limitations to our approach and, therefore, interesting possible extensions of our work.

Our approach requires the calculation of volumes of polyhedral sets in multi-dimensional space. This sometimes leads to numerical problems if the attributes of different products are colinear. It would be worthwhile to explore alternative volume calculation approaches. One possibility would be to use bootstrapping-like procedures, i.e., by uniformly drawing random points from weight space and testing the share of such points that belong to the different polyhedral convex sets.

Our approach is usable for locating "new" product opportunities that are not substantially different from existing brands. One must recognize that brand preferences are, to a considerable extent, conditioned by the particular set of alternatives that have been available over a length of time. It will generally not be possible to infer the demand for radically new or novel products with this framework since we will have no way of extracting the revealed values of novel attributes.

Our approach is also very deterministic. We assume that consumers have perfect information and make fully rational and consistent decisions. Even when working with nine features, some of the existing drugs should not rationally attract demand. To better understand the challenges of real-world product placement situations, it may therefore be useful to extend the framework with uncertainty.

Another interesting extension would be to allow for some inertia in the choice of product. A simple idea would be to introduce the improvement thresholds that are necessary to trigger a change in the drug. This requires the introduction of more complicated preference structures, such as the outranking methods from MCDM.

Finally, it should be noted that only the evaluation of drugs with given attributes, including the role of the drug price, have been considered above. This is only part of the problem of actually developing a drug that fits optimally into an already crowded space of existing drugs. We do not consider the larger problem of developing a drug. Part of such an extension would be to make the drug attributes more actionable, i.e., to link product development actions with the attributes that consumers value the most.

Finally, a natural empirical extension of this work would be to analyze a panel dataset with product prices and demands over several years. In this way, we could test how efficient our procedure is to predict demand ex-ante. We could also use such an

approach to calibrate extensions of our framework. We could, for example, introduce inertia thresholds and determine how they should be calibrated to best understand the demand that cannot be directly rationalized with our present framework.

Literature

Agha, H., S. Arora, and N. Sevdalis (2011). Quantitative assessment of expert and novice surgeons' thinking processes: An application to hernia repair. *The American Journal of Surgery*, 202:110–115.

Angelis, A. and P. Kanavos (2017). Multiple Criteria Decision Analysis (MCDA) for evaluating new medicines in Health Technology Assessment and beyond: The Advance Value Framework. *Social Science & Medicine*, 188: 137-156. doi: 10.1016/j.socscimed.2017.06.024

Baltussen R, and L. Niessen (2006). Priority setting of health interventions: the need for multi-criteria decision analysis. *Cost Eff Resour Alloc*., 4: 1-9. doi: 10.1186/1478-7547-4-14.

Bogetoft, P. (2012). Performance Benchmarking – Measuring and Managing Performance, Springer New York.

Bogetoft, P., and L. Otto (2011). Benchmarking with DEA, SFA and R, Springer New York

Bogetoft, P., and P. Pruzan (1991). Planning with Multiple Objectives: Investigation, Communication and Choice, pp.1-367, North Holland

Charnes A., W.W. Cooper, and E. Rhodes (1978). Measuring the efficiency of decision making units. *European Journal of Operational Research* 2:429–444.

Charnes A., W.W. Cooper, and E. Rhodes (1979). Short Communication: Measuring the Efficiency of Decision Making Units. *European Journal of Operational Research* 3:339.

Cohen, J. B., and K. Basu (1987). Alternative models of categorization: Toward a contingent processing framework. *Journal of Consumer Research*, 13: 455–472.

Combris, P., S. Lecocq, and M. Visser (2000). Estimation of a hedonic price equation for Burgundy wine. *Applied Economics*, 32: 961–967.

Einhorn, H. J. (1970). The Use of Nonlinear, Noncompensatory Models in Decision Making. *Psychological Bulletin*, 73(3): 221-230.

Einform, H.J. and N.J. Gonedes (1971), An Exponential Discrepancy Model for Attitude Evaluation. *Behavioral Science*, 16(2): 152-157.

Feenstra, R. C. (1995). Exact hedonic price indexes. National Bureau of Economic Research.

Green, P. E., and Y. Wind (1973). Multiattribute decisions in marketing: A measurement approach. Hillsdale, IL: Dryden Press.

Hotelling, H. (1929). Stability in Copetition. *Economic Journal*, 39(153): 41–57, doi:10.2307/2224214

Juslin, P., L. Karlsson, and H. Olsson (2008). Information integration in multiple cue judgment: A division of labor hypothesis. *Cognition*, 106: 259–298.

Juslin, P., H. Olsson, and A.C. Olsson (2003). Exemplar effects in categorization and multiple-cue judgment. *Journal of Experimental Psychology: General*, 132(1): 133–156.

Kardes, F. R., S.S. Posavac, and M.L. Cronley (2004). Consumer inference: A review of processes, bases, and judgment contexts. *Journal of Consumer Psychology*, 14: 230–256.

Keeney, R. L., and H. Raiffa (1993). *Decisions with multiple objectives: Preferences and value trade-offs*. Cambridge, UK: Cambridge University Press.

Komorita, S. S., and B. Rosen (1972). Multidimensional Models for the Evaluation of Political Candidates. *Journal of Experimental Social Psychology*, 8(1): 58-73.

Kotler P. A Framework for Marketing Management. Prentice-Hall, 2002
Lynch, J. G. Jr. (1985). Uniqueness issues in the decompositional modeling of multiattribute overall evaluations: An information integration perspective. *Journal of Marketing Research*, 22: 1–19.
Marsh, K. L. (2014). Assessing the value of healthcare interventions using multi-criteria decision analysis: a review of the literature. *Pharmacoeconomics, 32*(4): 345–365.
Marsh K, e.a. (2016). Multiple Criteria Decision Analysis for Health Care Decision Making–Emerging Good Practices: Report 2 of the ISPOR MCDA Emerging Good Practices Task Force. *Value Health, 19*(2): 125–137.
Roberts, J.H. and G.L. (1988). Urban, Modeling Multiattribute Utility, Risk, and Belief Dynamics for New Consumer Durable Brand Choice. *Management Science* 34(2): 167-185.
Rotundo, M., and P.R. Sackett (2002). The relative importance of task, citizenship, and counterproductive performance to global ratings of job performance: A policy-capturing approach. *Journal of Applied Psychology*, 87: 66–80.
Samuelson, P. A. (1948). Consumption Theory in Terms of Revealed Preferences. *Economica, 15* (60): 243-253. https://doi.org/10.2307/2549561
Shocker, A. D., and V. Srinivasan (1979). Multiattribute approaches for product concept evaluation and generation: A critical review. *Journal of Marketing Research*, 16: 159–180.
Smith, E. E., and D.L. Medin (1981). Categories and concepts. Cambridge, MA: Harvard University Press.
Sujan, M. (1985). Consumer knowledge: Effects on evaluation strategies mediating consumer judgments. *Journal of Consumer Research*, 12: 31–46.
Sundhedsstyrelsen. (2019). Anbefalinger om lægemidler. *https://www.sst.dk/da/Viden/Laegemidler/Anbefalinger*.
Thrane, C. (2004). In defense of the price hedonic model in wine research. *Journal of Wine Research*, 15: 123–134.
Tirole, J. (1990). The Theory of Industrial Organization, MIT Press.
Troutman, C. M., and J. Shanteau (1976). Do consumers evaluate products by adding or averaging attribute information? *Journal of Consumer Research*, 3: 101–106.
Tversky, A. (1972). Elimination by Aspects: A Theory of Choice, *Psychological Review*, 79(4): 281-299.

R-packages:

RCDD
https://CRAN.R-project.org/package=rcdd

Geometry:
https://CRAN.R-project.org/package=geometry

Benchmarking:
https://CRAN.R-project.org/package=Benchmarking

Drug studies:

PIONEER (Rybelsus/oral semaglutide): https://www.clinicaltrials.gov/ct2/show/NCT02849080: Pieber TR, Bode B, Mertens A, Cho YM, Christiansen E, Hertz CL, Wallenstein SOR, Buse JB; PIONEER 7 investigators. Efficacy and safety of oral semaglutide with flexible dose adjustment versus sitagliptin in type 2 diabetes (PIONEER 7): a multicentre, open-label, randomised, phase 3a trial. Lancet Diabetes Endocrinol. 2019 Jul;7(7):528-539. doi: 10.1016/S2213-8587(19)30194-9. Epub 2019 Jun 9. Erratum in: Lancet Diabetes Endocrinol. 2019 Sep;7(9):e21.

SUSTAIN (Ozempic/semaglutide): https://clinicaltrials.gov/ct2/show/NCT04572165: Zinman B, Bhosekar V, Busch R, Holst I, Ludvik B, Thielke D, Thrasher J, Woo V, Philis-Tsimikas A. Semaglutide once weekly as add-on to SGLT-2 inhibitor therapy in type 2 diabetes (SUSTAIN 9): a randomised, placebo-controlled trial. Lancet Diabetes Endocrinol. 2019 May;7(5):356-367. doi: 10.1016/S2213-8587(19)30066-X. Epub 2019 Mar 1. Erratum in: Lancet Diabetes Endocrinol. 2019 Mar 11;:. Lancet Diabetes Endocrinol. 2019 Aug;7(8):e20. Lancet Diabetes Endocrinol. 2019 Nov;7(11):e22.

LEADER (Victoza/liraglutide): https://www.clinicaltrials.gov/ct2/show/NCT01179048?term=victoza+liraglutide+leader&draw=2&rank=2: Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JF, Nauck MA, Nissen SE, Pocock S, Poulter NR, Ravn LS, Steinberg WM, Stockner M, Zinman B, Bergenstal RM, Buse JB; LEADER Steering Committee; LEADER Trial Investigators. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2016 Jul 28;375(4):311-22. doi: 10.1056/NEJMoa1603827. Epub 2016 Jun 13.

DURATION (Bydureon/exenatide): https://clinicaltrials.gov/ct2/show/NCT00308139: Drucker DJ, Buse JB, Taylor K, Kendall DM, Trautmann M, Zhuang D, Porter L; DURATION-1 Study Group. Exenatide once weekly versus twice daily for the treatment of type 2 diabetes: a randomised, open-label, non-inferiority study. Lancet. 2008 Oct 4;372(9645):1240-50. doi: 10.1016/S0140-6736(08)61206-4. Epub 2008 Sep 7.

REWIND (Dulaglutide/ Trulicity): https://clinicaltrials.gov/ct2/show/NCT01394952 Gerstein HC, Colhoun HM, Dagenais GR, Diaz R, Lakshmanan M, Pais P, Probstfield J, Riddle MC, Rydén L, Xavier D, Atisso CM, Avezum A, Basile J, Chung N, Conget I, Cushman WC, Franek E, Hancu N, Hanefeld M, Holt S, Jansky P, Keltai M, Lanas F, Leiter LA, Lopez-Jaramillo P, Cardona-Munoz EG, Pirags V, Pogosova N, Raubenheimer PJ, Shaw J, Sheu WH, Temelkova-Kurktschiev T; REWIND Trial Investigators. Design and baseline characteristics of participants in the Researching cardiovascular Events with a Weekly INcretin in Diabetes (REWIND) trial on the cardiovascular effects of dulaglutide. Diabetes Obes Metab. 2018 Jan;20(1):42-49. doi: 10.1111/dom.13028. Epub 2017 Jul 14.

ELIXA
(Lyxumia/Lixisenatide): https://clinicaltrials.gov/ct2/show/NCT01147250: Muskiet MHA, Tonneijck L, Huang Y, Liu M, Saremi A, Heerspink HJL, van Raalte DH. Lixisenatide and renal outcomes in patients with type 2 diabetes and acute coronary syndrome: an exploratory analysis of the ELIXA randomised, placebo-controlled trial. Lancet Diabetes Endocrinol. 2018 Nov;6(11):859-869. doi: 10.1016/S2213-8587(18)30268-7. Epub 2018 Oct 3.

CARMELINA
(Linagliptin/trajenta): https://clinicaltrials.gov/ct2/show/NCT01084005 Rosenstock J, Perkovic V, Alexander JH, Cooper ME, Marx N, Pencina MJ, Toto RD, Wanner C, Zinman B, Baanstra D, Pfarr E, Mattheus M, Broedl UC, Woerle HJ, George JT, von Eynatten M, McGuire DK; CARMELINA® investigators. Rationale, design, and baseline characteristics of the CArdiovascular safety and Renal Microvascular outcomE study with LINAgliptin (CARMELINA(®)): a randomized, double-blind, placebo-controlled clinical trial in patients with type 2 diabetes and high cardio-renal risk. Cardiovasc Diabetol. 2018 Mar 14;17(1):39. doi: 10.1186/s12933-018-0682-3.

EXAMINE
(alogliptin/Vipidia): https://clinicaltrials.gov/ct2/show/NCT00968708: White WB, Bakris GL, Bergenstal RM, Cannon CP, Cushman WC, Fleck P, Heller S, Mehta C, Nissen SE, Perez A, Wilson C, Zannad F. EXamination of cArdiovascular outcoMes with alogliptIN versus standard of carE in patients with type 2 diabetes mellitus and acute coronary syndrome (EXAMINE): a cardiovascular safety study of the dipeptidyl peptidase 4 inhibitor alogliptin in patients with type 2 diabetes with acute coronary syndrome. Am Heart J. 2011 Oct;162(4):620-626.e1. doi: 10.1016/j.ahj.2011.08.004. Epub 2011 Sep 14.

SAVOR-TIME 53
(saxagliptinønglyza): https://www.clinicaltrials.gov/ct2/show/NCT01107886?term=SAVOR-TIMI+53&draw=2&rank=1 Scirica BM, Bhatt DL, Braunwald E, Steg PG, Davidson J, Hirshberg B, Ohman P, Frederich R, Wiviott SD, Hoffman EB, Cavender MA, Udell JA, Desai NR, Mosenzon O, McGuire DK, Ray KK, Leiter LA, Raz I; SAVOR-TIMI 53 Steering Committee and Investigators. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. N Engl J Med. 2013 Oct 3;369(14):1317-26. doi: 10.1056/NEJMoa1307684. Epub 2013 Sep 2.

VERIFY (Galvus/Vildagliptin): https://clinicaltrials.gov/ct2/show/NCT01528254:
V Lukashevich, A Schweizer, Q Shao, P-H Groop, W Kothny: Safety and efficacy of vildagliptin versus placebo in patients with type 2 diabetes and moderate or severe renal impairment: a prospective 24-week randomized placebo-controlled trial, Diabetes Obes Metab,
2011 Oct;13(10):947-54.
doi: 10.1111/j.1463-1326.2011.01467.x.

TECOS (Januvia/Sitagliptin): https://clinicaltrials.gov/ct2/show/NCT00790205 : Green JB, Bethel MA, Armstrong PW, Buse JB, Engel SS, Garg J, Josse R, Kaufman KD, Koglin J,

Korn S, Lachin JM, McGuire DK, Pencina MJ, Standl E, Stein PP, Suryawanshi S, Van de Werf F, Peterson ED, Holman RR; TECOS Study Group. Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2015 Jul 16;373(3):232-42. doi: 10.1056/NEJMoa1501352. Epub 2015 Jun 8. Erratum in: N Engl J Med. 2015 Aug 6;373(6):586.

DECLARE TIMI 58
(Forxiga/Dapagliflozin): https://www.clinicaltrials.gov/ct2/show/nct00736879: Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, Silverman MG, Zelniker TA, Kuder JF, Murphy SA, Bhatt DL, Leiter LA, McGuire DK, Wilding JPH, Ruff CT, Gause-Nilsson IAM, Fredriksson M, Johansson PA, Langkilde AM, Sabatine MS; DECLARE-TIMI 58 Investigators. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2019 Jan 24;380(4):347-357. doi: 10.1056/NEJMoa1812389. Epub 2018 Nov 10.

CANVAS
(Invokana/Canagliflozin): https://clinicaltrials.gov/ct2/show/NCT01032629 : Cefalu WT, Stenlöf K, Leiter LA, Wilding JP, Blonde L, Polidori D, Xie J, Sullivan D, Usiskin K, Canovatchel W, Meininger G. Effects of canagliflozin on body weight and relationship to HbA1c and blood pressure changes in patients with type 2 diabetes. Diabetologia. 2015 Jun;58(6):1183-7. doi: 10.1007/s00125-015-3547-2. Epub 2015 Mar 27.

EMPA-REG
(Jardiance/Empagliflozin): https://clinicaltrials.gov/ct2/show/NCT01131676?term=empa-reg&draw=2&rank=2 Roden M, Weng J, Eilbracht J, Delafont B, Kim G, Woerle HJ, Broedl UC; EMPA-REG MONO trial investigators. Empagliflozin monotherapy with sitagliptin as an active comparator in patients with type 2 diabetes: a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Diabetes Endocrinol. 2013 Nov;1(3):208-19. doi: 10.1016/S2213-8587(13)70084-6. Epub 2013 Sep 9.

Working title	Are Danish national reimbursement priorities worthwhile for patients? An investigation using the discrete choice experiment to elicit type 2 diabetes patient preferences for the benefit and risk of injectable anti-diabetic treatment.
Authors	Laila Starr, MSc, PhD Fellow [1, 2] Trine Kjær, Professor[3] Lill-Brith von Arx, MSc, PhD [4]
Author affiliations	[1] Department of Economics, Copenhagen Business School, Denmark [2] Department of Public Health, University of Copenhagen, Denmark [3] DaCHE – Danish Centre for Health Economics, Department of Public Health, University of Southern Denmark, Denmark [4] Institute of Applied Economics and Health Research (ApHER), Copenhagen, Denmark
Corresponding author	Laila Starr, Department of Economics, Porcelænshaven 16b, DK-2000 Frederiksberg, Denmark, +4529858597, lst@eco.cbs.dk
Target journal	Cost Effectiveness and Resource Allocation
Status	Draft – June 14 2021
Acknowledgment	Financial support for the study on which this manuscript is based was provided as part of a PhD research grant co-funded by the Danish Innovation Fund (Danish Ministry of Education) and Novo Nordisk A/S.

1 Introduction

In publicly funded health care systems, patients' access to medicines is regulated based on national reimbursement decisions and clinical guidelines. It has been debated whether the concept of value in health care needs to be extended beyond the current value framework e.g. by incorporating patients' preferences for treatment aspects not captured in the frequently used cost-effectiveness analysis (Brazier et al., 2009; Dirksen, 2014; Garrison et al., 2017; Mott, 2018; van Overbeeke et al., 2019). In Europe, Health Technology Assessment (HTA) institutions have acknowledged the value of patient preferences in the EUnetHTA collaboration. Nationally IQWIQ (Institute for Quality and Efficiency in Healthcare) in Germany and NICE (National Institute for Health and Care Excellence) in the UK have similarly considered patient preference elicitation methods in their assessment frameworks (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWIQ), 2014; National Institute for Health and Care Excellence (NICE), 2019; Ørtenblad et al. 2017; Bouvy et al., 2020). Driven by a universal goal to deliver patient-centered care, criteria for priority setting for access to medicines increasingly include patient aspects beyond the clinical aspects in the assessment of pharmaceuticals (Angelis et al., 2017; European Commission, 2017; Manafò et al., 2018; Mangin et al, 2016).

In order to provide patient-centered care, it is important that the priorities and preferences of the patients are recognized and acknowledged in the national clinical guidelines. Incorporating the patient's priorities and preferences into their treatment is found to not just improve the primary health outcome, but also the proximal health outcomes related to communication as the patient feels understood, respected and engaged in their own care (Arora et al., 2009; Little et al., 2001; Ruland, 1998; Stewart et al., 2011). Thus, by incorporating preferences into treatment choice, treatment failure/drug discontinuation is mitigated when choosing a treatment concordant with patient choice in the first place.

Additionally, empirical research on concordance between national drug reimbursement strategies and patient and public preferences for funding of high-cost medicines is scarce (MacLeod et al., 2016; Muhlbacher & Juhnke, 2013; Rogge & Kittel, 2016).

With this study, it is our aim to examine 1) if preference for treatment differ between type 2 diabetes patients with similar demographic structure but receiving different types of insulin

2) if the national clinical guidelines in Denmark for pharmacologically glucose-lowering treatment are in alignment with Danish diabetes patients' stated preferences for treatment.

2 Background

Incorporating patient aspects holds the promise of better targeting and improving efficiency of health technology. E.g., by understanding the segments of a disease population with most benefit of treatment in the presence of multiple therapeutic options. Diabetes is an example of a disease in which several treatment options exist within the same drug classes. This is the case for basal insulins in which two types are available: human insulins and insulin analogues (Table 1).

Table 1: Safety and Efficacy Characteristics of NPH, Glargine, Detemir and Insulin Aspart

	Basal insulin, long-acting			Rapid/intermediate acting insulin
	Human insulin	Insulin analogue		
	Insulatard / NPH	Lantus / Glargine	Levemir / Detemir	NovoMix / insulin aspart
Change in HbA1c	Less than other insulins	Good	Good	Good
Risk of hypoglycaemia	Present – higher than other insulins	Low	Low	Low
Risk of nocturnal hypoglyceamia	Present – higher than other insulins	Low	Low	Low
Risk of severe hypoglycaemia	Present – higher than other insulins	Low	Low	Low
Injection site reaction	Less than glargine	Possible because of acidic pH	Rare	Rare
Weight gain	yes	yes	no	no
Timing of administration	Once or twice or thrice daily	At the same time every day	Once or twice daily	Once to four times daily
Onset	1 to 2 hrs	1 ½ hrs	3 to 4 hrs	15 min
Peak	4 to 10 hrs	No peak time. Insulin is delivered at a steady level.	6-8 hrs	1 to 3 hrs
Duration	13-20 hrs	20-24 hrs	Up to 24 hrs	3 to 5 hrs

Sources: https://www.ema.europa.eu

Both types of basal insulin are prescribed to patients who cannot control their blood sugar levels with oral therapies alone. Human insulin came on the market in the 1980s and was for long the only treatment and thus the standard treatment when initiating insulin treatment (Dansk Selskab for Almen Medicin (DSAM) [Danish College of General Practitioners], 2014). Evidence from clinical trials suggests that basal human insulin and insulin analogues differ primarily in their ability to reduce glycemic levels without leading to hypoglycemic events in patients, especially nocturnal hypoglycemic events, as a result of the improved absorption characteristics of the insulin analogues (Kristensen et al., 2012). Basal insulin analogues are indicated for patients with frequent hypoglycemic events. In the national diabetes recommendations for the use of basal insulin, it is concluded that the risk of hypoglycemia generally is lower in patients treated with insulin glargine (Lantus®) and insulin detemir (Levemir®) (insulin analogues) compared to human insulin. Insulin aspart (NovoMix®) is a mixture of the intermediate acting (70 %) and rapid acting (30 %) insulins with the benefit that it start to work as quickly as the fastest-acting insulin in the combination, and will last as long as the longest acting insulin in the mix. It is further noted, that it is uncertain if insulin analogues benefit the main group of type 2 diabetes patients, or only those at increased risk for hypoglycemia (due to heart disease or reduced kidney function) (IRF, 2017).

Globally, insulin analogues are sold at higher list prices than their human counterpart. In Denmark, insulin analogues are sold at about double the price of human insulin with the prices for a WHO defined day-dose by January 2021 being approximately one and two US$ respectively, whereas in US list prices of insulin analogues are up to ten-fold that of human insulin.

Cost-effectiveness analysis are in many countries used to guide the reimbursement decisions (Allen et al., 2017). The cost-effectiveness of insulin analogues has been evaluated in several studies (Cameron & Bennett, 2009; Shafie et al., 2017) with the effectiveness component based on either clinical outcomes or quality-adjusted-life-years (QALY).

Determining the reimbursement status of a drug regulates patient access to prescription drugs in primary health care; if a drug is not reimbursed the uptake will be lower. A second way to regulate is to develop national clinical guidelines supporting prescribers in their

choice of pharmacological treatment within different disease areas by defining clinical criteria for drug prescription.

Institute for Rational Pharmacotherapy (IRF), at the Danish Health Authority (DHA), issues the National Recommendation List (NRL) to support clinicians in their choice of treatment, with no consideration of price or grant status. The Danish Medicines Agency (DMA), based on advice and economic assessment by the reimbursement committee at the DMA, decides on the reimbursement status of drugs. These may receive general or conditional reimbursement, meaning that a drug may be prescribed to certain patient groups only or for the treatment of specific diseases. If the medicine is used for other purposes, no reimbursement is awarded (Barnieh et al., 2014; Lægemiddelstyrelsen, 2017). The prescriber, supported by the national recommendation list, is the gatekeeper of patient access to prescription drugs with a general reimbursement status. Drug consumption is monitored through national statistics, and deviations of prescription patterns to the national recommendation list may lead to changes in the reimbursement status of drugs from general to conditional (Statens Serum Institut, 2012). In many cases, the national recommendation lists restrict the use of generally reimbursed drugs to certain subgroups based on clinical criteria. At the time of the study, DHA recommended the use of insulin analogues over human insulin for the subgroup of patients at increased risk for hypoglycemic events (e.g. previous symptomatic events of hypoglycemia, reduced kidney function, heart disease or long-term diabetes) (IRF, 2017). In cases of large post-prandial fluctuations in blood sugar, and susceptibility to nighttime hypoglycemic events, an insulin analogue combination product insulin aspart (NovoMix®), combining rapid and intermediate acting insulin aspart is recommended as an alternative to the intermediary acting human insulin (Henriksen et al., 2021).

When choosing whether a patient is to be prescribed to human insulin or insulin analogues, the patient's hypoglycemic events in the past or certain health conditions rendering patients at a particular risk of hypoglycemic events are taken into account. From a patient perspective, reducing the risk of hypoglycemia may be driven by personal circumstances beyond the clinical assessment of risk, and hypoglycemia is known to be a major concern in diabetes management regardless of previous experience (Kalra et al., 2013).

2 Research design and methods

Study Sample

Respondents were recruited through Funen's Diabetes Database, a disease registry established in the county of Funen, Denmark. All insulin users with type 2 diabetes in the registry were eligible for participation and were invited to participate in a questionnaire survey combining a discrete choice experiment (DCE) with self-reported information on health status and socioeconomic position. The survey reported in this paper was distributed to 2370 patients during the period September to November 2014. Disease registry data included: demographic data, diabetes history and clinical measures, BMI, blood pressure, lipoproteins, waist circumference, diabetes complications, and cardiovascular history. Laboratory analyses, including HbA_{1c}, were performed at local laboratories and automatically transferred to the registry. Other information was entered manually by healthcare professionals (Beck-Nielsen, 2014).

Discrete Choice Experiment

The DCE was developed to examine patient trade-off between the benefit- and risk aspects of injectable insulin. The decision context of the DCE was pharmacological diabetes treatment, evaluating preference for health outcomes such as HbA_{1c}, weight change and hypoglycemic events rather than medication features such as mode of administration.

The attributes and levels were developed on the basis of information gathered from qualitative research according to good practice guidelines (Bridges et al., 2011; von Arx & Kjær, 2014).

The definition of attribute levels was based on clinical and epidemiological data. The descriptive levels were based on treatment guidelines for the use of insulin, and insights were gained from seven one-to-one patient and specialist interviews and four focus group interviews with insulin users. Participants in the focus groups were recruited through a diabetes clinic at Hillerød Hospital, Denmark (von Arx et al., 2017).

The DCEs differed in their description of treatment effectiveness and side effects but were designed to ensure consistency concerning the differences patients would experience

clinically based on epidemiological data and responses from interviews, for example, information from patients on which terminology to use (Johnson et al., 2013).

The information gained from the focus group interviews also guided the inclusion of certain attributes which were found to be of relevance by the patients, such as weight loss which was included as an attribute to represent a clinical benefit. Risk attributes included side effects in terms of severe and non-severe hypoglycemic events determined by the support required to manage the event. Incremental heart attack risk was included as a possible treatment-inherent risk.

The attributes of treatment evaluated, and their levels, are shown in Table 2.

Table 2. Attributes and levels in the discrete choice experiment

Treatment attribute	Level
HbA_{1c} (%)	6.0 % (very good) 7.5 % (good) 8.5 % (moderate)
1-year weight change (Kg)	None -4 Kg -10 Kg
Risk increase of hearth attack due to treatment, per year	Yes (3 additional people of 1000) No (no risk increase)
Low blood sugar requiring assistance from others, per year	None 1 per year 2 per year
Self-managed low blood sugar, per months	1 event per month 4 events per month 8 events per month

Source: von Arx et al, 2017

Software (Ngene, ChoiceMetrics Pty Ltd, Sydney, Australia) was used to construct an unlabeled, Bayesian, D-efficient design. The resulting experimental design consisted of 12 questions with two alternative choice answers. An in-depth description of the qualitative pre-work and experimental design is reported elsewhere (von Arx et al., 2017).

Survey Instrument

The survey instrument, in which the DCE was included, contained 27 items covering the following domains: Diabetes self-management, treatment beliefs, sociodemographic

position, and health data not included in the registry. The self-administered survey was distributed, through the Funen Diabetes Database register, to patients by postal mail. Completed questionnaires were scanned by optic recognition scanning and the data combined with the clinical registry data by personal identifier number anonymized to the researcher.

Analysis

Respondents were stratified by type of basal insulin prescribed, generating four groups of patients; insulin glargine (Lantus®), insulin detemir (Levemir®), insulin aspart (NovoMix®) and human insulin (Insulatard®) users. The SAS ANOVA procedure was used to test for differences in demographic and health characteristics between the groups.

The analysis of the DCE is based on the random utility approach and in accordance with the utility maximizing principle (McFadden, 1974). It is assumed that the true but unobservable latent utility (U_{in}) for alternative *i* of individual *n* consists of two components,

$$(1) \qquad U_{in} = \beta X_{in} + \epsilon_{in}$$

Where U_{in} is the systematic component of utility depending upon the attributes of the alternatives X_{in} and the β parameter vector. ϵ_{in} is unobservable to the researcher and treated as a random component. We assume, that the random components ϵ_{in} are independent and identically distributed extreme value random variables leading to the specification of the conditional logit model (MNL) (McFadden, 1974).

Accordingly, the model to be estimated becomes;

$$(2) \qquad Ui = \beta_0 0 + \beta_1 GC + \beta_2 WL + \beta_3 HA + \beta_4 nonSHE + \beta_5 SHE$$

where β_0 is the alternative specific constant, and $\beta_{1\text{-}5}$ are the estimated preference weights (parameters) for each of the defined treatment attributes including glycemic control measured by HbA_{1c} (GC), weight Loss (*WL*), incremental heart attack risk (*HA*), non-severe (*nonSHE*) and severe hypoglycemic events (SHE). Separate logit models were estimated for human insulin and insulin analogue users respectively. Insulin glargine (Lantus®) and insulin detemir (Levemir®) were combined into one group after testing for differences in preferences between the two separate groups of basal insulin analogue users.

To test for differences in preferences across all user groups we set up the following null-hypothesis

$$H_0^1: \quad \beta^{Insulatard} = \beta^{Lantus,Levemor} = \beta^{Novomix}$$

where β is a vector of the parameters specified in Equation (2). If H_0 is rejected we can reject the joint hypothesis that preferences structures are identical across all three user groups. We also conducted pairwise comparisons across user groups according to the following null-hypothesis;

$$H_0^2: \quad \beta^{User\ group\ 1} = \beta^{User\ group\ 2}$$

In total this resulted in five test results.

The null-hypotheses were tested using a log-likelihood ratio test statistics (Swait & Louviere, 1993)

(3) $$LR = -2(LL_{Combined} - \sum LL_{Separate})$$

Here $LL_{combined}$ is the log-likelihood of the combined logit model (full sample) allowing for heterogeneity in the error variance. $\sum LL_{separate}$ is the sum of the log likelihoods of the separate models estimated for each of the three user subgroups.

To illustrate the relative-importance of attributes across the evaluated treatment scenarios, the reference category for all categorical attributes was coded to represent utility gain (i.e. the worst level is the omitted category) and the preference weights from this model rescaled so that the most highly preferred attribute level had a value of 10 and the least preferred attribute level had a value of zero (von Arx et al., 2017).

The second study objective, to examine if national recommendations for pharmacologically glucose-lowering treatment compare with Danish diabetes patients' stated preferences for treatment, was addressed by reviewing the most current national reimbursement and

clinical guidelines. This review targeted the indication for use, and reimbursement status, of human insulin and insulin analogues included in the study.

Data management, descriptive analysis and the estimation of choice models were performed using SAS for Windows 9.3. (SAS Institute Inc., Cary, NC, USA) and StataIC version 15.

3 Results

As seen in Table 3, 787 people responded to the survey. Participants' mean age is 67.1 years with the majority (n = 480, 61%) being males. The mean duration with diabetes is 15.6 years with a mean HbA1c of 7.6 %. A large portion of the respondents are in the obese category with a mean BMI of 31.8 kg/m2 and the majority (60%) has high blood pressure. Close to half of the respondents (45.5%) have not experienced any hypoglycemic events in the last week and only a few (4%) have experienced more than 6 events. The majority of respondents (79.9%) have never experienced a severe hypoglycemic event.

Table 3 Demography and health (*N*=787)

Characteristic		
Age (years) mean (SD)		67.1 (10.2)
Duration of diabetes (years), mean (SD)		15.6 (7.6)
Male sex, n (%)		480 (61.0)
BMI, mean (SD)		31.8 (6.2)
HbA1c (%), mean (SD)		7.6 (1.2)
High BP (>130/80 mmHg), n (%)		467 (60.0)
Smoker, n (%)		112 (14.5)
Hypoglycemic events, n (%)		
	Non-severe, the past week	
	None	266 (45.5)
	1 to 5	296 (51.0)
	More than 6	23 (4.0)
	Severe, in a lifetime, n (%)	
	None	463 (79.0)
	1	66 (11.3)
	More than 1	57 (9.7)
	Night time, in a lifetime, n (%)	268 (46.0)
Self-measured blood glucose, per week, n (%)		
	None/don't know	95 (12.3)
	1 to 6	326 (42.1)
	7 or more	354 (45.7)
Education		
	Primary school/high school	261 (37.0)
	Technical college	222 (31.5)
	Medium length (≤ 4 years)	181 (25.7)
	Higher education (≥ 5 years)	41 (5.8)
Household income (DKK)		

	Up to 149,000	283 (39.3)
	150,000 to 249,000	242 (33.6)
	250,000- 374,000	112 (15.6)
	375,000 and above	83 (11.5)
Labor market attached		161 (21.0)
		BMI body mass index CVD cardiovascular disease

Of the total study population with sufficient data available for choice analysis, 617 are basal, or combination, insulin users. The majority of these (65%) use human insulin (Insulatard®), 35% are insulin analogue users distributed on insulin aspart (NovoMix®) (18%), insulin glargine (Lantus®) (11%), insulin detemir (Levemir®) (6%) and respectively.

According to Table 4, there are some differences in patient characteristics across user groups with differences between groups observed for age and HbA_{1c} levels. Insulin analogue users monitor their blood sugar more frequent than human insulin users. Insulin aspart (NovoMix®) users are older (69.9±8.8 years) than users of insulin glargine (Lantus®), insulin detemir (Levemir®) or human insulin (Insulatard®) (64.9±12.1, 65.9±10.7 and 67.3±9.9 respectively).

Table 4 - Demographic structure of the population stratified by basal insulin use (n=617)

	Human insulin (Insulatard®)	Insulin glargine (Lantus®)	Insulin detemir (Levemir®)	Insulin aspart (NovoMix®)	P-value[a]
	N=399	N=66	N=40	N=112	
Age (years) mean (SD)	67.3 (9.9)	64.9 (12.1)	65.9 (10.7)	69.9 (8.8)	0.012
BMI, mean (SD)	31.9 (6.1)	32.3 (6.8)	31.1 (5.7)	31.6 (5.6)	0.773
HbA_{1c} (%), mean (SD)	7.6 (1.2)	8.0 (1.3)	7.9 (1.3)	7.5 (1.2)	0.033
Diabetes duration (years) mean (SD)	15.4 (7.7)	14.3 (6.0)	15.4 (5.7)	15.9 (72)	0.618
Hypoglycaemic events, n (%)					
Moderate, the past week					
None	136 (45.6)	21 (45.7)	11 (42.3)	44 (50.6)	0.806
One to 5	150 (50.4)	22 (47.8)	15 (57.7)	39 (44.8)	
More than 6	12 (4.0)	3 (6.5)	0 (0.0)	4 (4.6)	
Severe, in a lifetime					
None	242 (81.2)	36 (76.6)	16 (61.5)	68 (78.1)	0.191
Once	29 (9.7)	5(10.6)	7 (26.9)	12 (13.8)	
More than once	27 (9.1)	6 (12.8)	3 (11.5)	7 (8.1)	
Night-time hypoglycemic events, n (%)					
None	164 (55.0)	22 (47.9)	15(57.7)	34 (39.5)	0.069
One or more	134 (45.0)	24 (52.2)	11(42.3)	52 (60.5)	
Self-measured blood glucose, n (%)					0.045
Never	54 (13.3)	7 (10.5)	1 (2.4)	12 (10.8)	
1-7 per month	181 (44.7)	19 (28.3)	19 (46.3)	49 (44.1)	
8-21 times per month or more	170 (42.0)	41 (61.2)	21 (51.2)	50 (45.1)	
Education n (%)					

	Primary school/high school	139 (37.7)	19 (32.2)	9 (26.5)	42 (41.2)	0.585
	Technical college	113 (30.6)	18 (30.5)	15 (44.1)	33 (32.4)	
	Medium length (≤ 4 years)	96 (26.0)	19 (32.2)	10 (29.4)	22 (21.6)	
	Higher education (≥ 5 years)	21 (5.7)	3 (5.1)	0 (0.0)	5 (4.9)	

Differences in patient preferences

The log-likelihood for models allowing for heterogeneity in the error variance, applied in the Swait-Louviere test, is shown in Table 5.

Table 5 Log-likelihood test statistics

	Type of Insulin	Chi-square	Df	Probability	Outcome
H_0^1:	$\beta^{Insulatard} = \beta^{Lantus,Levemir} = \beta^{Novomix}$	30.52096	13	0.003959474	rejected
H_0^2:	$\beta^{Insulatard} = \beta^{Lantus,Levemir}$	10.4482	12	0.576702713	accepted
H_0^3:	$\beta^{Novomix} = \beta^{Lantus,Levemir}$	26.35596	12	0.009555072	rejected
H_0^4:	$\beta^{Insulatard} = \beta^{Novomix}$	14.51276	12	0.269168793	accepted
H_0^5:	$\beta^{Insulatard} = \beta^{Novomix,Levemir,Lantus,Levemir}$	3.6554	12	0.988883069	accepted
	Df Degrees of Freedom				

The hypothesis H_0^1 that respondents' preferences are identical regardless of type of insulin use (human insulin, basal insulin analogue or combination insulin analogue users) is rejected for insulin aspart (Novomix®) versus insulin glargine (Lantus®)/insulin detemir (Levemir®) users, in other words users of insulin aspart (Novomix®) and insulin glargine (Lantus®)/insulin detemir (Levemir®) have different preferences. Preferences are stable across all other comparisons including long-acting human insulin versus insulin analogue users.

Estimated beta-parameters for the evaluated aspects of treatment are shown in Table 6. All attributes are coded with the worst level as reference category. With the exception of a negative beta estimate for a weight loss of 10 kg, the parameter signs are consistent with the expectation of being positive, representing utility gains.

Table 6 Estimated parameters of the conditional logit models (95% confidence intervals in parenthesis) stratified by basal insulin use

		Human insulin (Insulatard®)		Insulin glargine (Lantus®) and insulin detemir (Levemir®)		insulin aspart (NovoMix®)	
Attribute	Level	β	[CI]	β	[CI]	β	[CI]
ASC		0.08*	[0.01;0.15]	0.04	[-0.08;0.17]	0.10	[-0.04;0.23]
HbA_{1c}	6.0 % (very good)	0.18***	[0.06;0.30]	0.13	[-0.08;0.35]	0.14	[-0.10;0.37]
	7.5 % (good)	0.20***	[0.09;0.31]	0.14	[-0.06;0.35]	0.10	[-0.12;0.32]
	8.5 % (moderate)	Ref	-	-	-	-	-
1-year weight loss	0 kg	Ref	-	-	-	-	-
	4 kg	0.15**	[0.03;0.26]	0.21**	[0.00;0.42]	-0.09	[-0.31;0.12]
	10 kg	-0.04	[-0.17;0.08]	-0.04	[-0.28;0.20]	-0.42***	[-0.66;-0.17]
Incremental HA risk per year[1]	Yes	Ref	-	-	-	-	-
	None	0.63***	[0.52;0.73]	0.43***	[0.23;0.63]	0.70***	[0.49;0.91]
Non-severe hypoglycaemia, events per month	1	0.57***	[0.44;0.70]	0.38*	[0.14;0.61]	0.62***	[0.37;0.87]
	4	0.30***	[0.20;0.41]	0.19	[0.00;0.38]	0.38***	[0.17;0.59]
	8	Ref	-	-	-	-	-
Severe hypoglycaemia,	None	1.04***	[0.91;1.17]	1.10***	[0.86;1.34]	0.93***	[0.68;1.19]
Events per month	1	0.49***	[0.38;0.60]	0.51***	[0.30;0.71]	0.45***	[0.23;0.66]
	2	Ref	-	-	-	-	-
Log-likelihood (restricted)[2]		-2386.1		-695.4		-619.2	

Notes. 95% confidence intervals in parenthesis. ASC, alternative specific constant. HA, heart attack

* P ≤ 0.05; ** P ≤ 0.01; *** P ≤ 0.001.

Based on the estimated coefficients, the relative importance of level changes of treatment attributes is shown in Table 7.

Table 7 Relative importance[1] of level changes of treatment attributes (95%CI) stratified by basal and combination insulin medication

	Human insulin (Insulatard®) (n=547)	Insulin glargine (Lantus®) /insulin detemir (Levemir® (n=150)	Insulin aspart (NovoMix®) (n=155)
None versus 2 severe hypoglycemic events (per year)	10.0 (8.8-11.2)	10.0 (7.9-12.1)	10.0 (8.1-11.9)
No versus 0.003% annual incremental heart attack risk	6.2 (5.2-7.2)	4.1 (2.3-5.8)	8.3 (6.7-9.8)
One versus 8 non-severe hypoglycemic events (per month)	5.6 (4.5-6.8)	3.6 (1.5-5.7)	7.7 (5.8-9.5)
One versus 2 severe hypoglycemic events (per year)	4.9 (3.9-5.9)	4.8 (3.0-6.5)	6.4 (4.8-8.0)
Four versus 8 non-severe hypoglycemic events (per month)	3.2 (2.2-4.1)	2.0 (0.3-3.7)	5.9 (4.4-7.4)
Good glycemic control vs.moderate (HbA_{1c} of 7.5 vs 8.5%))(8.5%)	2.2 (1.2-3.3)	1.5 (-0.3-3.3)	3.8 (2.2-5.4)
Very good glycemic control vs.moderate (HbA_{1c} of 6.0 vs 8.5%)	2.1 (1.0-3.1)	1.5 (-0.4-3.4)	4.1 (2.3-5.8)
4 Kg weight loss versus no weight change	1.8 (0.7-2.8)	2.1 (0.3-4.0)	2.4 (0.8-4.0)
10 kg weight loss versus no weight change	0.0 (-1.2-1.2)	0.0 (-2.1-2.1)	0.0 (-1.8-1.8)

Relative attribute importance, on a scale from 0 to 10, over the evaluated choice scenarios. The highest rescaled coefficient value and 95% confidence interval within each attribute is shown

Avoiding severe hypoglycemic events and an incremental heart attack risk are drivers of preference for treatment across all groups of insulin users. Basal insulin analogue ((insulin glargine (Lantus®) and insulin detemir (Levemir®)) users prefer avoidance of frequent non-severe hypoglycemic events over avoidance of an incremental heart attack risk. Glycemic control (HbA_{1c} reduction) is preferred over weight loss in all groups of users, as shown in figure 1.

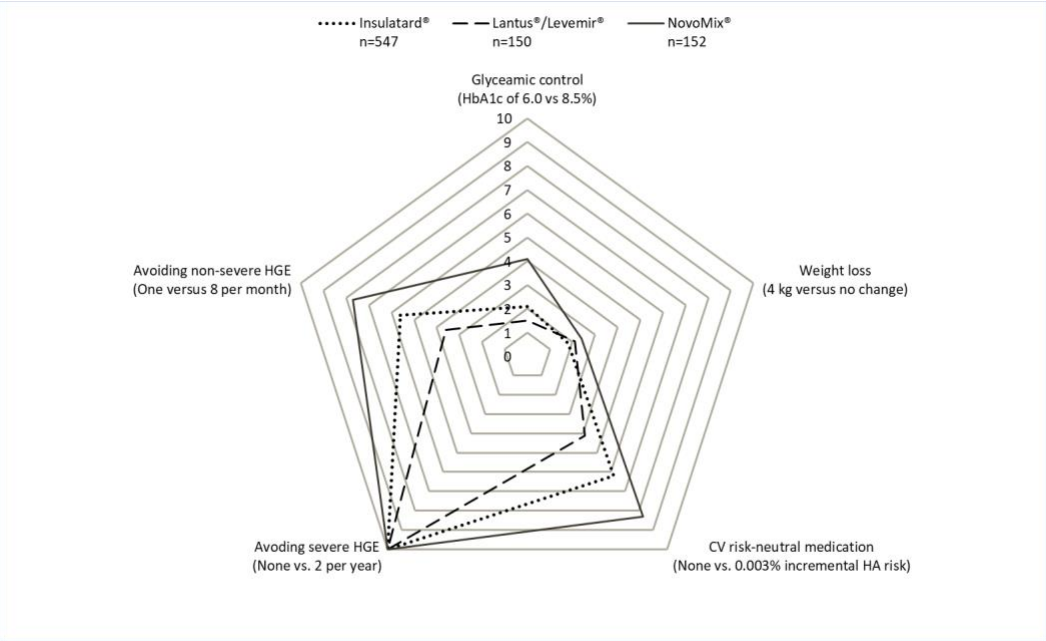


Figure 1 Rescaled (zero to 10) preference for diabetes treatment outcomes among basal insulin users. Rescaled beta-estimates for best level within each attribute is shown (for weight loss 4 and not 10 kg is shown).

HA heart attack *HGE* hypoglycaemic events, *CV* cardiovascular

Concordance between national recommendations and patient preferences

In general, respondents prefer treatments characterized by their safety profile: This means that most respondents prefer a medication with no severe hypoglycemic events, maximum one monthly self-managed hypoglycemic event, no incremental risk of heart attack, providing good (in relation to very good and moderate) glycemic control, and moderate weight loss (no more than 4 kilo) (See Table 1 for an overview of the safety and efficacy characteristics of the products). Users of insulin aspart (NovoMix®) and human insulin (Insulatard®) are less driven by individual risk aspects of treatment, whereas basal insulin analogue users (insulin detemir (Levemir®)) and insulin glargine (Lantus®)) gravitate towards avoiding severe hypoglycemic events relative to other risk aspects of treatment.

It is found, that the national diabetes treatment recommendations in Denmark at the time of drug prescription in this study are concordant with patient preference for treatment, for

patients prescribed to basal insulin analogues, but not human basal insulin users. Those prescribed to human insulin have equal preference for avoiding hypoglycemic events as the group of patients prescribed to basal insulin analogues. Treatment with combination insulin analogues (a mix between long and fast acting insulin) is recommended to people with diabetes at risk of hypoglycemia and with fluctuating post-prandial blood glucose levels. This is consistent with the difference in preference structure found between the basal insulin user group and combination insulin users. The latter do not trade-off glycemic control to the same extent as basal insulin users to avoid hypoglycemic events.

4 Discussion

In the Danish national diabetes treatment guidelines, patients are stratified by their clinical risk of hypoglycemic events. In our study, patients, regardless of which insulin they were prescribed, prefer treatments that lowers the risk of hypoglycemic events. A wide array of options are available for the treatment of hyperglycemia in type 2 diabetes patients. The newer generation of insulin analogues offer replacement strategies to human insulin, which is reflected in an increased prescription of insulin analogues in Denmark during the past decade (Statens Serum Institut, 2012). At the time of the study, most Danish type 2 diabetes patients were treated with human insulin (Statens Serum Institut, 2012) – in our sample 60%.

Since 2013 a number of new insulins have been introduced to the Danish market, hereunder the long-acting insulin degludec in late 2013 and a couple of biosimilar insulin analogues since 2016 (medicinpriser.dk, 2021; Agirrezabal, et al., 2020). This has had an impact on the treatment price and patterns, and hence the market share of the products. In general, more patients now, compared to when we collected our data, are treated with either short-acting insulins, such as insulin aspart, or long-acting insulins such as insulin glargine and insulin degludec. Furthermore, the number of patients on human insulin has halved and the number of patients on degludec has been reduced to only a third. Insulin aspart has driven the increased use of short-acting insulins, insulin glargine has increased its market share with more than 50 %, and the new product insulin degludec has obtained a 40% share of the long-acting insulin market (medstat.dk, 2021).

In 2019, DMA re-evaluated reimbursement status for treatment of diabetes including insulins. The evaluation stated that the most recent studies have shown there is a greater risk of hypoglycaemia when treated with Neutral Protamine Hagedorn (NPH) insulin compared to the long-acting insulin analogues. In addition, the treatment price for NPH insulin in pre-filled pen, which is primarily used, is higher than the cheapest basal insulin. Therefore, DMA concluded, that the other types of insulin are preferred over NPH insulin for patients at increased risk of hypoglycaemia, for example, previous symptomatic hypoglycaemia, renal impairment, heart disease or long-term diabetes. DMA further notes, that due to lack of long-term data in relation to the risk of cardiovascular events, insulin detemir (Levemir®) is only recommended in special cases, when other recommended insulins are not suitable. (Lægemiddelselstyrelsen, 2019). Despite this, insulin detemir still has the general reimbursement status. It can be noted that the recommendations have not had the intended effect when the reimbursement status does not follow the recommendations.

Although not significant, there is a tendency towards a stronger preference for a low-risk of hypoglycemic events among basal insulin analogue users. This is supported by the result of log-likelihood ratio test with differences in preferences observed between basal insulin analogue and insulin aspart (NovoMix®) users. Patients prescribed to insulin aspart (NovoMix®) have higher preferences towards avoiding minor as well as major hypoglycemic events, but not at the expense of an increased risk of heart attacks or good glycemic control.

Insulin aspart (NovoMix®) is being prescribed to patients who are experiencing difficulties in controlling their HbA_{1c}, are experiencing high fluctuations in glycose level after meals or to patients who have experienced nocturnal hypoglycemic events (Henriksen et al., 2021). Patients on insulin aspart (NovoMix®) are found to be older than users of the other modern insulins.

In Denmark, citizen's primary access point to the health care system is the general practitioner, and the general practitioner has the responsibility for the majority of drug prescriptions in Denmark. Therefore, general practitioners also play a vital role in ensuring that patients are prescribed to the adequate medications and understand proper usage.

Clinicians, including the general practitioner, demonstrate a wide variation in the choice and sequence of medications prescribed for diabetes management (Grant et al., 2007): On top of the objective patient clinical data e.g. age, glucose-level and frequency of hypoglycemia, the subjective patient factors such as adherence behavior or motivation by the patient can play a role when the clinician is to decide on the medication to prescribe. Additionally, factors like medical cost or the clinician's usual or prior practice and official guidelines might be factors that influence the prescription process.

Diabetes patients in our study are relatively old, with long-term diabetes. The majority of respondents have had diabetes for more than 15 years. One hypothesis is that with increased age it becomes harder to make behavioral changes, and age could thus be a factor in the resistance and motivation to change medication, as stability and regularity of the everyday life might weigh heavier than a potential slight improvement in the efficacy when considering changing medical behavior. This may be amplified, if the patient is currently experiencing only minor problems with blood sugar control, making the motivation for change very low. Therefore, both diabetes patient's own attitudes and the attitudes that others have, e.g., clinicians, can influence behavior. However, based on patient preference for treatment, insulin analogues more closely mimic the preferred benefit-risk profile of patients.

Motivation for changing to a new medication is thus both consisting of the cognitive (utilitarian) and affective (emotional) consequences of making a choice. Furthermore, the decision making process for drugs is not simply a sum of its benefits and safety attributes, but might show components which are functional as well as emotional, i.e. trustworthiness to the brand, loyalty to a medication and reluctance to change if clinicians and patients are satisfied with the current medication (Loewenstein, 2005).

Decision making is immensely complex and ideally rests on concordance between clinical judgement, patient preference for treatment and mutual agreement on the patient's ability to follow the prescribed regiment. In the general practitioner's gatekeeper role, there can be conflicts between the individual patient's wishes and the professional or/and resource considerations, but increasingly patient-related factors such as adherence and preferences are considered important. The endorsement of national priorities in the group of insulin

analogue users may reflect a high degree of shared medical decision making between clinicians and patients in the group of patients receiving insulin analogues. Although the demand for hypoglycemic event risk-lowering diabetes treatment seems to exceed what is accommodated within the health care system, the prescription patterns indicate some correlation between national priority setting and patient preference for diabetes treatment.

It has been an ongoing debate whether analogue insulins provide enough clinical benefit compared with human insulins to justify the higher cost (Grunberger, 2014) and real world evidence suggest that type 2 diabetes patients treated with insulin analog drugs do not have substantially better outcomes than those treated with less expensive human insulin (Lipska et al., 2018). Thus, in alignment with the national recommendations from IRF (IRF, 2017) many patients are likely to receive satisfying clinical results with human insulin. Fear of hypoglycemic events is subjective, and in many cases not related to previous experience. In some studies, hypoglycemic fear is found to be stronger in those with no previous experience as compared to those having experienced an event of low blood sugar which could be self-managed, but not in the case of severe events, requiring help from others (Hauber et al., 2009; Lloyd et al., 2011). With the introduction of more insulin alternatives and a lower price for many established diabetes products, more patients are prescribed a product with a low-risk profile for hypoglycaemic events in concordance with patients' preferences.

Limitations

This is a cross-sectional study, and caution should be made indicating causal mechanisms; We cannot with certainty state whether the patient's preferences are a result of the medication that the patient is on or whether the preferences are due to adaptation of use. This means that glycemic control and frequency of hypoglycemic events reported in this paper have no relation to clinical reality and medical decision making at the time of prescribing the current treatment to patients. Another limitation of this study is the small number of patients in the group of basal insulin analogue users (n=150) and combination insulin (n=155) versus the group of patients receiving human insulin (n=547). Attention was

given to the variance in the logit models, and the insulin glargine (Lantus®) and insulin detemir (Levemir®) user group was grouped to reduce the variance in beta estimates.

New products are frequently added to the cascade of diabetes products, and since the data was collected in 2013 a new generation of ultra-long-acting basal insulins has been added to the treatment options which going forward might make substantial changes to the market uptake of the other products.

5 Conclusion

Although the demand for diabetes treatments with a low-risk for hypoglycemic events seem to exceed what is provided by the health care system, our study has found that while the prescription patterns indicate some correlation between national priority setting and patient preference for diabetes treatment, the patients in our study did not all receive the treatment with the most optimal hypoglycemic profile.

Two-thirds of the respondents were prescribed human insulin, and the patient's treatment preferences for human insulin users are driven by a wish to avoid severe hypoglycemic events. This indicates that the demand for hypoglycemic event risk neutral medication exceeds what was provided by the Danish health care system. However, with the introduction of more alternative and cheaper options, more patients are now on long-acting insulin with a long-risk profile for hypoglycaemic events. Hence, there seem to be a better concordance between patient preferences and their actual prescribed medication now.

Literature

Agirrezabal, I., Sánchez-Iriso, E., Mandar, K., & Cabasés, J. M. (2020). Real-World Budget Impact of the Adoption of Insulin Glargine Biosimilars in Primary Care in England.Diabetes Care, 43(8), 1767-1773.

Allen, N., Walker, S. R., Liberti, L., & Salek, S. (2017). Health Technology Assessment (HTA) Case Stud- ies: Factors Influencing Divergent HTA Reimbursement Recommendations in Australia, Can- ada, England, and Scotland. Value in Health, 20(3), 320-328. doi:https://doi.org/10.1016/j.jval.2016.10.014

Angelis, A., Lange, A., & Kanavos, P. (2017). Using health technology assessment to assess the value of new medicines: results of a systematic review and expert consultation across eight Euro- pean countries. *Eur J Health Econ*. doi:10.1007/s10198-017-0871-0

Arora, N. K., Weaver, K. E., Clayman, M. L., Oakley-Girvan, I., & Potosky, A. L. (2009). Physicians' deci- sion-making style and psychosocial outcomes among cancer survivors. *Patient Educ Couns, 77*(3), 404-412. doi:10.1016/j.pec.2009.10.004

Barnieh, L., Manns, B., Harris, A., Blom, M., Donaldson, C., Klarenbach, S., . . . Clement, F. (2014). A synthesis of drug reimbursement decision-making processes in organisation for economic co- operation and development countries. *Value in Health, 17*(1), 98-108. doi:10.1016/j.jval.2013.10.008

Beck-Nielsen, H. (2014). Shared-Care. Presentation given at the HOPE (European Hospital and Healthcare Federation) exchange programme 2010. Retrieved from http://www.hope-ag- ora.eu/archives-2/hope-agora-2010/

Bouvy, J.A., Cowie, L., Lovett, R., Morrison, D., Livingstone, H., Crabb, N. (2020). Use of Patient Prefer- ence Studies in HTA Decision Making: A NICE Perspective. *The Patient – Patient-Centered Outcomes Research*, 13, 145-149

Brazier, J. E., Dixon, S., & Ratcliffe, J. (2009). The role of patient preferences in cost-effectiveness analysis: a conflict of values? *Pharmacoeconomics, 27*(9), 705-712. doi:10.2165/11314840- 000000000-00000

Bridges, J. F., Hauber, A. B., Marshall, D., Lloyd, A., Prosser, L. A., Regier, D. A., Johnson, F. R., & Mauskopf, J. (2011). Conjoint analysis applications in health—a checklist: A report of the ISPOR Good Research Practices for Conjoint Analysis Task Force. *Value in Health, 14*, 403–13.

Cameron, C. G., & Bennett, H. A. (2009). Cost-effectiveness of insulin analogues for diabetes mellitus. *CMAJ, 180*(4), 400-407. doi:180/4/400 [pii];10.1503/cmaj.081180 [doi]

Dansk Selskab for Almen Medicin (DSAM) [Danish College of General Practitioners]. (2014, 2014). Guidelines for type 2-diabetes. En fælles behandlingsvejledning med

enslydende kliniske be- handlingsmål. . Retrieved from http://www.dsam.dk/files/11/diabetesbehandling.pdf

Dirksen, C. D. (2014). The use of research evidence on patient preferences in health care decision- making: issues, controversies and moving forward. *Expert Review of Pharmacoeconomics & Outcomes Research, 14*(6), 785-794. doi:10.1586/14737167.2014.948852

European Commission. (2017). Mapping of HTA methodologies in EU and Norway. Retrieved from https://ec.europa.eu/health/sites/health/files/technology_assessment/docs/2018_map- ping_methodologies_en.pdf

Garrison, L. P., Kamal-Bahl, S., & Towse, A. (2017). Toward a Broader Concept of Value: Identifying and Defining Elements for an Expanded Cost-Effectiveness Analysis. *Value in Health, 20*(2), 213-216. doi:https://doi.org/10.1016/j.jval.2016.12.005

Grant, R. W., Wexler, D. J., Watson, A. J., Lester, W. T., Cagliero, E., Campbell, E. G., & Nathan, D. M. (2007). How Doctors Choose Medications to Treat Type 2 Diabetes - A national survey of spe- cialists and academic generalists. *Diabetes Care, 30*(6).

Grunberger, G. (2014). Insulin Analogs—Are They Worth It? Yes! *Diabetes Care, 37*(6), 1767-1770. doi:https://doi.org/10.2337/dc14-0031

Hauber, A. B., Mohamed, A. F., Johnson, F. R., & Falvey, H. (2009). Treatment preferences and medi- cation adherence of people with Type 2 diabetes using oral glucose-lowering agents. *Diabet Med, 26*(4), 416-424. doi:DME2696 [pii];10.1111/j.1464-5491.2009.02696.x [doi]

Henriksen, J. E., Nielsen, O. H., Beck-Nielsen, H., & Endokrinologisk Afdeling M. (2021) Insulinbehand- ling- OUH. Retrieved from http://www.sydvestjysksygehus.dk/wm441235

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWIQ). (2014). Patientenpräferen- zen mithilfe von Conjoint Analysis ermitteln [Examining patient preferences with conjoint analysis].

IRF. (2017). *Den Nationale Rekommendationsliste: Farmakologisk glukosesænkende behandling af type-2 diabetes*. Retrieved from https://www.sst.dk/da/viden/laegemidler/anbefalin- ger/den-nationale-rekommandationsliste-_nrl_/farmakologisk-glukosesaenkende- behandling-af-type-2-diabetes

Kalra, S., Mukherjee, J. J., Venkataraman, S., Bantwal, G., Shaikh, S., Saboo, B., . . . Ramachandran, A. (2013). Hypoglycemia: The neglected complication. *Indian Journal of Endocrinology and Me- tabolism, 17*(5), 819-834. doi:10.4103/2230-8210.117219

Kristensen, P. L., Pedersen-Bjergaard, U., Beck-Nielsen, H., Norgaard, K., Perrild, H., Christiansen, J.
S., . . . Tarnow, L. (2012). A prospective randomised cross-over study of the effect of insulin analogues and human insulin on the frequency of severe hypoglycaemia in patients with type 1 diabetes and recurrent hypoglycaemia (the HypoAna trial): study rationale and design. *BMC Endocr. Disord, 12*, 10. doi:1472-6823-12-10 [pii];10.1186/1472-6823-12-10 [doi]

Lægemiddelstyrelsen. (2017). The Reimbursement Committee. Retrieved from https://laege-middelstyrelsen.dk/en/reimbursement/reimbursement-committee/

Lægemiddelstyrelsen. (2019). Høringsversion – Revurdering af tilskudsstatus for insuliner. https://la- egemiddelstyrelsen.dk/da/nyheder/2019/hoering-om-medicintilskudsnaevnets-for- slag-til-tilskudsstatus-for-insuliner/~/me-dia/31B8136AA557421BBA6CA9FD805D8302.ashx

Lipska, K. J., Parker, M. M., Moffet, H. H., Huang, E. S., & Karter, A. J. (2018). Association of Initiation of Basal Insulin Analogs vs Neutral Protamine Hagedorn Insulin With Hypoglycemia-Related Emergency Department Visits or Hospital Admissions and With Glycemic Control in Patients With Type 2 Diabetes. *JAMA, 320*(1), 53-62. doi:10.1001/jama.2018.7993

Little, P., Everitt, H., Williamson, I., Warner, G., Moore, M., Gould, C., . . . Payne, S. (2001). Observa- tional study of effect of patient centredness and positive approach on outcomes of general practice consultations. *Bmj, 323*(7318), 908-911.

Lloyd, A., Nafees, B., Barnett, A. H., Heller, S., Ploug, U. J., Lammert, M., & Bogelund, M. (2011). Will- ingness to pay for improvements in chronic long-acting insulin therapy in individuals with type 1 or type 2 diabetes mellitus. *Clin Ther, 33*(9), 1258-1267. doi:S0149-2918(11)00509-1 [pii];10.1016/j.clinthera.2011.07.017 [doi]

Loewenstein, G. (2005). Hot-cold empathy gaps and medical decision making. *Health Psychol, 24*(4 Suppl), S49-56. doi:10.1037/0278-6133.24.4.s49

MacLeod, T. E., Harris, A. H., & Mahal, A. (2016). Stated and Revealed Preferences for Funding New High-Cost Cancer Drugs: A Critical Review of the Evidence from Patients, the Public and Pay- ers. *Patient, 9*(3), 201-222. doi:10.1007/s40271-015-0139-7

Manafò, E., Petermann, L., Vandall-Walker, V., & Mason-Lai, P. (2018). Patient and public engage- ment in priority setting: A systematic rapid review of the literature. *PloS one, 13*(3), e0193579-e0193579. doi:10.1371/journal.pone.0193579

Mangin, D., Stephen, G., Bismah, V., & Risdon, C. (2016). Making patient values visible in healthcare: a systematic review of tools to assess patient treatment priorities and preferences in the context of multimorbidity. *BMJ Open, 6*(6), e010903. doi:10.1136/bmjopen-2015-010903

McFadden, D. (1974). Conditional logit analysis of qualitative choice behavior. In P. Zarembka (Ed.), *Frontiers in econometrics* (pp. 105-142). New York: Academic Press. (Reprinted from: Not in File).

Medicinpriser.dk, data retrieved 2021. Medstat.dk, data retrieved 2021.

Mott, D. J. (2018). Incorporating Quantitative Patient Preference Data into Healthcare Decision Mak- ing Processes: Is HTA Falling Behind? *The Patient - Patient-Centered Outcomes Research, 11*(3), 249-252. doi:10.1007/s40271-018-0305-9

Muhlbacher, A. C., & Juhnke, C. (2013). Patient preferences versus physicians' judgement: does it make a difference in healthcare decision making? *Appl. Health Econ Health Policy, 11*(3), 163- 180. doi:10.1007/s40258-013-0023-3 [doi]

National Institute for Health and Care Excellence (NICE). (2019). NICE provides first scientific advice on patient preference study design. Retrieved from https://www.nice.org.uk/news/arti- cle/nice-provides-first-scientific-advice-on-patient-preference-study-design

Rogge, J., & Kittel, B. (2016). Who Shall Not Be Treated: Public Attitudes on Setting Health Care Priori- ties by Person-Based Criteria in 28 Nations. *PloS one, 11*(6), e0157018-e0157018. doi:10.1371/journal.pone.0157018

Ruland, C. M. (1998). Improving patient outcomes by including patient preferences in nursing care. *Proc AMIA Symp*, 448-452.

Shafie, A. A., Ng, C. H., Tan, Y. P., & Chaiyakunapruk, N. (2017). Systematic Review of the Cost Effec- tiveness of Insulin Analogues in Type 1 and Type 2 Diabetes Mellitus. *Pharmacoeconomics, 35*(2), 141-162. doi:10.1007/s40273-016-0456-2

Statens Serum Institut. (2012). *Flere diabetikere kommer i behandling med dyre lægemidler*. Re- trieved from ssi.dk

Stewart, R. J., Caird, J., Oliver, K., & Oliver, S. (2011). Patients' and clinicians' research priorities. *Health expectations : an international journal of public participation in health care and health policy, 14*(4), 439-448. doi:10.1111/j.1369-7625.2010.00648.x

Swait, J., & Louviere, J. (1993). The Role of the Scale Parameter in the Estimation and Comparison of Multinomial Logit Models. *Journal of Marketing Research (JMR), 30*(3), 305.

van Overbeeke, E., Whichello, C., Janssens, R., Veldwijk, J., Cleemput, I., Simoens, S., . . . Huys, I. (2019). Factors and situations influencing the value of patient preference studies along the medical product lifecycle: a literature review. *Drug Discovery Today, 24*(1), 57-68. doi:https://doi.org/10.1016/j.drudis.2018.09.015

von Arx, L. B., & Kjær, T. (2014). The patient perspective of diabetes care: Asystematic review of stated preference research. *Patient, 7*, 283–300.

von Arx, L. B., Johnson, F. R., Morkbak, M. R., & Kjaer, T. (2017). Be Careful What You Ask For: Effects of Benefit Descriptions on Diabetes Patients' Benefit-Risk Tradeoff Preferences. *Value in Health, 20*(4), 670-678. doi:10.1016/j.jval.2016.11.023

Ørtenblad, L., Jensen, L., & Lo Scalzo, A. (2017). EUnetHTA: Patients' Perspectives in the HTA Core Model®. In (pp. 289-298).

Value-Based Healthcare Classification and Experiences in Denmark

Laila Starr
lks@sund.ku.dk

Karsten Vrangbæk
kavr@sund.ku.dk

University of Copenhagen
Department of Public Health
Section of Health Service Research

2021

EIT Health is supported by the EIT,
a body of the European Union

Laila Starr & Karsten Vrangbæk: *Value-Based Health Care Classification and Experiences in Denmark,*
University of Copenhagen, Department of Public Health, Section of Health Service Research
European Institute of Innovation and Technology (EiT Health),
Published: 2021

ISBN: 978-87-92356-01-7

This study was supported by Integrated Personalised Diabetes Management goes Europe (iPDM-GO), a European Innovation project supported by EiT Health. EiT Health is supported by the EIT, a body of the European Union (euhealth.eu).

Table of Contents

Introduction

Increasing health expenditures are a challenge in all industrialised countries. Demographic transitions, rising expectations and new, expensive health technologies have led to higher demand, whereas stagnating economies have led to financial constraints[1]. Furthermore, significant variations in service quality have been observed in several countries.

Many different measures have been suggested to address such challenges. One of the most promising includes developing a stronger focus on value creation in health care and reorganising payment mechanisms to support this. *Value-based health care* (*VBHC*) is a framework that aims to encapsulate such ideas. It has gained significant international attention since Michael E. Porter and Elizabeth Olmsted Teisberg introduced the concept in the article: *Redefining Health Care: Creating Value-Based Competition on Results* [2]. VBHC makes the delivery of improved health outcomes for the same or at lower costs, the primary objective of the health care system. In this sense, VBHC is clearly aligned with traditional health economics. Yet, perspectives on value chains and measuring points go beyond most health economic frameworks and open up a range of questions in regard to the interpretation and practical implementation in specific health system contexts.

In Porter's terminology, it is important to assess the value from a patient standpoint and to evaluate costs and gains in a long-term perspective, including prevention, intervention, and follow-up. This assessment of costs and benefits of the entire treatment trajectory for each individual patient should be supported by an incentive structure where payments are linked to results in terms of value for patients.

[1] Regioner, D. (2015). Pres på sundhedsvæsenet: derfor stiger sygehusudgifterne – sådan holder vi væksten nede. https://www.regioner.dk/media/2209/2015-pres-paa-sundhedsvaesenet.pdf.
[2] Porter M.E & Lee, T. (October 2013). The Strategy That Will Fix Health Care. https://hbr.org/2013/10/the-strategy-that-will-fix-health-care.

VBHC promises to provide benefits for patients and the health care system in several ways. Patient outcomes can potentially be improved if more attention is paid to clinical value and the documented effects of pharmaceuticals and treatments. Financial impact may be reduced if purchasers, pharmaceutical manufactures and health care providers share the risk for suboptimal outcomes or if the VBHC contracts allow for personalized treatments that are more suited towards the individual patient's needs and wishes. Personalised medicine also has the potential to reduce expensive hospitalisations or emergency visits due to poorly controlled diseases. The shared risk that payers and providers agree on in the value-based contracts (i.e., outcome-based contracts) also has the potential to align stakeholder incentives to value. For the health care provider, value-based contracts can be used to differentiate and demonstrate the effectiveness of a product versus their competitors, which can then assist payers in making formulary decisions.

The intuitive appeal of VBHC has led many stakeholders to embrace the concept. However, the enthusiasm has only partially been converted to successful practices. Apart from the limited number of cases presented by Porter and associates, a number of pilot projects and partial implementation examples[3], there is limited experience with large-scale implementation[4].

Furthermore, both scholarly and policy debates have been characterised by a lack of consensus about the translation of VBHC into specific health system contexts. The diversity of interpretations combined with the evolving nature of several projects represent challenges to summarising developments in a systematic and comprehensive manner. A first step towards a more uniform mapping of experiences involves creating a set of dimensions to identify VBHC projects.

[3] EiT Health. (2020). Implementing Value-Based Health Care in Europe: Handbook for Pioneers (Director: Gregory Katz). EiT Health.
[4] Pedersen, K. (2017). Værdibaseret styring. Er det smitsomt? Odense, Denmark: COHERE discussion paper, no.3.

The aim of this paper is therefore to develop a framework for analysing core dimensions of VBHC projects and to demonstrate how this framework can be applied in analysis of such projects in Denmark. Secondary aims include presenting lessons from VBHC projects and determining design principles for future VBHC contracts while considering the ambiguities of VBHC concepts and implementation.

A key challenge for widespread implementation is that VBHC requires detailed patient-level data and a digital infrastructure to support the assessment of costs and value. The Nordic countries should, in principle, be in a favourable position to deal with this challenge due to a high level of digitalisation and extensive health registries that can be linked to a range of administrative and social data via personal ID numbers. Whereas some academic interest about VBHC in the Nordic region has been demonstrated, most contributions have focused on individual projects (e.g., the evaluation by McKinsey in 2019 of the Danish Regions' cross-regional VBHC projects[5] or general discussions about the phenomenon[6]. This paper aims to provide a broader collection of VBHC cases from Denmark.

Denmark has a culture of public and integrated health care system. The majority of funding for health care is derived through national, regional and local income taxes, and most hospitals are publicly owned and operated. However, there are also elements of private sector involvement and public-private collaboration. Danish regions typically have contracts with private hospitals and clinics to provide specific services, or these private entities serve as buffers in case of waiting times at public hospitals. General practitioners in Denmark are private enterprises, although they receive most of their income from public sources and are subject to regional planning and national-level agreements with the regions. VBHC may be applied as a steering mechanism within the public sector or as an instrument to optimise contracting and procurement from the private sector as will be explained in more detail below.

[5] McKinsey & Company. (2019). 20190114 Det tværregionale projekt om værdibaseret sundhed. https://www.regioner.dk/media/11405/20190114-det-tvaerregionale-projekt-om-vaerdibaseret-sundhed-pdf.pdf.
[6] Pedersen, K. (2017). Værdibaseret styring. Er det smitsomt? Odense, Denmark: COHERE discussion paper, no.3.

This study was supported by Integrated Personalised Diabetes Management goes (iPDM-GO), a Europe Innovation project supported by EiT Health. EiT Health is supported by the EIT, a body of the European Union (euhealth.eu).

Methods

Identifying VBHC cases is complicated as the concept is interpreted and applied differently by different actors and across different domains. Practices and projects may be labelled as VBHC even though they only include some of the core characteristics described in the literature regarding VBHC. Furthermore, projects may include elements of VBHC ideas without being labelled as such by project managers and initiators. This ambiguity about the concept means that a comprehensive mapping of cases is unfeasible. Instead, this report takes an explorative approach, aiming to identify as many cases as possible using a combination of internet searches and snowballing based on references in reports, media, workshops, conferences and so on.

The VBHC cases were identified by searching for the following search terms: ‘value-based management’, ‘value for the patient, ‘value-based health care’, ‘value-based procurement’, ‘pay for performance’, ‘outcome based health’, ‘performance-based health’, ‘værdibaseret’, ‘værdibaseret styring’ in the search engines PubMed, Google and InfoMedia and snowballing based on references in reports, media, workshops, conferences, etc.

Data collection has been ongoing during 2019/2020, with new cases being added to the database as they were identified. The rate of new cases identified has been declining. This trend indicates that the method provides a relatively good coverage of the field.

The Origins of Value-Based Health Care

VBHC as a concept or idea has been described and defined in different ways among researchers and clinical and health administrators. Common to all interpretations is the focus on the improvement in the patient's state of health and quality of life as a result of the health service's efforts for individual patients. This is defined as the value that is experienced by the individual[7]. At the system level, Porter defined value as the following relationship:

$$value = \frac{health\ outcomes}{costs\ of\ delievering\ the\ outcomes}$$

With health outcomes being the health results that matter for a patient's condition over the care cycle and the costs of delivering the outcomes, the total costs of care for a patient's condition over the care cycle. Therefore, it is a cost-effectiveness concept that expresses what one gets for the resource effort spent on the treatment. Ideally, the focus is thereby shifted number of e.g. operations to value, as the equation incentivises effective care delivery that prioritises outcomes that matter to patients.

A tricky concept in VBHC includes the idea that value is not a fixed concept and that perceptions of value can differ from person to person depending on the perspective of the value assessment[8]. It is therefore a critical part of VBHC to solicit information about patient experiences and to use these assessments as input for health care delivery and management.

[7] Porter, M. &. (2006). Redefining Health Care: Creating Value-Based Competition on Results. Harvard Business Press.
[8] Drummond, M. S. (2005). Methods for the Economic Evaluation of Health Care Programmes. Oxford University Press.

Another critical point in value-based management is that all stakeholders in the health care sector should work towards the same goal and that management tools should support this common goal that considers patients' experiences in management and treatment practices.

Porter's concept of VBHC is based on six dimensions. When combined, they should help maximise the value to the patient. They include the following: 1) organising into integrated practice units (IPUs), 2) measuring outcomes and costs for every patient, 3) moving to bundled payments for care cycles, 4) integrating care delivery across separate facilities, 5) expanding excellent services across geography and 6) building an enabling information technology platforms[9]. It is stated that the dimensions are all interconnected but that each dimension also has value in its own rights.

The six pillars of Porter's VBHC can be described in more detail.

1) *Organising into integrated practice units*

   Instead of a fragmented health care system that is not organised around the patient but to a larger extent around hospital departments, Porter proposed organising care around medical conditions over the full cycle of care and deliver services in IPUs.

2) *Measure outcomes and costs for every patient*

   Measuring patient outcomes and costs are key to VBHC. Outcomes should be condition-specific, multidimensional and reported by both clinicians and patients, and risk-adjustment factors should be considered. Porter proposes three tiers for outcome measurement: survival, process of recovery and long-term sustainability of health. To a large extent, existing quality data can be used in Denmark, but there might also be a need to develop new and uniform quality data on the patient's experience of value, such as patient-reported outcomes (PROs).

[9] Porter M.E & Lee, T. (October 2013). The Strategy That Will Fix Health Care. https://hbr.org/2013/10/the-strategy-that-will-fix-health-care.

In regard to costs, Porter recommends including downstream costs (not only the billable ones) for all procedures and personnel deployed for each case, including management of any complications, recurrences or medical errors.

The value of health care is supposedly maximised when outcome and cost are recorded continuously over time and made publicly available. Transparency enables providers to compete on value instead of price and therefore raise the overall standard of care and accelerate innovation.

3) *Moving to bundled payments for care cycles*

In a bundled payment model, a flat rate of reimbursement is paid for all the services performed by a provider to treat a patient undergoing a specific episode of care defined by a particular condition or period. Ideally, bundled payment encourages a careful allocation of resources and shared responsibility of all parties involved (e.g., primary and secondary care providers), and it also emphasises the patient's recovery.

4) *Integrating care delivery across separate facilities*

Porter suggested integrating care across the health care system to eliminate care fragmentation and duplication and to optimise the services delivered at each location through deepened expertise and better outcomes.

5) *Expanding excellent services across geography.*

Porter also supported disseminating excellent care models across a defined region and thereby serving a more significant patient population.

6) *Build an enabling information technology platform*

The IT landscape within health care is complex with a large variety of solutions for each department, location and type of data in use. A suitable digital platform that enables the collection and sharing of patient-centred, standardised and structured data is essential for successful implementation of VBHC.

Towards a national translation of VBHC in Denmark

In 2016, a Danish working group under the Danish Regions published a framework to support the development of VBHC models in a Danish context. This can be seen as an attempt to translate generic VBHC concepts into a health system with universal coverage based on public funding and predominant public service delivery. The framework consisted of the following elements.

Health policy objectives focusing on value for the patient:

1. focus on quality and effect;
2. coherent patient pathways in the hospital between hospitals and between sectors;
3. and cost-effectiveness.

These general principles were to be transformed into specific projects based on the following guidelines:

1. financing mechanisms must be transparent;
2. improvements are rewarded;
3. clinical staff involved in the design process to avoid negative side-effects on clinical practices;
4. continuous and clinically meaningful follow-up;
5. attention to all patient groups;
6. visible and valid data (baseline and evaluation);
7. and clear definition of prospective rules for risk and profit sharing.

Although there is clear inspiration from Porters framework, it is also obvious that the Danish translation represents a reformulation of the original VBHC concepts to consider some of the potential complications in translating the general concepts into practice. In particular, the framework takes in to account that projects can be entirely within the public sector focusing on quality development and relations between public payers and public provides. There is a stronger emphasis on the involvement of health care professionals in the formulation and implementation of VBHC concepts and a recognition of the need to

consider the complexity of multiple patient groups with heterogeneous care needs. The framework also recognises the critical issue of developing principles for fair and effective contracts to manage risk sharing between purchasers and providers or between public payers and public providers.

Developing a Framework for Classification of VBHC Projects in Public and Mixed Health Systems

Merging the adjusted guidelines from the Danish framework and the general principles from Porter and Teisberg, we developed a broad set of dimensions for classification of empirical case studies of VBHC. We refined this set of dimensions by considering the applicability to our preliminary list of empirical cases. This led to identification of the following themes for descriptive mapping of VBHC projects.

Patient scope

The transition to VBHC often involves pilot studies to gain experience in different settings. The scope of such pilots differs significantly, and this may have an impact on both the transferability and comparability of results. It is therefore crucial to distinguish between different scope ambitions. Several projects focus on particular population subsets. Most commonly, this refers to a specific group of patients with specific diagnoses, such as diabetes, cardiovascular diseases or chronic obstructive pulmonary causes and aims to incorporate the perspective of integrated care pathways and measurement of long-term value and costs as presented above. A major concern regarding such projects is how to deal with patients suffering from multimorbidity as this may heavily influence both costs and value assessments. In terms of scope, it is relevant to declare whether the projects are single diagnosis or include multimorbidity.

A second and broader scope option for VBHC is to include all citizens in a specific area. This type of population perspective addresses the core idea of bundling services, assessing and incentivising population-level value creation. However, it also raises a number of questions about how to account for population characteristics and broader determinants of health.

Another issue includes methods to assess and reward the contribution of different organisations and activities to value creation for individual patients. This is a key issue for the design of contracts as discussed in the later Section about “Risk-Sharing Contracts for Pharmaceuticals and Medical Devices”.

A third possible scope for VBHC studies includes taking an organisational entity, such as a hospital or a GP clinic, as the unit of analysis. In this case, the focus would be on health and ‘Quality of Life´ (QoL) performance for the entire population signed up with a particular GP or who receive treatment in a particular hospital department or ambulatory clinic.

In sum, we suggest that VBHC project characterisation should be defined in scope as single-group diagnosis, multimorbidity group diagnosis or population-level diagnosis.

Public, private or mixed?

As stated in the introduction, VBHC projects can be applied within the public sector as a steering mechanism for public hospitals and other health care providers. In this case, there is no market valuation of services, and the costing dimension can therefore be challenging. Whereas public provision may be the dominant form in some health systems, many others rely on a combination of public and private organisations to provide different parts of the care services. This means that the framework for VBHC analysis must be able to accommodate mixed provision chains across a set of public and private providers. We suggest that this dimension should be declared as public, private or mixed.

Conceptualisation of patient care trajectory

This leads to a second important dimension, namely the issue of how comprehensively the project conceptualises the patient trajectory. Some projects focus on specific parts of the care trajectory, such as care trajectories inside hospitals or departments, whereas others attempt a more holistic and integrated perspective, including care delivery in the entire care chain: namely, diagnostics (or even prevention), treatment, rehabilitation and follow-up. While the holistic perspective is most in line with the VBHC principles outlined above, it also

raises a number of issues for boundary setting, timing and assessment of the contribution of individual components of the care trajectory as previously explained.
We suggest that projects should be classified on a scale from single care elements to a full care chain from diagnosis to recovery.

Technological perspective

A third descriptive dimension concerns the breadth of the sociotechnical perspective of the projects. At one end of the scale are projects that focus narrowly on value creation associated with procurement and the use of specific drugs or medical equipment. At the other end of the scale are projects that integrate technology and its use into a broader care package.

The practice of value-based purchasing of pharmaceuticals belongs to the first category. Value-based purchasing contracts involve some degree of risk sharing through performance-based payment, conditional coverage or price-volume limits, with the latter being most common in Nordic countries. An example of a single technology focused project involving medical equipment can be found at Tampere Heart Hospital, where the hospital enters a long-term contract with a supplier of cardiac diagnostic equipment in which part of the payment is contingent upon long term quality performance. An example of a broader care management project is the provision of an integrated management package for diabetes patients, including measuring devices for blood sugar levels and digital capture of PRO-data from individual patients in Odsherred Municipality in Denmark.

We suggest that projects should be classified in terms of scale with a narrow technology perspective on the one hand and a holistic service package that can include a bundle of technology and care practices on the other hand.

Economic Incentives

An important part of VBHC is to develop economic steering mechanisms to support value creation. The incentive structure in VBHC can vary according to strength and design. Some

projects do not include incentives at all, while others rely heavily on economic incentives to facilitate a change in focus and operations.

Design includes several different dimensions, such as the type of performance measure and whether it is simple or composite (see below) and the time dimension (i.e., the time in which performance is evaluated and the distribution dimension specifying the weight assigned to different parts of the care chain when multiple providers are involved). Incentives may relate to the entire patient trajectory (bundled payments) or to specific parts as described above, and they may focus on performance for specific types of patients or entire populations (population-based payment). We suggest classifying projects according to the strength and design of economic incentives.

Performance dimensions

Typical performance dimensions include activities, such as diagnostic tests or surgical procedures, outputs, such as episodes of care, which are often classified as ´Diagnosis Related Groups´(DRGs) and outcome measures, which may include clinical measures of health and patient-reported measures of health, quality of life and satisfaction with the experience. ´Quality Adjusted Life Years´ (QALYs) are an example of a composite outcome measure based on self-reported health and quality of life combined with length of life.

We suggest classifying projects according to three types of performance measures: activity, output and outcome, as well as the subcategories within these main categories.

Organisational development

Some VBHC projects focus on the organisational development aspects without a framework of performance management or economic incentives. Ideas about care integration and utilisation of patient input has resonated well with ongoing quality improvement strategies in several public health systems, whereas the attempts to link quality improvement to payment schemes has generated critique as it entails a number of potentially unwanted or perverse side effects. Furthermore, the data infrastructure is not always in place to perform detailed and ongoing calculations of costs and value. For this reason, several pilot projects

have chosen to emphasise organisational developments, sometimes in the context of changing from activity-based payment to a global budgeting scheme to avoid the negative side effects of the former.

We suggest that VBHC projects should be characterised as pure organisation development projects or projects relying on economic incentives to create change.

Table 1 summarises the dimension:

Dimensions of Value-Based Healthcare	
Scope	Single diagnosis group, including multimorbidity? Population perspective (all citizens in a given area or affiliated with a given organisational entity)
Public/private	Public-private purchasing/contracting or public-public steering mechanism
Patient care trajectory	Single activity, treatment episode or full trajectory from prevention to recovery
Technology	Narrow/single technology, such as a drug or holistic technology and care package
Economic incentives	Strength and design of economic incentives
Performance measure	Activity, output, outcome (health and quality of life, patient reported or clinical, patient experience)
Organisational development perspective	Organisational quality development with or without performance related economic incentives

Table 1: Dimensions of Value-based Health Care

Examples of VBHC projects from Denmark

In this section, we illustrate how the framework developed in Table 1 may be used to characterise the translation of VBHC into pilot projects in the Nordic region.

Value-based delivery models

Mapping of VBHC practices is constrained by the fuzziness of the concept and the many different interpretations. This means that practices and projects may be labelled as VBHC even though they only include some of the characteristics described in the above. Indeed, many of the Danish cases focus on organisational optimisation or integration of PRO data

without a performance-based payment model or a specific focus on costs and outcomes for the individual patient.

Furthermore, it is possible that projects include elements of the general ideas within VBHC without being formally described as such by the project managers and initiators. Such projects would not necessarily be picked up in general Internet searches using keywords related to VBHC or through the process of snowballing based on references in reports, media, workshops, conferences and so on.

Our review of VBHC in Denmark found that several projects have been initiated at the regional level covering specific patient groups or organizations. There were no projects covering entire populations in specific areas, and only a few attempts to develop integrated VBHC projects to include the entire patient pathway across public and private provider structures were available.

We found that all regions had designated hospitals or hospital departments to participate in value-based management trial projects. Most of the Danish examples were initiated in response to a financial agreement between the state and the regions in 2016, which emphasised the need for alternatives to the activity-based settlement scheme and pointed to value-based management as a model that should be explored further[10]. Several of the regional trials include an exemption from the region's usual settlement models, which partly includes an element of activity management.

The dominant picture emerging is that VBHC has mostly been used within the public sector and primarily as a tool to develop new patient-reported outcome measures (PROMs) or to examine and reorganise specific organisational practices. There are very few examples of developing schemes that involve both public and private providers or that take a holistic view across care levels. Furthermore, few projects link performance to economic incentives.

[10] Regeringen, D. R. (2016). Aftale om regioners økonomi for 2016. Copenhagen, https://www.regioner.dk/media/1424/aftale-om-regionernes-oekonomi-2016.pdf.

Indeed, most of the regional projects were attempts to find alternatives to the dominant and rather stringent activity-based funding scheme with demands of 2% annual productivity increases, as this was perceived to have negative side effects.

Most projects concern particular hospital departments and/or specific diagnosis groups within these hospitals. Porter's theory indicates that a health care provider must organise and conduct the entire process to be responsible for all parts of the process. There are in many cases several administrative actors with their own budget (e.g., municipalities) conducting the rehabilitation efforts. This chain of actors responsible for each part distorts the incentive structure in relation to the goal of value-based governance. It must pay off for doctors to discourage readmissions and consider the patient's ability to function[11].

The Danish efforts that constitute the means to the goal often differ from those formulated in the theoretical concept of Porter's value-based management. Increased focus on compliance with the cancer packages and the treatment guarantee are process or output goals that cannot as isolated elements encapsulate value-based management outcome focus.

In the following are a few examples from Denmark to illustrate that Danish VBHC initiatives vary greatly in terms of content (e.g., the subcomponents of value-based management that are in focus) and scope (patient group or population or organisation level). Furthermore, generally the experiments had modest anchoring in the idealised theoretical framework for value-based management. A more comprehensive list can be found in Appendix 1.

- **Tariff management in the Capital Region:** The Capital Region has for many years had tariff management as a continuous control element and as a form of settlement in hospitals. In recent years, there has been a political desire in the Capital Region to develop 'a health care system that is being measured on the value we create for patients

[11] Porter M.E & Lee, T. (October 2013). The Strategy That Will Fix Health Care. https://hbr.org/2013/10/the-strategy-that-will-fix-health-care.

within for the financial framework we have ‘and to ‘work to eliminate unnecessary processes and strengthen documentation requirements and controls in the healthcare system‘[12].

- **Introduction to Integrated Care:** A collaboration between Odense Municipality, Region of Southern Denmark and Organisation of General Practice (PLO): The *Integrated Care* project in Odense Municipality is an example of Porter's first parameter, which emphasises that the treatment must be organised into integrated units. The Integrated Care project works precisely on how new forms of collaboration can help break the silo thinking. In this way, early efforts and coherent patient care could be ensured. The target group for the project was the elderly, medical patients and citizens with stress, anxiety and depression. In line with the value-based approach, cross-sectoral cooperation was coordinated through relationships based, among other things, on common goals. The common goals were defined by health care practitioners. The goals were individual specific rather than target specific, which precisely mirrored the value-based strategy of Porter's second parameter[13].

- **AmbuFlex using PRO:** In Central Denmark Region, work is structured on Porter's other parameter, which emphasises the importance of setting up patient-specific results at the start of treatment. PRO is used as a decision-making tool to determine whether a control visit is required for the individual chronic patient, but it does not measure the effect of the treatment.

  AmbuFlex, which is a generic web system, based on the patient's reported PRO data, creates a triage where the patient is categorised as either green (the patient can and wants to wait with control), yellow (notification of special conditions that the clinician

[12] Regeringen, D. R. (2016). Aftale om regioners økonomi for 2016. Copenhagen, https://www.regioner.dk/media/1424/aftale-om-regionernes-oekonomi-2016.pdf.
[13] Pedersen R, K. (2015). Værdibaserede strategier i sundhedssektorerne med fokus på medicinområdet: Fra skåltaler til virkelighed? KORA.

must evaluate on whether the patient should be contacted) or red (the patient needs a phone contact or check-in time).

According to a memo from the Danish Regions, the experience of AmbuFlex demonstrated that for the processes suitable for PRO, a large number of routine checks could be omitted. This results in an economic efficiency potential and at the same time a quality gain for patients in the form of a more flexible control process with less time consumption. Some research is under way with AmbuFlex, including research on the effect of PRO and AmbuFlex. Systems like these help ensure that health care can deliver better and more effective treatment[14].

- **New management in a patient perspective:** The trial 'New management in a patient perspective' was conducted in nine departments (medical department, emergency department, diagnostic centre, orthopaedic surgery department and the main neurocentre [five departments]), distributed over five hospitals. Together, the nine departments comprise approximately 13% of total economic activity. Several of Porter's parameters are included in the project (the first, second and sometimes the fourth). The aim of the project was to contribute knowledge about which patient-related goals could encourage the highest possible health-for-money effect and to determine whether these goals produced the desired health effect when managed according to patient-related goals, rather than only managing according to DRG value. During the trial period, the normal activity payment was put off, whereas general budget targets such as budget compliance requirements of at least 2% productivity growth and achievement of quality and service goals were maintained. The hospital departments have defined patient-centred goals, which have been found to be motivating for the staff as they feel that their knowledge and experience can be used in management. The departments also felt that the project gave rise to an increased focus on the patient's perspective, patient-perceived quality and patients' expectations for the treatment. Patient experience has

[14] Pedersen R, K. (2015). Værdibaserede strategier i sundhedssektorerne med fokus på medicinområdet: Fra skåltaler til virkelighed? KORA.

been collected through surveys or interviews. The involvement of patients' experiences has also led to changes in work processes. Furthermore, it has been argued that the wards have been given better cooperation opportunities with the other wards, since they must not take into account DRG value in the given patient treatment[15] [16].

- **Value for the citizen:** The hospitals in Region Zealand have been rewarded financially since 2012 for good quality and efficient utilisation of their resources, which leans on Porter's thinking. Value for the citizen uses an incentive structure constituting of a fixed percentage of the hospital's budgets on the basis of successfully reaching selected indicators that represent value for the patient. The focus has been on reaching compliance with the cancer packages in 95% of cases and to comply with the guarantee of treatment (30 days). As such, part of the hospital's budget is dependent on its performance and the incentive programme amounts to approximately 1.5% (or 103 million) of the six somatic hospitals' budgets [17].

Hence, Denmark has some structural advantages facilitating a successful implementation of VBHC, such as high-quality health data and national quality indicators that create a foundation for the collection and management of data and that provide a basis for clinicians to measure health outcomes. Denmark has a relatively advanced digitalisation within its health care system. Denmark has advanced and interconnected systems of electronic health records.

Risk-Sharing Contracts for Pharmaceuticals and Medical Devices

Until recently, Denmark had not used a risk-sharing contract for pharmaceuticals or medical devices. An external review of the national purchasing organisation Amgros from 2016 concluded that Amgros had very limited experience with such instruments. Few agreements

[15] Pedersen KM. (2015). Økonomisk styring i den offentlige sektor: Kvantitet, kvalitet og sammenhæng i opgaveløsningen (Financial management in the public sector: quantity, quality and service chains). COHERE. Odense: University of Southern Denmark.
[16] Midtjylland, R. (2015). Anden delevaluering – Ny styring i et patientperspektiv. Region Midtjylland.
[17] Pedersen R, K. (2015). Værdibaserede strategier i sundhedssektorerne med fokus på medicinområdet: Fra skåltaler til virkelighed? KORA.

on volume discounts had been entered, and no agreements with payment based on performance[18].

However, effective 1 January, 2019, the Danish Parliament adopted an amendment to the Danish Health Act, which introduced a three-year trial scheme for risk sharing in the drug supplement system[19]. The scheme ensures that patients who should receive reimbursement also receive it and without the authorities risking unforeseen expenses. Starting August 2019 the Danish Medicines Agency has selected the first two medications on the scheme, namely the blood clot drug Brilique (60 mg) and the psoriasis agent Skilarence; furthermore, the companies behind the drugs have undertaken to cover the public's subsidy costs if consumption is higher than anticipated: that is, a type of volume control contract[20].

The purpose of the legislative amendments has been to strengthen patients' access to reimbursement for prescription drugs, including faster and easier access to new innovative medicines. The legislative changes are expected to benefit the Life Science sector by enabling general reimbursement for drugs that do not currently meet the conditions[21]. Another possible benefit of the risk-sharing agreement is that it might help reduce the current geographical inequality around the prescription of medicines not covered by general reimbursement[22].

Under the trial scheme, the Danish Medicines Agency will be able to grant conditional reimbursement for medicines on the condition that the pharmaceutical company must share the risk. The fact that the drug is included in the risk-sharing trial does not entail any additional administration for doctors or pharmacies. On the contrary, there is actually less

[18] AMGROS. (2016). Ekstern analyse af Amgros' lægemiddelindkøb.
[19] Retsinformation. (2019). Lov om ændring af sundhedsloven. Hentet fra https://www.retsinformation.dk/eli/lta/2018/1556
[20] Lægemiddelstyrelsen. (2019). Medicin mod blodpropper og psoriasis kommer med i forsøgsordning om risikodeling. Hentet fra https://laegemiddelstyrelsen.dk/da/nyheder/2019/medicin-mod-blodpropper-og-psoriasis-kommer-med-i-forsoegsordning-om-risikodeling-/
[21] Retsinformation. (2019). Lov om ændring af sundhedsloven. Hentet fra https://www.retsinformation.dk/eli/lta/2018/1556
[22] LIF. (2019). Nyt forsøg med risikodeling. Hentet fra https://www.lif.dk/Nyheder/Sider/Nyt-forsøg-med-risikodeling.aspx

administration for the doctors, as they previously had to apply for individual reimbursement to each patient when prescribing these two drugs[23]. The health care system will cover the cost of reimbursement for a certain number of patients who meet the reimbursement requirements and when the treatment value is expected to be proportionate to the cost. The manufacturer must cover the region's reimbursement costs for the number of patients exceeding the target population[24]. The trial will be evaluated in 2021[25].

The status in regard to *medical equipment* is less transparent, as there is no central repository of contracts for medical equipment in Denmark. Indications can be found in a recent report on innovation and value-based purchasing in health care, commissioned by the Danish Ministry of Industry, Business and Financial Affairs in 2019. The report presented seven cases of public-private innovation through purchasing in health care. Two of the cases were presented as value-based purchasing, including the 'Odsherred' case presented above and an example from Region South, where payment for a specific type of knee-replacement was linked to outcomes. The report was based on a scanning of material from the five Danish Regions, and the other examples included public-private innovation and development contracts of various kinds. The fact that the report only lists two cases of performance-based purchasing indicates that this instrument is not used extensively in Denmark at the moment.

Lessons about VBHC implementation from Danish cases

Common challenges emerging from the reviewed cases include the following:

1) defining the necessary linkage in payment models across sectors or provider levels;

[23] Lægemiddelstyrelsen. (2019). Medicin mod blodpropper og psoriasis kommer med i forsøgsordning om risikodeling. Hentet fra https://laegemiddelstyrelsen.dk/da/nyheder/2019/medicin-mod-blodpropper-og-psoriasis-kommer-med-i-forsoegsordning-om-risikodeling-/
[24] Retsinformation. (2019). Lov om ændring af sundhedsloven. Hentet fra https://www.retsinformation.dk/eli/lta/2018/1556
[25] LIF. (2019). Nyt forsøg med risikodeling. Hentet fra https://www.lif.dk/Nyheder/Sider/Nyt-forsøg-med-risikodeling.aspx

2) developing measurement systems for tracking health outcomes and costs and building the advanced analytics platform necessary both to feed data to providers and to use it as a basis for value-based payments;
3) and creating systems to manage risk, both in terms of patient mix and providers' financial exposure.

A recent report from the Danish Ministry for Industry, Business and Financial Affairs, further elaborates on the barriers based on the investigation of value-based purchasing models in Denmark. The list of potential barriers includes the following. Focusing on price rather than long-term value creation. Lack of time, resources and competencies to engage in contracting negotiations, which tend to be highly complicated in regards to determination of performance targets, risk sharing models and contractual obligations. Tough risk-sharing demands can create uncertainty and deter some private sector suppliers from engaging in the project. Uncertainty about economic gains can be a hindrance for smaller firms with limited financial buffers. Furthermore, health personnel may dislike the increased transparency on their own performance.

In theoretical terms, this can be understood as increased risks, particularly as perceived from the private partner, and increased transaction costs related to preparation, negotiation and follow up of more complicated value-based contracts[26]. Value-based contracting requires a build-up of expertise and the capacity to handle complex performance and legal issues associated with contracting and follow-up as outlined in the section on **Error! Reference source not found.**.

Similar points have been raised in regard to risk-sharing models for pharmaceuticals and medical devices. A recent report from the central medicines purchasing agency in Denmark[27] argued that European experiences with performance-based risk modelling,

[26] Williamson OE. (87. November 1981). The Economics of Organisation: The Transaction Cost Approach. American Journal of Sociology, s. 548-77.
[27] AMGROS. (2016). Ekstern analyse af Amgros' lægemiddelindkøb.

particularly from Italy, have been mixed. They may facilitate earlier entry, but the costs of preparing, monitoring and enforcing contracts are significant, and this has led to a drop in the use of such contracts in Europe. Contracts based on economic risk sharing (without performance measurements) are seen as more promising but primarily in situations where the purchasing agency is in a strong bargaining position because the particular drug would otherwise not be granted access. This instrument has therefore only been used to a very limited degree in Denmark, prior to the trial period initiated in 2019. Instead, Denmark relies on regulatory measures such as general agreements with the pharmaceutical industry and evaluation by the Medicines Council since 2019.

The arguments for not using performance contracts focus on data availability, transaction costs, capacity and judicial issues. When using economic models, there has been a tendency to move from complex to simpler models. The main arguments for using such models in the first place are uncertainty about the economic burden of particular drugs[28]. Other European surveys have indicated similar mixed experiences and explanations in areas such as Eastern Europe[29] and the Netherlands[30].

Barriers against VBHC in delivery of health care services can also be found in the broader institutional context for health care in terms of legal frameworks and economic steering practices. A major unresolved issue is how to design payment schemes that support VBHC across multiple providers and organisational levels. There has been a reluctance to make decisions on this due to the inherent conflicts between different institutionalised interests. Furthermore, there is a lack of clear evidence for the optimal design of performance-based mechanisms across governance levels. Indeed, the international experiences with the use of ´Pay for Performance" (P4P) models in health care are quite mixed. Even without the added complexity of coordination across governance and organisational boundaries each with their

[28] Andersson, E. S. (April 2020). Risk sharing in managed entry agreements—A review of the Swedish experience. Health Policy, 124(4), s. 404-410.
[29] Rotar A.M., P. A. (Mar 2018). Rationalising the Introduction and Use of Pharmaceutical Products: The Role of Managed Entry Agreements in Central and Eastern European Countries. Health Policy, 122(3), s. 230-236.
[30] Makady A., V. A. (Mar 2019). Implementing managed entry agreements in practice: The Dutch reality check. Health Policy. Health Policy, 123(3), s. 267-274.

own decision structures and economic steering regime. One of the complications includes the fact that such cross-boundary schemes will require further investment in data and administrative capacity to track outcomes and costs and to identify the contribution of the different parts of the care chain to both costs and outcomes.

In the past, health care systems have relied on the division of labour: The responsibility for managing the costs to the health care system relied on the *Payers* (i.e., health insurance or health authorities) and *providers* (i.e., clinical personnel or pharmaceutical companies delivering care) were responsible for the quality of care delivered to patients. However, a core principle of VBHC is that payers and providers share accountability for and jointly manage costs and quality. The blurred line between being a provider or a payer (i.e., nurses and coaches hired by the pharmaceutical company) can lead to ethical dilemmas.

For VBHC to drive change in clinical practice, the payment models must be introduced in an environment of trust among providers and payers. As there are often conflicting interests between the different stakeholders, such as misalignment of incentives for fee-for-service reimbursement models between payers and providers, this can be challenging. To overcome this challenge, it is therefore important to emphasise and reflect that the focus for the incentive is not solely cost containment but also outcome improvement. Providers on the other hand should be involved in the design, implementation and refinement of payment models, including defining outcomes and reviewing performance bonus criteria.

The examples in Denmark have proven to be difficult in terms of engaging general practitioners in the projects. General practitioners have a multifaceted and central role in influencing the overall cost and quality of the health system. They are in a key position to encourage prevention and well-being and to intervene early for a chronic disease and aid in managing it over time in order to slow its progression. As the patients require more specialised health care, the general practitioners have critical roles as gate keepers and coordinators or communicators with the rest of the health system. It is therefore important to find ways to make them more engaged in VBHC projects if the projects are to succeed in the long run.

In most of the Danish cases provided in this report, only a subset of the care required to achieve the desired patient outcome was included in the payment model. Such a setup did not create incentives for providers to innovate across the full chain of care delivery or to manage the total cost of care. In an ideal implementation, the scope would be expanded to the full cycle of care across (economic) responsibilities by the Regions and municipalities (i.e., diagnostics, surgery and physical therapy), which would give the providers an incentive to share information, cooperate to redesign care pathways and provide the highest quality care in the most cost-effective manner. For patients, inconsistent and uncoordinated health care is one of the biggest challenges in the health care system, and efforts to improve collaboration and integrated care across sectors has been attempted numerous times[31] [32] [33] [34].

Requirements for further development of VBHC

So far, the health care sector lacks clear action models on how to scale pilots, which have only been tested in primary hospitals, to a national or regional implantation of VBHC programmes in Denmark as well as elsewhere. Even if individual payment initiatives demonstrate improved health care value, integrating it with a comprehensive and coherent system-wide care delivery and payment regime remains challenging.

A major unresolved issue is how to design payment schemes that support VBHC across multiple providers and organisational levels. Shying away from this is partly a reflection of mixed experiences with previous (and less complicated) pay-for-performance models internationally[35] and partly a recognition that such reconfiguration of incentive structures is

[31] Antunes, V. &. (2011). Approaches to developing integrated care in Europe: a systematic literature review. Journal of Management & Marketing in Healthcare, 4(2), s. 129-135.
[32] Sandberg Buch, M. (2012). Forløbskoordination for patienter med kronisk sygdom. Erfaringer fra Region Syddanmarks modelprojekt om udvikling af forløbskoordination på kronikerområdet, København: DSI.
[33] Sandberg Buch, M. and Anne Petersen(2017). Model for koordinerende indsatsplaner og tilhørende koordinatorfunktioner - Evaluering af et samarbejdsprojekt mellem Region Hovedstadens psykiatri og Københavns Kommune. København: KORA.
[34] Sundhedsstyrelsen. (2011). Forløbskoordinering i regioner og kommuner. Indsamling af erfaringer. Hørsholm: Sundhedsstyrelsen.
[35] Pedersen, K. (2017). Værdibaseret styring. Er det smitsomt? Odense, Denmark: COHERE discussion paper, no.3.

subject to substantial conflicts of interest. In any case, such cross-boundary schemes will require further investment in data and administrative capacity to track outcomes and costs and to identify the contribution of the different parts of the care chain to both costs and outcomes.

To make a successful VBHC, there is a need for systematic collection of patient-reported data (i.e., PRO data) to support clinical effect measures. It has proven very resource heavy to collect and maintain information on cost. At the administrative level, VBHC projects have been used to identify departments with improvement potential, where the clinical departments request individual data to make proper use of the VBHC solution.

A large part of monitoring quality within a VBHC system is to identify which indicators to monitor and which data support it. The Danish data registries are very rigorous in terms of data quality due to good registration practice, which includes extensive, comprehensive and complete data of an entire population over a long period of time, with a high level of registration within many disease areas. Furthermore, due to the unique personal ID, it is possible to combine data across registries. Examples of such registries include *De kliniske kvalitetsdatabaser*, *Dødsårsagsregisteret, Fælles Medicin Kort, Landspatientregisteret* (LPR), LUP (*Landsdækkende Undersøgelse af Patientoplevelser*), *Lægemiddelstatistikregisteret*, *Patientadministrative systemer* and *Ydelsesregisteret*. However, often times in the operationalisation of VBHC in Denmark, output rather than outcome is used, and the reimbursement is not based on the individual patient as stated in Porter's theory. The basis for being able to estimate the patient's risk profile and to relate current outcomes to expected ones is massive data entry on the patient: both clinical and personal data, as well as patient-reported data. It can potentially cause a considerable administrative burden on the hospital system.

Moreover, patients have considerable knowledge about themselves, their disease history and their current state of health, which can aid in qualification to determine the best treatment for individual patients. This information, as well as data already being collected, needs to be used better and more efficiently than currently. Self-registered health data can

aid in heightening the quality of the dialogue between the patient and health personnel to find the most suitable solution for patients. One challenge in the current set up includes discovering ways to make it easier for patients to share data with health personnel and ways for health personnel to easily access and use this data, as well as using data in combination with other patient data. Moreover, many health apps and technologies, either existing or in development, do process and share data better, but it is a challenging task for health care personnel to familiarise themselves with each health technology and a standardised rating of the quality of the app could possibly be an aid in this process.

In recent years, there have been extensive investments in upgrading Danish national data infrastructure, in particular for health personnel, and in strengthening data safety. However, Denmark does not have a combined data centre for all Danish National Health registries unlike other Nordic countries, such as Finland's Isaacus project and Norway's Helsedata programme. In Denmark, there is limited cross-functional organisation of health data, and each registry has its own approval, access and sharing procedure. The approval procedure for gaining access to data is complex and time consuming. When using the data, the different registries operate with different regulations and laws and without consistency in the manner data is made available to users. Users are not always aware of what data is available, of the content of each registry and the quality of the data in registries. The complexity and time-consuming nature of gaining access might make researchers and firms less likely to use data to its full potential [36]. Moreover, there is a lack of wider understanding of what data can be used for (i.e., explorative use or use for analytical models [AI] is currently not accepted).

[36] Deloitte. (2019). Værdien af bedre adgang til sundhedsdata - rapport resume. Deloitte.

Conclusion

We found that value-based health management is a growing trend in Denmark as well as in many other countries but that it was not used extensively within the Danish health care. The high degree of definitional inconsistency and the lack of comprehensive evaluations makes it difficult to compare value-based health care payment models and draw conclusions about their relative efficacy. Furthermore, the manner in which VBHC is used or understood in the Danish context omits parts of Porter's original concept, and numerous cases did not conform to the original strategic definition of VBHC. According to Porter, the use of outcome-based goals should be systematic throughout the course of treatment and done individually for each diagnosis. However, such goals have not yet been developed and tested in Denmark. Whereas Porter's theory indicates that a health care provider must organise and implement the entire process to be responsible for all parts of the process, Denmark has several administrative actors with their own budgets. The multitude of stakeholders responsible for various components of treatment and rehabilitation distorts the incentive structure in value-based governance. It must pay off for doctors to discourage re-admissions and to consider patients' ability to function. Often, components of the VBHC universe that make sense from the operational logic within the current institutional boundaries were used, and the schemes were implemented as limited pilot projects involving specific departments and patient groups. This approach makes sense as a starting point but does not fundamentally change the modus operandi or adhere to the full set of VBHC principles. Thus, value-based management is far from being a fully developed concept for managing the health care system in Denmark. To fulfil its promise, it is necessary to consider how clinical staff and patients can be involved and how the models can be developed to include collaboration across regions and sectors.

The initiatives we identified had a strong focus on outcome indicators. However, improved outcome in itself will most likely not lead to an increased effectiveness of payment models,

as other factors will also influence the effects on the quality of care and health care costs. Organisational optimisation to enhance value and development of various types of PROs and process quality tools have dominated the recent drive towards a more patient-centred health care sector as they motivate desired change towards more patient involvement and more cross-sectoral focus that reflects the overall patient pathway.

Data infrastructure, tele-health initiatives and other home-based capabilities are often regarded as an integral part of VBHC initiatives. The capacity to use tele-health has also been relevant in regards to pandemic scenarios such as the COVID-19 crisis of 2020. Furthermore, during the pandemic, other arrangements (often of easy-to-use or low technicality) have been put in place within a short time frame to meet the health and social needs of patients during the pandemic. Thus, the pandemic might thus aid in the shift towards a more suitable, less expensive and prevention-oriented health care system that better addresses patient's health and social needs in the future.

In sum, it appears that value-based models are not used extensively within the Danish health care, at least not in accordance with the full description of VBHC as presented by Porter and as outlined above. Instead, the progress so far could be characterised by a tendency to "cherry pick" and translate parts of the VBHC universe that make sense from operational logic within the current institutional structure. Organisational optimisation to enhance value and development of various types of PROs and process quality tools dominate the picture. Furthermore, there is a tendency for schemes to be implemented as limited pilot projects involving specific departments, patient groups, drugs or equipment. This approach makes sense as a starting point but does not fundamentally change the current modus operandi and does not adhere to the full set of VBHC principles. Furthermore, there is a lack of comprehensive and methodologically advanced evaluation of the effects, which leaves room for interpretation of the results of the numerous stand-alone projects.

However, several of the pilot projects have demonstrated a clear potential, and a number of actors are pushing for further development of various types of value-based contracting for

services, devices or drugs. It is crucial to follow this development in the future and to start accumulating more solid evidence for when and how such instruments provide most value and for when they may have unwanted negative side effects. So far, there is little solid evidence apart from case studies which have not undergone thorough evaluation or rigorous trials. There is also evidence of significant risks in terms of increased transaction costs, potential lock-in to specific solutions and disruption or resistance from health care professionals.

Appendix 1: Danish experiences with value-based health care

Below is a list of Danish value-based health care initiatives. The initiatives were identified searching for the terms: 'value-based management', 'value for the patient, 'value-based health care', 'value-based procurement', 'pay for performance', 'outcome based health', 'performance-based health', 'værdibaseret', 'værdibaseret styring' in the search engines PubMed, Google and InfoMedia and snowballing based on references in reports, media, workshops, conferences, etc. Data-collection has been ongoing during 2019/2020 with new cases being added to the database as they were identified.

We have used descriptive categories derived from the presentation above. However, it has not been possible to evaluate all criteria for all projects due to missing or ambiguous reporting in the source material.

Project name (and region / municipality)	Clinical application of PROM (Patient Reported Outcome Measures) in the cancer field, the "Health Barometer", the Danish Cancer Society (ten cancer departments throughout the country)[37]
Short description	The Danish Cancer Society (Kræftens Bekæmpelse) is behind the development of the Health Barometer (Helbredsbarometeret), which is a model for systematic use of patient-reported information. Ten cancer departments have tested the model for a period of two years (from 2013-2015). A model for the use of PROM has been developed at the ten project departments either as a dialogue support tool for outpatient consultations (ambulatoryPROM) or as a tool for need-controlled contact in the follow-up after the treatment (telePROM).
Target unit	Specific diagnosis groups (lung or prostate cancer patients)
Number of participants	2,087 cancer patients have participated in the project
Care trajectory	Partial
Technology or care focus	Technology focus
Status of the project	Work with PROM on the participating departments continued until 1st of May 2016, after which the departments had to decide whether they wanted to continue the project
Challenges	Barriers identified for the implementation of PROM: • The management does not show interest in the project • Clinicians feel that the purpose of PROM is unclear • Clinicians are not motivated for changing the existing practice • New staff is not introduced to the project • There are many simultaneous projects in the department during project start-ups • There is not sufficient resources for the nurses to carry out telePROM tasks • AmbulatoryPROM is too time consuming because of technical barriers, the content of the PROM scheme and the level of implementation • Increased risk of accidental events and delays in the patient course
Indicators	The questionnaires contain questions about patients' health, including physical health (symptoms, side effects, delays, etc.), mental health (sadness, concerns for the future, etc.) and social well-being (relationship with relatives, altered leisure activities, etc.).
Data	PROM are measurements based on patients' own assessments of health status and quality of life. PROM measurements allow clinicians to assess the impact of a given treatment from a patient's perspective. Two disease-specific questionnaires have been developed to measure PROM on cancer patients: one for lung cancer patients and one for prostate cancer patients. The AmbuFlex web system is used to collect and report PROM data.
Opportunities for scaling	Based on the experience that project departments have made with the use of PROM, there is considered a potential to spread clinical use of PROM to areas of disease other than lung and prostate cancer. In other areas of disease such as breast cancer, colorectal cancer, and ovarian cancer, there appear to be the same challenges for the systematic collection of health information and in adapting the patient course to patients' need for help and support.

[37] https://www.cancer.dk/dyn/resources/File/file/9/6659/1505726340/clinical-application-of-patient-reported-outcome-measures-prom.pdf

Project name (and region / municipality)	AMGROS[38]
Short description	Effective January 1st 2019, the Danish Parliament adopted an amendment to the Danish Health Act, which introduced a three-year trial scheme for risk-sharing in the drug supplement system. The first two medications are on the scheme; the blood clot drug Brilique 60 mg and the psoriasis agent Skilarence, and the companies behind the drugs have agreed to cover the public's subsidy costs if consumption is higher than anticipated – i.e. a type of volume control contract. The purpose of the legislative amendments has been to strengthen patients' access to reimbursement for prescription drugs, including faster and easier access to new innovative medicines. The legislative changes are expected to benefit the Life Science sector by enabling general reimbursement for drugs that do not currently meet the conditions.
Status of the project	On-going; Jan 2019-Dec 2021
Settlement models used	Volume control contract

[38] https://www.retsinformation.dk/Forms/R0710.aspx?id=205282.

Capital Region

Project name (and region / municipality)	Development Hospital Bornholm (Capital Region of Denmark)[39] [40]
Short description	Bornholm Hospital was exempted from "takststyring" from February 2016 to December 2018 to pilot value-based health care. The project also consisted of 8 sub-projects in different departments and a strategy for cultural development.
Target unit	Specific organizational unit
Number of participants	The entire hospital
Providers	Public
Status of the project	Finished December 2018
Care trajectory	Partial
Technology or care focus	Care focus
Challenges	Conditions that have challenged progress and results: • Continuous need to redefine goals and content in the sub-initiatives • Challenges in extracting valid data • Other contemporary development projects that have drawn on the same resources in the organization as the sub-projects • Continuous replacement in the project team and among resource persons at the executive level • Failure to anchor the sub-projects among the clinical managers which have led to unclear and/or slow decision-making paths
Indicators	Total activity is measured as the number of services provided in a given period. These are hospital activities where the rate of benefit does not count. A hospitalization counts as one activity. In addition, the number of unique patients treated, the number of admissions, the number of hospital days, the number of outpatient services, the number of emergency services and the number of scheduled services, is taken into account.
Data	For the register-based comparative study, data on hospital activity level and production value from the Lands Patient Register is used. Data covers the period from 1 January 2015 to the third quarter of 2018.
Settlement models used	Framework budget rather than tariff management
Opportunities for scaling	The process that took place at Bornholm Hospital has evolved along the way and is adapted to local conditions. Therefore, the process cannot be applied to other hospitals. However, the evaluation of Bornholm Development Hospital points to a number of factors that may be important to take into account when working with a new management framework.

[39] https://www.vive.dk/media/pure/13241/2888138

[40] https://www.vive.dk/en/udgivelser/udviklingshospital-bornholm-13241/

Project name (and region / municipality)	Ischemic heart disease (Rigshospitalet, Capital Region of Denmark)[41]
Short description	The focus of the project has been on establishing an analysis model that is clinically relevant and which can be used to assess the effect of the treatment on the basis of the patient's overall course over a 5-year period. The focus of the project was heart disease, dependent on atherosclerosis (ischemic heart disease, IHD), which, based on X-ray examination of the coronary artery (KAG), is treated with balloon expansion, by-pass surgery or medical treatment. The group of patients with IHD includes both elective and acute patients. The purpose of the project was: • A relevant analysis model must combine the effect of treatment (measured on a combination nation of patient-related efficacy goals, complications of treatment and long-term of treatment and rehabilitation) and resources. • Collection of data for use in treatment optimization and quality assurance. Effect based measures will aid in the dialogue and a relevant effect-based analysis tool should combine information about the status of the clinical quality with health information for the patient and resources ("personalized medicine")
Target unit	Specific
Providers	Public
Challenges	It was a wish in the sub-project to test the model on a limited patient course, clarify risk adjustment and test the possibilities with existing data sources in order to gain data experience with a broader patient pathway perspective, in order to be able to utilize the knowledge in the further work. Due to lack of data access it was not possible to test the model during the project period.
Indicators	Survival, stroke, re-admission, acute kidney failure, kidney failure, acute CABG, vascular complications within 30 days, sternum infection, re-operation, mortality, heart related readmission, angina or dyspnoea. Data sources was DHR, LPR, DHRD/QoL and PRO. The majority of outcome measures are observed within 30 days after treatment start; however some are observed 1/2-year, 1 year and 5 years after treatment start.
Economic incentives	Weak
Next step	In the further work, the project focuses on collecting PRO data, which can support the use and dissemination of value-based heart treatment. Use experience from other profiles to decide on the treatment. Opportunities for better estimate resource use and quality, benchmarking and -learning between departments, hospitals and regions.
Opportunities for scaling	Good

[41] https://www.regioner.dk/media/11349/bilag-c-oversigt-over-hvert-delprojekt.pdf

Project name (and region / municipality)	Anxiety and depression (Psychiatric Center Stolpegaarden, Capital Region)[42]
Short description	The objectives of the project were to create: • A relevant solution for effect-based measures, which support the experiences across treatment locations can 1) create knowledge across clinics, 2) create better dialogue, 3) visualize results and experiences. • All the psychiatric department make use of this tool for decision support and work tool in dialogue with the patient. In order to reach this, it is important, that data is first being used on section- and department- level. • A high response rate, so that the value of the data and solution can be optimized.
Providers	Public
Indicators	Burden of disease (SCL-10), remission (SCL-10), Side effects (PRISE-CAR 5+1), Social functionality (WHODAS 4), Life quality (WHO-5), Personal recovery (INSPIRE-5).
Data	Expenses are found by a) pull data from expense-database and link data with data from the Danish Health Data Protection Agency, b) add calculated expenses to the identified resource-data.
Opportunities for scaling	In the further work, the project focuses on the dissemination and use of treatment effect for several centers and more patients, and the use of data in the clinic and for management purposes, including bench-learning. The aim is to be integrated in current system and should be part of "sundhedsplatformen".

[42] https://www.regioner.dk/media/11349/bilag-c-oversigt-over-hvert-delprojekt.pdf

Project name (and region / municipality)	Precision medicine for patients with kidney cancer (Public-private-innovation project, Capital Region, Herlev and Gentofte Hospital)[43] [44]
Short description	In the project, the doctors include entirely new innovative tools, in which the patient's treatment is determined from a so-called DNA / RNA analysis of the patient's cancerous nodes. In this way, the treatment is targeted to the individual patient which is also called precision medicine. At the same time, you constantly monitor the patient's condition and side effects and adapt far more gentle treatments based on the individual's profile. This is done through Patient Reported Outcomes (PRO). The patient is more actively involved in the ongoing treatment, and gets blood pressure measured and selected blood tests at home to avoid fluctuations in treatment. It also gives the treating physician far more knowledge about the patient's condition and experience of the treatment throughout the course
Target unit	Specific organizational units
Providers	Public and private
Care trajectory	Partial
Technology or care focus	Technology focus
Indicators	PRO data: Data on the patient's state of health, including physical and mental health, symptoms, health-related quality of life and level of functioning.

[43] https://www.altinget.dk/sundhed/article/region-hovedstaden-dyr-medicin-boer-used-mere-intelligent
[44] https://www.regionh.dk/to-fagfolk/Om-Region-H/Indk%C3%B8b-og-udbud/S%C3%A5dan-workers-vi-med-indk%C3%B8b -and-supply / Pages / International-interest-by-region-work-with-v% C3% A6rdier.aspx

Project name (and region / municipality)	Orthopedic Surgery Department (Capital Region - Herlev and Gentofte Hospital)[45] [46]
Short description	Orthopedic surgical ambulatory for knees and hips at Herlev and Gentofte Hospital has been exempted from activity management since 2018. The purpose is to support activities regarding uniform project processes and optimization of resource consumption. The focus is on reducing the number of visits per patient, since it is the assumption that it is not the number of visits - but the right visits - that are value-adding
Target unit	Specific organizational units
Providers	Public
Care trajectory	Partial
Technology or care focus	Care focus
Data	The depart management has worked with the hospital management and staff to create the technical solution for obtaining PRO data.
Settlement models used	Exempted from activity management
Next step	A technical solution in Health Platform for obtaining the PRO data is awaiting before up scaling. The plan is to roll out to several orthopedic surgical diagnoses when the technical solution is available. The next step is to work on ensuring commitment among employees by involving patients' perceptions of the course

45 https://patientoplevelser.dk/files/documents/Presentation/temamoede2019/bilag_1_projektoverigt_erfaringsopsamling.pdf

46 https://www.regionh.dk/politics/political-committees-and-forums/Other-political-forums/committee-for-value-based-control/Documents/Anden%20interne%20exercise collection%20om%20v%C3 % A6rdibased% 20styrin_final.pdf

Project name (and region / municipality)	Joint Ambulatory at Amager Hospital (Capital Region of Denmark) [47, 48]
Short description	Establishment of the joint ambulatory in 2018, which runs across several specialties and departments and treats people with multi-diseases. The ambulatory has three tracks: • Track 1: Referred Patients. • Track 2: Chronic ill patients with connection to multiple ambulatory services. • Track 3: Patients with symptoms requiring subacute supervision by a specialist. In addition, cross-sectoral study visits are made, where nurses learn from each other across the municipality and hospital.
Target unit	Specific organizational unit
Providers	Public
Care trajectory	Partial
Technology or care focus	Care focus
Settlement models used	Not tax exempted.
Economic incentives	Weak
Next step	Currently the ambulatory is seeking money for: • Introducing feedback meetings. • To implement observational studies. • Cross-sectoral audit, in which patient cases are selected to map the communication and workflows in the sectoral transitions in specific patient courses linked to the subacute track of the Joint Ambulatory. This information should be used to adjust the course, offerings and written material according to the patients' needs.

[47] https://patientoplevelser.dk/files/documents/Presentation/temamoede2019/bilag_1_projektoverigt_erfaringsopsamling.pdf

[48] https://www.regionh.dk/politics/political-committees-and-forums/Other-political-forums/committee-for-value-based-control/Documents/Anden%20interne%20experience collection%20om%20v%C3 % A6rdibased% 20styrin_final.pdf

Project name (and region / municipality)	Diabetes Ambulatory (The Capital Region - Bispebjerg and Frederiksberg Diabetes Ambulatory)[49] [50]
Short description	The Diabetes Ambulatory at Bispebjerg and Frederiksberg Hospitals, which is part of the Endocronological department, has been working with value-based management since 2018. The project aims to create greater quality for patients with type 2 diabetes and create more coherent patient care while taking into account total resource consumption across sectors. The project is testing a new form of collaboration between general practice, the municipality and hospitals in a cross-sectoral organizational framework, for example: • Develop common goals across sectors for the treatment of patients with type 2 diabetes. • Develop and test knowledge sharing meetings between sectors. The individual patient is involved to ensure a tailor-made process based on the patient's wishes and needs. There are needs rather than fixed controls. A cross-sectoral collaboration project, Tværsam, has been built
Target unit	Specific organizational units
Number of participants	The department has reviewed its 821 type 2 diabetic patients and transferred the relevant to general practice (25 patients).
Providers	Public
Care trajectory	Holistic
Technology or care focus	Care focus
Next step	More funds are being sought from various groups, so that the cross-sectoral meeting activity can be continued

[49] https://patientoplevelser.dk/files/documents/Presentation/temamoede2019/bilag_1_project overview_experience collection.pdf

[50] https://www.regionh.dk/politics/political-committees-and-forums/Other-political-forums/committee-for-value-based-control/Documents/Anden%20interne%20experience collection%20om%20v%C3 % A6rdibased% 20styrin_final.pdf

Project name (and region / municipality)	Ambulatory operation, COPD patients (Capital Region of Denmark - Amager and Hvidovre Hospital)[51]
Short description	The COPD Ambulatory has been working on value-based management since 2018. The purpose is to develop and test a model to: • Reduce the number of outpatient visits. • Investigate the possibility of offering individual patients alternatives to the traditional booking of new outpatient visits, eg using MinSP. • End more hospital patients with COPD and transfer them to the primary sector • Create space for more investigative and treatment patients • The treatment must continue to be of a high professional standard and the patients must experience the treatment as valuable.
Target unit	Specific organizational units
Providers	Public
Care trajectory	Partial
Technology or care focus	Care focus

51 https://patientoplevelser.dk/files/documents/Presentation/temamoede2019/bilag_1_projektoverigt_erfaringsopsamling.pdf

Project name (and region / municipality)	CAPTAIN (Comprehensive and Prospective Treatment and Individual Nursing) (Capital Region) [52]
Short description	CAPTAIN is an outpatient needs-oriented offering for patients with COPD. The project was developed and implemented at the Pulmonary and Infectious Medicine Ambulatorium, North Zealand Hospital over a period of three years from 2013. It takes place on three different hospitals. The aim of the development of CAPTAIN is to raise the quality of palliative care for patients with severe COPD without adding extra resources. Previously, patients were routinely summoned for conversation in the outpatient clinic two to four times a year, and some patients were seen in the outpatient clinic after admission. With CAPTAIN, regular contacts are replaced by a more flexible contact, where conversations are planned to a greater extent according to patients' individual needs. In principle, the patient is only seen by a physician for regular consultation at least once a year or when there is a specific need for medical expertise, for example in case of acute deterioration.
Target unit	Specific organizational units
Number of participants	There are approx. 650-700 patients in a CAPTAIN course. Each month, approx. 20 new patients are added, while another 20 are transferred to the primary sector or are resigning on death.
Providers	Public
Status of the project	From 2016, CAPTAIN became the standard offer for all patients with COPD who are affiliated with North Zealand Hospital.
Care trajectory	Partial
Technology or care focus	Care focus
Indicators	Patient Reported Outcome (PRO) schedules are used in CAPTAIN to monitor the patient's condition. The CAT (COPD Assessment Test) is a disease-specific PRO scheme in which the patient rates his symptoms related to COPD, including shortness of breath, limitations in everyday activities, sleep impacts, etc. The questionnaire is answered by the patient at virtually all physical meetings, ie. conversations in the ambulatory or home visits. In cases where the nurse considers that a particularly intensive effort may be needed, palliative needs are identified with EORTC QLQ 15 PAL.
Opportunities for scaling	In 2018, a new, upscaling of CAPTAIN for several patient groups emerged at the Department of Pulmonary and Infectious Medicine at the North Zealand Hospital. The purpose is to test and implement a new organization in LIA that systematically promotes focused assessment based on an optimized screening process and needs-based treatment of outpatient patients [53]

[52] https://www.vive.dk/media/pure/13148/2775924

[53] https://www.regionh.dk/politics/political-committees-and-forums/Other-political-forums/committee-for-value-based-control/Documents/Anden%20interne%20experience collection%20om%20v%C3 % A6rdibased% 20styrin_final.pdf , p. 73

Project name (and region / municipality)	Lung and Infectious Medicine Department (Capital Region - North Zealand Hospital)[54]
Short description	Infection medical ambulatory at North Zealand Hospital has been released for activity management since 2018. The purpose is to test and implement a new organization in the Lung and Infectious Medicine Department, which systematically promotes focused assessment based on an optimized screening process and needs-based treatment of outpatient patients. • Fewer physical meetings, more use of email consultations and use of My Health Platform (Min Sundhedsplatform) • The best possible use of doctors' resources and skills and thus tasks moving from doctors to nurses • Focused and optimized assessment • More need-based treatment.
Target unit	Specific organizational units
Providers	Public
Care trajectory	Partial
Technology or care focus	Both technology and care focus
Indicators	• Patient satisfaction • Professional quality • Resource utilization • Employee well-being

54 https://patientoplevelser.dk/files/documents/Presentation/temamoede2019/bilag_1_projektoverigt_erfaringsopsamling.pdf

Project name (and region / municipality)	Open Ambulatorium - Knowledge Center for Rheumatology and Spinal Diseases (Capital Region - Rigshospitalet)[55] [56]
Short description	Open Ambulatory is a Needs Management offering for patients with inflammatory joint disease. It has been developed and implemented at the Knowledge Center for Rheumatology and Spinal Diseases at Rigshospitalet and is anchored in the ambulatory on the Glostrup matric. VRR is one of the region's test clinics for value-based management and has initiated several activities with the implementation of patient care. Since 2018.
Target unit	Specific organizational units
Number of participants	Open Ambulatory includes approx. 400 patients
Providers	Public
Care trajectory	Partial
Technology or care focus	Care focus
Indicators	Goals and success criteria are: • Higher patient satisfaction: Finding the right location for services. Less complex services may, for example, be outside of hospital management and will mean that the patient gets shorter to the place of treatment. To integrate the treatment provided at different sites or cross-sectorally. For example, a back surgery will take place in a hospital while the rehabilitation takes place locally in the municipality. Here it is important that the patient experiences coherence in the treatment and that it is coordinated and integrated across the treatment sites. • Clinical quality of treatment: Bringing together the services of a small number of providers to build expertise and thus achieve an improved treatment effect. • Number of patient rights: To have the scope of the services to be defined defined and thus to abolish the services that do not create value.
Settlement models used	Knowledge Center for Rheumatology and Spinal Diseases has been set free for the activity management with respect to the rheumatology since 2018, while back surgeries have not

[55] https://www.vive.dk/media/pure/13148/2775924

[56] https://patientoplevelser.dk/files/documents/Presentation/temamoede2019/bilag_1_projektoverigt_erfaringsopsamling.pdf

Project name (and region / municipality)	Value-based management at Finsenscentret, Rigshospitalet (Capital Region of Denmark)[57]
Short description	In 2018, Finsenscentret has been selected for a regional value-based pilot project. The project consists of a number of different value-based management initiatives for different patient groups, including: • Nursing consultations for patients operated on for breast cancer • Infectious disease clinic starts telemedicine patient course with cystic fibrosis patients. (10 patients) • Blood disease clinic restores autologous stem cell harvesting from hospitalized to outpatient course. (40 patients • Oncology clinic provides home treatment with chemotherapy for patients with testicular cancer. (25 patients) • Blood Disease Clinic teaches patients to manage central venous catheter • Home treatment with intravenous antibiotics • Oncology clinic tests phone calls with patients. (20 patients) • - And five other ongoing value-based management projects
Target unit	Specific organizational units
Number of participants	See number above in brackets for some of the projects.
Providers	Public
Care trajectory	Partial
Technology or care focus	Both technology and care focus
Challenges	
measurement Indicators	Professional quality, patient-experienced quality and resources. Indicators of patient quality: • Are you comfortable with the plan that is set for your treatment? • To what extent do you experience getting support and guidance to deal with symptoms / side effects during your treatment? Indicators of resources: Number of patients treated
Settlement models used	"Takstfrisat". Testing a new management paradigm with a more clinical and patient-centered priority than the previous financial management with a focus on activity and DRG
Next step	In the future, the center wants to work more with: • PRO data • To assist patients and staff in the choice of treatment, where rehabilitation and palliation are further integrated. • - Continued reorganization of the course, so that patients need less in the hospital due to the use of new technologies in combination with more systematic teaching of disease understanding and symptom management

[57] https://www.rigshospitalet.dk/presse-and-news/news/news/Documents/FIN%20-%20documents%20to%20news/VBS_folder231118_final.pdf

Region Zealand

Project name (and region / municipality)	Medical Joint Ambulatory and Video Consultations (Region Zealand - Holbæk Hospital)[58] [59]
Short description	Holbæk Hospital has established the Medical Joint Ambulatory (MFA) - an organizational unit across specialties with joint management. The MFA opened in the spring of 2016 under the heading "Same day under the same roof" and consists of six specialist ambulatories as well as the Unit for Interdisciplinary Investigation and Treatment (ETUB). MFA ensures faster and better progress and value for patients with multi-disease in Region Zealand. A patient with multiple chronic illnesses typically shows up 12 to 14 times in one year in different outpatient clinics, at different doctors and nurses. Now that patient may have to settle for four or five annual visits. This saves time for the seven per cent of the population in the Region Zealand who are multi-sick, and Holbæk Hospital ensures better coherence in the treatment. With the project "Virtual consultations in good coherent patient care", the department now goes a step further in creating coherence for the individual patient, as more and more consultations can take place from home. The project is about saving patients for a road trip if the conversation with the doctor or nurse can just as well take place at home at the desk. With the help of a smartphone, a tablet or a regular computer as well as a special app, the many annual consultations, especially chroniclers and multi-illness patients, can be reduced to a few. For patients, this means that they save on average 50 kilometers of transport per hour. visits - and patients of working age can also avoid taking time off from work to go to the hospital.
Target unit	Specific organizational units
Number of participants	For the virtual course: Holbæk Hospital has so far conducted virtual consultations for 200 outpatients, and another 450 consultations are planned in the coming months (from March 2019)
Providers	Public
Care trajectory	Partial
Technology or care focus	Both technology and care focus

[58] https://www.regionsjaelland.dk/sundhed/geo/holbaeksygehus/om-sygehuset/paa-forkant-med-udviklingen/Sider/Medicinsk-Faelles-Ambulatorium.aspx
[59] https://www.regionsjaelland.dk/news/Sider/Sammenhaengspris.aspx

Project name (and region / municipality)	Odsherred diabetes project[60]
Short description	In the municipality of Odsherred, they have applied Roche's Accu-Check Guide solution to their diabetic patients with the aim of improving citizens' health and satisfaction with diabetes care. The municipality's expenses depend on whether patients reach some pre-defined outcome measures.
Number of participants	30 adult type 2 diabetes patients have been enrolled through the 2-year trial period
Status of the project	Finalized (Project period Dec 2017- Dec 2019)
challenges	Difficult to get stakeholder engagement (e.g. difficult to recruit general practitioners, challenging to have patients stay on the program) Challenging to make a fair contract with relevant and comprehensive indicators
Indicators	An outcome index number established on the basis of comparison of three indicators (PROM (patient experienced quality), clinical effect (number of blood sugar measures, number of measures within target) and effectivity).
data	Individual patient data is available
Settlement models used	Pay-for-Performance
Next step	Unknown
Opportunities for scaling	Possibly scaling to other municipalities or other countries

[60] Interviews with representatives from Roche Diabetes Care and Odsherred Municipality

Project name (and region / municipality)	**Epilepsy (Neurologic Department at Zealand's University Hospital, Roskilde, Region Zealand)[61]**
Short description	The aim of this project was to gain experience with systematic and continuous follow-up of PRO measures and thereby examine how this in a real-life setting can support the dialogue and decision making. On the management level the strategic aim was to be able to use the effect measures to benchmark with other regions regarding quality and planning of treatments e.g. improve the distinction between periods with high need of support and periods with low level.
Providers	Public
Technology or care focus	Care
Challenges	Difficulties defining chronic ill patient treatment journeys makes it difficult to estimate effect (not a stsart and end date for treatment, heterogenous group of patients complications varies
Indicators	The outcome measures used correct diagnosis, social effect, reduction in number of attacks, quality of life, death because of epilepsy, reduction in side effects, patient safety, correct treatment.
Data	Sundhedsdatastyrelsen, LPR and PRO-epilepsy
Economic incentives	Weak
Next step	Benchmarking with other regions
Opportunities for scaling	Good

[61] https://www.regioner.dk/media/11349/bilag-c-oversigt-over-hvert-delprojekt.pdf

Project name (and region / municipality)	Value for the citizen (Værdi for borgeren) (Region Zealand)[62]
Short description	The Region Zealand has since 2012 worked with the concept Value for the Citizen, which aims to strengthen the quality of treatment and improve the incentive structure in hospitals, both somatic and psychiatric hospitals. This is done by setting quality and efficiency targets annually, which are incorporated into the operating agreements with the hospitals. An incentive pool is attached to Value for the Citizen, and achieving the agreed goals will trigger the payment of a bonus to the hospital.
Target unit	Specific organizational units
Providers	Public
Care trajectory	Partial
Technology or care focus	Care focus
Indicators	The efforts and goals related to Value for the Citizen are determined by the Regional Council. Hospitals' work on achieving individual goals is supported by a monitoring system that allows hospitals to continuously optimize efforts based on data on relevant goals / indicators.
Settlement models used	In Value for the Citizen, hospitals are honored for achieving predetermined quality and efficiency goals. The settlement to the hospitals is therefore no longer based solely on activity. The quality and efficiency goals that rewarded Value for the citizen, for example, compliance assessment and treatment court, however, has more the character of service / process measures than a genuine outcome - goal.

[62] https://www.vive.dk/media/pure/8799/2038887, page 36

Project name (and region / municipality)	AmbuFlex - University Hospital of Zealand (Region Zealand)[63] [64]
Short description	The University Hospital of Zealand has launched a project with AmbuFlex at the Department of Neurology and the Clinical Oncology Department. Patients with epilepsy and prostate cancer, respectively, are selected to be included in the project. The purpose of the project is to restructure the outpatient activity so that it targets the patients who are most in need. AmbuFlex is a web-based dialogue and decision support tool that can be used to assess whether the patient needs a visit or not. This is done on the basis of the patient's reported PRO data, where the patient is categorized as either green, yellow or red. If the patient is categorized as being green, the patient can and does want to wait with control; red indicates that there is a need or desire for contact (telephone or consultation); yellow patients may be needed. In the latter case, a clinician looks through the answer and assesses whether it is green or red.
Target unit	Specific organizational units
Providers	Public
Care trajectory	Partial
Technology or care focus	Technology focus
Data	Patient oriented outcome data.

[63] http://ambuflex.dk
[64] https://www.vive.dk/media/pure/8799/2038887

Region of Southern Denmark

Project name (and region / municipality)	Value-based purchase of knee implants (Region of Southern Denmark, Vejle Hospital)[65] [66]
Short description	Collaboration on solutions to improve patient outcome and streamline patient care. Vejle Hospital and the purchasing department in the Region of Southern Denmark have carried out an innovative promotion of knee implants focusing on the ongoing development cooperation with the private suppliers and a value-based settlement model in relation to the quality of treatment for the patients. In April 2018, eight-year contracts were signed with Stryker on the solutions for primary and revision patients and with Zimmer Biomet on the Uni knee solution.
Number of participants	Expected gross demand per years of the knee implants offered (number of patients): • Primary total knee arthroplasty: 425 • Total and partial revisions of knee arthroplasty: 90 • Primary medial unicompartmental knee joints: 200
Status of the project	Contract is made and the operation started from September 2018. Contract term of 8 years (if cooperation works)
challenges	The challenges and barriers to public organizations connection. Value-based purchasing processes: • Requirements for procurement departments on savings calculated on acquisition cost may stand in the way of more results-based procurement focusing on the long-term value creation for patients. • Lack of time and internal resources to carry out a value-based procurement process, as it involves greater complexity in relation to, for example, determining performance parameters, risk-sharing models and contract terms. Typically also places greater demands on the market dialogue. • Healthcare professionals may feel insecure about results-based payment from private providers, as it places greater emphasis on transparency about individual physicians 'performance when it has an impact on the value creation for patients and thus the private suppliers' bonus. • Increased requirements for joint procurement can make it more complex and demanding to implement value-based procurement and to set up joint risk-sharing models • Suppliers' business models are in no way compatible with risk sharing For private companies, the challenges and barriers in particular are linked to the increased risk and uncertainty of the value-based settlement model. The smaller Danish distribution company - which was part of the market dialogue but failed to tender for the tender - specifically points out that it was mainly the uncertainty about the variable settlement for audit processes that constituted a barrier
measurement Indicators	• Avg . patient admission time (24 hours) • Avg . primary osteoarthritis re-admission rate measured 30 days after discharge (in%)

[65] https://www.regions.dk/media/10379/indkoeb-ud-fra-patient-outcome-karsten-kirkegaard-og-per-wagner-kristensen.pdf

[66] https://irisgroup.dk/wp-content/uploads/2019/02/Kortl%C3%A6gning-and-exercise collection-of-IOI-i-health-sector.pdf

	• Avg . revision rate after primary surgery the first postoperative year (in%) • Avg . post-primary revision rate for the first 2 postoperative years (in%) • Avg . post-primary revision rate for the first 5 postoperative years (in%) • Proportion of patients with a very satisfactory overall experience 1 year after surgery • Proportion of patients with at least one satisfactory overall experience 1 year after surgery • Proportion of patients with a very satisfactory "functional lift" 1 year after surgery • Proportion of patients with at least a satisfactory "functional lift" 1 year after surgery
data	To measure the quality of treatment for patients, nine different presentation parameters have been established. The first five parameters are based on official and publicly available quality indicators from the Danish Knee Surgery Register. This includes about the average hospitalization time as well as the re-admission and revision rates. The other four performance parameters are based on patients' experiences and satisfaction, which are measured through first questionnaires (Oxford Knee Score and EQ-5D-5L Score). The nine performance indicators are all based on existing and available data sources, and thus there has been no need to initiate new independent data collection activities as a result of the value-based accounting model.
Settlement models used	Profit-based settlement and risk sharing. Value-based contracts with variable settlement of suppliers in relation to the quality of treatment for patients. The entire procurement process focused on three different knee implant solutions, each with their own contract. However, it was only within two of the solutions that value-based contracts were concluded with performance-dependent payment. These are the so-called Uni knees and solutions for primary patients who get the implant for the first time. The third contract included the patients who had previously received the implant, but here the region and Vejle Hospital assessed that there was too much uncertainty to make a value-based settlement model. Specifically, the value-based settlement consists of adjusting the suppliers' settlement prices in the individual operating year based on the performance of the previous operating year. Overall, settlement prices can be adjusted up to +/- 17 per cent. throughout the contract period. In addition, a special penalty was imposed for underperformance on the performance parameter. “Average audit rate after primary surgery during the first 2 postoperative years ” if the supplier does not meet the minimum requirement for the average audit rate or any guaranteed maximum revision rate.

Project name (and region / municipality)	Prostate cancer (Region of Southern Denmark)[67]
Short description	During the project period, the project has had particular focus on applying existing PRO data to assess the effect of treatment and care. This has been done in close cooperation with RKKP. The sub-project has thus gained access to data via RKKP within the framework of quality work.
Challenges	Survival, complications with chemotherapy, progression of disease, pain, incontinence, sexual dysfunction, tiredness and vitality, physical ability, quality of life, etc.
Next step	In the future, the project focuses on the processing of collected data in order to be able to present impact targets, including evaluating the applications of the existing PRO data.

[67] https://www.regioner.dk/media/11349/bilag-c-oversigt-over-hvert-delprojekt.pdf

Project name (and region / municipality)	Introduction of alternative financial management paradigm at Rygcenter Syddanmark (Region of Southern Denmark)[68]
Short description	In 2015, a new optimized spine course was introduced in the Region of Southern Denmark, which resulted in, among other things: 1) joint visitation at Rygcenter Syddanmark of all elective, regional spine patients, 2) the introduction of the joint specialized core assessment, so that all spine patients are assessed for an active medical coordinated course; 3) that relevant spinal medicine assessment and treatment options are tested before any surgery, and 4) that Rygcenter Syddanmark is fully responsible for ensuring the treatment of back patients in the Region of Southern Denmark.
Target unit	Specific organizational unit
Providers	Public
Care trajectory	Partial
Technology or care focus	Care focus
Indicators	Only one (quality goal 6) of the total eight quality goals included has the nature of an outcome goal, while the remaining more have the nature of service goals / process indicators. Quality Goal 6: Pain Score / Quality of Life. EQ-5D patients with spinal stenosis or disc prolapse who are first-time operated on are diagnosed. The average patient should be improved 0.12 on a scale of 0-1. Furthermore, the overall level must be better than or at the national average level.
Settlement models used	The center was fully managed, and from 2016 a smaller part of the economy (DKK 2 million) was made dependent on the center meeting eight quality goals. The center receives a settlement of DKK 250,000 per year.

[68] https://www.vive.dk/media/pure/8799/2038887 , page 38

Project name (and region / municipality)	Integrated Care (Region of Southern Denmark and Odense Municipality)[69] [70] [71]
Short description	With the project "Integrated Care", which is inspired by and supported by practical experience from an Integrated Care project in North West London, the Region of Southern Denmark, in collaboration with the Municipality of Odense, wants to try out a concrete collaborative model in which the actors Odense University Hospital, Psychiatry in the Region of Southern Denmark , general practitioners and the Municipality of Odense are part of a binding collaboration. The Integrated Care project addresses a number of basic barriers that have hitherto stood in the way of a more successful interdisciplinary and cross-sectoral collaboration for two selected patient groups; the elderly medical patient and citizens with stress, anxiety and depression. The project entails that the three main players in the area - hospital, general practice and local authority - must work more closely together under the auspices of the cross-sector in all teams (TST), where the professional professionals jointly with the citizen are responsible for planning a coordinated and coherent treatment effort. The aim of the project is to achieve better results for patients (eg slow down disease development) and to reduce costs (fewer preventable admissions and shorter periods of sick leave). During the period 2013-2014, the Interdisciplinary Patient Safety Group of the Zealand Region has worked purposefully to develop the cross-sectoral treatment co-operation on adult psychiatric patients living in residential areas in Region Zealand. The group is characterized by the fact that there are often several persons, bodies and sectors involved in the patient's treatment. In particular, the purpose is to promote patient safety and proper medication
Status of the project	An evaluation from 2016 shown e that the effort has not had the expected effect. The older patients took longer to recover than the patients in the control group and had more readmissions, and the citizens with stress, anxiety and depression were sick from work for a longer time than the citizens in the control group. In total, therefore, there were more expenditures on the consumption of health and social services during the project period of the citizens affiliated with Integrated Care than there was in the control group. The Regional Council of the Region of Southern Denmark has therefore decided to close the project
Settlement models used	Pay for performance.
Next step	The project has ended.

[69] https://www.regioner.dk/media/1313/afrapporting-management-for-vaerdi-for-patienten.pdf
[70] https://www.vive.dk/media/pure/8875/2040172
[71] https://www.regionsyddanmark.dk/wm485822

Project name (and region / municipality)	Happy Life with Osteoarthritis in Denmark (GLA: D)[72]
Short description	Good Life with Osteoarthritis in Denmark (GLA: D) consists of three parts: 1. Training of physiotherapists to conduct GLA: D courses for patients 2. Education and training of patients on GLA: D courses 3. Registration of patient data in the national GLA: D register Good Life with Osteoarthritis in Denmark (GLA: D) has meant better health for patients with limited expenses. The two conditions have now secured the GLA: D main prize at this year's award of the "Value Based Health Care Prize 2019".
Target unit	Specific diagnosis groups
Number of participants	More than 49800 patients have started GLA: D training to date. Of these, 31380 have been training for at least three months.
Providers	Private/public
Status of the project	Implemented and on-going
Care trajectory	Partial
Technology or care focus	Care focus
Indicators	The evaluations include demographic questions that describe different characteristics of patients, but also questions that can be used to evaluate the efficacy of GLA: D, e.g. pain level, medication consumption, quality of life and sick leave. The two physical tests in GLA: D measure how many times you can travel-sit in 30 seconds and how long it takes to walk 40 m, which is also included in the register as a target for respectively leg muscle function and walking speed. In addition, information on patient satisfaction and participation in patient education and training is recorded.
Data	The purpose of the GLA: D register is to gather knowledge about the group of the Danish population who have been diagnosed with knee and / or hip osteoarthritis. At the same time, it acts as a treatment register such as will enable future integration of data from e.g. Danish Knee Alloplasty Register and Danish Hip Alloplasty Register.

[72] https://www.glaid.dk/index.html

Midt - Central Denmark Region

Project name (and region / municipality)	AmbuFlex (Central Jutland Region, solutions for various diseases in different hospitals)[73]
Short description	AmbuFlex is the term for a clinical solution where the patient's own information is the focal point. Each AmbuFlex solution uses a questionnaire to collect information on patients' health and symptom burden. Each patient answers a questionnaire at home. The answer is used to assess whether the patient needs contact with the hospital. The answer can also be used to find out if the patient should see a doctor or a nurse. Therefore, AmbuFlex can be used to involve the patient's perspectives and create more flexible patient processes.
Target unit	Specific organizational units
Providers	Public
Care trajectory	Partial
Technology or care focus	Care focus
Status of the project	A wide range of solutions are active at the various hospitals in the Central Jutland region.
Data	Each AmbuFlex solution develops a questionnaire tailored to the patient group and purpose. This is done in close collaboration between the clinical specialists in the hospital and a project coordinator from AmbuFlex. The patient's response is loaded into the AmbuFlex system. Here, the answer is assigned a green, yellow or red color based on an automatic algorithm. The color will usually reflect symptom load. The clinics in the ambulatory are presented with the current questionnaire answer with color code, and an overview of the patient's response over time.

[73] http://ambuflex.dk/

Project name (and region / municipality)	New management in a patient perspective (midt-Central Denmark Region) [74] [75]
Short description	In January 2014, the Central Jutland Region launched the project "New management in a patient perspective", in which nine departments are kept free of activity management in order to work on selecting and developing other management goals instead. The purpose of the project is to investigate the consequences of failing to manage a number of departments according to DRG value and instead focus on more patient-related goals. The project ended in 2016.
Target unit	Specific organizational units
Providers	Public
Status of the project	Finished.
Care trajectory	Partial
Technology or care focus	Care focus
Indicators	Each department selected and developed their own management goals / metrics. Departments were asked to select three to five indicators that could measure their performance. The departments were unfamiliar with defining performance management, and it proved difficult to define indicators that were adequate for the good ideas - often because relevant data was not available. The indicators became much more than intended, and the quality of the indicators as input to results management was questionable according to common criteria for such indicators.
Settlement models used	During the project period, the nine departments had a fixed budgetary framework and are thus not subject to the DRG-based activity management model in the region, including the requirement for annual productivity increase. The departments shall remain subject to the general objectives included in the annual budget's. The objectives can be broadly divided into five categories: 1. Patient satisfaction and - security 2. Process objectives 3. Re-admissions and mortality 4. Patient-reported outcome (PRO) 5. Other goals that are less patient-centered

[74] https://www.vive.dk/media/pure/8799/2038887, p. 41
[75] https://www.defactum.dk/api/cfkpage/download/?fileid=637 , p. 13

Northern Jutland Region

Project name (and region / municipality)	Hip / knee replacement (Region North Jutland)[76] [77]
Short description	The ambition is to follow what the patients get out of the treatment as well as give the patients greater influence on their treatment. The orthopedic surgery department in Farsø, North Jutland, has teamed up with patients and medical experts from all five regions to select the effect targets that are most important to patients and which can be used to improve treatment from a clinical perspective. The dialogue between therapist and the patient has improved, because the doctor is able to follow and predict the patient's disease outcome. The patients can due to other patient's experiences get a better insight into their treatment options. There is also a financial rationale as there is a basis for assessing whether or not some patients should be operated on at all.
Indicators	Complications, re-operations (within 2 years), PRO data e.g. quality of life, functional level, work status, patient satisfaction, etc.
Next step	The next step in the project is to strengthen the hospital's collaboration with general practice and the municipality of Aalborg municipality. This way it is also possible to follow up on the patient's results after discharge from the hospital. The ambition of the collaboration is for staff across sectors to work in closer dialogue with each other on how they can together deliver better results for patients and create more coherent processes.
Opportunities for scaling	Good possibilities to scale to other treatment areas or other regional areas

[76] https://www.regioner.dk/media/11349/bilag-c-oversigt-over-hvert-delprojekt.pdf
[77] https://www.regioner.dk/media/11353/anbefalinger-for-det-fremtidige-arbejde-med-vaerdibaseret-sundhed.pdf

Project name (and region / municipality)	Multidisciplinary pain management (Danish Regions and Health Denmark)[78]
Short description	In the summer of 2017, a VBHC project was established on multidisciplinary pain management between the Danish Regions and Health Denmark (Sundhed Danmark), which represents private clinics and hospitals. All of the country's pain clinics participate in the project, both public and private. The effect measures which has been developed in the project must be applied to the majority of the approximately 10,000 patients with chronic pain who are treated annually at pain centers in Denmark. In the future, treatment at pain centers should include the answers the patients give in a questionnaire. This way, patients can have a greater influence on their treatment, which must be more organized according to the individual's wishes and needs.
Providers	Public and private
Indicators	The 10 most important efficacy targets for pain patients have been identified and a questionnaire has been prepared for follow-up with patients. Indicators are e.g. PRO related e.g. life quality, accept, social life, communication, employment status, physical status, sleep, handling of pain, mood.
Data	The questionnaire is implemented in a database (Paindata.dk) and is currently being tested at pain clinics.
Opportunities for scaling	The collected efficacy target data will be available to pain clinics across the country, which means long-term data can be used for quality development, learning and comparison of outcomes across the country.

[78] https://www.regioner.dk/media/11353/anbefalinger-for-det-fremtidige-arbejde-med-vaerdibaseret-sundhed.pdf

Project name (and region / municipality)	Prediction models for hip and knee surgery (North Jutland Region)[79]
Short description	The objective is to develop a data model that can predict the outcome of the respective hip and knee surgery process depending on the patient's characteristics.
Target unit	Specific organizational unit
Providers	Public
Care trajectory	Partial
Technology or care focus	Technology
Indicators	The model should be used to predict from medical indicators such as complications and reoperations as well as from PROM data (eg pain score, quality of life (measured on EQ-5D), functional score, return to the labor market and Oxford Hip and Knee Score). The goal is that the prediction model must be used partly as a tool for clinical decision support and partly as a basis for testing and simulation of new forms of accounting. The ambition is that the total resource consumption for each patient course is calculated, including regional costs in the form of outpatient visits, bedtime and complications, but also costs derived from, for example, the DREAM database (e.g. sickness allowance) are included in the calculation one of the resource consumption.
Settlement models used	Ideally, the prediction model could subsequently be used partly as a tool for clinical decision support, and partly to try new forms of settlement, where the payment for each treatment is either adjusted to the patient's severity or where specific criteria are set for which patients are included. in the individual settlement group.

[79] https://www.vive.dk/media/pure/8799/2038887 , p. 45

Project name (and region / municipality)	**Diabetes (Region Northern Jutland)[80]**
Short description	The aim of the project was to develop and pilot an IT-solution that could assist the clinical managers with information regarding efficacy (clinical quality), capacity utilization and resources. This is in order to secure data-supported information for continuous improvement and development of treatment, organization and planning for a more patient relevant treatment, ensure an improved health effect of the diabetes treatment for less resources overall. An additional purpose was to gain experience with a composite indicator of clinical quality. During the project period (2017-2018), the project has worked in two parallel tracks: • Developing a test tool that can compile e.g. costs and clinical quality goals for use by, for example, the clinic managers. Anchored in Region Northern Jutland, Department of Patient Care and Economy and Endocrinology Department, Aalborg University Hospital • initiated a long-term clinically anchored research project (Value-based Health Care and Patient Reported Outcomes in Diabetes (VBS-PRO-DIA)), which during the project period has worked on developing a solution for PRO. In the further work, the VBS PRO-DIA project focuses on testing the solution for PRO as well as further developing models and tools for VBHC, to be used regionally and nationally to optimize the value of the treatment for the patient and thereby deliver a better health effect. The project was anchored in Endocrinological Department at Aalborg University hospital and the Clinical Institute at Aalborg University.
Indicators	HbA1c, self-rated health, psychological wellbeing, symptom frequency and burden of disease, diabetes stress, diabetes influence of life quality, time within target blood sugar range, periphery neuropathy, albuminuria, retinopathy, cardiovascular disease, diabetic foot ulcer, amputation, cereal vascular disease, smoking, ketoacidosis, severe hypoglycemic events, hospitalization, blood sugar control, medicine satisfaction and dissatisfaction, diabetic specific treatment quality and support, confidence in own disease-management (personal goals, wishes and priorities for treatment).
Data	Data sources are: EPJ, PRO, CGH/Diasend, lab-results and anamneses

[80] https://www.regioner.dk/media/11349/bilag-c-oversigt-over-hvert-delprojekt.pdf

Assessment of Roche Diabetes Care / Odsherred Municipality Value-based Health Care Diabetes Project 2017–2019 Feasibility and transferability lessons

Author: Laila Starr

lks@sund.ku.dk
University of Copenhagen

Department of Public Health

Section of Health Service Research

April 2021

Introduction

In Denmark, 5% of the population has been diagnosed with diabetes and an additional 5% show pre-diabetes symptoms (Diabetes Foreningen, 2020). The costs of diabetes to Danish society are accordingly high – more than DKK 30 billion a year (roughly €4 billion) (Sortsø, 2016), of which medical costs amount to just over DKK 1 billion, thus a relatively minor part of the overall costs of the disease. Therefore, there is enormous potential for optimizing the rest of diabetes care, which includes services in the care sector, hospitalizations, medical visits and, not least, medical aids (Sortsø, 2016). Furthermore, the patient journey for an individual with Type 2 diabetes is often lifelong. After diagnosis, it typically consists of a combination of self-management, treatment and follow-up in hospital, visits to general practitioners (GPs) and municipal health services.

Many people diagnosed with Type 2 diabetes are managed in primary care, with a few monitoring visits a year, which means they manage the illness themselves most of the time. A large proportion of patients fail to achieve their treatment targets despite the availability of multiple therapeutic intervention strategies (Stone, 2013) (Currie, 2010). If diabetes is not well managed it can lead to premature death, blindness, amputation, cardiovascular disease and kidney failure (WHO, 2020). However, diabetes self-management is not a simple matter and patients need to master many skills, for example self-administering insulin in basal, bolus and correction doses (Drincic, 2016).

Value-based healthcare (VBHC) is a policy idea that has gained significant international attention since Michael E. Porter and Elizbeth Olmsted Teisberg introduced the concept in their article 'Redefining Health Care: Creating Value-based Competition on Results in 2006' (Porter ME & Teisberg EO 2006). In a value-based contracting scheme, the focus is on value for the patients, rather than volume. VBHC therefore makes the delivery of improved health outcomes for the same or a lower cost the primary objective of the healthcare system. As such, the concept is closely related to core ideas in traditional health economics. In Porter's terms, it is important to assess value from a patient perspective and to evaluate costs and gains in a long-term perspective, including prevention, intervention and follow-up. This assessment of the costs and benefits of the entire treatment trajectory for each individual patient is to be supported by an incentive structure, in which providers (e.g. Roche) and payers (e.g. Odsherred municipality) agree to link payments to the achievement of results in terms of value for patients.

In Denmark, the current agreements between public and private suppliers are typically concluded via public tenders, economy being the most important parameter. Quality in specialized healthcare is monitored by means of clinical databases and national quality indicators. Quality in municipal and homecare services is

not subject to the same level of monitoring, and there are few examples of the use of systematic, continuous outcome measurement at the municipal level.

The cost of diabetes equipment in a medium-sized Danish municipality is approximately DKK 45 million annually. Procurement generally takes place through tenders with specified criteria and conditions. Yet, a traditional procurement contract provides limited downstream information about the value as perceived by the patient; nor does it normally include specific targets for this. In this respect, the value-based healthcare concept can further more transparent and informed interaction between public and private domains in healthcare.

In the following we present preliminary lessons about value-based healthcare in Denmark based on a pay-for-performance project between Odsherred municipality and Roche Diabetes Care. Using these lessons as a starting point, we discuss issues of the feasibility and transferability of the VBHC concept to other settings.

In Odsherred municipality, a value-based diabetes project was introduced for a two-year period starting in December 2017. Payment was regulated by a pay-for-performance agreement between the medical device company Roche Diabetes Care and Odsherred municipality. The aim of the project was to ensure that Type 2 diabetic patients received the necessary support, counselling and tools, and the municipality's reimbursement depended on the value delivered to the patients. The tool used was the latest blood glucose monitoring equipment and an app that was installed on mobile phones or tablets of some of the municipality's diabetes patients.

The exploratory analysis presented here is built on semi-structured interviews carried out with a representative from Roche, one management consultant involved in the contract negotiations and a health manager from the municipality, as well as access to the contract between provider and payer. The interviews were given under anonymity. The semi-structured interview guide for the interview with the representative from the munipality is attached in appendix 1.

This study was supported by iPDM-GO (Integrated Personalized Diabetes Management), a European innovation project supported by EIT Health, a 'knowledge and innovation community' (KIC) of the European Institute of Innovation and Technology (EIT), a body of the European Union (EUHealth, 2019).

The outcome-based contract between municipality and provider

The aim of the personalized diabetes management project was to help diabetes patients make necessary lifestyle changes, encourage their motivation and determine opportunities that would enable them to

reach their individual health goals by spending more time within their blood sugar range. The project aimed to provide integrated solutions to monitor glucose levels, deliver insulin and track as well as contextualize relevant data points to contribute to a successful therapy regimen. It was expected that a more stable blood sugar level would reduce the need for treatment in the short term, compared to outpatient visits to the hospital, while also reducing the need for contact with municipal homecare or home nursing.

In order to establish a value-based healthcare model, it was necessary to define indicators for measuring value. The indicators were selected so that developments over time could be tracked. This was supposed to enable analysis of the relationships between indicators of costs and outcomes related to individual patient journeys.

The value-based settlement in the Odsherred project should encourage the provider (Roche Diabetes Care) to ensure as stable a blood sugar level as possible and likewise to obtain as many satisfied patients as possible. At the same time, the idea was that Odsherred municipality and Roche Diabetes Care should share the cost of the treatment if there was a lower than expected outcome from the treatment. Therefore, the settlement price was designed to vary depending on how well a treatment was realized in the individual diabetic patient, as measured by the outcome index.

The outcome index used for payment under the outcome-based model consisted of a clinical effect index, a patient experience index and a treatment index, each accounting for one-third of the total outcome index.

- The clinical effect index consisted of a number of observations to assess whether the patient's blood sugar level remained stable.
- The patient experience quality index was based on ongoing patient-reported outcome measures (PROMs).
- The treatment index measured various types of treatment.

The price mechanism was such that the settlement price would be higher if the actual treatment outcome was above the treatment baseline and, conversely, the settlement price would be lower if the treatment level was below the treatment baseline.

Lessons from the Odsherred project

Traditionally, the municipalities have procured aids in anticipation of their use by patients. In the coming years, the municipalities will face significant financial challenges, which will force them to set some clear and harsh priorities across all welfare areas. The VBHC project in Odsherred focused on reimbursement designed to support efficiency and innovation, with the healthcare needs of the patients as the focal point. The aim of the project was to ensure that the diabetic patients received the support, counselling and tools they needed, while the municipality's payment depended on the value delivered to patients. Measurements were based on the latest blood glucose monitoring equipment and an app on mobile phones or tablets, which was installed on some of the municipality's diabetes patients' devices.

Initially, the ambition for the project was to reach around a 1000 patients out of the municipality's 1900 diabetes patients. By the time the contract was signed, the target was reduced to 60 patients; however, only 30 patients have been enrolled in the project and only eight patients have remained within the project for the entire project period. In hindsight, the municipality admits that they did not spend enough time during the initial phases to consider what their expectations were and what was realistically possible. Since so relatively few patients were enrolled in the project, it is not possible to conduct a comprehensive quantitative evaluation in terms of value for the patient or economic impact. Therefore, the exploratory analysis below will focus on feasibility, i.e. an assessment of whether or not the ideas and findings are or can be shaped to be relevant and sustainable in future projects. The analysis is based on written material and a limited number of interviews with key stakeholders, as explained above. Roche Diabetes Care had aimed at using quantitative data in their effort to illustrate effects and expand their use of real-world evidence in value-based contract discussions, but, because of the small number of patients who participated, they were only able to carry out a qualitative evaluation of the project that took place in the autumn of 2019. The results from this evaluation have been solely for internal use. We have not had access to this evaluation, and the following is solely based on our investigation and the limited number of interviews conducted.

Stakeholder perspectives

The municipality of Odsherred was interested in this project because it was a means of testing if they could get more healthcare for the same amount of money as hitherto. The municipality therefore had an incentive to enter the contract to track the value in terms of improved health outcomes for the individual and value for money and to share the risk of new aids or treatment with the provider. However, entering a value-based contract in a new reimbursement environment with no possibility of putting it to tender also aroused some concern, as the options for negotiation were limited.

Despite the availability of multiple therapeutic intervention strategies, the municipality found that many diabetes patients failed to achieve their treatment targets. In many cases, diabetics either do not use the devices to which they have been introduced or do not use them as intended and therefore the expected clinical improvements do not occur, as confirmed in the literature (Khunti, 2018). Yet, the provider is still charging for the device. Therefore, it is vital to involve patients in their own short- and long-term healthcare, which empowers them, increases self-efficacy and reduces costs. Furthermore, a satisfactory and consistent diabetes treatment is much more than just the measurable areas such as blood sugar, blood pressure and cholesterol. The psychosocial dimension is crucial for the individual patient to be able to handle everyday self-care. Anxiety, stress and depression are considerably higher among diabetic patients than in the rest of the population (Strandberg, 2014) and, as pointed out by the medical device company, other aspects such as comorbidities, family, loneliness, finances, housing and employment play a major role in the individual patient's ability to care for his or her illness. In Odsherred, coaches and other healthcare professionals were able to spend more time with the patient and approach the diabetes treatment more holistically. However, it has been challenging to recruit enough patients and GPs and the resources spent on recruiting and implementing the treatment are not justifiable for so few patients.

For the provider, Roche Diabetes Care, the model in Odsherred municipality is regarded as a paradigm shift in business solutions within the Danish healthcare system, moving from economically based business models to business models that put patients' illness first (Mieritz K, 2019). The Danish diabetes unit is the first to offer a value-based private/public business solution for chronic diseases in both Denmark and throughout Roche's global organization. The incentive for Roche Diabetes Care to participate in a performance-based agreement could be that the targeted teaching and counselling give unique access to the patients, where they are able to differentiate their products from those of their competitors. Diabetes treatment is a highly competitive market, which offers Roche an opportunity to expand their business model beyond a device-driven business and allows them to circumnavigate wholesalers.

Roche is generally positive about the collaboration with the municipality, although the complexity of implementation and the difficulties of recruiting and retaining patients in the programme seems to have surprised both the medical device company and the officers of the municipality. The representative from Roche Diabetes Care also observed that one of the challenges for implementation was that too many activities were started at the same time and that a number of the planned activities did not take place.

Overall, acceptability by the municipality and the medical device company has been positive. Given the relatively small size of the Danish market, Denmark was perceived as a good place to incubate this new

business model in order to assess whether it should be used in more business-critical markets. However, although the company has presented a positive face externally about the project, internally the company does not appear to have been as engaged throughout the process. The company has argued that the human resources and money spent far exceeded the outcomes achieved and the programme has been paused on a number of occasions before being finally closed down after the initial 24-month trial period.

With regard to acceptability by health staff, some individuals, e.g. nurses and other professionals in the local healthcare sector, have feared losing their job, the representative from Roche said, as their role could potentially be replaced by, for example. a dietitian hired by the medical device company. However, only limited system changes would be required to introduce this programme into the existing healthcare infrastructure, and such concerns could, if clearly identified, potentially be dealt with. GPs had their reservations, as they have little incentive to spend a relatively large amount of time on this intervention, the municipality representative reported. There are already more than 165,000 health-related apps available for download, but few diabetes-focused apps have had supporting data described in medical literature or been approved for use by the authorities (Drincic, 2016). It is challenging for doctors to familiarize themselves with all the new apps that patients are using within different disease areas.

Diabetes patients are a heterogeneous group and, while some patients adopt the new technology and feel comfortable with it, others find it more difficult to adapt and are unsure of what to do, which complicates the set-up and implementation (Mieritz, 2019). Although the products are technically simple, some patients experience difficulties in mastering the use of smartphone apps and the kind of self-monitoring that means paying attention to diet and exercise. It may be a challenge for the municipality to adjust the treatment for those individuals who do not want or are not able to receive training and guidance in relation to their diabetes. The coaching was planned to last for six months, which some participants found to be too long, the representative from the munipality said. She further said, that the relatively large geographical extent of Odsherred posed a challenge in terms of recruitment, as a number of patients could not easily get to the introductory meetings. In addition, it was her experience, that some patients were sceptical about the fact that it was a private company principally driving the project. In hindsight, it might have been easier to recruit patients and GPs if the municipality had been the key patient-facing branding of the initiative. Further, the municipality could have played a larger operational role, for example utilizing local information on how to get patients to meetings (e.g. informing the patients about the option of using FlexTraffic).

Defining outcome measures

A general challenge in value-based contracts is to identify indicators and define the patient journey, as there is often no finite start date and chronic patients may therefore have different contacts within and

outside the healthcare sector (e.g. GP, short- and long-term stays at hospitals, municipality services, etc.). Depending on, for example, severity, complications and self-management, many different patient activities may be associated with the lifecycle of the disease. The contract in Odsherred relies on a few indicators, but the indicators are not all-embracing and many other factors may add to the perceived patient value. Nevertheless, for the payer and provider to develop and agree on the three parameters was a process that lasted 18 months. The party responsible for the data collection in Odsherred has been the provider. Overall data access in Denmark is excellent (although Patient Reported Outcomes (PRO) is in the implementation phase) and data collected for the project could be combined with data sources other than those currently utilized in Odsherred. The relatively long negotiation period for indicators reflects that this is a critical part of VBHC schemes and that the design of performance indicators is a far from trivial exercise, as reported in previous analyses of pay-for-performance schemes (Berg M et al 2005) (Søgaard R et al 2015).

Contract design

The baseline for the contract between the payer and the provider is the municipality's average expenditure on diabetes test strips of 10,000 DKK per year. If the patients entered in the project were normally distributed, the municipality would have the same expenditure as usual. In the differentiated reimbursement model, the payment is maximum DKK 13,000 per patient if the patient obtains an outcome far above the treatment baseline and minimum DKK 7,000 if the outcome is far below the treatment baseline. With a target of 1,000 patients, this would have a financial impact in the range of DKK 7,000,000 to DKK 13,000,000. The contract would be re-negotiated regularly to ensure fairness, as some patients require significantly more input than others. The municipality did not perceive the reimbursement model devised for this project as being appropriately transparent and found it difficult to follow the calculations, observing that the indicators could have been more precise and detailed.

If the uptake of the programme were to be higher, the incentives to GPs to become involved could be modified. In addition, consideration could be given to focusing on the group of patients who are most familiar with technology solutions. However, this type of cherrypicking raises questions about social inequality in healthcare treatment and the potential negative impact of burdening public healthcare systems with the most complicated and costly patients.

Conclusion

In conclusion, there is potential for increasing the patient-perceived value of the health services offered and for further developing public/private collaboration in Denmark. In principle, such solutions may be adapted to a range of chronic diseases such as chronic obstructive pulmonary disease (COPD) and cardiovascular disease (CVD). However, the experiences from the public/private collaboration between

Roche Diabetes Care and Odsherred municipality show that design and implementation require significant and continuing efforts. In particular, patient recruitment and the alignment of incentives for all stakeholders can be challenging. It is not feasible to apply the scheme at a larger scale when resources, time and commitment or some combination thereof are constrained, as they are in many municipalities. In this situation, designating an employee to deal with implementation issues may be too much of a commitment. Resource constraints are likely to apply in most settings wishing to implement VBHC. Indeed, it is often a main driver behind the decision on whether or not to pursue the project. This may dampen the likelihood of success in other areas, as initial investments are likely to be required in the implementation and follow-up. Yet, in this particular case, the municipality does confirm that they will engage in these types of partnerships in future.

Designated resources are needed to develop and follow up on projects like these. The importance of this is further underlined by the need to consider local conditions in clinical and social care practice when designing and implementing VBHC schemes. While some elements can be easily adapted in new settings, it also appears that a “one size fits all” approach is likely to fail.

The Odsherred case has shown that it would be relevant to look further into the barriers experienced by patients and GPs and to develop strategies for overcoming these barriers. Finally, it is important that the system design and strategies can encompass all groups of diabetes patients to preserve the equity and sustainability of the public health system.

References

Berg M et al. 2005. "Feasibility first: developing public performance indicators on patient safety and clinical effectiveness for Dutch hospitals." *Health Policy*, 1: 59–73.

Currie CJ, Gale EA & Poole CD. 2010. »Estimation of primary care treatment costs and treatment efficacy for people with Type 1 and Type 2 diabetes in the United Kingdom from 1997 to 2007.« *Diabetic medicine: a journal of the British Diabetic Association*, 938-948.

Diabetes Foreningen. 2020. *Diabetes i tal.* Mar 02. https://diabetes.dk/presse/diabetes-i-tal/diabetes-i-danmark.aspx.

Drincic, A., Prahalad, P., Greenwood, D., Klonoff, D. 2016. »Evidence-based Mobile Medical Applications in Diabetes.« *Endocrinol Metab Clin North Am.*, Dec: 943-965. doi:10.1016/j.ecl.2016.06.001. .

EU Health. 2019. euhealth.eu.

Khunti K et al. 2018. »Therapeutic inertia in the treatment of hyperglycaemia in patients with type 2 diabetes: A systematic review.« *Diabetes Obes Metab*, 427-437.

Mieritz K. 2019. *Nybrud: Højere betaling for gode resutater.* 20. Sep. Senest hentet eller vist den 22. Oct 2019. https://indblik.net/2019/09/20/nybrud-hoejere-betaling-for-gode-resultater/.

Porter ME & Teisberg EO. 2006. *Redefining Health Care: Creating Value-based Competition on Results.* Boston, MA, USA: Harvard Business Press.

Søgaard R et al. 2015. »Incentivising effort in governance of public hospitals: development of a delegation-based alternative to activity-based remuneration.« *Health Policy*, 1076–85.

Sortsø C et al. 2016. »Societal costs of diabetes mellitus in Denmark.« *Diabetic Medicine*, 877–885.

Stone MA et al. 2013. »Quality of care of people with type 2 diabetes in eight European countries: findings from the Guideline Adherence to Enhance Care (GUIDANCE) study.« *Diabetes care*, 2628-2638 udg.

Strandberg RB et al. 2014. »Relationships of diabetes-specific emotional distress, depression, anxiety, and overall well-being with HbA1c in adult persons with type 1 diabetes.« *J of Psychosom Res*, 174-9.

WHO. 2020. *Diabetes.* Senest hentet eller vist den 27. April 2020. https://www.who.int/diabetes/action_online/basics/en/index3.html.

Appendix 1: Semi-structured interview guide – examples of questions

- What was your motivation for joining the project?
- Did the project fulfill your expectations?
- What were the biggest challenges for you as a partner?
- How many patients participated?
    - Was the number as expected?
    - Was it difficult to recruit patients?
    - What prevented people from participating?
- What challenges did you experience for the doctors and other partners involved?
    - Was it difficult to recruit doctors for the project?
- Do you have any suggestions on how these challenges could be met?
- Is the project completed now?
    - If so, what was the reason it did not continue?
- Could the outcome have a real impact on your budget?
- Was it difficult to reach agreement on the design of the contract?
- Do you expect the municipality to use a value-based set-up in the future?
- Are you currently involved in other value-based health management project?

A Design Perspective on Value-Based Health Care Contracts

Lessons from a Danish Public/Private Pay-for-Performance Based Contract

Laila Starr
LKS@sund.ku.dk

University of Copenhagen
Department of Public Health
Section of Health Service Research
December 2020

This study was supported by Integrated Personalised Diabetes Management goes (iPDM-GO), a Europe Innovation project supported by EiT Health. EiT Health is supported by the EIT, a body of the European Union (euhealth.eu).

Abstract

A value-based healthcare contract is an innovative payment model in which two parties, typically the healthcare payer and the pharmaceutical company or health service provider, agree to make payments for services depend on value creation.

A VBHC contract might reduce the payer's risk of a sub-optimal purchase, facilitate earlier access to new health technologies because the risk is shared between payer and provider, provide higher value care for the patient since their feedback can be incorporated into the performance measures, and can serve as a catalyst for generating enhanced real-world medical evidence.

Despite the potential benefits, the use of VBHC contracts is still limited. One reason for this is that the design and implementation of value-based contracts are complicated. Agreeing on the terms of a contract can be challenging, especially under conditions of uncertainty and asymmetric information, involves difficult tradeoffs.

Designing a contract involves trade-offs between several different goals of contract design; coordinating (ensuring that the products are offered at the right time and place), motivation (ensuring that the contract parties have individual incentives to take socially desirable decisions), and transaction costs (ensuring that coordination and motivation are provided at the lowest possible cost). However, prioritizing one objective might come at the cost of another.

This paper gives a systematic coverage of a pay-for-performance contract between a private health service provider and a Danish public health care payer. This regulatory practice is compared with the theory of contract design outlined by Bogetoft and Olesen (Bogetoft P & Olesen HB, 2004). The systematic analysis of the contract is used to discuss specific and general issues of how to balance different goals of contract design within value-based health care. The discussion shows that focuses on some goals leads to downgrading others and that some trade-offs are crucial.

Key words: Contract design, incentive regulation, value-based health care, innovative contracting

Table of contents

1 Introduction

Healthcare providers, including clinicians, hospitals, and pharmaceutical companies, are typically paid through a combination of activity-based payments and global budgets. These traditional funding approaches are primarily focused on rewarding volume or emphasizing budget control instead of emphasizing clinical quality and patient experienced values. To address this lack of focus on value creation, health systems in a number of countries are testing different value-based payment models (The Economist - Intelligence Unit, 2018). Value-based healthcare (VBHC) has been presented as a way to promote more efficient and responsive health services:

In a VBHC model, providers are paid based on patients' health *outcomes* – as opposed to the fee-for-service or capitated approach, in which providers are paid based on the *amount* of healthcare services they deliver or the number of patients they serve. In these systems providers are, "rewarded for helping their patients improve their health, reduce the effects and incidence of chronic disease, and live healthier lives in an evidence-based way" (Porter ME, 2010). Hence, the "value" is derived from measuring health outcomes against the cost of delivering the outcomes.

Different payment models have been proposed to support a value orientation as follows:

- *pay-for-performance based payment* for meeting predefined thresholds for quality of care*,*
- *bundled payment* to encourage innovative and cost-effective treatments for the full cycle of care and to hold providers accountable for the health outcomes delivered to patients,
- *population-based payment* in which a provider agrees to accept responsibility for the health of a group of patients in exchange for a set amount of money, and
- *value-based purchasing of drugs and medical equipment* in which the purchasing power is used to stimulate competition on other parameters than price or price in combination with other criteria (Garrison LP, 2013).

More information on these different payment models can be found in Starr L & Vrangbæk K, 2021. However, these arrangements are still relatively new in the healthcare field; experiences using them in practice are still limited and there is room for interpretation in terms of both terminology and concept.

Therefore, a key issue in the transition to a VBHC model is determining how to design adequate, fair, and manageable contracts between payers and providers of health care. Contracting is complicated due to the

many types of information asymmetry and uncertainty that are inherent to healthcare (Donaldson C & Gerard K, 1993) . Market failures, rapid technological developments, and changes in demand make it difficult to foresee developments and risks. Additionally, while there is an abundance of data in many healthcare systems, it can be difficult to agree on appropriate indicators of value creation.

Several challenges need to be addressed in terms of building the contract between the payer and the provider. These include an agreement on causality between interventions and relevant outcome measures and indicators; how to ensure transparency and alignment in defining and measuring outcomes and how to ensure sufficient data to track outcomes. Ideally, a contract should be designed in a way that aligns incentives and alleviates problems of asymmetric information. This involves the trading-off of different goals of contract design: coordination (i.e., ensuring that the products are offered at the right time and place), motivation (i.e., ensuring that the contract parties have individual incentives to take socially desirable decisions) and transaction costs (i.e., ensuring that coordination and motivation are provided at the lowest possible cost). Prioritizing one objective might come at the cost of another. General contract theory, which analyses how contracts should be designed in order to achieve optimal and socially desirable outcomes, may help address such issues, especially under conditions of uncertainty and asymmetric information (Bogetoft P & Olesen HB, 2004).

Contract design is not new to health economics. It has been used to guide the setting of co-payments in a healthcare system, incentives for healthcare providers, pricing agreements between healthcare systems and pharmaceutical firms, and public-private healthcare provision.

Most papers in contract theory focus on just one or very few contract-based challenges (Bogetoft P & Olesen HB, 2004). This is not surprising from an academic perspective as the application of theoretical innovations often requires the use of stylized models in order to trace the effects analytically. However, it is not sufficient as a practical guidance as it risks solving one issue while creating new problems in other areas. It is therefore important to consider all aspects of a contract simultaneously. The advantage of the Bogetoft & Olesen's framework is that it provides a holistic perspective of contract design based on theories as well as the practicalities of contracting.

The objective of this paper is to discuss how a value-based health care contract prioritizes different goals of contract design. This paper uses a public-private pay-for-performance based contract between the health care provider Roche Diabetes Care and the Danish municipality of Odsherred. The health services offered as part of the contract is a combination of an app-based service and coaching. The project was initiated in

2017 as a pilot. This regulatory practice is compared with the theory of contract design outlined by Bogetoft and Olesen (2004). I also discuss insights that may be particularly useful in connection with similar value-based healthcare contracts in the future, both in Denmark and elsewhere.

2 Contract theory as applied within value-based healthcare

Most value-based healthcare (VBHC) projects require a formal contract framework. Real contracts balance a number of conflicting objectives that characterize the contracting situation as most economic systems involve several agents with conflicting interests, asymmetric information, and asymmetric possibilities to act. This section outlines a number of theoretical issues to be considered when designing and managing VBHC contracts including but not limited to risk sharing agreements, pay-for-performance based payment contracts, and innovative or outcome-based contracts.

Contract theory is based on the assumption of economic *rationality* (Bogetoft P & Olesen HB, 2004) in which individuals are depicted as choosing the best means to pursue their goals given the information they have with unlimited analytical capacity. Contract theory also relies on the idea of *opportunism*; individuals are depicted as selfish and are presumed to exploit the situation for their own benefit. Hence, an individual will only honor an agreement if it is beneficial for them and will otherwise seek to improve his position by withholding information, misreporting, or not acting according to the contract (Williamson O, 1985) (Bogetoft P & Olesen HB, 2004).

Within health care, there is limited experience that fit the specific contract situation. Therefore, many value-based contracts are developed through trial and error and are gradually improved as limitations appear (Bogetoft P & Olesen HB, 2004). As VBHC is still in its infancy in Denmark, not many contracts have been agreed upon yet and many of the previous pilot projects have lacked essential components such as the cost component (Vrangbæk K & Starr L, 2021). However, the trial-and-error approach is often lengthy, expensive, and, to some extent, random and sporadic (Bogetoft P & Olesen HB, 2004). Applying the theoretical contract framework may aid in this process and minimize errors. Two of the most important economic theories of contracts, the agency theory and the transaction cost theory, are explained as follows:

The agency theory is concerned with the design of incentive schemes in which one-person (the agent) acts on behalf of another person (the principal). In this relationship, a principal gives legal authority to an agent to act on the principal's behalf when dealing with a third party. The agent is obligated to act in the best

interests of the principal, but establishing the right incentive structure can be complicated by asymmetric information, which can then lead to adverse selection.

The contract in Odsherred is formally between Roche Diabetes Care as the agent and the Odsherred municipality as the principal that is delegating the task of providing municipal healthcare services on behalf of the public. However, patients may also receive health services from regional hospitals and general practitioners, both of which can be formally in charge of patient management. This means that payment from the Odsherred municipality to Roche depends on patient health outcomes, which in turn depend on the totality of services provided by Roche, GPs, and hospitals (if relevant).

The specific services that Roche delivers under the Integrated Diabetes Management solution use the Accu-Chek Guide Solution and are collectively called the “Stay in the Zone Health Program”. The solution offered by Roche is a supplement to the contract between the patient’s usual health professionals by adding what Roche defines as “additional education, motivation, and coaching”. Roche offers a digital solution for remote monitoring (a diabetes app), calls from customer support and certified coaches, a motivational community with other diabetics, group-based exercises such as weekly walks, a tele-dietician program, and group-based cooking class, easily accessible overviews of training materials, expert guidance accessible via telephone, and motivational elements (Roche, 2018).

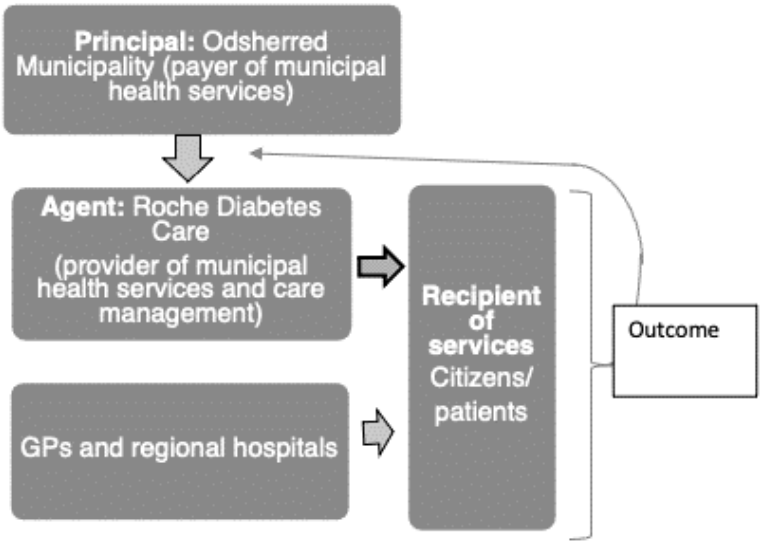


Figure 1: Principal-agent relationship

The resources involved in negotiating and administering a contract are largely ignored in agency theory (Bogetoft P & Olesen HB, 2004) but are covered in transaction cost theory. Transaction costs lead to incomplete contracts that do not specify all the possibilities. However, transaction cost theory has been criticized for being too broad in its explanatory aim and its limited ability to predict.

The context for a contract is essential as what might be the most important aspect of a successful implementation in one circumstance might not be true in another: The present case shows that general practitioners and regional hospitals play a critical role in achieving results. While neither the municipality nor Roche Diabetes Care has a direct principal-agent relation to these two entities, the contract assumes that they will not attempt to interfere when Roche Diabetes Care or Odsherred Municipality takes on more responsibility for the management of diabetes patients. This may be a problematic and somewhat naïve assumption but might be a consequence of the fact that there is an extreme demand for the service of general practitioners and hospitals focusing on specialized services for diabetics.

Regardless of the context, contract theory has identified a number of general issues in contract design. The literature on organization often focuses on problems with motivation and coordination of activities while transaction cost theory considers the costs of preparing and administering a contract (Milgrom P & Roberts J, 1992). In 2004, Bogetoft and Olesen developed a theoretical framework based on previous work in

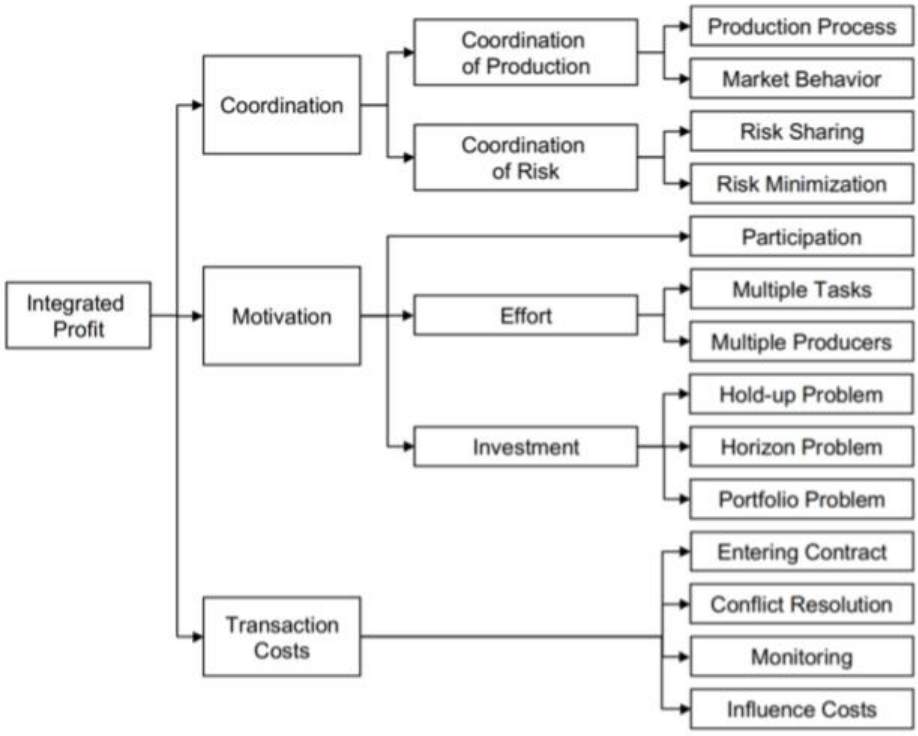
contract analysis that utilizes the concepts of coordination, motivation and minimization of transaction costs (Bogetoft P & Olesen HB, 2004) which are explained as follows:

1. **Coordination:** Ensuring that the right products are produced at the right time and place

2. **Motivation:** Ensuring that the contracting parties have individual incentives to make socially desirable decisions

3. **Transaction costs**: Ensuring that coordination and motivation are provided at the lowest possible cost

These are the three main factors that contribute to the overall goal of maximizing the sum of the profits of all the contracting parties in a production chain context as analyzed by Bogetoft and Olesen. In the context of healthcare, the overall goal would be to maximize value; maximize health outcome with minimum resources. Bogetoft and Olesen arrange the various aspects to consider when writing a contract in a hierarchy as illustrated in figure 2.



Source: (Bogetoft P & Olesen HB, 2004)

Figure 2: Hierarchy of goals for contract design

One reason that Bogetoft and Olesen developed this framework was to address the narrow focus of most of the alternative frameworks and develop a more holistic approach (Bogetoft P & Olesen HB, 2004). This paper uses this hierarchy to characterize and evaluate the contract between Roche Diabetes Care and the Odsherred municipality and to discuss the overall challenges with VBHC contracts. I find that, although the goal of hierarchy-based framework is more holistic than the alternatives, it risks being too complex. In the specific contract, some of the goals are however found to be somewhat overlapping and consequently, some goals are in the below section discussed more in-depth than others.

3 The value-based healthcare contract

Key elements of the contract that began in December 2017 between the provider, Roche Diabetes Care, and the payer, the municipality of Odsherred, are outlined below. It ran for 24 months.

The aim of this personalized diabetes management project was to encourage type 2 diabetes patients to make necessary lifestyle changes, motivate them, and determine opportunities that would enable patients to reach their individual health goals by spending more time within their ideal blood sugar range. The project aimed to provide integrated solutions for monitoring glucose levels, delivering insulin, and tracking as well as contextualizing relevant data points to contribute to successful treatment. It was expected that a more stable blood sugar level would reduce the need for treatment in the short term, which would potentially lead to reduced outpatient visits to the hospital (for which the municipality pays a co-payment) and/or reduced need for contact to municipal home care/home nursing.

In order to establish a VBHC model, Roche Diabetes Care and the municipality defined which indicators they believed would measure value for the patient. The indicators were selected to measure developments over time. This was supposed to enable analysis of relationships between indicators of costs and achievements related to individual patient journeys. The so-called outcome index - which was used for reimbursement under the outcome-based reimbursement model in Odsherred - consisted of a clinical effect index, a patient perceived quality index, and a treatment activity index, each accounting for one-third of the total outcome index:

- *The clinical effect index* consisted of consecutive observations of blood sugar levels that were compared with a target range.

- *The patient perceived quality index* was based on ongoing patient reported outcome measures (PROMs).
- *The treatment activity index* measured various types of treatment activity.

3.1 Clinical effect Index

It was agreed to measure how many observations of the blood glucose measurements that were within the established range for stable blood sugar. A baseline level was agreed upon for the proportion of observations to be within the range (clinical effect baseline). Ideally the baseline level was to be based on a population that had not been treated with the Accu-Chek Guide Solution (the intervention). In this case, a baseline was established based on general experience from the treatment of diabetes patients. The clinical effect baseline was initially in the contract set at 0.7, meaning that 70% of blood glucose readings should be within the agreed range for stable blood sugar levels.

Blood glucose was measured at least five times a day. All observations for a given period were collected and the proportion of observations within the desired range was calculated. If there was variation in the number of daily observations then the lowest number recorded during that period was used.

3.1.1 Calculation of index numbers (clinical impact index)

The calculation of the blood sugar index number was done by dividing the actual clinical effect for each patient with the baseline interval.

The formula is:

$$CEI_{mp} = \text{Clinical effect index}_{m,p} = \text{clinical effect actual level}_{m,p} / \text{clinical effect baseline}$$

Where *m* is the particular month to which the blood glucose measurement relates and *p* is the particular patient to which the observations relate.

A clinical effect index of 0.8 is used to determine the outcome index if measurements were not received for at least 50 percent of the days in the previous month.

3.2 Patient perceived quality index /PRO

A number of questions were created for the diabetic patients to answer on an ongoing basis to create a target for the patient-reported outcome (PRO). The questions focus on the patient-perceived quality of the treatment for diabetes as well as the satisfaction of treatment from the Accu-Check Guide solution.

3.2.1 Targets for patient perceived quality index

A common goal for the patient perceived quality index was to be found based on the following questions:

Questions	Answer-categories	Weight
1. How satisfied are you with your blood glucose level at the moment?	1 (low satisfaction) - 5 (high satisfaction)	0.5
2. How satisfied are you at the moment with the treatment you are receiving?	1 (low satisfaction) - 5 (high satisfaction)	0.5

Table 1: Patient perceived quality index

The above questions were considered patient reported outcome (PRO) measures.

Ideally, the baseline for answering question 1 will be based on a population of diabetics who have not been treated with the Accu-Chek Guide Solution yet, so that one has a starting point before starting treatment. It is noted, that a case-mix adjustment may be needed if the population is different from the population initiating treatment with the Accu-Chek Guide Solution. As there is no data from a previous population, the initial PRO baseline is determined on the basis of experience with satisfaction surveys in general.
The PRO baseline is set at a weighted response level of 4.0 from questions 1 and 2. This corresponds to the diabetic answering 4 to both questions or 3 in questions 1 and 5 in question 2.
Actual share based on ongoing observation. Based on the patient's answers, the actual satisfaction level (PRO actual answer) is determined, with each question weighing 0.5.

The actual satisfaction level was determined based on patient response with each of the two-question weighing an equal 0.5. The questions regarding satisfaction were sent to the enrolled diabetic patients once a month. Data was collected by Roche Diabetes Care for the purpose of calculating the monthly satisfaction index. If no data had been recorded, a value of 0,8 was used in the outcome index.

3.2.2 Calculation of index numbers for the patient perceived quality index

The calculation of the monthly patient perceived quality index was done by dividing the actual weighted satisfaction level by the baseline level. The formula is:

$$PPQI_{mp} = \text{Patient perceived quality index}_{m,p} = \text{PRO actual answer}_{m,p} / \text{PRO baseline}$$

Where *m* is the month in question and *p* is the patient to whom the observations relate.

The goal was to receive measurements from each patient each month. However, if no answer was received for a particular patient, a clinical effect index of 0.8 was used in the calculation of the outcome index.

3.3 Treatment activity index

The expectation is that a more stable blood sugar level will reduce the treatment activity index in the short-term regarding visits to the hospital and/or reduced dialogue with the municipality's home nurse. For now, this is not being taken into account in the overall treatment activity index calculations. The goal is that these measurements will be included in the long run but it is not clearly specified in the contract. For this reason, the treatment activity index TAI_{mp} is set to 1.0, and will weight 1/3 in the overall aggregated index score presented below.

3.4 Aggregate outcome index

The three index numbers (clinical effect index (CEI) , patient perceived quality index (PPQI), and treatment activity index (TAI)) are all included in an overall patient specific aggregated outcome index number. The total patient specific index can be between 0,42 (CEI= 1/3 x 0 + PPQI= 1/3 x 0.25 + TAI= 1/3 x 1.0) and 1.22 (CEI= 1/3 x 1.42 + PPQI=1/3 x 1.25 x TAI= 1/3 x 1.0), as seen in Table 2. The model is set up such that if baseline levels of clinical effect, patient-perceived efficacy, and treatment activity are achieved then the overall outcome index will be 1.0.

Finally, if a patient has missing data for both clinical effect and patient perceived quality index of 0.8 in both scores. This provides an overall outcome index of 0.64 for that month ((1/3 x 0.8) + (1/3 x 0.8) + (1/3 x 1.0)). This is the example provided in the far-right column below:

Index	Weight	Value interval	Treatment baseline	Index in case of missing data
Clinical effect $index_{m,p}$	1/3	0 – 1.42	1.0	0.8
Patient perceived quality $index_{m,p}$	1/3	0.25 – 1.25	1.0	0.8
Treatment activity $index_{m,p}$	1/3	1.0	1.0	1.0
Outcome index	**1.0**	***0 – 1.78***	***1.0***	***0.87***

Table 2: Example of calculations for the aggregate outcome index

These results indicate that it is disadvantageous for Roche Diabetes Care to have missing data in the clinical effect and patient perceived quality indexes, as the 0.8 is below the treatment baseline of 1.0. Conversely, if the patient would otherwise have measures below 0.8, reporting missing data could be an advantage for Roche Diabetes Care. As missing data can be considered to be evidence of patient non-compliance, an alternative could be that Roche Diabetes Care would carry some of the responsibility for the missing measurements.

It is clear from the table that the three elements of the index are given equal weight. This appears somewhat arbitrary and one might have expected the clinical component to carry more weight given the historical emphasis of clinical effect.

3.4.1 Determination of settlement baseline

A settlement price, i.e., the price that the payer will reimburse the provider, was determined for the use of the Accu-Chek Guide solution, which included diabetes testing strips. The baseline was set at the ordinary average cost for the municipalities, around DKK 10,000 per year per patient (DKK 5 x 6 daily measurements x 365 days per year) for purchasing strips. This was equivalent to Odsherred's direct costs associated with performing the task of chronic diabetic patients who were not in need of additional care.

A level of acceptable improvement of the target number was determined as a result of the treatment based on the baseline. This acceptable level was the starting point for pricing negotiations. At this level, the supplier receives the agreed settlement price for the treatment of the patient. If the outcome index after the treatment was above the agreed acceptable level, indicating that the treatment produced a greater effect than expected, then a higher settlement price was agreed upon. In Odsherred the agreed upon levels were that 10 and 30% respectively, meaning that 10 % and 30 % respectively were added to the agreed upon settlement price if the outcome index was at least 10 or 30% respectively above the acceptable level.

Similarly, the settlement price would be reduced if the outcome index was below the agreed acceptable level as illustrated in Figure 3. It was agreed, that these levels could be adjusted if needed.

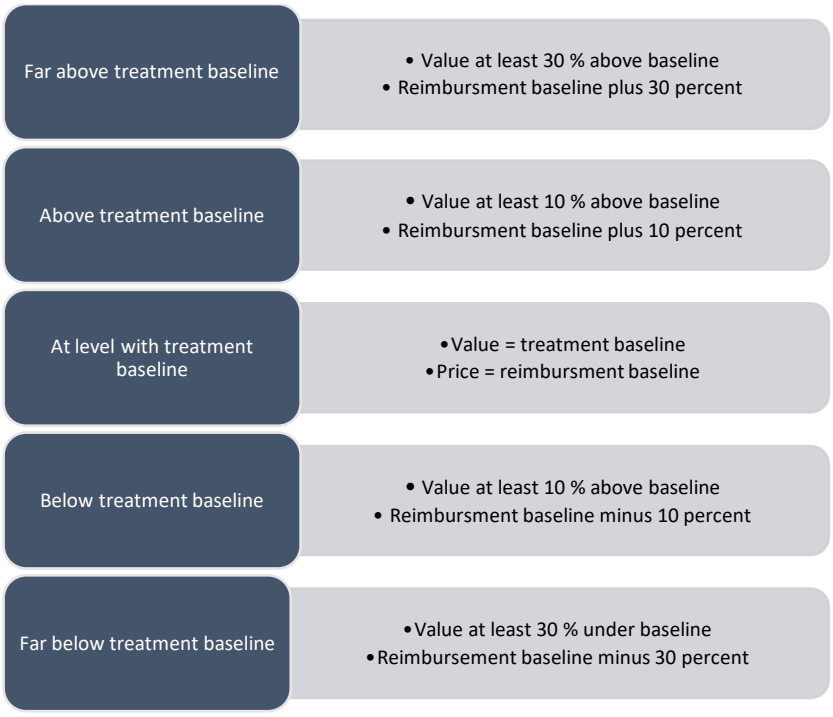


Figure 3: Model for differentiated reimbursement

3.4.2 Differential settlement model

As explained, the five settlement categories were defined based on the aggregate outcome index performance which sums the clinical effect, the patient perceived quality and the treatment activity. The five settlement categories range from below 0,5 to above 1,5 equaling a yearly payment ranging from between 7,000 DKK and 13,000 DKK depending on the aggregated outcome index (see Table 3).

	Level for the aggregated outcome index	**Difference from baseline, pct.**	**Actual reimbursement, monthly, DKK**	**Actual reimbursement, yearly, DKK**
Outcome far above treatment baseline	1,50 - max	+30 %	1.083	13.000
Outcome above treatment baseline	1,20-1,50	+10 %	917	11.000
Outcome on level with treatment baseline	0,80-1,20	0	833	10.000
Outcome below treatment baseline	0,51-0,80	-10 %	750	9.000
Outcome far below treatment baseline	Min-0,50	-30 %	583	7.000

Table 3 Categories for differential settlement

Figure 4 shows different levels of the outcome index depending on the percentage of blood glucose measurements within the agreed range (x-axis) and the level of patient satisfaction achieved (y-axis).

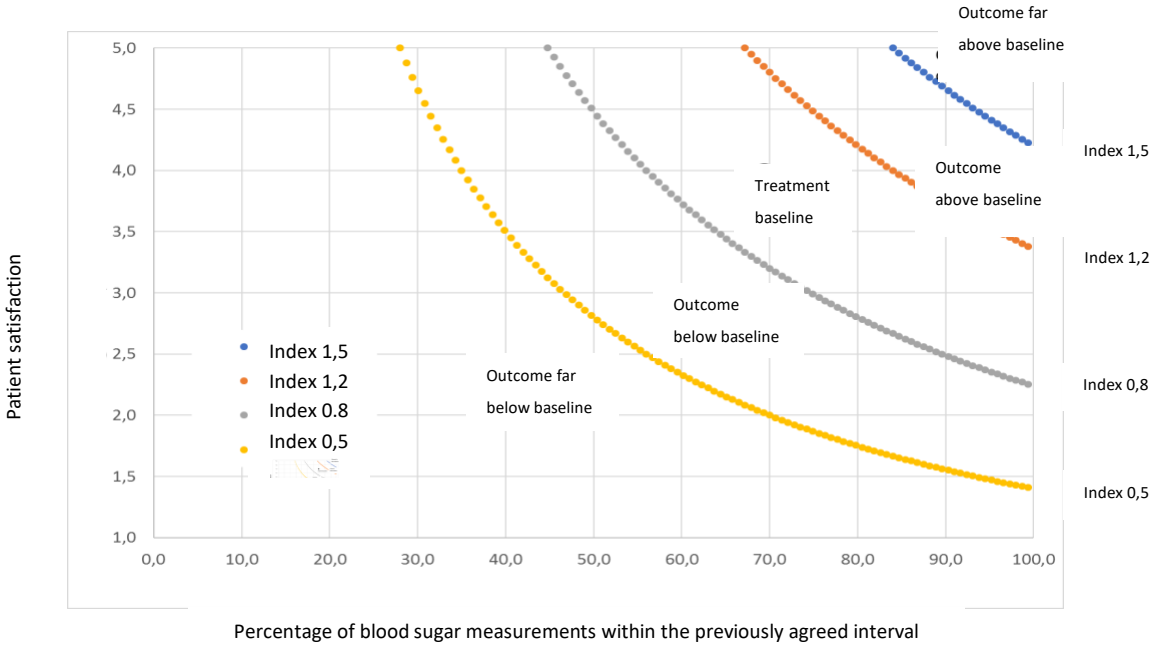


Figure 4: Relationship between clinical effect, patient-perceived quality and outcome level

3.5 Evaluation of the Odsherred project

In the article by Starr L (2021), the preliminary lessons about value-based healthcare in Denmark based on the Odsherred/Roche project were presented. Using these lessons as a starting point issue of the feasibility and transferability of the VBHC concept to other settings were discussed. Therefore, I refer to this article for a more in-depth discussion of the feasibility of the Odsherred project and VBHC in general.

It was found that very few patients (only 30 patients in total), and significantly fewer than expected, were enrolled in the project. Due to the few patients, it was not possible to do a formal evaluation of the outcome. It was found, that the design and implementation required significant and continuing efforts in all phases of the project. Resource constraints are likely to apply in most settings wishing to implement VBHC. This may dampen the likelihood of success in other areas, as initial investments are likely to be required in the implementation and follow-up. In regard to the contract itself, the contract was very time consuming to negotiate and to reach an agreement on which indicators to measure and which reimbursement level that would lead to indicating high transaction costs. It was found difficult for employees who had not been part of the contract negotiation to understand the contract and follow it as it was perceived very complex, and it was emphasized by clinicians that if they were to collect data it had to be of relevance for more than the

contract itself. While some elements of the contract and the case can be easily adapted in new settings, it also appears that a "one size fits all" approach is likely to fail. Hence, there is a great need to consider local conditions in clinical and social care practice when designing and implementing VBHC schemes.

In the below sections, the contract will be discussed up against the contract theory framework by Bogetoft and Olesen (2004).

4 Coordination

The behavior of the stakeholders must be coordinated such that the right services are being offered at the right time and place in order to achieve the best outcome:

4.1 Coordination of production

Coordination of production, in the context of healthcare, can for example refer to the alignment between the patient's preferences and the providers' deliverables. Coordination of production will ensure that the right combination of services is being offered compared to what patients would prefer given feasibility in terms of production possibilities. Therefore, the coordination of independent decision makers is probably the most important element in a contract. Sub-optimal coordination might lead to decision makers optimizing their own decisions without considering the consequences for the other decision makers in the production chain (Milgrom P & Roberts J, 1992).

The municipality of Odsherred had an interest in this project as it was a mean to test whether they could increase the value of healthcare for the same amount of money as their current level of spending. The municipality was incentivized to enter this contract in order to be able to track the value, i.e., improved health outcomes for the individual, for their spending and to share the risk of new aids or treatment with the provider, Roche Diabetes Care. However, entering a value-based contract in a new reimbursement environment where the project was not put to tender also created some concerns as the options for negotiation were not ideal given the set-up and the parties were locked-in with the services offered by the provider.

Despite the availability of multiple therapeutic intervention strategies, the municipality experienced that many diabetes patients failed to reach their treatment targets. The municipality found that, in many cases, patients would be introduced to new devices that the provider charged for but either not use them

properly or not use them at all, resulting in the expected clinical improvements not coming to fruition; this was also discussed in the literature (Khunti, 2018).

Diabetes patients are a heterogeneous group and while some patients adopt new technology and feel comfortable with it, others find it more difficult to adapt and are unsure of what to do, which complicates set-up and implementation (Mieritz, 2019). Although the products are technically simple, the municipality experienced that some citizens had trouble using smartphone apps and self-monitoring in ways that required them to pay attention to their own diet and exercise. It might be a challenge for the municipality to recognize and adjust treatment for those patients who do not want to or are not able to receive education and guidance in relation to their diabetes. Additionally, for some of the services offered, such as sessions with a coach, a number of the participants found the treatment period to be too long. According to the municipality, there was also challenge in recruiting the patients; the relatively large geographical size of Odsherred resulted in a number of patients being unable to attend the introductory meetings.

In other words, the municipality and Roche Diabetes Care underestimated the patient's perceived participation effort while patients felt that their effort exceeded the expected outcome. The program also seems to be based on a simplified perception of many patients' very complex realities and disease histories as it assumes that information and coaching/motivational interventions alone will incentivize patients to make an effort to improve clinical outcomes. Diabetes is a complex disease and many structural and contextual factors influence adherence to the treatment regime and the result of that regime over time (Hill J, 2013) (Young-Hyman, 2016) (Gonzalez JS, 2016) (Davies MJ, 2018).

4.2 Coordination of risk

Contract design should also be concerned with minimization of risk. A number of risks are present when initiating contracts in health care. Bogetoft and Olesen identify two ways to minimize the costs of risks; minimizing the risk by jointly making the total cost of risk-bearing as low as possible and creating the contract such that it minimizes the total risk (Bogetoft P & Olesen HB, 2004).

Minimizing risk and uncertainty can be done by choosing a robust contract that leads to reasonable outcomes even if the initial assumptions do not hold true.

4.2.1 Risk sharing

Risk-sharing agreements between providers and healthcare companies allow both parties to share the defined risks and opportunities of a shifting reimbursement landscape. Efficient contracts balance the cost of risk-bearing against the gains that come from providing incentives (Milgrom P & Roberts J, 1992). If the compensation to the provider depends only on the outcome, then the contract would provide the right incentives to the provider but it would also subject them with all the risks associated with the outcome. On the other hand, if the compensation to providers is made completely risk free and unrelated to outcomes or performance, companies would have little motivational incentive for a successful outcome as there would be neither rewards nor penalties related to performance levels. Shavell (Shavell S, 1979) showed that with a risk-averse agent, the optimal payment would always, to some extent, depend on the outcome, but the agent would never bear all the risk. There is thus a trade-off between protecting the companies from risk and providing motivational incentives.

In a VBHC contract like the contract in Odsherred, the contract is based on the idea that the payer and the provider should share the risk, i.e., the cost of the treatment if there is a very low outcome. For a diabetes patient, various factors can influence the outcome such as biological risks e.g., some patients responding better to the treatment plan than other or human behavior e.g., low compliance with the treatment plan. Therefore, the settlement price was designed to vary depending on how well a treatment was realized in the individual diabetic patient depending on the outcome index, as illustrated in Figure 3.

4.2.2 Risk minimization

The second aspect of minimizing the cost of risk is minimizing total risk. If the contract does not allow for adjustments to changes in production and market conditions the total risk in the producer-processor relationship can increase. A non-adjustable contract may prevent the parties from making mutually attractive adjustments to the production and marketing plans (Bogetoft P & Olesen HB, 2004).

It was agreed in the case of Odsherred that the contract could be adjusted every three months in cases such as, for example, the patients being significantly different than the average diabetes patient by e.g., having a lower socio-economic status or in other ways systematically being more difficult to be able to obtain a high outcome index. This option was not used in Odsherred. However, frequent adjustments might also cause motivational issues as the provider would not have the same incentive to over-perform. Frequent re-negotiations also require extra resources.

4.3 Sub-conclusion

In conclusion, in order to enter a successful contract, the behavior of the stakeholders must be coordinated such that the right services are being offered at the right time and place in order to achieve the best outcome. However, for the coordination of production, it seemed, that the municipality and Roche Diabetes Care underestimated the patient's perceived participation effort while patients felt that their effort exceeded the expected outcome. The program also seems to be based on a simplified perception of many patients' very complex realities and disease histories as it assumes that information and coaching/motivational interventions alone will incentivize patients to make an effort to improve clinical outcomes. In a VBHC contract like the contract in Odsherred, the contract is based on the idea that the payer and the provider should share the risk, i.e., the cost of the treatment if there is a very low outcome. The settlement price was designed to vary depending on how well a treatment was realized in the individual diabetic patient depending on the outcome index. The risk was thought minimized by making the contract adjustable every 3 months.

5 Motivation

As mentioned, contract theory assumes that people act opportunistically. Individuals are depicted as selfish and are presumed to exploit situations for their own benefit and thus will only reveal private information if it is in their interest to do so (Bogetoft P & Olesen HB, 2004). In order to motivate the parties to participate in a value-based contract, the contract must provide the parties with utilities at least equal to what they could obtain outside the contract, which is known as the individual rationality constraint. It is a requirement that the independent decision-makers are motivated in order to align their interests.

According to the hierarchy of goals outlined by Bogetoft and Olesen (Bogetoft P & Olesen HB, 2004), motivation is split between the objectives of participation, effort, and investment. A good contract needs to ensure that the contracting parties have individual incentives to make desirable decisions, and there is usually a stochastic relationship between actions and the resulting output. This implies that output-based incentives will expose the producers to risk because the payment depends on factors that are (partly) outside of their control. However, there might be a trade-off between providing incentives and minimizing the cost of risk (Bogetoft P & Olesen HB, 2004).

In other words, the cost of offering a pay-for-performance contract is that it imposes a risk on the compensation, which then might increase compensation. Consequently, when choosing higher

performance pay, firms' trade-off the benefits of more effort against higher costs (Prendergast C, 2002). The risk might be increased with higher uncertainty – uncertainty is an integral problem of healthcare.

Pay-for-performance based plans explicitly link provider remuneration to the quality of care provided with the aims of modifying provider behavior and improving patient outcomes. If implemented successfully, pay-for-performance based schemes could drive improvements in quality and efficiency of care. However, financial incentives could also erode providers' intrinsic motivations, narrow their focus, promote unethical behavior, and ultimately increase health care inequalities. This is in line with what Bengt Holmström demonstrated in his work (Holmstrom B, 1979) (Holmstrom B & Milgrom P, 1991). For the provider, rewards and punishments must be linked to those outcomes that can be influenced by the actions of relevant agents in order to avoid chance to play a dominant role. Evidence from plans implemented to date suggest that carefully designed pay-for-performance based schemes that align sufficient rewards with clinical priorities might lead to improvements in the processes of diabetic care and their intermediate outcomes (Latham LP and Marshall EG, 2014). There is limited evidence, however, on whether improvements in processes of care result in improved outcomes in terms of patient satisfaction, fewer complications, and increased longevity.

The lack of adequate control groups and the context specificity of many pay-for-performances based plans has limited the strength and transferability of research findings until now. More robust studies are needed to explore both the potential long-term benefits of pay-for-performance based schemes and their unintended consequences. Some of the unintended consequences has been presented here and include an overly narrow focus on just a few aspects of a patient's health (tunnel vision), which may potentially be at the expense of other key objectives (goal displacement). Other unintended consequence is the potential increase in the inequality of the patients who are not capable or willing to participate in these projects e.g., patients who do not already master the motivation to sign up or are not offered to participate in the first place. Another concern can be the monopoly-like situation that pay-for-performance can create when only one provider is responsible for the patient's treatment with the patient having limited possibility for changing provider.

5.1 Participation

In a contract, incentives must also be designed to address two inherent challenges due to conflict between interests of principal and agent. Hence, participation problems also involve adverse selection in which one party has information that is not shared before a contract is signed. In Odsherred, there is a risk that the

patients referred to the program by the municipality do not accurately represent the patient mix in the population. The payer has an incentive to refer patients whom they know have a more complex prognosis. It also has an incentive to refer patients for other reasons, such as social status, that could result in a slimmer chance of a successful outcome in the program. In other words, the municipality has an incentive to use its detailed knowledge about citizens to select individuals for the program that are likely to have below average outcomes, thus pushing the cost of treating these patients on to the private partner. The provider, on the other hand, would have an incentive to turn away patients whose treatment is expected to be more expensive than the average. In Odsherred, part of the solution for this was to set some objective requirements for the conditions of the citizens who could be included.

This may lead to a moral hazard, “the hidden action problem” in this case overuse of services, after contracting or that partners in the contract are not making the same efforts as prior to the contract. In value-based health care you attempt to avoid moral hazard by reward according to value produced and thus attempts to motivate the provider to find the right level of services. A risk could however be, that the indicators used are too easy to full-fill, this is however regulated the contract is up for re-negotiation every three months. This flexibility provides an opportunity to adjust to a fairer model if the patients referred to the program do not represent the diabetes population of the overall community (adverse selection) or if the indicator should be adjusted (moral hazards). No re-negotiation took place during the initial 24-month period of the project, which indicates that none of the parties perceive the contract to be unfair - at least not to an extent that would justify the effort of re-negotiation. After the initial test period, the project was terminated.

In practice it proved very difficult to attract patients, and so case-mix adjustments were not needed and all interested patients were included. This type of context induced self-selection into the program implies risks of bias and inequality that should be addressed in the contract negotiations.

If companies are offered a payment corresponding to the average reservation value of all companies it can be assumed that only companies with low costs will enter the contract, which will lead to an overcompensation of the low-cost companies (Bogetoft P & Olesen HB, 2004). Efforts needs to be made to ensure that companies are incentivized to carry out actions that will maximize social welfare and prevent moral hazard problems caused by unobservable actions (Bogetoft P & Olesen HB, 2004).

In Odsherred, as well as in other diabetes management programs, the value to the public sector of a diabetic patient achieving a more stable blood sugar level can be significant in the long run. A more stable blood sugar will reduce the risk of late complications that may lead to amputations. It can result in fewer co-morbidities, hospital admissions, and health care costs, and can also reduce the cost of income-compensating public benefits. The value of future savings in the public sector is therefore high and the municipality thus has a considerable incentive to participate. However, there must be a built-in risk premium for the municipality in relation to the uncertainty of the long-term effect. The normal framework for public financial management has a number of limitations in regard to the municipality being able to recoup the value of the discounted savings. On one hand, the municipality will not be able to realize (or include) potential future savings in their current budget and, on the other hand, the savings in terms of improved health and public benefits will primarily accrue to regions (hospital and GP services) and the state (unemployment benefits, etc.) and, to a lesser extent, the municipality. Therefore, the cost of payment for the Accu-Chek Guide solution in Odsherred is set to a maximum of 30% above the baseline.

For the provider in Odsherred, Roche Diabetes Care, the incentive to participate in a performance-based agreement could be that the targeted teaching and counseling gives them a unique access point to the patients through which they are able to differentiate their products from those of their competitors. Diabetes treatment is a very competitive market and this gives Roche Diabetes Care an opportunity to expand their business model and circumnavigate wholesalers. In addition to all of this, Roche Diabetes Care most likely used this arrangement as a pilot project, hoping that it could be deployed in other larger markets.

5.2 Effort

In a VBHC contract, rewards and penalties are linked to performance levels on certain outputs - as an indicator for effort - whereby the payment to companies varies with their output levels. A number of aspects have to be considered when deciding on the strength of the rewards and penalties. One of these aspects relates to the controllability of performance levels. Uncontrollable performance levels, which may be attributed to external factors, will lead to uncertainty in the evaluation of the company's efforts, while highly controllable outputs should lead to stronger incentives. The precision with which outputs are measured also affects the connection between unobservable actions and observed outputs. Therefore, incentivizing effort could make the payments to companies' dependent on random and uncontrollable factors, which would increase the cost of risk (Bogetoft P & Olesen HB, 2004) (Milgrom P & Roberts J, 1992).

A performance-based payment system aims to attract and retain the most productive agents and discourage the least productive to the principal's benefit (Milgrom P & Roberts J, 1992). In Odsherred, only one company was considered for the contract, which created a monopoly situation. It is a given in the contract that the patients enrolled in the program could only use Roche Diabetes Care products as products from other brands were not compatible with the app in question. This eliminated any competition and possibly created a negative payer-provider dependency where the parties are locked-in. As of now, only about 30 out of a possible 900 diabetes patients in the municipality are enrolled but if the enrollment reached higher numbers, it might become difficult for other companies to enter the market. Whether the real motivation for the provider could be that they are able to lock-in the patients is unknown and perhaps too cynical to speculate in.

This de facto monopoly situation may be negative for the overall efficiency, as incentives to make an effort are reduced, if there is no real threat of losing the market. This may also have negative implications from a patient perspective in terms of a lock-in to the specific services and devices provided by the monopoly provider (Roche Diabetes Care). The potential benefits of a pay-for-performance plan may therefore come at the cost of less flexibility and choice for both the municipality and the patients. Although it is claimed in the contract that data is solely collected for the purpose of this project, it might give Roche Diabetes Care a unique opportunity to further innovate their project or develop project with higher degree of patient loyalty. It also introduces ethical consideration in terms of whether the patients are aware of and have given their full consent for their personal information being collected and used when they entered the project.

Only few stakeholders are represented in the Odsherred contract, but many stakeholders can be expected to have an interest in the contract as well as the output. If the contract were expanded to include other stakeholders, such as other suppliers of medication, there might be conflicting interests. The business model of Roche Diabetes Care builds on the premise that patients are in control and can delay the progression of diabetes. Other suppliers of medication, might have an incentive to bring patients on to the next, often times more expensive, treatment option, which would result in a conflict of different stakeholders' interests.

Defining outcome measures is critical if the contract is to provide incentives to optimize efforts.

There may also be limitations regarding the clinical outcome measures of diabetes care or lipid management; studies have shown that, despite efforts to achieve glycemic control, patients rarely achieve the goal of bringing the hemoglobin A_{1c} (A1C) to < 7%. Even in studies with an unusual organization of care, i.e., an excess of health professionals far beyond what is available in routine clinical settings, most patients did not achieve glycemic control (The DCCT Research Group, 1993).

Patient reported outcomes (PROs) will often be classified as a process measure rather than a health outcome measure. PROs evaluate the level of patient satisfaction in terms of assistance and comfort during the care cycle and are therefore useful for health care provider assessment. It is also important to note, however, that PROs might reveal little about patient health outcomes (EiT Health, 2020) but rather become an approximation for the measurements of outcomes.

The combination of PROs and clinical effects create a synergistic approach for measuring success in health care. PROs are measured before, during, and after care. PRO measurements may also provide standardized measures for improvement, encourage patient engagement, and, most importantly, evaluate patient priorities (EiT Health, 2020). However, the PRO questionnaire in the Odsherred case is rather short and cannot be expected to capture all the quality relevant process measurements of relevance for the patients.

One way to get a more complete picture of the total measure of value without adding any extra administrative burden could be combining data from multiple sources; however, this also provide further risk of companies being able to pick, misuse, or simply get access to highly sensitive patient data without the awareness and consent of the patient. Typically, a person's health information is fragmented across multiple proprietary systems and data repositories (administrative, process, cost, PROs, etc.), and although not as relevant in Denmark as elsewhere, it makes it challenging to develop a holistic view of the patient's health or the care that they have received (World Economic Forum, 2018).

It is estimated in the contract that the cost of strips to the municipality for diabetes patients is DKK 10.000 per patient per year. This number can vary in the contract depending on the quality of the service from +/- 10 to 30 %. The relative low variance of reimbursement combined with the low number of enrollments results in a budget impact ranging from 210.000 DKK (30 patients x DKK 7.000 per patient) to 390.000 DKK (30 patients x DKK 13.000 per patient). Compared to the overall health budget, this has a relatively small impact but it might still be a good incentive for stakeholders to perform.

The contract in place in Odsherred might incentivize Roche Diabetes Care to perform well on just the few quality measures, that they are measured on, and pay less attention to the rest of the treatment that diabetes patients require. Agreeing on a contract is a compromise between being comprehensive enough and not being too complex. It would however be beneficial if there can be a higher incentive for the provider to maintain quality even if not all aspects of quality are being monitored.

5.3 Investment

Finally, to incentivize the contracting parties to invest in order to ensure future benefits, the contract must solve issues such as the hold-up problem, a situation where one party has invested in assets that are specific to a particular use and therefore worries about being forced to accept disadvantageous terms later (Milgrom P & Roberts J, 1992). The horizon problem, which concerns about reduced effort when a contract is not extended (Bogetoft P & Olesen HB, 2004). There is no indication that any of this was present in Odsherred, perhaps given the status as pilot project there was little incentive to put oneself in such a situation.

5.4 Sub-conclusion

In conclusion, there are many factors which might influence the motivation of the parties involved. In order to motivate the parties to participate in a value-based contract, the contract must provide the parties with utilities at least equal to what they could obtain outside the contract due to the limited number of citizens involved and the termination of the project after the pilot phase this must be concluded has over-all not been the case. If implemented successfully, pay-for-performance based schemes could drive improvements in quality and efficiency of care. However, financial incentives could also erode providers' intrinsic motivations, narrow their focus, promote unethical behavior, and ultimately increase health care inequalities. The contract in place in Odsherred might incentivize Roche Diabetes Care to perform well on just the few quality measures, that they are measured on, and pay less attention to the rest of the treatment that diabetes patients require. The financial impact of the project is deemed relatively small and in itself not a very high motivational factor to increase effort. The risk of adverse selection and moral hazards were attempted reduced by making the contract adjustable.

6 Transaction costs

The hypothesis of transaction costs economics is that transactions are organized to minimize transaction costs. The direct cost of contracting is the time and money spent on preparing the contract, collecting information, monitoring, bargaining, and conflict resolution; in other words, the cost of running the contract (Bogetoft P & Olesen HB, 2004). Ideally, these costs should be kept low as they do not directly generate a surplus. However, the cost of contracting is a relevant cost as it provides the information required for well-coordinated decisions (Milgrom P & Roberts J, 1992). Different types of transaction costs are analyzed below:

6.1 Entering contract

Bogetoft and Olesen (2004) outlines three primary sources of transaction costs when entering a contract: 1) The difficulty of foreseeing the possible contingencies in a complex world, such as the difficulty in setting up a complete set of possible outcomes, 2) the cost of wording the contract in which the parties find a common language to describe the different contingencies and the connected actions, and finally, 3) the cost of writing a legally binding contract so that it can be enforced by the judicial system if need be (Bogetoft P & Olesen HB, 2004).

Transaction costs in the initiation phase can cause the parties to enter incomplete contracts, i.e., contracts which do not give specific guidelines for every situation. Incomplete contracts might require subsequent negotiations to answer the unsolved questions, which can lead to hold-up situations and higher overall transaction costs.

In semi-structured interviews with representative for the provider and payer, both stated that it would be beneficial for the contract if it was more intuitive and less complex (Starr L, 2021), and that it is not clear how the different measures add up to the index number for example, and how that translates into the price to be paid.

6.2 Conflict resolution

Contracts cannot specify every eventuality and Hart argues that it can be helpful to agree now to agree later in cases of incomplete contracts (Hart O, 1995). In the Odsherred case this was not up for discussion. Within VBHC contracts in general, for example, pharmaceutical firms negotiate higher prices for drugs that demonstrate higher value or less uncertainty ex post. When the value of a new medicine is difficult to

ascertain ex ante at the initial contracting point between a payer and pharmaceutical company, an alternative is to track the performance of the product in a defined patient population over a defined time period so that reimbursement is based on the health and cost outcomes achieved (Garrison LP, 2013). Pay-for-performance-based risk-sharing arrangements represent a mechanism for reducing uncertainty at product launch and incentivizing investment in evidence collection while a technology is used within a health care system.

6.3 Monitoring

Treatment and settlement baselines are calibrated regularly in Odsherred in order to ensure continuous adjustment of baseline levels to the actual patient population and to the development in the expenditure level.

Ideally, the baseline for the answers to the first of the PRO related questions, “How satisfied are you with your blood glucose level at the moment?“, will be based on a population of diabetics who have not yet been treated with the Accu-Chek Guide Solution so that there is a starting point before treatment. It is important to note that a case-mix adjustment may be required if the population is different from the population initiating treatment with the Accu-Chek Guide Solution. Since there is no data from a previous population, the initial PRO baseline is determined based on satisfaction measurements in general.

In the case of a possible termination of the project there might be a failure in the continuity in patient management, which is essential in securing effective outcomes for the patients.

Since there is no empirical data to support the determination of clinical effect and PRO baselines, an iterative process is needed to qualify the baseline levels of clinical effect and patient satisfaction described above.

Previous studies have found that, regardless of the clinical care offered, the outcomes are substantially influenced by the clinical decisions made by patients independent of physician care. Demographic factors of the patients, such as their age and sex, and costs of drugs are important determinants of whether the patients chose to follow physician advice (Schultz JS & O'Connell JC et al, 2005) and there is a risk that pay-for-performance based schemes ignore the dependency of the outcomes of care on patient behavior independent of the excellence of the care provided. Therefore, there is a risk that challenging patients

might not be included in these efforts (adverse selection). One solution could be to make a high-risk tier in the contract.

The denominator of the value ratio is cost. However, there are several challenges in measuring this in a municipal health system; some reimbursement systems are based on department rather than patient-based data and hence there might not be sufficiently accurate information on the cost of the full cycle of care for a patient for a particular medical condition. As a result, cost allocations are often based on charges and not actual costs.

It is stated in the contract in Odsherred that the expectation is that a more stable HbA1c will reduce treatment activity, but there are no specific measures of activity incorporated into the aggregate outcome measure, even though the parties have stated an intention to include this later.

Another cost monitoring issue is the lack of clarity regarding which cost indicators have been perceived as associated with the intervention. It is therefore not possible to evaluate whether the new intervention creates more value than the status quo. Care pathway mapping is essential for understanding the processes and measure costs at the patient level. The pathway captures the baseline from which organizational changes can be tested and measured throughout improvement cycles (EiT Health, 2020)

In the contract in Odsherred, the cost is set using a baseline of 10.000 DKK per patient, which is equivalent to the average cost for the municipality of strips per year per patient while the cost covered by the provider; the value-based healthcare set up includes many more items associated with the management of diabetes. The cost of treating a diabetes patient must include not only the costs associated with endocrinological care but also the costs of managing and treating associated conditions and complications such as vascular, retinal, and renal disease as well as the costs of in primary care (EiT Health, 2020).

A prerequisite for improvements in efficiency, equity, and patient responsiveness is that both the payer and provider will have access to accurate information on the performance of the cost and quality.

6.4 Influence costs

Transaction costs have been described by Milgrom and Roberts as the costs of providing solutions to the problems of coordination and motivation (Milgrom P & Roberts J, 1992). In transaction cost economics, contractual designs are created to minimize transaction costs. However, minimization of transaction costs may conflict with the objectives of coordination and motivation. Following the hierarchy created by Bogetoft and Olesen (2004), four sources of transaction costs are to be considered: influence activities, entering a contract, monitoring, and conflict resolution.

For the first, influence activities, may involve manipulating information in terms of manipulating facts or suppressing unfavorable information in a way that emphasizes the arguments that support the preferred decision. To reduce influence activities, the principal can, for example, limit communication prior to decision making. This, however, entails a trade-off between reducing influence costs and obtaining information that could be valuable for decision making (Milgrom P & Roberts J, 1990).

The transaction costs of entering a contract include the resources involved in determining and writing a contract under the difficulty of foreseeing all possible outcomes and formulating a contract which describes the different contingencies and the actions that each party has to take with sufficient clarity (Milgrom P & Roberts J, 1992). The contract must also be enforceable. The transaction costs of entering a contract can be reduced by, for example, using a standard contract with all companies (Bogetoft P & Olesen HB, 2004). However, the transaction costs reflect activities which provide the information required to improve coordination and motivation. In the case of Odsherred, it seems like the transaction costs were high and the time spend on the initial steps were extensive.

Monitoring is a way to incentivize effort. The cost of monitoring can be related to having third parties verify financial statements or the cost of monitoring performance or outcome (Milgrom P & Roberts J, 1992). Within health care, the monitoring can be resource heavy and it is important that the monitoring does not create unnecessary paper work for e.g., clinicians. For Odsherred, it is unclear if the cost of monitoring played a role in the low enrollment and in the difficulties of getting health care professionals involved. It is however evident, that the number of daily monitoring activities are higher for a patient enrolled in the program than what most diabetes patients do on an average day. Furthermore, it is very important, than stakeholders find the monitoring activities important for the value of the treatment and not solely as a mean to fulfill the contract.

Lastly, conflict resolutions may be caused by incomplete contracts that can leave room for situations not covered by the contract, which can lead to conflicts. Parties act according to perceived incentives, which may differ from true incentives. It is therefore important that the contracts are simple and reflect their choices of action and how they correspond to the compensation scheme agreed to in the contract. Simple contracts may mean less complete ones, which can lead to interpretation issues. In order to have a motivational effect on the effort, the contract should be agreed to ex ante so that there is no motivation from an unexpected bonus (Bogetoft P & Olesen HB, 2004).

6.5 Sub-conclusion

In conclusion, the transaction cost of entering and maintaining this contract was found to be relative high: The time and money spent on preparing the contract, collecting information, monitoring, bargaining, and conflict resolution was found to be very high for this particular case, and the contract not found to be very intuitive which could lead to conflicts. The high cost, seems even more extreme given the few patients involved.

7 Conclusion

For quite some time it has been discussed among healthcare policymakers in Denmark as well as many other countries how to make a payment system transition from volume to value, i.e., value-based healthcare. Value-based healthcare contracts are a type of innovative payment model that brings together key stakeholders – often times the health care payers, patients, clinical decision makers and the providers - to deliver healthcare to patients. In the contract evaluated here, a value-based diabetes project was introduced for a two-year period starting in December 2017 with an aim to ensure that Type 2 diabetic patients received the necessary support, counselling and tools, and the municipality's reimbursement depended on the value delivered to the patients.

A VBHC contract has the potential of reducing the payer's risk of a sub-optimal purchase, facilitate earlier access to new health technologies for patients or consumers because the risk is shared between payer and provider, provide higher value care for the patient since their feedback can be incorporated into the performance measures, offer more efficient pricing mechanisms, and can serve as a catalyst for generating enhanced real-world medical evidence. The value-based settlement in the Odsherred project should encourage the provider (Roche Diabetes Care) to ensure as stable a blood sugar level as possible and

likewise to obtain as many satisfied patients as possible. At the same time, the idea was that Odsherred municipality and Roche Diabetes Care should share the cost of the treatment if there was a lower-than-expected outcome from the treatment. Therefore, the settlement price was designed to vary depending on how well a treatment was realized in the individual diabetic patient, as measured by the outcome index.

Despite the obvious benefits, the use of VBHC contracts is still limited. One reason for this is that the design and implementation of value-based contracts are complicated, logistically challenging and come with inherent risks for both parties. There further needs to be an appropriate incentive structure for stakeholders to pursue such contract.

Agreeing on the terms of a contract can be challenging, especially under conditions of uncertainty and asymmetric information. Economic transactions between self-interested economic agents; e.g., health care provider and payer, can give rise to conflicts of interests; designing a utility regulation involves tradeoffs. Trade-offs between several different goals of contract design takes place; coordinating (ensuring that the products are offered at the right time and place), motivation (ensuring that the contract parties have individual incentives to take socially desirable decisions), and transaction costs (ensuring that coordination and motivation are provided at the lowest possible cost).

In this paper it was discussed how a pay-for-performance based health care arrangement between a private health care provider and a public payer in Denmark, Roche Diabetes Care and Odsherred municipality, respectively, priorities different goals in contract design. While they may agree on a contract, it is clear that their goals may conflict in such a way that focusing on one objective comes at the cost of assigning a lower priority to other objectives. The trade-offs determine the relative importance of different objectives. A good alignment between patient preferences and provider outcomes as well as uncertainties about the future challenges within the healthcare sector are important factors to incorporate into the contract.

There need to be a consensus definition of value that all stakeholders can agree on. Hence there needs to be an agreement on which outcome measures to use and to make sure that monitoring these outcomes are not too resource consuming. In order to implement risk-based contracts tied to outcomes payers must have access to large volumes of e.g., clinical data, pharmacy and medical claims.

Some of the unintended consequences has been presented here and include an overly narrow focus on just a few aspects of a patient's health, which may potentially be at the expense of other key objectives. Other

unintended consequence is the potential increase in the inequality of the patients who are not capable or willing to participate in these projects e.g., patients who do not already master the motivation to sign up or are not offered to participate in the first place. Another concern can be the monopoly-like situation that pay-for-performance can create when only one provider is responsible for the patient's treatment with the patient having limited possibility for changing provider.

Thus, while value-based contracts are appealing because of the potential of an improvement in patient's health for equal or less money, there are many factors to take into consideration when agreeing upon a contract in terms of coordination, motivation, and transaction costs as outlined above, as well as ethical considerations in terms of flexibility trade-offs, data sharing, and equal access to care.

8 Literature

Bogetoft P and Olesen HB. 2004. *Design of Production Contracts.* Copenhagen : Copenhagen Business School Press, 2004.

Danske Regioner. 2015. *Pres på sundhedsvæsenet: derfor stiger sygehusudgifterne – sådan holder vi væksten nede.* s.l. : https://www.regioner.dk/media/2209/2015-pres-paa-sundhedsvaesenet.pdf, 2015.

Davies MJ, D'Alessio, et al,. 2018. Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care.* Dec 2018, Årg. 41, 12, s. 2669-2701.

Donaldson C & Gerard K. 1993. *Economics of Health Care Financing: The Visible Hand* . London : Palgrave, 1993.

EiT Health. 2020. *Implementing Value-Based Health Care in Europe: Handbook for Pioneers (Director: Gregory Katz).* s.l. : EiT Health, 2020. https://eithealth.eu/wp-content/uploads/2020/05/Implementing-Value-Based-Healthcare-In-Europe_web-4.pdf.

Garrison LP, Towse A, et al,. 2013. Performance-Based Risk-Sharing Arrangements - Good Practices for Design, Implementation, and Evaluation: Report of the ISPOR Good Practices for Performance-Based Risk-Sharing Arrangements Task Force. *Value in Health.* 2013, Årg. 16, s. 703-719.

Gibbons R and Murphy KJ. 1992. Optimal Incentive Contracts in the Presence of Career Concerns: Theory and Evidence. *Journal of Political Economy.* 1992, Årg. 100, 3, s. 468–505.

Gonzalez JS, Tanenbaum ML, Commissariat PV,. 2016. Psychosocial Factors in Medication Adherence and Diabetes Self-Management: Implications for Research and Practice. *Am Psychol.* 2016, s. 539-551.

Hart O. 1995. *Contratcs, and Financial Structure.* Oxford : Clarendon Press, 1995.

Hill J. 2013. Understanding the Social Factors That Contribute to Diabetes: A Means to Informing Health Care and Social Policies for the Chronically Ill. *The Permanenete Journal.* 2013, s. 67-72.

Holmstrom B & Milgrom P. 1991. Multitask Principal-Agent analyses: Incentives Contracts, Asset Ownership, and Job Design. *Journal of Law Economics and Organization.* 1991, Årg. 7.

Holmstrom B. 1979. Moral Hazard and Observability,. *The Bell Journal of Economics.* 1979, Årg. 10, 1.

Khunti K et al. 2018. Therapeutic inertia in the treatment of hyperglycaemia in patients with type 2 diabetes: A systematic review. *Diabetes Obes Metab.* 2018, Årg. 20, s. 427-437.

Klemp M, Frønsdal KB et al,. 2011. What principles should govern the use of managed entry agreements? *Int J Technol Assess Health Care.* 2011, s. 77-83.

Latham LP and Marshall EG. 2014. Performance-Based Financial Incentives for Diabetes Care: An Effective Strategy? *CJD.* October 2014, s. 83-87.

Mieritz K. 2019. Nybrud: Højere betaling for gode resutater. *Indblik.* [Online] 20. Sep 2019. [Citeret: 22. Oct 2019.] https://indblik.net/2019/09/20/nybrud-hoejere-betaling-for-gode-resultater/.

Milgrom P & Roberts J. 1990. An Economic Approac to Influence Activities and Organizations. *American Journal of Sociology.* 1990, Årg. 94, s. 154-179.

—. 1992. *Economics, Organization and Management.* New Jersey : Prentice Hall, 1992.

NEJM Catalyst. 2017. What is Value-Based Healthcare? *NEJM Catalyst.* Jan 2017.

Porter ME. 2010. What is value in health care? *N Eng J Med.* 2010, Årg. 363, s. 2477-81.

Prendergast C. 2002. The Tenuous Trade-Off between Risk and Incentives. *The Journal of Political Economy.* 2002, Årg. 110, 5, s. 1071-1102.

Roche. 2018. Stay in the Zone. [Online] 2018. www.stay-in-the-zone.dk.

—. 2018. *Vores bidrag i Danmark.* København : Roche a/s, 2018.

Schultz JS & O'Connell JC et al. 2005. Determinants of compliance statin therapy and low-density lipoprotein goal attainment in a managed care population. *Am J Manag Care.* 11 2005, s. 306 -312.

Shavell S. 1979. Risk Sharing and Incentivies in the Principal and Agent Relationship. *The Bell Journal of Economics.* 1979, Årg. 10, 1, s. 55-73.

Starr L. 2021. *Assessment of Roche Diabetes Care /Odsherred Municipality Value-based Health Care Diabetes Project 2017-2019 - Feasibility and Transferability Lessons.* Copenhagen : s.n., 2021.

Strandberg RB, Graue M et al,. 2014. Relationships of diabetes-specific emotional distress, depression, anxiety, and overall well-being with HbA1c in adult persons with type 1 diabetes. *J of Psychosom Res.* 2014, Årg. 77, s. 174-9.

The DCCT Research Group. 1993. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus,. *N Engl J Med.* 1993, Årg. 329, s. 977 -983.

The Economist - Intelligence Unit. 2018. *Value-based healthcare: A global assessment.* s.l. : The Economist, 2018.

Vrangbæk K & Starr L. 2021. Value-Based Health Care Classifications and Experiences in Denmark and Sweden. *Working Paper University of Copenhagen.* 2021.

Williamson O. 1985. The Goverance of Contractual Relations,. [forfatter] L. and R.S Kroszner (Ed.) Putterman. *The Economic Nature of the Firm.* Cambridge : Cambridge University Press, 1985.

Wohlin J, Stalberg H, et al,. 2012. *Uppföljningsrapport vårdval höft- och knäprotesoperationer Preliminär analys, slutsatser och rekommendationer Sammanfattning.* s.l. : Hälso- och sjukvårdsförvaltningen, Stockholms Läns Landsting, 2012.

World Economic Forum. 2018. *Value in Healthcare: Accelerating the Pace of Health System Transformation.* Davos, Schweiz : World Economic Forum, 2018.

Young-Hyman, de Groot et al,. 2016. Psychosocial Care for People With Diabetes: A Position Statement of the American Diabetes Association. *Diabetes Care.* Dec 2016, Årg. 39, 12, s. 2126-2140.

TITLER I PH.D.SERIEN:

2004

1. Martin Grieger
Internet-based Electronic Marketplaces and Supply Chain Management

2. Thomas Basbøll
LIKENESS
A Philosophical Investigation

3. Morten Knudsen
Beslutningens vaklen
En systemteoretisk analyse of moderniseringen af et amtskommunalt sundhedsvæsen 1980-2000

4. Lars Bo Jeppesen
Organizing Consumer Innovation
A product development strategy that is based on online communities and allows some firms to benefit from a distributed process of innovation by consumers

5. Barbara Dragsted
SEGMENTATION IN TRANSLATION AND TRANSLATION MEMORY SYSTEMS
An empirical investigation of cognitive segmentation and effects of integrating a TM system into the translation process

6. Jeanet Hardis
Sociale partnerskaber
Et socialkonstruktivistisk casestudie af partnerskabsaktørers virkelighedsopfattelse mellem identitet og legitimitet

7. Henriette Hallberg Thygesen
System Dynamics in Action

8. Carsten Mejer Plath
Strategisk Økonomistyring

9. Annemette Kjærgaard
Knowledge Management as Internal Corporate Venturing
– a Field Study of the Rise and Fall of a Bottom-Up Process

10. Knut Arne Hovdal
De profesjonelle i endring
Norsk ph.d., ej til salg gennem Samfundslitteratur

11. Søren Jeppesen
Environmental Practices and Greening Strategies in Small Manufacturing Enterprises in South Africa
– A Critical Realist Approach

12. Lars Frode Frederiksen
Industriel forskningsledelse
– på sporet af mønstre og samarbejde i danske forskningsintensive virksomheder

13. Martin Jes Iversen
The Governance of GN Great Nordic
– in an age of strategic and structural transitions 1939-1988

14. Lars Pynt Andersen
The Rhetorical Strategies of Danish TV Advertising
A study of the first fifteen years with special emphasis on genre and irony

15. Jakob Rasmussen
Business Perspectives on E-learning

16. Sof Thrane
The Social and Economic Dynamics of Networks
– a Weberian Analysis of Three Formalised Horizontal Networks

17. Lene Nielsen
Engaging Personas and Narrative Scenarios – a study on how a user-centered approach influenced the perception of the design process in the e-business group at AstraZeneca

18. S.J Valstad
Organisationsidentitet
Norsk ph.d., ej til salg gennem Samfundslitteratur

19. Thomas Lyse Hansen
Six Essays on Pricing and Weather risk in Energy Markets

20. Sabine Madsen
Emerging Methods – An Interpretive Study of ISD Methods in Practice

21. Evis Sinani
The Impact of Foreign Direct Investment on Efficiency, Productivity Growth and Trade: An Empirical Investigation

22. Bent Meier Sørensen
Making Events Work Or, How to Multiply Your Crisis

23. Pernille Schnoor
Brand Ethos
Om troværdige brand- og virksomhedsidentiteter i et retorisk og diskursteoretisk perspektiv

24. Sidsel Fabech
Von welchem Österreich ist hier die Rede?
Diskursive forhandlinger og magtkampe mellem rivaliserende nationale identitetskonstruktioner i østrigske pressediskurser

25. Klavs Odgaard Christensen
Sprogpolitik og identitetsdannelse i flersprogede forbundsstater
Et komparativt studie af Schweiz og Canada

26. Dana B. Minbaeva
Human Resource Practices and Knowledge Transfer in Multinational Corporations

27. Holger Højlund
Markedets politiske fornuft
Et studie af velfærdens organisering i perioden 1990-2003

28. Christine Mølgaard Frandsen
A.s erfaring
Om mellemværendets praktik i en transformation af mennesket og subjektiviteten

29. Sine Nørholm Just
The Constitution of Meaning – A Meaningful Constitution?
Legitimacy, identity, and public opinion in the debate on the future of Europe

2005

1. Claus J. Varnes
Managing product innovation through rules – The role of formal and structured methods in product development

2. Helle Hedegaard Hein
Mellem konflikt og konsensus – Dialogudvikling på hospitalsklinikker

3. Axel Rosenø
Customer Value Driven Product Innovation – A Study of Market Learning in New Product Development

4. Søren Buhl Pedersen
Making space
An outline of place branding

5. Camilla Funck Ellehave
Differences that Matter
An analysis of practices of gender and organizing in contemporary workplaces

6. Rigmor Madeleine Lond
Styring af kommunale forvaltninger

7. Mette Aagaard Andreassen
Supply Chain versus Supply Chain Benchmarking as a Means to Managing Supply Chains

8. Caroline Aggestam-Pontoppidan
From an idea to a standard
The UN and the global governance of accountants' competence

9. Norsk ph.d.

10. Vivienne Heng Ker-ni
An Experimental Field Study on the

Effectiveness of Grocer Media Advertising
Measuring Ad Recall and Recognition, Purchase Intentions and Short-Term Sales

11. Allan Mortensen
Essays on the Pricing of Corporate Bonds and Credit Derivatives

12. Remo Stefano Chiari
Figure che fanno conoscere
Itinerario sull'idea del valore cognitivo e espressivo della metafora e di altri tropi da Aristotele e da Vico fino al cognitivismo contemporaneo

13. Anders McIlquham-Schmidt
Strategic Planning and Corporate Performance
An integrative research review and a meta-analysis of the strategic planning and corporate performance literature from 1956 to 2003

14. Jens Geersbro
The TDF – PMI Case
Making Sense of the Dynamics of Business Relationships and Networks

15 Mette Andersen
Corporate Social Responsibility in Global Supply Chains
Understanding the uniqueness of firm behaviour

16. Eva Boxenbaum
Institutional Genesis: Micro – Dynamic Foundations of Institutional Change

17. Peter Lund-Thomsen
Capacity Development, Environmental Justice NGOs, and Governance: The Case of South Africa

18. Signe Jarlov
Konstruktioner af offentlig ledelse

19. Lars Stæhr Jensen
Vocabulary Knowledge and Listening Comprehension in English as a Foreign Language
An empirical study employing data elicited from Danish EFL learners

20. Christian Nielsen
Essays on Business Reporting
Production and consumption of strategic information in the market for information

21. Marianne Thejls Fischer
Egos and Ethics of Management Consultants

22. Annie Bekke Kjær
Performance management i Proces-innovation
– belyst i et social-konstruktivistisk perspektiv

23. Suzanne Dee Pedersen
GENTAGELSENS METAMORFOSE
Om organisering af den kreative gøren i den kunstneriske arbejdspraksis

24. Benedikte Dorte Rosenbrink
Revenue Management
Økonomiske, konkurrencemæssige & organisatoriske konsekvenser

25. Thomas Riise Johansen
Written Accounts and Verbal Accounts
The Danish Case of Accounting and Accountability to Employees

26. Ann Fogelgren-Pedersen
The Mobile Internet: Pioneering Users' Adoption Decisions

27. Birgitte Rasmussen
Ledelse i fællesskab – de tillidsvalgtes fornyende rolle

28. Gitte Thit Nielsen
Remerger
– skabende ledelseskræfter i fusion og opkøb

29. Carmine Gioia
A MICROECONOMETRIC ANALYSIS OF MERGERS AND ACQUISITIONS

30. Ole Hinz
Den effektive forandringsleder: pilot, pædagog eller politiker?
Et studie i arbejdslederes meningstilskrivninger i forbindelse med vellykket gennemførelse af ledelsesinitierede forandringsprojekter

31. Kjell-Åge Gotvassli
Et praksisbasert perspektiv på dynamiske
læringsnettverk i toppidretten
Norsk ph.d., ej til salg gennem Samfundslitteratur

32. Henriette Langstrup Nielsen
Linking Healthcare
An inquiry into the changing performances of web-based technology for asthma monitoring

33. Karin Tweddell Levinsen
Virtuel Uddannelsespraksis
Master i IKT og Læring – et casestudie i hvordan proaktiv proceshåndtering kan forbedre praksis i virtuelle læringsmiljøer

34. Anika Liversage
Finding a Path
Labour Market Life Stories of Immigrant Professionals

35. Kasper Elmquist Jørgensen
Studier i samspillet mellem stat og erhvervsliv i Danmark under
1. verdenskrig

36. Finn Janning
A DIFFERENT STORY
Seduction, Conquest and Discovery

37. Patricia Ann Plackett
Strategic Management of the Radical Innovation Process
Leveraging Social Capital for Market Uncertainty Management

2006

1. Christian Vintergaard
Early Phases of Corporate Venturing

2. Niels Rom-Poulsen
Essays in Computational Finance

3. Tina Brandt Husman
Organisational Capabilities, Competitive Advantage & Project-Based Organisations
The Case of Advertising and Creative Good Production

4. Mette Rosenkrands Johansen
Practice at the top
– how top managers mobilise and use non-financial performance measures

5. Eva Parum
Corporate governance som strategisk kommunikations- og ledelsesværktøj

6. Susan Aagaard Petersen
Culture's Influence on Performance Management: The Case of a Danish Company in China

7. Thomas Nicolai Pedersen
The Discursive Constitution of Organizational Governance – Between unity and differentiation
The Case of the governance of environmental risks by World Bank environmental staff

8. Cynthia Selin
Volatile Visions: Transactons in Anticipatory Knowledge

9. Jesper Banghøj
Financial Accounting Information and Compensation in Danish Companies

10. Mikkel Lucas Overby
Strategic Alliances in Emerging High-Tech Markets: What's the Difference and does it Matter?

11. Tine Aage
External Information Acquisition of Industrial Districts and the Impact of Different Knowledge Creation Dimensions

A case study of the Fashion and Design Branch of the Industrial District of Montebelluna, NE Italy

12. Mikkel Flyverbom
Making the Global Information Society Governable
On the Governmentality of Multi-Stakeholder Networks

13. Anette Grønning
Personen bag
Tilstedevær i e-mail som interaktionsform mellem kunde og medarbejder i dansk forsikringskontekst

14. Jørn Helder
One Company – One Language?
The NN-case

15. Lars Bjerregaard Mikkelsen
Differing perceptions of customer value
Development and application of a tool for mapping perceptions of customer value at both ends of customer-supplier dyads in industrial markets

16. Lise Granerud
Exploring Learning
Technological learning within small manufacturers in South Africa

17. Esben Rahbek Pedersen
Between Hopes and Realities:
Reflections on the Promises and Practices of Corporate Social Responsibility (CSR)

18. Ramona Samson
The Cultural Integration Model and European Transformation.
The Case of Romania

2007

1. Jakob Vestergaard
Discipline in The Global Economy
Panopticism and the Post-Washington Consensus

2. Heidi Lund Hansen
Spaces for learning and working
A qualitative study of change of work, management, vehicles of power and social practices in open offices

3. Sudhanshu Rai
Exploring the internal dynamics of software development teams during user analysis
A tension enabled Institutionalization Model; "Where process becomes the objective"

4. Norsk ph.d.
Ej til salg gennem Samfundslitteratur

5. Serden Ozcan
EXPLORING HETEROGENEITY IN ORGANIZATIONAL ACTIONS AND OUTCOMES
A Behavioural Perspective

6. Kim Sundtoft Hald
Inter-organizational Performance Measurement and Management in Action
– An Ethnography on the Construction of Management, Identity and Relationships

7. Tobias Lindeberg
Evaluative Technologies
Quality and the Multiplicity of Performance

8. Merete Wedell-Wedellsborg
Den globale soldat
Identitetsdannelse og identitetsledelse i multinationale militære organisationer

9. Lars Frederiksen
Open Innovation Business Models
Innovation in firm-hosted online user communities and inter-firm project ventures in the music industry
– A collection of essays

10. Jonas Gabrielsen
Retorisk toposlære – fra statisk 'sted' til persuasiv aktivitet

11. Christian Moldt-Jørgensen
Fra meningsløs til meningsfuld evaluering.
Anvendelsen af studentertilfredshedsmålinger på de korte og mellemlange videregående uddannelser set fra et psykodynamisk systemperspektiv

12. Ping Gao
Extending the application of actor-network theory
Cases of innovation in the telecommunications industry

13. Peter Mejlby
Frihed og fængsel, en del af den samme drøm?
Et phronetisk baseret casestudie af frigørelsens og kontrollens sameksistens i værdibaseret ledelse!

14. Kristina Birch
Statistical Modelling in Marketing

15. Signe Poulsen
Sense and sensibility:
The language of emotional appeals in insurance marketing

16. Anders Bjerre Trolle
Essays on derivatives pricing and dynamic asset allocation

17. Peter Feldhütter
Empirical Studies of Bond and Credit Markets

18. Jens Henrik Eggert Christensen
Default and Recovery Risk Modeling and Estimation

19. Maria Theresa Larsen
Academic Enterprise: A New Mission for Universities or a Contradiction in Terms?
Four papers on the long-term implications of increasing industry involvement and commercialization in academia

20. Morten Wellendorf
Postimplementering af teknologi i den offentlige forvaltning
Analyser af en organisations kontinuerlige arbejde med informationsteknologi

21. Ekaterina Mhaanna
Concept Relations for Terminological Process Analysis

22. Stefan Ring Thorbjørnsen
Forsvaret i forandring
Et studie i officerers kapabiliteter under påvirkning af omverdenens forandringspres mod øget styring og læring

23. Christa Breum Amhøj
Det selvskabte medlemskab om managementstaten, dens styringsteknologier og indbyggere

24. Karoline Bromose
Between Technological Turbulence and Operational Stability
– An empirical case study of corporate venturing in TDC

25. Susanne Justesen
Navigating the Paradoxes of Diversity in Innovation Practice
– A Longitudinal study of six very different innovation processes – in practice

26. Luise Noring Henler
Conceptualising successful supply chain partnerships
– Viewing supply chain partnerships from an organisational culture perspective

27. Mark Mau
Kampen om telefonen
Det danske telefonvæsen under den tyske besættelse 1940-45

28. Jakob Halskov
The semiautomatic expansion of existing terminological ontologies using knowledge patterns discovered

on the WWW – an implementation and evaluation

29. Gergana Koleva
European Policy Instruments Beyond Networks and Structure: The Innovative Medicines Initiative

30. Christian Geisler Asmussen
Global Strategy and International Diversity: A Double-Edged Sword?

31. Christina Holm-Petersen
Stolthed og fordom
Kultur- og identitetsarbejde ved skabelsen af en ny sengeafdeling gennem fusion

32. Hans Peter Olsen
Hybrid Governance of Standardized States
Causes and Contours of the Global Regulation of Government Auditing

33. Lars Bøge Sørensen
Risk Management in the Supply Chain

34. Peter Aagaard
Det unikkes dynamikker
De institutionelle mulighedsbetingelser bag den individuelle udforskning i professionelt og frivilligt arbejde

35. Yun Mi Antorini
Brand Community Innovation
An Intrinsic Case Study of the Adult Fans of LEGO Community

36. Joachim Lynggaard Boll
Labor Related Corporate Social Performance in Denmark
Organizational and Institutional Perspectives

2008

1. Frederik Christian Vinten
Essays on Private Equity

2. Jesper Clement
Visual Influence of Packaging Design on In-Store Buying Decisions

3. Marius Brostrøm Kousgaard
Tid til kvalitetsmåling?
– Studier af indrulleringsprocesser i forbindelse med introduktionen af kliniske kvalitetsdatabaser i speciallægepraksissektoren

4. Irene Skovgaard Smith
Management Consulting in Action
Value creation and ambiguity in client-consultant relations

5. Anders Rom
Management accounting and integrated information systems
How to exploit the potential for management accounting of information technology

6. Marina Candi
Aesthetic Design as an Element of Service Innovation in New Technology-based Firms

7. Morten Schnack
Teknologi og tværfaglighed
– en analyse af diskussionen omkring indførelse af EPJ på en hospitalsafdeling

8. Helene Balslev Clausen
Juntos pero no revueltos – un estudio sobre emigrantes norteamericanos en un pueblo mexicano

9. Lise Justesen
Kunsten at skrive revisionsrapporter. En beretning om forvaltningsrevisionens beretninger

10. Michael E. Hansen
The politics of corporate responsibility: CSR and the governance of child labor and core labor rights in the 1990s

11. Anne Roepstorff
Holdning for handling – en etnologisk undersøgelse af Virksomheders Sociale Ansvar/CSR

12. Claus Bajlum
Essays on Credit Risk and Credit Derivatives

13. Anders Bojesen
The Performative Power of Competence – an Inquiry into Subjectivity and Social Technologies at Work

14. Satu Reijonen
Green and Fragile
A Study on Markets and the Natural Environment

15. Ilduara Busta
Corporate Governance in Banking
A European Study

16. Kristian Anders Hvass
A Boolean Analysis Predicting Industry Change: Innovation, Imitation & Business Models
The Winning Hybrid: A case study of isomorphism in the airline industry

17. Trine Paludan
De uvidende og de udviklingsparate
Identitet som mulighed og restriktion blandt fabriksarbejdere på det aftayloriserede fabriksgulv

18. Kristian Jakobsen
Foreign market entry in transition economies: Entry timing and mode choice

19. Jakob Elming
Syntactic reordering in statistical machine translation

20. Lars Brømsøe Termansen
Regional Computable General Equilibrium Models for Denmark
Three papers laying the foundation for regional CGE models with agglomeration characteristics

21. Mia Reinholt
The Motivational Foundations of Knowledge Sharing

22. Frederikke Krogh-Meibom
The Co-Evolution of Institutions and Technology
– A Neo-Institutional Understanding of Change Processes within the Business Press – the Case Study of Financial Times

23. Peter D. Ørberg Jensen
OFFSHORING OF ADVANCED AND HIGH-VALUE TECHNICAL SERVICES: ANTECEDENTS, PROCESS DYNAMICS AND FIRMLEVEL IMPACTS

24. Pham Thi Song Hanh
Functional Upgrading, Relational Capability and Export Performance of Vietnamese Wood Furniture Producers

25. Mads Vangkilde
Why wait?
An Exploration of first-mover advantages among Danish e-grocers through a resource perspective

26. Hubert Buch-Hansen
Rethinking the History of European Level Merger Control
A Critical Political Economy Perspective

2009

1. Vivian Lindhardsen
From Independent Ratings to Communal Ratings: A Study of CWA Raters' Decision-Making Behaviours

2. Guðrið Weihe
Public-Private Partnerships: Meaning and Practice

3. Chris Nøkkentved
Enabling Supply Networks with Collaborative Information Infrastructures
An Empirical Investigation of Business Model Innovation in Supplier Relationship Management

4. Sara Louise Muhr
Wound, Interrupted – On the Vulnerability of Diversity Management

5. Christine Sestoft
Forbrugeradfærd i et Stats- og Livsformsteoretisk perspektiv

6. Michael Pedersen
Tune in, Breakdown, and Reboot: On the production of the stress-fit self-managing employee

7. Salla Lutz
Position and Reposition in Networks – Exemplified by the Transformation of the Danish Pine Furniture Manufacturers

8. Jens Forssbæck
Essays on market discipline in commercial and central banking

9. Tine Murphy
Sense from Silence – A Basis for Organised Action
How do Sensemaking Processes with Minimal Sharing Relate to the Reproduction of Organised Action?

10. Sara Malou Strandvad
Inspirations for a new sociology of art: A sociomaterial study of development processes in the Danish film industry

11. Nicolaas Mouton
On the evolution of social scientific metaphors:
A cognitive-historical enquiry into the divergent trajectories of the idea that collective entities – states and societies, cities and corporations – are biological organisms.

12. Lars Andreas Knutsen
Mobile Data Services:
Shaping of user engagements

13. Nikolaos Theodoros Korfiatis
Information Exchange and Behavior
A Multi-method Inquiry on Online Communities

14. Jens Albæk
Forestillinger om kvalitet og tværfaglighed på sygehuse
– skabelse af forestillinger i læge- og plejegrupperne angående relevans af nye idéer om kvalitetsudvikling gennem tolkningsprocesser

15. Maja Lotz
The Business of Co-Creation – and the Co-Creation of Business

16. Gitte P. Jakobsen
Narrative Construction of Leader Identity in a Leader Development Program Context

17. Dorte Hermansen
"Living the brand" som en brandorienteret dialogisk praxis:
Om udvikling af medarbejdernes brandorienterede dømmekraft

18. Aseem Kinra
Supply Chain (logistics) Environmental Complexity

19. Michael Nørager
How to manage SMEs through the transformation from non innovative to innovative?

20. Kristin Wallevik
Corporate Governance in Family Firms
The Norwegian Maritime Sector

21. Bo Hansen Hansen
Beyond the Process
Enriching Software Process Improvement with Knowledge Management

22. Annemette Skot-Hansen
Franske adjektivisk afledte adverbier, der tager præpositionssyntagmer indledt med præpositionen à som argumenter
En valensgrammatisk undersøgelse

23. Line Gry Knudsen
Collaborative R&D Capabilities
In Search of Micro-Foundations

24. Christian Scheuer
Employers meet employees
Essays on sorting and globalization

25. Rasmus Johnsen
The Great Health of Melancholy
A Study of the Pathologies of Performativity

26. Ha Thi Van Pham
Internationalization, Competitiveness Enhancement and Export Performance of Emerging Market Firms:
Evidence from Vietnam

27. Henriette Balieu
Kontrolbegrebets betydning for kausativalternationen i spansk
En kognitiv-typologisk analyse

2010

1. Yen Tran
Organizing Innovationin Turbulent Fashion Market
Four papers on how fashion firms create and appropriate innovation value

2. Anders Raastrup Kristensen
Metaphysical Labour
Flexibility, Performance and Commitment in Work-Life Management

3. Margrét Sigrún Sigurdardottir
Dependently independent
Co-existence of institutional logics in the recorded music industry

4. Ásta Dis Óladóttir
Internationalization from a small domestic base:
An empirical analysis of Economics and Management

5. Christine Secher
E-deltagelse i praksis – politikernes og forvaltningens medkonstruktion og konsekvenserne heraf

6. Marianne Stang Våland
What we talk about when we talk about space:
End User Participation between Processes of Organizational and Architectural Design

7. Rex Degnegaard
Strategic Change Management
Change Management Challenges in the Danish Police Reform

8. Ulrik Schultz Brix
Værdi i rekruttering – den sikre beslutning
En pragmatisk analyse af perception og synliggørelse af værdi i rekrutterings- og udvælgelsesarbejdet

9. Jan Ole Similä
Kontraktsledelse
Relasjonen mellom virksomhetsledelse og kontraktshåndtering, belyst via fire norske virksomheter

10. Susanne Boch Waldorff
Emerging Organizations: In between local translation, institutional logics and discourse

11. Brian Kane
Performance Talk
Next Generation Management of Organizational Performance

12. Lars Ohnemus
Brand Thrust: Strategic Branding and Shareholder Value
An Empirical Reconciliation of two Critical Concepts

13. Jesper Schlamovitz
Håndtering af usikkerhed i film- og byggeprojekter

14. Tommy Moesby-Jensen
Det faktiske livs forbindtlighed
Førsokratisk informeret, ny-aristotelisk ἦθος-tænkning hos Martin Heidegger

15. Christian Fich
Two Nations Divided by Common Values
French National Habitus and the Rejection of American Power

16. Peter Beyer
Processer, sammenhængskraft og fleksibilitet
Et empirisk casestudie af omstillingsforløb i fire virksomheder

17. Adam Buchhorn
Markets of Good Intentions
Constructing and Organizing Biogas Markets Amid Fragility and Controversy

18. Cecilie K. Moesby-Jensen
Social læring og fælles praksis
Et mixed method studie, der belyser læringskonsekvenser af et lederkursus for et praksisfællesskab af offentlige mellemledere

19. Heidi Boye
Fødevarer og sundhed i senmodernismen
– En indsigt i hyggefænomenet og de relaterede fødevarepraksisser

20. Kristine Munkgård Pedersen
Flygtige forbindelser og midlertidige mobiliseringer
Om kulturel produktion på Roskilde Festival

21. Oliver Jacob Weber
Causes of Intercompany Harmony in Business Markets – An Empirical Investigation from a Dyad Perspective

22. Susanne Ekman
Authority and Autonomy
Paradoxes of Modern Knowledge Work

23. Anette Frey Larsen
Kvalitetsledelse på danske hospitaler
– Ledelsernes indflydelse på introduktion og vedligeholdelse af kvalitetsstrategier i det danske sundhedsvæsen

24. Toyoko Sato
Performativity and Discourse: Japanese Advertisements on the Aesthetic Education of Desire

25. Kenneth Brinch Jensen
Identifying the Last Planner System
Lean management in the construction industry

26. Javier Busquets
Orchestrating Network Behavior for Innovation

27. Luke Patey
The Power of Resistance: India's National Oil Company and International Activism in Sudan

28. Mette Vedel
Value Creation in Triadic Business Relationships. Interaction, Interconnection and Position

29. Kristian Tørning
Knowledge Management Systems in Practice – A Work Place Study

30. Qingxin Shi
An Empirical Study of Thinking Aloud Usability Testing from a Cultural Perspective

31. Tanja Juul Christiansen
Corporate blogging: Medarbejderes kommunikative handlekraft

32. Malgorzata Ciesielska
Hybrid Organisations.
A study of the Open Source – business setting

33. Jens Dick-Nielsen
Three Essays on Corporate Bond Market Liquidity

34. Sabrina Speiermann
Modstandens Politik
Kampagnestyring i Velfærdsstaten.
En diskussion af trafikkampagners styringspotentiale

35. Julie Uldam
Fickle Commitment. Fostering political engagement in 'the flighty world of online activism'

36. Annegrete Juul Nielsen
Traveling technologies and transformations in health care

37. Athur Mühlen-Schulte
Organising Development
Power and Organisational Reform in the United Nations Development Programme

38. Louise Rygaard Jonas
Branding på butiksgulvet
Et case-studie af kultur- og identitetsarbejdet i Kvickly

2011

1. Stefan Fraenkel
Key Success Factors for Sales Force Readiness during New Product Launch
A Study of Product Launches in the Swedish Pharmaceutical Industry

2. Christian Plesner Rossing
International Transfer Pricing in Theory and Practice

3. Tobias Dam Hede
Samtalekunst og ledelsesdisciplin
– en analyse af coachingsdiskursens genealogi og governmentality

4. Kim Pettersson
Essays on Audit Quality, Auditor Choice, and Equity Valuation

5. Henrik Merkelsen
The expert-lay controversy in risk research and management. Effects of institutional distances. Studies of risk definitions, perceptions, management and communication

6. Simon S. Torp
Employee Stock Ownership:
Effect on Strategic Management and Performance

7. Mie Harder
Internal Antecedents of Management Innovation

8. Ole Helby Petersen
Public-Private Partnerships: Policy and Regulation – With Comparative and Multi-level Case Studies from Denmark and Ireland

9. Morten Krogh Petersen
'Good' Outcomes. Handling Multiplicity in Government Communication

10. Kristian Tangsgaard Hvelplund
Allocation of cognitive resources in translation - an eye-tracking and key-logging study

11. Moshe Yonatany
The Internationalization Process of Digital Service Providers

12. Anne Vestergaard
Distance and Suffering
Humanitarian Discourse in the age of Mediatization

13. Thorsten Mikkelsen
Personligsheds indflydelse på forretningsrelationer

14. Jane Thostrup Jagd
Hvorfor fortsætter fusionsbølgen udover "the tipping point"?
– en empirisk analyse af information og kognitioner om fusioner

15. Gregory Gimpel
Value-driven Adoption and Consumption of Technology: Understanding Technology Decision Making

16. Thomas Stengade Sønderskov
Den nye mulighed
Social innovation i en forretningsmæssig kontekst

17. Jeppe Christoffersen
Donor supported strategic alliances in developing countries

18. Vibeke Vad Baunsgaard
Dominant Ideological Modes of Rationality: Cross functional

integration in the process of product innovation

19. Throstur Olaf Sigurjonsson
Governance Failure and Icelands's Financial Collapse

20. Allan Sall Tang Andersen
Essays on the modeling of risks in interest-rate and inflation markets

21. Heidi Tscherning
Mobile Devices in Social Contexts

22. Birgitte Gorm Hansen
Adapting in the Knowledge Economy Lateral Strategies for Scientists and Those Who Study Them

23. Kristina Vaarst Andersen
Optimal Levels of Embeddedness The Contingent Value of Networked Collaboration

24. Justine Grønbæk Pors
Noisy Management A History of Danish School Governing from 1970-2010

25. Stefan Linder
Micro-foundations of Strategic Entrepreneurship Essays on Autonomous Strategic Action

26. Xin Li
Toward an Integrative Framework of National Competitiveness An application to China

27. Rune Thorbjørn Clausen
Værdifuld arkitektur Et eksplorativt studie af bygningers rolle i virksomheders værdiskabelse

28. Monica Viken
Markedsundersøkelser som bevis i varemerke- og markedsføringsrett

29. Christian Wymann
Tattooing The Economic and Artistic Constitution of a Social Phenomenon

30. Sanne Frandsen
Productive Incoherence A Case Study of Branding and Identity Struggles in a Low-Prestige Organization

31. Mads Stenbo Nielsen
Essays on Correlation Modelling

32. Ivan Häuser
Følelse og sprog Etablering af en ekspressiv kategori, eksemplificeret på russisk

33. Sebastian Schwenen
Security of Supply in Electricity Markets

2012

1. Peter Holm Andreasen
The Dynamics of Procurement Management - A Complexity Approach

2. Martin Haulrich
Data-Driven Bitext Dependency Parsing and Alignment

3. Line Kirkegaard
Konsulenten i den anden nat En undersøgelse af det intense arbejdsliv

4. Tonny Stenheim
Decision usefulness of goodwill under IFRS

5. Morten Lind Larsen
Produktivitet, vækst og velfærd Industrirådet og efterkrigstidens Danmark 1945 - 1958

6. Petter Berg
Cartel Damages and Cost Asymmetries

7. Lynn Kahle
Experiential Discourse in Marketing A methodical inquiry into practice and theory

8. Anne Roelsgaard Obling
Management of Emotions in Accelerated Medical Relationships

9. Thomas Frandsen
Managing Modularity of Service Processes Architecture

10. Carina Christine Skovmøller
CSR som noget særligt
Et casestudie om styring og meningsskabelse i relation til CSR ud fra en intern optik

11. Michael Tell
Fradragsbeskæring af selskabers finansieringsudgifter
En skatteretlig analyse af SEL §§ 11, 11B og 11C

12. Morten Holm
Customer Profitability Measurement Models
Their Merits and Sophistication across Contexts

13. Katja Joo Dyppel
Beskatning af derivater
En analyse af dansk skatteret

14. Esben Anton Schultz
Essays in Labor Economics
Evidence from Danish Micro Data

15. Carina Risvig Hansen
"Contracts not covered, or not fully covered, by the Public Sector Directive"

16. Anja Svejgaard Pors
Iværksættelse af kommunikation
- patientfigurer i hospitalets strategiske kommunikation

17. Frans Bévort
Making sense of management with logics
An ethnographic study of accountants who become managers

18. René Kallestrup
The Dynamics of Bank and Sovereign Credit Risk

19. Brett Crawford
Revisiting the Phenomenon of Interests in Organizational Institutionalism
The Case of U.S. Chambers of Commerce

20. Mario Daniele Amore
Essays on Empirical Corporate Finance

21. Arne Stjernholm Madsen
The evolution of innovation strategy
Studied in the context of medical device activities at the pharmaceutical company Novo Nordisk A/S in the period 1980-2008

22. Jacob Holm Hansen
Is Social Integration Necessary for Corporate Branding?
A study of corporate branding strategies at Novo Nordisk

23. Stuart Webber
Corporate Profit Shifting and the Multinational Enterprise

24. Helene Ratner
Promises of Reflexivity
Managing and Researching Inclusive Schools

25. Therese Strand
The Owners and the Power: Insights from Annual General Meetings

26. Robert Gavin Strand
In Praise of Corporate Social Responsibility Bureaucracy

27. Nina Sormunen
Auditor's going-concern reporting
Reporting decision and content of the report

28. John Bang Mathiasen
Learning within a product development working practice:
- an understanding anchored in pragmatism

29. Philip Holst Riis
Understanding Role-Oriented Enterprise Systems: From Vendors to Customers

30. Marie Lisa Dacanay
Social Enterprises and the Poor
Enhancing Social Entrepreneurship and Stakeholder Theory

31. Fumiko Kano Glückstad
Bridging Remote Cultures: Cross-lingual concept mapping based on the information receiver's prior-knowledge

32. Henrik Barslund Fosse
Empirical Essays in International Trade

33. Peter Alexander Albrecht
Foundational hybridity and its reproduction
Security sector reform in Sierra Leone

34. Maja Rosenstock
CSR - hvor svært kan det være? Kulturanalytisk casestudie om udfordringer og dilemmaer med at forankre Coops CSR-strategi

35. Jeanette Rasmussen
Tweens, medier og forbrug
Et studie af 10-12 årige danske børns brug af internettet, opfattelse og forståelse af markedsføring og forbrug

36. Ib Tunby Gulbrandsen
'This page is not intended for a US Audience'
A five-act spectacle on online communication, collaboration & organization.

37. Kasper Aalling Teilmann
Interactive Approaches to Rural Development

38. Mette Mogensen
The Organization(s) of Well-being and Productivity
(Re)assembling work in the Danish Post

39. Søren Friis Møller
From Disinterestedness to Engagement
Towards Relational Leadership In the Cultural Sector

40. Nico Peter Berhausen
Management Control, Innovation and Strategic Objectives – Interactions and Convergence in Product Development Networks

41. Balder Onarheim
Creativity under Constraints
Creativity as Balancing 'Constrainedness'

42. Haoyong Zhou
Essays on Family Firms

43. Elisabeth Naima Mikkelsen
Making sense of organisational conflict
An empirical study of enacted sensemaking in everyday conflict at work

2013

1. Jacob Lyngsie
Entrepreneurship in an Organizational Context

2. Signe Groth-Brodersen
Fra ledelse til selvet
En socialpsykologisk analyse af forholdet imellem selvledelse, ledelse og stress i det moderne arbejdsliv

3. Nis Høyrup Christensen
Shaping Markets: A Neoinstitutional Analysis of the Emerging Organizational Field of Renewable Energy in China

4. Christian Edelvold Berg
As a matter of size
THE IMPORTANCE OF CRITICAL MASS AND THE CONSEQUENCES OF SCARCITY FOR TELEVISION MARKETS

5. Christine D. Isakson
Coworker Influence and Labor Mobility
Essays on Turnover, Entrepreneurship and Location Choice in the Danish Maritime Industry

6. Niels Joseph Jerne Lennon
Accounting Qualities in Practice
Rhizomatic stories of representational faithfulness, decision making and control

7. Shannon O'Donnell
Making Ensemble Possible
How special groups organize for collaborative creativity in conditions of spatial variability and distance

8. Robert W. D. Veitch
Access Decisions in a Partly-Digital World
Comparing Digital Piracy and Legal Modes for Film and Music

9. Marie Mathiesen
Making Strategy Work
An Organizational Ethnography

10. Arisa Shollo
The role of business intelligence in organizational decision-making

11. Mia Kaspersen
The construction of social and environmental reporting

12. Marcus Møller Larsen
The organizational design of offshoring

13. Mette Ohm Rørdam
EU Law on Food Naming
The prohibition against misleading names in an internal market context

14. Hans Peter Rasmussen
GIV EN GED!
Kan giver-idealtyper forklare støtte til velgørenhed og understøtte relationsopbygning?

15. Ruben Schachtenhaufen
Fonetisk reduktion i dansk

16. Peter Koerver Schmidt
Dansk CFC-beskatning
I et internationalt og komparativt perspektiv

17. Morten Froholdt
Strategi i den offentlige sektor
En kortlægning af styringsmæssig kontekst, strategisk tilgang, samt anvendte redskaber og teknologier for udvalgte danske statslige styrelser

18. Annette Camilla Sjørup
Cognitive effort in metaphor translation
An eye-tracking and key-logging study

19. Tamara Stucchi
The Internationalization of Emerging Market Firms:
A Context-Specific Study

20. Thomas Lopdrup-Hjorth
"Let's Go Outside":
The Value of Co-Creation

21. Ana Alačovska
Genre and Autonomy in Cultural Production
The case of travel guidebook production

22. Marius Gudmand-Høyer
Stemningssindssygdommenes historie i det 19. århundrede
Omtydningen af melankolien og manien som bipolære stemningslidelser i dansk sammenhæng under hensyn til dannelsen af det moderne følelseslivs relative autonomi.
En problematiserings- og erfarings-analytisk undersøgelse

23. Lichen Alex Yu
Fabricating an S&OP Process
Circulating References and Matters of Concern

24. Esben Alfort
The Expression of a Need
Understanding search

25. Trine Pallesen
Assembling Markets for Wind Power
An Inquiry into the Making of Market Devices

26. Anders Koed Madsen
Web-Visions
Repurposing digital traces to organize social attention

27. Lærke Højgaard Christiansen
BREWING ORGANIZATIONAL RESPONSES TO INSTITUTIONAL LOGICS

28. Tommy Kjær Lassen
EGENTLIG SELVLEDELSE
En ledelsesfilosofisk afhandling om selvledelsens paradoksale dynamik og eksistentielle engagement

29. Morten Rossing
Local Adaption and Meaning Creation in Performance Appraisal

30. Søren Obed Madsen
Lederen som oversætter
Et oversættelsesteoretisk perspektiv på strategisk arbejde

31. Thomas Høgenhaven
Open Government Communities
Does Design Affect Participation?

32. Kirstine Zinck Pedersen
Failsafe Organizing?
A Pragmatic Stance on Patient Safety

33. Anne Petersen
Hverdagslogikker i psykiatrisk arbejde
En institutionsetnografisk undersøgelse af hverdagen i psykiatriske organisationer

34. Didde Maria Humle
Fortællinger om arbejde

35. Mark Holst-Mikkelsen
Strategieksekvering i praksis
– barrierer og muligheder!

36. Malek Maalouf
Sustaining lean
Strategies for dealing with organizational paradoxes

37. Nicolaj Tofte Brenneche
Systemic Innovation In The Making
The Social Productivity of Cartographic Crisis and Transitions in the Case of SEEIT

38. Morten Gylling
The Structure of Discourse
A Corpus-Based Cross-Linguistic Study

39. Binzhang YANG
Urban Green Spaces for Quality Life
- Case Study: the landscape architecture for people in Copenhagen

40. Michael Friis Pedersen
Finance and Organization:
The Implications for Whole Farm Risk Management

41. Even Fallan
Issues on supply and demand for environmental accounting information

42. Ather Nawaz
Website user experience
A cross-cultural study of the relation between users´ cognitive style, context of use, and information architecture of local websites

43. Karin Beukel
The Determinants for Creating Valuable Inventions

44. Arjan Markus
External Knowledge Sourcing and Firm Innovation
Essays on the Micro-Foundations of Firms' Search for Innovation

2014

1. Solon Moreira
Four Essays on Technology Licensing and Firm Innovation

2. Karin Strzeletz Ivertsen
Partnership Drift in Innovation Processes
A study of the Think City electric car development

3. Kathrine Hoffmann Pii
Responsibility Flows in Patient-centred Prevention

4. Jane Bjørn Vedel
Managing Strategic Research
An empirical analysis of science-industry collaboration in a pharmaceutical company

5. Martin Gylling
Processuel strategi i organisationer
Monografi om dobbeltheden i tænkning af strategi, dels som vidensfelt i organisationsteori, dels som kunstnerisk tilgang til at skabe i erhvervsmæssig innovation

6. Linne Marie Lauesen
Corporate Social Responsibility in the Water Sector: How Material Practices and their Symbolic and Physical Meanings Form a Colonising Logic

7. Maggie Qiuzhu Mei
LEARNING TO INNOVATE: The role of ambidexterity, standard, and decision process

8. Inger Høedt-Rasmussen
Developing Identity for Lawyers Towards Sustainable Lawyering

9. Sebastian Fux
Essays on Return Predictability and Term Structure Modelling

10. Thorbjørn N. M. Lund-Poulsen
Essays on Value Based Management

11. Oana Brindusa Albu
Transparency in Organizing: A Performative Approach

12. Lena Olaison
Entrepreneurship at the limits

13. Hanne Sørum
DRESSED FOR WEB SUCCESS? An Empirical Study of Website Quality in the Public Sector

14. Lasse Folke Henriksen
Knowing networks How experts shape transnational governance

15. Maria Halbinger
Entrepreneurial Individuals Empirical Investigations into Entrepreneurial Activities of Hackers and Makers

16. Robert Spliid
Kapitalfondenes metoder og kompetencer

17. Christiane Stelling
Public-private partnerships & the need, development and management of trusting A processual and embedded exploration

18. Marta Gasparin
Management of design as a translation process

19. Kåre Moberg
Assessing the Impact of Entrepreneurship Education From ABC to PhD

20. Alexander Cole
Distant neighbors Collective learning beyond the cluster

21. Martin Møller Boje Rasmussen
Is Competitiveness a Question of Being Alike? How the United Kingdom, Germany and Denmark Came to Compete through their Knowledge Regimes from 1993 to 2007

22. Anders Ravn Sørensen
Studies in central bank legitimacy, currency and national identity Four cases from Danish monetary history

23. Nina Bellak
Can Language be Managed in International Business? Insights into Language Choice from a Case Study of Danish and Austrian Multinational Corporations (MNCs)

24. Rikke Kristine Nielsen
Global Mindset as Managerial Meta-competence and Organizational Capability: Boundary-crossing Leadership Cooperation in the MNC The Case of 'Group Mindset' in Solar A/S.

25. Rasmus Koss Hartmann
User Innovation inside government Towards a critically performative foundation for inquiry

26. Kristian Gylling Olesen
Flertydig og emergerende ledelse i folkeskolen
Et aktør-netværksteoretisk ledelses-studie af politiske evalueringsreformers betydning for ledelse i den danske folkeskole

27. Troels Riis Larsen
Kampen om Danmarks omdømme 1945-2010
Omdømmearbejde og omdømmepolitik

28. Klaus Majgaard
Jagten på autenticitet i offentlig styring

29. Ming Hua Li
Institutional Transition and Organizational Diversity:
Differentiated internationalization strategies of emerging market state-owned enterprises

30. Sofie Blinkenberg Federspiel
IT, organisation og digitalisering:
Institutionelt arbejde i den kommunale digitaliseringsproces

31. Elvi Weinreich
Hvilke offentlige ledere er der brug for når velfærdstænkningen flytter sig – er Diplomuddannelsens lederprofil svaret?

32. Ellen Mølgaard Korsager
Self-conception and image of context in the growth of the firm – A Penrosian History of Fiberline Composites

33. Else Skjold
The Daily Selection

34. Marie Louise Conradsen
The Cancer Centre That Never Was
The Organisation of Danish Cancer Research 1949-1992

35. Virgilio Failla
Three Essays on the Dynamics of Entrepreneurs in the Labor Market

36. Nicky Nedergaard
Brand-Based Innovation
Relational Perspectives on Brand Logics and Design Innovation Strategies and Implementation

37. Mads Gjedsted Nielsen
Essays in Real Estate Finance

38. Kristin Martina Brandl
Process Perspectives on Service Offshoring

39. Mia Rosa Koss Hartmann
In the gray zone
With police in making space for creativity

40. Karen Ingerslev
Healthcare Innovation under The Microscope
Framing Boundaries of Wicked Problems

41. Tim Neerup Themsen
Risk Management in large Danish public capital investment programmes

2015

1. Jakob Ion Wille
Film som design
Design af levende billeder i film og tv-serier

2. Christiane Mossin
Interzones of Law and Metaphysics
Hierarchies, Logics and Foundations of Social Order seen through the Prism of EU Social Rights

3. Thomas Tøth
TRUSTWORTHINESS: ENABLING GLOBAL COLLABORATION
An Ethnographic Study of Trust, Distance, Control, Culture and Boundary Spanning within Offshore Outsourcing of IT Services

4. Steven Højlund
Evaluation Use in Evaluation Systems – The Case of the European Commission

5. Julia Kirch Kirkegaard
AMBIGUOUS WINDS OF CHANGE – OR FIGHTING AGAINST WINDMILLS IN CHINESE WIND POWER
A CONSTRUCTIVIST INQUIRY INTO CHINA'S PRAGMATICS OF GREEN MARKETISATION MAPPING CONTROVERSIES OVER A POTENTIAL TURN TO QUALITY IN CHINESE WIND POWER

6. Michelle Carol Antero
A Multi-case Analysis of the Development of Enterprise Resource Planning Systems (ERP) Business Practices

Morten Friis-Olivarius
The Associative Nature of Creativity

7. Mathew Abraham
New Cooperativism:
A study of emerging producer organisations in India

8. Stine Hedegaard
Sustainability-Focused Identity: Identity work performed to manage, negotiate and resolve barriers and tensions that arise in the process of constructing or ganizational identity in a sustainability context

9. Cecilie Glerup
Organizing Science in Society – the conduct and justification of resposible research

10. Allan Salling Pedersen
Implementering af ITIL® IT-governance - når best practice konflikter med kulturen Løsning af implementerings-problemer gennem anvendelse af kendte CSF i et aktionsforskningsforløb.

11. Nihat Misir
A Real Options Approach to Determining Power Prices

12. Mamdouh Medhat
MEASURING AND PRICING THE RISK OF CORPORATE FAILURES

13. Rina Hansen
Toward a Digital Strategy for Omnichannel Retailing

14. Eva Pallesen
In the rhythm of welfare creation
A relational processual investigation moving beyond the conceptual horizon of welfare management

15. Gouya Harirchi
In Search of Opportunities: Three Essays on Global Linkages for Innovation

16. Lotte Holck
Embedded Diversity: A critical ethnographic study of the structural tensions of organizing diversity

17. Jose Daniel Balarezo
Learning through Scenario Planning

18. Louise Pram Nielsen
Knowledge dissemination based on terminological ontologies. Using eye tracking to further user interface design.

19. Sofie Dam
PUBLIC-PRIVATE PARTNERSHIPS FOR INNOVATION AND SUSTAINABILITY TRANSFORMATION
An embedded, comparative case study of municipal waste management in England and Denmark

20. Ulrik Hartmyer Christiansen
Follwoing the Content of Reported Risk Across the Organization

21. Guro Refsum Sanden
Language strategies in multinational corporations. A cross-sector study of financial service companies and manufacturing companies.

22. Linn Gevoll
Designing performance management for operational level
- A closer look on the role of design choices in framing coordination and motivation

23. Frederik Larsen
Objects and Social Actions – on Second-hand Valuation Practices

24. Thorhildur Hansdottir Jetzek
The Sustainable Value of Open Government Data
Uncovering the Generative Mechanisms of Open Data through a Mixed Methods Approach

25. Gustav Toppenberg
Innovation-based M&A – Technological-Integration Challenges – The Case of Digital-Technology Companies

26. Mie Plotnikof
Challenges of Collaborative Governance
An Organizational Discourse Study of Public Managers' Struggles with Collaboration across the Daycare Area

27. Christian Garmann Johnsen
Who Are the Post-Bureaucrats? A Philosophical Examination of the Creative Manager, the Authentic Leader and the Entrepreneur

28. Jacob Brogaard-Kay
Constituting Performance Management A field study of a pharmaceutical company

29. Rasmus Ploug Jenle
Engineering Markets for Control: Integrating Wind Power into the Danish Electricity System

30. Morten Lindholst
Complex Business Negotiation: Understanding Preparation and Planning

31. Morten Grynings
TRUST AND TRANSPARENCY FROM AN ALIGNMENT PERSPECTIVE

32. Peter Andreas Norn
Byregimer og styringsevne: Politisk lederskab af store byudviklingsprojekter

33. Milan Miric
Essays on Competition, Innovation and Firm Strategy in Digital Markets

34. Sanne K. Hjordrup
The Value of Talent Management Rethinking practice, problems and possibilities

35. Johanna Sax
Strategic Risk Management – Analyzing Antecedents and Contingencies for Value Creation

36. Pernille Rydén
Strategic Cognition of Social Media

37. Mimmi Sjöklint
The Measurable Me - The Influence of Self-tracking on the User Experience

38. Juan Ignacio Staricco
Towards a Fair Global Economic Regime? A critical assessment of Fair Trade through the examination of the Argentinean wine industry

39. Marie Henriette Madsen
Emerging and temporary connections in Quality work

40. Yangfeng CAO
Toward a Process Framework of Business Model Innovation in the Global Context
Entrepreneurship-Enabled Dynamic Capability of Medium-Sized Multinational Enterprises

41. Carsten Scheibye
Enactment of the Organizational Cost Structure in Value Chain Configuration A Contribution to Strategic Cost Management

2016

1. Signe Sofie Dyrby
Enterprise Social Media at Work

2. Dorte Boesby Dahl
The making of the public parking attendant
Dirt, aesthetics and inclusion in public service work

3. Verena Girschik
Realizing Corporate Responsibility Positioning and Framing in Nascent Institutional Change

4. Anders Ørding Olsen
IN SEARCH OF SOLUTIONS
Inertia, Knowledge Sources and Diversity in Collaborative Problem-solving

5. Pernille Steen Pedersen
Udkast til et nyt copingbegreb
En kvalifikation af ledelsesmuligheder for at forebygge sygefravær ved psykiske problemer.

6. Kerli Kant Hvass
Weaving a Path from Waste to Value: Exploring fashion industry business models and the circular economy

7. Kasper Lindskow
Exploring Digital News Publishing Business Models – a production network approach

8. Mikkel Mouritz Marfelt
The chameleon workforce: Assembling and negotiating the content of a workforce

9. Marianne Bertelsen
Aesthetic encounters
Rethinking autonomy, space & time in today's world of art

10. Louise Hauberg Wilhelmsen
EU PERSPECTIVES ON INTERNATIONAL COMMERCIAL ARBITRATION

11. Abid Hussain
On the Design, Development and Use of the Social Data Analytics Tool (SODATO): Design Propositions, Patterns, and Principles for Big Social Data Analytics

12. Mark Bruun
Essays on Earnings Predictability

13. Tor Bøe-Lillegraven
BUSINESS PARADOXES, BLACK BOXES, AND BIG DATA: BEYOND ORGANIZATIONAL AMBIDEXTERITY

14. Hadis Khonsary-Atighi
ECONOMIC DETERMINANTS OF DOMESTIC INVESTMENT IN AN OIL-BASED ECONOMY: THE CASE OF IRAN (1965-2010)

15. Maj Lervad Grasten
Rule of Law or Rule by Lawyers?
On the Politics of Translation in Global Governance

16. Lene Granzau Juel-Jacobsen
SUPERMARKEDETS MODUS OPERANDI – en hverdagssociologisk undersøgelse af forholdet mellem rum og handlen og understøtte relationsopbygning?

17. Christine Thalsgård Henriques
In search of entrepreneurial learning – Towards a relational perspective on incubating practices?

18. Patrick Bennett
Essays in Education, Crime, and Job Displacement

19. Søren Korsgaard
Payments and Central Bank Policy

20. Marie Kruse Skibsted
Empirical Essays in Economics of Education and Labor

21. Elizabeth Benedict Christensen
The Constantly Contingent Sense of Belonging of the 1.5 Generation Undocumented Youth
An Everyday Perspective

22. Lasse J. Jessen
Essays on Discounting Behavior and Gambling Behavior

23. Kalle Johannes Rose
Når stifterviljen dør…
Et retsøkonomisk bidrag til 200 års juridisk konflikt om ejendomsretten

24. Andreas Søeborg Kirkedal
Danish Stød and Automatic Speech Recognition

25. Ida Lunde Jørgensen
Institutions and Legitimations in Finance for the Arts

26. Olga Rykov Ibsen
An empirical cross-linguistic study of directives: A semiotic approach to the sentence forms chosen by British, Danish and Russian speakers in native and ELF contexts

27. Desi Volker
Understanding Interest Rate Volatility

28. Angeli Elizabeth Weller
Practice at the Boundaries of Business Ethics & Corporate Social Responsibility

29. Ida Danneskiold-Samsøe
Levende læring i kunstneriske organisationer
En undersøgelse af læringsprocesser mellem projekt og organisation på Aarhus Teater

30. Leif Christensen
Quality of information – The role of internal controls and materiality

31. Olga Zarzecka
Tie Content in Professional Networks

32. Henrik Mahncke
De store gaver
- Filantropiens gensidighedsrelationer i teori og praksis

33. Carsten Lund Pedersen
Using the Collective Wisdom of Frontline Employees in Strategic Issue Management

34. Yun Liu
Essays on Market Design

35. Denitsa Hazarbassanova Blagoeva
The Internationalisation of Service Firms

36. Manya Jaura Lind
Capability development in an off-shoring context: How, why and by whom

37. Luis R. Boscán F.
Essays on the Design of Contracts and Markets for Power System Flexibility

38. Andreas Philipp Distel
Capabilities for Strategic Adaptation: Micro-Foundations, Organizational Conditions, and Performance Implications

39. Lavinia Bleoca
The Usefulness of Innovation and Intellectual Capital in Business Performance: The Financial Effects of Knowledge Management vs. Disclosure

40. Henrik Jensen
Economic Organization and Imperfect Managerial Knowledge: A Study of the Role of Managerial Meta-Knowledge in the Management of Distributed Knowledge

41. Stine Mosekjær
The Understanding of English Emotion Words by Chinese and Japanese Speakers of English as a Lingua Franca An Empirical Study

42. Hallur Tor Sigurdarson
The Ministry of Desire - Anxiety and entrepreneurship in a bureaucracy

43. Kätlin Pulk
Making Time While Being in Time
A study of the temporality of organizational processes

44. Valeria Giacomin
Contextualizing the cluster Palm oil in Southeast Asia in global perspective (1880s–1970s)

45. Jeanette Willert
Managers' use of multiple Management Control Systems: The role and interplay of management control systems and company performance

46. Mads Vestergaard Jensen
Financial Frictions: Implications for Early Option Exercise and Realized Volatility

47. Mikael Reimer Jensen
Interbank Markets and Frictions

48. Benjamin Faigen
Essays on Employee Ownership

49. Adela Michea
Enacting Business Models
An Ethnographic Study of an Emerging Business Model Innovation within the Frame of a Manufacturing Company.

50. Iben Sandal Stjerne
Transcending organization in temporary systems
Aesthetics' organizing work and employment in Creative Industries

51. Simon Krogh
Anticipating Organizational Change

52. Sarah Netter
Exploring the Sharing Economy

53. Lene Tolstrup Christensen
State-owned enterprises as institutional market actors in the marketization of public service provision:
A comparative case study of Danish and Swedish passenger rail 1990–2015

54. Kyoung(Kay) Sun Park
Three Essays on Financial Economics

2017

1. Mari Bjerck
Apparel at work. Work uniforms and women in male-dominated manual occupations.

2. Christoph H. Flöthmann
Who Manages Our Supply Chains? Backgrounds, Competencies and Contributions of Human Resources in Supply Chain Management

3. Aleksandra Anna Rzeźnik
Essays in Empirical Asset Pricing

4. Claes Bäckman
Essays on Housing Markets

5. Kirsti Reitan Andersen
Stabilizing Sustainability in the Textile and Fashion Industry

6. Kira Hoffmann
Cost Behavior: An Empirical Analysis of Determinants and Consequences of Asymmetries

7. Tobin Hanspal
Essays in Household Finance

8. Nina Lange
Correlation in Energy Markets

9. Anjum Fayyaz
Donor Interventions and SME Networking in Industrial Clusters in Punjab Province, Pakistan

10. Magnus Paulsen Hansen
Trying the unemployed. Justification and critique, emancipation and coercion towards the 'active society'. A study of contemporary reforms in France and Denmark

11. Sameer Azizi
Corporate Social Responsibility in Afghanistan
– a critical case study of the mobile telecommunications industry

12. Malene Myhre
The internationalization of small and medium-sized enterprises: A qualitative study

13. Thomas Presskorn-Thygesen
The Significance of Normativity – Studies in Post-Kantian Philosophy and Social Theory

14. Federico Clementi
Essays on multinational production and international trade

15. Lara Anne Hale
Experimental Standards in Sustainability Transitions: Insights from the Building Sector

16. Richard Pucci
Accounting for Financial Instruments in an Uncertain World Controversies in IFRS in the Aftermath of the 2008 Financial Crisis

17. Sarah Maria Denta
Kommunale offentlige private partnerskaber Regulering I skyggen af Farumsagen

18. Christian Östlund
Design for e-training

19. Amalie Martinus Hauge
Organizing Valuations – a pragmatic inquiry

20. Tim Holst Celik
Tension-filled Governance? Exploring the Emergence, Consolidation and Reconfiguration of Legitimatory and Fiscal State-crafting

21. Christian Bason
Leading Public Design: How managers engage with design to transform public governance

22. Davide Tomio
Essays on Arbitrage and Market Liquidity

23. Simone Stæhr
Financial Analysts' Forecasts Behavioral Aspects and the Impact of Personal Characteristics

24. Mikkel Godt Gregersen
Management Control, Intrinsic Motivation and Creativity – How Can They Coexist

25. Kristjan Johannes Suse Jespersen
Advancing the Payments for Ecosystem Service Discourse Through Institutional Theory

26. Kristian Bondo Hansen
Crowds and Speculation: A study of crowd phenomena in the U.S. financial markets 1890 to 1940

27. Lars Balslev
Actors and practices – An institutional study on management accounting change in Air Greenland

28. Sven Klingler
Essays on Asset Pricing with Financial Frictions

29. Klement Ahrensbach Rasmussen
Business Model Innovation The Role of Organizational Design

30. Giulio Zichella
Entrepreneurial Cognition. Three essays on entrepreneurial behavior and cognition under risk and uncertainty

31. Richard Ledborg Hansen
En forkærlighed til det eksisterende – mellemlederens oplevelse af forandringsmodstand i organisatoriske forandringer

32. Vilhelm Stefan Holsting
Militært chefvirke: Kritik og retfærdiggørelse mellem politik og profession

33. Thomas Jensen
Shipping Information Pipeline: An information infrastructure to improve international containerized shipping

34. Dzmitry Bartalevich
Do economic theories inform policy? Analysis of the influence of the Chicago School on European Union competition policy

35. Kristian Roed Nielsen
Crowdfunding for Sustainability: A study on the potential of reward-based crowdfunding in supporting sustainable entrepreneurship

36. Emil Husted
There is always an alternative: A study of control and commitment in political organization

37. Anders Ludvig Sevelsted
Interpreting Bonds and Boundaries of Obligation. A genealogy of the emergence and development of Protestant voluntary social work in Denmark as shown through the cases of the Copenhagen Home Mission and the Blue Cross (1850 – 1950)

38. Niklas Kohl
Essays on Stock Issuance

39. Maya Christiane Flensborg Jensen
BOUNDARIES OF PROFESSIONALIZATION AT WORK An ethnography-inspired study of care workers' dilemmas at the margin

40. Andreas Kamstrup
Crowdsourcing and the Architectural Competition as Organisational Technologies

41. Louise Lyngfeldt Gorm Hansen
Triggering Earthquakes in Science, Politics and Chinese Hydropower - A Controversy Study

2018

1. Vishv Priya Kohli
Combatting Falsifi cation and Counterfeiting of Medicinal Products in the E uropean Union – A Legal Analysis

2. Helle Haurum
Customer Engagement Behavior in the context of Continuous Service Relationships

3. Nis Grünberg
The Party -state order: Essays on China's political organization and political economic institutions

4. Jesper Christensen
A Behavioral Theory of Human Capital Integration

5. Poula Marie Helth
Learning in practice

6. Rasmus Vendler Toft-Kehler
Entrepreneurship as a career? An investigation of the relationship between entrepreneurial experience and entrepreneurial outcome

7. Szymon Furtak
Sensing the Future: Designing sensor-based predictive information systems for forecasting spare part demand for diesel engines

8. Mette Brehm Johansen
Organizing patient involvement. An ethnographic study

9. Iwona Sulinska
Complexities of Social Capital in Boards of Directors

10. Cecilie Fanøe Petersen
Award of public contracts as a means to conferring State aid: A legal analysis of the interface between public procurement law and State aid law

11. Ahmad Ahmad Barirani
Three Experimental Studies on Entrepreneurship

12. Carsten Allerslev Olsen
Financial Reporting Enforcement: Impact and Consequences

13. Irene Christensen
New product fumbles – Organizing for the Ramp-up process

14. Jacob Taarup-Esbensen
Managing communities – Mining MNEs' community risk management practices

15. Lester Allan Lasrado
Set-Theoretic approach to maturity models

16. Mia B. Münster
Intention vs. Perception of Designed Atmospheres in Fashion Stores

17. Anne Sluhan
Non-Financial Dimensions of Family Firm Ownership: How Socioemotional Wealth and Familiness Influence Internationalization

18. Henrik Yde Andersen
Essays on Debt and Pensions

19. Fabian Heinrich Müller
Valuation Reversed – When Valuators are Valuated. An Analysis of the Perception of and Reaction to Reviewers in Fine-Dining

20. Martin Jarmatz
Organizing for Pricing

21. Niels Joachim Christfort Gormsen
Essays on Empirical Asset Pricing

22. Diego Zunino
Socio-Cognitive Perspectives in Business Venturing

23. Benjamin Asmussen
Networks and Faces between Copenhagen and Canton, 1730-1840

24. Dalia Bagdziunaite
Brains at Brand Touchpoints A Consumer Neuroscience Study of Information Processing of Brand Advertisements and the Store Environment in Compulsive Buying

25. Erol Kazan
Towards a Disruptive Digital Platform Model

26. Andreas Bang Nielsen
Essays on Foreign Exchange and Credit Risk

27. Anne Krebs
Accountable, Operable Knowledge Toward Value Representations of Individual Knowledge in Accounting

28. Matilde Fogh Kirkegaard
A firm- and demand-side perspective on behavioral strategy for value creation: Insights from the hearing aid industry

29. Agnieszka Nowinska
SHIPS AND RELATION-SHIPS Tie formation in the sector of shipping intermediaries in shipping

30. Stine Evald Bentsen
The Comprehension of English Texts by Native Speakers of English and Japanese, Chinese and Russian Speakers of English as a Lingua Franca. An Empirical Study.

31. Stine Louise Daetz
Essays on Financial Frictions in Lending Markets

32. *Christian Skov Jensen*
Essays on Asset Pricing

33. Anders Kryger
Aligning future employee action and corporate strategy in a resource-scarce environment

34. Maitane Elorriaga-Rubio
The behavioral foundations of strategic decision-making: A contextual perspective

35. Roddy Walker
Leadership Development as Organisational Rehabilitation: Shaping Middle-Managers as Double Agents

36. Jinsun Bae
Producing Garments for Global Markets Corporate social responsibility (CSR) in Myanmar's export garment industry 2011–2015

37. Queralt Prat-i-Pubill
Axiological knowledge in a knowledge driven world. Considerations for organizations.

38. Pia Mølgaard
Essays on Corporate Loans and Credit Risk

39. Marzia Aricò
Service Design as a Transformative Force: Introduction and Adoption in an Organizational Context

40. Christian Dyrlund Wåhlin-Jacobsen
Constructing change initiatives in workplace voice activities Studies from a social interaction perspective

41. Peter Kalum Schou
Institutional Logics in Entrepreneurial Ventures: How Competing Logics arise and shape organizational processes and outcomes during scale-up

42. Per Henriksen
Enterprise Risk Management Rationaler og paradokser i en moderne ledelsesteknologi

43. Maximilian Schellmann
The Politics of Organizing Refugee Camps

44. Jacob Halvas Bjerre
Excluding the Jews: The Aryanization of Danish-German Trade and German Anti-Jewish Policy in Denmark 1937-1943

45. Ida Schrøder
Hybridising accounting and caring: A symmetrical study of how costs and needs are connected in Danish child protection work

46. Katrine Kunst
Electronic Word of Behavior: Transforming digital traces of consumer behaviors into communicative content in product design

47. Viktor Avlonitis
Essays on the role of modularity in management: Towards a unified perspective of modular and integral design

48. Anne Sofie Fischer
Negotiating Spaces of Everyday Politics: -An ethnographic study of organizing for social transformation for women in urban poverty, Delhi, India

2019

1. Shihan Du
   ESSAYS IN EMPIRICAL STUDIES BASED ON ADMINISTRATIVE LABOUR MARKET DATA

2. Mart Laatsit
   Policy learning in innovation policy: A comparative analysis of European Union member states

3. Peter J. Wynne
   Proactively Building Capabilities for the Post-Acquisition Integration of Information Systems

4. Kalina S. Staykova
   Generative Mechanisms for Digital Platform Ecosystem Evolution

5. Ieva Linkeviciute
   Essays on the Demand-Side Management in Electricity Markets

6. Jonatan Echebarria Fernández
   Jurisdiction and Arbitration Agreements in Contracts for the Carriage of Goods by Sea – Limitations on Party Autonomy

7. Louise Thorn Bøttkjær
   Votes for sale. Essays on clientelism in new democracies.

8. Ditte Vilstrup Holm
   The Poetics of Participation: the organizing of participation in contemporary art

9. Philip Rosenbaum
   Essays in Labor Markets – Gender, Fertility and Education

10. Mia Olsen
    Mobile Betalinger - Succesfaktorer og Adfærdsmæssige Konsekvenser

11. Adrián Luis Mérida Gutiérrez
    Entrepreneurial Careers: Determinants, Trajectories, and Outcomes

12. Frederik Regli
    Essays on Crude Oil Tanker Markets

13. Cancan Wang
    Becoming Adaptive through Social Media: Transforming Governance and Organizational Form in Collaborative E-government

14. Lena Lindbjerg Sperling
    Economic and Cultural Development: Empirical Studies of Micro-level Data

15. Xia Zhang
    Obligation, face and facework: An empirical study of the communicative act of cancellation of an obligation by Chinese, Danish and British business professionals in both L1 and ELF contexts

16. Stefan Kirkegaard Sløk-Madsen
    Entrepreneurial Judgment and Commercialization

17. Erin Leitheiser
    The Comparative Dynamics of Private Governance
    The case of the Bangladesh Ready-Made Garment Industry

18. Lone Christensen
    STRATEGIIMPLEMENTERING: STYRINGSBESTRÆBELSER, IDENTITET OG AFFEKT

19. Thomas Kjær Poulsen
    Essays on Asset Pricing with Financial Frictions

20. Maria Lundberg
    Trust and self-trust in leadership identity constructions: A qualitative exploration of narrative ecology in the discursive aftermath of heroic discourse

21. Tina Joanes
Sufficiency for sustainability Determinants and strategies for reducing clothing consumption

22. Benjamin Johannes Flesch
Social Set Visualizer (SoSeVi): Design, Development and Evaluation of a Visual Analytics Tool for Computational Set Analysis of Big Social Data

23. Henriette Sophia Groskopff
Tvede Schleimann
Creating innovation through collaboration – Partnering in the maritime sector

24. Kristian Steensen Nielsen
The Role of Self-Regulation in Environmental Behavior Change

25. Lydia L. Jørgensen
Moving Organizational Atmospheres

26. Theodor Lucian Vladasel
Embracing Heterogeneity: Essays in Entrepreneurship and Human Capital

27. Seidi Suurmets
Contextual Effects in Consumer Research: An Investigation of Consumer Information Processing and Behavior via the Applicati on of Eye-tracking Methodology

28. Marie Sundby Palle Nickelsen
Reformer mellem integritet og innovation: Reform af reformens form i den danske centraladministration fra 1920 til 2019

29. Vibeke Kristine Scheller
The temporal organizing of same-day discharge: A tempography of a Cardiac Day Unit

30. Qian Sun
Adopting Artificial Intelligence in Healthcare in the Digital Age: Perceived Challenges, Frame Incongruence, and Social Power

31. Dorthe Thorning Mejlhede
Artful change agency and organizing for innovation – the case of a Nordic fintech cooperative

32. Benjamin Christoffersen
Corporate Default Models: Empirical Evidence and Methodical Contributions

33. Filipe Antonio Bonito Vieira
Essays on Pensions and Fiscal Sustainability

34. Morten Nicklas Bigler Jensen
Earnings Management in Private Firms: An Empirical Analysis of Determinants and Consequences of Earnings Management in Private Firms

2020

1. Christian Hendriksen
Inside the Blue Box: Explaining industry influence in the International Maritime Organization

2. Vasileios Kosmas
Environmental and social issues in global supply chains: Emission reduction in the maritime transport industry and maritime search and rescue operational response to migration

3. Thorben Peter Simonsen
The spatial organization of psychiatric practice: A situated inquiry into 'healing architecture'

4. Signe Bruskin
The infinite storm: An ethnographic study of organizational change in a bank

5. Rasmus Corlin Christensen
Politics and Professionals: Transnational Struggles to Change International Taxation

6. Robert Lorenz Törmer
The Architectural Enablement of a Digital Platform Strategy

7. Anna Kirkebæk Johansson Gosovic
Ethics as Practice: An ethnographic study of business ethics in a multi-national biopharmaceutical company

8. Frank Meier
Making up leaders in leadership development

9. Kai Basner
Servitization at work: On proliferation and containment

10. Anestis Keremis
Anti-corruption in action: How is anti-corruption practiced in multinational companies?

11. Marie Larsen Ryberg
Governing Interdisciolinarity: Stakes and translations of interdisciplinarity in Danish high school education.

12. Jannick Friis Christensen
Queering organisation(s): Norm-critical orientations to organising and researching diversity

13. Thorsteinn Sigurdur Sveinsson
Essays on Macroeconomic Implications of Demographic Change

14. Catherine Casler
Reconstruction in strategy and organization: For a pragmatic stance

15. Luisa Murphy
Revisiting the standard organization of multi-stakeholder initiatives (MSIs): The case of a meta-MSI in Southeast Asia

16. Friedrich Bergmann
Essays on International Trade

17. Nicholas Haagensen
European Legal Networks in Crisis: The Legal Construction of Economic Policy

18. Charlotte Biil
Samskabelse med en sommerfugle-model: Hybrid ret i forbindelse med et partnerskabsprojekt mellem 100 selvejende daginstitutioner, deres paraplyorganisation, tre kommuner og CBS

19. Andreas Dimmelmeier
The Role of Economic Ideas in Sustainable Finance: From Paradigms to Policy

20. Maibrith Kempka Jensen
Ledelse og autoritet i interaktion - En interaktionsbaseret undersøgelse af autoritet i ledelse i praksis

21. Thomas Burø
LAND OF LIGHT: Assembling the Ecology of Culture in Odsherred 2000-2018

22. Prins Marcus Valiant Lantz
Timely Emotion: The Rhetorical Framing of Strategic Decision Making

23. Thorbjørn Vittenhof Fejerskov
Fra værdi til invitationer - offentlig værdiskabelse gennem affekt, potentialitet og begivenhed

24. Lea Acre Foverskov
Demographic Change and Employment: Path dependencies and institutional logics in the European Commission

25. Anirudh Agrawal
A Doctoral Dissertation

26. Julie Marx
Households in the housing market

27. Hadar Gafni
Alternative Digital Methods of Providing Entrepreneurial Finance

28. Mathilde Hjerrild Carlsen
Ledelse af engagementer: En undersøgelse af samarbejde mellem folkeskoler og virksomheder i Danmark

29. Suen Wang
Essays on the Gendered Origins and Implications of Social Policies in the Developing World

30. Stine Hald Larsen
The Story of the Relative: A Systems-Theoretical Analysis of the Role of the Relative in Danish Eldercare Policy from 1930 to 2020

31. Christian Casper Hofma
Immersive technologies and organizational routines: When head-mounted displays meet organizational routines

32. Jonathan Feddersen
The temporal emergence of social relations: An event-based perspective of organising

33. Nageswaran Vaidyanathan
ENRICHING RETAIL CUSTOMER EXPERIENCE USING AUGMENTED REALITY

2021

1. Vanya Rusinova
The Determinants of Firms' Engagement in Corporate Social Responsibility: Evidence from Natural Experiments

2. Lívia Lopes Barakat
Knowledge management mechanisms at MNCs:
The enhancing effect of absorptive capacity and its effects on performance and innovation

3. Søren Bundgaard Brøgger
Essays on Modern Derivatives Markets

4. Martin Friis Nielsen
Consuming Memory: Towards a conceptualization of social media platforms as organizational technologies of consumption

05. Fei Liu
Emergent Technology Use in Consumer Decision Journeys: A Process-as-Propensity Approach

06. Jakob Rømer Barfod
Ledelse i militære højrisikoteams

07. Elham Shafiei Gol
Creative Crowdwork Arrangements

08. Árni Jóhan Petersen
Collective Imaginary as (Residual) Fantasy: A Case Study of the Faroese Oil Bonanza

09. Søren Bering
"Manufacturing, Forward Integration and Governance Strategy"

10. Lars Oehler
Technological Change and the Decomposition of Innovation:
Choices and Consequences for Latecomer Firm Upgrading: The Case of China's Wind Energy Sector

11. Lise Dahl Arvedsen
Leadership in interaction in a virtual context:
A study of the role of leadership processes in a complex context, and how such processes are accomplished in practice

12. Jacob Emil Jeppesen
Essays on Knowledge networks, scientific impact and new knowledge adoption

13. Kasper Ingeman Beck
Essays on Chinese State-Owned Enterprises:
Reform, Corporate Governance and Subnational Diversity

14. Sönnich Dahl Sönnichsen
Exploring the interface between public demand and private supply for implementation of circular economy principles

15. Benjamin Knox
Essays on Financial Markets and Monetary Policy

16. Anita Eskesen
Essays on Utility Regulation: Evaluating Negotiation-Based Approaches inthe Context of Danish Utility Regulation

17. Agnes Guenther
Essays on Firm Strategy and Human Capital

18. Sophie Marie Cappelen
Walking on Eggshells: The balancing act of temporal work in a setting of culinary change

19. Manar Saleh Alnamlah
About Gender Gaps in Entrepreneurial Finance

20. Kirsten Tangaa Nielsen
Essays on the Value of CEOs and Directors

21. Renée Ridgway
Re:search - the Personalised Subject vs. the Anonymous User

22. Codrina Ana Maria Lauth
IMPACT Industrial Hackathons: Findings from a longitudinal case study on short-term vs long-term IMPACT implementations from industrial hackathons within Grundfos

23. Wolf-Hendrik Uhlbach
Scientist Mobility: Essays on knowledge production and innovation

24. Tomaz Sedej
Blockchain technology and inter-organizational relationships

25. Lasse Bundgaard
Public Private Innovation Partnerships: Creating Public Value & Scaling Up Sustainable City Solutions

26. Dimitra Makri Andersen
Walking through Temporal Walls: Rethinking NGO Organizing for Sustainability through a Temporal Lens on NGO-Business Partnerships

27. Louise Fjord Kjærsgaard
Allocation of the Right to Tax Income from Digital Products and Services: A legal analysis of international tax treaty law

28. Sara Dahlman
Marginal alternativity: Organizing for sustainable investing

29. Henrik Gundelach
Performance determinants: An Investigation of the Relationship between Resources, Experience and Performance in Challenging Business Environments

30. Tom Wraight
Confronting the Developmental State: American Trade Policy in the Neoliberal Era

31. Mathias Fjællegaard Jensen
Essays on Gender and Skills in the Labour Market

32. Daniel Lundgaard
Using Social Media to Discuss Global Challenges: Case Studies of the Climate Change Debate on Twitter

33. Jonas Sveistrup Søgaard
Designs for Accounting Information Systems using Distributed Ledger Technology

34. Sarosh Asad
CEO narcissism and board composition: Implications for firm strategy and performance

35. Johann Ole Willers
Experts and Markets in Cybersecurity On Definitional Power and the Organization of Cyber Risks

36. Alexander Kronies
Opportunities and Risks in Alternative Investments

37. Niels Fuglsang
The Politics of Economic Models: An inquiry into the possibilities and limits concerning the rise of macroeconomic forecasting models and what this means for policymaking

38. David Howoldt
Policy Instruments and Policy Mixes for Innovation: Analysing Their Relation to Grand Challenges, Entrepreneurship and Innovation Capability with Natural Language Processing and Latent Variable Methods

2022

01. Ditte Thøgersen
Managing Public Innovation on the Frontline

02. Rasmus Jørgensen
Essays on Empirical Asset Pricing and Private Equity

03. Nicola Giommetti
Essays on Private Equity

04. Laila Starr
When Is Health Innovation Worth It? Essays On New Approaches To Value Creation In Health

TITLER I ATV PH.D.-SERIEN

1992

1. Niels Kornum
Servicesamkørsel – organisation, økonomi og planlægningsmetode

1995

2. Verner Worm
Nordiske virksomheder i Kina
Kulturspecifikke interaktionsrelationer ved nordiske virksomhedsetableringer i Kina

1999

3. Mogens Bjerre
Key Account Management of Complex Strategic Relationships
An Empirical Study of the Fast Moving Consumer Goods Industry

2000

4. Lotte Darsø
Innovation in the Making
Interaction Research with heterogeneous Groups of Knowledge Workers creating new Knowledge and new Leads

2001

5. Peter Hobolt Jensen
Managing Strategic Design Identities
The case of the Lego Developer Network

2002

6. Peter Lohmann
The Deleuzian Other of Organizational Change – Moving Perspectives of the Human

7. Anne Marie Jess Hansen
To lead from a distance: The dynamic interplay between strategy and strategizing – A case study of the strategic management process

2003

8. Lotte Henriksen
Videndeling
– om organisatoriske og ledelsesmæssige udfordringer ved videndeling i praksis

9. Niels Christian Nickelsen
Arrangements of Knowing: Coordinating Procedures Tools and Bodies in Industrial Production – a case study of the collective making of new products

2005

10. Carsten Ørts Hansen
Konstruktion af ledelsesteknologier og effektivitet

TITLER I DBA PH.D.-SERIEN

2007

1. Peter Kastrup-Misir
Endeavoring to Understand Market Orientation – and the concomitant co-mutation of the researched, the re searcher, the research itself and the truth

2009

1. Torkild Leo Thellefsen
Fundamental Signs and Significance effects
A Semeiotic outline of Fundamental Signs, Significance-effects, Knowledge Profiling and their use in Knowledge Organization and Branding

2. Daniel Ronzani
When Bits Learn to Walk Don't Make Them Trip. Technological Innovation and the Role of Regulation by Law in Information Systems Research: the Case of Radio Frequency Identification (RFID)

2010

1. Alexander Carnera
Magten over livet og livet som magt
Studier i den biopolitiske ambivalens