Master's Thesis

MSc in Business Administration and Innovation in Healthcare

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The Lack of Innovation in Female Contraception

*"So it's not that we need more s***, that doesn't work, or is dangerous. We just need stuff that works really, really nicely for us. We should not have pain just because we are women."*
(End-user 09)

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Abstract

Objective: The study took departure from the notion of the high rates of unintended pregnancies in Europe despite the availability of safe and effective birth control options. A dual research question was conducted and assessed women's perceptions with current contraceptives and their influence on innovation as well as insights from the pharmaceutical industry's hindrances to innovate.

Methods: The study applied an explorative mono-method qualitative design by conducting semi-structured interviews with two informant groups, end-users of contraception (n=20) as well as industry experts (n=6) within the pharmaceutical drug development. The data was triangulated and analyzed based on grounded theory in the scope of template analysis.

Results: The study identified three misfits which hinder innovation within female contraception. (1) The 'Lack of say' reflected in the shortcoming of assessing their pain, needs and desires, (2) The 'Systematic barriers and bias' within the pharmaceutical industry mirrored through a profit-driven approach, bias and the double standard of protecting women by not including them into pharmaceutical development, (3) The 'Lack of ownership' driven by an economic pressure and fragmented health-care system distinguished as a market failure.

Conclusion: Female contraceptives lack innovation due to a limited assessment of users' conception of pain. Without accurate and commulated data of perceived pain the "proven" value to ensure reimbursement is not given. The distinguished market failure stresses for a public health imperative within contraception.

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We are very proud of our women-lead contribution on such an important topic.

And lastly for all the women who persist: keep on being bloody difficult!

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List of Abbreviations

BMGF	Bill and Melinda Gates Foundation
ECP	Emergency Contraception
ECRR	European Center for Reproductive Rights
EMA	European Medical Agency
FAB	Fertility Awareness Based Methods
FDA	Food and Drug Administration
GMP	Good Manufacturing Practice
GT	Grounded Theory
HIC	High Income Countries
HIV	Human Immunodeficiency Virus
HMA	Heads of Medicine Agency
IUD	Intrauterine Devices
LARC	Long-acting Reversible Contraceptives
LIC	Low Income Countries
LMIC	Low and Middle Income Countries
M&A	Mergers and Acquisitions
NDA	New Drug Applications
NGO	Non-governmental Organizations
NICHD	National Institute of Child Health and Human Development
NRM	Natural Rhythm Methods
OC	Oral Contraceptives
OECD	Organisation for Economic Co-operation and Development
PC	Population Council
PPP	Public-private partnerships
PRH	Family Planning and Reproductive Health
PV	Predictive Value
R&D	Research and Development
ROI	Return on Investment
SARC	Short-acting Reversible Contraceptives
STD	Sexually Transmitted Diseases
TA	Template Analysis
UN	United Nations
UNDESA	United Nations Department of Economic and Social Affairs
WHO	World Health Organisation
WO CBP	Women Of Child Bearing Potential

Terminological glossary

This section aims at describing the terms used along the paper in a way we wish them to be perceived by the reader. The reader may refer to this glossary at any point in time when doubting the understanding of a word during the lecture of this thesis.

Contraception: In the context of this research the terms ‘contraceptives’, ‘birth control’, ‘family planning’ and ‘fertility control’ are used interchangeably. Our analysis is based on modern forms of contraception, which are technological advances that enable the prevention of pregnancy through a medical device or drug. In the scope of this paper we refer to barrier methods, SARCs and LARCs when using the wording ‘contraception’.

End-user vs. women: The term 'end-user’ is defined as women (she/her/they) who are currently using a modern form of birth control or have done so in the past. The broader term of ‘women’, applies to all women whether they are users of contraceptives or not.

Non-invasive: In this context, ‘non-invasive’ refers to an insertion method of a contraceptive that doesn’t require a medical insertion. For instance, the insertion of an IUD is seen as invasive, whereas, the intake of the pill is non-invasive.

Non-hormonal vs. hormonal: Non-hormonal contraceptives are methods that do not require the intake of hormones. Therefore they do not interfere with a body’s natural hormonal cycle. Some examples are the copper IUD, diaphragm, cervical sponges or natural family planning methods. The latter one however is not assessed in the context of this thesis, as it is considered a traditional and not a modern form of contraception.

Patient vs. end-user: A patient refers to a person in need of care or medical treatment. However in the scope of this thesis, the medication taken is preventive, therefore the users of contraception are not considered to be patients as they are not sick in any way. Thus, we refer to them as end-users instead.

Payer vs. government vs. reimbursement: Payer is used interchangeably with the entity reimbursement. Within a single health care system the government is embodying the payer. Within a universal health care system the payer encompasses different entities such as employer, government and health insurances.

Sexual education: For the purpose of this paper it is defined as education about the reproductive system as well as contraception, with regards to their existence, the availability of methods, their side-effect and safety profile.

Systemic barriers: Systemic barriers are referred to when addressing the linear way in which the pharmaceutical company operates, it involves the policies, practices or procedures embedded in the system that result in some innovations receiving unequal attention or being excluded from further research or development.

The system of contraceptive development: When using the wording ‘the system’ in relation to contraception, we wish to designate the interaction among the main three players that are researched in the context of this paper: the end-users, the pharmaceutical industry and the government iterating with each other. As a whole, they define what makes the system of contraceptive development. In the real world, other players may also interact and interfere with the aforementioned players.

Chapter I: Introduction

1. Introduction and problem formulation

This thesis takes departure in the premise of the high rates of unintended pregnancies in Europe, where access and cultural acceptance towards contraceptive use is very high (De Irala et al., 2011). Besides contraceptives' main purpose to avoid unintended pregnancies, it offers women around the world more freedom in family planning, better health outcomes for themselves and their children, and, as a result of this, an increase in social and educational outcomes (Liu & Raftery, 2020). With the introduction of the pill in the 1960s, society experienced a social revolution allowing women to plan their families and enter the workforce. Since then the field of hormonal female contraception showed continuous incremental innovation, as seen with improvements and adaptation of the pill. Pharmaceutical companies stopped their research and development (R&D) activities within female contraception at the beginning of the 21st century (Callahan et al., 2020).

However, despite pharmaceutical past R&D activities and available contraceptives, an unmet need for new contraceptive methods among men and women can still be identified. This is shown by the fact that around 171 million women worldwide between the age of 15 and 49, which represents one out of 11 women, are not using contraception, yet want to avoid pregnancy (UN, 2020). Reasons linked to this number are a lack of access, medical concerns, strong side effects and difficulty of use (Callahan et al., 2020). Around 40% of all pregnancies are unplanned, half of which end in induced abortion. Astonishingly a high proportion of unintended pregnancies occur where contraception is relatively accessible and cultural stigma against it is generally low, such as in North America (48%) and Europe (43%). This indicates that access is not the driving factor, rather it appears to be an active choice by women to not choose a contraceptive. This expresses dissatisfaction with the current options. Therefore, new, effective, and more desirable contraceptive options are urgently needed (Bearak et al. 2020).

Reasons behind the decreasing efforts of the pharmaceutical industry to research contraceptives can be linked to the (1) "*existence of many effective, low-cost products in the market, some over-the-counter; (2) the high bar for developing commercially successful new products with such highly effective existing options already marketed; (3) liability concerns since, unlike other therapeutics that treat a medical problem/disease, contraceptives are generally used for long periods of time by healthy individuals; and (4) the high cost of R&D*" (Callahan et al., 2020, p.158).

An additional burden for the possible innovation in contraceptives are the demanding clinical trials and regulations required to comply with (HMA, 2014).

Nevertheless, the same difficulties occur in most other medical treatment research, where innovation and R&D are still ongoing and funded by the pharmaceutical industry. As opposed to other drugs, contraceptives are merely a preventive option that is not related to disease treatment. However, research persists in for example vaccines, which, similarly to birth control, is a form of prevention (Moyle & Tote, 2013). Fostering research in preventive therapeutic areas is crucial in the improvement of global health, the alleviation of the healthcare system, and the reduction of cost burdens. That also goes for the continuous innovation in birth control, which would benefit healthcare systems and the health of women, by avoiding all the side effects from contraception, unsafe abortions but also abortion costs and related emotional distress (Grossman et al., 2016).

The last decade's research efforts within the area of contraception were mainly driven by non-profit organisations, philanthropic foundations (Gates Foundation), and academia (ibid). There is a lack of investment that is required to elaborate on new innovative methods like non-hormonal contraceptives (Johnston & Goldberg, 2020). Callahan et al. underline the importance of cross-sectional collaboration in mitigating the barriers to new contraceptive development. New partnerships between governments, academia, NGOs, and the pharmaceutical industry need to be established so that the accumulated risk and financial investment can be shared (Callahan et al., 2020).

2. Purpose statement and gap analysis

The perspectives women have on the available current methods of contraception and the need for new ones are limited and under-researched. Further, it appears that if the need for the development of new contraceptives was researched, most literature dates back to the 1990s (Mastroianni et al., 1990). The existing literature on preferred birth control amongst known methods, such as the CHOICE project, provides insights on what women favor but doesn't assess the need for new ones (Secura et al., 2010). As recent research elucidates, unintended pregnancy rates will remain high until the lived experience of women's relationships with contraception is investigated (Alspaugh et al., 2019). Yet, the reasons for the discontinuation of contraceptives in Europe and the desire for new products have not been addressed sufficiently. This calls for a need to mitigate and close the lack of granularity to improve data accessibility about end-users needs and desires.

Further, we identified a gap in the literature on the reasons behind the disengagement of the pharmaceutical industry after the late 2000s. Thus, there has been limited interest, investment, and innovation within the field over the last twenty years. This highlights the lack of transparency in the available data as well as the lack of research on the reasons behind the exit of the pharmaceutical industry in this context.

Therefore, we aim at contributing to the existing literature by investigating women's perceptions, desires, and needs on their modern contraceptive methods and addressing the barriers of the pharmaceutical industry to innovate those.

3. Research questions

This thesis aims to evaluate the lack of innovation within birth control. As such, the leading research question follows:

'Why do female contraceptives lack innovation ?'

In order to evaluate the implications of this analysis, the thesis will focus on the two major players: the pharmaceutical industry and the end-users (women). On the one hand, we attempt to explore women's perceptions of their satisfaction and their desires for new contraceptives. Thus, the first sub-question elucidates:

'How do end-users perceive contraceptives,
and how does a potential lack of satisfaction foster the need for innovation?

On the other hand, we seek to investigate the role and the reasons behind the interest of pharmaceutical companies in investing in female contraceptive methods and assess what the barriers and opportunities to do so, involve. Subsequently, the second subordinate question states:

'What are the barriers for the pharmaceutical industry to innovate female contraceptives?'

4. Scope and delimitation

4.1. Germany

The research area will be explored by delimiting the scope of this thesis to Germany. Firstly, this delimitation to Germany has been decided upon, as it represents one of the most prominent and

research-incentive areas for pharmaceutical players in the World. Some of the key players in the development of contraception stem from Germany, such as Bayer AG, leader in the therapeutic area of women's health (GVR, 2019). Secondly, the German market embodies one of the key health markets within Europe with a population of 83 million inhabitants, of which 50,61% is of female gender (World Bank, 2020). A large part of this population is at a reproductive age, which makes Germany a developed country that relies heavily on contraception. Thirdly, the country offers a context where the use of contraception is widely accepted and not constrained by cultural or ethical stigmas (De Irala et al., 2011). Further reasoning behind the choice of Germany is due to the fact that contraception is covered by health insurance until the age of 21 years. Therefore, the questioning of satisfaction with a contraceptive method may arise even more as one has to carry the financial burden of it. As such, expensive drugs are known to come along with high patient expectations (Center of Reproductive Rights, 2012). These reasons make Germany a viable market to investigate the reasons behind a lack of innovation in contraceptives.

It has to be noted, that even though this thesis is written in the context of Germany, not all available literature and theories can be applied to this specific background. Thus, when elucidating the role of the pharmaceutical industry, the drug development process and innovation theories, the national limitation will not be taken into consideration.

4.2. Focus on female and not male contraceptives

Further on the scope of this thesis is restricted to the area of female birth control methods. The safety and acceptability of contraceptives are especially important to women who use them as they are the ones carrying the burden of side effects. Further, the current availability of contraceptive choices limits the possibilities to effectively share the responsibility of contraception. This restriction in the scope of this paper has also been concluded for feasibility reasons as the female contraceptive market is already fragmented and separated into medical devices, oral contraceptives and traditional methods of contraception (Chandra, 2016). Therefore, male contraceptives will not be considered a part of the research under the scope of this study.

4.3. Early drug discovery focus

Focus will be given to the early stage of the drug development process, in particular on the first gate: early discovery in R&D, which will be elucidated upon in the background section of this paper. This has been decided upon as we noted, that hardly any contraceptives are currently seen in the pipeline of drug-development companies. Thus, if a drug candidate for birth control was considered they did not pass to the second stage. As such, the first stage is considered to be crucial. However,

as the different stages of the drug development influence each other significantly, the thesis will also mention bottlenecks visible in the later stages of the drug-development process if relevant to the case of contraceptives.

4.4. Radical innovation rather than incremental innovation

Lastly, as mentioned in the leading research question, this thesis will investigate the lack of innovation in female contraceptives. However, when referring to the term innovation, only radical innovations that have the potential to transform the business model will be considered as additions to the existing contraceptive methods. Thus, incremental innovation, which invokes small improvements such as upgrades in the shape of an IUD for example, will not be considered as innovation. Therefore, only completely new modes of action are seen as innovations in the context of this paper.

Chapter II: Background

In the following chapter, a first part will introduce the key concepts of female contraception, its benefits and needs. It will then be followed by a presentation of the European female contraceptive market, its drivers and challenges. Subsequently, pharmaceutical research and development (R&D), new drug development and the value chain of female contraceptives will be introduced. In the last part of this section, the main theories and factors leading to innovation in life science will be addressed.

1. Female contraception

The following section will start by providing an overview of the definition of contraception. Further, the reproductive choices and rights along with the benefits of contraception will be outlined. Lastly, the different types of contraceptive methods will be introduced along with their current usage.

1.1. Introduction to contraceptives

Contraception is defined by any device, method, or drug used whose primary purpose is to prevent pregnancy. It is seen as an essential health service that improves health outcomes and reduces health care costs (Moniz et al, 2017). This can be done both from the male and the female side. The scope of this paper focuses solely on modern forms of female contraceptive methods which are characterized by technological advances, under the form of a product or a medical procedure that are created in order to overcome biology, by interfering with reproduction from sexual intercourse. Its aim is to enable couples to have mutually desired sexual intercourse at any desired time (Hubacher & Trussel, 2015).

Opposed to that, traditional contraception encompasses methods such as abstinence, withdrawal, calendar rhythm and lactational amenorrhoea to control fertility (WHO, 2006). Sexually active women that are amenorrhoeic (menstruating), not pregnant and not infertile represent the population at risk of pregnancy. Over her lifetime, the mean span of a woman's reproductive age ranges from 15 to 49 years. Women at reproductive age are considered as a woman of childbearing potential (WOCBP) until becoming post-menopausal or permanently sterile (Hayunga et al., 1996). As such, whether or not they decide to give birth to a child, women are in need of sexual and reproductive health services and depend on preventive birth control methods from their adolescence onwards for more than 30 years (Gutmacher, 2014).

1.2. Reproductive choices and rights

Since the 1968 International Conference on Human Rights, family planning has been included as a key human right and became an obligation to respect and provide support from every government, country and policy-maker. Thus, every human should be allowed adequate information and education with respect to contraceptive choices (UNFPA, 2018). Particularly for women, family planning and reproductive choice is a fundamental human right that liberates them from a continuous cycle of pregnancy, breastfeeding and childcare. The informed decision to have children, how many and with whom are key aspects of the rights of family planning, which also represents an enormous step towards greater gender equality (Cleland et al., 2012).

According to the World Health Organisation (WHO), sexual and reproductive health involves the inclusion of provision of contraceptive choices, safety and infertility services. Education on available birth control has shown to increase people's informed decision-making in their family planning preferences, as well as better satisfaction and continued use of contraceptives. Family planning standards as set out in the Proclamation of Teheran (1968) entails the nine following aspects: non-discrimination (1), availability (2), accessibility (3), acceptability (4), good-quality (5), informed decision making (6), privacy and confidentiality (7), participation (8) and accountability (9) of birth control options (UNFPA, 2018).

1.3 The benefits of contraception

The central aspect of contraceptive use is that a couple or a woman can plan if they/she desires to have a child, how many children are wanted and how many years apart the children should be (Yaya et al., 2018). The freedom of family planning is one of the essential aspects and advantages of contraception. Further family planning offers improved health outcomes for mother and child (Kavanaugh & Anderson, 2013) as studies have shown the connection between closely-timed pregnancies and an increased child-mortality rate (Hobcraft et al., 1983). Moreover, contraceptives are linked to women’s empowerment through more autonomy in their decision-making, enabling more participation in the labor force due to fewer children, resulting in an economical uplift (Yaya et al., 2018; Liu & Raftery, 2020). Family planning is therefore key to poverty reduction, sustainable development, economic growth, gender equality and social inclusion for women (Bendix et al., 2017).

Even though not all unintended pregnancies are unwanted they may come along with some other health risks for mother and child. For instance, unintended pregnancies can lead to the practice of unsafe abortions (Shah et al., 2012). Unplanned births in the US are estimated to have cost 21

billion US dollars to the American healthcare system in 2010 only (Sonfield et al, 2015). These costs could be dramatically reduced by avoiding the need of abortion due to correct contraceptive use. On top of that the mental and physical burden that women undergo when deciding to abort can be avoided (Fergusson, 2018). Lastly, more than just providing freedom of decision-making and avoiding pregnancies, certain types of birth control also allow the protection against certain sexually transmitted diseases (STDs) and human immunodeficiency virus (HIV) (CDC, 2013).

1.4. The unmet need of family planning

Worldwide, 1,9 billion women are at a reproductive age, between the age of 15 and 49 years old. Of all these women, 1,1 billion are estimated to be in need of modern forms of contraception (UNDESA, 2019). Among the European population, a total of 23% at a reproductive age is currently not using any modern form of birth control methods (UNDESA, 2019).

Behavior trends and choice in contraceptives vary depending on age, civic status, pre-or post children and country in Europe (Skouby, 2012). Therefore, different needs, values and desires can be identified in people using contraceptives, which reflects that a variety of different methods can best meet women's expectations. Moreover, besides differing in their contraceptive preferences, the needs of an individual change through the course of a reproductive lifetime. As such, adolescents' needs for contraception contrast to women who have terminated their family planning, but are still at a reproductive age. On top of that, women react differently to contraceptives methods, which further emphasizes the need for an array of birth control choices (Mastrioanni et al.,1990).

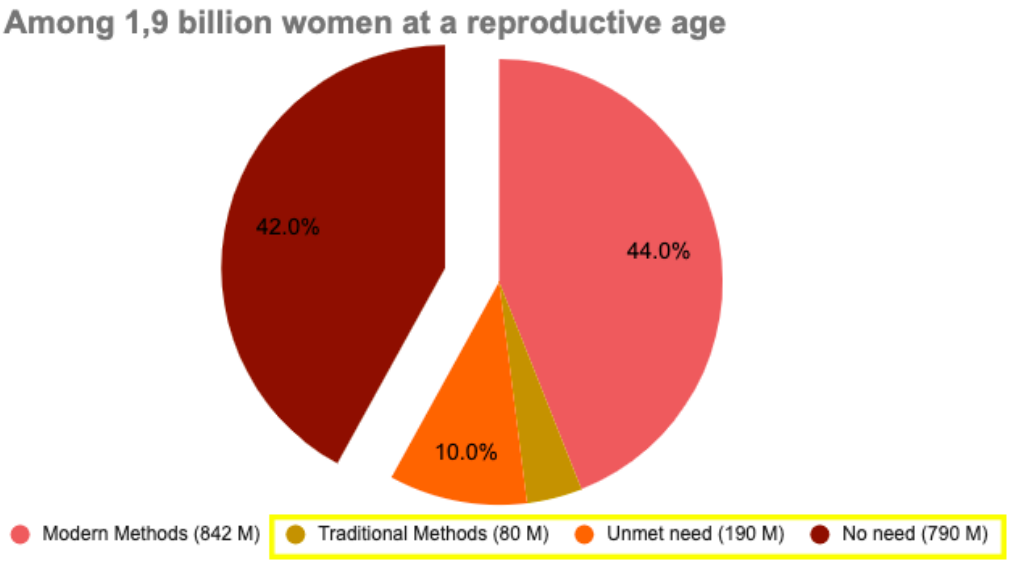

Figure 1: Usage and need for modern contraception of women at reproductive age (15-49)
Data Source: Estimates and Projections indicators of family planning 2019

The figure above depicts the estimated number of women of reproductive age worldwide using modern and traditional contraceptive methods. It also shows women having an unmet need for family planning, meaning those who want to avoid pregnancy but do not use any contraceptive method, and women who do not need contraception as they desire children. This paper aims at assessing the unmet need of women using modern methods of contraception, using traditional methods or not using any contraception because of potential side-effects, health concerns or else. As such, the three aforementioned categories are encircled in yellow to demonstrate that within each of these groups, there is a certain percentage of dissatisfaction, despite the fact that modern or traditional contraceptives may be used.

1.5. Types of birth control

Overall, modern female types of contraceptive methods can be classified under three main groups: (1) long-acting reversible contraceptives (LARCs); such as intrauterine devices (IUD) and hormonal implants. (2) Short-acting reversible contraceptives (SARC); such as oral contraceptive pills, female condoms, spermicides and injectable hormones and (3) permanent methods which involve sterilization through tube litigation (Tibajuka et al., 2017). Oral contraceptives remain the most used method through all age groups, followed by LARCs (Skouby, 2012).

(1) LARC methods are birth controls that are usually inserted by a medical practitioner and depending on the method last from three to ten years. The efficiency rate of LARCs is mostly independent of the user attributes and are thus recognized as very efficient methods of contraception.

(2) SARC methods on the other hand, are birth control methods that need to be prescribed by a doctor in most European countries and are effective for a given period of time. They require to be taken on a regular basis, which can be daily, weekly or monthly depending on the chosen option.

(3) Female sterilization refers to a form of birth control that prevents pregnancy for the rest of a woman's life through a medical procedure where the tubes are ligated. This method holds an effectiveness rate of 99% and is permanent.

(4) Barrier methods are another form of pregnancy prevention that needs to be used during every sexual intercourse.

(5) Fertility awareness-based methods (FAB) or Natural Rhythm Methods (NRM) are included as part of the previously mentioned traditional methods of contraception. As such these methods do not use any type of modern contraceptive device or pill but instead control for a woman's fertile days in her cycle and use abstinence, withdrawal or lactational amenorrhea (WHO & PRH, 2018).

(6) Emergency contraception (ECP) helps women to avoid becoming pregnant after having unprotected sex, where no contraception was used. Products such as combined oral contraceptives and progestin-only pills can act as emergency contraceptives. Emergency contraceptives classify as a form of hormonal birth control. They do not disrupt an ongoing pregnancy and can be taken up to five days after having had unprotected sex, however, the sooner emergency contraception is taken the higher its efficacy. The so-called ‘morning-after pill’ works by delaying or preventing the release of eggs from the ovaries. The insertion of an IUD after unprotected sex can also be used as a form of emergency contraceptive (ibid).

Further female contraceptives can be divided into hormonal and nonhormonal forms of female contraception. Hormonal contraceptives include combined contraceptives such as the combination-pill, vaginal ring, and the contraceptive patch and progesterone-only methods, which encompass the progestin-only pill, implants, injections and IUDs. They act by changing a woman's cycle and body chemistry. Based on which hormonal birth control is used, they either prevent ovaries from releasing, thinning the uterus to avoid implantation or thicken the overall cervical mucus to prevent sperm from reaching the eggs. The most common side effects are mood swings, weight gain, acne, headaches and migraines as well as menstruation changes. The side effects vary depending on every woman’s body. These hormonal options are, however, often linked with high efficacy rates (Visser et al., 2013). On the contrary, non-hormonal contraceptives don’t interfere with a female's reproductive system at all. They act as a barrier method between the sperm and the egg to prevent pregnancy. This non-interference with the female reproductive system also means that fewer side effects occur (Lam, 2020). However, increased pain linked to heavier uterine bleedings and spotting between the periods leads around 15% of women to remove their Copper IUD within the first year of insertion (Hubacher, 2008).

The following table displays an overview and classifies which type belongs to which concept. Information regarding side effects and effectiveness rate is provided. The choice of contraceptives taken by the end-user depends on one's age, education and geographical location (Chandra, 2016). Thus, the table presents information regarding the usage, price range and sociodemographics for Germany as an example:

Concept	Barrier Methods	SARCs	LARCs	Sterilization	Fertility Awareness Methods	Emergency Pill
Function	Creates a physical barrier to prevent sperm from entering a woman's uterus	Hormones are taken into the body to prevent the ovaries from releasing eggs	Exist with and without hormones - the device is inserted in the uterus and makes it inhospitable to sperm	Permanent surgical intervention that prevents men or women to have children in the future	Monitoring and recording of a women's cycle in order to work out when she is most likely to get pregnant (length of cycle, temperature, changes to cervical secretion)	Can be taken up to 5 days after having had unprotected sex
Type	Condom, spermicides, diaphragm, cervical cap, contraceptive sponge	Pill, implants, injections, skin patches, vaginal rings	IUD - with or without hormones, coil	Tubal ligation	Possibility to use fertility monitors, Apps, or fertility charts that help track the cycle	Emergency contraceptive pill or the IUD inserted after having had unprotected sex
Usage	Every time	Daily or regularly	Insertion and retrieval	Permanent	Regular tracking	One time
Effectiveness- perfect use	92 to 99% (varies by method)	99% (varies by method)	99% (varies by method)	99%	99%	99%
Effectiveness- typical use	71 to 88 % (varies by method)	91% (varies by method)	98%	-	76%	95%
Reversible	Yes	Yes	Yes	No	Yes	Yes
Benefits	- No need for prescription - Some methods can prevent STDs - Can be used in combination with other methods to increase the effectiveness -Can be used whilst breastfeeding	- Possible lighter periods and less pain - Can improve hormonal acne - Fertility returns soon after stopping use - May reduce the risk of ovarian cancer	- Longest lasting reversible birth control available - Possible to become pregnant directly after removal - Can be used when breastfeeding - Possibility to choose a hormone-free method	- Single time intervention - Stays for the rest of the life - No hormones	- Natural and doesn't cause any side effects - No hormones - Awareness of body and cycle performance - Free of costs - Development of an understanding of one's body	- Reliable - Convenient - Single-use - No harm done to the fetus

Germany						
Usage*	46% of the population uses condoms	47% of the population uses the pill	10 % of the population uses an IUD	2% of the women have tubal ligation	5% of the population temperature or calendar method	n.a.
Socio-demographic information in age**	(condom) 18 - 29: 58 % 30 - 39: 44 % 40 - 49: 34 %	(pill) 18 - 29: 56 % 30 - 39: 45 % 40 - 49: 39 %	(IUD) 18 - 29: 5 % 30 - 39: 6 % 40 - 49: 20 %	(Tubal ligation) 18 - 29: 0 % 30 - 39: 3 % 40 - 49: 13 %	n.a.	n.a.
Price Range	Condom: 3- 20€/ pack	- Pill: 6 - 13€ / month - Vaginal ring: 17€/ month	- Hormonal IUD: 310 - 610 €/ 3-5 years - Copper IUD: 180 - 300€/ 3-5 years + added costs for ultrasound examination	500 - 1000€/ for life	No costs unless use of Apps like 'Clue ' (3,30€/month) or 'Natural Cycles' (65€/ year)	16 - 35€ / one time
Overall Trends in Germany	• 67% of the German population actively uses contraception • In comparison to 2011, there has been a decrease in the use of the pill and an increase of condom use • In particular, in the age group between 18 - 29 years, the usage of the pill as the main method of contraception has significantly decreased • Major reasons for not using contraception are because of a wish to have children, not having a sexual partner or not wanting to use hormones • Safety to prevent pregnancies is advanced as the main reason for the use of contraceptives • The majority of the population identifies hormonal contraception as a risk (BZgA, 2018)					

Table 1: Main contraceptive methods overview, by type, use, effectiveness, benefits, and side-effects

Sources: Based on various literature reviews (NHS, 2020; BZgA, 2018)

**The usage of contraceptives in Germany is above 100% as some women rely on several types of contraceptives (e.g. condom and the pill)*

*** The sociodemographic information is including men in the percentage of the use of condoms*

1.6 The current state of contraception

1.6.1. Addressing satisfaction

Patient satisfaction with healthcare, their medication or medical device is a topic that has drawn a lot of attention in the past decade. The perception of value from a patient's perspective has become a central aspect also for pharmaceutical manufacturers, who wish to obtain feedback about their products (Shikiar & Rentz, 2004). For contraception, this value perception is particularly important, as the drugs or medical devices are used in a healthy and young population, where satisfaction is key to ensure adherence and continuation of a chosen birth control method (ibid.).

Satisfaction with female contraceptive methods is a topic that can easily be overlooked due to the fact that being pregnant is not a disease. Thus, the advancement in birth control does not challenge a life-threatening disease but is merely a preventive measure (Mastroianni et al., 1990). However, unwanted pregnancies and abortion still represent a huge cost factor to healthcare systems, in addition to being a physical and psychological burden to women (Grossman et al., 2016). Furthermore, placing a measurement on the perception of pain is very difficult with contraceptive measures. Besides describing pain on a numerical scale, the notion of pain can also be described as one's impact on the quality of life (Katz, 2002). This is a crucial point in the discussion of satisfaction of birth control as it affects a woman's everyday life.

In order to place a measurement on the term of satisfaction, the quality of the taken medication and the experience with it has to be assessed. In the healthcare sector it can be difficult to obtain consumers' preferences, as everyone's needs vary and one might have different perceptions of pain and side-effects of the same medication (Shikiar & Rentz, 2004). This also goes for female contraceptives, as every woman's body, cycle and approach to it is different. As such, it is a challenge to have a contraceptive method that suits the needs and wants of every woman. Some recent studies have shown that women's contraceptive needs are changing over the course of a lifetime but also with increased information. For pill users, 36% of the participants of Johnson's et al.' Europe-based study wished to change birth control options in the near future. The most common reason for change was due to concern over side-effects. Knowledge about non-hormonal contraceptives in return was estimated to be low (Johnson et al., 2013) A study on contraceptive use done in Germany, showed that the majority of the German contraceptive users identify hormonal contraception as a risk because of side effects or potential health concerns (BZgA, 2018). Furthermore, reasons for discontinuation of contraceptive methods are often linked to side-effects, concerns of these or the desire to switch to a more effective method (Ali et al., 2012)

Colwell et al. designed a birth control satisfaction assessment tool (ORTHO BC-SAT) for hormonal contraceptives. Their research shows that women's reason for using hormonal contraception is firstly to avoid pregnancy and secondly to allow for regulation of their menstrual cycle. This framework includes the following attributes to measure the satisfaction of female birth control users: ease of use and convenience, level of symptoms and side effects bother, menstrual impact, lifestyle impact, compliance and adherence, assurance and confidence, future fertility concerns and lastly overall confidence (Colwell et al., 2006). These various attributes pave a way to determine the overall satisfaction of women with a given contraceptive method by touching upon aspects impacting daily life, physical and mental health.

1.6.2 Assessing dissatisfaction of modern contraceptives

The available literature on dissatisfaction can be composed of three major points of dissatisfaction for modern methods: (1) Physical and psychological harm experienced by the users, which refers to all the side-effects mentioned in section 1.5. of this paper. Secondly, (2) the shortcomings of the intake are put forward. Certain pregnancy-preventive methods require discipline, memory, frequent consultations with the doctor for prescription renewals and even skills to use (Clealand et al., 2012). Lastly, (3) the continued use of contraception despite dissatisfaction with the chosen method is displayed. Some women opt to continue to use a specific contraception by dealing and suffering from side-effects and disadvantages, just to be protected from pregnancy (Fatizadeh et al, 2011).

1.6.3. Measuring satisfaction through effectiveness and safety

Efficacy plays a crucial role in understanding contraceptive methods. The most important criteria for women to use birth control is to prevent pregnancy, therefore having low failure rates of those is essential (Grady et al,1999). Measures of efficacy for contraceptives in clinical trials are reported either with the Pearl Index or with the Life Table Analysis. The term ‘efficacy’ refers to how well an intervention works in a clinical trial setting, whereas ‘effectiveness’ shows its functioning in practice (Trussel, 2013). The effectiveness is often distinguished between ‘perfect use’ and ‘normal use’. The latter reflects evidence studies regarding the real-life usage by patients and users (ibid.).

2. The contraceptive market

The following section will present an overview of the contraceptive market, its history and its main stakeholders involved in shaping the development, manufacturing and distribution. It will be followed by a description of the market environment with its main characteristics and requirements. In a third step, the thesis will shed light on the regulatory steps framing the development of new birth controls.

2.1. Historical development of pharmaceutical engagement in contraceptives

The involvement of the pharmaceutical industry has shifted over the last sixty years in the R&D of contraceptives. In order to get a better understanding of how the incentive structure and the engagement of the pharmaceutical industry within contraceptive development take place, the historical dynamics will be outlined.

The contraceptive revolution began around 1951 when Carl Djerassi at Syntex filed a patent for norethindrone. Through serendipity, he accidentally developed a synthetic progesterone which acts as an anti-ovulent drug. By collaborating with the activist Margaret Sanger the first development of an oral contraceptive (OC) started (Harrison & Rosenfield, 1996). In 1960 the first OC was approved and introduced to the market. The ease of use and the empowerment of limiting and spacing children made the pill a fast-growing success (Sitruk-Ware et al., 2013). The hesitancy of cultural and politicized discourse about contraception was overridden by the steady and huge market of contraceptives. The period was marked by less stringent FDA approval processes and fewer regulatory hurdles (Harrison & Rosenfield, 1996).

In the second phase of the contraceptive progress, however, many litigation cases and scrutiny of contraceptive products arose. These developments resulted in the increase of regulatory requirements within the sphere of contraceptive development. R&D spending on contraceptive development sank by 25% between 1972 to 1983 (Lincoln & Kaeser, 1988). While the pharmaceutical industry withdrew or decreased its efforts, several public and non-profit organizations came into play. Caused by the fierce litigation cases in the US, research and development shifted towards European pharmaceutical companies, where Organon, Schering AG and Roussel-Uclaf initially took part in (Gelijns & Pannenborg 1993). The time around the turn of the millennium was characterized by several mergers and acquisitions (M&A), which led to a further decrease of R&D spending for contraceptives and even the complete shut down of women's health branches. In the mid-2000s the remaining pharmaceutical companies abandoned both their female and male hormonal and nonhormonal drug discovery R&D programs (Callahan, 2020). As such, the women’s health sector was minimized and not seen as needing new development anymore (Herper, 2020). In the following ten years, no effort or change of strategy was visible from big pharma. Yet, in 2019 the pharmaceutical company MSD, announced a spin-off with Organon with a sole focus on women's health to increase the importance of the field (Merck, 2020).

These dynamics and the withdrawal of big pharma from the field are also reflected in the product history of contraceptives. Whilst contraceptives between the 1960s to the 1980s were produced and innovated from pharmaceutical in-house R&D, last decades products stem from small biotech companies as well as NGOs like the Population Council. The latest products encompass fertility tracking apps (Clue, Natural Cycles), hormonal long-term vaginal rings (Annovera), a non-hormonal gel (Phexxi), smaller barrier methods (Ballerine) and a non-hormonal vaginal ring (Ovapren), which is still under development (Bloomberg, 2020). None of the mentioned products originated from big pharma.

2.2. Market size

The contraceptive market is divided into drugs and medical devices. The contraceptive market is a sub-market of the Women's Health market has an estimated worth of 6,35 Billion US dollars in 2016 and is expected to grow by 6,5% until the end of 2025. In comparison, the women's health market has an estimated worth of 41 Billion US dollars (Chandra, 2016). The US market is the leading market and accounts for one-third of the shares worldwide, followed by the European one, as depicted in the figure below:

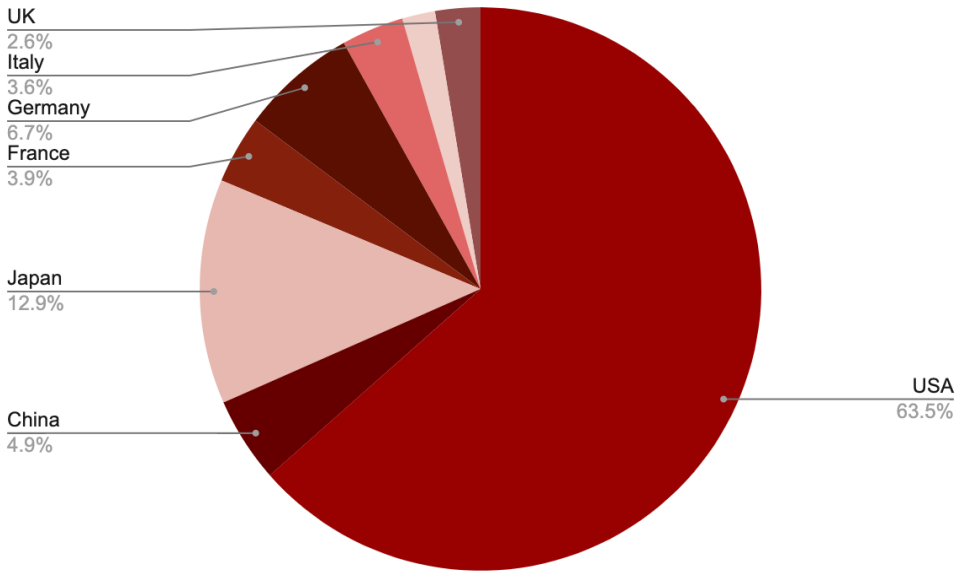

Figure 2: Global contraceptive market by market shares
Source: Global Data, 2019

In 2015, oral contraceptives accounted for more than 85% of the overall revenue share in the contraceptive drugs market, which makes them the most common type of reversible contraception drug used worldwide. The reason for this widespread use can be attributed to government initiatives encouraging the market growth, by putting forward the attributes of high effectiveness and the benefits of contraception (e.g. Planned Parenthood). In particular, the adoption of modern contraceptives in developing countries is forecasted as a drive for future market growth (Global Data, 2019).

The major operating pharmaceutical companies today are Bayer, Pfizer, MSD (today Organon), Teva Pharmaceuticals, Novartis, Agile Therapeutics, Johnson & Johnson (Mordor, 2020). However, their revenue share is not an indicator for innovation in new female birth control methods. Rather it

presents their income from already established contraceptives. On the contrary, only 2% of the R&D investments in pharmaceutical companies operating in women's health are disbursed to contraception, when for other therapeutic areas, R&D costs usually account for 20% (Chamberlain, 2020).

2.3. Market players

As market participants, the thesis defines players involved in the development and distribution of contraceptives, which will later be referred to as the 'system' in which contraceptive development emerges. The area of contraception requires an array of expertise such as excellent science, the ability to master and comply with complex regulatory requirements as well as managing financial, manufacturing, and marketing activities simultaneously (Mastroianni et al., 1990; Callahan et al., 2020). These tasks are covered by a diverse organizational landscape of institutions, all of which play different roles in contraceptive development and belong to a network marked by dependencies. This will be outlined in the following section.

2.3.1. The private sector - big pharma

Large pharmaceutical companies, so called big pharma, are vertically integrated with major research divisions, manufacturing, marketing and distribution channels. Pharmaceutical companies are bound to making strategic decisions on therapeutic areas they would like to pursue research in, on the grounds of the provision of a satisfactory return on investment (ROI) to ensure corporate growth. As such, the market size of a given indication as well as the considerations of profitability play a crucial role. Further on, large pharmaceutical companies focus on patentable research rather than basic research to maximize profitability (Mastroianni et al., 1990). In order to mitigate risk in big pharma, corporate portfolio strategies are used, which include the diversification of the therapeutic areas they are invested in. Whilst some companies prefer to focus on one specific area, and believe it spurs innovation, others rely on diversification of their product lines to spread opportunity costs (Thunecke, 2017).

2.3.2. The public sector

The profit-driven approach of the pharmaceutical industry results in R&D decisions towards drug targets that have the highest ROI, as seen in blockbuster lines, that are drugs, which generate annual sales of at least USD 1billion in return (Barlow, 2017). Therefore the public sector has an important role in steering research in areas that may be overlooked due to their lack of financial returns, which contraceptives can arguably be considered part of. Thus, the public sector is essential in providing funding and contributing to educating the population on reproductive health

matters. Secondly, the development of contraception requires clear regulations of how the development process can take place, which is set up by governmental entities. Lastly, the public sector is crucial for reimbursement and co-payments strategies that can play a role in ensuring access to contraception (Mastroianni et al., 1990; Callahan et al., 2020). Some of the key public institutions involved in the three tasks in Europe and the US are the National Institute of Child Health and Human Development (NICHD); Office of Population at the Agency for International Development and the European Center for Reproductive Rights (ECRR) (ibid). For the German market the Bundeszentrale für gesundheitliche Aufklärung (BZgA) is an important national participant. Some institutions are part of the regulatory sector which also shape the contraceptive landscape, they will be addressed in section 3.4.2.

2.3.3. The nonprofit sector

NGOs, philanthropic foundations and international organizations such the WHO and the UN constitute another component of the contraceptive development field. They also fund research that is not covered through the private sector. The engagement of the non-profit sector varies widely and encompasses basic R&D, to the distribution of contraceptives methods, or the improvement of knowledge and education about those (Callahan et al., 2020). The main NGOs and philanthropic organizations in the contraceptive field were historically the Rockefeller foundations as well as Andrew W. Mellon foundations. Today the Bill and Melinda Gates Foundation (BGFM), the Population Council and FHI360 have large commitments to strengthen the contraceptive field (PC, 2018).

2.3.4. Academia - universities

Lastly, universities can bring important contributions through university scientists and researchers in contraceptive development activities. However, effective collaboration between academia and the private sector is sometimes difficult because the non-translational and open source approach from academia doesn't align with the patent and profit-driven approach of the private industry (Mastroianni et al., 1990).

2.3.5. Dynamics among market players

The fluctuant dynamics of the contraceptive market participants indicate a trend of decreased private sector engagement and increased non-profit and philanthropic commitment. In the past years, pharmaceutical companies and R&D development have gradually switched from being fully integrated to relying on innovation from the outside. Hence, they have relied on new strategies such as acquisitions, licensing in late-stage technologies and creating strategic partnerships

(Harrison et al., 1996). The changing environment resulted in the appearance of many small biotech firms that are nowadays seen as the main contributors to innovation in the pharmaceutical industry (Schumacher et al., 2016). Thus, the market shifted from a private enterprise sector with multinational firms to a diverse setup encompassing small biotech companies, NGO's and philanthropic institutions (Mastroianni et al., 1990; Callahan et al., 2020). The private sector has large fixed costs to cover, which is one of the main barriers when investing in new potential markets, regardless of their size. Most contraceptives serve a small share of the whole market only. Therefore, executives of big pharma do not believe that the relatively small markets they see for the proposed contraceptive innovations justify the substantial development costs (Mastroianni et al., 1990). However, even though foundations, NGOs and public institutions have been driving the development of new contraceptive products in recent years, the involvement of pharmaceutical companies is crucial in terms of distribution and manufacturing possibilities. That shows the interdependence and the difficulty of revitalizing the field of contraception without big pharma. Therefore novel and viable academic–public-private partnerships are required to succeed (Callahan et al., 2020).

2.4. Market environment - the revenue streams of the pharmaceutical industry

The following section will highlight the standards, regulations and approval measures that the pharmaceutical industry is constrained to whilst being bound to profit returns. Thus, the importance of patents, the fragmentation of the market, the regulatory requirements as well as the reimbursement system will be presented.

2.4.1. Patent structure

Bringing a new drug to market ranges in between USD 850 million and USD 1.9 billion. The biggest percentage of these costs are related to the failure of components regarding the safety, efficacy, quality, and purity of a potential drug before it is allowed on the market (Rees, 2011). In order to mitigate these costs, the patent structure has crucial implications on the revenue stream of pharmaceutical companies. Initially, the patent structure was introduced to incentivize and compensate for the risk-taking of pharmaceutical companies. In addition, the profits were meant to be used in order to fuel further research. Nevertheless, due to the long time period between the patent application, until a new drug is launched, pharmaceutical innovations receive a much shorter patent exclusivity, usually between seven to eight years, than any other patent-dependent industry (Lehman, 2003). The structure of the patent system resulted in governments and healthcare systems encouraging physicians to prescribe generics as soon as the patent protection

expires. In return, for innovators and patent owners, the generic prescription leads to a shorter life cycle and thus revenue erosion (ibid).

2.4.2. Regulatory requirements

Pharmaceutical products and drug development are subject to a number of laws and guidelines that have to comply with the regulatory bodies. Regulations are defined as a number of texts, that include guidelines, recommendations, procedures and policies that have different legal grounds (Lezotre, 2014). These are designed to make sure that safe, efficacious and high-quality drugs are available to consumers. In Europe, the European Medical Agency (EMA) and in the US, the Food and Drug Administration (FDA) is responsible for providing access and authorizing that the novel drugs intended for use in the diagnosis, treatment, prevention and cure of diseases meet the requirements. This is ensured over the course of a drugs life cycle, starting in the initial drug development phase, with constant evaluation and regulations around the manufacturing, drug labeling and surveillance before and after a drug's approval (Olson, 2014).

Further, New Drug Applications (NDA) have to be in line with the Clinical Trials Directive in the EU, which entails an assessment by a scientific ethical committee, respecting the good manufacturing practice (GMP), as well as many other rules that ensure consistency in clinical trials throughout the EU, in providing the highest standards of safety and transparency for participants of clinical trials. Suspected adverse events in the course of a clinical trial have to be sent to the pharmacovigilance committee (EMA, 2020).

2.4.3. Health care system, reimbursement options and pharmaceutical pricing

Healthcare systems widely vary in their ways in enhancing access and providing healthcare services to people around the globe. In the context of the German healthcare system, it is based upon a social security health system that is financed through statutory health insurance funds, employee and employer contributions (Döring & Paul, 2010).

A number of European countries subsidize contraceptives on the grounds of fundamental rights and public health. As such, the healthcare system in most EU member states allows for reimbursement policies that enable partial or total reimbursement of birth control options. In Germany for instance, the pill is covered by the statutory healthcare system until the age of 21 years, after which it is considered non-reimbursable unless a medical condition for its use applies (CFRR, 2009). How these reimbursement rates and pricing policies are being placed depend on national governmental authorities, who have a right to exercise price control through defined processes and regulations during the market authorization period of a new pharmaceutical product.

Pricing policies of medication are thus strongly linked to its reimbursement possibilities. In European countries reimbursement criteria are based on the medical necessity, safety, cost-effectiveness, therapeutic benefit and the added value in comparison to already existing alternatives (WHO, 2016; OECD, 2008).

3. Processes in the pharmaceutical industry

After having provided an overview of the contraceptive market and the hurdles and regulations the industry is subject to, an introduction to the drug development process and the current trends will be elucidated, and links will be made to birth control when suitable.

3.1. The drug development process

The next section will focus on the process of drug development. In order to identify at which stage barriers to the development of new female contraceptive methods can happen, the whole process will be described.

Drug development is a fragmented and highly complex process involving different tasks such as chemical and biochemical sourcing, preclinical development, clinical development, regulatory affairs, quality assurance, finance, marketing, informatics and information systems, business development, licensing, pharmacovigilance and sophisticated project management (Rees, 2011). The overall failure rate in drug development is 96%, which shows the low chances of bringing a new drug to market (Hingorani, 2019). Thus big pharma follows the idea of “fail early and often”. Spending too much time and extending expensive processes should be prevented as effectively as possible. To ensure objective and timely decision-making and to minimize non-productive activities the process flow is structured through different steps and go/no go cr along the pathway, (Callahan et al., 2020).

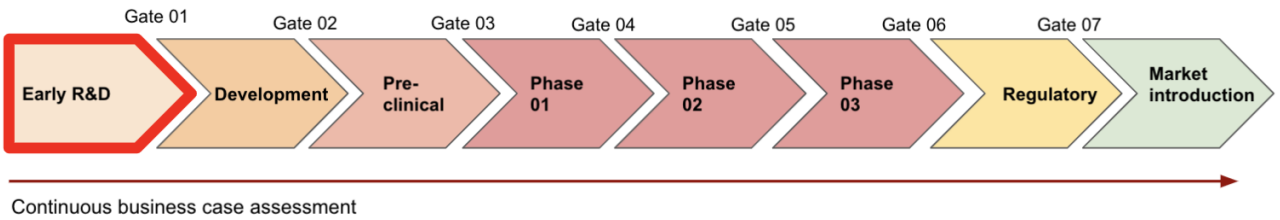

Figure 3: The stages of pharmaceutical drug development

Source: (Callahan et al., 2020) adapted for the purpose of this research

As depicted in the figure above, the drug development process encompasses eight steps, from R&D to market introduction. A total of seven ‘Gates’ have to be passed to launch a new product.

Throughout the steps the main goal is to secure a stable ROI, displayed as the business case arrow in the figure. As outlined in the scope this thesis has a focus on the first stage highlighted in red in which target identification, validation and screening for new compounds takes place. This process can be unstructured and creative while the following step, the development phase, must be rigorous and controlled (Rees, 2011). As defined in the scope of this paper, the first step of the drug-development process will build the basis of the analysis. The leading compound defined in the development phase must be assessed in preclinical studies. Before a novel drug can be administered to humans it requires a clean toxicology bill from animal in-vitro tests.[1] Simultaneously a regulatory strategy is developed and a scale-up to good manufacturing practice for clinical trial batches is initiated (Rees, 2011).

If that stage is reached the drug development process continues with the clinical phase. Clinical Phase 1 tests the new compound in healthy human volunteers. In general volunteer studies do not prove therapeutic effects, the focus lies on the dosage. The Phase 2A aims for “proof of concept” and evidence for the therapeutic effect, while 2B is used to test dosage and proof efficacy. Phase 3 of the clinical studies are the most expensive phase. It includes large studies among different settings and continents. They are designed to show that a drug is effective and safe (Rees, 2011). In clinical trials, WOCBP are often excluded due to the potential risks to the participants and the foetus. However, this exclusion criteria can hinder gain of new clinical knowledge that is crucial for improving the care of women (Phelan et al., 2016).

After the completion of all three mandatory trials the final drug approval is required. As previously explained all countries have agencies charged with national stewardship (e.g. FDA, EMA) of development, marketing, and general use of new pharmaceutical drugs. Meeting prior to clinical trials can be useful to exchange knowledge and align on expectation management. With the final approval the market-introduction and scale-up phase begins. Manufacturing, packaging and labelling needs to be coordinated in the last phase of the drug development process (Rees, 2011).

3.2. Trends and dynamics in drug discovery

The environment of drug discovery is characterized by the increasing length of preclinical and clinical phase trial research, the increasing number of investigational drugs that fail during the clinical trials and the overall opportunity costs considering increasing R&D costs comparable to the expected ROI. These characteristics lead to an increase in complexity, bias and economical pressure (Rao, 2021). As introduced in the market players section, the drug discovery is balanced

[1] There are 3 tests (toxicology, metabolism and pharmacokinetics and chemical and biopharmaceutical)

by a robust pipeline at the core business of the pharmaceutical companies. In order to succeed, managing and ensuring pipeline portfolios becomes a requisite to establish a foundation for economic growth (Rao, 2021). The R&D process requests a high financial commitment and has to take losses into the equation. Until today there is no way of identifying only successful drug components (ibid).

The cost of developing a new drug roughly doubles every nine years. Despite improvements within technology like high-throughput screening, biotechnology, combinatorial chemistry and open source concepts the drug discovery is slowing down and simultaneously becoming more expensive since the 1980s, which is captured through Eroom's Law (Lowe, 2012). The literature provides different explanations for the described trend. The so-called "better than the Beatles problem" refers to the fact that first-generation products are hard to outperform and therefore the development of second-generation products requires additional resources. Further, the literature is presenting the "low hanging fruit theory" which describes the concept that introduced drugs were the ones that were easy to detect and develop. Second-generation products could be described as "high hanging fruits" and difficult to reach. Thirdly the increasing costs of R&D are explained through the "cautious regulator problem". This problem can be defined by a decrease in risk-taking of the industry and due to the increase in regulation. As such R&D is more restricted in its ability to evolve. Lastly, the "basic-brute-force-bias" is referenced by scholars, which refers to the tendency to overestimate the first promising molecules to increase the probability that the given component will be effective and safe in clinical trials. This approach to new drug candidates in the pharmaceutical industry may explain the high failure rates in phases II and III of the drug-development process (ibid).

3.3. Specifications within contraception in drug development

Despite the aligned process across all drugs, the drug development of contraceptives faces some specific challenges. The fact that contraceptives entail prevention rather than treatment and are taken in by healthy women increases the safety as well as the efficacy profile of new drugs. The tolerance of undesirable side effects is very low (Nass & Strauss, 2004; Callahan et al., 2020). For example in phase 1 trials of female methods, requiring women to be at low risk of pregnancy yet not using hormonal contraceptives can lead to difficulties in recruitment (ibid).

The medication of healthy individuals is underlining the liability risk. As presented in the historical development, lawsuits lead to a decrease in resource allocation among pharmaceutical companies and litigations have been particularly marking the contraceptive development. Mastroianni et al.

claim that pharmaceutical companies should not carry the whole risk, in case of adverse events (Mastroianni et al., 1990). Further researchers introduce the idea of indemnification for pharmaceuticals that serve the greater good of public health, as comparable to vaccines (Nass & Strauss, 2004). These options would help to share the risk-taking that the pharmaceutical industry has to carry.

Regulatory guidelines simplify the whole process of drug development and have a large influence on the whole efficient process flow. With regard to contraceptives, the EMA issued a guideline for clinical investigations of steroid contraceptives to help developers to set up their study design in 2005. In 2019, the FDA followed and released a draft largely aligned with the EMA document. Nevertheless, a big gap remains for guidelines of non-hormonal contraceptive development as well as male contraceptives. Thus early engagement with regulatory agencies is crucial for innovative contraceptives (Callahan et al., 2020).

Lastly, the social and politicized context of contraception should be mentioned. Reproduction is a highly personal issue that is affected by culture and social norms and acceptance is decisive for usage. Therefore, market research and user insights are crucial (Nass & Strauss, 2004; Callahan et al., 2020).

3.4. Preliminary summary of the background

With the previously presented background, the thesis outlines the benefits, the need and the missing or decreasing interest of big pharma, especially within the last two decades. Further, we touched upon general and specific challenges within contraceptive development. While big pharma decreased engagements, players outside of the industry are driving new research. However, due to the requirement of high risk-taking and high capital resources in order to develop and market new innovative contraceptives the involvement of pharmaceutical companies is needed (Skrepnek & Sarnowski, 2007).

Chapter III: Theoretical approaches

The following chapter aims at identifying and introducing some key theories on innovation in drug discovery. It will draw on the term of innovation and evoke some of its facilitators in the drug development process.

1. Defining innovation

In line with our research question, this paper intends to assess the lack of innovation within female contraceptives. The healthcare sector more than other industries is characterized by uncertainty and risks. The challenge to innovate in healthcare is related to the fact that budgets are often limited, whilst demand and expectations from the population are increasing, as people live longer. On top of that, it is a sector that is renowned for its slow adoption of innovations (Herzlinger, 2006).

However, in science more than in other sectors, innovations in products and services are essential as they contribute to the development and the maintenance of human health (Harada et al., 2021). The term ‘innovation’ is a subjective concept and has many different definitions. Within the scope of our research, we recognize innovation as ‘the complex process of introducing novel ideas into use or practice’ (Monti, 2004) and as ‘the introduction of something new " where that something could be an idea, process, or product (Correia, 2009). Further on, a novel idea in order to be classified as an innovation, should have clear benefits in comparison to the current methods and be both usable and desirable to be a successful innovation (Kelly, 2017). According to Shumpeter’s Theory of Economic Development (1934) five different types of innovation can be distinguished: ‘new products, new methods of production, new sources of supply, the exploration of new markets, and new ways to organize businesses. This complexity of the term of innovation needs to be reflected in any used definition or theory in order to embrace it, by referring to the whole process of an invention from coming up with an idea, to its adoption and diffusion of, in our case, a new female contraceptive method (Yezersky, 2007).

There are four main classifications of innovation: (1) radical innovation refers to a significant improvement or change of an existing process or product using a different technology or knowledge-based approach. (2) Incremental innovation designates a small improvement to an already existing process or product. (3) Disruptive innovation is known to slowly change the standards of an industry by starting to impact only low market segments. Lastly, (4) revolutionary innovation is known to change the entire industry (Tidd, 2006).

In general, innovation is driven by a market push, market pull or the interactive link between them. The classic innovation theory depicts the market push as a force driven by technological advancement. It refers to the development of a new product that is introduced to the market without doing previous market research or knowing if it will satisfy a user's need (Tidd, 2006). In contrast the market pull refers to an innovation derived from a need that is identified in the market, by doing extensive market research through end-users. The interactive link is the combination of the push from a technological side with the market need (Rosenberg & Kline, 1986).

2. Innovation within drug development

As elaborated in the drug discovery section, trends towards increasing R&D spendings are not linked with an increase of NPDs entering the market each year. The so-called 'innovation productivity crisis' in the pharmaceutical industry is backed up by Eroom's law, which suggests that the costs are related to the increase of regulatory approvals, which slows down drug discovery (Barlow, 2017). Due to the extensive theoretical literature available on the increasing costs of R&D and recommendations on how to mitigate this crisis, the paper aims at elucidating four approaches that foster innovation within the specific phase of early drug development. Thus, the concepts of patient involvement, drug discovery alliances, private-public partnerships, and lastly decision-making will be outlined.

2.1. Patient involvement

Since recent years, health care systems aim at establishing a switch to a patient-centric paradigm, which entails having patients at the center of the decision-making and as a driving source of innovation (Loewe et al., 2016). It aligns with the concept of value-based healthcare, a healthcare delivery model built around value for the patient, where care is paid for in accordance with patient health outcomes (Porter, 2012).

In contrast to the efforts seen in healthcare settings, the pharmaceutical industry is still reluctant to switch to a patient-centered focus and mostly follows the linear model of innovation: "Science finds, Industry applies, Man conforms" (Smits & Boon, 2008). However, for the pharmaceutical industry to be innovative and demonstrate the value of their products to patients, the perceived patient outcomes need to be taken into account. As such, it is supported that similarly to healthcare, pharmaceutical companies should involve patients in the whole product life cycle and spend resources to build sustainable communication channels with users to align with their expectations (Lowe et al., 2016).

Further, Smits & Boon display five reasons on how innovation is fostered through user involvement within pharmaceutical drug development. Firstly, the inclusion of users facilitates the identification of societal problems which are insufficiently addressed on a global agenda (Smits & Boon, 2008). Secondly, the interaction with the users increases adaptability, due to early involvement as well as conducted patient data. Thirdly, the collaboration with patient advocacy groups enables the pharmaceutical industry to receive more funding from philanthropic and public entities which increases the cost-effectiveness ratio. Fourthly, the interaction with the users reveals moral and ethical difficulties among activist or religious groups. Thus, a dialogue can be initiated in an early stage (e.g. animal protection or pro-life activists). Especially for politicized areas, like contraception, the early engagement with users appears to be beneficial. The last reason refers to the moral right of including users. Drugs are administered by users and therefore the pharmaceutical industry should have an interest in satisfying their expectations. As such, some pharmaceutical companies have succeeded in making the change towards patient involvement in drug development. This resulted in strengthened pipelines that reflected patients' expectations, whilst decreasing the R&D budget because of the early user engagement (Smits & Boon, 2008). Therefore, even though patient involvement was neglected from a pharmaceutical perspective for a long time, practice shows that patients can be a source of innovation through revealing radical ideas, unforeseen demands and suggestions for application and administration (ibid).

2.2. Partnerships

Through the aforementioned increasing criticism towards the linear drug development process in a pharmaceutical setting, partnerships can be considered as another way to drive innovation within R&D. These partnerships are seen in drug-discovery alliances as well as cross-sectional collaborations.

2.2.1. Drug discovery alliances

So-called Drug Discovery Alliances are scientific collaborations between biotech start-ups, academia and pharmaceutical companies (Schuhmacher et al., 2016). In light of the regulatory and R&D burden that pharmaceutical companies are facing, business alliances with biotech startups are seen as a sustainable solution to address those challenges. They have over the past decade generated promising biomedical products and become the leading innovators of drug discovery (Harada et al., 2021).

The collaborative efforts among the alliances include knowledge and technology sharing. Studies have demonstrated the catalyzing effects of such alliances on innovation within drug development (Cheng et al., 2020; Romasanta et al., 2020).

2.2.2. Public-private partnerships

Public-private partnerships (PPP) represent another prominent collaboration model that has proven to be successful. They are funded and operate through the involvement of a governmental entity and one or more private entities (Schuhmacher et al., 2016). The current challenges in drug development require the mobilization of a large pool of stakeholders as well as a need for significant resources. PPPs can help in facilitating this process and gaining on the benefits of new approaches (WHO, 2004). These types of partnerships are usually driven when a major challenge arises that could not be addressed by a sole entity in an adequate manner (Schuhmacher et al., 2016). To name a few, in recent times of public health crisis, as part of the Covid-19 response, PPP between governmental entities and the pharmaceutical industry have played a crucial role in the fast-tracked development of vaccines. Worldwide collaborative frameworks have emerged that allowed for the prioritization of drug candidates, coordination of regulatory processes and the streamlining of clinical trials (NIH, 2020).

3. Decision making

Lastly, decision-making has a central role when it comes to innovation within drug development. As illustrated previously, all eight gates of the drug development process are defined by “go/no-go decisions”, that determine if a drug candidate will proceed further in the development or be terminated. Decision-making and allocating resources are essential and are the key determinants of the success of a drug company (Skrepnek & Sarnowski, 2006).

In their decision-making process, pharmaceutical companies apply experience, intuition and human judgment to 85% when making a choice. However, past research advances, that when facing a new R&D decision that comes along with the evaluation of data, one needs to rely on reason and analysis over personal instinct (Bonabeau, 2003). Two main errors can impede traditional drug development and NPD. One type occurs when managers ignore evidence challenging their assumption that a project will succeed, thus being too optimistic about future success. The other type of error occurs when a project is terminated prematurely for a lack of evidence that it could succeed, thus being too negative regarding future success. Both of these errors are influenced by the business-case and the possible return on investment, which has to be assessed in order to invest further. The so-called “late-stage mindset” of the pharmaceutical industry manifests the long-term vision of the drug development process. As such, pharmaceutical companies predict the success rate (ROI) of possible components, even though this new drug may

not be marketed before years. This mindset and approach to NPD can lead to a failure to conduct the right experiments to reveal a product's potential (Bonabeau et al., 2008).

To overcome these decision-making errors the literature suggests seeking external advice and a diverse decision-making committee (Robbins & O'Gorman). As such, decision-making gates of new drug candidates encompasses a heterogeneous set of actors. Thus, non-traditional actors should be involved to ensure diversity. While the pharmaceutical industry intensified the cross-sectional collaboration the last decade, the structural integration on an organisational level is lacking (ibid.). The user, as one non-traditional actor, appears to be a source of innovation (ibid.). Further, the literature refers to modelling the degree of variability among decision-makers to overcome subjectivity and bias of decision makers (Cowlrick et al., 2011). Thus if a decision appears to have a high sensitivity, external advice could provide support for an increased rational decision making. Lastly, Scannell et al. suggests to overcome the intuitive driven approach by introducing a systemic process by establishing a lingua-franca to express and identify the predictive value (PV) of new compounds and methods of action (Scannell & Bosley, 2016). The predictive value facilitates the assessment of compounds by classifying them into a numerical scale. Thus, transparency can be created with the PV as it quantifies new compounds and therefore enables decision-makers to compare compounds based on their rating.

Chapter IV: Methodology

The following section presents the description of the methods applied over the course of the thesis. The research structure will be outlined in a categorical manner and will elaborate on the reasons why the applied methods were chosen in order to best answer the investigated research question.

The research design aligns with the “research onion” as described by Saunders et. al (2019). The illustrated research onion highlights the many layers affecting the data collection as well as the data analysis. The section will go through every layer starting with (1) the research philosophy, (2) the research approach, (3) the research purpose, (4) the research method, (5) the time horizon, (6) the data collection and lastly (7) the data analysis technique. The illustrated research onion below aims at giving an understanding of our research approach in the investigation of our research questions, starting from the research philosophy (1) ’Pragmatism’ at the top of the depicted graph and working towards the data analysis technique (7), which was done with the template analysis.

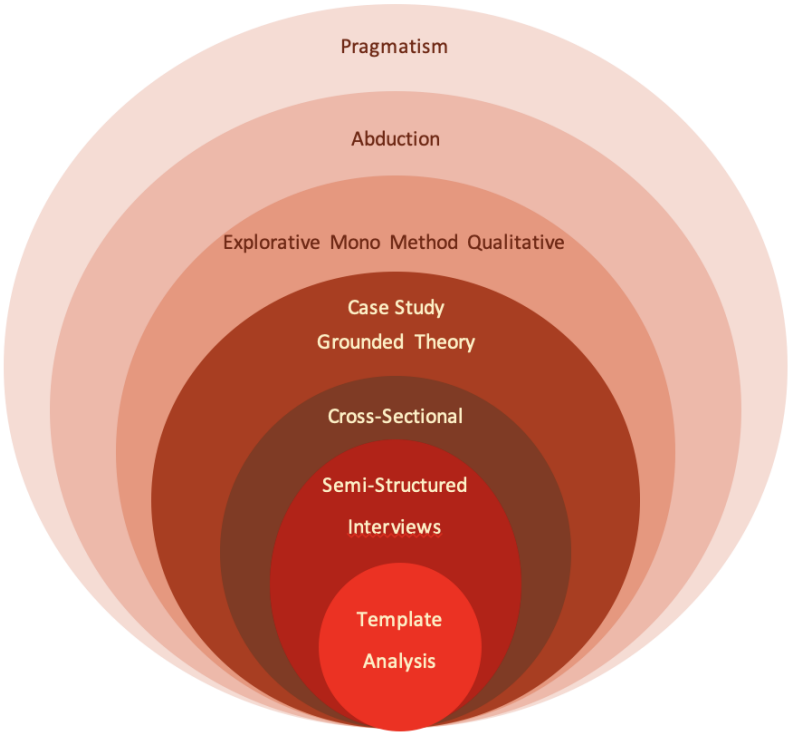

Figure 4: Research onion describing the methods used for the purpose of the paper
Source: (Saunders et al., 2019) adapted for the purpose of this research

1. Philosophical assumption

Every study builds upon a framework of assumptions and understanding that evolves with the increasing knowledge developed in the particular field of research. These assumptions can be chosen consciously or not, but they affect the way of conducting research and are therefore important to describe. Some assumptions define which realities are encountered (ontological assumption), others how human knowledge is perceived (epistemological assumption), or in which way the researcher affects the research process by his own values and the choice of data collection (axiological assumptions). Therefore making assumptions is seen as inevitable and guides the selection of methods as well as the interpretation of data (Crotty, 1998). A consistent set of assumptions enables a coherent study design, in which all elements of the study fit together.

When reflecting on different research philosophies against each other, pragmatism has been defined as most suitable in the context of this research. It considers the inclusion of several perceptions as strengthening the study and suggests that concepts are only relevant when supporting action. For pragmatists research starts with a problem and aims to deliver a solution that can help in future practice (Saunders et. al, 2019). As such, we have opted to use pragmatism as a philosophical assumption as our thought process when deciding on the topic of this thesis was initiated by the feeling that we couldn't grasp the reason behind the lack of innovation in female contraception. Thus, we wanted to assess the reasons behind this gap in new products.

Further, pragmatism reconciles subjectivism and objectivism, acts and values, accurate and rigorous knowledge and different contextualised experiences (Saunders et. al, 2019). It appears to be suitable as it rejects the ontology of positivism and does not align with the exclusive socially constructed reality of interpretivism and postmodernism. As researchers, we define ourselves as "subtle realists" which is positioned between positivism and a "contextual constructivist" approach (Hammersley, 1992). The delimitation towards critical realism is more nuanced. However, this study has a strong problem focus and incorporates several varying perceptions, as such the philosophical assumption of pragmatism is suitable.

Within pragmatism, the *ontological assumption* considers that reality is external, multiple and complex. The view that best enables the researcher to answer the research question should be adopted (ibid.). We believe that reality is not only shaped by measurable data. Reality consists as well through subjective meanings of social phenomena shaped by processes, experiences and practices. The *epistemology* of pragmatism considers theories as true if those enable successful action (ibid.). We define practical subjective meaning of knowledge in specific contexts as

knowledge, if it contributes to answering the research question. Our *axiological persuasion* is value-bond to the observed context. The axiological persuasion involves the transfer of young people's perceptions of value in the process of gaining knowledge and as such takes place on the premise of cultural values (ibid). Thus, we as researchers are master's students and do not work within the pharmaceutical industry and therefore, no conflict of interest can be identified. However, besides being students, we both identify ourselves as women and have our own perceptions and thoughts on the topic of contraception. To counter our perceptions on the subject under the scope of the research and as we were aware that we are bound to our values and it might have shaped our research, we followed an integral and reflexive practice. We adopted a detached perspective when dealing with the value of the research participants. As such, we used reflexivity in forming our analysis by using several different approaches, such as reviewing codes, talking about our research with external people, using a hypothesis tracker to see how our thoughts evolved, this will be explained with more details further below. Moreover we also reflected our thoughts with our supervisors to ensure that we were not biased by our own perceptions and to ensure the reflexivity of our thought processes.

2. Research approach

In order to define the focus within theory testing or theory building the question of the underlying research approach is crucial. There are two main contrasting research approaches, namely induction and deduction. Deduction occurs when the conclusion is obtained logically from a set of theory-derived premises where the conclusion is true when all the premises are true (Saunders et al., 2019). Induction on the other hand reasons that there is a gap in the logic argument between the premises observed and the conclusion, and therefore presents a theory building approach. A third approach is abduction which lies within deduction and induction. Abduction starts with a "puzzle" being observed and is moving back and forth from theory to data and data to theory devoted to explaining the puzzle (Bell & Harley, 2018). The puzzle was manifested by the discrepancy of demand for innovative contraceptives and a lack of supply. As the thesis aimed at challenging previous theories through the collection of data, an abductive approach was applied. As such, the research was conducted in a way that the theories around innovation presented in the background chapter were researched, whilst the data was collected. The data was then analysed and findings were found, which were then compared to previous theories once more. Thus abduction, as an approach that moves back and forth between theory and data was chosen.

3. Research purpose

In general, the research methodology can be subdivided into qualitative and quantitative approaches. The quantitative approach requires quantifiable variables and often applies a range of statistical and graphical techniques in order to find patterns, predictors or establish causal relationships. As such, it is especially suitable for large and standardized measuring study designs. Qualitative research is particularly suitable for analyzing people, groups, organizations, and societies in contrast (Gay et al., 2009).

In qualitative research, researchers elaborate and “make sense” of the subjective and socially constructed meanings expressed by the investigated phenomena by identifying and leveraging nuances of expression (van Aken, 2018; Saunders et al., 2019). Due to the pragmatism as the nature of the philosophy in this study, which perceives reality as an outcome built through subjective meanings, qualitative research was chosen. Further on, it was seen as appropriate, as the needs, feelings, thoughts of the interviewed women were wished to be explored. The qualitative approach enabled us to explore the “why” and understand the perception of women in a more embedded context. This was especially important in the context of contraception, which can be considered an intimate and sensitive topic. As such it is even more important to build trust and a common area of understanding and safety, to enable the participants to feel at ease. This further enabled us to assess and access the nuances of subjective meanings (Edmondson & McManus, 2007, Saunders et al., 2019).

On the other hand, the use of qualitative research also enabled for a more thorough and in-depth understanding of the pharmaceutical industry's challenges to innovate, as we were able to dig deeper and ask follow up questions, which would not have been possible with quantitative research. In particular the nuances perceived when interacting with industry experts that were both representative of the industry but also users of contraceptives themselves, enabled us to capture feelings and a sense of understanding that was not necessarily expected coming from an industry perspective. Thus, semi-structured interviews were suited to grasp interviewees contributions and to identify the nature of the different perceptions and allowed us to identify patterns.

More specifically, a mono-method qualitative study was undertaken. We chose to conduct semi-structured interviews as a single data technique followed by a qualitative analytical procedure. This reasoning was decided upon, as it enabled us to ask the similar questions to all the interviewees, but adapting it to the specific context. Further on it also enabled follow-up

questions if necessary. The semi-structured interview method was applied to multi informants by taking end-users of contraceptives and industry experts into account.
As such, the study applied a two-fold perspective, which aligns with the concept of a “holistic study design” (Khan, 2014). Recent organisational research advances the spectrum of qualitative study design by suggesting to investigate a problem from “different lenses” and assess a combination of perspectives rather than focusing on a single view (Khan, 2014). By applying a holistic study design, the depth of the research phenomena can be enriched. Further it enabled us to investigate the phenomena from different perspectives and thus had the capacity to display interactions and may detect inflection points among different perspectives. With regard to the multiplayer environment of contraceptive development outlined in the background section, a multi-informant strategy was chosen. This was done in order to understand the perceptions of women, and get a feeling for the magnitude of the issue, but also to assess if that issue was captured in a similar manner by the pharmaceutical industry. The first group consisted of 20 end-users of contraception, women, while the second group encompassed six industry experts within contraception and big pharma. A more thorough description of the sample will be displayed below.

In general, research can be designed to fulfill either a descriptive, exploratory, evaluative or explanatory purpose, or a combination of these. The purpose of research, which may change over time, defines the approaches that the researchers take to answer the research question (Saunders et al., 2019). To do so successfully, more than one research purpose was applied. In order to investigate “how” the perception of the end-user evolves around female contraceptives an *exploratory research purpose* was applied. The exploratory purpose seeks to understand the perception of women and starts with a broad focus and will become more narrow as the research progresses (ibid.). In addition, a *descripto-explanatory purpose* was applied to the second informant group of industry experts. In the interest to identify “what” fosters innovation in the pharmaceutical industry within contraception, the conducted interviews seeked to gain a deeper understanding about processes and systems. As such, the purpose showed a descriptive nature (ibid.). However, the descriptive part was accompanied with an explanatory purpose to explain the reasoning, the incentives and thought-processes of the experts (ibid.). The combination of different purposes enabled a thorough understanding of how structures, processes and perceptions are intertwined and co-dependent on each other.

4. Research method

Based on our research questions and the described research design, our research strategy was defined. The research strategy can be described as the logic of the thesis, as it is the

methodological link between the research design and the subsequent choice of methods to collect and analyse data (Saunders et al., 2019).

The study chose Grounded Theory (GT) as the single methodology in order to identify patterns in the collected data. GT is a systematic inductive analytical method that is used to identify patterns and conceptual hypotheses from collected data (Birks&Mills, 2015). The aim of GT is to produce or construct an explanatory theory that uncovers a process inherent to the substantive area of inquiry (Saunders et al., 2019). GT emerged within the constructivism philosophy and emphasized the inductive way of new theory construction. Since then GT has developed in many different directions (Tie et al., 2019). As such, the meaning of GT is different for everybody (Bryant&Charmaz, 2007). In general, GT aims to develop theoretical explanations of social interactions and processes (Saunders et al., 2019). GT is commonly referred to as taking an inductive approach (ibid.). Recent literature claims the inevitability of possessing prior knowledge and the value of abduction in order to provide tentative conclusions. Thus, this strengthens pragmatism as a basis for GT (Morgan,2020). As pragmatists, we agree with these claims and thus decided to apply GT as our research methodology. The leading rationale behind GT is “to make sense” of the gathered data through reorganizing and categorizing data by building codes. The relationship of the codes emerges and guides the interpretation and should be tested through additional data until conceptual density has been reached (Glaser,1992).

5. Time horizon

The time horizon applied to the study follows a cross-sectional approach, which entails that the study is investigating a phenomenon at a particular point in time (Saunders et al., 2019). Due to the time constraints, the study can be seen “as a snapshot” of the current contraceptive field in which the semi-structured interviews were conducted over a short period of time. Thus, the interviews were conducted during a time period between mid-January and the end of March 2021. Despite having talked to our interviewees a single time the data provided information on future challenges and expectations, stemming from both groups of informants.

6. Data collection

This research relied exclusively on the collection of primary data through semi-structured interviews with the two aforementioned informant groups: end-users and industry experts. The interviews were conducted via Zoom and captured by audio-recording. After which, they were transcribed. In correspondence with our axiological assumption, we collected the data through the role of an external researcher .

6.1. Interviews

Semi-structured interviews are suitable for research designs with an exploratory and explanatory element. Thus, aligning with the previous presented study design. Semi-structured interviews focus not only on the “how” and “what” but also on the “why”, which appears to be essential to investigate the reasons behind the lack of contraceptives innovation. The semi-structured form uses a list of specific questions but leaves sufficient room for additional information that may appear during the interview. The form consists of a sequence of questions that are open to change, and follow-up questions. The structure seeks to obtain descriptions by the interviewee in order to interpret the meaning of the described phenomena. Therefore, they generate rich data on experiences, perspectives and ensure that nuances are coming through (van Aken, 2018; Saunders et al., 2019). Semi-structured interviews are most advantageous, if a large number of questions need to be answered and the questions embody a complex or open-end character. Within a complex and embedded system it is necessary to analyse related units as well (Yin, 2003). Based on this information, we decided to investigate two crucial actors in the contraceptive field: the end-users as well as members of the pharmaceutical industry. Both actors are part of the system of contraceptive development but evolve and take part in the value creation or in the drug development process. Whilst women embody the end-user and therefore are at the end of the product cycle, the industry experts have a crucial role in the starting point of the contraceptive development. The interaction of both actors within one case study seeks to provide extensive insights.

6.2. Recruitment and sample description

The procedure of identifying the informant groups is called sampling. Generally, there are three different sampling approaches: complete population, random sampling, purposeful sampling. The latter is the standard in qualitative research (Patton, 2002). It was also the chosen method in the scope of this research, as it represents the intentional selection of participants in accordance with their ability to elucidate a specific concept, theme or phenomenon (Robinson, 2014). Thus, participants of the industry expert group were selected in order to give an insight and a possible explanation to our research question, whilst women were selected based on set criterias and their ability and will to share their contraceptive journey.

6.2.1. End-user

6.2.1.1. Recruitment strategy

A two-folded recruitment strategy was used to gather the end-user along the principals of the above mentioned purposeful sampling, as seen in the strategic way we undertook the recruiting of participants. Approximately half of the participants were recruited over social media, by publishing an announcement on social media platforms. A post was announced on several Facebook groups and included an informative flyer about the studys' aims and length of the interview, which can be found in (Appendix E). The targeted Facebook groups were chosen upon their group size and a topic which should be rather broad like housing, plant-sharing and city groups. These groups were mostly bound to a specific city and included over 5000 group members on average. As the recruiting strategy did not perform sufficiently, the Facebook group targets were adjusted. As such, groups engaged in women's health related topics and women activist groups were aimed at when trying to reach out to potential participants. In the recruited participant group through social media, the snowballing technique was used. Thus, some of the participants forwarded the information of our study to other potentially interested participants, some of which became study participants in the end. These groups usually had between 100 to 1000 participants, some groups were more socially active than others based on their online presence. The study recruited a total of 14 end-users through the Facebook groups. The flyer that was part of the post, included a barcode that when scanned, could redirect the users on a booking platform for the interviews. There, study participants could inform themselves on the exact scope of the research, agree to the data protection and data collection rules (GDPR) as well as book a time slot that best suited their schedule.

The remaining six participants were recruited through three German gynecologists. Both researchers reached out to OBGs in their direct environment and asked them to place the same printed flyers in their gynecological practice. Thus, two gynecologists were reached through personal acquaintances. The last OBG was recruited through cold calling directly and also agreed to ask his patients in person if they were willing to participate in the study. Reaching out to gynecologists turned out to be more difficult than initially expected, as due to the ongoing Covid-19 pandemic, many were constrained to consult their clients through telemedicine, making it more difficult to talk to patients into participating in a Master thesis project. The flyers were the same as in the social media recruitment strategy and interested participants could reach out to the interviewers directly, if questions arose or alternatively book a time slot for the interview.

6.2.1.2. Selection requirements

With the goal of gathering as many women of a reproductive age a high variety of cases was desired. Some common criterias were set that end-users had to fulfill in order to participate within interviews. Thus, women had to be at a reproductive age, which according to the definition set up in the background section of this paper, takes women aged 15-45 years into account. Because we did not want to face any legal issues or have a need for parental authorisation, all women below the age of 18 years were excluded. As such, requirements to participate were in a first place to range in between the age of 18 to 45 years old. Furthermore, we decided upon interviewing 10 women below the age of 30 and 10 women above the age of 30, as we wanted a sample that was well distributed but also because we wished to capture the contraceptive needs of women who at some point in their lives desired to have children, had children or had terminated her family planning.

Another requirement for the women was to live in Germany and preferably to have attended the compulsory years of education in a German school. This criteria was chosen in order to have a sample population facing similar cultural values and having had the same chances at receiving knowledge and education on contraceptive choices and availability. Only one participant did not attend school in Germany, but had spent several years in the country.

6.2.1.3. Sample description

The displayed table outlines the attributes of the sample of the end-user. A total of 20 women were interviewed. The first part of the table indicates the distribution along different attributes. The second part presents some trends extracted through data plotting. While the goal was not to compare women in between age or education, we still identified generational differences in the analysed data, which the results section will be elaborating on. The shared experience among the sample group remains that they currently are or were at some point in their life using or switching contraceptive methods.

Variables	Distribution
Age	The age was distributed between 19-44. Average age 29,6
Profession	The sample included students, the rest of the sample was employed in various industries such as international marketing, tattoo artist, gynecologist, teacher, social workers, service industry, sales
Religion	The sample included six catholic, three protestant, one muslim and ten atheist.

Martial/ Relationship status	Twelve women were in a relationship, and six of them married.The other eight women defined themselves as singles or not in a closed relationship.
Children	The sample encompassed seven women with children
Current contraceptive use	The current contraceptives were distributed as such: Condom 7, Copper IUD 3, Hormonal IUD 3, Pill 3, Implany 1, No (modern) contraception: Vasectomy 1, NFP 3
Hormonal vs. non-hormonal	The sample included seven women using hormonal and 13 women using non-hormonal contraception.
LARC/ SARC	Non-hormonal and SARC 10, Hormonal and SARC 3 Non-hormonal and LARC 3, Hormonal and LARC 4
Plotting of attributes	**Distribution**
Differences in contraceptive use with or without children	In the collected sample more women with children use hormonal contraception than women without children
Differences between age groups	Women below 30 have a stronger desire for non-hormonal contraception.

Table 2: Demographic distributions of collected data from end-users

Source: Data Attributes: Demographics retrieved from NVivo

The interviews with end-users took between 20 and 45 minutes depending on the responses received by the participants on given questions. To make participants more at ease, the interviews were conducted in German as it appeared to be important that the end-user can talk in their native tongue. The transcripts were afterwards translated into English.

6.2.2. Industry experts

6.2.2.1. Recruitment strategy

The second informant group aimed to recruit pharmaceutical experts within drug development and preferably with a connection to women's health. A total of six experts were recruited and interviewed. The interviewees were identified through the participation in online conferences within female contraception as well through the network of the Bio-Innovation Institute in Copenhagen.

6.2.2.2. Selection requirements

Requirements to be a participant as an industry expert required to possess one or more of the following characteristics: have worked within women's health or contraception, have knowledge of the R&D process and decision-making, work for a pharmaceutical company, for investment in the healthcare sector or within provision of family planning services. With this technique, six experts with extensive knowledge on contraceptives, drug development and capital investment in the pharmaceutical industry were recruited.

6.2.2.3. Sample description

Amongst the interviewees, one participant works in healthcare venture capital, another represents a philanthropic foundation within family planning, a further interviewee works for a mid-sized pharmaceutical company specialises in women's health and the last three participants are representatives of big pharma in R&D positions. Moreover, two of the industry experts are gynecologists on top of their pharmaceutical functions. Lastly, out of the six interviewed experts, four were women and two were men. As such, the interviewed women could have had a two-folded perspective on contraceptive innovation, one based on their knowledge of the industry and one on their perception of contraceptives as a woman and potential user of those. The interviews with industry experts were about one hour long and were all conducted in English.

6.2.3 Interview guide

For both interviews we set up an interview guide divided into different blocks (Appendix A). The interview guide for the end-user was tested on two women and afterwards readjusted. The initial interview guide included questions regarding the participants' sexual activity. While testing the interview guide, the question appeared to be too sensitive, difficult to define and not mandatory to elaborate on the guiding research question. Thus, the interview guide was adjusted. Both interview guides followed a chronological order of past, present and future. Questions asked to the end-users included demographic ones, inquiries about their acquired knowledge on contraceptives through education, questions concerning their gynecologist, their current, past and future contraceptive use as well as their wishes in terms of birth control. On the other hand, questions addressed to the industry experts encompassed questions specific to their company and its perceptions towards women's health and contraceptives. Further, questions were asked regarding past and future development of the market, the R&D process, decision-making processes in the

companies and financial allocation of resources. In order to reinforce validity through data triangulation, similar questions were applied in both interview guides.

6.2.4 Sample size and saturation

A total of 26 interviews were conducted, 20 end-users and 6 representatives from the industry. In general, the basic principle of the sample size depends on the analysis saturation (Eisenhardt, 1989). An analysis is saturated when additional cases don't seem to change and to add further insights to the findings (Kvale, 2016). Despite the main goal of saturation, our sample size was influenced by time constraints. As such, we used a pragmatic approach but after 20 interviews, the data was rich enough to answer the research question. More interviews would have allowed us to better understand the nuances between women with different experiences or backgrounds. However, distinct patterns could be identified and no new themes were coming up when analyzing the end-users interviews. This was thus seen as a sign of saturation.

Out of six industry experts, only one participant was working in a big pharma company that is still active within female contraception. This was due to the fact that there are only three active companies in the field. All three of those were contacted and one of them agreed to the interview. In addition, three other experts from pharmaceutical R&D could be recruited experienced within female contraceptives due to previous positions. The analysis enabled distinct patterns which can as with the first informant group seen as saturation.

7. Data analysis

In order to analyze the data, all conducted interviews were audio recorded and fully transcribed. For the transcription the service of the transcription platforms otter.ai and f4x.audiotranskription.de was used and adapted by the researchers.

7.1. Hypothesis tracker

Following our integral and reflexive practice, we introduced a hypothesis tracker throughout the research. As the conducting and transcription of the interviews takes a considerable amount of time and every interview is debating the research phenomenon out of his or her own perspective, ideas and hypotheses arise. In order to decrease our perception and to ensure less bias, thus, transparent thought patterns, we introduced a hypothesis tracker. This tracker can be compared to other note-techniques like document summaries, self memos, research notebooks and reflective

diaries (Saunders et al., 2019). By continuously documenting arising hypotheses, we could assess which hypotheses were further emphasized or lost strength throughout the process. The hypothesis tracker is displayed in the Appendix (Appendix D).

7.2. Template analysis

From raw data material to explanation outcomes and results many studies lack transparency (van Aken, 2018). Thus, the following sub section aims to describe each step of the final data analysis. In order to analyze the data the concept of *Template Analysis (TA)* was applied. The TA is a type of *Thematic Analysis* and based on a systematic text analysis, in which the material is gradually structured and filtered. TA corresponds to the “subtle realist” position as well as with the chosen research method Grounded Theory. The TA suggests combining *a priori* themes, themes which are defined before the data analysis, with emerging *in vivo* themes, themes which emerge while doing the analysis. The key difference between the Thematic Analysis and Template Analysis is that the search for global themes starts during the procedure of coding (Saunders et al., 2019; Brooks et al., 2015). Further, the TA approach offers extra flexibility of developing and revising a coding template by coding subsequent data. Thus, it allowed the researchers to undertake the stages of analysis (e.g. coding, devising and linking themes, exploring relationships, sense-making) in a more holistic way (Saunders et al., 2019).

The study followed the main six procedural steps in carrying out a template analysis: (1) Becoming familiar with the data and reading through all transcripts, (2) Carrying out a preliminary coding set by highlighting anything in the transcripts which may contribute to the understanding of the research phenomena and define some *a priori* themes, (3) Organizing the themes into meaningful clusters and building hierarchical relationship to identify how they interact with each other, (4) Defining an initial coding template by coding a rather small proportion of the gathered data, (5) Applying the template to further data and modifying the initial template if necessary, (6) Finalizing the template and apply it to the full data set (Brooks et al., 2015).

The initial coding template was built after completing the analysis of two end-user transcripts and one industry transcript. We considered applying two different code books for each informant group. Nevertheless, we decided to focus on a single code book to leverage the data triangulation and enable a stronger interaction between the two informant groups within the code book. This approach resolved in strong codes where perspectives and views challenged each other and therefore offered rich and insightful nuances. The code book was applied by aductive means with the qualitative analysing program NVivo. Nvivo was used to classify the most relevant statements

into a system of codes and thus reduce the complexity. With the help of categories, the content was to be interpreted, counted, evaluated and stored in relation to other text passages. During the whole process codes could be defined or refined. The following categories were identified:

	Themes	Description
1	Drivers of dissatisfaction	Covers expressions of dissatisfaction with the current contraceptive method
2	Tolerance	Covers expression of acceptance rather then satisfaction; unawareness of pain, high-level of tolerance
3	One size doesn't fit all	Covers categories regarding Individuality of desires, contraception as an intimate and personal topic
4	Sexual education and empowerment	Builds upon critic of sexual education provided by school, gynecologists, social structure
5	Lack of say	Captures nuances of "feeling lost", "feeling alone", "nobody to turn to" as well as confusion who to report discomfort
6	Healthy Women Argument	Build upon the paradox of safety vs. risk, underrepresentation of female medical health data
7	Economic pressure	Covers how the liberal market system is shaping the behaviour and incentives of all market players
8	Unconscious bias	Covers how cognitive patterns shape structures, processes and cognitive patterns
9	Fragmentation	Builds upon diversity of market players and decentralization of drug development but as well as on the healthcare system
10	No added value – reimbursement	Outlines the rationale of how new medical products enter the market
11	Perception of development of contraception	Covers expressions of how the development of contraceptives is perceived, reflection on society dynamics and changes

Table: Overview of main identified categories in code book (Appendix B)

Source: Retrieved from NVivo

8. Data quality consideration

The main purpose of displaying the research design is to provide transparency on how the answers for the research questions emerged. The transparency of the research methodology shall

“reduce the possibility of getting the answer wrong” (Saunders et al., 2019). As described by psychologist Carl Roger, scientific methods are applied to prevent “subjective hunches'" which have developed through the relationship between researcher and data (1961). Therefore, a reliable and valid research design is required. While the concept of reliability and validity are mainly used in quantitative studies, they do not fit well when assessing the quality of the qualitative research. In the interest of demonstrating a high quality of the collected qualitative data, the following section elaborates on ethical considerations, dependability (reliability), forms of bias, generalisability and credibility (validity).

8.1. Ethical consideration

In general, research design should not subject the investigated groups to the risk of embarrassment, pain, harm or any other disadvantage. Consent of the research group is necessary and compliant with the GDPR rules. As such, the data was collected and transcribed, whilst being stored in a cloud platform with secured access through our university. As soon as the project is finished, the collected data will be deleted from the cloud platform. Further on, interviewees were anonymized. The interview guides for the respective informant groups were approved by trained qualitative researchers and consent was given by each interview participant. Further, we offered the option to skip a question and provided a comfort space for the interviewees, where they could stop the interview at any time. As briefly mentioned previously, the interview guide for the end-user was tested on two women and readjusted in accordance with the felt perceptions and feedback received by the voluntary test-participants.

8.2. Dependability

Reliability refers to the ability of replication. However, a qualitative research design is not necessarily intended to be replicated, due to the socially constructed interpretations of participants, the specific setting as well as the set time (Saunders et al., 2019). A modification of reliability for qualitative research, so-called dependability, is meant to be delivered through recording all of the changes made in the research focus, as the study progresses, and by precisely describing the research design. As such, in order to produce a reliable study design which is guiding through the emerging research focus and can be comprehended as well as evaluated by others (ibid.). According to that, the study displayed the hypothesis tracker (Appendix D) to outline how the main themes were identified and how the research focus changed throughout the process. The flexibility provided by the semi-structured interview was essential to explore the complex, dynamic and personal views on contraception.

8.3. Bias consideration

In order to provide a successful and transparent research design, the nature of bias should be discussed. The awareness of “why” a particular research topic and a specific research design got chosen as well as “how” the researcher is interacting with the topic is crucial to provide data in an unbiased and meaningful way (Denzin & Lincoln, 2011). The study acknowledges that biases could be mitigated but never fully removed. Within semi-structured interviews the dependability is influenced through the *interviewer bias.* This is where comments, tone or non-verbal behaviour of the interviewer creates bias in the way that interviewees respond to the questions being asked (Saunders et al., 2019). Further the *response bias* appears which refers to the interviewees’ perceptions about the interviewer. This bias could also be linked to the interviewee not feeling comfortable about every question and therefore only providing partial insights. The following biases are difficult to overcome. However, by conducting the interviews in pairs the diversity of whom is asking the question as well as the response bias can be mitigated. The *participation bias* is given by the nature of individuals participating and agreeing to be interviewed and is reflected in the study. Furthermore challenges regarding cultural differences were considered. However, due to the requirements for informant groups one cultural homogeneity, defined as the same home country, was given, except for one participant. One of the end-users grew up in Australia, but lived in Germany for several years. Differentiation towards the other women could only be noted around specific country details (e.g. reimbursement system Australia) otherwise the main patterns were confirmed. While the second informant group presented a larger variety of nationalities, the cultural differences fade within the international setting of pharmaceutical companies. Here as well, the study applied a reflective practice, by using the hypothesis tracker and challenging the views within the research team.

8.4. Credibility and validity

Validity refers to the appropriateness of the measures, accuracy of the analysis of the results and the generalisability of the findings. Semi-structured interviews can achieve a high level of validity by using clarifying questions, probing meanings and by exploring responses from a variety of angles (Saunders et al., 2019). In order to strengthen validity the technique of data triangulation was applied. Data triangulation involves using more than one source of data collection to confirm the validity, credibility and authenticity of research data, analysis and interpretation (Brantlinger et al., 2005). The purpose of the triangulation is to approve the links the data is presenting through two different independent sources (Denzin & Lincoln, 2011). The study performed triangulation by collecting data of two different informant groups and following a multi-informant strategy embedded

in a holistic approach. The different perspectives by the two informant groups add depth, breadth, complexity and richness.

8.5. Summary of chapter III

In the method section we described the whole research onion and defined the research philosophy, research approach, research purpose, research design and research strategy. As such, we have highlighted that the research question calls for an exploratory and descripto-explanatory purpose and is answered from a “subtle realist” philosophy. Furthermore, both purposes relate to an abductive approach in which previous industry and background knowledge of the contraceptive fields and the collected data are interacting. Through the use of grounded theory methodology, semi-structured interviews were conducted with two different informant groups. The first informant group, the end-user of female contraception, have been selected through a two-folded recruiting strategy (facebook groups, OBG flyer) to mitigate bias and ensure a broad spectrum. The second informant group, encompassing industry experts, have been selected due to their industry knowledge within drug development and contraception. The data analysis took place in the scope of the template analysis.

Chapter V: Results

The following chapter will outline the main empirical findings through the previously described qualitative study method. This implies that the section is not driven by established theory or literature but by the data that has been gathered and analyzed for the purpose of this research. In light of the chosen research methods, a pragmatic and abductive design was followed, which implies that the results are influenced through previous theoretical knowledge (Saunders et al., 2019). The data has been triangulated, thus the evidence of both target groups will be reflected simultaneously in the results (Brantlinger et al., 2005). The interviewees will be referred to as (End-User X), (Pharma X), (Investor X) or (Foundation X), where X is the number in accordance with the order in which the interview was conducted.

Based on the empirical analysis of both interviewed target groups, we have identified patterns which are summarized into three major misfits. Each of these misfits corresponds to an issue that hinders the contraceptive development and is composed of three to four sub-themes. Further, the misfits can be allocated to three main stakeholders involved in contraception that act on different levels: the end-users, the pharmaceutical industry and the government. As such, on a (1) Micro-level the reflections of the end-users are defined, (2) the Meso level is associated with the pharmaceutical industry, and lastly (3) the Macro level relates to society as a whole incorporated by the government. All of these three levels build what we define as the ‘system of contraceptive development’, referred to in the background section of this paper as the market players, who work together as an interconnected and complex entity. The different levels are suggested to follow a clear line of argumentation and thus the findings will be discussed separately, following the separation of the levels. However, it is to be kept in mind that all of the identified levels are co-dependent. Their interactions and dependencies will be discussed in Chapter VI.

Overall, the major misfit identified on a micro level will be described as a ‘lack of voice’, on the meso level the misfit of “systemic barriers and biases” will be proposed and lastly on macro level we will define the misfit of “a lack of ownership”. These will be elucidated whilst unfolding the empirical analysis and will answer the research questions. The below graphical representation depicts the aforementioned levels along with the corresponding misfits and the sub-themes of those.

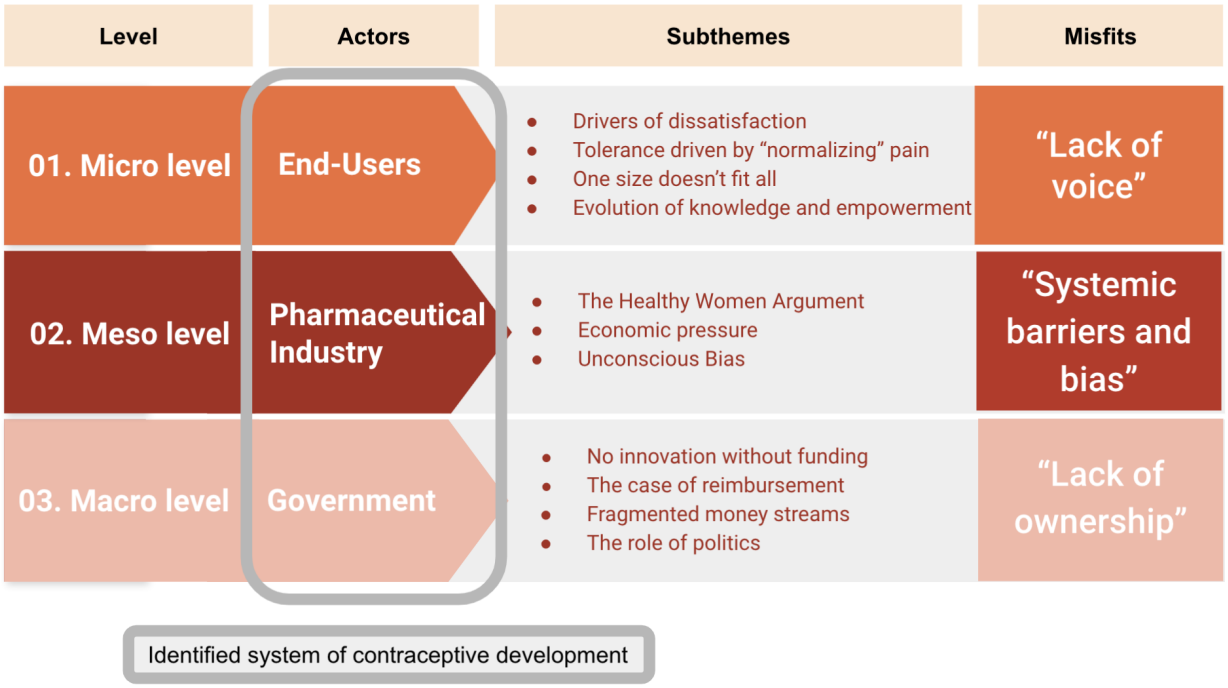

Figure 5: A three-level approach to the lack of innovation in contraceptives

1. Micro-level: a lack of voice - the perception of contraceptives

The result indicates that one reason behind the lack of innovation in female contraception is the end-users' lack of voice within the embedded system of contraceptive development. Even though an unmet need and dissatisfaction with current contraceptives is identified in female contraception, this need is not reflected in the innovation of new, desired methods. Four themes unfolding the dissatisfaction among women have been identified: (1) Drivers of dissatisfaction, (2) Tolerance: continuation despite dissatisfaction, (3) One size doesn't fit all and (4) Evolution of knowledge and empowerment. All of these elements establish the absence of say on women's contraceptive needs.

1.1. Drivers of dissatisfaction

First, the data analysis showed that women are dissatisfied with current methods. The dissatisfaction expressed by the assessed sample unfolded along two main drivers: Side-effects and the desire to not interfere with women's natural system by taking contraceptives. The following quote exemplifies the experience of side-effects caused by contraception: *"I tried the hormone ring for a year. I was about 26, no, 27, exactly 27, which was a disaster, because I had permanent PMS with the hormone ring. [...] I have pretty heavy PMS and then just the whole family suffers from it. If you have that as a permanent condition. I was then also with a psychologist and then thought I have depression. She tried antidepressants and then I described to her how I felt. And then she*

said no, you don't have depression. Because the medication didn't do what it was supposed to do. And at that time I read this article about the ring and stopped taking it, and afterwards she also said that it was probably related to that. It was totally burdening!" (End-user 01)
The quote illustrates how the side-effects decreased the quality of life and affected not only her as a user, but also her surroundings. Thus, the wide extent of side-effects is emphasized. Within the findings other physical side-effects like irregular bleeding, heavy bleeding, extended bleeding, headaches, weight gain, iron malsufficents, digestion problems, fungal infection, herpes and complexities to get pregnant are causing dissatisfaction among the assessed sample. Further, psychological side-effects encompassing stress, anxiety, mood swings, depression, PMS, decrease in sexual desire or libido decrease as well as concerns about the ability to become pregnant in the future are adding on to the malcontentment amongst the interviewees.

The extent of the perception of side-effects were perceived differently from women to women, which is exemplified by the following quote: *"So he [her partner] said I was like completely changed after I got the IUD and stopped the pill. Also mentally much much happier. I felt so much better"* (End-user 10). This statement draws on the fact that the dissatisfaction is first realized when the method has been changed. Some women experienced immediate changes in their bodies whilst for others it took time to sense discomfort and realize that it may be connected to their contraceptive method.

Secondly, the data shows discomfort of taking a method which interrupts women's natural reproductive cycle. This is elucidated by this interviewee:
"And just all these hormones, that's just not so natural with the whole cycle. And so on. And yes, I didn't really have any problems with the pill. But now I feel better somehow. So much freer, so I don't know exactly how to say it. But I just feel better now that I know that there isn't anything else in my body." (End-user 07)
Here, the desire of women towards methods in which their *"bodies remain their bodies"* is identified, to ensure a continuous communication channel with themselves and receive signals that can be transmitted with an irregular cycle, such as stress for example. Our sample shows hesitation to disrupt natural processes and have the desire to *"feel"* and *"be in contact"* with their bodies. This strengthens the dissatisfaction among women and illustrates that current available methods are violating the desire of natural physical processes.The reflected importance of being in contact with one's body and the tendency to be more aware of the effects hormones can have, is reflected especially amongst younger women in our sample. In particular women in their early

twenties discontinue their contraceptive method because of hormones and opt for a less invasive method instead.

In addition, mothers within our sample express worries regarding the influence of hormonal contraception for their daughters. As expressed in this quote: *"But when I think of my daughter, what she can take, there is only the pill. Even if hormones provide protection, I don't really agree with that. There has to be a better option, except to shoot the body full of hormones at that age."* (End-user 18). This emphasizes the wishes and the hopes that the previous generation has for the following one: to be able to choose a contraceptive that doesn't require the intake of hormones. Thus, we identify a need for new products through women's expressions of dissatisfaction with hormones and their desires for their own children.

The findings further present that both the desire of no intervention in natural processes as well as the side-effects are perceived by the expertise of pharmaceutical companies. The latter is proven by the following quote: *"I think that a lot of patients just have bad side effect profiles [...] it is the number one reason I think"* (Pharma 05). The acknowledgement is shared among the full sample of industry experts and reflects that market research resulted in the awareness of the pharmaceutical industry on the dissatisfaction caused by side-effects. The quote also reflects on the hierarchy of the reasons for discontinuation. As such, it appears that the industry agrees that side-effects play a crucial role within dissatisfaction and discontinuation of current contraceptive methods. Further, the industry is aware of the desire of women, not to have any interruption in their natural processes caused by contraceptive use. The younger generation is described as *"hormone sceptic"* by the industry experts and their demands for contraceptives are acknowledged to "*not disturb the hormonal balance*" and "*something completely non-hormonal*". It can thus be identified that an unmet need is present and known by the industry, because of the high side-effect profile of current birth control options combined with a wish for new non-hormonal methods.

Moreover, the study assessed if time effort and economic reasons are key drivers of dissatisfaction with contraceptives. The time effort component designates the obtention of the contraceptive method as well as the complexity in intake. The economic component referred to the burden of costs for the individual. The latter was mainly mentioned by younger women currently pursuing their studies. As outlined in the background, the results highlighted that contraceptives in Germany are reimbursed until the age of 21. Further one woman highlighted the possibility to request additional funding by providing evidence for limited income to the health department of the

municipality. In general, we identified that financial reasons outweighed the time-consuming ones. However, the data shows that both factors are not the overriding factors of dissatisfaction.

1.2. Tolerance: continuation despite dissatisfaction

A second finding of the gathered data is reflected in the trend that women continue to use their contraceptive method despite the mentioned dissatisfaction with it. Thus, three rationals could be identified: continuation because of no alternative, continuation because of perceived and "normalized" pain and lastly continuation caused through dominance of benefits.

At first, the data displays that women continue their contraception despite discomfort driven by the perception of having *"no better alternative"* or *"no choice",* which strengthens the case of a lack of options. Further the conception of pain is shown to be a reason to continue with a contraceptive that is not fulfilling the actual desires as exemplified in this statement:
"But you know, women, we deal with a lot of crap, you know, so if we have headaches or something, because we're taking our birth control pills, or we're menopausal, and we're having hot flashes. It's kind of just like a well, it's part of being a woman just deal with it. [...] I don't know, it's really unfortunate, but I think that women are more used to dealing with their problems quietly. And so that gets reflected in the market space" (Pharma 05). The quote indicates how women tend to interact with pain and side-effects and that they are used to "deal" with a certain degree of pain. As such, women are not seen as complaining about felt side-effects but just deal and recognize it as what makes them a woman. Further it indicates how the industry endorses this observation. The continuation of a method despite dissatisfaction is an indication that women as well as the pharmaceutical industry "normalizes" the pain inflicted by contraceptive use and does not contribute to the need of alleviating the endured pain.

Lastly, continuation is presumably caused by the prevailing benefits of contraceptives, as stated: *"So yeah, it's a little freaky, and it's a little uncomfortable. But um, I just kind of gotta suck it up, honestly. And it is satisfying that you can feel it, and it's there. So you know that it's doing its job, and you are safe."* (End-user 09).
Here, the strongest benefit of the chosen method is given by the high safety profile and the ability to rely on that, thus taking away the worry of a possible pregnancy. Further the quote illustrates how the "uncomfort" is identified as a reminder that the contraceptive offers protection. Hence, this can be seen as a paradox, as uncomfort has a negative connotation, but women seem to assert that the increased feeling of discomfort is positively related to a feeling of better safety of a contraceptive. Other benefits such as less bleeding, no bleeding, predictable bleeding, less pain, good skin and steady mood are mentioned regularly across the data. While these benefits often

come along with strong discomfort, women express that the benefits, especially the attribute of feeling safe, is outperforming the disadvantages and therefore accept to deal with possible side-effects.

1.3. One size doesn't fit all

In alignment with the described dissatisfaction caused by the wish for less interference in the reproductive system, the data raises a wish for new contraceptive products.

There is a strong overlap of desired attributes for new products. Especially features like *"no side-effects*", *"non-hormonal"*, *"not invasive"*, *"not something to think about everyday"*, *"cheap"* and *"shared responsibility"* are reflected in the data. There is a discrepancy in the wish for having regular bleeding or no bleeding. While for some women the regular bleeding is welcomed and seen as a connection and confirmation that everything "works", some women experience it as a big burden as exemplified: *"For some women it is a positive signal that they are healthy, that everything is fine, for others it is a burden"* (End-user 06).

Therefore, we can assume that women know what they desire with their contraceptive options, but that these wishes may vary from person to person and that "one size does not fit all". Moreover, no pattern could be identified in between participants who preferred to have regular bleedings and those who would rather suppress their period. On this premise, additional new product features mentioned by the interviewees were *"no interference with mental sanity"*, *"no risk for infertility/complications of getting pregnant"* , *"no interference with diet or other drugs"* as well as *"protection against sexual transferrable diseases (STD)"* . Similarly, no particular pattern was identified on these preferences in relation to age or current relationship status, on the above mentioned desired product features.

Additionally, another variance is seen regarding the wish for self-administered or self-controlled methods as exemplified in the following:

"*Because I also wanted to have this personal responsibility, that I somehow have it in my own hands. And then it would also be important if you could control it. Yes, I don't know exactly how. But you could simply check whether it still fits properly.* " (End-User 03)

This emphasizes some women's wish for a method where they can make sure by themselves that they can rely on it's efficacy. Thus, while some women would like to be in control and administer their method independently, others prefer to have a one time procedure and don't have to spend any further thoughts on their choice of birth control. Thus there are also women wishing for *"episodic products"*, which can just be used shortly before sexual intercourse. The wish to administer the drug or the new product influences how women feel and think about *"putting*

something in their vagina" or "*touching themself"* in order to insert a pregnancy preventive method. Whilst for some women the self-administration feels liberating, others feel uncomfortable and overwhelmed and are afraid of doing something wrong that would put at risk the efficacy of their birth control choice. While the data underscore the alignment for non-hormonal and non-invasive new products, heterogeneity evolves around women's views on the administration, use and duration of a contraceptive.

The desire for non-hormonal and non-invasive products is also reflected in the data collected from the industry experts as expressed with the quote: *"I would hope that a new mechanism of action really comes through, especially a non hormonal one."* (Investor 01) This statement builds on the development of new medical products that, as referred to in Chapter II, starts with the identification of a new mode of action. As such, the heterogeneity in the desires of women on new contraceptives that have been outlined previously, could impose a challenge for pharmaceutical companies towards NPD based on heterogeneous market research. However, the data displays distinct results that a non-hormonal mode of action is desired. The data emphasizes the expectation towards *"pharma"* to identify a new target (non-hormonal) and the need to find a solution *"to get around the procedure of insertion"* (non-invasive).

1.4. Evolution of knowledge and empowerment

The last theme elucidates how sexual and contraceptive education leads to empowerment and the ability to better express the felt pain, dissatisfaction or the need for innovation on existing birth control methods. The following quote exemplifies that: *"And then I talked to a pharmacist on the phone, and I talked to the manufacturer of the diaphragm on the phone for a very long time, and asked exactly how everything works, what happens, and what I need to do [...] But it was the only time where I really felt like someone was explaining to me how this contraception works. And that was the only time I felt someone was interested that a young woman somehow gets some knowledge around her contraception." (End-user 11).*

Here, the end-user expresses that in the past she hasn't encountered many people willing to inform her on the mode of action of a specific contraceptive method. Thus, it also emphasizes the fact that women have a need and an interest in gaining knowledge in the field and resent that they are lacking sexual education. As such, this feeling is further strengthened, by a common trend in the collected data: contraceptives were addressed rarely when growing up neither with family nor with friends. Further the findings outline a shortcoming of sexual education in schools. This lack of education is reflected in the data by a myriad of expressions such as "*feeling left alone*" or *"not taught sufficiently"*, suggesting that the sexual education received wasn't enough to enable women

to make an informed decision on their contraceptive choices. Therefore a lack of empowerment stemming from a shortcoming of sexual and reproductive education is present in the data, which surprisingly was reflected across all age groups. Even though the data exhibited that the younger generation felt more at ease to address contraceptives with their family and friends, they all wished for a better education during their school years.

Additionally, the interaction with gynecologists (OBG) presents a variety of emotions. This finding is indicated in quotes like: *"I have now changed my gynecologist three times. The first time it was because I didn't feel I was in good hands when it came to contraceptive inquiries. I changed practitioners, and then when it got really bad with my menstrual pain and I was only advised to take painkillers and was also told that maybe pregnancy would be a good thing, I was like okay, that's not the medical advice I need and I changed again. So this is now the third gynecologist I am consulting and I'm satisfied for the time being"* (End-user 05).

While some women are satisfied with their consultation, two third of the women (n=13) in our sample data express dissatisfaction with their gynecological consultations, which often resulted in a change of doctor. The concept of the principal-agent problem is strongly confirmed in the data, which is defined by the information asymmetry between the principal (women) and the agent (OBG). The theory also suggests that the agent is able to make decisions and/or take actions on behalf of the principal (Gauld, 2018). Thus, this theory can also be applied on the mismatch of knowledge and information sharing on contraceptives in between women and their OBGs. In return, this leads to a strong dependency of women on their gynecologist. This imbalance of knowledge stems from the little education previous to the first appointment with a gynecologist.
Further, the results display that women recognize and partly criticize that OBGs have their own agenda and a "*favourite method*", that women often feel incited to. As such, some women feel that their doctor convinces them to opt for a specific birth control method, without really considering their wishes. The own agenda setting combined with the strong dependence women have on their gynecologist shows how influential the opinion of an OBG and the consultation received is on women's contraceptive choices.

Another criticism grasped from the data is a lack of time for individual consultation, expressed through statements such as: *"It's so time-consuming to really do this educational work about all the different contraceptives and to highlight the advantages and disadvantages and reflect on what the individual's needs are. And no doctor can fully finance this."* (End-user 04). This expresses, that besides the above mentioned feeling to be given a prescription for a specific contraceptive method

that is preferred to the gynecologist, a lack of time in the consultation further strengthens the feeling not to have one's birth control wishes satisfied. From a patient's perspective the lack of time can hint towards not having enough time to feel comfortable to talk about an intimate topic and thus not having the possibility to ask all the questions of interest. On the other hand, from a practitioners view, the many patients that need to be consulted don't allow for more explanations on contraceptives. This relationship thus reflects that the lack of time hinders knowledge sharing that allows for women' actual wishes to get overridden by the favorite methods of the respective OBG.

The data further shows that women express doubt about the causality between a used contraceptive method and the felt side-effects. This is exemplified by: *"I was always tired and then had to take iron supplements [...] decrease in sexual desire. But I don't know, maybe other psychological factors also played into that"* (End-user 05). Thus, the lack of knowledge about contraceptives seems to foster uncertainties in attributing experienced discomfort with the respective contraceptive used. This uncertainty is enhanced by younger women starting to use contraceptives around the age of 14. Through the data analysis a struggle to differentiate or relate to how they felt before taking contraception was identified. This can be explained by the fact that as soon as they started menstruating they started using (hormonal) contraceptives. The uptake in contraceptive use was thus at the same time as hitting adolescence, when natural hormonal changes occur. Therefore it can be difficult to differentiate which feeling or perceived pain can be attributed to the use of birth control, when they are not aware of what their female body at a reproductive age feels like without the birth control.

On top of that, the combination of the uncertainty of linking pain with contraceptives and the influence of OBGs can lead to confusion about end-users' own perceptions and discouragement to take action. This is displayed in the following expression: "*I had super many infections and then asked again and again my gynecologist, can it be that it is because of the IUD? Could it be that my body no longer tolerates the copper? But then I would always hear no, no, that can't be the case, that has nothing to do with it"* (End-user 11). Thus, the role of the gynecologist in helping women navigate their contraceptive choices and possible side-effects of these is exemplified. The uncertainty of side-effects in relation to contraceptive methods that women experience, is not perceived due to a lack of attention that it could be linked to contraceptives, as it is a topic that is underestimated. Therefore, this argument builds on the lack of voice women have in communicating their feelings on birth control.

Lastly the data indicates a trend driven by the younger generation spreading knowledge and getting informed on contraception through social media. The following quote elucidates that: *“Younger women are growing up, they're growing up in a different sort of atmosphere, I think that people are more empowered, they're more comfortable talking about sex, their bodies, their options. And so I think that space is making a little bit more of a, it's sort of evolving a little bit more [...] I do like the newer, younger contraceptive patients, they seem much more open about asking for what they need. And you know, having that honest discussion.I think a lot of it comes from social media. So especially, you know, TikTok, Instagram, Twitter, etc“* (Pharma 05)

Through educational content available on social media sexual education can take place outside of the traditional institutions such as school, family or gynecologists. This allows women to feel empowered and deconstruct the taboo topic of birth control by sharing experiences and enabling sophisticated criticism. This trend is recognized by the private industry and translated into a larger incentive to innovate. It occurs that within the field of women's health contraception is *“evolving a bit more”* than other topics. This is ascribed to more visibility through social media. Young women speak up about their pain, wishes and desires. Through social media they established a communication channel among each other, which results in mitigating the aforementioned feeling of *“being alone”*. Further by exchanging experience and knowledge through social media, data is generated. This data can often be assessed by other instances and could therefore be the starting point of having a direct communication channel with the end user (e.g. Instagram analytics). The results present that social media strongly emphasizes the link between contraceptive knowledge-sharing and empowerment, and as such can be a way to provide a voice to (young) women.

1.5. Preliminary conclusion of perception on contraceptives

Despite the different nuances to dissatisfaction, the results strongly emphasize across the assessed sample, that side-effects as well as the wish of no interference in the natural system are the main aspects mentioned in the dissatisfaction of women with their chosen contraceptive method. The tolerance among women to cope with products, which cause pain and discomfort comes along with a clear desire for new products. The industry is aware of the side-effects and the wish of no-interference with the reproductive system. However, the perception of pain women suffer does not seem to be adequately documented. Further on, even though an unmet need and dissatisfaction with current contraceptives is identified, this need is not reflected in the innovation of more methods. A reason behind the lack of innovation in female contraception can thus be identified in the end-users’ lack of voice which is fostered through a shortcoming of sexual and contraceptive knowledge. The current instances encompassing family, friends, schools and OBGs

are not succeeding in providing women a context to feel safe and understood when talking about discomforts of contraceptive methods. Therefore, along with the outlined results the study identified the misfit of a “Lack of voice”. The new generation however, presents how the use of social media could be a facilitator in overcoming this misfit and finding a common voice that can be heard, to lead the change.

2. Meso-level: systemic barriers and biases

The second aspect of the research investigates the barriers for pharmaceutical companies to innovate in the field of female contraceptive methods. In this section, patterns are established in the way the interviewees express their views on how female contraceptives are approached from an industry perspective. When relevant, end-users perceptions will be incorporated.

By applying the template analysis, we determined several barriers that lead to a lack of innovation in the pharmaceutical industry. However, some of these are not specific to contraception and have been depicted in depth in previous studies. Thus, the following trends can be confirmed by the collected data, but will not be further elaborated in this chapter due to the limited scope of the research: (1) Outsourcing of R&D and the fragmentation of drug development process (2) Regulatory approval challenges (3) the “Better than the Beatles problem” and (4) The rising costs of R&D. Since these trends are not specific to the case of female contraceptive development, focus will be given to the results that apply to contraception only and leave room for interpretation of how to overcome those to enable NPDs. The three sub-themes discussed are: (1) The healthy women argument, (2) Economic pressure and lastly (3) Unconscious bias. The three sub-themes are summarized within the identified misfit of “Systemic barriers and biases”.

2.1. The healthy women argument

The sub-theme of the ‘healthy women argument’ has been distinguished in the results. As such, we find three categories to belong to that topic: (1) The complexity of the reproductive system, (2) Clinical trials, and (3) Litigations.

The complexity of the reproductive system is emphasized in the preclinical stage of animal modelling as exemplified in the following quote: “*So I would say the biggest bottleneck in the reproductive area is the lack of animal models”* (Pharma 2). This statement points out that the preclinical stage is perceived as a crucial phase which blocks the contraceptive case from moving on to the clinical stage, as animal models have very different reproductive systems than human women. The reasoning of the healthy women is apparent as testing will not be performed in a

healthy population before the safety threshold in an animal model is high enough. Thus the complexity and the high safety threshold blocks the development of new creative approaches. However, the data displays that it is rather a question of commitment to find new ideas to model a woman's reproductive system than a lack of possibilities. This finding is underlined by the data through displaying the advancement of cancer treatment modeling within animals, which highlights that with the right funding progress can be achieved.

Secondly, hurdles in the clinical phase are highlighted through stringently regulated clinical trials due to the high barrier of safety. The following quote underscores safety as a key concern: "*So I think that hurdle to basically come up with something that's a true innovation in that area and the investment that is necessary, and a really, really high threshold for safety in clinical trials as well because we are treating healthy young women"* (Pharma 03). This emphasizes the fact that many risks and responsibilities do come along with running clinical trials in young and healthy women as opposed to performing a trial in a person that is already suffering from a medical condition. In addition, the financial aspects of clinical trials that involve a revolutionary birth control method add on to the list of perceived barriers as pointed out in the collected data. Investing in incremental innovation is perceived as less risky compared with *"true innovation"* in contraception because of fewer financial risks at the clinical stage. Even though clinical trials are crucial and necessary in order to bring the best possible product to market, clinical trials in contraceptives are seen as particularly costly and difficult to perform in terms of data, ethicy and safety for a healthy population. Overall, the traditional drug development path within big pharma can thus be seen as a hindrance for contraceptives as it does not adapt to another type of situation. The fact that healthy women (WOCBP) need to take part in drug development processes will not disappear. As such, the argument of pharmaceutical companies that testing needs to be performed on a fit population and that the regulatory hurdles of safety are high appears like an excuse. This enables a main barrier in contraceptive research. Thus, instead of coming up with new processes which would shape the way to revolutionary products, the industry is driven by a conservative approach to perform incremental innovations to family planning methods.

Thirdly, the lack of a diversified sample population in contraceptive trials is mentioned as a potential bottleneck to innovate. As displayed by the industry experts: *"It's a problem with a lot of data, because you know, you want these patients who are healthy. Obviously, we don't want to be having patients who have a high BMI, or risk factors and all these other things, that's not really very indicative of the population. You know, we want people who are Hispanic or black women who are, you know, all these different races, and they end up being very predominantly white women, which*

I think is a problem as well" (Pharma 05). The quote outlined the importance of an increased variety in clinical sample studies and states that with more differences perceived in the tested population, the more will be known about the possible side-effects of a new contraceptive method on different body types. To serve this diversity the recruiting of suitable candidates can be a bottleneck especially for Phase 3, the largest clinical trial. A contraceptive specific issue in clinical trials is that participants not only need to be healthy women, they also need to be at a reproductive age, not pregnant and willing to take risks with their fertility when participating in a trial. These requirements for contraceptive trials may be the reason that make it difficult to obtain a diverse group of participants where all 'races' are represented in the data. Once more, this highlights the case of the 'healthy women' as participant recruitment can turn out more complex than for other indications.

Finally, past litigation cases in birth control have shaped the pharmaceuticals view on product development in the field. As such, major risks associated with litigation are described by "*there was a lot of litigation going on in the US so it was not an attractive field. All the companies were sued. Basically, every company selling contraceptives was sued in that context*" (Pharma 03). This statement presents that companies are taking on a considerable risk when coming up with a new contraceptive. The empirical data strengthens that most of big pharma even left the field because of the many litigation cases.

Furthermore, lawsuits impact a company's branding and perception for both end-users and employees. Bad light is shed when introducing new contraceptives on the market from the interviewees point of view "*that's also in the public perception and that of these newspaper articles, my beautiful 22 year old daughter died of a blood clot. Horrible, no one wants to see that. It's so super sad, and also not good for your public reputation*" (Pharma 03). This statement really accentuates the fact that legal disputes are a major risk in terms of reputation and innovating in contraceptives. The risk of causing harm to a young and healthy woman's life is related to huroundes compensation, high litigation payments and reputation damage. Thus, contraceptive products really *"need to be perfect"* before being distributed as the damaging impacts at stake are too high for a pharmaceutical company. Once more the extent of side-effects from hormonal contraceptives argue in favour of the high risks perceived by the industry when placing a new product to market that is designated for a healthy and young population.

2.2. Economic pressure

The empirical data has shown that a further hindrance is revealed caused by the need to generate revenue in the pharmaceutical industry. This constant search for return on investment (ROI) is exemplified by the following categories: (1) Business case (2) and Public-driven companies.

A barrier to innovation is presented through the required business case which forecasts how profitable a new product will be, (ROI), underscored by the following: ***"****But providing a business case is the first step"* (Pharma 02). All industry experts manifest the importance of the business case at an early-stage of the drug-development process. The business case defines if a drug will be pursued within the R&D process or not. The data highlights the doubts of having a business case in the field of female contraception. Even though female birth control affects half of the world's population, and has therefore a large target group, its business case is perceived as not providing enough financial returns, as exemplified by another quote: "*And I think the number of unintended pregnancies speak exactly to your case, there is a need for contraception. But maybe not for big pharma , at least that's why big pharma has decided to leave the field*" (Pharma 03). The increasing reliance on a business case by big pharma emphasizes their justification to avoid investments in new contraceptive methods, as the costs and risks will not be covered by the little ROI of a new contraceptive product. The persistence of the business case as a decisive factor adds a barrier to explore areas outside of the strict monetary scope and overcome incremental innovation and discover disruptive NPD.

Secondly, the monetary pressure is even more present in publicly traded companies, which big pharma mostly is. The collected data exemplifies this: "*As a private company, we can take the decision that we want to address this, but from a listed company, if you have a stock exchange expecting a return of your investment, I think that decision is basically that no companies are actively pursuing development in this space* "(Pharma 02). Thus, the pharmaceutical industry is led by profit and can not decide where to innovate based on their preferences. We recognize the role of listed companies as a barrier to contraceptive drug development, as their freedom and creativity to innovate in the field is cut. This aspect is related to the business case and to the fact that female contraceptives already exist. As such, they would have to compete with already existing pregnancy-preventive products in terms of pricing, where the costs of development would probably outweigh its returns. Therefore, in publicly-traded companies, where the aim is profit and not to contribute to wellbeing and reducing pain, innovation in contraceptives for big pharma is out of reach, embodied in the quote "We are not a charity!" (Pharma 03).

Further the data displays that the constant evaluation of financial returns limits creativity and room for exploration as described by the industry: *"I don't think it is the lack of ideas. It's really just the attractiveness of that field. Yeah, that would be my guess and that's why [own company] left research in contraceptives 10 years ago now [...] the business simply wasn't there anymore."* (Pharma 03). This expression of the scientific breakthrough, contradicts the position that science in contraception is at the end. The data presents that the increasing importance of the business case which defines the "attractiveness" of the market is negatively associated with scientific breakthrough within contraceptive research. Thus, only incremental innovations in female contraception are bound to take place.

Following on that, the weight of the business case is scrutinized based on the long-term horizon of contraceptive development and ongoing changes exemplified in this statement: *"To be honest, yeah [...] things change so rapidly, it doesn't make sense in my mind to do a full blown business case, if you have six years to the market. Because in that six years, the entire treatment algorithm, the patient population, the reimbursement issue can change considerably and will change. So all those factors influencing a business case are constantly moving into the target."* (Pharma 02) The quote underscores the lack of predictability and therefore mitigates the significance of the business case, especially within early drug development.

2.3. The unconscious Bias

The last point of the meta-level addresses the bias of the industry influencing the decision-making process that doesn't allow for further female birth control developments. This tendency unfolds in two categories: (1) Agenda-setting and (2) Gender imbalance.

Having the authority to decide on a global strategy for a company is decisive in indicating the goals a company will pursue. Affirmations such as "*I mean, this is like a strategic question. Do we want to be within women's health? Do we want to be in contraception?* " (Pharma 02), presents the shift and decision-making of pharmaceutical companies to either leave women's health, or contraception as a part of the women's health portfolio. In general, the data unfolds that if contraception is not on the global strategy agenda, then, no innovation in the field will take place. Overall the collected data shows a trend of the pharmaceutical industry to leave the women's health field. Contraception is not perceived as an allurating division anymore and therefore the managerial decision has been taken to leave the field. Strategic trendsetting is therefore recognized as an immense barrier to innovate in the scope of the research.

A further aspect invigorated in the performed interviews is the individual agenda-setting which strongly influences the decision-making process. As presented in the following quote: "*Each of us has certain areas. I sort of happened to be the person who knows most about women's health investment. When we don't think in terms of departments, we also don't have a fixed allocation,[...] It's really driven by the individual opportunity* "(Investor 01). Across all hierarchy levels within big pharma (board, scientific committees, discovery board, etc.) the individual agenda appears to influence decision-making. This stresses the question of how decisions in the field are being made. Due to the lack of systemic systems, the current setting is based on a case to case approach, which is indirectly heavily influenced by individual agenda-setting and bias. Moreover, currently the agenda is not set towards specifically targeting and advancing NPDs in female birth control, therefore it is unlikely that something will breakthrough in the field. With a lack of data infrastructure, decisions can not be tracked or explained. This presented lack of transparency allows for biased decisions.

Tying onto this finding, the way in which decisions are made and the person responsible for taking those, plays a crucial role. As such, the reason why in many big companies women's health is not in the foreground can be explained by the fact that board members are often men. The following statement substantiates the advanced hypothesis: "*One pervasive issue in women's health investments and development is of course, sort of gender imbalance in management teams and investor teams, right? [...] 88% of decision makers in venture capital are men at this point. And in the pharma industry, maybe looks a little bit better, but not that much*" (Investor 01). The hypothesis drawn upon indicates that the gender imbalance in members of the board may be the reasons why women's health topics, such as contraceptives are not on the agenda and not taken into account. Therefore, we see the unequal gender distribution as a reason for the lack of innovation in female contraception. Furthermore, one interviewee even thematizes that contraception was initially developed for women due to the gender imbalance, phrased as "o*f course, I don't think it's a coincidence that contraceptives were developed for the female part. You can do the exact same thing for the male part. That science has been known for 50 years. So of course, that reflects how the boardrooms were populated in those times"* (Pharma 04), which reflects these thoughts and sheds light on the unequal gender distribution in higher management and the way contraceptive innovation is fostered. Gender imbalance is yet another finding that contributes towards the perceived systemic barriers and bias in advancing research in female contraception.

2.4. Preliminary conclusion meso level

The data shows a variety of information that can answer the leading research questions. It really embodies the complexity of the topic and offers arguments towards the lack of innovation, by bringing forward divergent perspectives from both industry experts as well as end-users.

The landscape of contraceptive development is strongly influenced by risks, uncertainties and complexity. Animal modeling, clinical trials and litigation are all procedural barriers that can not be removed in the drug development process and offer particular complications in the case of female contraceptive advancement. These barriers are stringently incorporated in the way the pharmaceutical industry works and has been performing for decades. The ideation of new contraceptives is undermined by the traditional processes of the pharmaceutical industry, taking away the space for creativity and science to come up with novel ideas. The barriers to innovate in female contraceptives are all intertwined and can be summarized under the misfit of “systemic barriers and biases”. The misfit unfolds along the argument of “working with” healthy women, which increases the risk and the regulatory hurdles, which in return damps the business case for innovation. This finding is accompanied by individual agenda-setting and gender imbalance. Thus, NPD in contraception is not identified as an attractive business which entails that the resources of big pharma are distributed across other areas. Therefore, the hypothesis can be advanced, that as the industry becomes more regulated, the less incentives and interests are left to come up with new contraceptives. With regards to agenda-setting and gender imbalance, a rather systematic and transparent decision process as well as the goal to balance gender-equality across pharmaceutical companies are recognized as ways that could steer innovation in the field of female contraception.

3. Macro-level: lack of ownership

As a last finding we identified the misfit described as a “Lack of ownership” on a macroeconomic level. The misfit is driven by four categories: (1) No innovation without funding, (2) Reimbursement, (3) Lost in fragmentation and (4) The role of the government.

3.1. No innovation without funding

In order to yield new contraceptive methods additional funding in research is required as exemplified in the following quote: *“I don't think it is the lack of ideas. It's really just the attractiveness of that field. Yeah, that would be my guess and that's why Bayer left research in contraceptives 10 years ago now, I mean, we had top notch scientists, they could have found targets for the next 100 years, I'm sure yeah.”* (Pharma 03). Drawing upon that quote the data

shows that the scientific possibilities are not saturated yet and that it is rather a question of financial commitment than a shortcoming of science. The data draws a distinct link on how "*putting more dollars into research"* would *"unleash the creativity of researchers and scientists"* (Investor 01). Thus, the association between adequate funding and ground-breaking science is underscored. Hence, the lack of innovation within female contraception does not stem from a lack of ideas nor possibilities, rather the industry doesn't believe in the potential ROI new contraceptives could have. Thus, the findings impose the question whose responsibility it should be to provide sufficient funding to enable the development of new groundbreaking contraceptive options. Overall, we find that the pharmaceutical sector seems to be aware that if more funding was made available for contraceptive research, innovation in the hormonal and the non-hormonal area would be enabled.

3.2. Reimbursement

The data analysis suggests that the reimbursement system plays a role in determining the price of a new medical product. The price of a given drug is impacted by governments dependent on the healthcare system, but will affect the ROI for the company as outlined by this industry expert: *"I think it really comes down to who pays for this, right. And this is different in different countries and for different types of populations. And in some European countries, where the government will pay for your contraception, and then they actually determine the price if it's a good thing, but they also then determine the price effect."* (Investor 01). The quote displays the importance of the payer who will have to cover the costs of a new contraceptive. The payer refers to the reimbursement system and is embodied by the government solely (single-payer system) or by the government and others as the private health insurances (universal system). However, in the latter health insurances are dependent on the price setting through public regulatory bodies, thus, the government. Therefore, two results can be unfolded: firstly that health insurances have tremendous implications in the previously discussed business case. Secondly, the influence of the government as determining the price level of a drug is emphasized.

Further, reimbursement only covers new products if there is a significant improvement, an added value, of the already existing products and if this can be demonstrated. The following quote comparing contraceptives to oncology drugs outlines the payers thinking process: *"Looking at like a cancer drug and how much you pay for cancer drug. Well, you sort of look at how many life years it saves, and then you put a price on that. [...] That's why some cancer drug costs $100,000 a year. [...] But here you quote unquote, just "address the woman's desire to have no hormonal contraceptive" and then the payer says, well I mean, that's your personal choice, we already have a perfectly sort of safe and effective contraceptive. If you don't want to take a hormonal one then*

you should pay for it out of pocket." (Investor 01). The quote indicates that the need and therefore the value for new contraceptives is not acknowledged. The data describes the existing methods as suitable contraceptives, because they are safe and effective. This perception can be identified as a barrier to foster innovative methods. Further, the data emphasizes that the payer is not covering for the aspect of *"convenience"*. Thus, the payer is not acknowledging the magnitude of the need for new contraceptives by end-users. Downplaying the need and defining it as convenience presents the misconception of the payer and the implication for a lack of reimbursement. Thus, the findings from the empirical data distinguish a market failure on a macroeconomic level. This theory is recognized, as there is a clear misconception of the payer regarding the true demand by women and the willingness to foster supply by providing reimbursement. As per our findings, this entails the government to ensure that demand and supply match and therefore to overcome the lack of investment and of ownership.

3.3. Fragmented money streams

Another barrier on the macro-level is identified in the fragmentation of money streams among the involved players, which results in an immense complexity and lack of oversight as exemplified here: *"So for example, a woman is missing or not showing up for work, because she has some side effect from her contraception, there is, of course, like an economic sort of problem and, you could put a sort of dollar price on that. But then that dollar price is not borne by the healthcare payer who pays for the contraception, right?[...] If you have like this fragmentation, and you may save problems, save money somewhere, but it's not the same person who has to pay for the extra cost"* (Investor 01).

The illustrated example presents how the economic-costs of side effects are not borne by the health insurances despite their provider role. Rather it affects the general economy or as mentioned in the example above the employer. Therefore, it reflects how the fragmentation of the healthcare system is skewing the link between costs and benefits.

Rooted in the above finding, the data presents how the players involved in contraception are concerned about their cost-benefit ratio. Whilst the private industry points out that they are *"no charity"* and are constrained to researching on projects that have a stable ROI, philanthropic institutions outline that they *"can't fund the whole process and that that is not their goal"* (Pharma 03, Foundation 01). Lastly, the investors only fund scientific projects if they see an *"exit strategy and can either make [the new contraceptive company] public or sell them"* (Investor 01). Moreover, as outlined previously the payer is only covering the costs of a new product if there is a sufficient added value to it. Therefore we find that the data reflects on how every entity involved in

developing new contraceptives is restrained in the ability to provide funding as they are all bound to reach a given goal or provide ROI. Further, it appears that the non-profit sector which, based on their raison d'être, aims at building bridges within the described skewed funding scheme, instead adds a further complexity by being involved. As such, we find that this complexity appears because NGOs are mainly engaged in LMIC, where they have the important function of funding research of new contraceptives that are more suitable in that specific country setting as well as increasing access of contraception. However the needs in LMIC aren't necessarily the same as in HICs, as such it doesn't go hand in hand with steering against a lack of innovation in female contraceptives in countries under the scope of this research. Therefore, the data outlines a paradox of how the agenda of NGOs can be counter-productive in the necessity of advancing contraception within HIC and how their role within the system draws an image of "*this is a third world problem"*. The outlined findings underline the complexity and the lack of ownership of all actors involved in being aware of which entity is responsible for funding which part of the drug development process.

The misfit of the lack of ownership is also reflected in the data collected from end-users. Thus, women mentioned governmental institutions, health insurances, investors, pharmaceutical companies, schools, gynecologists and friends as entities to take on responsibility and drive innovation. It hints towards a complex market that is difficult to understand from an end-user's perspective.

3.4. The role of politics and the government

The last finding on the macro-level elaborates and presents which role politics and the government has within the identified system of contraceptive development.

The results depict the role of politics and the government as having the ability to influence the agenda and to drive contraceptive change. This is exemplified in the following statement: *"The role of government is huge. I mean, when Obama was in power, and he passed the Affordable Care Act, and had these mandates that women had to have access to contraception, it was just such a big win. And there is still way too much power of government over women's reproductive rights, and women's bodies and women's choices, and it drives me insane.[..] These government officials have power to limit access and limit options. It's just a disaster.* (Pharma 05) The quote underscores the capacity of the government to shape regulations and the agenda around contraceptives, or, in a broader sense, reproductive health. As such, it becomes visible that in order to foster innovative contraceptives it needs to become a "*top priority"* for governments

(Investor 01). In line with that finding, the data further emphasizes how the priority on a political level could have a spill-over effect among further market players.

In addition, we find that politicians are not concerned or engaged in the contraceptive discussion, as made apparent through:*"Yes, and in the end, politics will have to do something. Yes, but this is a generation [...] it's never been relevant, because 80 percent of them are white old men. They've never had to deal with the issue. And now we have to really get on their nerves. Here they cant say you, on the one hand, impose women if they have an abortion and then criminalize them, and on the other hand, say yes, but contraception is not our issue at all. And that is a private matter. No, it is not a private matter. It is a public task to facilitate people to become pregnant when they want to get pregnant or maybe not at all"* (End-user 05). This quote sheds light on the responsibility seen within the government and the political agenda. It unfolds the paradox that the government has the ability to position itself strongly against abortion, however is not strongly involved in the development of new contraceptives, that could help to prevent unintend pregnancies ending in abortion. A misbalance is therefore identified between topics that affect public health, discussed on a political level. Lastly, the quote also emphasized on the gender imbalance of people in governmental positions and pins out the underrepresentation of women. This last finding is therefore also in line with the misfit of a lack of ownership, as governments are not found to be involved in shaping the contraceptive revolution.

Overall the analysis of the findings has enabled us to present the aforementioned misfits on three levels. It has drawn on the lack of voice identified by the end-users, suggested that the systemic barriers and biases the industry is subject to may hinder innovation, and lastly, has presented a lack of ownership of all market participants.

Chapter VI: Discussion

1. Summary of the results

This research set out to explore the lack of innovation in female contraceptive methods. Across interviews with end-users and representatives of the pharmaceutical industry, we have identified three themes that we have categorized as misfits, seeing that they represent barriers which hinder the contraceptive development. These misfits have been discussed in the analysis on the three following levels:

- **Micro-level:** The majority of women stated a clear dissatisfaction and all women expressed a desire for new products. The lack of satisfaction has been deducted by the high threshold to tolerance and acceptance of pain, which is not measured by the pharmaceutical industry. Nevertheless, the unmet need in terms of the high side-effect profiles of current methods was acknowledged and perceived by the pharmaceutical industry. Younger women appeared to be more informed and question the lack of evolution, whereas the elder women seemed to have come to terms with current contraceptives, but still expressed their hope for improvements for the generation to come. Further, current contraceptive methods as well as the infrastructure around it: education, OBGs, societal involvement has been described as not sufficient. The empirical analysis advanced that the young generation can pave a way for providing a voice to women on their contraceptive needs by generating more data, through the use of social media and other knowledge-sharing platforms. Therefore the misfit of a ‘lack of voice’ was identified, as women did not have a lobby to share their feelings and pains in relation to their birth control choice. The absence of the integration of women’s perceived pain in the contraceptive development process creates a barrier to innovation.
- **Meso-level:** The private industry appeared to be fragmented by systemic processes, and to be driven by economic profit, in particular for publicly-traded companies. Thus, the constant drive for profit has been identified as impacting scientific creativity in coming up with new birth control options. Further the condition that contraceptives are administered to healthy women added an additional complexity layer to the already manifold process of drug development. Additionally, the data outlined a perceived saturation of the market which lowered the incentive to invest in research for new products and rather suggested a tendency towards incremental contraceptive innovation. Lastly, the analysis made it evident that the company's strategic goals, the individual agenda-setting, gender-balance among

decision-makers as well as unconscious bias hampered decision-making that could strengthen NPD in female contraception. As such, the misfit of the ‘systemic barriers and biases’ has been identified to draw back on innovation.

- **Macro-level:** On a macro level several barriers have been identified that form the misfit of ‘the lack of ownership’. Firstly, a connection between the little funding and innovation has been established. It became apparent that more funding in the contraceptive field would yield innovation. Secondly, the reimbursement system, which is steered by the government in a lot of countries, has been depicted as a hindrance to innovation due to the fact that it only allows for better reimbursement policies when the added value of a new birth control method can be proven. Further on, the analysis pointed out that the fragmentation of the money streams resulted in skewed cost-benefit outcomes for the involved entities. Hence, players involved were funding one specific part of the drug development process, thus not enabling transparency or ownership-taking. Lastly, the role of the government has been presented as crucial. The results showed that contraceptives are not part of the political agenda and that it is a topic where no awareness is spread. Thus, all of the aforementioned barriers determine the misfit of ‘the lack of ownership’, which suggests that no stakeholder is taking on the responsibility of being fully involved in the development of new birth control methods.

In order to assess the reasons behind a lack of innovation in female contraception, the following chapter discusses the theoretical contributions and implications of the above stated results. As mentioned, each of these three observational units is depicted by a misfit. Due to the fact that all three levels build the system of contraceptive development, the levels are reciprocal, co-dependent and intertwined. Therefore the identified misfits can not be discussed in isolation and should be investigated within the embedded system. In the coming chapter, we aim to challenge the relationship between the levels and investigate if interactions amongst those would enable to drive innovation in female contraception.

The discussion will assess the findings in comparison to previous literature in order to answer the research question accordingly. We bring forward unique findings that align with previous contributions to theories around innovation and the drug development process. However, our findings also challenge some of the already existing theories and reveal that some aspects of previous studies are not specific to the case of contraceptives only. In addition, we will reflect on the applied methodology, before concluding by giving an answer to our research questions. Lastly we will outline implications for research and practice.

2. Discussion of the findings in relation to previous contributions

2.1. The challenge of defining the value of new innovative female contraceptives

In a first part, hindering factors to contraceptive development will be discussed, by taking into account end-users, the industry and institutional views on the concept of value in birth control.

2.1.1. Need for new methods

Our empirical data suggested that women have a desire for new and better products. Despite the fact that the literature about satisfaction with modern contraceptives is scarce, some previous studies show that there is a need for new methods due to side effect profiles, inconvenience and medical concerns of the existing products (Callahan, 2020). Our results confirm this and expand these findings by pointing out that in particular, the wish for non-hormonal and non-invasive methods strikes in the sample population that we interviewed. These findings are in line with research that advocates for a contraceptive revolution and that the development of non-hormonal contraceptives is crucial in order to increase a variety of available options for women (Anderson et al., 2019; Hemmerling et al., 2020; Mastroianni et al., 1990). Further on, we have identified that especially young women in our sample are demanding better contraceptives. Opposed to that, women above the age of 30, seemed to have come to terms and accepted to choose amongst the existing contraceptives. The desire for new contraceptives was however expressed for their children. These generational differences have not been presented in previous research with relation to gaining knowledge on contraceptives.

2.1.2. Patient involvement

Further, the overall misfit of the ‘lack of voice’ and lobby of women to share their perception on contraception has been established in the analysis. The identified desire for new products results in the fact that there should be an emphasis on a two-sided discussion channel, where a voice is given to end-users to share their pain, questions and desires on new contraceptive development. As pointed out by Loewe in prior studies, building sustainable communication channels with users (patients) would enable the alignment of the expectations of drug users (Lowe et al., 2016). Put in perspective the results present a lack of understanding of the patient journey from the industry’s perspective. The trend to align pharmaceutical products with patients expectations empowers the patient by ensuring his/her needs are met. Further, moving away from the linear model in the industry to include users' feedback is seen as crucial in the innovation process (Smith & Boon, 2008). The industry needs to prove the value of their methods in relation to the outcomes

experienced by the users (Lowe et al., 2016). Thus, by receiving feedback on women's contraceptive journey and involving patients throughout the process would enable the creation of a system where the user is placed at the center.

2.1.3. The dimension of pain

Moreover, dissatisfaction was assessed as women were continuing to use birth control methods, despite their dissatisfaction and built up a tolerance to the pain caused by side-effects. Previous research about satisfaction in contraceptives refer to the physical and psychological harm experienced by users through side-effects and put forward the deficiencies of the intake (Clealand, 2019). The continuation despite side-effects because of the promise of safety has also been identified in precedent research (Fatizadeh et al., 2011). For most users in our sample population, a high safety profile is the most important factor in choosing a birth control method, which aligns to previous studies that refer to safety as being the crucial element to pregnancy preventive options (Grady et al.,1999). Other studies assess the discontinuation of birth control methods because of side effects and health concerns (Sedgh et al., 2016; Callhan et al., 2020). Further the results delineate that 'one size doesn't fit all' when it comes to contraceptives as women's own perception on suffering varies for every person as also studied by Mastroianni et al., (1990). Thus, our results confirm previous contributions on dissatisfaction with modern contraceptive methods.

In addition to what has been previously researched, we have identified that dissatisfaction is closely related to a lack of the assessment of pain. Pain can be seen as '*whatever the experiencing person says it does'* and plays an important role in one's perceived quality of life (Kumar & Elvarasi, 2016). Thus, we assume that tackling the issue of pain in birth control methods would significantly improve women's quality of life. As presented in the results, many of the interviewed participants pointed out the pain of insertion with LARCs. Others emphasized on the side-effects that increased their menstrual pain or had constant bleedings, for some it provoked headaches, fatigue and others experienced heavy psychological side-effects. The wide-range of suffering due to contraception was often downplayed and tolerated by the users. The normalization of pain was expressed when women suggested that they learnt to deal with the side-effects as they have no alternative options. The normalization of pain appeared to be deeply rooted, displayed by the sample questioning the efficacy of the methods if they would not feel any discomfort with it. Thus, the discomfort by using contraception is not only normalized it is deeply internalized and perceived as an indicator of security. This, in turn, indicates a social construct linking pain and safety reinforced by society.

Pain is overseen because it is generally normalized in women's health and women do not have a channel to communicate the extent of their suffering. This finding was suggested by the fact that many women did not feel comfortable with their gynecologist or felt ill consulted. As such, we find that this setting allows women to share their felt pain only to a limited extent with their gynecologists, and on top of that, have no means to share it with the pharmaceutical industry. This finding is a crucial contribution in the contraceptive field, as pain is questioned with other types of medication. One could assume that women are cautious to complain about the felt pain from side-effects, because of a sense of gratitude to have the ability to prevent pregnancies, which other generations did not have. On top of that, acceptance to pain may come more naturally in women's health, as reproductive health, menstruation and giving birth are all related to pain and discomfort. As such acceptance to pain in childbirth for instance is unique as it is more easily accepted than other types of pain and perceived as necessary to give new life (Loewe, 2002). However, the results of our research challenge this perception with a division between age groups. As such young women in the interviewed sample tend to be less tolerant to the felt pain and more engaged towards making a change in contraceptive products, whereas their older counterparts, are more accepting in dealing with pain in contraception. This may be due to the fact that they have accumulated more experiences and some of them even experienced childbirth.

Even though the pharmaceutical industry is normalizing pain, the empirical analysis has asserted that the industry is aware of the unmet need in female contraceptives. The acknowledgment of the unmet need isn't to the best of our knowledge, stated as such in previous contributions, rather the cessation of investment in female contraception after the late 2000 is mentioned (Calhan et al., 2020). However, the analysis suggests that if the industry would be aware of the dimensions of pain, the unmet need would be recognized as very urgent, and could set incentives to overcome the identified issue of '*the healthy women*' argument in contraceptives by designing new ways of preclinical and clinical trials. Thus, placing a measurement of the felt pain from contraception is crucial to shed light on the magnitude of suffering and incentivize the pharmaceutical industry to overcome the industry barriers. This finding too, is an addition to previous satisfaction studies and assessment tools for birth control, such as the ORTHO BC-SAT, discussed in Chapter I of this paper, where complaints and feelings on the amount of suffering are not taken into account (Colwell et al., 2006). Re-defining the concept of value in contraception, by giving a central role to pain in patient-reported outcomes would enable to capture the real views women have on contraception. As in previous contributions, understanding what brings value to a patient and placing her/his needs at the center has become a benchmark in healthcare (Porter, 2012). Additionally, pharmaceutical manufacturers wish to capture feedback on the perceived value for

users (Shikiar & Rentz, 2004). As such, our research adds on to these contributions by adding the dimension of pain measurement to the definition of value.

2.1.4. Pain and Reimbursement

Furthermore, the reimbursement system is a drawback to innovation as from a payer's perspective (reimbursement), the pain experienced by the users is normalized as well. Thus, our findings on adding a measurement of pain also applies to the healthcare system, with a need to show what contributions a better birth control method, with less side effects can bring. This aligns with one classification of innovation, emphasizing that in order for an innovation to be called as such, it needs to have clear benefit in comparison to the current method (Kelly, 2017). Even though fertility planning has provided an undebatable advancement in helping to lift women out of poverty and attain a higher educational status (Liu & Raftery, 2020), our findings suggest that the side-effects and pain felt from contraceptive use can also have an impact on women's ability to contribute to the overall economy and their surrounding. Thus, we consider that irregular bleeding, increased menstrual pain or future health concerns to name a few, have a huge effect on how efficient a woman can be in her everyday life and determine if she is able to go to work. Paradoxically, the analysis of the results presented that reimbursement systems do not redeem it necessary to add yet another contraceptive option to the market, in line with findings that advance the high efficacy profile of the existing contraceptives. Thus, the research suggests that value-based reimbursement systems are a positive trend for contraception, if the concept of value would incorporate the dimension of pain. In line with Porter's approach to provide value for the patient, value-based reimbursement encompasses the need to recognize value over volume (Saleh et al., 2016).

2.1.5. Desire for more education and exchange among women

Moreover, the empirical data implies that all women, no matter which age group they belong to, have a desire for better education around available contraceptives to be more aware of possible options and know who to address in this regard. The misinformation on contraception, as well as the need for more counselling of modern contraceptives to allow women to make an informed choice aligns with previous research (Lopes da Silva-Felho et al., 2016; Nielsen et al, 2012). A facilitator for fostering innovation is embodied through social media as an exchange and educational platform by the interviewed sample. Through our analysis we put forward that as long as women do not have the means to communicate their suffering, new developments in the field will not be steered as currently the pain is normalized by the industry. Not having a platform where to discuss issues and not being able to state one's expectations with a product and the perceived

needs is hindering contraceptive innovation. The lack of voice and lobby around female contraceptives has not been identified in previous research. Further from the conducted research, we consider the young generation as being able to lead the change as they appear to want the possibility to make better informed choices and are more sceptical towards the current available female contraceptives, especially regarding the hormonal intake. Moreover, the younger generation is more open on sharing their issues over social media and reading up on things to increase their knowledge (Goodyear & Armour, 2019). As such, the research proposes that a similar development can take place in sharing one's perception and pain with birth control methods. Some digital birth control methods, such as ‘Clue’ , ‘Natural Cycles’ or ‘Inne’ are already taking part in collecting data on women’s reproductive cycle and are informing women on how their own reproductive health works. Through the conducted interviews, we emanate the need to convince more women to talk about their pain in order to generate data. The evaluation of that data, could provide the means to come up with disruptive products, maybe even in the non-hormonal area, by presenting the real extent of the unmet need when taking pain into account. Further the socially constructed link between pain and safety could be scrutinized and disrupted.

2.2. Theoretical contributions I

Overall the research aligns with most previous contributions on the need for new contraceptive products. Through the exploration of end-users and industry experts' knowledge on contraceptives, we have identified several factors that are an addition to the existing literature. We therefore propose to include a measurement of pain both in the drug development process as well as in the creation of reimbursement policies, to capture the real value in women’s eyes. In order to do that, patient involvement is necessary. Further we have identified the dismissal of pain as lack of voice and lobby from the end-users. The ignorance about the topic of pain can be mitigated by empowering women through knowledge exchange. We find that the young generation can play a role in sharing knowledge and generating data on pain and contraceptive use through social media platforms and therefore challenge the internalized link between safety and pain.

2.3. Systematic barriers and bias within the pharmaceutical industry

The second part of this section will address the challenges perceived by the pharmaceutical industry to innovate in the contraceptive field and will therefore answer our second sub-research question.

2.3.1. R&D

Firstly, one of the barriers declared by previous research is the high cost of R&D (Callahan et al., 2020). These costs are attributed to Eroom's-law and the “productivity crisis”, which implies that despite improvements in technology drug discovery is slowing down and becoming more expensive because of the multiple regulatory approvals (Hall, 2018). This aligns with our findings from the industry that suggest that the high regulatory barriers and costs resulted in hindering innovation. However in the analysis, we find that the mentioned innovation crisis appears to be an industry trend rather than a specific circumstance for contraceptive development (PWC, 2020).

2.3.2. Existing and effective products

Further, previous studies argue for the existence of many contraceptives that are effective and cheap as a reason that hinders innovation (Callahan et al., 2020). Firstly, our research confirms the availability of two female contraceptive concepts, hormonal and copper, which both provide a high perfect-use efficacy ratio. As such, undoubtedly hormonal contraceptives have a very high safety profile when in perfect use, but the normal use of those products considerably decrease the efficacy whilst coming along with a lot of side-effects (Trussel, 2013). Therefore, the findings stress the necessity of more transparency within research and practice when talking about safety profiles. In addition, we want to discuss how the side-effect profile and the efficacy should be balanced. With the presumption that unintended pregnancies in HIC are mainly driven by dissatisfaction because of side-effects, the argument of the high safety profile is questioned. As such, the hypothesis can be advanced, that a decrease in efficacy with improvement in side-effects could lower the percentage of unintended pregnancies. This is seen in the young generation being more inclined towards non-hormonal options and are willing to take the trade-off into account: a higher risk of becoming pregnant but not having to deal with potential side-effects.

Secondly, our findings further unfold that small improvements are happening around hormonal contraceptives, rather than disruptive innovation, which is defined by the “Better than the Beatles problem” disclosed in the introduction (Ringel et al., 2020; Scannell et al., 2016). In line with our findings, the high efficacy of the affordable and low-price segment products strengthens the industry perception that they “solved” the problem of preventing pregnancies. Thus, the industry can therefore not be held accountable for coming up with a new method (Callahan et al., 2020). An insightful comparison can be drawn upon the case of Viagra, that was first introduced on the market to treat erectile dysfunction. While a cure was found in 1998, that became the fastest selling drug on the market, Viagra as a low-price drug is still researched and outnumbers studies

within womens health by five times (Slawson, 2019). On the other hand, with female contraceptive methods, innovations are not considered necessary due to the low-price segment even though it affects half of the world's population. As such, we challenge that Callhan's argument of low-price drugs is a sufficient reason to name it as a barrier of innovation.

2.3.3. The paradox of safety and a lack of representation

Further, the liability issues in dealing with a healthy population combined with demanding clinical trials and regulations required to comply with are highlighted as barriers and can be confirmed by our study (Callahan et al., 2020; HMA, 2014). However, this barrier can also be observed within other therapeutic areas like vaccines (Xue & Ouellette, 2020).

The presence of high regulatory hurdles and the treatment of a healthy population within other areas like vaccines, where a continuous allocation of resources can be seen, fosters scrutiny on the differentiation of contraceptives. The findings question if the regulatory barriers are a reason enough why innovation isn't taking place and display the "healthy individual" argument as an excuse. As such, several informants underline the safety argument in testing novel drugs in women as it can affect not only them, but potentially also their future children. The set priority on safety reveals an established and accepted double-standard where advancing the argument of protecting women, is in return hindering the initiation of scientific research to develop suiting therapeutics for women. Shown in the findings, the reluctance of advancement already appears in the preclinical phase by the lack of good animal models that resemble the female reproductive system. The described phenomenon is reflected in the "medical-gender gap", that refers to the underrepresentation of women in clinical trials (Del Carmen et al., 2015; Phelan et al,, 2016). In retrospect, this drives the lack of female data and the inadequate representation of women.

The excuse of the 'healthy women' is further underlined as not taking ownership to develop sustainable and suiting ways to test novel therapeutics on healthy women, by this study. To specify, the argument is seen as invalid, as other preventive treatment areas face the same issues in needing to pass regulatory barriers and demanding clinical trials. As such, within the conducted interviews comparisons were drawn to the two following cases: vaccines and orphan diseases. Vaccines are used as a comparison caused by the preventative nature of the drug. While orphan diseases are mentioned because of the lack of representation. Both therapeutic areas are part of a "public imperative", that implies the need for indemnification by public health interventions and is seen as essential in changing the burden of diseases (The Lancet, 2017). The fact that a therapeutic area which affects half of the population and the reproduction of the whole society is

compared to orphan disease is a finding in itself that emphasizes the lack of representation and ownership in the case of female contraceptives.

2.3.4. The pharmaceutical industry integrated in the capitalistic system

Through our results we have identified a further addition in comparison to past research in the significance of the financial returns. As such, our findings suggest that the industry relies on the existence of a business case and is driven by profit return, in particular for publicly traded companies, which are even more bound to returning profit to their investors and stakeholders. Especially the early drug discovery phase, detailed commercial planning is seen as a hindrance to innovation. This has been studied previously in other medical fields and diagnosed as the 'fuzzy front end' (FFE), which encompasses the period of time when a new product idea is first considered. It is often characterized as the key decision-making process in many large corporations (Robbins & O'Gorman, 2015; Owens et al., 2015). In line with prior research, we thus underline the early need for assessing the ROI as a significant barrier to innovate in the field of contraceptives. Nevertheless, the research acknowledges the need of a business case to assess products and help determine their value and prioritisation. Therefore, our findings suggest that in an ideal world, reducing the weight of the business case early in the drug development process (Stage 1) would allow for more innovation. Moreover, previous literature advances that economic pressure in the pharmaceutical industry negatively correlates to innovative drug discovery (Scannell et al., 2016). Thus, as presented in our findings, the sole focus on profit, that the pharmaceutical is subject to in order to survive, is 'killing the science', in particular when the focus on ROI is placed early on in the drug development process.

2.3.5. Bias within decision-making nurtured through complexity

Lastly, our findings have given new insights into the lack of contraceptive development in relation to the industry's bias in making decisions. Thus, the study presents that the "who" and "how" of decision-making has an impact on the designated scientific targets in the industry. As such the gender imbalance in leadership positions is seen as a bias in setting a contraceptive focused agenda, which is a reason that hinders innovation.

Another decision-making bias is visible in determining a research strategy that involves the research of contraceptives. Previous research has assessed that scientists tend to overestimate their own research and prioritize projects in areas they are experts in. The latter bias is discussed in existing research as the "basic-brute-force-bias", which is defined in the introduction of this

paper and in line with the ‘individual agenda setting’ outlined in the results (Scannell et al., 2016). As such, a bias is seen in the research, as investments in the contraceptive field are so little that few scientists within the pharmaceutical industry are presumably representing the reproductive areas nowadays. Thus “the basic brute force bias” does not appear to be boosting the field of contraception.

In order to act against these existing biases stemming both from the scientists and from the gender imbalance, our study stresses the importance of diversity and structured processes in decision-making (Clowrick et al., 2012; Roobins & O’Gormans). The findings also present that most decisions in the pharmaceutical management are still based solely on intuition and individual experience. Existing literature in the field of decision-making suggests that when facing several options to decide in between, making an evaluation based on data, helps in reasoning with sense instead of personal instinct (Bonabeau, 2008). As such, it could be recommended that R&D decision-making in pharmaceutical companies should be revisited to avoid personal bias in setting scientific research targets. This is of particular importance, as in the early drug discovery stages, scientific committees face approximately 250-500 different compounds for which they have to decide if research will be pursued (Rees, 2011). As outlined in Chapter 3, in the R&D stage, two types of errors can be made, either by terminating the compounds too early or too late (Bonabeau et al., 2008). Both of these errors lead to sunk costs. The lack of practical knowledge and example cases on how to pursue the different stages within contraception development indicate that the first error, stopping the project too early, is very likely to happen. Thus, the necessity to systemize and structure decision-making is striking. Therefore, approaches measuring the variance of go/no-go decisions and if a high variance is obtained external advice is seeked, could be applied.

Further, establishing domains of validity which indicate the predictive value of new compounds would allow for cross-comparison among compounds and weaken intuition (Scannell et al., 2016; Cowlrick et al., 2011). Because of the aforementioned biases and barriers in decision-making, it seems unlikely that female contraceptives are prone to be placed as a scientific target in the near future. Future research within the field of decision-making is necessary and would help to overcome these biases in order to enable the placement of contraceptives on top of the research agenda.

2.4. Theoretical contributions II

To sum up, the data analysis has enabled us to confirm previous contributions, but also to challenge these and supplement new findings. Overall the results presented that the industry is

characterized by many regulatory and process barriers that can hinder the innovation process at large. Callhans main lines of argumentation, relying on four barriers, have been identified as general industry barriers rather than specific to female contraception. Instead we have identified supplementary findings that are seen as a barrier to innovate. For instance, the lack of animal models that can imitate the female reproductive system are one barrier. With regards to the assertion of the existence of many effective contraceptives, the data presents that other therapeutic fields continue their advancements in research in spite of the existence of other drugs. Further, the liability concerns of treating a healthy population have been confirmed as a major risk for pharmaceutical companies to innovate. However, the research challenges this perspective by advancing that the pharmaceutical industry may instrumentalize the past litigation cases and therefore limits the initiation of scientific research in contraception. Thus, it contributes to the problem of the medical gender gap, as better contraceptives will not be developed. Additionally, the requirement of a business case at an early-stage of the drug-development process has been presented as detrimental to advancing innovation in contraception. Lastly, our research has contributed by bringing forward the role of decision-making biases as a main hindrance to innovation, as there is an unequal gender distribution as well as a tendency to research specific fields of interest to scientists.

2.5. The need for more transparency, collaboration and common efforts

Lastly, the identified 'lack of responsibility' of the involved market players is going to be assessed in relation to previous literature.

2.5.1. The hidden market failure driven by the fragmented healthcare system

The findings from the study suggest that investing more money in the scientific research and drug development process would have the potential to result in a contraceptive innovation. As such, our results exemplify this by comparing contraceptives to other preventive areas such as vaccines, where an increase in funding and the involvement of public-private partnerships has resulted in innovation, as seen with the Covid-19 vaccines (Xue & Ouelette, 2020). This finding has not been mentioned in previous studies with regards to contraception. Therefore, it unfolds that the lack of innovation within female contraception is rather a question of funding than a question of scientific possibilities.

However, the decentralization and fragmentation of the drug development process questions which entities are responsible for providing the required funding. This has been assessed in our results by the lack of ownership in the contraceptive development system. The decentralization and

fragmentation of the pharmaceutical industry as well as the healthcare system is discussed extensively in previous research (Khanna, 2012; Lowman et al., 2012). As such, it appears that fragmentation and a lack of transparency is hindering ownership and therefore hampers innovation within female contraception. Further our results distinguished a market failure. In the light of liberal market theory, one could assume that the liberal market dynamics regulate the supply and demand of contraceptives independently (Buchanan, 1998). However, the fragmentation and the lack of ownership hinder direct communication between supply and demand and therefore undermine the market failure. In accordance with market theory, the presence of a market failure calls for governmental intervention and action (ibid.). The call for governmental engagement is strengthened by studies undermining that research within preventive therapeutic areas is crucial in the improvement of global health, the alleviation of the healthcare system and the reduction of cost burdens (Grossman et al., 2016). For the greater good of developing better contraceptives and in order to cut costs, the government could take the responsibility to co-finance R&D; or create a framework for cross-collaboration among other players in order to enable better communication between supply and demand. The collaboration should result in strategies on how to share financial commitment, liability-risk as well as research funding in order to drive innovation. The distinguished market failure has not been pointed out previously and should be additionally studied in the context of a government mandate on contraceptives.

Further, the role of non-profit organizations is highlighted. Previous research has identified that efforts to underline the contraceptive agenda are mainly driven by non-profit organisations and philanthropic foundations (Callahan et al., 2020). Thus, even if the nonprofit sector has been steering the agenda of contraceptives, our findings display that their involvement imposed an additional layer of complexity. The layer of complexity is built upon the NGO's strong focus on LMIC. As such, their focus relies mainly on providing access to contraceptives rather than assessing satisfaction and developing new contraceptives for HICs. As stated in the introduction, the unintended pregnancy rate in Europe (43%) rather appears to be an active choice than a lack of access (Bearak et al., 2020). Nevertheless, this presents a mismatch on the current perspective of contraceptive development, as the non-profit sector is perceived as being the leading force behind the research and main investor in new contraceptives. This depicts the lack of ownership presented in the results, as it shows how no player in the contraceptive innovation space is currently taking on the responsibility. Further, there seems to be a lack of transparency on what aspects of contraceptive development NGOs are responsible for. Therefore, Callhan's view on the investment of NGOs in the contraceptive development field can be undermined by the findings advanced through the discussion with industry experts in our research.

2.5.2. Partnerships and the call for a public health imperative

Further, previous literature has identified a strategy to act on the limited funding options of the involved market players by investing into cross-sectional collaborations (Callahan et al., 2020). Our results align with previous literature that cross-sectional collaborations and new partnerships between governments, NGOs, academia and the pharmaceutical industry are necessary to share the responsibility and the financial hazards of innovation (Callahan et al., 2020). However, our findings additionally indicate that in order to build sustainable partnerships a common understanding of the importance of new contraceptive methods as well as an ethical responsibility to act is required. Based on that, for the greater good of contraceptive development, the government could intervene. Our results emphasize that governmental intervention has the capacity to shape an agenda that takes innovation in female contraception into account. As such, the implication of a successful political agenda-setting is reflected in cases, where the governments have set a public health imperative, meaning that a specific public health issue is placed as a priority and support and investment is given in order to reduce the burden. This has been the case with HIV for instance, where the government has been funding and launching campaigns to help prevention and inform people of the risks of HIV. Campaigns on the use of condoms have greatly contributed in rising awareness and overcoming the discomfort to address an intimate topic that can be related to shame (Piot et al., 2017). Through large funding campaigns, the case of HIV was considered as a public health imperative. A public imperative can be defined as “a call for sustained and coordinated action initiated by the government” and is known among others in the areas of epilepsy, vaccines and women's health (WHO, 2019; Malone&Hinman, 2003). With regard to contraceptives, the findings display the positive effects of ensuring women’s health and safety by placing innovation in birth control on the political agenda.

2.5.3. Government and reimbursement

Lastly, national governmental authorities have a right to exercise price control through defined processes and regulations during the market authorization period of a new pharmaceutical product. Therefore, they are capable of shaping reimbursement possibilities which have long-term ramifications for the whole contraceptive development process. (WHO, 2016; OECD, 2008). In line with the aforementioned literature, and, as discussed in the beginning of this section the perceived value of a new pharmaceutical product is guiding price setting by governmental entities. The perceived added value is strongly influenced by the measurement of existing methods which was discussed further above. If the reimbursement does not acknowledge the added value of a new contraceptive, the business case for a given pharmaceutical company will be hard to prove.

However, as previously mentioned in the results, the business case is the key step in defining if a product will be further researched. As such, the findings suggest that the government plays a role in subsidizing or enabling reimbursement regulations that facilitate the development of new contraceptive methods. Co-investment or cost-sharing possibilities for example, would help to make a case where the added value of a new contraceptive could be proven, whilst being profitable enough for the pharmaceutical industry to have an interest in contributing to its R&D. The need to prove that a specific medicine is better than an already existent one has been studied in prior literature (WHO, 2016; OECD, 2008). Nonetheless, our contributions emphasize the importance of the reimbursement system as a crucial force to incentivise future research and to help mitigate the risks and barriers associated with NPD in the pharmaceutical industry.

2.6. Theoretical contributions III

All in all, the last section of this discussion has put forward the need for common efforts of all the levels mentioned in the results section. All of these are seen as interdependent. In particular the role of the government has been advanced in creating a call for a public health imperative, in order to enable a reimbursement system that favours the development of new contraceptive methods. Furthermore, our findings have in addition to previous ones, detected a market failure, where the needs of the women are not reflected in the contraceptive products that are available on the market. In addition, the fragmentation of the market space allows for a lack of ownership, which results in the fact that no entity is fully responsible for fostering contraceptive development. These are all findings that have not been studied previously and that would require further investigation.

2.7. The vicious circle of innovation in contraception in an utopian world

This thesis has suggested results on different societal levels by analysing the perception of contraceptives from an end-users perspective, the barriers to develop those by the industry and lastly the need to incorporate governmental action was identified. In the discussion the need for interaction of the different levels has been suggested. By coming back to the assessment of value and the earlier outlined importance of incorporating pain, a vicious circle can be established. The illustrated figure below therefore presents the three different actors: End-user, the pharmaceutical industry and the government. The three misfits outlined in the results are illustrated as thunderbolts and should be interpreted as a lack of mutual perception between entities. The end-users position is highlighted by the need of suiting instruments assessing their pain, needs and desires. The government is misguided through the high use of contraception and the lack of lobby within the political sphere and therefore does not confirm an added value by new contraceptive methods. This resolves in limited reimbursement opportunities which hampers the business case for the

pharmaceutical company and limits their efforts of allocating resources through market research. Therefore market research stagnates on the surface and the vicious circle continues.

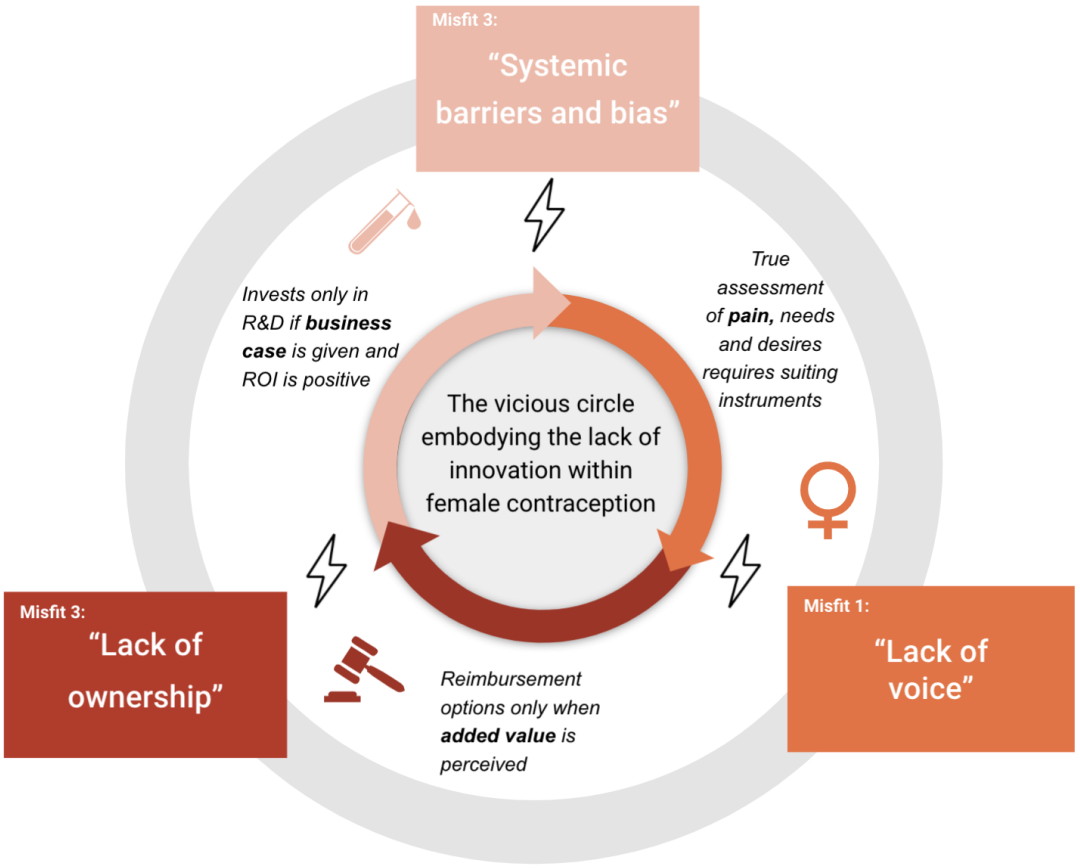

Figure 6: The vicious circle of contraceptives in a simplified world

3. Evaluation of research strategy and methods

The aim of this section is to discuss the limitations and strength of the applied research methods and to assess the influence of these issues on our findings.

The strengths of our study included the abductive practice facilitating us to transition continuously between the collected data, our previous perception as well as our background section (Saunders et al., 2019). Further, the data triangulation intertwining the perspectives of both target groups enabled us to follow a holistic study design, by investigating the perceived need of end-users and industry experts (Khan, 2014; Brantlinger et al., 2005). By assessing the research question from

two ‘different lenses' the study design displayed how the two perspectives align or contradict. Moreover the diversity of the recruited sample population in both target groups are distinguished as a strength. This can be seen in the distribution of age, relationship status, children, profession and contraceptive methods in the target group of the end-users as well as in the variety of backgrounds in our second target group, the industry experts, working with life science investment, in the pharmaceutical industry or philanthropy. In addition the semi-structured interviews allowed us to address the sensitivity of the subject to obtain rich nuances through proximity, flexibility as well as providing our end-users a safe environment (Saunders et al., 2019). Lastly, all of the interviews were conducted simultaneously by both researchers. This approach enabled us to mitigate possible biases through the use of a reflexive approach. Reflexivity was undertaken by discussing the interviews once conducted between each other but also with our supervisors, further the use of a hypothesis tracker as described in the methodology section was ensured, as well as reviewing the codebook on several occasions. It allowed us to be detached from our findings and is therefore seen as a strength in the composition of the study.

The weaknesses of the applied study design is reflected in the limited sample size of the semi-structured interviews. Thus, reliability could have been strengthened by enlarging the assessed sample size and include further demographic attributes (Saunders et al., 2019). Further, validity could have been improved by applying a mixed method strategy in combining different qualitative approaches, or quantitative strategies like surveys (ibid.). Looking in retrospect, a large quantitative survey strategy assessing the gender balance among scientific drug discovery committees and the application of decision tools, would have strengthened the relationship between innovative power and decision-making. However, this was outside of the scope of this thesis and resulted as one of our findings.

Limitations were identified in the sampling of the two target groups. It has to be noted that the first population sample, the end-users, who were willing to participate in an interview on contraceptive perception and use, were expected to be more open-minded and aware about the topic. As presented in the sample description half of the younger women (n=5) were recruited over a social media platform for activists on contraceptive rights. Further, a few women had a medical background (n=3). While the latter is presumed to have little influence, because the medical background can not be linked to being an expert in contraceptives, the recruited activist could have biased the results more firmly. As such, the findings may be biased in a sense that these women in our sample feel strongly about the need for new birth control options. However, in comparison to the younger women not recruited from the activist group distinct differences were not identified.

Hence, the bias of being an “activist” had a limited effect on our results. Further, due to the limited scope of the research, 20 women were interviewed, all of them were German with the exception of one participant who originated from Australia, but has lived in Germany for several years. The exception of one non-German was not perceived to have an effect on the results. The majority of the sample had attained higher education. Hence, the level of education reflects that all women in the sample were taught about sexual education to some extent in their academic path. This results in the fact that the interviewed women were aware of different contraceptive options and grew up in a society where the use of birth control is accepted and encouraged. Thus the findings mirror women living in HIC and can not be applied to the global south.

Further, in light of the second research question, drawbacks are identified by the fact that one NGO and one venture capital are part of the sample population that addresses and analyzes the pharmaceutical industry’s positioning on contraceptive development. Thus, they have an external view on the operations of the pharmaceutical industry. The remaining participants are representatives of bigger pharmaceutical companies that are, or were active in the women’s health field or contraceptive area. Two of the interviewees were additionally gynecologists on top of their business functions. As such, they may be inclined to protect the interest of the given entity they represent. This resulted in statements that either strengthened their engagements within contraceptives or if little engagement of a given company was visible, reasons were highlighted to underscore why the company can not engage within the area. Therefore, this inclination towards protecting the strategic decision of their company is reflected as having an influence on our findings on the importance of contraceptives within the industry.

Another condition has to be pointed out, as of the six interviewed parties, four were women and two men. Therefore, their contributions involved a two-folded perspective: first as a representative of the industry, and secondly as a woman, partner or father of someone with contraceptive needs. Although the questions of the interview did not focus on their perspective as women, partner or father or mother, their position could have influenced their responses as representatives of the industry. Thus the results were affected through stronger attachment which were mirrored in a mix of industry knowledge and personal opinion in their answers. In the analysis of our data, women seem to have stronger opinions and identification with the topic.

On the basis of the discussed strengths and weaknesses, the applied mono research strategy built upon grounded theory appears to have succeeded in collecting rich data, including different perspectives within a complex theme. The 20 conducted interviews within the target group of

women have not provided distinct differences within the assessed demographic characteristics such as relationship status, religion or profession. Other characteristics such as living area or socioeconomic status were not assessed. However, the study design allowed us to reach saturation and to identify findings that were homogeneous across the data (Kvale, 2016). The acknowledged limitations of the study declare a large potential for other approaches and methods to contribute new insights which generate additional academic insights and practical implications and may reinforce validity.

4. Conclusion

This study took departure from the notion of the high rates of unintended pregnancies in Europe despite the availability of safe and effective birth control options. In order to understand this mismatch, the aim of this thesis was to provide an answer to the leading research question, investigating the reasons behind the lack of innovation in female contraception. Further, the study set out to explore two subordinate questions: firstly, the perception of end-users on current birth control options was assessed as well as if a potential lack of satisfaction resulted in fostering the need for innovation. Secondly, the barriers of the pharmaceutical industry to innovate female birth control options were analysed.

We found that end-users' perception of the available contraceptives are malcontentment with side-effects despite the tolerance of those, a trend towards preferences of non-hormonal methods and a wish for non-invasive methods, demonstrating a high degree of dissatisfaction. As such, the research has identified new contraceptive development as a priority area to innovate. However, the lack of satisfaction has not resulted in fostering innovation despite the fact that the pharmaceutical industry acknowledges the unmet need of contraception. Our findings suggest that on an end-user level, the real need is not perceived as women lack a voice to communicate their pain. As such the extent of the pain is not known and therefore normalized by both, the industry and the end-users, which stagnates innovation in the field.

In light of the second research question, we find that the pharmaceutical industry is subject to several barriers that hinders the drug-development process in female contraceptives. Barriers recognized as contraceptive specific are the lack of animal models that can mimic the female reproductive system, a difficult litigation past, manifested in high risks by testing a healthy population. Further a lack of funding directed towards scientific research in female contraception driven by the limited prospects of a positive return on investment are advanced. On top of that, biases in the decision-making process due to gender imbalance and strategic agenda-setting have

been identified. Lastly, a lack of ownership and transparency of all actors involved in developing new birth control methods are presented in our findings.

In spite of the fact that it is unlikely that unintended pregnancies will disappear completely as it is assumed that some cultural stigma towards contraception will always persist; and the perfect use never reached by all women, the need to tackle the 43% rate of unplanned pregnancies in Europe has never been greater. We therefore conclude that there is a need for new birth control methods and that light should be shed on ways to facilitate birth control innovations for the pharmaceutical industry. Lastly, we highlight the fact that women's voices should be heard to express their demands on modern birth control options and move from tolerance to satisfaction.

5. Implications for research and practice

This paper assessed the lack of innovation in the female contraceptive field and has derived (1) a lack of end-users' voice in sharing their perception of pain, (2) systemic industry barriers and bias and (3) a market failure driven by a lack of ownership and transparency, as misfits that are reasons for the hindrance of innovation. Thus, implications on how to mitigate the aforementioned misfits will be presented. In light of the limited scope of the research, some propositions that evolved over the course of the study are advanced for future research suggestions.

5.1. Implications for practice

In order to counter the dissatisfaction with current contraceptive methods and facilitate innovation in the area, our research argues that innovation policies should address the market failure by involving policy makers in increasing funding and fostering public-private partnerships. Six main areas of consideration have been identified to act against the misfits of contraceptive development.

Implication: Pain as a measure of value

Firstly, the research suggests incorporating a measurement of pain with birth control methods on all steps of the market research to perceive real patient-feedback and move away from normalizing pain in women’s health. Transforming the linear model of the industry towards an approach based on patient-inclusion would foster a faster change. Implementing a sustainable communication channel with patients and users would break the traditional industry approach to R&D and foster innovation. Similarly, a pain index needs to be accounted for in a value-based reimbursement system.

Implication : Financial support for female data capturing companies through PPP

Further on, recommendation is given to strengthen the already existing infrastructure of companies positioning themselves in the female health area through public-private-partnerships. By providing financial and technical resources, the reach of the companies such as "Clue" could be extended. This would allow more data to be collected and facilitate accessing women for future studies and assessments.

Implications: Public Health Imperative through agenda-setting

The government's ability to position contraceptives on a national political agenda by defining it as a public imperative may lead to countering the market failure. This governmental mandate is suggested as it could raise awareness on the topic and therefore facilitate a way for women and others to raise their voices and form a contraceptive lobby. Hence, this may lead to facilitating the creation of public-private partnerships by leveraging transparency and joining forces among women, families, OBGs, academia, the pharmaceutical industry, biotech companies, NGOs, key opinion leaders and already existing contraceptive companies.

Implication: Diversify decision-making

In order to act against biases, it is advanced that decision-making processes need to increase diversity and systematic approaches. As such, we advocate for an improved gender balance within scientific drug development committees and further suggest the inclusion of external advisors (e.g. women using contraceptives, scientists, academia). Lastly, we pledge for an increase in systematic decision-making tools which are not based on intuition but instead rely on data and economical models. With these implications we presume that decision-making would mitigate subjective views in the process and allow for steering innovation in the contraceptive field.

Implication: Mitigate the weight of the business case from FFE

In light of the above mentioned decision-making process, we suggest to decrease the importance of the business case in the early phase of the drug development process. This is proposed based on the knowledge that the development of a drug takes several years and a business case at a given point in time may not reflect the market changes until a new contraceptive is introduced on the market. Nevertheless, the need for pharmaceutical companies to provide significant profit is undeniable, therefore we advance that giving less weight to the business case in the beginning of the process and re-assessing it when closer to the market introduction would potentially foster scientific drug development. This may enable the new drug candidate to pass the first gate and

prove its potential before being systematically rejected because the commercial perspectives can not be recognized.

5.2. Implication for future research

In the latter, future research suggestions are advanced with regards to the findings suggested in this paper.

Research on online platforms and applications

In light of Goodyear & Armour' perspective social platforms could have a positive effect on empowerment and knowledge sharing. As such, it may improve the sensibilisation of pain amongst women and depict their wishes for new contraceptives. The platforms may enable women to share contraceptive expectations encompassing administration, safety, side-effect profile, duration and price. We therefore suggest that future research could assess the implementation of those platforms and the criterias needed to ensure usage and data privacy.

Research on holistic market research

Further, we identified that academic research on the topic of satisfaction with contraceptives lacks both depth and quantity. Even though some studies research the satisfaction and use amongst the existing methods, the need for new ones appears to be under researched. Based on the findings advanced in this thesis, we think that a more sophisticated approach should be taken in order to specify how side-effects and current contraception in general are perceived. We therefore suggest that future studies should evaluate the current satisfaction methods and adjust (in-depth) and extend them (quantity). As such, we suggest future research to investigate quantitative studies that include a pain index. Further, qualitative assessments are suggested as a research area to capture the real unmet need through the dimensions of suffering, the desires and the expectation on current and future contraceptives on a larger number of women.

Research on decision-making

Lastly, the study displays that the decision-making process and bias in scientific committees is a bottleneck that may be removed by including external participants and by using decision-modelling relying on the use of systematic economical models. Thus, we believe that future research should investigate the assessment and decision-making of novel ideas in a pharmaceutical drug development context with a special focus on the aforementioned FFE stage (early-stage). In particular the evaluation of a gender inclusive steering committee should be researched. Furthermore, weight should be given to the used decision-modelling in different companies to

enable the determination of a new unified and quantitative assessment tool that takes away the bias on how strategic choices are determined nowadays and eventually give further insights on how these can be improved to avoid bias.

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Appendix

Appendix A.1 Interview guide end-user

Interview Guide: End-users		
Block	**Number**	**Question**
General		
	Intro	To start we would like to ask you some demographic questions to ensure comparability and clustering.
	1	How old are you?
	2	Did you grow up in Germany?
	3	What is your confession?
	4	Do you currently have a partner?
	5	Since when?
	6	Do you have children?
	7	How many and how old are your children?
	8	Do you intend to get more?
	9	What is your profession and what is your educational background?
Social and Education		
	Intro	
	11	Tell me how and when did you learn about contraceptives?
	12	Were you taught about contraceptives by your teachers in school?
	13	If yes, thinking back, how informative and long-lasting were these learnings for you? If no, would you have wished to be taught about contraception in school?
	14	Did you talk about contraceptives with your family and friends growing up?
	15	How did it make you fell and how did it shape/influence your view on contraceptive methods today?
	16	How do you feel talking about contraceptives today?

Contraception		
	Intro	
	17	Are you sexually active? (what does it mean: benchmark once per month)
	18	Are you taking contraceptives?
	19	If yes, which contraceptive are you using?
	20	Why are you taking contraceptives?
	21	If not, why are you not taking contraceptives?
	22	How do you avoid getting pregnant then?
	23	Are you satisfied with your approach (taking or not taking)?
	24	Why, why not?
	25	What were your experiences with the different contraceptive methods?
	26	What were the reasons for changing the contraceptive?
	27	Thinking about the future, do you think you will stick to the same contraceptive method?
	optional	How safe do you consider your choice of contraception ?
	optional	How do the side effects affect/impact your daily life?
	optional	How do you finance your contraception and how do you feel about it?
	optional	How time-consuming is contraception for you?
Contact person / Prescription		
	Intro	In the next section we will ask more about the contraceptive

		methods purchasing
	28	How do you get access/prescription to your contraceptives?
	29	
	30	How long are you already at your OB GYN practice?
	31	Do you feel well consulted by your OB GYN regarding the different contraceptive methods?
	optional	Did you discuss the different side effects and intakes?
Innovation		
	Intro	In our final set of questions, we'd like to talk to you about the future of contraceptives.
	32	How do you think we can communicate these changes?
	33	Do you think we need more birth control methods on the market?
	34	Why?
	35	If yes, what would an ideal birth control method look like for you?
	36	Why are these 'ideal' contraceptive methods that you just described not visible on the market?
	37	Have you ever shared these thoughts with someone, who?
	38	How do you think we can communicate these ideas?
	39	Do you have any additional comments, something you would like to add?

Appendix A.2 Interview guide industry-experts

Interview Guide: Pharma		
Block	**Number**	**Question**
General		Intro
Block 1	**Job**	
	1	Where are you working currently?
	2	Since when?
	3	What is your position?
	4	What did your professional path look like?
	5	What is the value proposition of your company?
	6	Who are the stakeholders you are working with?
	7	Who are your competitors?
Block 2	**Women's Health/ Contraception**	
	8	How did women's health from your perspective develop in the last years?
	9	What about contraceptives?
	10	What were the biggest break-throughs the last years within women's health/contraception?
	11	Do you have a women's health department? and what is the main focus in that department?
	12	Do you have any contraceptives in your portfolio?
	13	Do you have any other contraceptives in the pipeline or in the R&D process at the moment?
	14	Why not?
	15	Is a big part of your budget dedicated to women's health?
	16	Why not?
Block 3	**Value-chain drug development**	
	Intro	Pitch value-chain process

	17	Is that drafted process different within women's health?
	18	Did the process change in recent years?
	19	Where would you locate your company within the drug development path?
	20	What are the biggest hurdles in that process?
	21	Who are the key stakeholders and players within the process of developing a new drug?
	22	Did the stakeholders change in the recent years?
	23	If yes, what do you think about the change?
	24	What are the crucial parts to foster innovation within drug development in general?
	25	Does innovation within drug development within women's health differ from other areas?
	26	If yes, why?
Block 4	**R&D**	
	27	Do you have experience within R&D investment decisions?
	28	If yes, what are the parameters leading to a positive investment decision?
	29	Who drives the drug development R&D?
	30	What are the incentives of investing into R&D?
	31	What are the requirements and resources needed to perform R&D in the most successful way?
	optional	Do you see geographical differences within pharmaceutical R&D commitment in women's health? (US/EU)
	32	Why did pharma stop their investments within female health in 2008?
	33	Why?
Block 5	**End-user**	
	34	Do you feel like the public conversation about contraceptives changed?

	35	Do you think there is an unmet need within female contraception from an end-user perspective?
	36	If yes, why?
	37	How do you address consumer needs in your product?
	38	How do you communicate with your consumers?
	39	Does a lack of satisfaction among end-users foster (a need for) innovation?
	40	How?
Block 6	**Future**	
	Intro	In our final set of questions, we'd like to talk to you about the future of contraceptives.
	41	How do you think the contraceptives market will develop in the next few years?
	42	What innovative approaches do you think will be successful?
	43	Why?
	44	What do you think future products in female contraception will look like?
	45	Why?
	46	Why is all the innovation that can currently be seen driven by small companies and others (philanthropic, NGO's) instead of big pharma?
	47	Do you think a collaboration between universities and VC or life science investment could be successful in leveraging innovative female contraception?
	48	Why, why not?
	optional	Can innovation also be driven by NGO and philanthropic engagement?
	End	

Appendix B. Coding book

Codes

Name	Description	Files	References
Current Method of Contraception		20	20
Drivers of dissatisfaction	Covers expressions of dissatisfaction with the current contraceptive method	23	78
Benefits of NO Contraception		8	17
Connection to own body		7	17
Change in contraceptive method	Experience with different contraceptive methods	9	13
Future of own contraception	Indication of following contraceptive path; indicates also satisfaction with current used methods	5	5
Disadvantage of taking Contraception		0	0
Economical		9	11
Non-physical		12	18
Side-effects	Expressions of participants regarding medical side-effects	15	42
Male contraception		14	21
Need for new methods	Expressions regarding new methods - indication about satisfaction with current available methods; one size doesn't fit all	17	64
Perception of development of contraception	Expressions if participants have the impression that there are many new products within the last years; if much has changed	18	53
The perfect contraception	Expressions about ideas and criteria of desired contraceptives and new methods as well as male contraception	15	28
Drivers of Innovation	Expressions how innovation within female contraception could be bosted	9	78

Agenda Setting	Person/Institution/Dynamics pushing that contraceptives are addressed	5	13
Ecosystem		4	17
Financial Investment		4	5
Market Research		6	25
Partnerships		6	34
Process Innovation RD		3	9
Open innovation		5	8
Potential market growth		1	1
Serendipity		3	7
Economic pressure	Covers how the liberal market system is shaping the behaviour and incentives of all market players	10	46
End of the curve		3	4
Fragmentation	Builds upon diversity of market players and decentralization of drug development but as well of the healthcare system	8	65
Better than the beatles		3	4
Incremental Innovation		3	9
Pharma		5	6
Physicians		9	11
Politics		12	19
R&D		6	23
School		4	5
Science Research		14	40
Society		15	28
Healthy Women Argument	Build upon the paradox of safety vs. risk, underrepresentation of female medical health data	5	33
Clinical Trials		6	10
Legal		4	12
Pre-Clinical		5	8

Lack of say	Captures nuances of “feeling lost”, “feeling alone”, “nobody to turn to” as well as confusion who to report discomfort	15	62
No added value - Reimbursement	Outlines the rationale of how new medical products enter the market	10	41
Benefits of contraception		28	32
Safety		10	14
Disadvantage of NO contraception		15	18
One size doesn't fit all	Covers categories regarding Individuality of desires, contraception as an intimate and personal topic	15	31
Sexual Education and Empowerment	Sexual education and empowerment Builds upon critic of sexual education provided by school, gynecologists, social structure	2	6
Family & Friends		16	28
Initial contact with contraception		9	12
MedSchool		1	1
OBG Consultation		15	30
Principal-Agent Relation		10	19
School		13	22
Intimacy of topic		2	2
Social Media		1	1
Society		15	34
Vulnerable Age		2	2
Tolerance	Expression of acceptance rather then satisfaction; unawareness of high-level of acceptance/tolerance of side-effects + sole responsibility	17	52
Unconscious Bias	Covers how cognitive patterns shape structures, processes and cognitive patterns	8	55

Appendix C. Categories and quotes

Theme	Quote
Dissatisfaction	*“But I do notice that I suffer more from period pain now because of the IUD, which was never a big issue before. [...] I worked in the hospital and was in the operating room almost every day for a very, very long time. And when you're just standing in the surgery room and you can’t just go to the bathroom to change the bandage, it naturally requires more advance planning. It's just physically more exhausting.”* (End-user 05)
	“I first took the pill [...] I had so much flatulence and I had stomach pain all the time and I was lying in bed with a stomach bottle. Yes, then I stopped it again pretty quickly.” (End-user 03)
Uncertainty about causal link between side-effect and own body	*or “I have gained weight in the time, but that can also be due to something else.“* (End-user 02)
	“Because I thought I don’t know my sexuality at all without hormones, what is it like” (End-user 05) or *“But in retrospect I would say that I am more balanced without the pill. But I didn't know that before, I didn't know how I would feel without hormones.”* (End-user 07) or
Side-effect acknowledgement through pharma	*“It's not surprising that, you know, with hormonal methods that, you know, the dislikes are around the side effects. I mean, I will say, by far, the repeated information we get is on the side effects in the bleeding disrupt disruptions.” (NGO 01)*
Connection to own body, no interference with natural system	“*where their body continues to be my body. That, that just really, that my cycle itself remains, that my body continues to react to stress and things like that.”* (End-user 04)

	"I've been taking it for ten years now. In principle, I've never really had a normal period, because with the pill you only have the withdrawal bleeding." (End-user 05)
	"So I don't want to take the pill anymore, because there are a lot of side effects involved. And simply all these hormones, that is just not so natural with the whole cycle. And so on." (End-user 07)
Acknowledg ment of pharma	"*"How I see it is that there are things going on in, you can see a non-hormonal approach. So finding contraceptives, that does not disturb the hormonal balance"* (Pharma 02) or *"When we discuss it, we call it that most of the younger generations are 'hormone sceptic"* (Pharna 03) or *"And so we made an explicit decision that we it's gonna take a long time, but we really like the field needs something that is a non hormonal."* (Pharma 06)
Economic and time reasons	Especially the one-time payment of 450 Euro for the IUD is perceived as a larger burden as the continuous monthly payment of 30 Euro for the hormonal pill. However the data indicated that in case of financial hurdles, public entities can be contacted: *"I financed the first IUD myself and at that time I didn't have a partner. And now, the second I have once through Pro Familia, a help / support program for low-income people in my hometown, where you get paid and they have taken it over completely."* (End-user 03)
Need for new contraceptives	*"So one topic is contraception on demand, why do I need to take something every day, if I only have sex, once a month? That is one obviously, non-hormonal idea of how we can tend to have something local. That's obviously, like I want something that is self determined where I don't need to basically have a physician insert something into me, that's something you hear from women, yes, trying to find solutions for, for what women really request where they feel that they don't have any opportunities." (Pharma 03)* *or "I think that IUDs are great. I think they're effective. A lot of patients tolerate them well. But there is a problem with that insertion procedure. I*

	know a lot of patients are just, they think it's gonna hurt. They're nervous about it. So they might buy into the idea of an IUD but don't want the procedure. So I don't know how to get around that." (Pharma 05)
Principal-Agent Problem	*"When you go to talk to a doctor, they seem to have their favourite method that they just want everybody to be on" (Pharma 05); "So I have the impression that the gynecologists like to prescribe the pill without really explaining the arguments for it" (End-user 07); And I have the feeling that they always focus on one thing. And I just don't have the feeling that you get advice. Because advice should be objective, because you should be informed about the pros and cons and supported in making a decision." (End-user 11); "I remember I had some questions because I was unsure myself if I wanted to take the pill. But she didn't tell me much about other methods" (End-user 17)*
Social Media	"*What has changed is the mentality of talking about it.[...] So the surrounding, but not the hardware, hasn't changed at all."* (End-user 05) or *"It's also such an exponential curve how much space these topics of sexuality, contraception, menstruation have taken up. From my observation it's analogous to a development in the media. When we started to study, it had become a topic. It just took more and more space in social media. A lot of things that were more shame-faced are now so normal to address."* (End-user 06)
Animal Trials	*"If you think about a complex like a hormonal system, a particular reproductive system works very differently, in a mouse versus a human. [...] I would say there are no super good animal models for individuals" (Investor 01)*
Litigations	*"if you look at Bayer/Schering with Yasmin, I mean they were in the US news and also in the European news all the time [...] but that's of course terrible" (Investor 01)*

Financing	*a big part is the financial aspect, with the pill they probably earn a lot of money*" (End-user 01) "*the issue must be the financing*" (End-user 03). *"We invest in a company, they make the development and then a few years later, we either take them public through an IPO, or we sell them to a pharma company, for example. That's how we make a return. And so we are dependent on finding an exit"* (Investor 01) "*these are not drugs that sell for $100,000 a year like a cancer drug, right? I mean, they sell for a few $100 a year*" (Investor 01). "*in too many big companies the Women's Health Department is kind of in the background and not getting very much love and money"* (Pharma 05)
Business Case	*"I think there is a business case for sure. It's definitely as I said, if they can find solutions to this non-hormonal approach"* (Pharma 02). "*the business case has more and more focus*" (Pharma 04)
Publicly-traded companies	"*we're a publicly traded company. So I would imagine that that was sort of a necessity at some point to go public to raise all that capital*" (Pharma 05).
Necessity of governmental involvement	*"Yes. I think that's actually a very good argument. Why don't we have a dedicated like we have with orphan disease, rare disease, you have specific tracks, you have reimbursement tracks? Why don't we have that in the female part? It's a very good argument. And that needs to come from the governments and the political society."* (Pharma 02) *"So we are facing several governments around the world who doesn't reimburse fertility treatment, because it's not a life threatening disease. It's not a right to have a child. So why would we pay for it."* (Pharma 02)

No ROI	"*And I think we have seen that the innovation step in contraception, for example, needs to be so big, that the hurdle is so high, that the investment really doesn't make sense for most companies. And in the end basically companies are there to get a return on investment*" (Pharma 03).

Appendix D. Hypothesis Tracker

Research Question: Why do female contraceptives lack innovation?

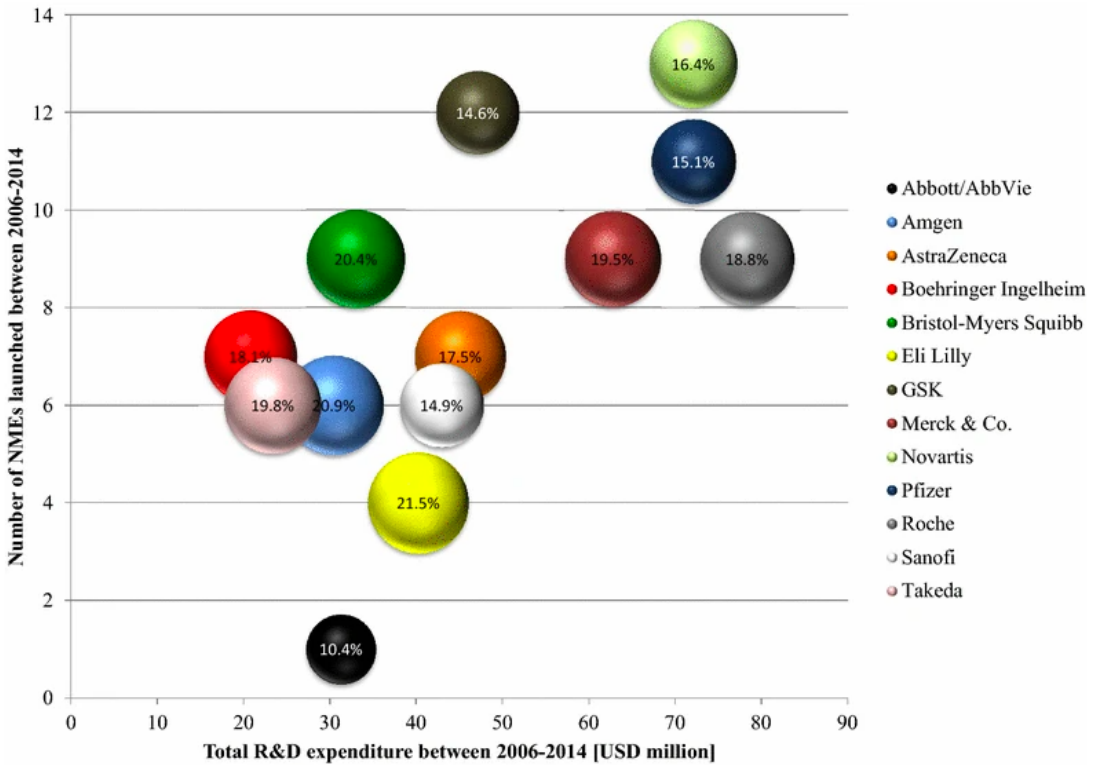
1. How do end-users perceive contraceptives, and how does (a potential lack of satisfaction)/ their view/expectations (?) foster the need for innovation?
2. What are the barriers for the pharmaceutical companies to innovate in female contraception?

Hypothesis Tracker	
	Why does no one invest in a 30-years chronic condition with an ongoing and not changing demand?
	Unintended pregnancies indicate the dissatisfaction with current products
	Does pharma spin off women's health branches because they don't believe in it?
	Does NGO hinder innovation by putting more requirements and more complexity towards the topic ?
	Difficult to find the perfect method as there is no one size fits all, every women has different needs
	Critical mass with components within R&D needs to be tackled,
	Reimbursement of contraceptives is an issue different from country to country, US out of pocket, Germany half reimbursed, Denmark single payer system
	Engaging and educating more/ young men in the problem? Not making it a female issue but a common one
	Education needs to be fostered to achieve bottom up process and that women speak up about their needs and wishes
	“And pharma companies have like this corporate venture fund. Because what we feel like, especially in women's health, the problem is that pharma companies don't really see the business case, or they're like, yeah, we need mature science. The venture capitalists are even more conservative in that sense that they are like there is no exit strategy. So we are not going to invest in that. And then we have the NGOs, which are like, yeah, we invest in that. But we have a primary focus on low and middle income countries, which is like putting another complexity to everything. So I feel like and then our goal is to kind of find what is the first step and who is the driver, who could overcome that, because I think it is a bottleneck. And as soon as VCs understand that there is a business case, then they're coming in, but I feel like there is a responsibility or there is a driving force within and I'm not sure how you see it. Maybe you can comment on that. That pharma is kind of his signalising: we take it further, but you need to help in the death valley. “

	Change in R&D process: ideas, molecules and targets come from the outside - leads back to case study: for pharma there is no need for innovation there is already enough products
	Foundations: have the Money, see the need, but are not steering innovation in the right way
	Incremental innovation in contraceptives vs groundbreaking stuff - important to differentiate
	Psychological effect of reproductive life: difficult to block that ‘natural’ process: religion, social construct, catholicism (southern Europe)
	Its contradictory that business cases are more and more important as well as unmet need for pharmaceutical companies - are they interflicting?
	Unmet need and rare diseases are not the ones making a lot of money? - answer: portfolio strategy?
	You should have focus area within your contraception - to less pharma take women’s health as a focus - less synergies, less serendipity, less innovation
	Gates: lack of data on what women want
	Public traded companies need to ensure ROI and therefore have to follow the popular diseases and can’t focus on more alternative markets (quote therapeutics MD)

Appendix E. Recruitment flyer

Appendix F: NPD vs. R&D expenditures



Appendix F: Changing Models in research-based pharmaceutical industries, by total number of NMEs (new molecular entities) approved by the FDA contrasted to the total R&D expenditure per company between 2006–2014

Source: Schumacher et al., 2016