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Document Version
Final published version

Published in:
Preventive Medicine

DOI:
10.1016/j.ypmed.2023.107521

Publication date:
2023

Preventive Medicine 172 (2023) 107521

Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

The association between commuting and cardiovascular disease: A biomarker-based analysis of cross-sectional cohort data from the UK Biobank

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ARTICLE INFO

Keywords:
Active commuting
Biomarker
cardiovascular disease risk
Cycling
Physical activity

ABSTRACT

This study used cross-sectional UK Biobank data to estimate the influence of active and passive commuting modes and commuting distance on cardiovascular disease (CVD) -related biomarkers as measures of health outcomes. The analysis applied logistic regression to assess the risk of exhibiting individual biomarker values outside a predefined reference interval and standard linear regression to estimate the relation between commuting practices and a composite CVD index. The study sample comprised 208,893 UK Biobank baseline survey participants aged 40 to 69 who use various modes of transport to commute to work at least once a week. Participants were recruited and interviewed between 2006 and 2010 at 22 centers geographically dispersed across England, Scotland, and Wales. The data set included these participants' sociodemographic and health-related information, including lifestyle indicators and biological measures. The primary outcome was a shift from low to high-risk blood serum levels in eight cardiovascular biomarkers: total cholesterol, low density lipoprotein, high density lipoprotein, triglycerides, apolipoprotein A and B, C-reactive protein, and lipoprotein (a). Our results indicated a small negative association between the composite risk index for CVD biomarkers and weekly commuting distance. Although estimates for active commuting modes (cycling, walking) may admittedly be sensitive to different covariate adjustments, our specifications show them to be positively associated with select CVD biomarkers. Commuting long distances by car is negatively associated with CVD-related biomarkers, while cycling and walking might be positively associated. This biomarker-based evidence, although limited, is less susceptible to residual confounding than that from distant outcomes like CVD mortality.

1. Introduction

A growing body of literature has documented the association between active commuting and a range of health outcomes (Bassett Jr et al., 2008; Pucher et al., 2010; Celis-Morales et al., 2017; Panter et al., 2018; Raustorp and Koglin, 2019; Baker et al., 2021; Schäfer et al., 2020; Künn-Nelen, 2016) . Results have shown that active commuting such as cycling and walking is associated with a lower risk of cardiovascular disease (CVD), cancer, and even all-cause mortality (Celis-Morales et al., 2017; Panter et al., 2018; Hamer and Chida, 2008; Patterson et al., 2020; Dutheil et al., 2020). Active commuting has also been associated with better mental health (Jacob et al., 2021; Morris, 2015; Scheepers et al., 2014). Although this literature provides strong evidence for the beneficial health outcomes of active commuting, two issues warrant further investigation: first, very little is known about the transmission mechanism, that is the way through which active commuting influences certain distant health outcomes. The general conclusion that can be drawn from the existing literature is that active commuting may contribute to cardiorespiratory fitness and that this may lower all kinds of mortality (Celis-Morales et al., 2017). Second, existing literature acknowledges that residual confounding is always possible and that this may lead to an overestimation of the true effects (Panter et al., 2018; Hamer and Chida, 2008). Residual confounding is particularly pertinent when the outcome variable is not only dependent on a wide range of factors, but also when the duration between an activity and a health outcome is long. Thus, active commuting may indeed eventually

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https://doi.org/10.1016/j.ypmed.2023.107521
Received 27 October 2022; Received in revised form 24 March 2023; Accepted 24 April 2023
Available online 28 April 2023

influence cancer or even all-cause mortality, but with a cross-sectional design, the influence of residual confounding is potentially very large.

In order to address these two issues, this study takes a look at biomarkers as health outcomes. Biomarkers are more proximal to active commuting and thus are less susceptible to residual confounding. Furthermore, by using a wide-range of biomarkers we are able to shed some light on the transmission mechanism of active commuting. Our general premise is that if active commuting affects distant health outcomes such as CVD, cancer or all-cause mortality, then this should be clearly observable in relevant biomarker data. In other words, changes in biomarkers are more proximal to active commuting in the sense that long before the influence of active commuting can be observed on say CVD mortality, the influence should be measurable in related biomarkers. Our focus is on the association between commuting and CVD outcomes as measured by biomarkers. Besides looking at the different forms of commuting, we also analyse how commuting intensity affects CVD biomarkers for different forms of commuting. As in much of the leading literature on this topic, we use data from the UK Biobank.

2. Methods

2.1. Study design

Our biomarker-based regression analysis drew on data from the 2006–2010 baseline survey of the UK Biobank project, a population-wide cohort study of over 500,000 adults aged 40 to 69 that combined sociodemographic data with a wide range of health-related information, including lifestyle indicators (e.g. leisure-time and occupational physical activity, diet, alcohol and cigarette consumption) and biological measures (e.g. anthropometries such as body fat measurements and grip strength) (Sudlow et al., 2015; Bycroft et al., 2018). One unique survey feature was the collection of participant blood, urine, and saliva samples at 22 geographically distributed centers across England, Scotland, and Wales, which were then used to analyse a range of biological markers and are now available for further analysis of known disease associations (Sudlow et al., 2015). Our sample comprises 208,893 employed or self-employed baseline survey participants who commuted to work at least once per week using both active and passive modes of transportation.

2.2. Procedures

Using the biological data for this baseline survey sample, we defined our health outcome measures as the eight different biomarkers commonly employed to assess individual cardiovascular risk (Varbo and Nordestgaard, 2018; Sniderman et al., 2011; Zanoni et al., 2016; Hopewell et al., 2014; Shrivastava et al., 2015; Nordestgaard and Varbo, 2014): total cholesterol, direct low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides, apolipoprotein A and B, C-reactive protein, and lipoprotein (a). For each of these eight biomarkers, we considered whether the respective value was within or outside the range clinically considered an elevated risk for developing cardiovascular disease (Ginsburg et al., 1991; Kannel, 1995; InformedHealth.org [Internet], 2013; Stone et al., 2005; Haidari et al., 2001; Kamboh et al., 1997; Iwata et al., 2006; Jubran et al., 2019) (see Table S1 in the Appendix for the cutoff values). For example, we classified a male participant's HDL as low risk if its value was higher than 1 mmol/L. We were thus also able to calculate a composite cardiovascular risk index using the following formula:

$$CVD_{index} = 1 - \frac{\sum_{i=1}^{8} \mathbf{1}_{A_i}(x)}{8}$$

where $\mathbf{1}_{A_i}$ is an indicator function equal to 1 if the measured value x of a particular biomarker i is outside the set of values associated with a low risk for cardiovascular disease (i.e., A_i denotes the set of values associated with a high risk for cardiovascular disease). Unlike the individual biomarkers, this composite measure allows a holistic assessment for each participant of cardiovascular risk, our main outcome variable. (one can discuss whether or not to include lipoprotein (a) to calculate CVD_{index} as physical activities are considered to have limited influence on lipoprotein (a) levels (Reyes-Soffer et al., 2022). However, since recent research (Enkhmaa and Berglund, 2022) has identified a potential association between various lifestyle factors and changes in lipoprotein (a) levels, and since including it will not cause any bias, we decided to incorporate it).

The explanatory variables of most interest were the weekly distance traveled to the workplace in miles (weekly commuting frequency x twice the distance) and the mode of transportation (car, public transport, cycling, or walking). We also included several other measurements (e.g., smoking status, total household income, or processed meat intake) to minimize any bias from potential confounders (Celis-Morales et al., 2017) (see Table S2 for all measurements and their baseline characteristics). To increase analytic robustness, we excluded all implausibly valued data points for any variable used, as well as commuters reporting more than one transportation mode (whose frequency or active versus passive status were unspecified in the database).

2.3. Statistical analyses

We analyzed the relation between CVD-related biomarkers and commuting in two primary ways: a logistic regression model that assessed the individual risk of biomarker values outside the predefined reference interval and, given the composite CVD measure's seemingly normal distribution between 0 and 1, a standard OLS regression that estimated the relation between commuting and the CVD index. Because the analytic aim was to use cross-sectional data to derive an unbiased estimate of commuting's effect on each biomarker without exploiting any exogenous variation in commuting, it was imperative to make sufficient adjustment for relevant confounders without overcontrolling. This latter would have resulted from the regression models including as controls any of the mediator variables on the causal pathway between commuting and the CVD biomarkers (Babyak, 2009). We thus adjusted for variables that were probable confounders but arguably not a consequence of individual choice of commuting distance or mode. This specification, which closely mimicks prior work on the topic (Celis-Morales et al., 2017; Panter et al., 2018; Hamer and Chida, 2008), covers sex; age; household members and number of vehicles; average household income before taxes (£); a Townsend deprivation index; consumption of cooked vegetables or salad (heaped tablespoon per day), fresh fruit or dried fruit (pieces per day), oily fish or processed meat (times per week), and alcohol (frequency); mode of transportation (excluding work); frequency and duration of walks for pleasure in the past 4 weeks; handgrip strength (in kg); smoking status (never/formerly/now); time spent watching TV and using computer (hours per day); intake of vitamin and mineral supplements or pain relief, constipation or heartburn medication (yes/no); job involves heavy manual or physical work (yes/no); ever diagnosed with diabetes, cancer, depression, or vascular/heart problems (yes/no); bone fractures in the past 5 years (yes/no); long-standing illnesses (yes/no); air pollution from nitrogen dioxide and particulate matter in 2007 and 2010 in the local vicinity of the participant's home; traffic intensity on the nearest road, and distance to the nearest road in 2009. As regards three additional covariates controlled for in previous studies – body fat percentage, individual waist-to-hip ratio, and existing use of CVD medications – despite no statistical confirmation, we suspected that they might induce underestimation of the potentially positive commuting effect of more active commuting modes. We thus omitted these variables from our main models and assessed their relevance by contrasting the estimates from additional regression specifications, briefly referenced in the main text but fully reported in the supplementary information. All analyses used robust standard errors and were conducted using STATA 17.

2.4. Patient involvement

Because our UK Biobank source comprised anonymised data from a typically healthy general population, we had no control over recruitment and no patients were involved in the design, implementation, or conducting of this study or had any influence in research question formulation, data interpretation, or the writing up of results. The results of the UK Biobank project itself are routinely made available to study participants via the project website and social media.

2.5. Ethical approval

The UK Biobank project received ethical approval from the North West Multi-centre Research Ethics Committee (REC reference: 11/NW/03820). All participants gave written informed consent before enrolment in the study, which was conducted in accordance with the principles of the Declaration of Helsinki.

3. Results

The number of observations with complete information (i.e., usable in each model) varied from 720 to 35,421 depending on which outcome variables and/or specific subsamples were analyzed (see Tables 1 to 3). Whereas cars were by far the most used mode of transportation (165,540 out of 208,893), only 5883 respondents regularly commuted by bicycle (see Table S2). The descriptive statistics highlight that deriving unbiased estimates requires careful adjustment of covariates, as 37.7% of the bicycle commuters reported also cycling or walking in their leisure time, only 8% of car commuters did so. Dietary habits also differed: around 16% of the bicycle commuters reported never eating processed meat but only about 10% of the car commuters. This latter subgroup also emerged as the main driver of the negative relation between commuting distance and the composite CVD index (see Table 1), with a subgroup value equal to that of the entire sample ($\beta = -0.0006$, $p < 0.01$). No other subgroup showed a statistically significant distance-to-index association, but only in a regression that pooled walking and cycling as the active commute modes was the relation significant and positive (β=0.0037, $p < 0.05$).

In terms of specific biomarkers, 10 miles (around 16 km) of extra commuting distance per week was significantly associated with an increased relative risk of high total cholesterol (odds ratio (OR): 1.0041, $p < 0.01$), high LDL (OR: 1.0057, p < 0.01), high triglycerides (OR: 1.0047, $p < 0.01$), and high (or too low) apolipoprotein A (OR: 1.0042, $p < 0.01$) and B (OR: 1.0046, p < 0.01) (see Table 2). Of the separate transportation modes, walking was overall linked to a lower risk for low HDL (OR: 0.7841, p < 0.01) and low apolipoprotein A (0.7821, p < 0.01) than driving, with lower HDL risk also related to cycling (OR: 0.6659, p < 0.01). In fact, cycling was also associated with a lower risk for high triglycerides (OR: 0.7288, p < 0.01), low apolipoprotein A (OR: 0.7042, p < 0.01), high (or low) apolipoprotein B (0.7657, $p < 0.05$), and high C-reactive protein (OR: 0.6673, p < 0.05).

Applying these findings separately to each of the four subsamples (see Table 3), for car commuters, each extra 10 miles (or 16 km) of weekly commuting increased the relative risk for elevated total cholesterol (1.0038, $p < 0.01$), high LDL (OR: 1.0055, p < 0.01), high triglycerides (OR: 1.0046, p < 0.01), low apolipoprotein A (OR: 1.0045, p < 0.01) and high (or low) apolipoprotein B (OR: 1.0045, p < 0.01). Among walking commuters, in contrast, each additional mile was associated with a lower relative risk of high triglycerides (OR: 0.8790, $p < 0.05$). No statistically significant associations emerged, however, for those who cycled or used only public transport.

As regards our conjecture that the regression estimates might suffer from residual confounding if participants with higher body fat (or waist-to-hip ratio) or current intake of CVD medication were less likely to engage in non-car commuter modes, the answer was difficult to determine. For instance, our descriptive statistics showed a substantially lower body fat percentage for those who cycled to work relative to all other commuter subgroups (cycling: 24.5% vs. car: 30.51%). Cycling commuters reported an average weekly commuting distance of 34.2 miles (around 54 km), which equates to roughly 1000 to 2000 extra kcal burned, depending on intensity. Holding all other factors constant, such a comparative caloric imbalance would need to persist over several months if not years to explain the observed differences in body fat. However, weight differences prior to the commuter mode decision or other unmeasured confounders might explain some if not all of these differences. To entertain this possibility, we re-estimated our results from Tables 1-3 with all these measures included as additional control variables. The results, reported in Tables S3-S5, highlighted the sensitivity of the relation between commuting behaviour and biomarkers for the alternative model specifications. Whereas the overall negative effect of commuting distance and the corresponding negative effect of car commute remained robust, virtually all benefits of alternative commute modes disappeared when the model was augmented with these additional variables that cannot be clearly categorized as good or bad controls.

4. Discussion

In the existing documentation of a relation between active commuting and a lower probability of CVD incidence and mortality (Celis-Morales et al., 2017; Panter et al., 2018; Hamer and Chida, 2008), some associations are very strong. For example, one recent study linked a walking commute to a significant 0.64 hazard ratio, implying that,

Table 1
Marginal effects of commuting distance on CVD biomarkers, conditional on the type of commuting.

		Subsample by type of commute				
	Full sample	Car	Walking	Public transport	Cycling	Active[2]
	b/se	b/se	b/se	b/se	b/se	b/se
Commuting distance [1]	−0.0006***	−0.0006***	−0.0001	−0.0006	0.0025	0.0037**
	(0.000)	(0.000)	(0.006)	(0.000)	(0.002)	(0.002)
Car	*Reference category*					
Walking	0.0039					
	(0.005)					
Public transport	0.0050					
	(0.004)					
Cycling	0.0276***					
	(0.007)					
Observations	23,885	18,619	1505	3041	720	2225

Note. b = unstandardized regression coefficients, se = robust standard errors in parentheses. * $p < 0.1$, ** p < 0.05, *** $p < 0.01$.
All models included the covariates listed in Table S2 except for *body fat percentage*, *waist to hip ratio*, and *current CVD medication*.
[1] Distance measured as 10 miles equal around 16 km.
[2] Active commuting mode includes those cycling and walking.

Table 2
Odds ratios for CVD biomarkers by commuting distance and type of commuting.

Individual biomarkers as outcomes								
	Total cholesterol	LDL direct	HDL cholesterol	Triglycerides	Apolipoprotein A	Apolipoprotein B	C-reactive protein	Lipoprotein (a)
	OR/se	OR/se	OR/se	OR/se	OR/se	OR/se	OR/se	OR/se
Commuting distance[1]	1.0041***	1.0057***	1.0026*	1.0047***	1.0042***	1.0046***	1.0003	0.9983
	(0.001)	(0.002)	(0.002)	(0.001)	(0.002)	(0.001)	(0.002)	(0.001)
Car				*Reference category*				
Walking	1.0226	1.0122	0.7841***	1.0149	0.7821***	0.9725	0.9276	0.9569
	(0.056)	(0.079)	(0.057)	(0.055)	(0.059)	(0.058)	(0.080)	(0.062)
Public transport	0.9449	0.9244	0.8988*	0.9955	0.9155	0.9422	0.9589	1.0330
	(0.040)	(0.055)	(0.050)	(0.042)	(0.051)	(0.045)	(0.065)	(0.052)
Cycling	0.9821	0.8840	0.6659***	0.7288***	0.7042***	0.7657***	0.6673**	0.9583
	(0.074)	(0.096)	(0.079)	(0.058)	(0.084)	(0.071)	(0.109)	(0.087)
Observations	33,146	33,095	30,007	33,121	35,421	33,012	33,087	26,538

Note. OR = odds ratio, se = robust standard errors in parentheses. * p < 0.1, ** p < 0.05, *** p < 0.01.
All models included the covariates listed in Table S2 except for *body fat percentage*, *waist to hip ratio*, and *current CVD medication*.
[1] Distance measured as 10 miles equal around 16 km.

Table 3
Odds ratios for CVD biomarkers by commuting distance conditional on the type of commuting.

	Individual biomarkers as outcomes							
	Total cholesterol	LDL direct	HDL cholesterol	Triglycerides	Apolipoprotein A	Apolipoprotein B	C-reactive protein	Lipoprotein (a)
	OR/se	OR/se	OR/se	OR/se	OR/se	OR/se	OR/se	OR/se
				Type of commute subsample: Car				
Commuting distance[1]	1.0038***	1.0055***	1.0030*	1.0046***	1.0045***	1.0045***	1.0009	0.9983
	(0.001)	(0.002)	(0.002)	(0.001)	(0.002)	(0.001)	(0.002)	(0.002)
Observations	25,880	25,841	23,375	25,859	27,647	25,778	25,830	20,716
				Type of commute subsample: Public transport				
Commuting distance	1.0059	1.0070	0.9997	1.0059	1.0047	1.0052	0.9918	0.9992
	(0.005)	(0.006)	(0.006)	(0.005)	(0.006)	(0.005)	(0.008)	(0.005)
Observations	4159	4153	3831	4155	4446	4133	4153	3334
				Type of commute subsample: Cycling				
Commuting distance	1.0159	0.9541	0.9283*	0.9839	0.8990*	1.0069	1.0432	0.9970
	(0.026)	(0.030)	(0.041)	(0.024)	(0.049)	(0.029)	(0.054)	(0.027)
Observations	979	976	884	979	1026	964	966	803
				Type of commute subsample: Walking				
Commuting distance	1.0480	1.1125	0.9215	0.8790**	1.0025	0.9140	0.9615	1.0125
	(0.062)	(0.094)	(0.075)	(0.055)	(0.083)	(0.067)	(0.095)	(0.069)
Observations	2128	2125	1917	2128	2302	2125	2126	1685

Note. OR = odds ratio, se = robust standard errors in parentheses. * p < 0.1, ** p < 0.05, *** p < 0.01.
All models included the covariates listed in Table S2 except for *body fat percentage*, *waist to hip ratio*, and *current CVD medication*.
[1] Distance measured as 10 miles equal around 16 km.

relative to passive commuting modes, walking to work induces a 36% lower risk of CVD mortality (Celis-Morales et al., 2017). This same study associated a cycling commute with a 0.48 hazard ratio, an approximately 50% lower risk of mortality than passive commuter modes. Such associations, however, may be strongly affected by residual confounding, especially when active commuting's beneficial effects take considerable time to translate into lower probabilities of mortality. The potential biases caused by residual confounding can be partially mitigated by examining more proximal health outcomes such as biomarkers.

Our results for the different commuting modes revealed a discernable association between them and CVD biomarkers, with walking showing significant benefits for two of the eight biomarkers (HDL and apolipoprotein A), and cycling being significantly positively linked to five of the eight (HDL, triglycerides, apolipoprotein A and B, and C-reactive protein), as well as the composite biomarker measure. While cycling distance - in line with evidence from a randomized controlled trial in a previous study (Schmied et al., 2020) - had no statistically significant effect on the different biomarkers, the distance walked was positively associated with better triglycerides. Not only did these results support the existing evidence of a beneficial association between active commuting and CVD incidence and mortality, but the significant biomarkers (especially HDL and apolipoprotein A) suggested a transmission mechanism of physical activity and cardiorespiratory fitness. Commuting by car, in contrast, was associated with a low composite CVD biomarker, while the distance traveled was linked to poorer measures of total cholesterol, LDL, triglycerides, apolipoprotein A and B. This finding corroborated previous evidence that driving to work is detrimental to both physical (e.g. obesity) and mental health outcomes (Sugiyama et al., 2013; Roberts et al., 2011; Flint and Cummins, 2016). On the other hand, the insignificant (albeit mostly positive) association between commuting by public transport and CVD biomarkers calls for a more detailed investigation of both public transport modes (e.g., bus, subway, and train) and their quality (e.g., waiting times, capacity), especially in light of previous literature (Rojas-Rueda et al., 2012) suggesting benefits from commuting by public transport compared to commuting by car.

The general picture given by our analysis is that CVD biomarkers, and the health outcomes they represent, are beneficially related to active

commuting, particularly cycling, but negatively associated with long commutes by car. Our results also highlighted the complex nature of commuting's influence on health, implying that past research may not only have been parsimonious in investigating this relation but may have underestimated the influence of residual confounding on the estimated associations. As shown in the appendix, the estimated effects of commuting on health are very susceptible to the choice of confounders, making the careful consideration of covariates a requirement for cross-sectional analyses, especially in assessments of commuting's long-term health implications (e.g. CVD mortality). Evidence from longitudinal and causal research designs emphasize the potential bi-directional relationship between obesity and physical activity indiscernible in our correlational study (Carrasquilla et al., 2022; Petersen et al., 2004; Wareham et al., 2005). We see that particularly the positive associations between cycling and CVD biomarkers vanish when augmenting the model with measures of body fat and CVD medication use. While we are unable to statistically isolate the relevant causal dynamics, we observe that the positive differences for cyclists were primarily observed at the extensive margin rather than the intensive margin, suggesting that the additional variables capture important group differences between cyclists and non-cyclists rather than differences between cyclists that routinely bike longer or shorter commutes.

In addition to commuting mode and distance, such diverse factors as quality of public transport, road congestion, climate, work-time arrangements, and even childcare facilities can influence the health effects of different commuting practices. A far more nuanced analysis of health effects than is currently common is thus necessary, a shift in which this analysis of individual biomarkers is a first step.

4.1. Study strengths and weaknesses

The primary strength of this study is its very large sample size and wide range of biomarkers used. The main limitation is that, although residual confounding may be less pertinent than in studies of long-term health outcomes, the cross-sectional nature of the data limits the results to associations rather than causal relations. Moreover, the method we used to calculate our risk index (CVD_{index}) has not been tested against well-established risk assessment scores, and a more complex approach may have yielded slightly different results. However, in order to maintain the interpretability of our results, and given that the primary focus of our study was on different modes of transportation, we opted for a simplified index that is consistent with the individual biomarker assessments presented in Tables 2 and 3.

We also cannot completely rule out self-selection bias, as some previous studies have suggested that participants in the UK Biobank cohort were, on average, somewhat healthier and less ethnically diverse than the general population (Panter et al., 2018; Fry et al., 2017). In addition, although our preferred specification indicated some benefits of active commuting, our models omitted three covariates commonly controlled for in earlier research models, whose more conservative estimates provided no evidence for the benefits of active commuting. We therefore interpret these findings with caution. Our comparison of several associations between commute distance, mode, and individual biomarker also made our results subject to a multiple comparison problem inflating the type 1 error-rate. Nonetheless, the observation that longer commuting distances by car seems to have a negative effect on healthy levels of CVD-relevant biomarkers remained robust across all our specifications. Finally, we do not have information on how long participants had been commuting before participating in the UK Biobank study, which could – in fact - increase the variance of our estimates. However, the lack of this information is not an underlying confounder that could bias our results. Such bias would only occur if we assumed that the duration a participant was traveling a certain distance (and by a certain mode of transport) before participating would have a direct influence on biomarker levels and – at the same time - would differ systematically between the different modes of transport. Although we cannot completely rule out the possibility, we consider such a systematic correlation to be very unlikely.

5. Conclusions

Our study results confirmed robust associations between passively commuting long distances by car and adverse CVD biomarkers and suggest a potential link between actively commuting by bicycle or walking and better CVD biomarkers. Hence, by addressing a perceived methodological imitation in the previous literature, our analysis provided supportive evidence that active commuting might improve serum levels of CVD-related biomarker such as HDL and triglycerides.

CRediT authorship contribution statement

Micha Kaiser: Conceptualization, Methodology, Formal analysis, Data curation, Writing – original draft, Writing – review & editing, Project administration. **Jan M. Bauer:** Conceptualization, Methodology, Validation, Writing – original draft, Writing – review & editing. **Steffen Otterbach:** Data curation, Methodology, Writing – original draft. **Lucia A. Reisch:** Supervision, Funding acquisition. **Alfonso Sousa-Poza:** Conceptualization, Writing – original draft.

Funding

This work has been funded by the European Union's Seventh Framework Programme for research, technological development and demonstration (Grant No. 607310; Nudge-it). Although the UK Biobank project received support from the Wellcome Trust, Medical Research Council, Department of Health, Scottish government, Northwest Regional Development Agency, Welsh Assembly government, and British Heart Foundation, the authors designed, conducted, analysed, and interpreted the research entirely independent of these funding sources.

Declaration of Competing Interest

All authors declare no conflict of interest with regard to the study design, data collection, analysis, interpretation, or publication of the findings.

Data availability

The authors do not have permission to share data.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2023.107521.

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