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The two-way relation between socioeconomic status and risk factors for cardio-metabolic health: Implications for prevention and social policy

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List of abbreviations

BMI	Body-mass-index
DALY	Disability adjusted life years
GWAS	Genome-wide association study
IV	Instrumental variable
LOC	Locus of control
MR	Mendelian randomization
RDD	Regression discontinuity design
SEM	Structural equations modelling
SES	Socioeconomic status
WHR	Waist-to-hip-ratio

List of publications

1. Pedron, S., Schmaderer, K., Murawski, M., & Schwettmann, L. (2020). The association between childhood socioeconomic status and adult health behavior: the role of locus of control. *Social Science Research*, 65, 102521.
2. Pedron, S., Maier, W., Peters, A., Linkohr, B., Meisinger, C., Rathmann, W., Eibich, P. & Schwettmann, L. (2020). The effect of retirement on biomedical and behavioral risk factors for cardiovascular and metabolic disease. *Economics & Human Biology*, 38, 100893.
3. Pedron, S., Kurz, C.F., Schwettmann, L. & Laxy, M. (2021). The effect of BMI and type 2 diabetes on socioeconomic status: a two-sample multivariable Mendelian randomization study. *Diabetes Care*, 44(3), 850-852.

Additional Manuscript

4. Pedron, S., Emmert-Fees, K., Laxy, M., & Schwettmann, L. (2019). The impact of diabetes on labour market participation: a systematic review of results and methods. *BMC Public Health*, 19(1), 1-13

1. Introductory summary

In the last decades, advances in medical treatment and technology and improvements in living conditions led to an unprecedented increase in life expectancy, in high income as well as in low and middle income countries (Mathers et al., 2015). While this trend could be regarded as a great achievement, it was also accompanied by a reduction in fertility rates, leading to society aging, and by an increase in the burden of morbidity and mortality due to chronic non-communicable conditions. In most countries with a comprehensive welfare system, these trends started to threaten the economic viability and sustainability of pension and healthcare systems[1] (Bloom et al., 2015).

In order to secure said sustainability, the measures taken focus predominantly on maximizing labor market participation of older individuals and preventing non-communicable diseases (Beard and Bloom, 2015, Bloom et al., 2015, WHO, 2013). The former involves the reshaping of pension benefits, progressively reducing pension levels and increasing the retirement age in most systems (Börsch-Supan and Coile, 2021). The latter targets mainly lifestyle changes for the prevention of non-communicable illnesses with a strong behavioral component, such as obesity, type 2 diabetes and cardiovascular diseases, which cause together a very high share of the burden of disease (Prince et al., 2015).

However, the policy debate surrounding the challenges posed by population aging is still narrow. One reason is that calendar age is not always related to the same levels of functioning, which are very heterogeneous, especially among the older workforce. Besides genetic predisposition, the other two main factors contributing to different levels of functioning are behavioral and socioeconomic factors (Brooks-Wilson, 2013, Elo, 2009). In fact, research has shown that individuals from more disadvantaged backgrounds are more likely to work in physically demanding jobs and adopt unhealthy behaviors, thus being at higher risk for health impairments (Clark et al., 2009, Cutler et al., 2012, Moor et al., 2017). These in turn might jeopardize their ability to be productive and might lead them to fail to achieve an adequate level of economic security in older age (Kwan and Walsh, 2018, Seuring et al., 2015, Pedron et al., 2019, Gordois et al., 2016).

This interrelation between socioeconomic factors and health is therefore a fundamental one, which should be considered while shaping retirement incentives as well as targeted prevention strategies. A growing body of research on this interrelation calls for a more diversified policy action, in order to secure economic viability and directly considering equity aspects. This thesis represents a contribution to deepen our understanding of these complex societal mechanisms by focusing on selected issues in the two-way interrelation between socioeconomic status (SES) and cardio-metabolic health and its risk factors, which are among the most important drivers of morbidity and mortality worldwide. The

[1] Full disclosure: at the time this thesis is being written, the world is fighting against the Covid-19 pandemic. While this represents a serious emergency, it will also probably lead to an aggravation of the trends described in this thesis for two reasons. First, the pandemic caused an unprecedented rupture in the continuity of medical treatment, preventive actions and scientific research in the usual areas of critical care (such as cardio-metabolic conditions and other non-communicable diseases), which however still represent a substantial burden of morbidity and mortality (Zeggini et al., 2020). Second, the pandemic led to an economic recession, adding serious concerns to the sustainability of pension and healthcare systems (IMF, 2020).

presented manuscripts offer some starting points for the improvement of evidence-based solutions, working towards more equitable strategies to prevent illness and maintain work ability of individuals.

SES and health: a two-way relation

The literature has demonstrated that SES and cardio-metabolic health are strongly intertwined (Chaker et al., 2015, Pedron et al., 2019, Clark et al., 2009, de Mestral and Stringhini, 2017, Everson et al., 2002, Galobardes et al., 2006, Hoffmann et al., 2018). In fact, this relation could run in both directions. On the one hand, the SES of an individual, conceived as personal educational endowment, social and economic background, personal and familiar income levels, and occupational hazards and prestige, is one of the most important risk factors for health (Cutler et al., 2012, Clark et al., 2009). This mechanism has been termed the *social causation* hypothesis (Hoffmann et al., 2018). As the literature has shown, this influence might run through several mechanisms, the most important of which are a better access to healthcare, a healthier behavior and advantageous personal resources of individuals with a higher SES (Moor et al., 2017, Pampel et al., 2010, Petrovic et al., 2018). Therefore, based on this evidence, SES is one of the most important aspects that need to be considered in order to shape effective prevention programs.

On the other hand, cardio-metabolic health can affect labor market participation in form of employment status, early retirement, disability pension, absenteeism and presenteeism, thus subsequently affecting personal income, occupational and social prestige and generally the socioeconomic position of an individual in society (Chaker et al., 2015, Pedron et al., 2019, Seuring et al., 2015, Gordois et al., 2016). This mechanism has been termed the *health selection* hypothesis (Hoffmann et al., 2018). These effects represent the indirect costs of illness and pose a serious burden on healthcare and pension systems by significantly reducing productivity and participation. They also threaten the efficacy of measures aiming at prolonging productive age beyond the conventional pension cutoffs, since workers with cardio-metabolic conditions might be at higher risk of unemployment, early retirement, and disability pension (Gordois et al., 2016, Pedron et al., 2019). Therefore, once these conditions have been diagnosed, it is essential to estimate and reduce their effect on labor market participation and offer suitable retirement benefits and secondary prevention services to the individual.

The main contribution of this thesis is to focus on both directions with separate pieces of research, which tackle selected parts of these extremely complex mechanisms. The thesis is divided in two parts. In the first part (section 1.1), the role of SES and changes thereof as determinants of behavioral and biomedical risk factors for cardio-metabolic health are investigated (Manuscripts 1 and 2). The second part of the thesis (section 1.2) includes one systematic review and one original contribution gathering evidence on the effect of type 2 diabetes and body-mass-index (BMI) on labor market participation and other closely linked indicators of SES, namely income and deprivation (Manuscript 3, Additional Manuscript).

The biggest threat: cardio-metabolic conditions

Cardio-metabolic illnesses represent the biggest threat for morbidity and mortality worldwide. Among these, the most common causes of DALYs and mortality are ischemic heart disease, ischemic stroke and type 2 diabetes (Vos et al., 2020). Furthermore, the prevalence and incidence of these conditions have been steadily rising in the last few decades, making them the target of large research efforts and preventive strategies (Beard and Bloom, 2015, Prince et al., 2015).

At the center of these preventive strategies lie the metabolic precursors of these illnesses, including hypertension, obesity, impaired glucose tolerance and dyslipidemia (Bellou et al., 2018, WHO, 2017). Early diagnosis and effective management of these conditions has proven to be the most effective way of preventing serious health deteriorations, leading to chronic cardio-metabolic conditions (WHO, 2013, Alberti et al., 2007). In fact, besides genetic predisposition and family history, the single most important risk factor to cause such metabolic impairments and their complications is individual health behavior, including unhealthy diet, lack of exercise, excessive alcohol consumption and smoking (Bellou et al., 2018, WHO, 2017). Despite being rooted in habits, routines, social norms and groups, health behavior is a potentially modifiable aspect of individual life. Therefore, by tackling behavior, these conditions bear a tremendous prevention potential (WHO, 2013, Alberti et al., 2007).

However, successfully modifying behavior and achieving an effective management of the metabolic precursors is a challenging task (Dalle Grave et al., 2010, Fischer et al., 2020). This calls for more evidence on the underlying mechanisms generating behavioral habits and on the groups who are more at risk, both of which are strongly affected by sociodemographic factors, in order to generate evidence-based prevention strategies and increase the efficacy of existing ones. In this thesis, these issues are tackled by investigating the role of childhood socioeconomic circumstances and control beliefs in determining adult health behavior (Manuscript 1) and by investigating the effect of retirement on health behavior and on the metabolic precursors of cardio-metabolic conditions (Manuscript 2), identifying target risk groups after this important socioeconomic transition.

Furthermore, estimating the effects of BMI and diabetes on SES is difficult, not only because of the reverse causation between health and SES, but also because these illnesses mostly coexist, hampering the isolation of the underlying causal effects (Chaker et al., 2015, Pedron et al., 2019). In this thesis, this issue is addressed by estimating the independent effects of BMI and type 2 diabetes, two often coexisting conditions, on socioeconomic indicators (Manuscript 3).

Estimating effects: causal inference methods

As emerges from the above-cited literature, the relation between different aspects of SES and cardio-metabolic health and its behavioral precursors is a complex one. Besides the fact that causality can run in both directions, further challenges of modelling such relations are the presence of unmeasured confounding and measurement error. These problems lead to a fundamental endogeneity issue.

Consequently, most literature available focused on the associations between these variables, rather than investigating causation under consideration of endogeneity (Pedron et al., 2019, Seuring et al., 2015). This is in fact a difficult task, which can be resolved only if suitable methods and data are available. Most applications estimating causal effects in this context focus on the use of the instrumental variable (IV) method and its further declinations (Angrist and Pischke, 2008). In a nutshell, the intuition behind this method is the inclusion of an exogenous variable in the model, which (1) is significantly related with the endogenous exposure and (2) influences the outcome exclusively via the exposure. In this way, the endogenous regressor can be instrumented using this exogenous variable, producing estimates that are free of bias due to reverse causation and omitted variables.

In two of the three manuscripts presented in this thesis, we make use of this technique to produce causal estimates. In Manuscript 2, we resort to a regression discontinuity design (RDD) method to estimate the causal effect of retirement on markers of behavior and metabolic health, using the exogenously determined retirement cutoffs as instrumental variables (Lee and Lemieux, 2010). In Manuscript 3, we investigate the independent effect of BMI and type 2 diabetes on income and regional deprivation, using genetic information as instrumental variable in a multivariable two-sample Mendelian randomization (MR) approach (Burgess and Thompson, 2015, Davey Smith and Hemani, 2014).

Thesis outline

The remainder of this thesis is organized as follows. In section 1.1, two manuscripts investigating the effects of SES and changes thereof on health behavior and metabolic markers of health are presented. In section 1.2 the results of a systematic review on the effects of diabetes on labor market outcomes and the results of an investigation on the effect of BMI and type 2 diabetes on income and deprivation are presented. Section 1.3 presents concluding remarks and a final outlook.

1.1. Part 1: The effect of SES on risk factors for cardio-metabolic health

This part of the thesis is concerned with investigating the effect of SES and changes thereof on risk factors for cardiovascular and metabolic health, including health behavior and clinical parameters.

Childhood SES and adult health behavior: control beliefs as significant mediator (Manuscript 1)

Several pieces of research have highlighted that SES is an important determinant of cardio-metabolic health and mortality (Clark et al., 2009, Everson et al., 2002). This influence is not only deriving from the SES one person achieves during his or her lifetime, but also from the socioeconomic background in which individuals were born and grown, independently from one´s own achievements (Elo, 2009, Hayward and Gorman, 2004, Pakpahan et al., 2017).

One of the most important mechanisms explaining this “long-arm of childhood” on later health and mortality is a substantial socioeconomic gradient in health behavior (Moor et al., 2017, Pampel et al.,

2010, Petrovic et al., 2018). As literature has shown, this is the results of multiple factors. These include lower educational levels of the offspring, but also a lower access to resources for healthy lifestyle, adverse socialization conditions and a higher likelihood of being exposed to peers and neighbors with unhealthy behaviors (Cohen et al., 2010, Due et al., 2011, Matthews et al., 2010, Pampel et al., 2010). Moreover, psychosocial and personal characteristics, such as stress, hopelessness and cynical hostility, have been increasingly analyzed as factors determining this social gradient in health behavior (Matthews et al., 2010, Murray et al., 2012, Pampel et al., 2010).

The first study included in this thesis focuses on one of these psychosocial mechanisms, potentially linking childhood SES with adult health behavior, namely individual control beliefs. This concept originates from Rotter´s social learning theory (Rotter, 1966) and proves useful in measuring personal beliefs in controllability of life, operationalized using the concept of locus of control (LOC). Individuals with a more internal LOC believe that life outcomes depend on their own actions, while individuals with a more external LOC rather believe that life is in the hands of fate or "powerful others".

Several pieces of research have demonstrated that individuals from lower SES families are more likely to develop a more externally oriented LOC (Whitehead et al., 2016). Furthermore, external control beliefs were previously linked with a lower frequency of physical activity, a less healthy diet and a higher probability of smoking, while results for alcohol were inconsistent (Bailis et al., 2001, Cobb-Clark et al., 2014, Whitehead et al., 2016). Previous studies have investigated these separate pathways or closely related mechanisms, but none of them linked these factors in a comprehensive mediational model (Bosma et al., 1999, Boylan et al., 2016, Gale et al., 2008, Oi and Alwin, 2017, Pudrovska et al., 2005, Ross and Mirowsky, 2011). Therefore, based on this evidence, we constructed a mediational model, hypothesizing that LOC is a significant mediator between childhood SES and adult health behavior.

The data we used to analyze this question draw from the largest socioeconomic annual panel survey of households in Germany, namely the Socio-Economic Panel (SOEP) (Goebel et al., 2018). This rich dataset (n= 33,119) allowed the consideration of a large sample from a wide range of socioeconomic positions and circumstances. In order to estimate our mediational model we used Structural Equation Modelling (SEM) techniques (Brown, 2014).

Our results indicate that externally oriented LOC is a significant partial mediator between lower childhood SES and lower physical activity and smoking, independently from adult SES and other confounders. Furthermore, no associations could be highlighted for dietary behavior, while the effect for alcohol is inverted, since a lower childhood SES and a more external the LOC are associated with a less frequent alcohol consumption. This counterintuitive association was shown in several other pieces of research, which hypothesize that the cause lies in the incapacity of coping with alcohol effects or in the lower frequency of social contacts (Caliendo and Hennecke, 2020, Cobb-Clark et al., 2014). The stratified analysis indicates that these mechanisms affect women rather than men, and younger and middle-aged individuals rather than older ones.

These results show that childhood SES remains a powerful determinant of adult lifestyle, contributing to a substantial problem of socioeconomic inequalities that are passed on from one generation to another. The paper is mostly concerned with investigating the issue in the framework of socioeconomic health inequalities. However, the results can also be considered in perspective of a greater preventive effort, as described in the introductory summary. In fact, by investigating how socioeconomic inequalities in behavior arise and persist across generations, one investigates also one of the most important risk factors for the burden of cardio-metabolic conditions later in life. Equally, by tackling such inequalities, the efficacy of prevention strategies could be increased by identifying and targeting specific subgroups of the population.

These results make a compelling argument for targeting control beliefs as a way of improving behavior and reducing inequalities. Further research should consider investigating if and how control beliefs can be influenced towards more internally oriented beliefs. While it is reasonable to suggest that such beliefs are more malleable during beliefs formation in childhood and adolescence, highlighting the role of educational institutions, it should also be investigated if they could also be the target of specific programs aiming at improving lifestyle of adult individuals.

The effect of retirement on health behavior and clinical risk factors (Manuscript 2)

Beyond investigating how the general socioeconomic background of an individual influences behavior and health, the literature has also investigated the impact of changes in the SES of an individual, such as job and income losses (Browning and Heinesen, 2012, Michaud et al., 2016, Salm, 2009, Sullivan and Von Wachter, 2009, Benzeval and Judge, 2001, Boyce et al., 2013). Furthermore, in the context of the present aging trend, the transition from productive age to "leisure time" old age is also receiving increasing attention (Coe et al., 2012, Coe and Zamarro, 2011, Eibich, 2015).

Retirement marks a major socioeconomic transition in the life of a working individual. In fact, retiring from productive life goes along with profound changes, not only in the daily routine, but also in the personal identity, material possibilities and social contacts of an individual. This could have both negative and positive effects on lifestyle and health care utilization, with potential consequences for cardio-metabolic health (Atchley, 1976, Gall et al., 1997, Kasl and Jones, 2000, Palmore et al., 1984). In fact, previous studies have demonstrated that retirement has a positive effect on physical activity, smoking cessation, subjective health, but also mixed findings on physical health, including depression, cognitive decline and the incidence of chronic conditions (a thorough review of the literature is provided in Manuscript 2). Furthermore, only few studies focused on the clinical risk factors for cardio-metabolic diseases, including BMI and blood pressure, reporting both positive and negative effects (Behncke, 2012, Chung et al., 2009, Eibich, 2015, Godard, 2016, Goldman et al., 2008, Johnston and Lee, 2009, Xue et al., 2017, Xue et al., 2019).

The aim of the second manuscript was therefore to add to this literature by investigating the causal effect of retirement on a large number of behavioral and clinical risk factors for cardio-metabolic

disease. In fact, these factors might be highly responsive to changes in daily routines and might have a large impact on the deterioration of health conditions in the years following retirement.

In order to answer our research question we resorted to epidemiological data from the KORA study platform (Cooperative Health Research in the Region of Augsburg), including 11,168 observations (Holle et al., 2005). This allowed us to study the impact of retirement on several self-reported health behaviors (physical activity, smoking, alcohol consumption) and objectively measured clinical biomarkers (BMI, WHR, systolic and diastolic blood pressure, cholesterol levels and glycosylated hemoglobin). In order to disentangle the causal effect of retirement, which is a complex task given the substantial problems of reverse causation and omitted variables, we adopted a regression discontinuity design (RDD). This technique exploits the random variation generated around the fixed age cutoffs for retirement: by comparing individuals just before and after the cutoffs, the causal effect can be estimated (Lee and Lemieux, 2010).

Our results show that, for individuals retiring regularly, retirement does not have any impact on behavior or clinical markers, but rather increases their subjective health, probably due to a general relief from work-related stress. As some authors have already argued, these results suggest in fact an accumulation of work-related strains before retirement (Mazzonna and Peracchi, 2015, Westerlund et al., 2010). From the point of view of social and work policy this result is of high importance and worth further explorations, especially in light of current policies aiming at extending productive life. In fact, prolonging working life might be associated with an increasing burden in the last years before retirement, with potential detrimental effects for health, which would counterbalance the gains in productivity. A deeper understanding of this issue should drive the creation of new forms of flexible exit and participation of older workers.

For individuals retiring early, we noticed an increase in physical activity. However, this increase was not enough to counterbalance the parallel increase in BMI and WHR after retirement. Stratified analyses revealed that these effects concern especially women and low educated individuals retiring early, which might therefore be considered as potential high-risk groups for a worsening of important risk factors after retirement. From the point of view of prevention, these results offer clear starting points for targeted interventions. Potential strategies should aim at incentivizing a more health-conscious reshaping of daily activities upon retirement in these groups, in order to use the additionally available time to establish healthier habits and consequently helping to slow down the age-related health deterioration.

1.2. Part 2: The effect of metabolic health on SES

This part of the thesis investigates the effects of BMI and diabetes on SES, presenting the results of a systematic review and of an original contribution.

The effect of BMI and type 2 diabetes on labor market participation (Additional Manuscript)

The prevalence of obesity and type 2 diabetes is increasing worldwide at an unprecedented pace (Chooi et al., 2019, Saeedi et al., 2019). These trends are largely interrelated, since a high BMI is one of the major risk factors for type 2 diabetes, sharing with it both pathophysiological mechanisms and genetic risk (Eckel et al., 2011, Goodarzi, 2018). The two factors were also found to be independently responsible for a large part of the burden in cardiovascular morbidity and mortality (Thomas et al., 2005, Yusuf et al., 2020) and for higher health care costs (Cawley, 2015, Dixon et al., 2020, Kurz and Laxy, 2020, Seuring et al., 2015).

Furthermore, the literature indicates that high BMI is associated with poorer labor market prospects and lower productivity, including absenteeism, employment chances and early retirement (Cawley, 2015). The same detrimental effects were found also for diabetes, as we demonstrate in an own systematic review investigating the effects of diabetes on labor market participation (Pedron et al., 2019) (Additional Manuscript), complementing existing summaries on income and ability-to work (Breton et al., 2013, Seuring et al., 2015). These disadvantages might accumulate over time, influencing available income, living circumstances and deprivation (Cawley, 2015, Harrison et al., 2019, Seuring et al., 2015, Tyrrell et al., 2016), thereby leading diabetes and BMI to define the SES of an individual on multiple dimensions.

However, the identification of clear causal effects of BMI and type 2 diabetes on SES is a challenging task. In fact, intrinsic problems of unmeasured confounding, measurement error, and reverse causation largely prevent the identification of causal effects (Cawley, 2015, Pedron et al., 2019, Seuring et al., 2015). As showed in the cited reviews, previous approaches to investigate causal effects of BMI or diabetes in this context used the disease status of biological parents or siblings as instrumental variable (Cawley, 2015, Pedron et al., 2019, Seuring et al., 2015). However, the studies using this approach and investigating causal effects are still scarce. Furthermore, the use of disease status of parents as instrumental variable could lead to a violation of one of the fundamental IV assumptions, since its effect on the SES of the offspring could be mediated by other factors. This calls for more evidence on the socioeconomic effects of BMI and diabetes, making use of different instruments and methods.

The effect of BMI and type 2 diabetes on income and regional deprivation (Manuscript 3)

Responding to this call, more recent studies have focused on the use of genetic characteristics as exogenous sources of variation in a Mendelian randomization (MR) approach to estimate the effects of BMI or type 2 diabetes on SES (Böckerman et al., 2019, Davey Smith and Hemani, 2014, Harrison et al., 2019, Tyrrell et al., 2016). However, the use of these approaches is further complicated by the fact

that BMI and type 2 diabetes share several genetic determinants (Goodarzi, 2018). Therefore, estimating the effect of one exposure without considering the other might violate the fundamental IV assumption that the instruments must affect the outcome only through the exposure, otherwise leading to biased estimates (Burgess and Thompson, 2015, Davey Smith and Hemani, 2014). The aim of this study was to overcome these challenges by adopting a novel multivariate two-sample MR approach. This allowed us to take into account the shared genetic components of BMI and diabetes, in order to jointly estimate their independent causal effects on income and regional deprivation (Burgess and Thompson, 2015). To carry out these analyses, we used summary data from published meta-analyses of GWAS (Locke et al., 2015, Mitchell et al., 2019, Scott et al., 2017).

The results of the univariable analysis show a negative effect of BMI on household income and regional deprivation, but no effect of diabetes. Multivariable MR successfully took care of the bias generated by the overlapping loci, showing a slightly lower coefficient for BMI and again no effects of diabetes on the outcomes.

Our results add to previous literature by providing a new causal estimate of the effect of BMI and type 2 diabetes on measures of SES by using novel MR techniques. The negative effect of BMI is in line with previous literature (Böckerman et al., 2019, Cawley, 2015, Harrison et al., 2019, Tyrrell et al., 2016). On the contrary, the effect of type 2 diabetes contradicts previous evidence, which found a negative association between diabetes and income (Seuring et al., 2015). For this reason, this result should be treated with caution and investigated in further studies, making use of more powerful instruments from the new generation of GWAS (Mahajan et al., 2018, Yengo et al., 2018).

These results have far-reaching implications that should inform and guide preventive efforts and public or company-specific health policies. First and foremost, these results indicate that preventive efforts to reduce weight may prove helpful in reducing not only the burden of cardio-metabolic conditions and their complications, but also the negative effects of body weight on SES.

Further implications for health policy might result from a deeper understanding of the underlying mechanisms leading to this result. A closer look at the existing literature suggests that, for obese individuals, discrimination, lower ability-to-work, higher absenteeism and presenteeism and a higher probability of work-related injuries play a key role in determining labor market prospects and therefore income and deprivation (Cawley, 2015, Puhl and Heuer, 2009, Schulte et al., 2007). This underlines again the need of targeted and efficient measures to reduce weight, but also the need of a general effort to uncover and tackle these underlying problems, for example by adopting more inclusive company-level policies. The scarce but already existing company-level efforts aimed at understanding if racial or gender discrimination in the workplace exist, could be accompanied by efforts to understand if discrimination or self-selection are also present due to body weight. If so, further research and actions should be taken to understand the roots of these factors and tackle them, in order to achieve a companywide higher sensibility to the issue and avoid adverse SES effects of BMI.

Finally, our results open a new perspective on the interrelation between high BMI and deprivation. This result adds to previous studies on the "obesogenic environment", showing that specific environmental characteristics can impact BMI (Mackenbach et al., 2014). In fact, our study also indicates the presence of (self-) selection of obese individuals in more deprived areas, which offer generally more affordable housing and food options. This might create a vicious cycle, which calls for new social policies to break this connection, for example by increasing the offer of fitness activities, green spaces, and gyms or by increasing the supply of healthy food options in socially deprived areas.

1.3. Conclusions and outlook

The presented manuscripts offer detailed insights in three selected research questions tackling the interconnection between SES and cardio-metabolic health or its behavioral risk factors. They represent small pieces of a very complex puzzle, but still offer some practical implications and starting points for creating and improving evidence-based prevention strategies and social policy.

The first manuscript indicates that the effect of childhood SES on adult health behavior is partially mediated by control beliefs, adding to a growing body of research pointing at psychosocial characteristics as potential additional targets in prevention and adherence strategies. The second manuscript demonstrates that the effects of retirement on health depend on timing, gender and education, identifying women and low educated individuals retiring early as potential targets of prevention strategies fostering a healthier adaptation to retirement. For regular retirees this transition is a positive one, but the development of their health status prior to retirement should be object of further research in order to sustain future evidence-based changes to the current retirement rules. The third manuscript provides new evidence of the detrimental causal effect of BMI on socioeconomic outcomes, controlling for type 2 diabetes. This result highlights the need of targeted strategies to reduce the adverse effects of high levels of BMI, involving weight reduction and company-wide efforts to recognize and tackle potential mechanisms, such as self-selection and discrimination. Further concrete policy recommendations would profit from understanding the reasons behind the null results obtained for the effects of diabetes, involving the new generations of more powerful GWAS studies.

Finally, this thesis as a whole entails complementary examples of the two-way relation of SES and behavioral and health markers and therefore underlines the need of considering such reverse causation in further research in order to obtain causal estimates.

2. Included manuscripts

2.1. Manuscript 1

Pedron, S., Schmaderer, K., Murawski, M., & Schwettmann, L. (2020). The association between childhood socioeconomic status and adult health behavior: the role of locus of control. *Social Science Research*, 65, 102521.

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The association between childhood socioeconomic status and adult health behavior: The role of locus of control

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ABSTRACT

The socioeconomic environment in childhood is a powerful determinant for health behavior in adulthood, subsequently influencing health outcomes. However, the underlying mechanisms are insufficiently understood. This study assesses locus of control (LOC) as a mediator linking childhood socioeconomic status (SES) with health behavior (smoking, regular alcohol consumption, unhealthy diet and low physical activity). Drawing on a representative sample from Germany (SOEP), we investigated these relations using structural equations modelling. Results show that externally oriented LOC explains up to 6% of the relationship between childhood SES and health behavior in adulthood, independently from adult SES. Stratification indicates that these results hold in women but not in men, in younger and middle-aged individuals but not in older ones. Hence, control beliefs play a modest yet significant role in shaping the socioeconomic gradient in health behavior and might have far-reaching consequences on how morbidity and mortality arise and persist across generations.

1. Introduction

Socioeconomic inequalities in health persist in all Western countries despite extensive research on structural explanations and policy action, tackling for example environmental and occupational health risks, housing conditions, and access to healthcare (Mackenbach, 2012; Mackenbach et al., 2008). Individuals from disadvantaged socioeconomic backgrounds have a higher probability of being obese, suffering and dying from chronic conditions, experiencing mental health issues and having a lower self-reported health (de Mestral and Stringhini, 2017; Clark et al., 2009; Elo, 2009; Everson et al., 2002; Moor et al., 2017; Galobardes et al., 2006). Furthermore, studies adopting a life course approach have shown that the influence of socioeconomic circumstances on health begins as early as childhood and affects older age morbidity and mortality (Elo and Preston, 1992; Elo, 1998; Hayward and Gorman, 2004;

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Haas, 2008; Montez and Hayward, 2014; Pakpahan et al., 2017; Glymour et al., 2008; Birnie et al., 2011; Tampubolon, 2015; Elo, 2009; Martikainen et al., 2020).

The mechanisms behind the association of SES with health are complex and multifaceted (Ben-Shlomo and Kuh, 2002; Cohen et al., 2010; Due et al., 2011; Moor et al., 2017; Petrovic et al., 2018; Whitehead et al., 2016; Matthews et al., 2010). Besides direct effects and physiological mechanisms, for example via sustained reactions to stress or environmental exposures, a social pattern in health behavior including smoking, diet, physical activity and alcohol consumption was shown to be one of the most important mechanisms through which socioeconomic inequalities in health arise and persist (Due et al., 2011; Petrovic et al., 2018). Health behavior is in fact a powerful determinant of cardiovascular and metabolic health and, therefore, contributing to one of the major causes of morbidity and mortality worldwide (Yusuf et al., 2020). Additionally, it can also affect mental health and wellbeing, life satisfaction and quality of life (Godos et al., 2020; Biddle et al., 2019; McNeill, 2001; Proctor et al., 2009). Thus, health behavior can have a large impact on society and socioeconomic inequalities, not only because of its impact on health and mortality but also because of a wide range of far-reaching consequences for employment chances, productivity and health care costs (Cawley and Ruhm, 2011).

Despite the importance of health behavior for socioeconomic inequalities in health, the complex mechanisms linking SES with behavior are neither fully understood nor backed with sufficient empirical evidence (Moor et al., 2017; Pampel et al., 2010; Petrovic et al., 2018). So far, personal characteristics, such as personality traits, cognitive abilities and sense of control, have been investigated as increasingly important drivers for the social gradient in health behavior (Mackenbach, 2012). Among these, personal beliefs in controllability of life, such as locus of control (LOC) and mastery, have earned increasing attention (Bailis et al., 2001; Bosma et al., 1999, 2005; Cobb-Clark et al., 2014; Gale et al., 2008; Murray et al., 2012; Oi and Alwin, 2017; Pudrovska et al., 2005). These concepts refer to attitudes and beliefs in having control over one's life outcomes and circumstances: individuals with an internal LOC strongly believe in their power and possibilities, while individuals with an external LOC rather believe that life is mostly influenced by chance or powerful others (Rotter, 1966).

On the one hand, these control beliefs follow a social gradient, with individuals from disadvantaged social backgrounds perceiving less control over life circumstances than their better-off counterparts (Mittal and Griskevicius, 2014; Shifrer, 2018; Ward, 2013). As several studies have pointed out, both the experience of disadvantaged socioeconomic environments in childhood and the socialization process of individuals from economically weaker backgrounds might lead individuals to believe that they have less control over life circumstances, influencing their control beliefs throughout life (Whitehead, 2016).

On the other hand, beliefs in controllability of life determine how a person acts and relates to the present circumstances, determining behavior and lifestyle choices (Bailis et al., 2001; Cobb-Clark et al., 2014; Whitehead et al., 2016; Murray et al., 2012). In fact, having an external LOC might lead to passive or aggressive response patterns or to different expectations regarding the benefits of investing in health, thus influencing lifestyle choices (Cobb-Clark et al., 2014; Whitehead et al., 2016).

This body of literature makes a strong case for LOC as a mediator between childhood socioeconomic circumstances and adult health behavior, but no study formally investigated this mediating role of LOC. Closely related studies of Gale et al. (2008) and Ross and Mirowsky (2011) included this mechanism in their models but did not test the mediational contribution of LOC formally. Furthermore, some studies have focused only on the mediational role of LOC between childhood SES and health, but without considering health behavior (Bosma et al., 1999b; Boylan et al., 2016; Oi and Alwin, 2017; Pudrovska et al., 2005; Ross and Mirowsky, 2011). Other authors have investigated the mediational role of LOC between adult SES and behavior, without considering childhood SES (Bailis et al., 2001; Murray et al., 2012; Stephenson-Hunter, 2018; Wardle and Steptoe, 2003). Among this literature, only few studies made use of rigorous structural equations modelling techniques to analyze complex pathways and correlations between the mediators (Murray et al., 2012; Ross and Mirowsky, 2011; Bailis et al., 2001; Oi and Alwin, 2017).

Our study aims at investigating whether LOC is a potential pathway through which childhood SES affects health behavior in adulthood by estimating a comprehensive mediational model. In our analysis, we included adult SES as an additional pathway through which childhood SES impacts adult health behavior. Additionally, we extensively considered potential sources of heterogeneity, such as sex and age cohort.

To this aim, we performed a formal effect decomposition using structural equations modelling (SEM). The most useful advantage of this method is that it allows testing complex relations between multiple exposures and mediators in a standardized and rigorous framework and incorporating measurement error in the analysis (Brown, 2014). Moreover, using SEM we included LOC as a latent construct, using a measurement model depending on multiple observed dimensions. Last, we modelled adult SES as an additional mediator, itself strongly determined by childhood SES and related to LOC.

Our contribution to the literature is threefold. First, we provide novel evidence on the mediational role of LOC between childhood SES and adult health behavior as important modifiable determinants of health. Second, we test a comprehensive model including childhood SES as a precursor and relevant determinant of LOC while controlling for the potential role of adult SES. Third, drawing from a large panel survey, we consider relevant sources of heterogeneity, including sex and age cohort effects.

The results from this investigation shed light on one of the mechanisms through which socioeconomic inequalities in health behavior arise, with potential far-reaching consequences on physical and mental health, productivity, satisfaction and quality of life. They identify the contribution of LOC and, thereby, motivate further research for new and effective methods to decrease the impact of socioeconomic circumstances on the development of external sense of control in children and adolescents and to foster more internal control beliefs among adults with a more disadvantaged background.

2. Background

The hypothesis investigated in the present study draws from a large body of literature surrounding the effects of the "long arm of

childhood". In fact, in these studies, the deleterious impact of early socioeconomic childhood conditions on later health and mortality has been vastly researched and documented (Elo and Preston, 1992; Elo, 1998; Hayward and Gorman, 2004; Haas, 2008; Montez and Hayward, 2014; Pakpahan et al., 2017; Glymour et al., 2008; Birnie et al., 2011; Tampubolon, 2015; Elo, 2009; Martikainen et al., 2020). However, as several reviews have pointed out, the potential mechanisms linking these factors are multiple and highly complex (Ben-Shlomo and Kuh, 2002; Cohen et al., 2010; Conroy et al., 2010; Due et al., 2011; Matthews et al., 2010), posing serious problems to the operationalization of the research questions across the life course without incurring in generalizations and simplifications.

Several theories and pieces of evidence have shown that the mechanisms linking childhood socioeconomic circumstances with later health and mortality involve physiological, psychosocial and behavioral factors (Elo, 2009; Due et al., 2011; Cohen et al., 2010; Ben-Shlomo and Kuh, 2002). Summarizing, the most frequently investigated mechanisms involve three pathways. First, the disadvantaged physical and psychological conditions experienced in childhood might lead to a sustained stress reaction and to lasting physiological influences, which affect later health and mortality. Second, individuals with a lower SES in childhood are less likely to achieve higher levels of education and SES as adults, thereby sustaining the early disadvantage throughout life. Third, disadvantaged conditions in childhood might foster and promote unhealthy behavior, which leads to health impairments.

The contribution of the last mechanism, i.e. the social gradient in behavioral risk factors, is high, but still lower compared to the other two pathways (Moor et al., 2017; Pampel et al., 2010; Petrovic et al., 2018). However, understanding what causes this social gradient in health behavior is challenging, because the mechanisms connecting childhood SES and behavior in adulthood are various, complex and still poorly understood. In our model (Fig. 1), we are specifically interested in investigating the socioeconomic gradient in health behavior, by focusing on the role of LOC as a potential mediator between childhood SES and adult health behavior. In the following subsections, we describe each pathway separately, summarize the leading theories and mechanisms, and cite relevant sources for a more comprehensive and detailed overview thereof.

2.1. Path A: childhood SES and adult health behavior

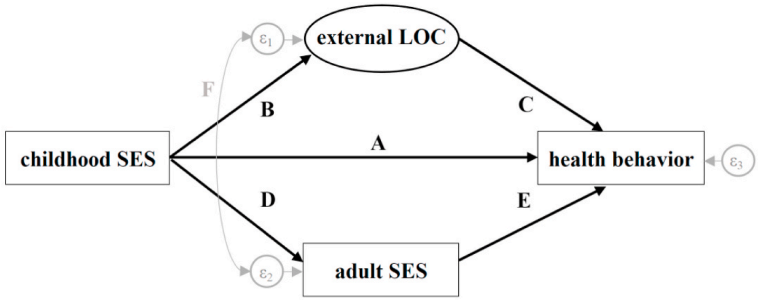
Existing evidence has identified the role of childhood SES as one determinant of health behavior in adulthood (Pampel et al., 2010; Petrovic et al., 2018; Moor et al., 2017; Due et al., 2011). The mechanisms linking these two factors are various. On the one hand, children from more disadvantaged households may have less access to resources for healthy behavior, such as parks, sport facilities, fresh fruit and vegetables. On the other hand, they might be exposed to social or community environments where parents, neighbors and peers function as role models for less healthy behavior. Both the material environment and the societal/community exposures could lead children and adolescents to develop unhealthy habits, which track and grow into adulthood (Due et al., 2011; Cohen et al., 2010; Conroy et al., 2010; Ben-Shlomo and Kuh, 2002; Pampel et al., 2010; Evans, 2004).

Furthermore, children from higher SES households are more likely to have better cognitive abilities and to achieve higher levels of education, leading to a higher SES in adulthood. This might be linked not only to increased material possibilities to access healthy options, but also to a higher cultural capital and health consciousness, which drive their attitude to a more healthy behavior (Cohen et al., 2010; Due et al., 2011; Matthews et al., 2010; Mckenzie et al., 2011; Oi and Alwin, 2017; Pampel et al., 2010; Sheikh et al., 2014). We explore these pathways in more detail in section 2.3 (*paths D, E & F*).

An additional factor which could be responsible for the social pattern in health behavior in adulthood is the health status during childhood and adolescence. In fact, several studies have shown how health in adolescence, involving low back pain, migraines, asthma, overweight, obesity and depression, is socially patterned (Due et al., 2011; Ben-Shlomo and Kuh, 2002). These conditions may influence health behavior in adolescence, which then tracks into adulthood leading to a social gradient in health behavior (Due et al., 2011; Ben-Shlomo and Kuh, 2002).

A further part of the research has focused on the psychosocial and personal mechanisms. Previous studies have investigated the role of stress, negative emotions (hopelessness, depression, cynical hostility), future orientation, self-control, effective agency, LOC and social support linking SES with behavior (Pampel et al. 2010; Murray et al., 2012). However, most of these studies focused on the effect of adult SES on behavior, with only a few including childhood SES.

Additionally, the available sources indicate that adult health behavior is not only socially patterned, but also strongly dependent on



Note: SES Socioeconomic status, higher values indicate lower SES; *LOC* locus of control, ε(1, 2, 3) error terms. Squares indicate manifest variables; circles indicate latent variables. For each health behavior, a model was estimated in the formal analysis.

Fig. 1. Path diagram of the investigated relations.

sex and age (Baker and Wardle, 2003; Wardle et al., 2004; Courtenay, 2000a, 2000b). In a review, Courtenay (2000a) showed that women consistently choose healthier behaviors compared to men. While the source of these gender differences is not yet well understood, some authors suggested a connection with typical characteristics of masculinity and femininity: the former being linked to risk taking, the latter to protective behaviors, ideal body image, and health knowledge (Courtenay, 2000b; Wardle et al., 2004). Thus, a stratification of the outcomes and mechanisms by sex and age should be considered while investigating the relation between childhood SES, personal characteristics and health behavior.

2.2. Childhood SES, LOC and adult health behavior

2.2.1. The concept of LOC

The concept of LOC originates from the social learning theory developed by Rotter (Rotter, 1966; Skinner, 1996). He described LOC "as a generalized attitude, belief, or expectancy regarding the nature of the causal relationship between one's own behavior and its consequences" (Rotter, 1966). People with a more external LOC tend to doubt in the personal controllability of life. Instead, they may believe that life is determined by chance, fate or "powerful others". In contrast, people with a more internal LOC tend to believe that life outcomes depend on themselves (Rotter 1966). These beliefs have a strong influence on the person-environment interaction, so that LOC could be connected with a variety of life outcomes and behaviors (Whitehead et al., 2016).

2.2.2. Path B: childhood SES and LOC

A growing body of evidence has shown that a lower SES in childhood is related to more externally oriented control beliefs (Mittal and Griskevicius, 2014; Shifrer, 2018; Ward, 2013). The mechanisms were summarized in a review by Whitehead et al. (2016), who divided them depending on their influence at the micro, meso and macro level. At the micro level, children growing up in less advantaged families are more likely to be exposed to harsh or unpredictable situations and to a lack of material and psychosocial resources. These children more often experience an actual "lack of control" and feel determined by external forces like chance, fate or powerful others, developing more externally oriented control beliefs (Mittal and Griskevicius, 2014; Whitehead et al., 2016; Evans, 2004). Furthermore, they could also be exposed to a process of adverse socialization, for which external control beliefs and personality traits of "important others" like parents, siblings and peers might be transferred to the child (Belsky et al., 1991; Anger, 2012).

Mechanisms at the meso level involve environmental factors, including peers and neighbors but also the community in which individuals live and the broader circumstances to which they are daily exposed to. Individuals from more disadvantaged households are more likely to be exposed to instability as well as more dangerous and less resourceful neighborhoods, which can contribute to create a sense of lack of control (Whitehead et al., 2016; Evans, 2004).

Finally, mechanisms at the macro level refer to societal factors that impact the whole society, such as gender discrimination and adverse political or societal circumstances (Whitehead et al., 2016).

These levels of influence are widely interconnected and dependent on sex and age. In fact, the socialization process is different for male and female, since a clear societal division between the two genders still exists, regarding both social behaviors and psychosocial factors (Stockard, 2006; Eagly and Wood, 1991). In a cross cultural review of gender differences in LOC, Dyal (1984) showed that women were generally more externally oriented than men. However, the changing role of women in society may help to increase their internal control beliefs (Smith et al., 1997). Additionally, more internal control beliefs in men could be related to masculine traits, such as self-assertion and independence from others, while women might be more subject to a feminine socialization, with traits such as expressiveness, supportiveness and affectivity (Dyal, 1984).

Furthermore, regarding age, a cross-temporal meta-analysis showed how individuals became more externally oriented in the time period between 1960 and 2002, with birth cohort explaining a large part of the change (Twenge et al., 2004). The authors stated that the results are consistent with an "alienation model" of modern society, in which individuals are becoming more cynic and individualistic, leading them to the belief that their actions are not meaningful and valuable. Additionally, societal and political circumstances and changes may have affected individuals from distinct age cohorts differently. For these reasons, a stratification of results by sex and age is necessary.

2.2.3. Path C: LOC and health behavior

Several previous studies have shown that external LOC is generally related to unhealthy lifestyles, including less physical activity, a higher probability of smoking and unhealthy dietary behavior (Whitehead et al., 2016; Cobb-Clark et al., 2014; Bailis et al., 2001; Steptoe and Wardle, 2001; Mercer et al., 2018; Mendolia and Walker, 2014; Lassi et al., 2019; Gale et al., 2008). Moreover, the case of alcohol consumption is singular: an external LOC is related to alcohol consumption, but both positive and negative effect directions have been identified (Bailis et al., 2001; Caliendo and Hennecke, 2020; Cobb-Clark et al., 2014; Gale et al., 2008; Murray et al., 2012; Cheng and Furnham, 2018; Kiecolt et al., 2013; Lassi et al., 2019; Mendolia and Walker, 2014; Mercer et al., 2018; Norman et al., 1998; Steptoe and Wardle, 2001).

Explanations derived from the public health and sociological literature were summarized by Whitehead et al. (2016). One theory postulates that the belief to have less control may induce a *passive response pattern.* This can lead people to miss chances to change their lives or discourage them to invest in their health via healthy behaviors (e.g. by increasing their physical activity levels or by adopting a healthy diet), or to stop health damaging behaviors (e.g. smoking or alcohol consumption). Another approach states that the belief to have insufficient control over life may strongly correlate with distress and negative emotional responses, like frustration, anger and anxiety, leading to a direct detrimental effect on health. Furthermore, frustration, anger and anxiety may trigger an *aggressive response pattern* leading to a higher tendency for health damaging behavior, like smoking or alcohol consumption (Whitehead et al., 2016).

Further insights into the mechanisms connecting LOC with health behavior can be gained from the model of health capital and health investments (the "human capital model") (Grossman, 1972, 2000). In this approach, health is modelled as a stock, depending on an initial health endowment, depreciating with age and potentially increasing with investments in the form of medical care, health behavior and prevention. Recent developments of this model included non-cognitive skills such as future orientation, self-efficacy and LOC, as factors potentially affecting individual health investments decisions (Chiteji, 2010; Cobb-Clark et al., 2014).

The human capital model allows theoretical deductions and is helpful in providing explanations of empirical results on the effect of LOC on health behavior. Several mechanisms have been already identified (Cobb-Clark et al., 2014). First, LOC could influence individual expectations regarding the benefits from healthy behaviors. Internally oriented individuals may believe that their investments, like exercising regularly, avoiding tobacco and alcohol, and eating healthy food, have a stronger effect on health (i.e. a higher return on investment) compared to what their more externally oriented counterparts think. Second, LOC could be related to patience, self-control, and time preferences. Internal individuals may be more patient in waiting for the results of their investments to materialize, leading to a higher persistence to regular exercising and healthy diets. Third, LOC could be related to motivation and satisfaction: internal individuals maintain healthy habits because they might derive a greater satisfaction from those actions than external individuals do (Cobb-Clark et al., 2014; Cobb-Clark, 2015).

Recent empirical research has provided further evidence for these mechanisms and has shown substantial gender differences in explaining the connection between LOC and health behavior. In fact, for men, LOC impacts health behavior via different expectations regarding the return on their investments, while for women satisfaction is the leading mechanism (Caliendo and Hennecke, 2020; Cobb-Clark et al., 2014).

2.2.4. Paths B & C: LOC as mediator between childhood SES and adult health behavior

The evidence cited in the previous paragraphs suggests a mediational role of LOC in linking children's socioeconomic conditions with health behavior in adulthood, but only few studies have explored related hypotheses. In this context, Gale et al. (2008) investigated the single pathways of influence of childhood SES on LOC and, in turn, of LOC on behavior. However, without a formal model, they concluded that LOC might be a mediator in the relation between childhood SES and adult behavior. In addition, Ross and Mirowsky (2011) investigated the role of childhood and adult SES on health behavior and health outcomes in a complex model, considering LOC as a mediator. Their results suggest that this is an important pathway in the creation of socioeconomic differences in health behavior and health in adulthood.

Further research is worth to be mentioned in this context. Some studies have identified a significant mediational role of perceived control between adult SES and physical activity, but not for other risk factors including smoking or alcohol consumption (Bailis et al., 2001; Murray et al., 2012; Stephenson-Hunter, 2018; Wardle and Steptoe, 2003). Additionally, few studies have focused on the mediational role of LOC between childhood SES and health outcomes, but without considering health behavior or other potential risk factors (Oi and Alwin, 2017; Pudrovska et al., 2005; Bosma et al., 1999b; Boylan et al., 2016).

2.3. Paths D, E & F: the role of adult SES as intermediate confounder

Another relevant factor influencing health behavior is the individual's own SES in adulthood. First, adult SES and LOC may interact over the life course (Whitehead et al., 2016) (*path F*). On the one hand, an external LOC may reflect an actual lack of control caused by a lower SES (Bailis et al., 2001; Murray et al., 2012; Whitehead et al., 2016). On the other hand, a more external LOC may induce a passive and ineffective coping style by not exploiting ones full potential, which may lead to poorer socioeconomic outcomes in life (Cobb-Clark, 2015; Infurna et al., 2016; Schnitzlein and Stephani, 2016).

Second, adult SES is itself a mediating pathway between childhood SES and health behavior in adulthood (Mckenzie et al., 2011; Cohen et al., 2010; Ben-Shlomo and Kuh, 2002). Individuals from households with a higher socioeconomic background are in fact more likely to reach a higher SES later in life (Chetty et al., 2014; Lee and Solon, 2009; Ben-Shlomo and Kuh, 2002; Cohen et al., 2010) (*path D*). This represents the *intergenerational mobility* between parents and their offspring. Recent research has shown that low mobility between social classes is still an issue despite extensive efforts to achieve equality in many high-income countries (Chetty et al., 2014). Furthermore, own adult SES is itself a powerful determinant of health behavior in adulthood (*path E*) (Due et al., 2011; Pampel et al., 2010; Petrovic et al., 2018). For these reasons, we considered adult SES in our analysis as an important intermediate confounder (VanderWeele, 2016).

As shown in several pieces of research, there are profound gender differences shaping the relation between LOC and labor market outcomes (Cobb-Clark, 2015; Infurna et al., 2016) and in the intergenerational mobility (Chetty et al., 2014; Lee and Solon, 2009). Additionally, due to both an increased participation of women and fluid dynamics in the labor market, these trends are also likely to change over time and to be different for distinct age cohorts (Chetty et al., 2014; Lee and Solon, 2009).

2.4. Hypothesis

Following the overview presented, we hypothesize that external LOC is a mediator between childhood SES and adult health behavior, independent of adult SES and differing for sex and age cohort. In fact, as highlighted in the background section, these are important determinants of LOC, adult SES and health behavior and may therefore significantly influence the dynamics between the factors analyzed.

3. Methods

3.1. Data

The German Socioeconomic Panel (SOEP) is a nationally representative annual panel study of private households (Goebel et al., 2018). In the dataset, the main exposure (childhood SES) was collected retrospectively upon entrance in the survey. Adult SES information and a LOC scale are available in the survey years 2005 and 2010.[1] Data for all health behaviors considered is available for the subsequent years (2006 or 2007, 2011 or 2012) or for the same year in which LOC was measured (e.g. 2010 in the case of alcohol consumption). Hence, the chronological order stated in Fig. 1 can be reflected by the data available.

For the present study, we pooled observations for the years 2005 and 2010. After excluding individuals who were younger than 18 years old and individuals from three subsamples whose questionnaire did not include any measure of LOC, the sample comprised 39,661 observations. An overview of the sample construction, missing data and original sample descriptive statistics is available in Appendix A.

To deal with missing data, we adopted a *full information maximum likelihood strategy* (FIML), assuming that missing values were *missing at random* (MAR) (Brown, 2014). Following this strategy, all observations with missing values on the included covariates were dropped from the estimation (see Table A.1 in Appendix A). After excluding these observations, the final estimation sample included 33,119 observations, half of which were female (Table 1). The average age was 48.7 years and 16% of our sample was living alone. Bivariate correlations between childhood SES, health behaviors, and confounders are reported in Appendix B.

The population in 2005 was comparable with the population in 2010 for all variables included (Table A.3, Appendix A). Since the sample contained repeated observations at the individual level, a total of 11,177 individuals were surveyed in both years (50% of the total number of included individuals). As the loss to follow-up was rather large (34%), and since LOC is generally stable over time (Caliendo and Hennecke, 2020; Cobb-Clark and Schurer, 2013), we analyzed the data as a repeated cross section.

3.2. Variables

3.2.1. Childhood and adult socioeconomic status

We operationalized SES using the International Socio-Economic Index (ISEI) (Ganzeboom et al., 1992), a continuous scale ranging from 16 (lowest SES) to 90 (highest SES). It ranks participants based on their occupational status as well as the educational level and income usually associated with that occupation. For the analysis, we reverse-coded the score, with higher values indicating a lower status.

For childhood SES we used parental ISEI values. This variable is based on general information on the occupation and job position of parents when the participant was 15 years old. This information was retrospectively collected for all participants with a one-time questionnaire about childhood and adolescence upon their entrance in the SOEP (i.e. in the first or second year of participation) (Schnitzlein et al., 2018). In the main analysis, we defined childhood SES as father's ISEI in childhood. If this information was missing, we used mother's ISEI as an alternative proxy for childhood SES.[2]

For adult SES we used the ISEI score of the participant for the same year in which the LOC was measured (i.e. 2005 and 2010). For individuals who were not employed at the time of the survey, the last available information on occupation and job position was used to compute adult ISEI (DIW, 2019).

The ISEI is a complex measure of SES, pooling information about occupation, job position, education and income and thus reflecting several aspects of this multidimensional concept (Cutler et al., 2012). However, the available variables contained a rather high number of missing values, both for childhood SES (16%) and adult SES (23%) (see Appendix A). For this reason, we carried out a sensitivity analysis using educational status (high/low) as an alternative indicator for both parental and adult SES (Appendix F), defined as having a degree higher than high school based on schooling and vocational training information (Grabka, 2017). For childhood SES we used father's educational status (high/low). Again, if this information was not present, we used mother's educational status as proxy. Both adult educational status and parental educational status presented a lower number of missing values (3% and 13%, respectively - Appendix A).

3.2.2. Locus of control: measurement model

LOC was assessed in 2005 and 2010 with ten items based on a scale developed by Krampen (Krampen, 1981; Nolte et al., 1997; Richter et al., 2013). The ten statements concern several dimensions including own abilities, fate or luck, powerful others or social conditions and their potential to drive life outcomes (Appendix C). Agreement to each statement was measured via a 7-point-Likert

[1] The same LOC scale is also available for the year 2015. In this study, we pooled data from the years 2005 and 2010 as for both years we could draw on the same health behavior dimensions, measured in the same way. In successive years, the definition of alcohol consumption slightly changed and healthy dietary behavior was not part of the questionnaire anymore.

[2] This choice was motivated by theoretical and data-driven reasons. First, most studies in the literature operationalize childhood SES using only (or mostly) the socioeconomic status of the family head or of the father, as he was in most cases the principal earner in the family (Bosma et al., 1999b; Pudrovska and Anikputa, 2012; Hayward and Gorman, 2004; Montez and Hayward, 2014). Second, data on mother's ISEI was available for only 37% of observations, opening concerns for missing data. Third, in 80% of the cases father's ISEI was higher than or equal to mother's ISEI. In only 16% mother's ISEI was higher than father's ISEI, while for 4% only mother's ISEI was available.

Table 1
Distribution from the SOEP study sample with frequencies of health behaviors, SES and confounders.

					Male			Female		
		N	Mean (SD)/proportion		N	Mean (SD)/proportion		N	Mean (SD)/proportion	
Smoking		26,674			12,708			13,966		
	(0) No	19,383	73%		8782	69%		10,601	76%	
	(1) Yes	7291	27%		3926	31%		3365	24%	
Physical activity		27,370			13,050			14,320		
	(1) every week	10,155	37%		4632	35%		5523	39%	
	(2) every month	2129	8%		1100	8%		1029	7%	
	(3) seldom	5048	18%		2599	20%		2449	17%	
	(4) never	10,038	37%		4719	36%		5319	37%	
Alcohol		31,530			15,041			16,489		
	(1) never	3945	13%		1311	9%		2634	16%	
	(2) seldom	9050	29%		3149	21%		5901	36%	
	(3) sometimes	13,097	42%		6592	44%		6505	39%	
	(4) regularly	5438	17%		3989	27%		1449	9%	
Healthy Diet		26,653			12,699			13,954		
	(1) very strongly	2463	9%		810	6%		1653	12%	
	(2) strongly	10,988	41%		4291	34%		6697	48%	
	(3) a little	11,661	44%		6511	51%		5150	37%	
	(4) not at all	1541	6%		1087	9%		454	3%	
SES										
Low Ch. SES		33,119	65.14	(16.56)	15,846	64.98	(16.65)	17,273	65.30	(16.47)
Low Ad. SES		25,305	59.78	(16.6)	12,822	59.34	(17.25)	12,483	60.24	(15.89)
Low parental education		31,861	73%		15,198	70%		16,663	76%	
Low adult education		31,080	85%		14,889	85%		16,191	85%	
Covariates										
Age		33,119	47.92	(17.69)	15,846	47.64	(17.5)	17,273	48.17	(17.85)
	(1) 18-40	12,051	36%		5785	37%		6266	36%	
	(2) 41-65	14,676	44%		7096	45%		7580	44%	
	(3) >65	6392	19%		2965	19%		3427	20%	
Female		33,119	52%		–			–		
Living alone		33,119	15%		15,846	14%		17,273	17%	
West Germany		33,119	75%		15,846	75%		17,273	75%	
Migration Background		33,119	12%		15,846	11%		17,273	12%	
German		33,119	96%		15,846	96%		17,273	96%	
Number of children in HH		33,119	0.48	(0.86)	15,846	0.47	(0.85)	17,273	0.49	(0.86)
Season		33,119			15,846			17,273		
	(1) winter	10,844	33%		5172	33%		5672	33%	
	(2) spring	17,278	52%		8293	52%		8985	52%	
	(3) summer	3334	10%		1606	10%		1728	10%	
	(4) autumn	1663	5%		775	5%		888	5%	
Year		33,119			15,846			17,273		
	2005	17,086	52%		8197	52%		8889	51%	
	2010	16,033	48%		7649	48%		8384	49%	

Notes: SES: socioeconomic status; Ch. SES: childhood SES (reversed ISEI); Ad. SES: adult SES (reversed ISEI); SD: standard deviation.

scale ranging from (1) "agree completely" to (7) "disagree completely".

In the literature, some studies operationalized the same scale by using either separate (sum or average) scales for external and internal components (Hajek and König, 2017) or one continuous index (Offerhaus, 2013; Caliendo and Hennecke, 2020). In contrast, we measured the latent construct "external LOC" by carrying out an exploratory and a confirmatory factor analysis (EFA and CFA, respectively) and creating a measurement model (Brown, 2014) (detailed steps and results in Appendix C). This also allowed us to test its goodness-of-fit.

More specifically, based on the EFA we identified four out of the ten items loading highly onto one factor, which we termed "external LOC". These items reflect beliefs of (1) having little control over life circumstances (item 10), (2) doubting one's own abilities (item 7), (3) life being controlled by powerful others (item 5), and (4) having achieved what deserved (item 2). Based on these items, we constructed a measurement model for the factor "external LOC" using CFA and estimated the model applying the standard maximum likelihood approach. Similarly to Caliendo and Hennecke (2020), we pooled observations from both 2005 and 2010 to compute the factor loadings.[3]

The resulting measurement model showed sufficient goodness-of-fit (Chi-square = 3.98; p = 0.046), while all other goodness-of-fit (GOF) measures considered (RMSEA, SRMR, CFI, TLI) indicated very good model fit, being consistently below the usually accepted

[3] As the authors explain (Caliendo and Hennecke, 2020), in this way, the factor loadings are assumed to be constant over time, but the specific values of LOC for 2005 and 2010 for each participant were allowed to change due to possible changes in the answer patterns.

cutoff values (Brown, 2014). Robustness checks confirmed the robustness of the model, which was adopted for the main analysis (Appendix C).

Finally, our construct of "external LOC" presented metric invariance between different groups, i.e. male/female and age groups (Appendix D), which is a necessary assumption for the stratified analysis (Brown, 2014).

3.2.3. Outcome: health behavior

We included a range of self-reported health behaviors, i.e. smoking, alcohol consumption, dietary behavior, and physical activity. All behaviors were coded in the way that a higher category represented more unhealthy behavior. Hence, current smoking status was coded 1 if participants reported to smoke currently, otherwise it was coded 0. Participants were asked about their frequency of consumption of different sorts of alcohol. Possible answers reached from (1) "never" to (4) "regularly". Concerning dietary behavior, individuals stated to what extent they follow a health-conscious diet ranging from (1) "very strongly" to (4) "not at all". Finally, they were asked about practicing physical activity. Corresponding categories ranged from (1) "at least once a week" to (4) "never".

Since the answer categories for alcohol consumption are very prone to subjective interpretation (Caliendo and Hennecke, 2020), we carried out a sensitivity analysis using data from the years 2015 and 2016. In fact, in 2016 a new question on alcohol consumption was introduced, asking participants how often they consume alcohol based on a set of more objective frequency categories, ranging from (1) never to (6) every day (Appendix G). The LOC scale was computed based on the 2015 values using the method already described above. The same observation applies to the categories for healthy diet, which are equally prone to subjective interpretation. However, due to a lack of objective information on dietary habits, we were not able to provide a robustness check for this outcome. The sensitivity analysis for alcohol could reveal whether this problem is present and in which way the bias is directed. This result might also apply to other items with strongly subjective categories such as healthy diet.

3.3. Model and analytic strategy

To assess the mediating role of external LOC in the relationship between childhood SES and adult risk factors, we estimated the model depicted in Fig. 1 using structural equation modelling (SEM). Childhood SES and the outcomes were introduced as manifest variables, while LOC was included as a latent mediator after applying the measurement model described above (Appendix C). Additionally, we included manifest adult SES as potential intermediate confounder and further mediator in our model. In fact, intermediate confounders are mediator-outcome confounders, which are themselves affected by the exposure (VanderWeele, 2016). Hence, they should be considered in the analysis to ensure the correct modelling of mediational pathways. However, causality between the mediators LOC and adult SES could run in both directions (Bailis et al., 2001; Cobb-Clark et al., 2014; Infurna et al., 2011; Murray et al., 2012; Schnitzlein and Stephani, 2016). For this reason, we did not specify a causal relationship between the two factors but rather assumed a covariance between their error terms (path F in Fig. 1).

All analyses were adjusted for age, sex, living alone, living in territories of former East/West Germany, being a German citizen, having a direct or indirect migration background, number of children in the household, seasonality and year of survey. Additionally, we computed cluster robust standard errors, with clusters at the individual level to consider dependency of observations across years. We weighted our models using individual-specific sampling weights. Since all our outcomes were either dichotomous (smoking) or categorical (physical activity, alcohol consumption, diet), we estimated each model applying the weighted least square mean and variance adjusted estimator (WLSMV) (Brown, 2014).

Based on this estimation, we obtained results of the effect decomposition computing standardized direct, indirect, and total effects as well as the respective cluster-robust bootstrapped confidence intervals with 1000 replications (Nitzl et al., 2016). More specifically, the *total effect* is the effect of childhood SES on health behavior controlling only for confounders. The *direct effect* is the effect of childhood SES on the risk factors controlling for mediators and confounders (path A). The *indirect effect* via the single mediators was computed using the product method, namely by multiplying the coefficient of the exposure on the mediator (paths B or D) with the coefficient of the mediator on the outcome (paths C or E) (Nitzl et al., 2016; VanderWeele, 2016). Furthermore, we computed the proportion mediated (PM) by the single mediators as share of the total effect (Brown, 2014).

To test the presence of mediation, we used the proof logic described in Nitzl et al. (2016). Accordingly, we tested the significance and direction of the indirect effect and then defined whether there is full, partial or no mediation by looking at the significance of the direct effect. For all models, we reported goodness-of-fit measures (CFI, SRMR) and R squared values of the respective outcome (Appendix E).

In order to deal with missing data, we adopted a *full information maximum likelihood strategy* (FIML) assuming a *missing at random* (MAR) pattern (Brown, 2014) (Appendix A). However, if the missing mechanism is non-ignorable, i.e. if the probability of missing data on a variable depends on its values, concerns regarding potential bias of the FIML estimates could arise. However, the MAR assumption cannot be tested. Therefore, we took these considerations into account by carrying out a sensitivity analysis adopting a listwise deletion strategy, which is regarded to be the most robust method to violations in the MAR assumption (Allison, 2001) (Appendix F).

To consider potential differential effects, we estimated separate models for different sex (male/female) and age ("young" (18–40), "middle" (41–65) and "old" (66–97)) groups, setting the factor loadings for the latent variable equal across groups (Appendix D – test of metric invariance).

Due to the large number of tests carried out, reservations regarding multiple testing could arise. To avoid concerns of type II errors, we adopted a conservative approach basing our evaluation on 99% bootstrapped confidence intervals. Additionally, to highlight potential type II errors we marked also results whose 95% confidence interval did not include the null.

All analyses were carried out using Mplus Version 8.3 (Muthén and Muthén, 2017).

4. Results

We report results of the effect decomposition in Table 2 and visualize the complete model for one outcome (smoking) as an example in Fig. 2. For smoking, a lower childhood SES was associated with a more external LOC (path B). In turn, a more external LOC was related with a higher probability of smoking (path C). Hence, the indirect effect via external LOC on smoking was positive ($\beta = 0.004$ [0.001; 0.009]) (Table 2). Furthermore, a lower childhood SES also corresponded to lower adult SES (path D). Therefore, given that a lower adult SES was associated with higher probability of smoking (path E), the resulting indirect effect via adult SES was positive ($\beta = 0.046$ [0.033; 0.058]) (Table 2). Finally, after controlling for the two mediators, childhood SES still had a significant effect on smoking (path A). Hence, in the case of smoking, we observed a partial mediation of the effect of childhood SES via the mediators. The proportion mediated (PM) by LOC was 4%, while adult SES played a major role (PM = 50%) (Table 3).

A similar partial mediation could be observed for low physical activity (Table 2), in which case lower childhood SES was significantly related with a higher probability of low levels of physical activity, despite controlling for the mediators (path A). The proportion mediated by the different factors was similar to smoking, with LOC mediating up to 6% of the effect.

For unhealthy diet, we could observe only a partial mediation via adult SES, while LOC showed a significant indirect effect, but only at the 95% significance level.

In contrast, a lower childhood SES was associated with less frequent alcohol consumption (path A). Again, external LOC and low adult SES partially mediated this effect. In fact, the more external the LOC, the less frequent was alcohol consumption (paths B x C). Additionally, a lower adult SES was associated with a more frequent alcohol consumption (paths D x E).

Our goodness-of-fit statistics showed reasonable but not exceptional model fit, with SRMR ≤ 0.06 and CFI ≥ 0.85 for all outcomes (Appendix E).

4.1. Stratification for sex

The sex stratification showed that LOC was a partial mediator only for women, but not for men (Table 2). For males, LOC was a partial mediator only for physical activity, while we observed larger confidence intervals for all other outcomes. However, it should be noted that the point estimates did not differ much between sexes, whereas the coefficients for men's indirect effects constituted potential type II errors due to the conservative approach we adopted.

Additionally, more information on these effects can be obtained by looking at the underlying effects composing the indirect effect (Fig. 3). For the indirect effect, we observed that the impact of childhood SES on external LOC (path B) was significant for both sexes. Therefore, the non-significant indirect effect via external LOC for men must be due to non-significant effects of external LOC on the health behaviors (path C). In addition, results for the indirect effect via adult SES indicated that men had a significantly lower intergenerational mobility than women (path C), driving the difference observed.

Again, goodness-of-fit statistics indicated reasonable model fit of the models, with CFI > 0.92 and SRMR < 0.10 for all outcomes (Appendix E).

Table 2
SEM results for all health behaviors, with effect decomposition (in SD, 99% CI) and with sex stratification.

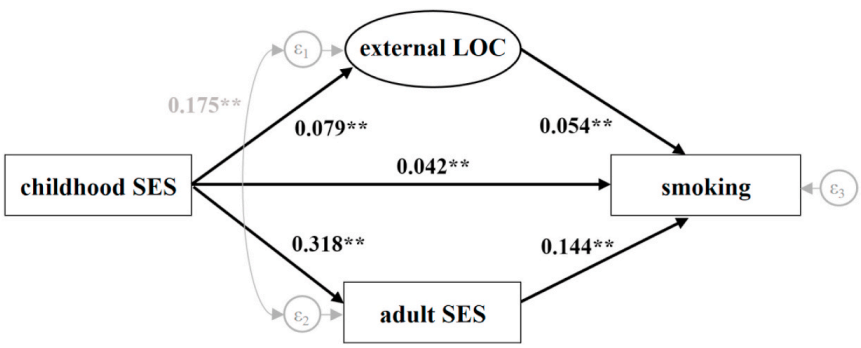
		All				Male				Female			
		est.		*95% CI*	*PM*	*est.*		*95% CI*	*PM*	*est.*		*95% CI*	*PM*
Smoking													
DE	**A**	0.042	**	[0.001; 0.084]	46%	0.040		[−0.015; 0.095]	38%	0.045	*	[−0.012; 0.102]	58%
IE (adult SES)	**D x E**	0.046	**	[0.033; 0.058]	50%	0.063	**	[0.044; 0.083]	59%	0.027	**	[0.012; 0.045]	35%
IE (LOC)	**B x C**	0.004	**	[0.001; 0.009]	4%	0.003		[−0.002; 0.01]	3%	0.005	**	[0.001; 0.011]	6%
TE		0.092	**	[0.055; 0.131]	100%	0.106	**	[0.054; 0.154]	100%	0.078	**	[0.022; 0.13]	100%
Freq. Alcohol consumption													
DE	**A**	−0.063	**	[−0.091; −0.038]	65%	−0.045	**	[−0.094; −0.001]	60%	−0.092	**	[−0.133; −0.056]	71%
IE (adult SES)	**D x E**	−0.028	**	[−0.038; −0.018]	29%	−0.026	**	[−0.042; −0.009]	35%	−0.032	**	[−0.046; −0.017]	25%
IE (LOC)	**B x C**	−0.005	**	[−0.009; −0.002]	5%	−0.005	*	[−0.009; 0.000]	7%	−0.006	**	[−0.012; −0.002]	5%
TE		−0.097	**	[−0.123; −0.068]	100%	−0.075	**	[−0.116; −0.033]	100%	−0.130	**	[−0.166; −0.093]	100%
Low physical activity													
DE	**A**	0.065	**	[0.038; 0.093]	45%	0.055	**	[0.016; 0.099]	36%	0.072	**	[0.036; 0.11]	53%
IE (adult SES)	**D x E**	0.070	**	[0.058; 0.082]	49%	0.087	**	[0.069; 0.104]	57%	0.056	**	[0.04; 0.072]	41%
IE (LOC)	**B x C**	0.009	**	[0.005; 0.014]	6%	0.011	**	[0.004; 0.018]	7%	0.008	**	[0.003; 0.015]	6%
TE		0.144	**	[0.118; 0.172]	100%	0.153	**	[0.114; 0.193]	100%	0.136	**	[0.101; 0.172]	100%
Unhealthy diet													
DE	**A**	0.038	**	[0.005; 0.067]	49%	0.010		[−0.044; 0.054]	20%	0.067	**	[0.022; 0.11]	63%
IE (adult SES)	**D x E**	0.036	**	[0.025; 0.048]	47%	0.039	**	[0.021; 0.056]	76%	0.037	**	[0.019; 0.053]	35%
IE (LOC)	**B x C**	0.003	*	[0.000; 0.006]	4%	0.003		[−0.002; 0.008]	6%	0.003	*	[0.000; 0.008]	3%
TE		0.077	**	[0.047; 0.102]	100%	0.051	**	[0.001; 0.091]	100%	0.107	**	[0.068; 0.147]	100%

Note: SEM: structural equation model; est: estimate; CI: bootstrapped confidence interval; PM: proportion mediated; DE: direct effect; IE: indirect effect; TE: total effect; LOC: locus of control; SES: socioeconomic status, higher values indicate a lower SES. All models controlled for age, sex, living alone, West Germany, German citizen, children in the household, migration background, seasonality and year. **99% CI does not entail the null. *95% CI does not entail the null.

Table 3
SEM results for all health behaviors, with effect decomposition (in SD, 99% CI) and with age group stratification.

		Young (≤40)				Middle (41–65)				Old (>65)			
		est.		*95% CI*	*PM*	*est.*		*95% CI*	*PM*	*est.*		*95% CI*	*PM*
Smoking													
DE	**A**	0.098	**	[0.032; 0.164]	62%	0.028		[−0.033; 0.081]	38%	−0.107	**	[−0.219; −0.004]	195%
IE (adult SES)	**D x E**	0.052	**	[0.031; 0.074]	33%	0.043	**	[0.024; 0.061]	59%	0.051	**	[0.004; 0.097]	−93%
IE (LOC)	**B x C**	0.007	**	[0.001; 0.016]	4%	0.003		[−0.002; 0.009]	4%	0.001		[−0.014; 0.014]	−2%
TE		0.157	**	[0.092; 0.22]	100%	0.073	**	[0.018; 0.126]	100%	−0.055		[−0.145; 0.033]	100%
Freq. Alcohol consumption													
DE	**A**	−0.080	**	[−0.127; −0.032]	82%	−0.048	**	[−0.097; −0.004]	57%	−0.051	*	[−0.113; 0.007]	50%
IE (adult SES)	**D x E**	−0.014	*	[−0.031; 0.002]	14%	−0.031	**	[−0.044; −0.017]	37%	−0.040	**	[−0.075; −0.007]	40%
IE (LOC)	**B x C**	−0.004		[−0.01; 0.001]	4%	−0.005	**	[−0.01; −0.001]	6%	−0.010	**	[−0.021; −0.002]	10%
TE		−0.098	**	[−0.145; −0.053]	100%	−0.084	**	[−0.128; −0.043]	100%	−0.101	**	[−0.147; −0.05]	100%
Low physical activity													
DE	**A**	0.069	**	[0.025; 0.116]	49%	0.060	**	[0.018; 0.1]	41%	0.067	**	[0.008; 0.13]	39%
IE (adult SES)	**D x E**	0.062	**	[0.039; 0.082]	44%	0.075	**	[0.058; 0.09]	52%	0.094	**	[0.049; 0.13]	55%
IE (LOC)	**B x C**	0.010	**	[0.003; 0.02]	7%	0.010	**	[0.003; 0.02]	7%	0.009	**	[0.001; 0.021]	5%
TE		0.141	**	[0.095; 0.185]	100%	0.145	**	[0.105; 0.186]	100%	0.170	**	[0.113; 0.22]	100%
Unhealthy diet													
DE	**A**	0.059	*	[0.000; 0.108]	62%	0.036	*	[−0.013; 0.083]	51%	0.000		[−0.068; 0.064]	0%
IE (adult SES)	**D x E**	0.032	**	[0.013; 0.052]	34%	0.034	**	[0.021; 0.048]	48%	0.057	**	[0.022; 0.094]	93%
IE (LOC)	**B x C**	0.004	*	[0.000; 0.011]	4%	0.001		[−0.003; 0.006]	1%	0.004		[−0.006; 0.013]	7%
TE		0.095	**	[0.046; 0.143]	100%	0.071	**	[0.021; 0.114]	100%	0.061	**	[0.008; 0.114]	100%

Note: SEM: structural equation model; est: estimate; CI: bootstrapped confidence interval; PM: proportion mediated; DE: direct effect; IE: indirect effect; TE: total effect; LOC: locus of control; SES: socioeconomic status, higher values indicate a lower SES. All models controlled for age, sex, living alone, West Germany, German citizen, children in the household, migration background, seasonality and year. **99% CI does not entail the null. *95% CI does not entail the null.



Note: SES socioeconomic status. LOC locus of control. Results in standard deviations. *99% CI does not include the null.

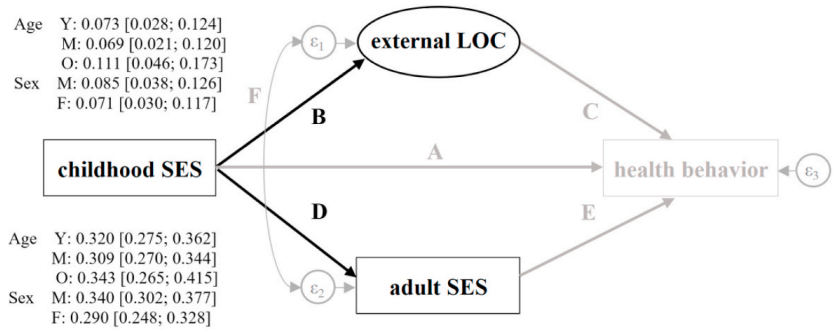
Fig. 2. Structural equation model for the outcome smoking (full results as example).

4.2. Stratification for age

The results stratified by age indicated that the mediational effect of LOC in different age groups differed among the outcomes. For physical activity, LOC was a partial mediator in all age groups, mediating 7% of the total effect in young and middle-aged with a decreasing contribution for the older (PM = 5%). External LOC was a partial mediator for smoking only in the young age group (age ≤ 40). For the outcome unhealthy diet, external LOC was not a significant mediator. In this case, adult SES fully mediated the effect of childhood SES. Additionally, alcohol consumption represented again an exception. External LOC was a successful mediator only for the middle-aged and older groups, showing an inverted mediational role.

As before, single effects showed that the effect of lower childhood SES on external LOC remained stable across age cohort (path B) (Fig. 3). The effect of lower childhood SES on adult SES (path D) showed a weaker association in the younger and middle-aged cohort, indicating increasing social mobility, although coefficients are not significantly different. Hence, the fluctuations in the indirect effect, either via external LOC or adult SES, were due to changes in the effect of the mediators on the single outcomes (paths C & E) (Fig. 3).

Goodness-of-fit statistics showed again reasonable but not exceptional model fit for all outcomes (CFI > 0.87 and SRMR < 0.13) (Appendix E).



Notes: estimate and 99% confidence interval; M: male; F: female; Y: young (18-40); M: middle (41-65); O: old (>65). Effects of the exposure and mediators on the health behaviors (paths A, C, E, F) for sex and age groups are available upon request.

Fig. 3. Effect of childhood SES on the mediators for sex and age groups (in SD, with 99% CI).

4.3. Sensitivity analysis

Using educational status of parents as a marker of childhood SES led to slight changes in the coefficients and proportions mediated, but did not alter the results considerably (Appendix F). Due to listwise deletion, almost 40% of observations got lost in each model, but results remained stable for the reduced sample, showing good robustness (Appendix F), albeit with some coefficients turning significant only at the 95% level.

The results of the analysis using the alcohol frequency definition from the year 2016 not only confirmed the results of the main analysis, but also revealed an even stronger effect of LOC as a mediator (Appendix G). For men, the proportion mediated was highest, reaching 12%, while for women the proportion mediated was 8%. Interestingly, in these models, LOC was not a significant mediator for the middle and older aged, but it was for the younger (PM = 10%), albeit at the 95% significance level.

5. Discussion

Our study provides novel evidence on the role of external LOC as a partial mediator in the relation between childhood SES and adult health behavior. This mediational role is especially relevant and robust for women and younger or middle-aged individuals. Furthermore, the effect is independent from adult SES and other demographic characteristics. Therefore, the study shows that LOC is an important mechanism linking childhood conditions and health behavior, with potential far-reaching consequences on chronic disease, mental health, and direct and indirect health care costs (Biddle et al., 2019; Cawley and Ruhm, 2011; Godos et al., 2020; McNeill, 2001).

More specifically, we could confirm our hypothesis regarding the mediational role of external LOC in linking childhood SES with health behavior in adulthood. The mediational effect and the proportion mediated by external LOC are stronger for low physical activity, where LOC mediates up to 6% of the association with childhood SES. These results indicate that external LOC has a mediational role not only for active health damaging behaviors, like smoking and drinking, but also for passive health damaging behaviors, like low levels of physical activity, where an active physical and cognitive effort would be needed to engage in health promotion. Thus, recalling the logic postulated in the theoretical explanations of LOC, our results indicate that external LOC mediates the effect of socioeconomic circumstance in childhood, leading to both aggressive and passive response patterns (Whitehead et al., 2016). Further investigations should try to gain a deeper understanding of how the LOC impacts these outcomes, i.e. whether its influence runs mainly via different expectations, patience or motivation, as key mechanisms previously highlighted in the literature (Cobb-Clark et al., 2014; Cobb-Clark, 2015).

Alcohol consumption represents an exception. While external LOC also partially mediates this association, both low childhood SES and external LOC show a protective rather than a deleterious impact on this risk factor. This counterintuitive relation has already been observed in the literature (Bailis et al., 2001; Caliendo and Hennecke, 2020; Cobb-Clark et al., 2014; Gale et al., 2008; Murray et al., 2012; Cheng and Furnham, 2018; Kiecolt et al., 2013; Lassi et al., 2019; Mendolia and Walker, 2014; Mercer et al., 2018; Norman et al., 1998; Steptoe and Wardle, 2001). In a recent study, Caliendo and Hennecke (2020) investigated the relation of LOC with alcohol consumption in the SOEP data, providing evidence for two explanations. On the one hand, they showed that almost 30% of the effect of internal LOC could be explained by a higher frequency of social opportunities and activities, which in turn influences the frequency of drinking. On the other hand, their analysis indicated that individuals with an internal LOC may underestimate the effects of drinking and, as such, engage more frequently in this unhealthy behavior. To show this, they exploited differences in risk willingness, showing that this mechanism is only visible in men. This explanation was also discussed by Cobb-Clark et al. (2014), who found that people with more internal control beliefs are less likely to avoid binge drinking, probably because they feel more confident in coping with its effects. Another explanation is that individuals may not directly link alcohol consumption to their health status and potential health consequences (Bennett et al., 1998; Bailis et al., 2001; Caliendo and Hennecke, 2020). Finally, measuring frequency of consumption may lead to different results compared to quantity or alcohol type, showing only a part of the consumption behavior (Collins, 2016).

This relation is robust to all sensitivity analyses, including a more objective definition of frequency of alcohol consumption using

2015–2016 data. This analysis shows that the self-reported definition was probably subject to individuals' specific understanding of what "frequent" alcohol consumption means, potentially influenced by SES and LOC itself (Caliendo and Hennecke, 2020). The same consideration applies to unhealthy diet since the question does not contain objective categories of what exactly a "healthy diet" is and therefore answers could be subject to interpretation. Unfortunately, we did not have any other measure of diet to verify the robustness of this results, but it could be assumed that the same downward bias observed for alcohol applies for this outcome as well.

All these results are robust to alternative definitions of childhood and adult SES (using educational status of parents and of the individual) and to a different approach to deal with missing values.

5.1. Heterogeneity: sex

This is the first study to investigate sex differences with respect to LOC as a mediator in linking childhood SES with health behavior. Our analysis shows that external LOC has a mediational effect in women but not in men. This observation results from the fact that external LOC is not associated with the outcomes in the male population, except for the outcome physical activity.

Furthermore, these results are mostly driven by sex differences in the effect of LOC on health behavior (path C), since no differences could be reported for the effect of childhood SES on LOC (path B). This result can be explained in light of previous research, indicating that the way LOC affects behavior differs between men and women (Caliendo and Hennecke, 2020; Cobb-Clark et al., 2014). These authors have shown that a more external LOC in men is linked with lower expectations regarding their return on investment: this would explain the strong and robust effect found for physical activity, but not for smoking and alcohol, where also the social and addiction components play a role. Instead, this mechanism is not evident in women, whose internal LOC seems to be more linked to motivation and satisfaction driving health behavior. These differences may explain our results and should be investigated further to gain a deeper understanding of these complex mechanisms.

Furthermore, the indirect effect via adult SES (paths D & E) is stronger in men than in women. Interestingly, this difference is due to the fact that childhood SES is a stronger predictor of adult SES in men compared to women (path D), indicating that males have a lower intergenerational mobility compared to females, as already documented in other studies (Chetty et al., 2014; Lee and Solon, 2009).

5.2. Heterogeneity: age cohorts

The results for the age-stratified analysis shows that the mechanisms investigated differ between age cohorts, depending on the health behavior regarded. For young and middle-aged participants, we observe a mediational effect for passive (low physical activity) and active health damaging behaviors (alcohol consumption, smoking). The latter might reflect not only the tendency of externally oriented individuals to start smoking, but also the capacity of less externally oriented individuals to quit once they have started. For the young age group, external LOC plays a very important role for behavior, as it mediates a rather large part of the effects of lower SES in childhood. For older participants we observe a significant mediational effect of LOC for alcohol consumption and physical activity. However, this result did not withstand most robustness checks.

In addition, our results could also reproduce the increasing trend in intergenerational social mobility for Germany (path D, Fig. 3), detected in previous research for other countries (Chetty et al., 2014; Lee and Solon, 2009). However, despite noting an increasing trend, no significant differences could be observed among the age groups.

These results complement existing research, which has demonstrated that individuals have become increasingly individualistic and externally oriented in the last decades (Twenge et al., 2004). In fact, our results show that the role of LOC as mediator for the social gradient in health behavior is stronger in the younger generations compared to middle-aged and older ones, indicating that LOC is becoming not only more external (Twenge et al., 2004), but also increasingly important for socioeconomic inequalities. However, it could also be that generally, the mediational role of LOC is more important for younger individuals and diminishing with age. Therefore, these age-stratified results should be treated with caution: given the cross-sectional nature of our data, we could not disentangle possible life-stage effects from cohort effects. Further research may use longitudinal information to take this limitation into account.

Moreover, our model might not capture the true underlying dynamics, especially for the older age group. In fact, for this group, the gap between exposure and mediators/outcomes is very large, probably causing our general model to exclude relevant factors that could have influenced behavior and LOC itself. Most importantly, our model did not take into account previous changes and deteriorations in the health status, which may have influenced both reporting of LOC and health behavior, for this group more than the others. Therefore, more complex modelling strategies, for example taking a life course approach using longitudinal data, are needed to investigate this relation in the older age group.

5.3. Strengths and limitations

In the present study, the use of SEM allowed us to investigate the complex mechanisms underlying the socioeconomic gradient in health behavior. Compared to previous studies, we were able to enhance established methods by including external LOC as a latent variable and using a measurement model with convincing goodness-of-fit levels. Moreover, we also tested multiple mediator effects within a single model and allowed the specification of covariance between the error terms of the two mediators (Brown, 2014). We could test our hypothesis stratified for sex and age groups and against several alternative models with adequate statistical power. Furthermore, our investigation was based on a large representative sample of the German population, including a large variation in the SES exposure included, thus producing results with high external validity.

Despite these strengths, our study contains some limitations. First, health status in childhood and its effects on LOC, SES, and behavior in adulthood could not be taken into account due to lack of information. Furthermore, our model did not consider previous values of health status as potential determinants of behavior. This is especially important for the older age group, where the temporal gap between exposure and mediators/outcomes was larger. Second, our investigation is based on repeated observations for some participants, but we did not exploit the longitudinal nature of the data due to a substantial loss to follow-up (34%). Hence, we did not consider temporal interrelations among the factors included and potential changes of external LOC. Third, despite the additional sensitivity analysis using listwise deletion, our way of dealing with missing data may still be flawed, leading to potentially biased estimates (Allison, 2001). To overcome this limitation, the missing mechanism should be modelled, but this would require a large amount of information, most of which is not available. These first three limitations may cast some doubt on the causal interpretation of our model, mainly due to omitted variable bias. Hence, our results should be further investigated considering these limitations. Finally, an additional limitation concerns the operationalization of the exposure using mainly father related information. Recent studies have shown in fact that maternal education and employment status play an important role for the offspring's health outcomes (Cutler et al., 2012; Huebener and Marcus, 2019).

5.4. Further issues and further research

Further improvements of this model should focus on exploiting the longitudinal nature of the data to include also previous values of health status as a potential determinant of LOC and health behavior. In order to consider this, rich longitudinal information is needed to model these complex temporal dependencies between health and behavior, allowing the model to adequately capture recursive dependencies (e.g. behavior influences health which in turn could influence behavior), time changes and avoiding concerns of reverse causation and omitted variables.

In addition, further psychosocial and personal traits could be investigated, thus complementing this piece of research and shedding more light on the mechanisms of socioeconomic inequalities in behavior.

Moreover, some studies have investigated the role of LOC as a moderator of the effect of socioeconomic circumstances on health or behavior (Montez and Hayward, 2014; Ross and Mirowsky, 2011; Taylor and Seeman, 1999; Pudrovska et al., 2005). In fact, according to these studies, LOC could be an important resource in case that disadvantaged events or circumstances occur, helping to reduce the adverse effect of childhood socioeconomic SES on behavior and health. Hence, LOC would function not only as a mediator but also as a moderator in the relation between childhood SES and health behavior. Further studies should integrate this potential mechanism in a more complex model, allowing for exposure-mediator interactions and analyzing effect decomposition using the appropriate framework (Muthén and Asparouhov, 2015; Valeri and VanderWeele, 2013).

5.5. Policy implications

Our results support the creation of intervention strategies that contribute to diminish the negative influence of disadvantaged SES on the formation of control beliefs in children and adolescents and fostering a more internal LOC in adults from lower socioeconomic backgrounds. This is in line with the recommendation of Mackenbach, who suggested that "a direct attack on the personal, psychosocial and cultural determinants of health inequalities may be necessary to achieve a substantial reduction of health inequalities" (Mackenbach, 2012).

Despite the growing evidence that psychosocial factors such as LOC might be important targets to reduce socioeconomic inequalities, the research and debate surrounding corresponding interventions are still young. Among adult individuals, available interventions have shown promising results in internalizing LOC, involving few resources and with consequences lasting in the medium run (Mehrtak et al., 2017; Reijnders et al., 2017; Wolinsky et al., 2009). However, their efficacy and cost-efficacy in the long-run is not yet clear. This depends strongly on whether LOC is a deeply-rooted construct or can be influenced in advanced age. If the first is true, policy actions to break the negative connection between childhood SES and LOC formation should begin earlier in life, when the socioeconomic environment starts shaping one's own personality and beliefs. This would imply complementing school curricula with educational tasks that foster the creation of internal control beliefs of children and adolescents, empowering their choices over their own life and life circumstances (Seligman et al., 2009). This underlines once again the importance and the potential roles of educational systems and structures outside of the parental home and environment in diminishing the negative impact of low SES on behavior, thus diminishing inequalities (Walker et al., 2019). Future research should investigate these issues to create innovative policy recommendations.

Achieving a more internally oriented LOC in the population could have far-reaching implications beyond the individual health behaviors considered in the present study. In the context of primary and secondary behavioral prevention, internal LOC could help to improve health outcomes, especially in those cases where adherence to specific behavioral components (e.g. healthier dietary choices after hypertension diagnosis) or medication regimes is an important component of therapy and prevention. Strategies to internalize control beliefs could also lead to higher efficacy of policy action in the context of environmental/structural prevention. In fact, structural policies targeted at improving availability and reach of services (e.g. healthy food choices in the local shops, fitness and sport facilities, smoke quitting groups/services) might be a necessary albeit not sufficient condition to improve behavioral choices of individuals from disadvantaged socioeconomic contexts, since a more external LOC could still prevent them from taking those services into account. This would suggest not only the necessity of strategies to internalize LOC, but also the use of more paternalistic measures and nudges to prompt individuals to take those services and opportunities into account.

6. Conclusion

The persistence of socioeconomic inequalities in health despite extensive evidence and policy action calls for more research on the subject, also including behavioral and psychosocial factors as important determinants and potential targets for prevention and therapy. Our study provides novel evidence on the role of LOC as a factor partly explaining the relationship between a low SES in childhood and health behavior in adulthood, independent from adult SES. We observe the presence of this mechanism in women but not in men, in young and middle-aged adults but not in older participants. These results indicate that LOC is a potential target for diminishing socioeconomic inequalities in health behavior, which in turn might contribute to drive inequalities in physical and mental health, quality of life and productivity.

Our results may encourage the creation of targeted interventions, which effectively diminish the connection between childhood SES and LOC and actively strengthen and internalize control beliefs, such as mentoring programs, cognitive therapies or educational strategies. Potential effects could include improving the efficacy of existing behavioral and environmental or structural prevention policies.

Research involving human participants

The database we used is the German Socioeconomic Panel (SOEP), an annual socioeconomic survey of households in Germany. The survey was approved by the German Council of Science and Humanities (Drs. 9503–09). No ethics approval was needed. We accessed anonymized SOEP data via project agreement.

Informed consent

Participants were asked for informed consent before participating in the data collection process in accordance with German and European law.

Funding

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Availability of data and material

Data from the SOEP study is available online via project agreement.

Code availability

Code can be made available upon request.

Declaration of competing interest

All authors declare no conflicts of interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ssresearch.2020.102521.

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2.2. Manuscript 2

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The effect of retirement on biomedical and behavioral risk factors for cardiovascular and metabolic disease

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ABSTRACT

Retirement is a major life event potentially associated with changes in relevant risk factors for cardiovascular and metabolic conditions. This study analyzes the effect of retirement on behavioral and biomedical risk factors for chronic disease, together with subjective health parameters using Southern German epidemiological data. We used panel data from the KORA cohort study, consisting of 11,168 observations for individuals 45–80 years old. Outcomes included health behavior (alcohol, smoking, physical activity), biomedical risk factors (body-mass-index (BMI), waist-to-hip ratio (WHR), glycosylated hemoglobin (HbA1c), total cholesterol/HDL quotient, systolic/diastolic blood pressure), and subjective health (SF12 mental and physical scales, self-rated health). We applied a parametric regression discontinuity design based on age thresholds for pension eligibility. Robust results after p-value corrections for multiple testing showed an increase in BMI in early retirees (at the age of 60) [$\beta = 1.11$, corrected p-val. < 0.05] and an increase in CHO/HDL in regular retirees (age 65) [$\beta = 0.47$, corrected p-val. < 0.05]. Stratified analyses indicate that the increase in BMI might be driven by women and low educated individuals retiring early, despite increasing physical activity. The increase in CHO/HDL might be driven by men retiring regularly, alongside an increase in subjective physical health. Blood pressure also increased, but the effect differs by retirement timing and sex and is not always robust to sensitivity analysis checks. Our study indicates that retirement has an impact on different risk factors for chronic disease, depending on timing, sex and education. Regular male, early female, and low educated retirees should be further investigated as potential high-risk groups for worsening risk factors after retirement. Future research should investigate if and how these results are linked: in fact, especially in the last two groups, the increase in leisure time physical activity might not be enough to compensate for the loss of work-related physical activity, leading thus to an increase in BMI.

1. Introduction

Cardiovascular and metabolic diseases are among the major causes of morbidity and mortality in the population in high and middle income countries (World Health Organization, 2018). They are associated with a large economic burden on healthcare systems (Bloom et al., 2012), with extensive losses in quality of life (Glasgow et al., 1997; Juenger et al., 2002) and productivity (Chaker

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et al., 2015; Pedron et al., 2019). Their incidence increases sharply beyond the age of 55 (Tamayo et al., 2016; Mozaffarian et al., 2015), making this age group a primary target of public health preventive measures. Among the most prominent modifiable risk factors for these illnesses are unhealthy behaviors, whereas other critical determinants include physical and psychosocial occupational stressors and socioeconomic conditions (Nyberg et al., 2013; Winkleby et al., 1992).

In the life of a working individual, retirement marks a major event, often perceived as a transition from middle age to old age, which goes along with a reshaping of one's own identity and daily activities (Atchley, 1976; Gall et al., 1997; Palmore et al., 1984). As such, retirement is connected with several important changes in the aforementioned risk factors for chronic disease, both in a positive and negative way (Kasl and Jones, 2000). On the one hand, for those who strongly identify themselves with their role as working individuals, this transition could be connected with a loss in sense of purpose and social contacts. On the other hand, at retirement individuals are relieved from occupational strains and can dedicate themselves to other meaningful and fulfilling activities (Atchley, 1976; Gall et al., 1997; Palmore et al., 1984). Through the reshaping of daily activities, individuals could become more or less active than during their working age, with direct and lasting consequences for their cardiovascular and metabolic health (Zantinge et al., 2013).

Careful consideration of potential health effects of retirement is mandatory to shape effective and successful labor market and health policies aimed at keeping the older workforce active, extending working life, and reshaping flexible retirement exit routes. These mark important societal and political challenges, that will influence the sustainability of healthcare and pension systems in the next decades (Carone et al., 2016). Despite an increased interest in the literature regarding the effect of retirement on health, evidence concerning potential effects for physical health and the underlying mechanisms remains inconclusive if not completely lacking. Understanding the effect of retirement on biomedical and behavioral risk factors for chronic diseases is crucial. In fact, risk factors are directly related to the aforementioned changes at retirement and might have long lasting consequences on cardiovascular and metabolic health later in life, on disability, longevity and health care costs.

In our study, we aimed at estimating the causal effect of retirement on a large set of biomedical and behavioral risk factors for cardiovascular and metabolic disease, including glycosylated hemoglobin, total cholesterol/HDL-cholesterol ratio, blood pressure, body-mass-index (BMI), waist-to-hip ratio (WHR), physical activity, smoking and alcohol consumption. We also investigated the effect on subjective health indicators. We analyzed the research question by using a German epidemiological dataset, which included objectively measured and validated observations on risk factors and self-reported health behavior information.

Estimating the effect of retirement on health is not straightforward. In fact, selection problems and potential unobserved confounding might considerably bias the results, jeopardizing the identification of a causal effect (Nishimura et al., 2018; Barnay, 2016). Therefore, in our study we used a regression discontinuity design, exploiting the retirement age thresholds as exogenous sources of variation to obtain valid causal effect estimates (Lee and Lemieux, 2010). The same method was already employed by other authors for the identification of the effects of retirement on a wide range of health outcomes (Coe and Zamarro, 2011; Eibich, 2015; Godard, 2016; Insler, 2014; Johnston and Lee, 2009; Müller and Shaikh, 2018; Zhao et al., 2017). However, unlike many of these studies on the effect of retirement using a regression discontinuity design, we applied a parametric identification strategy, which allowed us to include a larger period of time around the cutoff by choosing the correct modelling of the health-age relationship (Lee and Lemieux, 2010). Furthermore, we extensively explored the robustness of our findings using a set of specification curves (Christensen and Miguel, 2018; Simonsohn et al., 2015).

Our study contributes to the available literature in two ways. First, we are among the first to estimate the causal effect of retirement on a large set of biomedical risk factors for chronic cardiovascular and metabolic conditions (Behncke, 2012). Not only do these represent clinical parameters, directly relevant in the daily clinical practice. Estimating the impact of retirement on these outcomes might also help in understanding the concrete long run effects of retirement on cardiovascular and metabolic health, providing insights in an area in which evidence is either scarce or even lacking. Second, by including a large set of behavioral parameters, subjective health indicators and heterogeneity sources, we are able to provide a complete picture of the effects of retirement, identifying effects, relevant mechanisms and risk groups. Furthermore, this allows us to establish a link between previously reported changes in health behavior and effects on chronic diseases, providing evidence-based targets for public health policies.

Our results show that regular retirement (at the age of 65) leads to an increase in CHO/HDL levels. Stratified results indicate that this increase might be driven especially by men retiring regularly and is accompanied by increasing subjective physical health. Furthermore, early retirement (age 60) leads to a robust increase in BMI. This is confirmed by an increasing tendency in WHR, despite an increase in physical activity. Early female and low educated retirees seem to be particularly affected by these negative changes. Combining these results, a possible interpretation is that these groups are not able to compensate the loss in work-related physical activity with enough leisure time physical activity after early retirement, leading thus to an increase in the risk of cardiovascular and metabolic disease later in life. Yet, this interpretation should be appreciated with caution and further investigated especially for women, due to their more selective labor market participation. Nevertheless, following our current results, men retiring regularly and women and low educated individuals retiring early should be considered as high-risk targets for behavioral interventions for a healthy adaptation to retirement, targeting also the other risk factors considered, which did not show any change.

This paper is structured as follows. First, a literature overview of the most relevant evidence on the effect of retirement on health is presented. Hereby, we particularly focus on behavioral and biomedical risk factors, chronic disease incidence, and subjective health. In the "Methods" section the analyzed survey data and empirical strategy are presented. Follows a "Results" section, which also contains the heterogeneity analysis and extensive robustness checks. Concluding we discuss, interpret and compare our results with the available literature.

2. Related literature

In the last few years, the question regarding the effect of retirement on health has received increasing attention. The empirical evidence shows a generally positive impact of retirement on subjective health and behavior. Studies which estimated the causal effect of retirement used mainly instrumental variables strategies and generally showed a positive effect of retirement on physical activity and smoking cessation (Eibich, 2015; Insler, 2014; Müller and Shaikh, 2018; Zhao et al., 2017; Celidoni and Rebba, 2017; Kämpfen and Maurer, 2016; Motegi et al., 2016; Oshio and Kan, 2017; Zhu, 2016). Furthermore, most studies evidenced an increase in subjective health (Coe and Zamarro, 2011; Eibich, 2015; Insler, 2014; Johnston and Lee, 2009; Oshio and Kan, 2017; Zhu, 2016; Blake and Garrouste, 2013; Coe and Lindeboom, 2008;

DeGrip et al., 2012; Hessel, 2016; Mazzonna and Peracchi, 2015; Neuman, 2007; Kolodziej and Garcia-Gomez, 2019; Messe and Wolff, 2019), with few exceptions showing either a negative or no effect (Johnston and Lee, 2009; Sahlgren, 2012; Dave et al., 2006). A recent study by Anxo et al. (2019) revealed that individuals who continued working past age 65 reported on average a better self-rated health during retirement than those who retired at 65. The effect however was found only in the short run, since no difference was present after 6 years.

However, a closer look at the mental health component displays no effects of retirement on depression, measured with different scales (Coe and Zamarro, 2011; Blake and Garrouste, 2013; Neuman, 2007; Latif, 2013; Heller-Sahlgren, 2017). Furthermore, studies investigating the impact of retirement on cognitive functioning report accelerated cognitive decline after retirement (Bonsang et al., 2012; Clouston and Denier, 2017; Mazzonna and Peracchi, 2012; Rohwedder and Willis, 2010), while some other studies detected unclear effects (Coe and Zamarro, 2011; Coe et al., 2012; de Grip et al., 2015). A recent study using European SHARE data showed that the effect of retirement on cognition is more sophisticated and strongly depends on timing: for regular retirees it has a detrimental effect, while for early retirees it has rather a protective effect (Celidoni et al., 2017).

Regarding physical health, the empirical evidence has not yet been able to disentangle the complex and ambiguous effect of retirement, producing scarce and mixed findings. This is probably not only due to the inherent complexity of modelling this transition (Nishimura et al., 2018; Barnay, 2016), but also to scarce data availability of objectively measured physical health parameters in large socioeconomic surveys.

Specifically relevant for the sake of the present work are studies investigating the association between retirement and the risk of chronic cardiovascular and metabolic conditions, which generally reported mixed findings (Insler, 2014; Johnston and Lee, 2009; Behncke, 2012; Hessel, 2016; Neuman, 2007; Horner and Cullen, 2016; Shai, 2018; Moon et al., 2012; Xue et al., 2019). However, results of instrumental variables approaches showed no effects of retirement on the risk of chronic conditions or composite indices, which include indistinctly a large number of cardiovascular and metabolic conditions such as myocardial infarction, stroke, cardiovascular disease, hypertension and diabetes (Johnston and Lee, 2009; Hessel, 2016; Neuman, 2007; Horner and Cullen, 2016). Here, the risk of diabetes marks an exception since Horner and Cullen (2016) reported increased risk, while Insler (2014) noted a protective effect of retirement for this condition. The study by Behncke (2012) on the effect of retirement on chronic cardiovascular conditions and metabolic syndrome as a risk factor is directly relevant for the present study. The author used data from England and an identification strategy primarily based on nonparametric matching, which leaves open concerns of potential residual bias. In contrast, we draw on a regression discontinuity design to address such concerns of bias and provide new evidence for Germany. Finally, while Behncke (2012) primarily used a composite outcome based on self-reported diagnoses (metabolic syndrome), we use single and objectively measured biomarkers, which can also capture preclinical conditions.

Another possible reason why no effect of retirement on cardiovascular disease and diabetes could be observed is that, in the short run, the effect of retirement might rather concern their biomedical risk factors, which respond quicker to changes in lifestyle and which are directly related to an increased risk for chronic conditions later in life. However, evidence regarding the causal effect of retirement on biomedical risk factors for chronic diseases is scarce and mainly focused on weight or body-mass-index (BMI). Most studies reported a modest increase (Godard, 2016; Behncke, 2012; Chung et al., 2009; Goldman et al., 2008), while others found either negative or no effects (Eibich, 2015; Johnston and Lee, 2009). Few studies have investigated the association with blood biomarkers, such as blood pressure and cholesterol levels (Behncke, 2012; Xue et al., 2017), as emerges also from a recent review (Xue et al., 2019). However, they differ substantially in their methodology, so that concerns regarding residual bias remain. Furthermore, in this context, very few studies have investigated causal effects on both health behavior and health outcomes based on one unique dataset, allowing them to draw conclusions regarding possible underlying mechanisms (Eibich, 2015; Insler, 2014; Zhu, 2016). Available studies report no effects on alcohol consumption, increased physical activity and reduced smoking, together with increased self-rated health (Eibich, 2015; Godard, 2016; Insler, 2014; Zhu, 2016), and showed again different effects on BMI (Eibich, 2015; Godard, 2016). Interestingly, this leads to different scenarios and interpretations from different authors. In a study using European SHARE data, Godard (2016) showed that men tend to increase their BMI after retirement, without changing their levels of physical activity. On the contrary, women tend to increase (albeit not robustly) their leisure time physical activity levels, thus compensating the loss of work-related physical activity and preventing an increase in BMI after retirement. Although his study was also based on a large dataset from a German population, Eibich (2015) found slightly different results: both men and women tend to increase their physical activity after retirement, more than compensating their loss in work-related physical activity leading also to a significant decrease in BMI.

Furthermore, other authors investigated the impact of retirement on grip strength, as predictor for disability and mortality in the elder population (Leong et al., 2015). They reported a short-term positive effect of retirement, but also an increase in the rate of muscle strength loss (Bertoni et al., 2018). Other studies directly investigated mortality and life expectancy, reporting mixed results depending on retirement timing, sex and socioeconomic status (Hallberg et al., 2015; Brockmann et al., 2009; Hult et al., 2010).

The presence of mixed findings in the above-mentioned literature could also be due to the presence of several sources of heterogeneity, which mark differential effects of this transition on health. First, retirement timing (early vs. regular) might be associated with distinct groups and retirement motives, which potentially influence subsequent health and behavior. One study already showed different effects on the considered outcomes depending on this factor (Eibich, 2015). Second, the effect of retirement could be different for men and women. This might be due to the rather selective labor market participation of women especially at older ages, but also to different retirement rules and incentives for both sexes in most countries (US Social Security Administration, 2019). Nevertheless, studies that differentiated for sex, found similar improvements in physical activity in both males and females (Eibich, 2015; Celidoni and Rebba, 2017; Kämpfen and Maurer, 2016; Motegi et al., 2016), but also unclear effects on weight (Eibich, 2015; Godard, 2016; Forman-Hoffman et al., 2008). Third, socioeconomic status might be responsible for differential retirement effects. Most studies that stratified for occupational characteristics found that the positive effect of retirement was stronger for individuals retiring from strenuous occupations (Godard, 2016; Hessel, 2016; Mazzonna and Peracchi, 2015; Kolodziej and Garcia-Gomez, 2019; Shai, 2018; Westerlund et al., 2009) while others found no differential effects (Moon et al., 2012). Additionally, a higher education could also be connected with lower physical occupational strain but also stronger work attachment (Hessel, 2016), representing a source of heterogeneity. Results are however scarce and indicate no heterogeneous effects for different educational groups.

3. Methods

3.1. Data: the KORA survey

We used data from the population-based KORA study (Cooperative Health Research in the Region of Augsburg). We pooled data from two separate surveys, namely S3 (1994–95) and S4 (1999–2000), and the respective follow-up studies [F3 (2004–5), F4 (2006–8), FF4 (2013–14)]. The two baseline surveys were sampled to be population representative, while the loss to follow-up was about 30 %. All participants received a computer-assisted personalized interview (CAPI), several medical examinations, and blood tests. The study was approved by the Ethics Committee of the Bavarian Medical Association (Ethics number: S3 Bundesdatenschutz – F3 03097, S4 99186, F4 and FF4 06068). All study participants gave written informed consent. A detailed description of the KORA study can be found elsewhere (Holle et al., 2005).

For our main model, we focused on individuals who were between 45 and 80 years old. The pooled dataset thus included 11,168 observations, with an average age of 59 years, 49 % males, and 33 % high educated individuals (Table 1).

We analyzed a set of health behaviors, risk factors for chronic disease, and subjective health parameters (Table1). We dichotomized the health behavior variables, including regular physical activity (at least one hour/week)[2], current smoking, no alcohol consumption, and excessive alcohol consumption. The last two variables were calculated based on average self-reported consumption, assessed using a validated recall method (Keil et al., 1997), in which participants were asked how much beer, wine, and spirits they consumed on the previous weekday and weekend. We defined alcohol excess for men (women) as consumption $\geq$24 g/day ($\geq$12 g/day) (Burger et al., 2004).

We analyzed relevant biomedical risk factors for chronic cardiovascular and metabolic disease. These include glycosylated hemoglobin (HbA1c, %), total cholesterol/HDL-cholesterol ratio (CHO/HDL, %), diastolic and systolic blood pressure (mmHg), body-mass-index (BMI, kg/m^2), and waist-to-hip ratio (WHR). All parameters were measured following current standards at the time of data collection. A detailed description of each procedure can be found elsewhere (Laxy et al., 2016; Meisinger et al., 2006; Meisinger et al., 2002). Based on the interquartile range method, severe outliers for each risk factor were identified and excluded from the analysis.

Subjective health status was assessed using the SF12 questionnaire, including a mental and a physical health scale (Ware et al., 1996). Additionally, we assessed self-rated health as a predictor of mortality, especially among the older population (Idler and Benyamini, 1997). The original variable was measured on a 5-point Likert scale from "bad" (1) to "very good" (5) and was dichotomized to indicate "satisfactory health" (score $\geq$3).

Other relevant factors considered were sex, education, living alone, and the intake of antihypertensive medications (AHM). High education was defined as having had at least 12 years of schooling (roughly equivalent to high school). Intake of AHM was determined by a computer-assisted drug recording procedure, involving both self-reported information and drug package collection.

Retirement was defined based on self-reported information. Individuals were considered retired if they reported their current employments status as “retired”. We decided to include in the control group all other employment types, i.e. employed, unemployed, others (homemakers, long-term sick), since according to Nishimura et al. (2018), relevant differences in the effect size across studies investigating the impact of retirement were not due to the sample composition but rather to the methodology applied.

3.2. The German pension system

In Germany, the public pay-as-you-go pension system is still one of the major sources of old age security, although other private and mixed forms are growing in importance (Federal Ministry of Labor and Social Affairs, 2016).

The German pension system offers several alternative pension plans. In Table 2 we provide a brief description of the relevant schemes during the period covered in this study (1994–2014).

In this system, the receipt of a public pension is subject to specific age thresholds. At the age of 65, all individuals with at least 5 years of contributions were entitled to leave their job and receive a full old-age pension, i.e. without deductions in the standard old-age pension plan. Certain subgroups of the population were allowed to retire earlier under alternative schemes, depending on their contribution years and their year of birth (Table 2). At the time of data collection, individuals with a disability, long-term unemployed, partially retired individuals, and women were allowed to retire early at the age of 60 years. Another pension plan allowed long-term insured individuals (with at least 35 years of social security contributions) to retire early with deductions, at the age of 63 (Börsch-Supan et al., 2018; Deutsche Rentenversicherung Bund (DRV), 2019).

In the long period considered, the German pension system underwent some changes. A comprehensive description of the evolution of the system is provided by Börsch-Supan et al. (2018). However, only a small group of individuals surveyed in the last follow-up was affected by these reforms (FF4, 2013–2014). In fact, with the 1999 pension reforms, a stepwise increase in the regular retirement threshold was introduced starting from the year 2012. As the changes in retirement age were very small and progressive, we decided not to control for this issue (Deutsche Rentenversicherung Bund (DRV), 2019). Further modifications in the pension plans during the time period considered are described in Table 2. Most changes involve a stepwise increase of thresholds or a complete deletion of the pension plan. Again, since these modifications were introduced stepwise and regarded only a small group of individuals surveyed in the last follow up, we decided not to control for these issues.

At the time data were collected, most individuals retired either in the standard old-age pension plan at 65 (33 % in 1995 and 42 % in 2013) or in the early retirement plans at age 60 (57 % in 1995 and 37 % in 2012). The other available pension plan (i.e. pension for long-term insured at 63 or 65) was chosen by a smaller number of individuals (Deutsche Rentenversicherung Bund (DRV), 2018).

As depicted in Fig. 1, at the retirement thresholds, the share of retirees increases disproportionately, creating two prominent discontinuities in the probability of retirement, one at 60 years (“early retirement age” – ERA) and one at 65 years (“official retirement age” – ORA). No discontinuity is however visible at 63 years, probably because this pension plan is usually chosen by a relatively small number of individuals (Table 2) (Deutsche Rentenversicherung Bund (DRV), 2018). Additionally, the two discontinuities can be observed for sex and education stratified groups (Appendix A in Supplementary data). Based on these considerations, we exploited the “early” (ERA – retirement at 60) and “official” (ORA – retirement at 65) retirement cutoffs as instruments in our analysis but abstained from considering the retirement age at 63 years as a further cutoff point.

[2] We adopted the same dichotomization used in other studies (Eibich, 2015; Zhao et al., 2017), in order to increase interpretability and comparability of our results. Nonetheless, we also tested the robustness of our results using the original categorical variables. The direction and significance of the effects did not change.

Table 1
Descriptive statistics of covariates and outcome variables included.

			Not retired		Retired	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Covariates						
Age	11,168	59.28 (8.68)	6,809	54.20 (6.43)	4,359	67.22 (5.00)
Male	11,168	0.49 (0.50)	6,809	0.46 (0.50)	4,359	0.53 (0.50)
High education	11,118	0.33 (0.47)	6,773	0.38 (0.49)	4,345	0.25 (0.43)
Living alone	11,168	0.16 (0.37)	6,809	0.13 (0.33)	4,359	0.22 (0.41)
Antihypertensive med.	11,156	0.31 (0.46)	6,803	0.20 (0.40)	4,353	0.47 (0.50)
Health behavior						
No alcohol	11,155	0.30 (0.46)	6,806	0.28 (0.45)	4,349	0.33 (0.47)
Alcohol excess	11,168	0.32 (0.47)	6,809	0.33 (0.47)	4,359	0.30 (0.46)
Physical activity	11,154	0.49 (0.50)	6,804	0.51 (0.50)	4,350	0.45 (0.50)
Smoking	11,165	0.18 (0.38)	6,809	0.22 (0.41)	4,356	0.12 (0.33)
Risk factors						
HbA1c	10,902	5.53 (0.72)	6,679	5.44 (0.63)	4,223	5.66 (0.82)
BMI	11,083	28.02 (4.50)	6,772	27.61 (4.49)	4,311	28.66 (4.43)
WHR	11,131	0.89 (0.09)	6,790	0.88 (0.09)	4,341	0.91 (0.08)
CHO/HDL ratio	11,024	4.30 (1.43)	6,737	4.24 (1.43)	4,287	4.39 (1.42)
Diastolic BP	11,133	79.93 (11.09)	6,795	80.75 (11.05)	4,338	78.64 (11.05)
Systolic BP	11,146	130.99 (20.38)	6,799	128.07 (19.45)	4,347	135.55 (20.95)
Subjective health						
SF12 mental	7,591	51.48 (9.22)	4,803	51.18 (9.20)	2,788	52.00 (9.25)
SF12 physical	7,591	47.13 (9.04)	4,803	48.49 (8.39)	2,788	44.78 (9.62)
Satisfactory health	10,559	0.84 (0.37)	6,604	0.86 (0.35)	3,955	0.79 (0.41)

Notes: HbA1c (%): glycosylated hemoglobin, BMI (kg/m^2): body mass index, WHR: waist–hip ratio, CHO/HDL ratio: total cholesterol/HDL-cholesterol ratio, BP (mmHg): blood pressure.

Table 2
Overview of the available pension plans in the German pension system in the study period considered (1995-2014).

		Retirement age		Number of retirees (as of 31.12)				Number of new retirees (whole year)			
	Min. yrs of contribution	ERA	ORA	1995		2013		1995		2013	
Standard old-age pension[a]	5		65	10,165,298	(76 %)	8,039,899	(46 %)	327,781	(33 %)	274,082	(42 %)
Pension for long-term insured[b]	35	63	65	539,991	(4%)	1,564,978	(9%)	97,516	(10 %)	114,023	(18 %)
Pension for especially long-term insured[c]	45		63	–		28,860	(0.2 %)			16,197	(2%)
Pension for women[d]	15	60	65	1,202,343	(9%)	3,856,264	(22 %)	233,832	(23 %)	97,680	(15 %)
Pension for long-term unemployed/partial retirement[e]	15	60	65	872,915	(7%)	2,388,958	(14 %)	294,133	(29 %)	66,703	(10 %)
Pension for severely disabled[f]	35	60	63	554,010	(4%)	1,777,289	(10 %)	47,563	(5%)	79,484	(12 %)
Total				13,334,557		17,656,248		1,000,825		648,169	

[a] With the 1999 pension reforms, the official retirement age was increased stepwise from 65 to 67 for individuals born between 1947–1964. These changes started in 2012. As such they affected a small group of individuals surveyed in the last follow-up included (FF4 - 2013/2014).
[b] For individuals born 1949–1963 the official retirement age threshold was increased stepwise from 65 to 67, starting from 2012. This change is only relevant for a small group of individuals surveyed in the last follow-up (FF4 - 2013/2014). The early retirement threshold for this group remained constant and is connected with deductions.
[c] This type of pension was introduced in 2013. For individuals born from 1953 to 1964, the age threshold is increased stepwise from 63 to 65. Early retirement with deductions is not possible under this plan. This change is only relevant for individuals surveyed in the last study (FF4 - 2013/2014).
[d] Women born between 1940–1951 were allowed to retire early with deductions from their final pension. Early retirement for women was eliminated for individuals born 1952 onwards: this change is only relevant for individuals in the last included study (FF4 - 2013/2014). Starting from 1999 (birth cohorts 1940–1944) the ORA threshold was increased stepwise from 60 to 65.
[e] Individuals born 1936–1945 could retire early with deductions. For individuals born 1946–1948 the ERA was raised stepwise from 60 to 63. This type of pension was eliminated for individuals born 1952 onwards. These changes are only relevant for individuals surveyed in the last included study (FF4 - 2013/2014). Starting from 1996 (birth cohorts 1937–1941) the ORA threshold was increased stepwise from 60 to 65.
[f] For individuals born 1952–1964, a stepwise increase of the ERA to 62 years was introduced. This change is only relevant for individuals surveyed in the last study (FF4 - 2013/2014). Starting from 2000 (birth cohorts 1941–1943) the ORA threshold was increased stepwise from 60 to 63.Sources: Börsch-Supan et al. (2018),Idler and Benyamini (1997), Federal Ministry of Labor and Social Affairs (2016); Deutsche Rentenversicherung Bund (DRV) (2019), Deutsche Rentenversicherung Bund (DRV) (2018); own modification based on Eibich (2015).

3.3. RDD rationale and identification strategy

In order to estimate the causal effect of retirement, we used a regression discontinuity design (RDD). This method has already been widely used in health economics in previous studies of retirement and health (Coe and Zamarro, 2011; Eibich, 2015; Godard, 2016; Insler, 2014; Johnston and Lee, 2009; Müller and Shaikh, 2018; Zhao et al., 2017).

RDD can be applied when treatment is determined by whether a continuous "assignment variable" exceeds an exogenously determined threshold. If the assignment variable is not manipulable by individuals and if pretreatment covariates are continuous around the threshold, the exogenous assignment rule creates a local randomization in the treatment status and in the covariates around the threshold (Lee and Lemieux, 2010; Bor et al., 2014). As a result, individuals just below the threshold can be considered as a

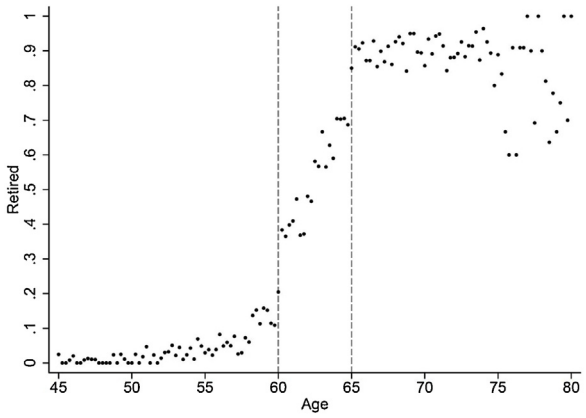

Fig. 1. Share of retirees by age group (bins of 3 months).
Note: each dot represents the share of retired individuals in age groups of 3 months. The drop in the share of retirees after 75 years is due to a decrease in the number of observations, so that each age quarter consists of only a few individuals. If, among these few, a couple are classified as others or are still working, this would have a big impact on the share of retirees computed for those age quarters.

valid control group for those just above the threshold, allowing valid estimation of causal treatment effects.

In our case, as treatment (retirement) is assigned probabilistically, the average treatment effect must be scaled by the difference in the probability of obtaining treatment at the threshold or, in other words, by the discontinuity in the treatment ("fuzzy" RDD) (Lee and Lemieux, 2010). This amounts to estimating a local average treatment effect (LATE) for compliers, i.e., those individuals whose treatment assignment would change with the instrument (Lee and Lemieux, 2010). This effect can be estimated using a Wald estimator, using the exogenous threshold as instrumental variables (IVs), in a two-stage least squares model (Lee and Lemieux, 2010; Bor et al., 2014). For the main specification, we included both thresholds simultaneously as IVs. As the compliers are likely to be different for both cutoffs, we also estimated separate models for ERA (60) and ORA (65) thresholds. In the main model, we estimated the following equations:

$$r_{it} = \gamma_0 + \gamma_1 f(age)_{it} + \delta_1 ERA_{it} + \delta_2 ORA_{it} + u_{it} \quad (1)$$

$$health_{it} = \beta_0 + \beta_1 f(age)_{it} + \tau_1 \widehat{r}_{it} + \varepsilon_{it} \quad (2)$$

In the first stage (Eq. 1), we regressed the retirement status on a function of age and two binary variables taking on value 1 if the individual i is above the retirement thresholds at 60 (ERA) or 65 (ORA), and 0 otherwise. In the second stage (Eq. 2), we regressed the outcomes on a function of age and the estimated retirement status from the first stage.

Owing to limited sample size, we adopted a parametric regression including the whole sample of observations (from 45 to 80 years old for the main model, i.e., adopting a bandwidth of 15 years on both sides of each cutoff) (Lee and Lemieux, 2010; Moscoe et al., 2015). A parametric approach offers the advantage of using more data in the estimation, and thus provides more precise estimates (Lee and Lemieux, 2010). Since also data far away from the cutoff are used, the challenge of a parametric estimation is the correct modeling of the health–age relationship around the cutoff, in order to exclude the possibility that eventual non-linearities are mistaken for the effect of treatment (Lee and Lemieux, 2010; Angrist and Pischke, 2008). To evaluate the age specification that best fitted our data, we used the Akaike Information Criterion (AIC) (Lee and Lemieux, 2010), comparing specifications with age polynomials up to the second degree (linear and quadratic). Following the suggestion by Burnham and Anderson (2004), the simpler linear specification was preferred, unless the more complex quadratic specification was better by more than 10 points (Δ_{AIC} >10) (Burnham and Anderson, 2004). For the complete analysis, see Appendix B in Supplementary data.

Despite dealing with panel data, we decided not to include individual-specific fixed effects. In fact, according to Lee and Lemieux (2010), the inclusion of individual-specific fixed effects is not necessary for the identification in a regression discontinuity design. Furthermore, including fixed effects would have caused a loss of observations due to panel attrition. Panel attrition might have been caused by several reasons, among others health deterioration or a direct retirement effect, but also moving away from the area of Augsburg or other reasons not related to employment or health (e.g. care of relatives). To test for the effects of panel attrition we carried out a sensitivity check including only individuals who are present in the sample at least two times.

In a further step, we investigated heterogeneous effects stratifying by sex and educational level. All analyses were performed using STATA 14 (Stata Corporation, College Station, TX, USA).

Since we were conducting multiple estimations to investigate the effect of retirement on a large number of parameters, concerns regarding type I errors due to multiple testing could arise. To control for this issue, we reported corrected significance levels based on p-values following a stepdown correction procedure (Romano and Wolf, 2016; Clarke, 2018). Effects were considered significant if they showed a p-value<0.05.

All assumptions for a valid estimation with regression discontinuity design were satisfied. The assignment variable (age) was continuous around the cutoff and by construction was not manipulable by individuals (see Appendix C in Supplementary data). Furthermore, we carried out a graphical analysis of potentially relevant predetermined covariates in the dataset (male, education, living alone) to test their continuity around the cutoff. If they were not continuous, doubts regarding the causal interpretability of estimates may arise (Lee and Lemieux, 2010). However, in our sample the variables investigated were comparable on both sides of the cutoffs (Appendix D in Supplementary data). The analysis for AHM revealed a positive discontinuity in this factor at retirement. Hence, the results for diastolic and systolic blood pressure should be interpreted with caution (Appendix E in Supplementary data).

Visual analysis of the outcomes revealed a discontinuity in both ERA and ORA cutoffs. However, results were strongly dependent on the outcome considered (Appendix D in Supplementary data).

4. Results

Results of the first-stage regression (Table 3) showed that both ERA and ORA instruments are highly significant and have a positive effect on the retirement probability. Hence, the relevance assumption of IV regression was satisfied and the age thresholds can be used as relevant instruments.

The main results are reported in Table 4. All models showed a Kleibergen–Paap Wald F-statistic (Fstat) larger than the cutoff value of 10 for validity of the instruments (Staiger and Stock, 1994). This indicates that the instruments were not weak in all models. Furthermore, instruments in the official retirement models (ORA) were weaker than instruments in the early and combined models. Results of the Sargan-Hansen overidentification test could not reject the null hypothesis that the instruments are jointly valid, also indicating no heterogeneity between the two instruments. Nevertheless, the institutional setting suggests that heterogeneous effects are plausible, and we therefore carried out a stratified analysis.

Table 3
First-stage results.

	linear			quadratic		
	Both	ERA	ORA	Both	ERA	ORA
ERA	0.413***	0.397***		0.41***	0.385***	
	(0.014)	(0.014)		(0.013)	(0.014)	
ORA	0.323***		0.252***	0.346***		0.329***
	(0.013)		(0.016)	(0.015)		(0.015)
Age	0.007***	0.022***	0.035***	(0.026)***	−0.083***	0.201***
	(0.001)	(0.001)	(0.001)	0.005	(0.005)	(0.008)
Age^2				0.000***	0.001***	−0.001***
				(0.000)	(0.000)	(0.000)
N	11,168	10,935	9,290	11,168	10,935	9,290
R^2	0.618	0.589	0.52	0.618	0.603	0.539

Notes: Fuzzy regression discontinuity design first-stage coefficients. 95 % confidence intervals in brackets. Both: model including both cutoffs as instruments; ERA: model including only the early retirement cutoff (60) as instrument; ORA: model including only the regular retirement cutoff (65) as instrument. Significance: * p < .05; ** p < .01; ***p < .001.

Table 4
Fuzzy regression discontinuity analysis results.

	Both				ERA			ORA		
	Effect (SE)	N	Fstat	Hansen	*Effect (SE)*	N	Fstat	*Effect (SE)*	N	Fstat
Health behavior										
Alcohol excess	−0.010	11,168	1,591	0.059	0.039	10,935	699	−0.053	9,290	242
	(0.028)				(0.04)			(0.066)		
No alcohol	0.040	11,155	1,589	0.691	0.038	10,922	697	0.008	9,279	243
	(0.027)				(0.039)			(0.065)		
Physical activity	0.046	11,154	1,589	0.065	0.125**	10,921	696	−0.009	9,279	244
	(0.031)				(0.044)			(0.071)		
Smoking	−0.027	11,165	1,591	0.827	−0.023	10,932	698	−0.034	9,287	243
	(0.022)				(0.031)			(0.047)		
Risk factors										
HbA1c	−0.020	10,902	1,567	0.386	0.005	10,670	683	0.001	9,047	395
	(0.044)				(0.064)			(0.093)		
CHO/HDL	**0.280*** **	11,024	1,245	0.094	0.014	10,792	649	**0.471** **	9,165	404
	(0.085)				(0.125)			(0.159)		
BMI	0.640**	11,083	1,262	0.191	**1.111** **	10,851	670	0.125	9,211	397
	(0.248)				(0.352)			(0.488)		
WHR	0.001	11,131	1,262	0.029	0.014*	10,900	672	−0.015	9,255	400
	(0.005)				(0.007)			(0.009)		
Diastolic BP	**2.102** **	11,133	1,255	0.209	0.408	10,904	666	0.325	9,258	242
	(0.673)				(0.973)			(1.557)		
Systolic BP	**5.647*** **	11,146	1,259	0.052	−0.513	10,914	698	4.962	9,270	242
	(1.263)				(1.708)			(2.948)		
Subjective health										
SF12 mental	1.175	7,591	1,258	0.087	1.990	7,392	470	−0.078	6,208	234
	(0.687)				(1.032)			(1.362)		
SF12 physical	1.594*	7,591	1,258	0.527	1.412	7,392	470	2.310*	6,208	353
	(0.66)				(1.015)			(1.15)		
Satisfactory health	0.079*	10,559	953	0.452	0.064	10,552	665	0.108	8,713	250
	(0.031)				(0.035)			(0.059)		

Notes: Fuzzy regression discontinuity design second-stage coefficients. Cluster-robust standard errors in parentheses. Both: model including both cutoffs as instruments; ERA: model including only the early retirement cutoff (60) as instrument; ORA: model including only the regular retirement cutoff (65) as instrument. HbA1c (%): glycosylated hemoglobin, CHO/HDL ratio: total cholesterol/HDL-cholesterol ratio, BMI (kg/m^2): body-mass-index, WHR: waist–hip ratio, BP (mmHg): blood pressure. Choice of the age polynomial (linear or quadratic) was based on the Akaike-Information Criterion (AIC) (Appendix B in Supplementary data), only the results of the preferred specification are

The results indicated no significant impact of retirement on alcohol consumption and smoking. In contrast, retirement increased the probability of regular physical activity in the early retirees by more than 10 percentage points ($p < 0.01$). This effect was however not significant anymore after correcting the p-value for multiple testing. The effects for the general and ORA models also showed positive coefficients, but with large confidence intervals (Table 4).

Some biomedical risk factors showed a significant worsening after retirement, which were in most cases robust to p-value corrections. In the general population, retirement led to an increase in CHO/HDL and BMI. Regular retirees showed a strong increase in CHO/HDL (corrected $p < 0.01$). Early retirees (ERA) showed a strong increase in BMI (corrected $p < 0.01$), alongside with an increase in WHR (Table 4). Furthermore, the analysis showed an increase in diastolic and systolic blood pressure after retirement (corrected $p < 0.01$). However, this result should be interpreted with caution, not only because the assumptions testing revealed a parallel increase in AHM intake (Appendix E in Supplementary data), but also due to the weaker and non-significant coefficients highlighted in the separate analyses for ERA and ORA reported in Table 4.

The effect on subjective mental health (SF12 mental) showed positive, albeit not significant coefficients for all groups

Table 5
Fuzzy regression discontinuity analysis results for sex groups.

	Male			Female		
	Both	ERA	ORA	Both	ERA	ORA
Health behavior						
Alcohol excess	−0.054	0.041	−0.116	0.028	0.023	0.043
	(0.043)	(0.06)	(0.086)	(0.037)	(0.053)	(0.066)
No alcohol	0.078*	0.076	0.098	0.021	0.031	−0.017
	(0.032)	(0.046)	(0.086)	(0.042)	(0.06)	(0.076)
Physical activity	0.086	0.122*	0.122	0.006	0.129*	−0.091
	(0.045)	(0.062)	(0.115)	(0.043)	(0.062)	(0.076)
Smoking	−0.045	−0.053	−0.019	−0.014	−0.001	−0.040
	(0.034)	(0.048)	(0.080)	(0.028)	(0.040)	(0.055)
Risk factors						
HbA1c	−0.090	−0.049	−0.147	0.053	0.061	0.096
	(0.067)	(0.099)	(0.145)	(0.059)	(0.082)	(0.143)
CHO/HDL	0.279*	−0.244	0.729*	0.232*	0.185	0.082
	(0.128)	(0.182)	(0.312)	(0.107)	(0.158)	(0.195)
BMI	0.067	0.730	−0.330	0.822*	1.514**	0.058
	(0.306)	(0.439)	(0.783)	(0.381)	(0.555)	(0.733)
WHR	−0.007	0.000	−0.013	−0.002	0.014	−0.018
	(0.005)	(0.007)	(0.010)	(0.005)	(0.007)	(0.009)
Diastolic BP	1.505	0.114	3.356	2.428**	0.217	1.192
	(0.976)	(1.391)	(1.919)	(0.914)	(1.317)	(1.946)
Systolic BP	4.933**	0.512	1.954	2.464	−2.237	8.150*
	(1.759)	(2.364)	(4.586)	(1.705)	(2.402)	(3.838)
Subjective health						
SF12 mental	1.467	1.692	2.036	0.870	2.235	−1.703
	(0.922)	(1.431)	(1.827)	(1.008)	(1.474)	(1.974)
SF12 physical	1.490	0.478	3.117	1.664	2.256	1.795
	(0.946)	(1.466)	(1.668)	(0.922)	(1.404)	(1.855)
Satisfactory health	0.076	0.046	0.147	0.062	0.072	0.068
	(0.044)	(0.052)	(0.087)	(0.036)	(0.048)	(0.085)

Notes: Fuzzy regression discontinuity design second-stage coefficients. Cluster-robust standard errors in parentheses. Both: model including both cutoffs as instruments; ERA: model including only the early retirement cutoff (60) as instrument; ORA: model including only the regular retirement cutoff (65) as instrument. HbA1c (%): glycosylated hemoglobin, CHO/HDL ratio: total cholesterol/HDL-cholesterol ratio, BMI (kg/m^2): body-mass-index, WHR: waist–hip ratio, BP (mmHg): blood pressure. Choice of the age polynomial (linear or quadratic) was based on the Akaike-Information Criterion (AIC), only the results of the preferred specification are reported here. Fstat: Kleibergen-Paap Wald F-statistic. Significance: * $p < .05$; ** $p < .01$; ***$p < .001$; no results were significant after Romano-Wolf correction for multiple testing.

considered. The effect on subjective physical health (SF12 physical) was positive and significant, but not robust to p-value corrections. The same positive result can be observed for self-rated health. After retirement, participants were more likely to report at least satisfactory health (Table 4).

4.1. Heterogeneity

The sex-stratified analysis is shown in Table 5. In the pooled analysis, we observed increases in CHO/HDL, BMI and diastolic blood pressure for women. Furthermore, females who retired early improved their physical activity significantly, but at the same time, they presented also a significant increase in BMI. Men tended to improve their health behavior after retirement (eg. significantly higher frequency of no alcohol consumption and higher physical activity), but with large confidence intervals for most parameters. They also showed an increase in systolic blood pressure and CHO/HDL. The latter was especially present in regular retirees.

Regarding subjective health, we observed increasing albeit non-significant trends in both groups. The only exception was subjective mental health in women retiring regularly, for which large negative effects cannot be ruled out.

The analysis stratified by educational level is reported in Table 6. In the pooled analysis, low educated individuals showed increased CHO/HDL, BMI and diastolic blood pressure. Furthermore, low educated individuals retiring early significantly increased their physical activity after retirement, but also revealed significant increases in BMI and WHR.

Additionally, low educated individuals also presented significant increases in subjective physical health and satisfactory health. In contrast, high educated individuals did not show any significant effect of retirement, except a non-robust increase in systolic blood pressure in the general population.

Romano-Wolf p-value corrections showed however that only the increase in physical activity and systolic blood pressure in the low educated group are robust results, while none of the other coefficients are robust to correction for multiple testing. Despite some notable differences in the sign as well as the magnitude of the point estimate, due to the small sample sizes for the subgroups the differences between men and women and high and low educated individuals were never significant.

4.2. Robustness checks

We tested the robustness of our results, as suggested by different guidelines, using both a specification curve, in which we plotted estimates for linear and quadratic specification coefficients for different successively declining bandwidths (15, 12, 10, 7 and 5 years around the cutoffs), and a sensitivity analysis table (Appendix F, Table F.1 in Supplementary data) (Lee and Lemieux, 2010; Bor et al., 2014; Moscoe et al., 2015; Christensen and Miguel, 2018; Simonsohn et al., 2015). In Figs. 2–4 we presented examples of specification curves for selected outcomes and models.

The visual inspection of the curves showed robust results for almost all outcomes for different bandwidth and polynomial choices (Appendix F, Table F.1 in Supplementary data). Obviously, confidence intervals generally increased with decreasing bandwidth. Furthermore, most non-significant results from the main analysis still showed large confidence intervals, in some cases with volatile point estimates including opposite values (e.g. smoking,

Table 6
Fuzzy regression discontinuity analysis results for educational groups.

	Low education			High education		
	Both	ERA	ORA	Both	ERA	ORA
Health behavior						
Alcohol excess	0.002	0.018	−0.013	−0.040	0.104	−0.086
	(0.034)	(0.045)	(0.096)	(0.049)	(0.088)	(0.085)
No alcohol	0.033	0.024	0.005	0.049	0.076	0.010
	(0.035)	(0.046)	(0.100)	(0.041)	(0.074)	(0.073)
Physical activity	0.073	**0.170*****	−0.044	0.023	0.013	0.113
	(0.038)	(0.05)	(0.079)	(0.052)	(0.09)	(0.089)
Smoking	−0.020	−0.013	−0.066	−0.039	−0.062	0.017
	(0.027)	(0.036)	(0.072)	(0.036)	(0.062)	(0.055)
Risk factors						
HbA1c	−0.042	0.002	−0.080	0.046	0.001	0.099
	(0.058)	(0.079)	(0.137)	(0.064)	(0.109)	(0.117)
CHO/HDL	0.261**	0.043	0.449*	0.294	−0.097	0.154
	(0.101)	(0.137)	(0.221)	(0.159)	(0.312)	(0.241)
BMI	0.665*	0.974*	0.292	0.366	0.709	−0.233
	(0.295)	(0.39)	(0.696)	(0.454)	(0.677)	(0.629)
WHR	0.006	0.016*	−0.011	−0.005	0.002	−0.015
	(0.006)	(0.007)	(0.013)	(0.008)	(0.013)	(0.012)
Diastolic BP	2.074**	0.421	1.224	2.291	1.002	2.466
	(0.803)	(1.057)	(2.326)	(1.234)	(2.546)	(1.709)
Systolic BP	**5.244*****	−0.493	7.277	5.581*	−0.334	5.723
	(1.514)	(1.957)	(4.466)	(2.285)	(3.545)	(3.208)
Subjective health						
SF12 mental	1.654	2.325	−0.193	0.896	1.715	0.464
	(0.883)	(1.260)	(2.016)	(1.059)	(1.874)	(1.676)
SF12 physical	2.257**	1.974	3.030	0.529	1.207	1.214
	(0.860)	(1.247)	(1.609)	(1.008)	(1.769)	(1.741)
Satisfactory health	0.079*	0.053	0.142	0.064	0.104	0.030
	(0.036)	(0.041)	(0.081)	(0.038)	(0.066)	(0.082)

Notes: Fuzzy regression discontinuity design second-stage coefficients. Cluster-robust standard errors in parentheses. Both: model including both cutoffs as instruments; ERA: model including only the early retirement cutoff (60) as instrument; ORA: model including only the regular retirement cutoff (65) as instrument. HbA1c (%): glycosylated hemoglobin, CHO/HDL ratio: total cholesterol/HDL-cholesterol ratio, BMI (kg/m^2): body-mass-index, WHR: waist–hip ratio, BP (mmHg): blood pressure. Choice of the age polynomial (linear or quadratic) was based on the Akaike-Information Criterion (AIC), only the results of the preferred specification are reported here. Fstat: Kleibergen-Paap Wald F-statistic. Significance: * $p < .05$; ** $p < .01$; ***$p < .001$; in bold: significant coefficients after Romano-Wolf correction for multiple testing.

HbA1c). However, for the effects of retirement on physical activity, CHO/HDL, BMI, WHR, and subjective health, which were already found to be significant in the main analysis, the curves confirmed positive effects, with strongly robust point estimates to alternative bandwidth choices (Fig. 2). Finally, the results for blood pressure parameters showed much volatility of the effect and large confidence intervals mostly including the zero (Fig. 3). For this reason, no robust effect of retirement on these parameters could be determined for the overall population.

For the sex-stratified analysis, the specification curves confirmed the robustness of our results for physical activity, CHO/HDL, BMI, WHR and subjective health (Appendix G, Table G.1–2 in Supplementary data). They also helped to shed light on effect estimates for CHO/HDL in the pooled analysis (Fig. 4). As emerged from the graphs, this factor was strongly dependent on sex and timing: men who retired early showed a decrease while men who retired regularly showed a robust increase in CHO/HDL. The opposite was true for women (Fig. 4). Also, in the sex-stratified analysis, the curves revealed that the effects on blood pressure parameters are not robust to different modeling choices and should thus be interpreted with caution. Finally, the curves pointed towards another interesting result regarding HbA1c levels: independently from retirement timing, women showed mostly increasing effects, while men showed mostly decreasing effects of retirement on this factor. Although the confidence intervals were very large, they mainly stretched in one direction, excluding the possibility of very large opposite effects.

Specification curves for the stratification by educational level largely confirmed the results of the main analysis (Appendix H, Table H.1-2 in Supplementary data). The only exceptions concern again systolic blood pressure, whose coefficients were very volatile depending on modelling choices. Instead, the effect on diastolic blood pressure in low educated individuals was increasing and robust with respect to almost all specifications considered.

Furthermore, we carried out additional robustness checks. First, we ran the same analysis focusing only on employed or self-employed and retired individuals. In this way we excluded some observations which could potentially attenuate the effect, since for the excluded group the change from non-retired to retired should have fewer consequences. By observing results tables in Appendix I (in Supplementary data), we see that the point estimates largely confirm the results of the main analysis. Standard errors on all parameters increase due to a decrease in sample size, leading thus to a loss in significance for some parameters. For women and low educated we observe a general increase in the parameter estimates, with coefficients significantly different from zero and, thereby, confirming the results highlighted in the main analysis despite a decrease in sample size. This is probably due to the fact that the excluded group included a large share of women and low educated individuals (share of male is now 56 % instead of 49 % as in the main analysis) and indicates that the results of the main analysis should be interpreted as lower bounds of the true underlying effect.

As the exogenously determined cutoffs create a local randomization, there is no need to adjust for potential confounders (Lee and Lemieux, 2010; Calonico et al., 2020). Nevertheless, we ran a robustness check, comparing models with and without covariates (male, education, month, and year fixed effects) (Appendix J in Supplementary data). The curves showed slightly different point estimates, but generally confirmed the results of the main analysis.

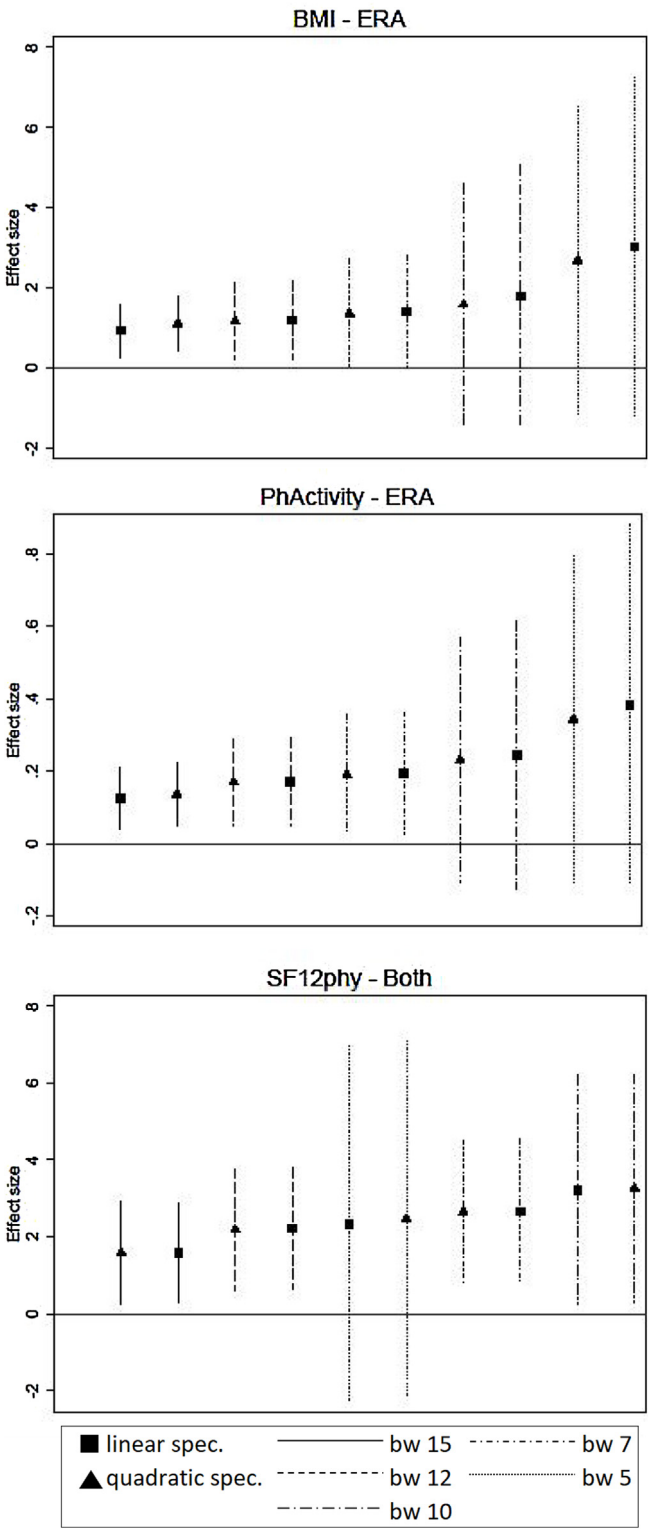

Fig. 2. Selected specification curves.
Note: the full set of specification curves for all outcomes is available in Appendix F (in Supplementary data). Bw: bandwidth. BMI (kg/m^2): body-mass-index. PhActivity: physical activity. SF12phy: subjective physical health. Both: model including both cutoffs as instruments; ERA: ealy retirement age.

Additionally, the dataset we investigated presented a relatively low dropout rate between the follow-ups (30 %). However, if the dropouts are not missing at random, as assumed in the main estimation, loss to follow-up could cause selection bias issues. Therefore, we tested robustness by including only individuals for whom at least two observations were available (Appendix K in Supplementary data). Also, these curves generally confirmed the results of the main analysis.

Furthermore, as higher order polynomials or age–cutoff interactions would likely cause an over-specification of the model, we decided to limit our model selection to continuous linear and quadratic specifications. However, we extensively tested the robustness of our results using higher order polynomials or age-cutoff interactions (Appendix L–M in Supplementary data). Results showed larger confidence intervals, but point estimates generally confirmed the results of the main analysis. In some cases, results from the age-cutoff interactions models showed a much higher volatility of point estimates with some very large effects. These results confirmed our assumption that higher order polynomials and age-cutoff interactions are very likely to overfit our model and are thus not suitable to be considered as main specifications.

5. Discussion

The study results show that retirement leads to an increase in BMI and CHO/HDL levels. These might be accompanied by increases in WHR and blood pressure, but at the same time also by positive effects on physical activity and subjective physical health. While the effect on subjective health is similar in all models considered, the effect on health behavior and biomedical risk factors strongly depends on retirement timing and sex, and thus on the underlying population of compliers considered. This is not surprising as the two retirement thresholds mark two different exit routes (Deutsche Rentenversicherung Bund (DRV), 2019; Gruber and Wise, 2008).

Results indicate that individuals retiring regularly (at the age 65 years cutoff) benefit from retirement especially on a subjective level, as their subjective physical health increases with retirement. This probably results from a relief in work-related stress and fatigue symptoms, as other authors have already shown (Mazzonna and Peracchi, 2015; Westerlund et al., 2010). In contrast, most risk factors and health behaviors did not display any robust change, implying that, for most regular retirees, retirement represents a smooth transition regarding the considered parameters. In this group, no significant differences between men and women, high and low educated individuals could be highlighted. The only exception is a significant increase in CHO/HDL, especially for regular male retirees. Interestingly, this result is robust to multiple testing p-value corrections and several sensitivity analyses, including different bandwidth choices.

At the early retirement threshold, only individuals with a disability, long-term unemployed, partially retired individuals, and women were allowed to retire early (Deutsche Rentenversicherung Bund (DRV), 2019). Results show positive effects of early retirement on physical activity, together with a strong increase in BMI and WHR. Other risk factors, such as CHO/HDL or systolic blood pressure, display consistently worsening coefficients, indicating that, if an effect of retirement on these factors exists, it is likely to be small and deleterious.

In the case of early retirees, however, the results of the stratified analysis might be more informative. In fact, in this group, the characteristics of the underlying complier population and the retirement reasons might be strongly related to sex, as women were allowed to retire early, while men were allowed to retire early only if they had a disability or were long-term unemployed or in partial retirement (Deutsche Rentenversicherung Bund (DRV), 2019). For men retiring early, health-related reasons might play an important role in the decision to retire, much more so than for their female counterparts. However, when comparing results for male and female retirees, it should be noted that labor market

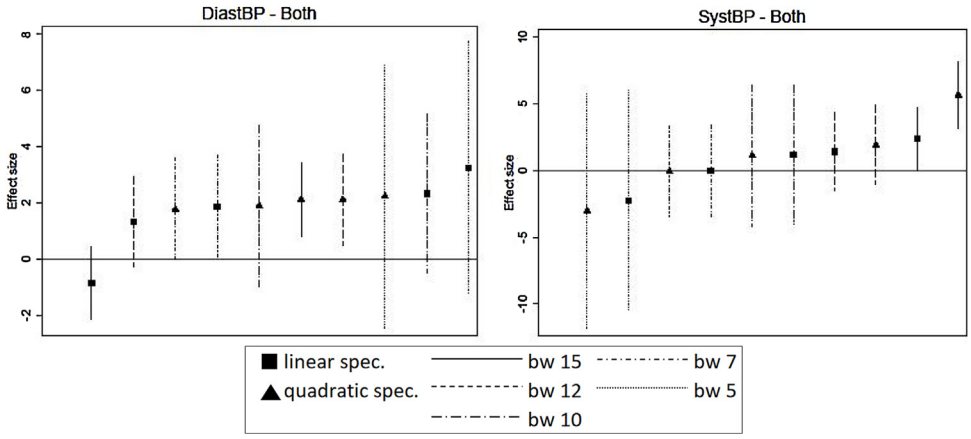

Fig. 3. Selected specification curves.
Note: the full set of specification curves for all outcomes is available in Appendix F (in Supplementary data). Bw: bandwidth. DiastBP (mmHg): diastolic blood pressure; SystBP (mmHg): systolic blood pressure.

participation of older women is more selective than participation of older men. At the time the data were collected, women had a lower labor market participation before retirement than men and those who worked were more likely to be high educated (Börsch-Supan and Ferrari, 2017; OECD, 2020). This does not threaten the internal validity of our RDD estimator. However, it implies that the local average treatment effect estimated in the RDD model applies to a specific subgroup, and it cannot be generalized to the overall population of women. Results from the sensitivity analysis focusing only on employed and retired individuals confirmed that the results in the main analysis can be interpreted as a lower bound of the true underlying effect for women retiring directly from employment. However, based on our data we could not investigate how specific work characteristics (such as work-related physical activity, job strain, job satisfaction), which might be responsible for a higher occupational selection in women, generate heterogeneity in the results.

Our analysis indicates that, for men retiring early, retirement marks a positive transition, leading to a significant increase in physical activity. Risk factors show no effect or generally negative coefficients, with confidence intervals mainly stretching on the negative side, supporting the hypothesis of a positive effect of retirement in this group. For women, the same increase in physical activity could be observed. However, this is also accompanied by a significant increase in BMI, WHR, and increasing trends on CHO/HDL and HbA1c. The same result of increasing physical activity alongside increasing BMI and WHR was observed also for low educated individuals who retired early. It has to be remarked that these results are robust to different model specifications, but after correction for multiple testing, only the increase in BMI in the ERA population remains significant. One could speculate on the link between these results, which leads to interesting potential interpretations regarding the mechanisms of retirement on health for the group of early female and low educated retirees. In fact, our results might indicate that in women and low educated individuals who retire early the increase in leisure time physical activity is probably not enough to compensate for the decrease in work-related activity, as BMI and WHR tend to increase. Other authors suggested similar compensation mechanism between physical activity and BMI, albeit with different results (Zantinge et al., 2013; Goldman et al., 2008). Other possible mechanisms, such as changes in dietary and sleep patterns, found only selective support in previous studies (Eibich, 2015; Goldman et al., 2008). For low educated individuals this result is not surprising, since they are more likely to retire from physically demanding occupations than high educated individuals. Despite a general relief from occupational strain, which is reflected in the increase in subjective physical health, working seemed to have had a protective effect on their BMI and WHR. For women the interpretation of this result is less clear and should be further investigated, as their labor market participation is more selective in terms of occupation than men. Besides potential interpretations and links between the parameters observed, these findings suggest that early female retirees and retirees with low education should be considered as high-risk groups for a negative effect of retirement on biomedical risk factors, which could in turn affect their long-run risk of cardiovascular and metabolic disease.

The effects we found are also interesting in light of previous research. Godard (2016) reveals in fact that women tend to increase their physical activity after retirement. However, women also showed no significant changes in BMI. The author thus suggested that women are able to fully compensate for the loss of work-related physical activity by increasing their leisure time physical activity after retirement. The study of Eibich, based on German Socio-Economic Panel (SOEP) data, projected a different scenario: both men and women tend to increase their physical activity and decrease their BMI after retirement. In this case thus, it seems that both groups are able to more than compensate their loss of work-related physical activity (Eibich, 2015). This comparison with the literature highlights more than any other result the complexity and strong heterogeneity of the effects of retirement and its potential underlying mechanisms. We strongly encourage further research, especially aiming at including further determinants of BMI, such as diet and sleep patterns.

The results for blood pressure show a detrimental effect of retirement on both systolic and diastolic pressure. However, these results should be interpreted with caution, not only because of the poor robustness of the effects to different specifications and bandwidths but also because of the increased AHM intake upon retirement. The effect might thus be downward biased, hampering the clear identification of the effect of retirement on blood pressure. However, increasing blood pressure despite increasing AHM intake corroborates the result that retirement might have a deleterious effect on this parameter. Further analysis is needed to establish the direction of causality and the presence of unobserved confounders (e.g., more frequent doctor visits).

The results from the analysis of health behaviors are generally in line with previous literature. The role of retirement on alcohol

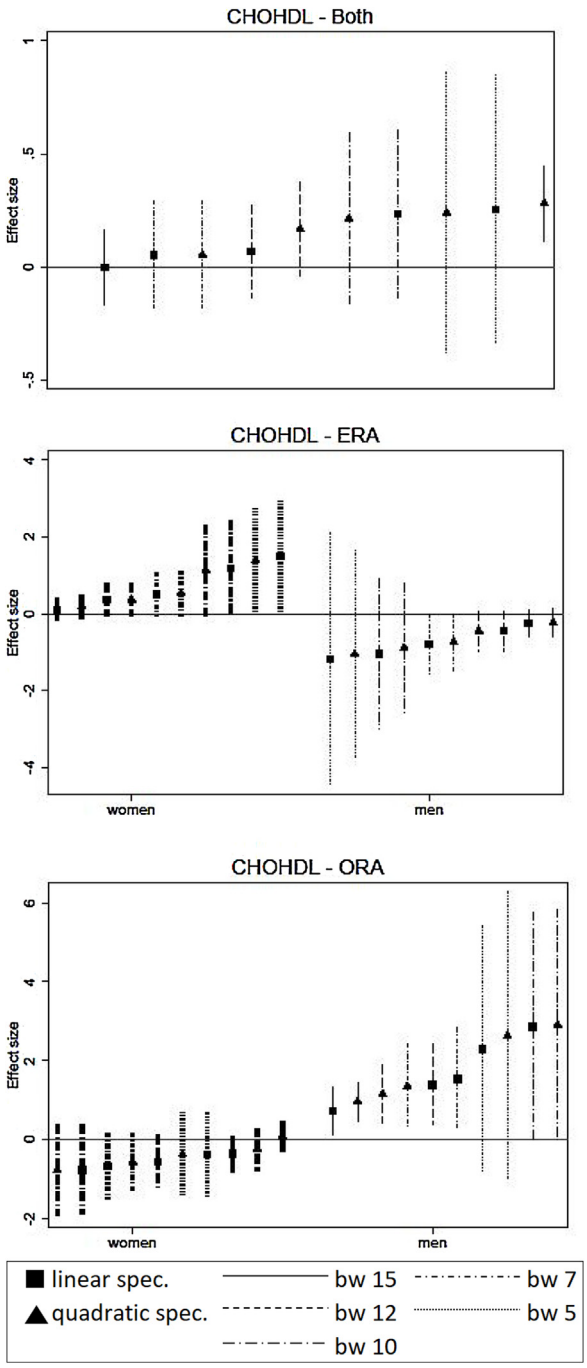

Fig. 4. Selected specification curves – stratification.
Note: the full set of specification curves for all outcomes is available in Appendix F & G (in Supplementary data). Bw: bandwidth. ERA: early retirement age. ORA: official retirement age.

consumption is ambiguous and, as our study also shows, depends on the indicator used and on the group considered (Eibich, 2015; Müller and Shaikh, 2018; Zhao et al., 2017; Celidoni and Rebba, 2017; Motegi et al., 2016; Zhu, 2016). The effect on smoking, albeit non-significant, is also comparable with previous findings, which show that retirement causes a reduction in smoking probability by a few percentage points in the overall population (Eibich, 2015; Insler, 2014; Zhao et al., 2017; Celidoni and Rebba, 2017; Kämpfen and Maurer, 2016; Zhu, 2016). The increase in physical activity, in both men and women, is generally in line with previous research (Eibich, 2015; Insler, 2014; Müller and Shaikh, 2018; Zhao et al., 2017; Celidoni and Rebba, 2017; Kämpfen and Maurer, 2016; Motegi et al., 2016; Zhu, 2016). However, the only study differentiating the analysis for early and regular retirees, also based on German data, showed that the increase in physical activity is actually driven by the regular retirees and not by the early retirees group (Eibich, 2015).

Our study corroborates the evidence that retirement leads to an increase in BMI in the early-retired population, in line with the increase in WHR. No effect was shown for regular retirees. The available evidence regarding BMI is ambiguous: the majority of studies report an increase in BMI, but some report negative or null effects (Eibich, 2015; Godard, 2016; Johnston and Lee, 2009; Behncke, 2012; Chung et al., 2009), with different but mixed effects between timing, sex, and education (Eibich, 2015; Godard, 2016; Hessel, 2016; Forman-Hoffman et al., 2008). As BMI marks a very important risk factor for chronic disease, this heterogeneity should be investigated further. Regarding the other risk factors considered, few comparable studies are available. Behncke (2012) showed a similar worsening of metabolic syndrome symptoms as aggregated parameter including cholesterol levels and blood pressure. However, she used a different methodology, which leaves open concerns of potential residual bias.

The same increasing trend in self-assessed health upon retirement was reported in most previous studies (Coe and Zamarro, 2011; Eibich, 2015; Johnston and Lee, 2009; Oshio and Kan, 2017; Zhu, 2016; Blake and Garrouste, 2013; Hessel, 2016; Mazzonna and Peracchi, 2015; Neuman, 2007) with a few exceptions (Johnston and Lee, 2009; Sahlgren, 2012; Dave et al., 2006).

Basing our analysis on epidemiological data gave us the opportunity to investigate simultaneously the effect of retirement on objectively measured biomedical risk factors for chronic disease, self-reported health behavior, and subjective health indicators, allowing the identification of possible mechanisms. The methodology we used enabled us to estimate the causal effect of retirement, taking the problem of unmeasured confounding and reverse causation into account. However, the study presented some limitations, mainly related to a limited sample size. First, although we used the whole sample and focused on low polynomial specifications, we still obtained large standard errors, which increased with decreasing bandwidth. As most effects resulting from retirement are probably small, a larger sample size would be needed to detect them and would allow using higher polynomial specifications and age–retirement interactions without overfitting concerns. Second, a related limitation is that several results were not robust to p-value corrections for multiple testing. While this might indicate the presence of type I errors, it is also possible that our study lacks the necessary power to detect such specific effects with sufficient certainty. In either case, there is greater uncertainty around these specific results, and they should be considered in future analyses involving larger sample sizes. Third, because of lack of data or inconsistent questioning across surveys, we did not include other mechanisms, such as doctor visits or dietary habits, which may have contributed to explain the results in the health domains. Fourth, our strategy to take panel attrition into account might not be enough to fully eliminate those concerns, as the panel we selected might present further problems of selection bias and lack of representativeness.

Finally, although the two baseline surveys were drawn to be representative for the Augsburg region, and the panel attrition of about 30 % is relatively low, if and how the findings are generalizable for the whole German population remains uncertain. On the one hand, differences between participants and non-participants were found to be small (Hoffmann et al., 2004). About 600,000 people live in the study area, which consists of both urban and rural parts including 80 small towns and villages. On the other hand, regional differences with respect to health behavior and health status have

been reported for Germany (e.g. diabetes prevalence) (Schipf et al., 2014), showing that KORA participants are somewhat healthier than individuals from other German cohort studies. This indicates that our analyses might have overestimated positive effects from retirement, as participants in other samples are less likely to adopt a healthier lifestyle. Furthermore, we also might have underestimated negative effects, given the concerns that the population might be healthier than the general German population.

6. Conclusions

The present study provides novel evidence regarding the effect of retirement on biomedical risk factors for chronic cardiovascular and metabolic diseases. It also contributes to a growing body of research on the effect of retirement on health behavior and subjective health, using an analysis design that allowed causal inference. Retirement mostly represents a smooth transition for regular retirees, generally connected with improvements in subjective health but also with an increase in CHO/HDL levels, especially visible in regular retired males. Early retirement relates to worsening BMI, despite an increase in physical activity, which might have a long-lasting effect on the incidence of chronic disease, health care costs and longevity. Early female and low educated retirees (age 60) are mostly concerned by these negative effects. They should thus be regarded as high-risk groups and should represent potential targets for behavioral interventions. These should incentivize a more effective and health-conscious use of the additionally available time and changes in the daily routines in the retirement adaptation phase, targeting not only an adequate increase in leisure-time physical activity but also the other behavioral risk factors considered, which showed room for improvement.

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Data and code to replicate the results

All the data used in this submission can be requested from the KORA platform via project agreement (https://www.helmholtz-muenchen.de/kora/fuer-wissenschaftler/zusammenarbeit-mit-kora/index.html). The code used to analyze the data is available upon request from the corresponding author.

CRediT authorship contribution statement

Sara Pedron: Conceptualization, Project administration, Methodology, Formal analysis, Visualization, Writing - original draft, Writing - review & editing. **Werner Maier:** Conceptualization, Investigation, Data curation, Writing - review & editing. **Annette Peters:** Conceptualization, Methodology, Resources. **Birgit Linkohr:** Data curation, Resources, Writing - review & editing. **Christine Meisinger:** Methodology, Investigation, Writing - review & editing. **Wolfgang Rathmann:** Methodology, Investigation, Resources, Writing - review & editing. **Peter Eibich:** Methodology, Formal analysis, Supervision, Writing - original draft, Writing - review & editing. **Lars Schwettmann:** Conceptualization, Supervision, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no conflicts of interest.

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Appendices A–M. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ehb.2020.100893.

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2.3. Manuscript 3

Pedron, S., Kurz, C.F., Schwettmann, L. & Laxy, M. (2021). The effect of BMI and type 2 diabetes on socioeconomic status: a two-sample multivariable Mendelian randomization study. *Diabetes Care*, 44(3), 850-852.

The Effect of BMI and Type 2 Diabetes on Socioeconomic Status: A Two-Sample Multivariable Mendelian Randomization Study

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OBJECTIVE

To assess the independent causal effect of BMI and type 2 diabetes (T2D) on socioeconomic outcomes by applying two-sample Mendelian randomization (MR) analysis.

RESEARCH DESIGN AND METHODS

We performed univariable and multivariable two-sample MR to jointly assess the effect of BMI and T2D on socioeconomic outcomes. We used overlapping genome-wide significant single nucleotide polymorphisms for BMI and T2D as instrumental variables. Their causal impact on household income and regional deprivation was assessed using summary-level data from the UK Biobank.

RESULTS

In the univariable analysis, higher BMI was related to lower income (marginal effect of 1-SD increase in BMI [$\beta = -0.092$; 95% CI −0.138; −0.047]) and higher deprivation ($\beta = 0.051$; 95% CI 0.022; 0.079). In the multivariable MR, the effect of BMI controlling for diabetes was slightly lower for income and deprivation. Diabetes was not associated with these outcomes.

CONCLUSIONS

High BMI, but not diabetes, shows a causal link with socioeconomic outcomes.

Previous evidence indicates that high BMI and type 2 diabetes (T2D) are associated with poorer labor market prospects, lower productivity, and higher absenteeism (1–6). These disadvantages may accumulate over time and affect income and living circumstances, leading to a selection of individuals in more regionally deprived areas.

However, identifying the causal effect of BMI or diabetes on socioeconomic outcomes is challenging, mainly due to intrinsic problems of unmeasured confounding and reverse causation (1–3). Earlier approaches focused on the use of instrumental variable (IV) methods, exploiting the disease status of biological parents as IV (1–3). Recent studies have used genetic characteristics in one-sample Mendelian randomization (MR) approaches and showed an effect of BMI on socioeconomic status (4–6), while no effect of diabetes could be revealed (5).

This study aims at estimating the causal effect of BMI and T2D on household income and regional deprivation using a multivariable two-sample MR approach. This approach allows considering the shared genetic components of BMI and diabetes (7) to jointly estimate their causal effects on these socioeconomic outcomes (8).

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L.S. and M.L. share last authorship.

RESEARCH DESIGN AND METHODS

MR

The principle of MR roots in Mendel's laws of inheritance (i.e., the individual genotype is largely independent of external factors and therefore independent of potential confounders). In MR techniques, significant single nucleotide polymorphisms (SNPs) that are associated with the exposure are exploited as exogenous genetic variation in the form of IVs (8,9).

Genome-wide association studies (GWAS) have shown significant independent associations between several SNPs and BMI or T2D (10,11) but also the presence of distinct signals influencing both conditions (7). While the relevance assumption and exclusion criteria are satisfied for our data (see Supplementary Material 1), this overlap could lead to horizontal pleiotropy that violates the exchangeability assumption (i.e., the same SNP independently influences multiple phenotypes) and could result in biased estimates (9). Horizontal pleiotropy can be overcome by using multivariable MR methods (i.e., by considering the overlapping instruments directly in the estimation) (8).

Data

For the associations between SNPs and socioeconomic outcomes, we used publicly available summary-level data from a GWAS of UK Biobank data (12,13), including 464,708 individuals of European ancestry. Our outcomes were household income, defined as the average total household income before tax, and regional deprivation, defined using the Townsend deprivation index (14) (Supplementary Material 1).

Regarding the exposures, we used summary-level data on the associations between SNPs and BMI or T2D from published meta-analyses of GWAS (10,11), excluding UK Biobank participants, because independency of data of the SNP-exposure and SNP-outcome association is a key prerequisite for the validity of the two-sample MR approach (9) (Supplementary Materials 1 and 2).

Statistical Analysis

First, we performed a univariable MR analysis, testing the single effects of BMI and diabetes on the outcomes (8). Second, we estimated two-sample multivariable MR analysis of the effects of BMI and diabetes on the outcomes, using the set of overlapping SNPs as instruments (10,11).

We estimated the effects using the inverse-variance weighted (IVW) method (9). Furthermore, we tested their robustness against other estimation methods, including median-based, MR Egger, and MR-robust adjusted profile score (RAPS) methods (Supplementary Materials 1 and 3). Moreover, we tested the sensitivity of the results by excluding other potentially pleiotropic SNPs (Supplementary Material 4).

In both the univariable and the multivariable analyses, we tested the effects of two exposures on two outcomes. We therefore assumed a conservative Bonferroni-corrected P value for statistical significance of $0.05/4 = 0.0125$.

RESULTS

In total, we included 69 SNPs for BMI and 42 SNPs for T2D, which overlapped at two distinct loci: FTO and TCF7L2 (Supplementary Table 2).

Results of the univariable MR analysis indicated that a higher BMI was associated with a lower household income ($\beta = -0.092$; 95% CI -0.138; -0.047) and with a higher regional deprivation ($\beta = 0.051$; 95% CI 0.022; 0.079) (Table 1). Diabetes did not have any effect on the socioeconomic outcomes considered.

All analyses, except for BMI on income, presented low to middle levels of heterogeneity ($I^2 = 0$–57%), indicating good validity of the instruments. The difference between MR Egger and IVW estimates and a significant MR Egger intercept indicated the presence of horizontal pleiotropy, highlighting the need for multivariable MR analysis. The resulting effects from the multivariable MR analysis (Table 1) revealed that the direct effect of BMI controlling for diabetes was lower than in the univariable setting but still significant for both household income ($\beta = -0.089$; 95% CI -0.13; -0.048) and regional deprivation ($\beta = 0.049$; 95% CI 0.023; 0.075). Again, no effect of diabetes on socioeconomic outcomes could be observed.

The results from the MR Egger regression were almost identical to the estimates resulting from the IVW regression, indicating that the multivariable approach successfully accounted for the bias resulting from horizontal pleiotropy in the univariable setting.

All results were robust to the use of alternative estimation methods (Supplementary Material 3) and to the exclusion of other potentially pleiotropic SNPs (Supplementary Material 4).

CONCLUSIONS

In this study, we estimated the independent effects of BMI and T2D on household income and regional deprivation using a novel multivariable MR technique (8). Our results indicate negative effects of BMI but no effect of diabetes.

These findings strengthen the evidence of the deleterious role of BMI on income and regional deprivation reported in previous observational and one-sample MR studies (1,4–6). The potential underlying mechanisms include a lower ability to work, higher absenteeism, higher probability of musculoskeletal injuries, and higher discrimination, which may lead to poorer career prospects, decreasing labor market participation, and lower income (1). A lower income could in turn affect living standards, leading individuals to self-select into more deprived areas with more affordable housing and food options.

Similar to a previous one-sample MR study (5), our results did not show any significant effect of T2D on household income or regional deprivation. In contrast, other studies that did not use a multivariable two-sample MR approach showed a negative effect of diabetes on socioeconomic outcomes (2,3). This result should be object of further studies, aiming at establishing whether this null effect can be replicated or whether it is mainly due to methodological shortcomings in our study.

In fact, this study has some methodological limitations. First, despite the fact that genetic characteristics are independent of possible confounders, high BMI or diabetes genetic risk of parents might be an unmeasured confounder, causing a "dynastic bias" (15). Second, although the relevance assumption of our IVs is satisfied, the explanatory power of the set of SNPs used in the analysis for both the exposures and the outcomes is limited (10,11). Finally, because the UK Biobank population is a selected one (13), our results might suffer from selection bias.

In conclusion, the current study provides evidence of a negative causal effect of higher BMI on income and regional deprivation, controlling for diabetes. In contrast, T2D does not have an effect on these two socioeconomic outcomes. Further studies should investigate this

Table 1—MR results for the effect of BMI and diabetes on household income and regional deprivation

	Household income (SD)						Deprivation (SD)					
Method	β	95% CI	pval	Q pval	I^2 (%)	Int pval	β	95% CI	pval	Q pval	I^2 (%)	Int pval
Univariable MR												
BMI												
IVW	−0.092	−0.138; −0.047	<0.001	<0.001	71		0.051	0.022; 0.079	0.001	<0.001	57	
MR Egger	−0.045	−0.11; 0.019	0.080	<0.001	71	0.359	0.013	−0.036; 0.057	0.282	<0.001	55	0.045
T2D												
IVW	−0.002	−0.005; 0.008	0.793	<0.001	50		0.002	−0.005; 0.008	0.634	0.524	0	
MR Egger	−0.005	−0.014; 0.02	0.312	<0.001	49	0.702	0.003	−0.012; 0.019	0.346	0.516	0	0.375
Multivariable MR												
BMI												
IVW	−0.089	−0.13; −0.048	<0.001				0.049	0.023; 0.075	<0.001			
MR Egger	−0.089	−0.131; −0.048	<0.001				0.049	0.023; 0.076	<0.001			
T2D												
IVW	−0.001	−0.016; 0.013	0.854				0.0004	−0.009; 0.01	0.940			
MR Egger	−0.001	−0.016; 0.013	0.866				0.0003	−0.009; 0.01	0.958			

The estimates for BMI indicate the change in the outcomes for a 1-SD increase in the genetically predicted level of BMI. The estimates for T2D can be interpreted as the change in outcomes in response to a 1-unit increase in the $\log_e$ odds of genetic risk of diabetes. All changes in outcome are expressed in SD units. β, marginal effect; Int pval, intercept *P* value; pval, *P* value; Q pval, *P* value of the Cochran *Q* statistic.

result, using new generations of GWAS with a higher explanatory power and including a more representative population. Furthermore, applied research may help to improve the understanding for the underlying mechanisms and to create targeted strategies to break the negative connection between BMI and socioeconomic outcomes.

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4. Appendix A: Additional Manuscript

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The impact of diabetes on labour market participation: a systematic review of results and methods

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Abstract

Background: Diabetes mellitus is a major chronic disease, which is connected to direct and indirect costs and productivity losses. However, its effects on labour market participation are not straightforward to identify, nor are they consistently included in cost-of-illness studies. First, this study aims to synthesise existing evidence regarding the impact of diabetes on labour market outcomes that imply a complete absence of work. Second, the analysis takes a particular look at relevant methodological choices and the resulting quality of the studies included.

Methods: We conducted a systematic literature research (PubMed, Embase, PsychINFO), by applying a standard screening, selection and results extraction process, which considered all types of studies including cross-sectional and longitudinal approaches. Risk-of-bias and quality within the studies were assessed and results were compared. We dedicated special attention to the modelling of potential reverse causality between diabetes and labour market outcomes and the consideration of comorbidities and complications.

Results: Overall, 30 studies satisfied our inclusion criteria. We identified four main labour participation outcomes: absence of employment, unemployment, early retirement, and disability pension. The studies reviewed show a negative impact of diabetes on the labour market participation outcomes considered. However, only a few studies controlled for endogeneity, differentiated between type 1 and type 2 diabetes or modelled the impact of comorbidities. We report how modelling choices affect the directions and interpretations of the effects.

Conclusions: The available evidence mainly suggests a negative impact of diabetes on several outcomes indicating labour market participation. The methodological limitations identified can guide future research with respect to both outcomes and methods. This study provides therefore an empirical contribution to the discussion on how to model the economic impact of diabetes.

Keywords: Diabetes mellitus, Labour market, Indirect cost, Employment, Unemployment, Early retirement, Disability pension, Systematic review

Background

Diabetes mellitus is a major chronic disease with increasing public health relevance in high-, low- and middle-income countries. According to recent estimates, the number of people suffering from this condition worldwide will rise from 425 million in 2017 to 629 million by 2045 [1]. The progressing prevalence of this illness is especially due to type 2 diabetes, which constitutes 90–95% of diabetes cases, and the increasing average age of populations [2–5]. Due to this increase, total health care expenditures resulting from diabetes mellitus are estimated to rise from $727 billion in 2017 to $776 billion in 2045 [1].

Type 2 diabetes is closely linked to environmental and lifestyle risk factors, such as unhealthy diet, smoking and physical inactivity. Furthermore, the management of both type 1 and type 2 requires a high level of patient awareness and self-management [1]. For these reasons, many countries have established prevention and disease management programs to reduce incidence rates and to help affected people coping with the illness [6–8]. If

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poorly managed, both types of diabetes could lead to severe medical complications, which can affect an individual's ability to work and may lead to lower productivity at work (presenteeism) or missing workdays (absenteeism) [9].

Existing systematic reviews suggest a clear effect of diabetes on economic costs [10, 11], work ability, work functioning, macroeconomic productivity and socio-economic consequences [9–11]. Despite this evidence, most cost-of-illness studies base their calculations of indirect costs on productivity losses due to short or long term morbidity (absenteeism, presenteeism and disability pension) and mortality [12]. However, as suggested by the American Diabetes Association [13], considering only these factors might result in a rather conservative approach, since individuals with diabetes might have lower workforce participation rates than the overall population, which would not be adequately captured simply accounting for such short and long term productivity losses. Although the underestimation caused by this flaw could be mitigated by adopting a friction cost approach, the effect remains of key importance in the correct computation of individual and general societal costs due to diabetes.

However, understanding and empirically estimating the effects of diabetes on workforce participation is not straightforward. The correct empirical strategy to examine the relationship between diabetes and workforce participation requires careful consideration of potential confounding, of reverse causality between the illness and workforce participation - otherwise termed "endogeneity" -, of different types of diabetes mellitus and of its associated complications.

Given the growing importance of diabetes, the complex assessment of its productivity losses, and the potential heterogeneity in the applied econometric methods to address this question, a careful pooling and critical assessment of the existing evidence regarding the impact of diabetes on labour market participation is needed. Therefore, the aim of the present review is twofold: First, we gather all existing evidence regarding the relation between diabetes and workforce participation outcomes (employment/unemployment, early retirement, and permanent disability pension). Second, we distinguish and assess methodological characteristics in existing studies. Hence, this review contributes to the discussion on the appropriate modelling of diabetes impact, provides methodological guidance for future studies and, therefore, fosters informed decisions in health policy and research.

Methods

Search strategy

The review was conducted and reported following the PRISMA guidelines [14]. We applied a structured approach, combining keywords and Medical Subject Headings (MeSH®) or Embase Subject Headings (Emtree®) on diabetes and labour market outcomes. The full set of the search terms for one database is represented in detail in Additional file 1. We applied the search on three databases: PubMed, Embase and PsychINFO. All databases were accessed using our institutional login. Additionally, at the end of the selection process, eligible studies, but also economic modelling studies focusing on the impact of diabetes on the selected outcomes, were screened for references.

Inclusion and exclusion criteria

Included original studies had to be published in a peer-reviewed journal between 1st January 2000 and 28th March 2017 in any language and had to focus on the general population of adults aged 18–64. Papers focusing on women or specific ethnic groups were also considered eligible whereas studies, which only aim at specific subpopulations of patients suffering from other diseases were excluded. All articles screened by abstract had an English version of the abstract available, and for none of the eligible studies the use of a translator was necessary.

We focused on studies which evaluated the impact of diabetes or its biomarkers, such as hyperglycaemia or haemoglobin A1c (glycosylated haemoglobin) higher than 6.5% [15], on labour market outcomes indicating the complete absence of an occupation, i.e. employment, unemployment, early retirement or reception of a permanent disability pension, but not mortality or other measures of productivity covered in other reviews [9, 11]. In addition, studies were considered not eligible if diabetes appeared as a cluster of several conditions (e.g. metabolic disorders, cardiovascular risk factors) or if the outcome of interest could not be distinguished from other outcomes.

We included both cross-sectional and longitudinal studies with the primary aim of estimating the impact of diabetes on the selected outcomes, while economic modelling studies (cost-of-illness studies and simulations) were not included.

Study selection process

After pooling the results in EndNote (Version X7) and eliminating duplicates, two authors (SP, KEF) carried out an independent three-step successive screening process of the articles regarding titles, abstracts and full-texts, by considering the predefined inclusion criteria described above. Disagreements were first discussed between the two authors and afterwards with the other authors (LS, ML).

Data extraction and synthesis

After the identification of all eligible studies, we collected the results by using a predefined extraction form based on the well-established *Cochrane Consumers and Communication Review Group data template* [16]. From each paper we extracted a standardised set of information including

the general characteristics of the study, the data source and the study population, the outcome measure considered and its definition, the analysis method used, the type of results reported, and finally the magnitude of corresponding effects. For those studies, which take endogeneity into account, we also added the necessary information allowing the evaluation of their methodological rigor. In all cases, missing information was retrieved by consulting survey web pages, reading explanatory publications or contacting authors. Furthermore, we grouped the studies in four different outcome categories. Studies which analysed the impact of diabetes on a binary variable indicating the presence of an occupation were grouped under the term "employment". Other studies considered a binary variable indicating the absence of an occupation or the status "unemployment", i.e. currently not employed but actively looking for an occupation. Furthermore, we identified two other clusters, i.e. studies which focused on "early retirement" and studies which focused on the full receipt of a permanent "disability pension".

Quality appraisal

We assessed the quality and the risk of bias of each eligible study based on the Newcastle-Ottawa Scale [17]. Two authors (SP and KEF) assessed each study independently and discussed disagreements with the other two authors. The scale entails three domains (selection, comparability, and exposure) with several sub-questions, focusing on representativeness of the dataset, measurement of exposure/outcome, and control variables included. Since the original scale is only available for cohort and case-control studies, we based our quality analysis on a modified version of the scale [9, 10]. Cross-sectional studies could be awarded a maximum of 6 points, while longitudinal studies had a maximum of 8 (see Additional file 2 for further details).

Due to the high heterogeneity of outcomes, we limited our analysis to a comparison of results based on their direction and level of significance. Furthermore, we focused our qualitative synthesis on methodological differences and how they influenced results in the studies. Finally, as a robustness check we focused our qualitative synthesis on studies which were awarded more than half of the maximum quality score indicating a low risk of bias.

Results

Description of included studies

Our search yielded 5674 records, resulting in 3570 papers after elimination of duplicates (Fig. 1). Through reference screening we identified 4 other articles. After the three-step screening process, thirty studies were considered eligible for the qualitative synthesis (Fig. 1).

As reported in Table 1 and detailed in Table 2, nineteen out of these thirty studies had a cross-sectional design [18–36], ten had a longitudinal design [37–46] and one study used both kinds of designs [47]. Most studies were based on data from North America (15 studies), Europe (7 studies) or Australia (6 studies), while low and middle-income countries (LMICs) from Asia [24, 39] or Central America [31] were object of three studies only.

Most data were collected through large population-based surveys, while only four of these studies linked those data to morbidity or administrative registries [28, 37, 38, 40]. Almost half of the studies evaluated recent data collected from the year 2000 onwards. The other half analysed data collected in the last century, dating back until 1979.

Only a minority of studies focused on specific groups of employees [37, 38] or women [25, 42, 44], whereas the majority considered (population-based) samples from the general population.

While half of the studies focused on the elderly, the other half included samples from the whole working age population (aged 18–64). However, they generally carried out a stratified analysis for different age groups, so that the results are generally comparable among all studies on this regard.

Table 2 and Additional file 2 show that no study reached the maximum quality score. Three cross-sectional and three longitudinal studies gained half of the available points. This indicates a high risk of bias. The majority of studies were assigned a low score because, among other reasons, they used self-reported diabetes status as the exposure variable. Only a few studies based their analysis on more objective information from morbidity registries or formal blood tests [21, 26, 28, 37, 41]. Furthermore, the studies which adopted an "objective" definition of diabetes did not clearly indicate which pieces of information were used to carry out such definition, i.e. whether the status was defined on the basis of blood parameters (glycosylated haemoglobin, fasting or plasma glucose) or on the basis of a previous medical diagnosis reported by the participants. Additionally, in most cases the labour market outcomes were defined through structured interviews or questionnaires, resulting in a low scoring for several studies (Additional file 2).

In Table 2, we clustered the available studies according to the outcome(s) of interest. Despite the sorting into similar outcomes groups, the definitions of outcomes and control groups still varied considerably within each cluster, limiting the comparability of the studies included. For these reasons, any generalized comment or comparison of effect magnitude among the studies in this framework is not feasible, unfortunately.

Effects on employment

In general, as can be inferred from Table 2, the studies show a negative and statistically significant association between the presence of diabetes and the outcome

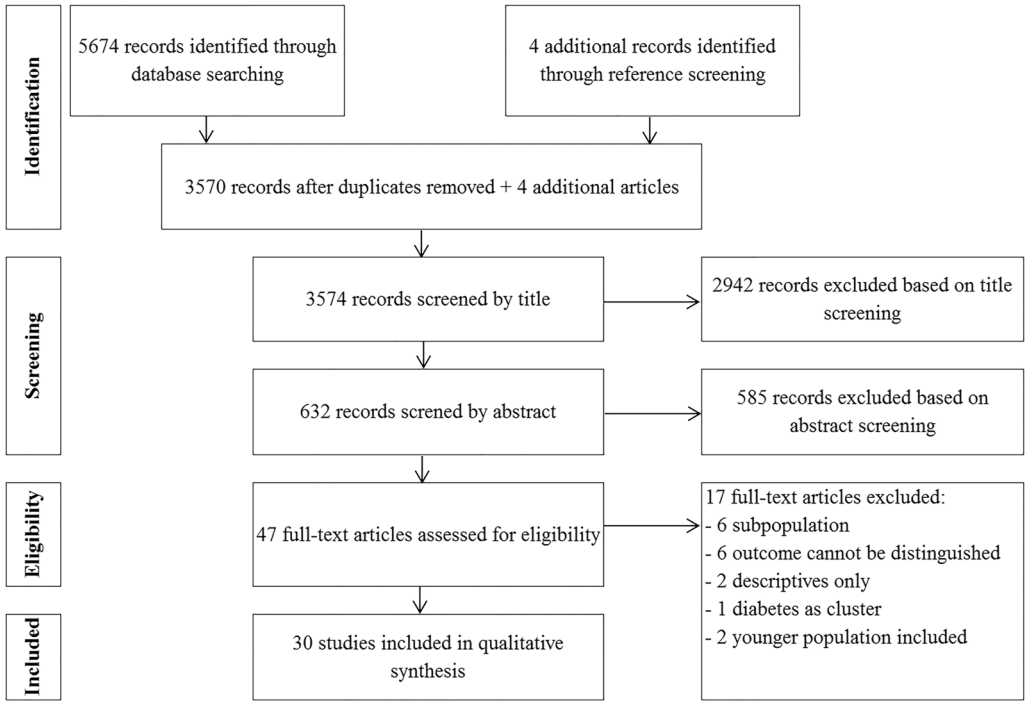

Fig. 1 PRISMA flowchart

"employment". However, the magnitude of the effect varies greatly between the studies considered. This might be due to differences in the mean sample ages, modelling techniques or outcome definitions. This negative effect does not change when we focus only on studies with a low risk of bias. Furthermore, considering the overall evidence, statistically significant coefficients for both genders are reported. However, within studies, estimated coefficients are generally higher in men than in women, indicating a stronger effect of diabetes on employment in males (see Table 2).

When focusing on studies from LMICs [24, 31, 39], diabetes does not show any effect on the employment chances of women, while the effect for men remains negative. This finding is in line with the overall results, but shows a much lower, if non-existent, effect in women compared to the other studies from HIC (high income countries). Furthermore, a few studies differentiated the analysis between type 1 and type 2 diabetes (T1DM and T2DM) [25–28, 43]. They show that the negative effect of diabetes is actually driven by T2DM, since the coefficients on type 1 are generally insignificant or in some cases positive and statistically significant.

By applying different statistical methods, seven out of thirteen cross-sectional studies considering employment as the outcome variable tested for endogeneity of diabetes. In order to take this factor into account, authors employed either recursive multivariate probit models, jointly estimating the probability of diabetes, other comorbidities/complications (cardiovascular disease, depression, etc.) and employment, or used an instrumental variable (IV) approach, when genetic information (diabetes status of parents or siblings) was available. Not all studies detected the presence of endogeneity. Furthermore, if endogeneity was found to be present, modelling approaches aiming to account for endogeneity revealed either an under- or an overestimation of the coefficients compared to models without endogeneity. Hence, the overall picture is rather inconsistent.

To model the presence of comorbidities or complications, some studies included relevant variables as confounders in the analysis, without discussing the implications of their modelling choices [21, 22, 36, 44]. In contrast, other authors used these factors as additional controls in more complex model specifications, discussing their role with regard to the magnitude and the significance of the coefficients compared with simpler model specifications [43, 46]. As a result, some coefficients on the diabetes variable lost their significance (see Table 2) or decreased (c.f. Table 2). In contrast, Ng et al. (2001) [27] carried out an additional analysis focusing only on the diabetes group and tested the impact of comorbidities. Their analysis shows that people suffering from diabetes and other comorbidities have a 12% lower probability of being in the labour force than people suffering from diabetes but without any complication.

Table 1 Descriptive table of included studies

Category	Characteristics	Number of studies
Design[a]	Cross sectional	20
	Longitudinal	11
Context		
Area[a]	North America	15
	Europe	7
	Australia	6
	Asia	2
	Central America	1
Period of data collection	Before 2000	14
	After 2000	16
Dataset	Survey only	26
	Survey + Register	4
Participants		
Number of participants	< 10,000	11
	≥10,000 to < 50,000	13
	≥50,000 to < 100,000	5
	> 100,000	1
Population	General population	28
	Employees in the energy sector	1
	Employees in the public sector	1
Sex	Both	27
	Only Women	3
	Only Men	0
Age[b]	18 or older	16
	45 or older	7
	50 or older	7
Definitions		
Diabetes definition	self-report	25
	register data	3
	laboratory analysis	2
Diabetes type[a]	T1DM only[c]	1
	T2DM only[c]	1
	Both distinguished	4
	Both undistinguished	24
	Haemoglobin A1c > 6.5%	1
Outcome[a]	Employment	16
	Unemployment	8
	Early retirement	8
	Disability pension	5

[a]These studies do not sum up to 30. Some studies included more than one of the characteristics indicated
[b]The indicated age refers to the youngest participant. Generally, the studies included only people maximum 64 or 65 years old. For details see Table 2
[c]T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus

Effects on unemployment

For the second outcome considered, i.e. "unemployment", heterogeneity in the outcome definition is particularly apparent. Groups of employed individuals are compared with very different samples of persons without occupation. From pooling corresponding evidence, it emerges that the presence of diabetes has no impact on the probability of having no occupation but still being economically active [18, 33, 40, 41]. However, it is associated with a complete exit from the labour market [30, 32, 34, 41]. Furthermore, by differentiating the exposure variable in diabetes with/without complications, Kraut et al. (2001) [41] revealed that people suffering from diabetes with complications are more likely to exit the labour force compared to individuals not suffering from diabetes, whereas this observation does not hold for people with diabetes without complications.

Effects on early retirement and permanent disability pension

In general, studies focusing on early retirement revealed a positive association between the presence of diabetes and the probability of retiring early. In contrast, two studies stratified their analyses with respect to gender and revealed only weak evidence for either women or men [29, 39]. However, one of these studies shows a high risk of bias [29], while the other one entails a low number of observations, probably leading to a lack of significance in the final result [39].

Studies evaluating the fourth outcome, viz. "permanent disability pensions", revealed a positive association with the presence of diabetes. In the paper by Ervasti et al. (2016) [37] several models with different comorbidities and complications are reported. After introducing corresponding confounders, coefficients on diabetes remained positive and statistically significant, but their magnitude diminished (see Table 2).

Robustness checks

Generally, leaving out studies at high risk of bias does not change the pattern of synthesised results remarkably for different outcomes. No study focusing on unemployment, early retirement or disability pension distinguished between T1DM and T2DM or considered endogeneity of diabetes. Furthermore, only two studies stratified the analysis for gender, and several studies included comorbidities or complications as confounders, potentially adding other sources of bias to the analysis.

Discussion

Summary of evidence and interpretation

We identified 30 studies, which evaluated the impact of diabetes on labour market outcomes, which imply a complete absence of any occupation. The available

Table 2 Eligible studies evaluating the effect of diabetes on labour market outcomes

Study	Methods					Results				Other			
	Study design[a]	Outcome definition	Age group	Exposure	Statistical method	Summary measure[d]	Overall	Men	Women	Confounders[e]	Comorbidities/ complications modelling	Endogeneity[g]	Quality score
Employment													
Ng et al. (2001) [27]	C	Currently working (vs. currently not working)[b]	18–65	Diabetes	Probit regression	PC	−0.04 *			A, CC, E, F, G, L, MS, SH	Stratification	no	5/6
				T1DM	Probit regression	PC	0.11 *						
Bastida et al. (2002) [19]	C	Currently working (vs. currently not working)	45+	Diabetes	Probit regression	ME		−0.08 *	−0.07	A, E, F, H, I, MS, O	–	no	5/6
Yassin et al. (2002) [34]	C	Being employed for most of the time in the last 12 months	18–64	Diabetes	Multinomial logistic regression	OR		0.53	0.48 *	A, E, I, MC, MS, O, SM	–	no	5/6
Brown et al. (2005) [20]	C	Currently working (vs. currently not working)[b]	45+	Diabetes	Probit regression	PC		−1.02 *	−0.34 *	A, E, F, H, I, MS, O	–	yes	5/6
					Recursive bivariate probit IV	PC		−1.71 *	0.51				
Klarenbach et al. (2006) [22]	C	Working at a job or business and being present at that job for the week before	20–59	T2DM	Logistic Regression	OR	0.70 *			A, CC, E, G, L, MS, O	Confounders	no	4/6
Harris (2009) [21]	C	Currently employed (vs. not working but not retired)	> 25	Diabetes	Endogenous multivariate probit model	ME		−0.07 *	−0.09 *	A, CC, E, F, I, MS, PA, SM	Confounders	yes	4/6
Latif (2009) [23]	C	Having had a job in the last 12 months	15–64	Diabetes	Probit regression	PC		−0.65 *	−0.44 *	A, E, H, L, MS	–	yes	5/6
				Diabetes	Recursive bivariate probit regression IV	PC		0.96	0.19				
Zhang et al. (2009) [36]	C	Currently working (vs. currently not working)[b]	18–49	Diabetes	Endogenous recursive multivariate probit model	TE (%)		−3.91 *	−3.70	A, CC, E, MS, O, Y	Confounders	yes	4/6
			50–64	Diabetes	Endogenous recursive multivariate probit model	TE (%)		−11.47 *	−0.20				
Lin (2011) [24]	C	Currently working (vs. currently not working)	45–65	Diabetes	Recursive bivariate probit model	ME	−0.24 *	−0.19 *	−0.15	A, E, G, I, MS	–	yes	5/6
Minor (2011) [25]	C	Worked for pay at some point during the last year	20–65	Diabetes	IV estimation (model 1)	ME	−0.42 *			A, E, F, F, J, L, MS, O, SH	–	yes	5/6
				T1DM	IV estimation (model 2)	ME	−0.06						
				T2DM		ME	−0.45 *						
Seuring et al. (2015) [31]	C	Having worked or carried out an activity that helped with the household expenses for at least 10 h over the last week	15–44	Diabetes	Probit regression	ME		−0.01	0.00	A, E, F, I, L, MS, O, PE	–	yes	5/6
			45–64			ME		−0.110 *	−0.06 *				

Table 2 Eligible studies evaluating the effect of diabetes on labour market outcomes *(Continued)*

Study	Methods					Results					Other			
	Study design[a]	Outcome definition	Age group	Exposure	Statistical method	Summary measure[d]	Overall	Men	Women		Confounders[e]	Comorbidities/ complications modelling	Endogeneity[g]	Quality score
Nielsen et al. (2016) [28]	C	Currently working (vs. currently not working)	18–103	T1DM	Linear regression	RD	−9.10 *	− 5.30 *	− 12.20 *		A, E, G, SH	–	no	4/6
Minor et al. (2016) [26]	C	Currently working (vs. currently not working)	18–65	A1c levels > 6.5%	Probit regression (model 1)	ME		−0.02	− 0.16		A, E, F, MS, O, Y	–	no	5/6
				T2DM		ME		−0.11 *	− 0.19 *					
				T1DM		ME		−0.17	0.18 *					
				T2DM	Probit regression (model 2)	ME		−0.09 *	− 0.19 *					
				T1DM		ME		−0.16	0.175 *					
Tunceli et al. (2005) [46]	L	Working for pay outside the home (vs. Not working for pay outside home)	51–61	Diabetes	Probit regression (model 1)	ME		−0.09 *	− 0.06 *		A, BMI, E, F, I, J, MS, O	Confounders SA[f]	no	6/8
				Diabetes	Probit regression (model 2)	ME		−0.07 *	− 0.04		A, BMI, E, F, I, J, MS, O, CC			
Pit et al. (2012) [44]	L	Employment last week (more than one hour spent on an occupation with or without pay) (vs. less than one hour spent last week on an occupation or unemployed)	51–61	Diabetes	Robust nested multivariate longitudinal analyses (GEE)	OR	0.82 *				BMI, CC, E, F, L, MS, SM, Y	Confounders	no	4/8
Minor (2013) [43]	L	Currently working (vs. currently not working)[b]	45–53	T1DM	Logistic regression	LC		0.22	−0.03		A, E, F, FH, J, L, MS, O, Y	Confounders SA[f], modelling time from diagnosis	no	6/8
				T2DM		LC		−0.42 *	− 0.37 *					
				T1DM	Logistic regression	LC		0.02	0.28		A, BMI, CC, E, F, FH, J, L, MS, O, Y			
				T2DM		LC		−0.28	−0.36 *					
Unemployment														
Alavinia et al. (2008) [18]	C	Currently unemployed (vs. Having done any kind of paid work in the last four weeks)	50–65	Diabetes	Logistic regression	OR	1.38				A, AL, BMI, CC, E, G, MS, PA, SM	Confounders	no	4/6
Smith et al. (2014) [32]	C	Currently not employed due to health reasons (vs. currently employed)	25–74	Diabetes	Logistic regression	OR	2.22 *				A, BMI, CC, E, F, G, I, L, MS, Y	Confounders	no	3/6
Van Der Zee-Neuen et al. (2017) [33]	C	Currently unemployed (vs. currently employed)	18–65	Diabetes	Multinomial logistic regression	OR	1.88				A, BMI, E, G, SM	–	no	4/6
Yassin et al. (2002) [34]	C	Transition from employment to no employment due to health reasons	18–64	Diabetes	Logistic r egression	OR		3.1 *	2.9		A, E, I, MC, MS, O, SM	–	no	5/6
Rumball-Smith et al. (2014) [30]	C	More than one year of absence from the labour force or retirement	> 50	Diabetes	Cox proportional hazards models (matching diabetes	HR	1.30 *	1.26 *	1.34 *		A, E, G, L	–	no	5/6

Table 2 Eligible studies evaluating the effect of diabetes on labour market outcomes *(Continued)*

Study	Methods					Results					Other			
	Study design[a]	Outcome definition	Age group	Exposure	Statistical method	Summary measure[d]	Overall		Men		Women	Confounders[e]	Comorbidities/ complications modelling	Endogeneity[g]	Quality score
		(vs. Currently employed)			subject with seven non-diabetes matches)										
Kraut et al. (2001) [41]	L	Not in the labour force (not employed and not seeking job) vs. in the labour force	18–64	Diabetes (w comp)	Logistic regression	OR	2.07	*				A, G, L, MS, O	Exposure	no	6/8
				Diabetes (w/o comp)	Logistic regression	OR	1.20								
		Unemployed (no job but actively looking for it) vs. employed (with job)	18–64	Diabetes	Logistic regression	OR	1.45								
				Diabetes (w comp)	Logistic regression	OR	1.69								
				Diabetes (w/o comp)	Logistic regression	OR	1.35								
Kouwenhoven-Pasmooij et al. (2016) [40]	L	Transition from employment to unemployment	> 50	Diabetes	Multinomial logistic regression	OR	1.17					A, CC, E, G, L, MS,	Confounders	no	6/8
Majeed et al. (2015) [42]	L	"Early paid work" (vs. "mostly in the labour force")[c]	45–50	Diabetes	Multinomial logistic regression	OR	1.44	*				BMI, E, F, I, MS, SM	–	no	4/8
Early retirement															
Vijan et al. (2004) [47]	C	Currently retired (vs. currently working)	51–61	Diabetes	Logistic regression	OR	1.3					A, E, F, G, MS, O	–	no	4/6
Alavinia et al. (2008) [18]	C	Currently retired (vs. Having done any kind of paid work in the last four weeks)	50–65	Diabetes	Logistic regression	OR	1.33	*				A, AL, BMI, CC, E, G, MS, PA, SM	Confounders	no	4/6
Pit et al. (2013) [29]	C	Retirement due to health reasons (vs. Working)	45–65	Diabetes	Multinomial logistic regression	OR			1.44	*	1.30	A, CC, E, MS	Confounders	no	3/6
		Retirement for other reasons (vs. Working)							1.16		1.07				
Yen et al. (2011) [35]	C	Age at retirement	50–75	Diabetes at age 50	OLS regression	OLS	−1.39	*				CC, E, G, I, J, L, O	Confounders	no	3/6
Vijan et al. (2004) [47]	L	Incremental duration of retirement over the 8 years follow-up	51–61	Diabetes at baseline	Two-part multivariable model (logistic regression + OLS)	OLS	0.14	*				A, E, F, G, MS, O	–	no	6/8
Shultz et al. (2007) [45]	L	Transition from employment to retirement	47–64	Diabetes at baseline	Multinomial logistic regression	OR	3.37	*				A, CC, G, I, O	Confounders	no	4/8
Herquelot et al. (2011) [38]	L	Transition from employment to retirement	35–60	Diabetes (in at least three consecutive	Cox proportional-hazard regression	HR	1.6	*				A, BMI, G, J	–	no	6/8

Table 2 Eligible studies evaluating the effect of diabetes on labour market outcomes *(Continued)*

Study	Methods					Results				Other			
	Study design[a]	Outcome definition	Age group	Exposure	Statistical method	Summary measure[d]	Overall	Men	Women	Confounders[e]	Comorbidities/ complications modelling	Endogeneity[g]	Quality score
				yearly questionnaire)									
Kang et al. (2015) [39]	L	Transition from employment to early retirement due to health problems	45–70	Diabetes at baseline	Cox proportional hazard model	HR	1.47 *	1.52	1.40	A, AL, BMI, CC, G, I, J, PA, SH, SM	Confounders	no	5/8
Kouwenhoven-Pasmooij et al. (2016) [40]	L	Transition from employment to retirement	> 50	Diabetes	Multinomial logistic regression	OR	1.06			A, CC, E, G, L, MS,	Confounders	no	6/8
Disability pension													
Vijan et al. (2004) [47]	C	Currently receiving a disability pension (vs. currently working)[a]	51–61	Diabetes	Logistic regression	OR	3.1 *			A, E, F, G, MS, O	–	no	4/6
Van Der Zee-Neuen et al. (2017) [33]	C	Currently receiving a disability pension (vs. Currently employed)	18–65	Diabetes	Multinomial logistic regression	OR	2.32 *			A, BMI, E, G, SM	–	no	3/6
Vijan et al. (2004) [47]	L	Incremental duration of disability pension over the 8 years follow-up	51–61	Diabetes at baseline	Two-part multivariable model (logistic regression + OLS estimation)	Cumulative impact of diabetes (years)	0.79 *			A, E, F, G, MS, O	–	no	6/8
Herquelot et al. (2011) [38]	L	Transition from employment to disability pension	35–60	Diabetes (in at least three consecutive years)	Cox proportional-hazard regression	HR	1.4			A, BMI, G, J	–	no	6/8
Ervasti et al. (2016) [37]	L	Transition from employment to disability pension	30–65	Diabetes at baseline (vs. No metabolic condition)	Cox proportional-hazard regression (model 1)	HR	1.84 *			A, G, SES	Confounders SA[f]	no	7/8
				Diabetes at baseline (vs. No metabolic condition)	Cox proportional-hazard regression (model 2)	HR	1.56 *			A, AL, BMI, CC, G, J, PA, SES, SM			
Kouwenhoven-Pasmooij et al. (2016) [40]	L	Transition from employment to disability pension	> 50	Diabetes or high blood glucose levels	Multinomial logistic regression	OR	2.37 *			A, CC, E, G, L, MS,	Confounders	no	6/8

*p-value< 0.05
[a]C: cross-sectional study; L: longitudinal study;
[b]Not clearly stated but understood from context, interpretation, questions asked in survey
[c]Other outcomes considered ("increasingly paid work", "gradually not in paid work", "mostly not in paid work") are not reported here
[d]OR: Odds Ratio HR: Hazard Ratio ME: Marginal Effect PC: Probit Coefficient LC: Logit Coefficient TE: Treatment Effect RD: Risk Differences OLS: OLS-Coefficient
[e]*A* Age, *AL* Alcohol use, *BMI* Body-Mass-Index, *CC* Comorbidities/complications, *E* Education/Years of schooling, *F* Family related features (Number of children; Family size; People living in household; Household size; Living with someone who needs care; Competing activities;); *FH* Family health, *G* Gender, *H* Owns home, *I* Income/Wealth, *J* Employment characteristics, (Self-employment; Job tenure; Work experience; Part time; Occupational status;) *L* Region, Area of living/residence, *MC* Medical cost, *MS* Marital status, *O* Origin (Race, Australian born, Immigrant status) 0 *PA* Physical activity, *PE* Parental education, *SH* Subjective health/health related quality of life, *SM* Tobacco use/Smoking, *Y* Year
[f]Complications were used in the sensitivity analysis as confounders;
[g]Presence of endogeneity: yes = endogeneity of diabetes was detected; no = endogeneity of diabetes was not detected
Other information (e.g. sample size, country, method of data collection, results of IV tests) are not included in the table due to space limitations and are available from the corresponding author upon request

studies were quite heterogeneous in terms of definition of outcomes, age of the population considered and statistical method used even within the four outcome clusters we identified. Generally, the studies included provide consistent evidence that diabetes is negatively associated with employment and that diabetes patients are more likely to retire early, be fully out of the labour force and to receive a full and permanent disability pension, although effects may vary across subgroups.

The studies included also show considerable differences in the methods used, which could significantly impact the results. Furthermore, evaluations are often based on an extremely simplified modelling of diabetes, its dynamics and its progression, resulting in potential sources of bias. In this context, the majority of data is based on self-reported diabetes status and often no heterogeneity factors or endogeneity of the labour market outcomes are considered, resulting in lower quality scores for several studies included.

Specifically, a stratified analysis using potential sources of heterogeneous effects, such as gender, age, age at retirement or diabetes type, was inconsistently carried out throughout the studies, limiting the comparison of results regarding different groups within the scope of this review. In fact, a consistent stratified analysis between genders is available only for the outcome "employment". For the other outcomes, only isolated evidence with a high risk of bias could be found [29, 30, 34, 39]. As shown in many of the studies included [16, 19, 25, 27, 30, 32, 35, 39, 42] and in a previous review [7], both men and women suffering from diabetes have higher chances of adverse labour market outcomes, but within the same studies, the effect is generally higher for men than for women. However, no study furnished an evidence-based explanation of this result. The main interpretation is that, since the employment chances of elder females are already low due to several other factors (e.g. providing informal care, traditional household regimes), diabetes influences the employment chances of women in a less disruptive way than those of men. In this context, also the differences between studies from LMICs and other countries should be emphasized: the effect of diabetes for the employment and early retirement chances of women in LMICs is never significant, while the effect for men is in line with those observed in HIC [24, 31, 39]. The non-significant effect for women should be put in the right context and should be interpreted in the light of labour market differences, regarding most notably the social security systems and the role of women in society, which still characterize the divide between HIC and LMICs and which could significantly affect the employment chances of women in the first place. However, in line with previous studies [11], this review highlights also the paucity of evidence regarding the differences between HIC and LMICs, since only three of the included studies focused on the latter [24, 31, 39], and thus highlights the need for more research on these differences.

Most studies were based on large survey data, where diabetes status was self-reported (see Table 1). Although previous studies showed that there is a high correspondence between self-report and objective diagnosis [48, 49], this implies that most of the available evidence regarding the effect of diabetes on labour market outcomes bases its analysis and conclusions on a subjective measure of diabetes and is thus potentially open to bias. This bias is expected to be upwards, since the undiagnosed cases are probably those who also do not show any symptom or impairment from the disease, and as such are much less likely to leave the labour force due to diabetes. This potential pitfall is reflected in the lower quality score assigned to those studies based on self-report of diabetes and should be considered as an important limitation of the available evidence in this field.

Furthermore, in the same studies, no other information about age at onset, diabetes type, severity or medications was available, according to the publications identified. One important distinction in this context is that between T1DM and T2DM. Although the prevalence of T1DM is usually low [1], not controlling for this difference could cause a downward bias and, thus, an underestimation of the effect of T2DM on employment. In fact, the few studies that distinguish between the two diabetes types show that the negative effect of diabetes on employment is actually driven by T2DM, since the coefficients on T1DM are either insignificant or even significantly positive. Furthermore, T1DM and T2DM are two distinct conditions, with two different aetiologies and ways of coping with the illness. Therefore, this difference should be taken into account when modelling diabetes. For example, in absence of more detailed information, the age at onset could offer a good approximation, as already done in some of the studies included [25, 26].

Most studies also adopted a very simplified modelling of comorbidities and complications. These factors can play a crucial role in the ability to work of diabetes patients over the life course and, thus, should be considered when modelling diabetes and labour market outcomes. There is no consensus on how to take them into account. In most of the studies considered, they are either not taken into account or are modelled as confounders. However, as highlighted by some authors [25], simply adding them as confounders could be problematic, since they might be highly correlated with diabetes or a result of common unobserved factors. Therefore, including them as covariates into the model could result in biased estimates for the diabetes variable. In isolated cases comorbidities and complications are included [1] as confounders in different

versions of the model as further specification [37, 43, 46], [2] as a way to differentiate the exposure variable (diabetes with/without complications) [41] or [3] as exposure in a further analysis focusing only on the diabetes group [27]. These three implementations show that adding such confounders leads to a change in the magnitude or in the significance of the coefficient on the diabetes variable [37, 43, 46]. In addition, Kraut et al. (2001) [41] showed that only diabetes with complications leads to a full labour market exit. Ng et al. (2001) [27] also revealed that people suffering from diabetes with complications have a higher chance of being out of the labour force than people suffering from diabetes without complications.

A further issue, only addressed in a few studies, is the problem of reverse causality or endogeneity of diabetes in labour market outcome models. Typical ways for taking this problem into account include recursive multivariate probit approaches [20, 21, 23, 24] or the use of genetic instrumental variables [25, 31]. Results from studies taking endogeneity into account generally differed in two aspects: (i) the actual endogeneity of the diabetes variable and (ii) the direction of the bias in the regression coefficients with respect to the basic model without endogeneity. Overall, diabetes was not found to be consistently endogenous in each study considered and for every gender subgroup. Furthermore, while comparing the results from models with and without endogeneity within the same study, no clear direction of the bias of the coefficients could be highlighted (see Table 2). Therefore, since the pattern of presence and effect is not clear, endogeneity should always be tested for in this context and the limitations of results should be discussed carefully.

Strengths and limitations

This review specifically gathered evidence regarding the effect of diabetes on all labour market outcomes involving the complete absence of occupation. Hence, it complements related reviews, which focused on other productivity outcomes [9] or reviewed part of the included outcomes as a secondary aim [11]. Furthermore, in the present review, we paid specific attention to the methods used, providing ground for an evidence-based discussion on how to produce credible and robust findings both from an economic and a statistical point of view.

However, our study may suffer from some limitations. First, we have adopted rather restrictive inclusion criteria. We searched three databases and we included only articles already published in peer-reviewed journals, starting from the year 2000. Therefore, the review might suffer from publication bias. However, the large number of studies initially retrieved after an independent screening by two researchers and a comprehensive reference check allowed us to apply such restrictive criteria in order to report the most robust evidence available. Second, we based our quality and risk of bias assessment on the Newcastle-Ottawa Scale [17], as already done in similar reviews [9, 10]. Besides the transparent procedure of evaluation, the scale had to be modified for our specific case, which prevents comparability to a certain extent (for detailed explanation see Additional file 2). Furthermore, the scale is actually suitable for evaluating epidemiological studies involving clinical outcomes but could still be adapted to our specific question and context. Although the scale represents the best instrument available to our knowledge, this problem should be taken into account in further studies, aiming at improving also quality and risk of bias assessment.

Implications for practice, policy, and research

The aggregated evidence available reveals that generally, individuals suffering from type 2 diabetes mellitus are more likely to fully exit the labour market early, retire early and receive a permanent disability pension. Both men and women are affected, but the probability of employment of men is affected stronger than that of women. Diabetes can be endogenous in the labour market outcomes, but it is not clear why and in which cases it is present and how coefficients are influenced.

Maintaining and possibly also extending the ability to work of older workers is one of the primary goals of current pension reforms. This study shows, however, that chronically ill individuals suffering from T2DM, might not be able to maintain their employment status and will therefore exit the labour market earlier. Since T2DM prevalence is rising, not only in high- but also in low- and middle-income countries [1], a considerable effort should be undertaken to improve and prolong the ability to work of diabetes individuals. Specific attention should be paid to developing and increasing the efficacy of evidence-based prevention and management programs.

Finally, the existing evidence should be improved, specifically investigating the underlying dynamics and establishing and strengthening the link to practice. First, future cost studies investigating the indirect costs of diabetes should take the complete absence of an occupation due to diabetes or its complications into account. Failing to consider this aspect could lead to a severe underestimation of the burden this condition is imposing. Second, future studies will need to differentiate between gender and/or diabetes type, while also checking specifically for the endogeneity of diabetes. These methods should be applied for every outcome, not only for the presence versus absence of employment. Third, the issue of diabetes endogeneity should be discussed for each study, since no pattern of presence and effect could be found. Understanding how the underlying processes and effects work, being it through reverse causality or through unobserved factors, could also prove helpful in understanding how a

chronic life-style illness impacts the outcomes considered. Lastly, the available studies adopt an extremely simplified definition and modelling of diabetes, its progression, its severity and its complications and comorbidities. Further research should rely on more objective ways to determine diabetes. Also, it should improve the understanding of which factors and dynamics actually lead to adverse labour market outcomes and should include different modelling strategies on how comorbidities and complications actually work. Furthermore, additional aspects of the illness, such as efficiency of management, health literacy, and medication adherence [50, 51], should be included in the analysis, to gather further understanding on underlying factors and allow for the individualisation of concrete starting points for practical intervention.

Conclusions

This systematic literature review indicates that type 2 diabetes mellitus, but not type 1, is associated with lower productivity. We further found that the effect of diabetes is generally stronger in men than in women. In addition, the present study reveals that one of the largest potential sources of bias is the use of self-reported measures of diabetes, not confirmed by physicians or formal blood tests. Finally, the studies showed no consensus regarding the correct modelling strategy of diabetes and labour market outcomes. Only some of them considered possible endogeneity, or only partly discussed their modelling choices regarding the role of complications and comorbidities. Thus, the review highlights the need for improving the current practice of modelling diabetes and for understanding how the illness is connected with the outcomes. This is not only important for the accurate determination of indirect costs, but could also prove useful in the establishment of evidence-based prevention and disease management programs.

Additional files

Additional file 1: Search strategy. This file contains a detailed account of the databases and terms/keywords and restrictions used in our search strategy for one database (PubMed). (PDF 156 kb)

Additional file 2: Newcastle-Ottawa Scale and quality scores. This file contains a detailed overview and explanation of the Newcastle-Ottawa Scale used to assess quality of the retrieved studies. The file entails also a detailed overview of the scores for each study in each dimension. (PDF 271 kb)

Abbreviations

T1DM: Type 1 Diabetes Mellitus; T2DM: Type 2 Diabetes Mellitus; Haemoglobin A1c: glycosylated haemoglobin; LMIC: Low and middle income countries; HIC: High income countries

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Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

Authors' contributions

All authors conceptualized the review and formulated the research question. SP and KEF developed and carried out the research strategy, independently screened the manuscripts, retrieved the information and evaluated the results. Disagreements were discussed with ML and LS, who provided guidance during the process. SP drafted the manuscript. KEF, ML and LS critically revised and contributed to the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

The authors declare that they have no competing interests.

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Own contribution to the publications

4.1. Contribution to manuscript I

S. Pedron (SP) and K. Schmaderer conceptualized the original idea. SP co-supervised the first exploratory analysis in the master thesis of K. Schmaderer. SP further developed the model, re-conceptualized the analysis using the SEM framework and rewrote the manuscript accordingly, including a thorough enlargement of the theoretical basis, interpretations and policy implications. With the contributions of M. Murawski and L. Schwettmann, SP edited and reviewed the manuscript.

4.2. Contribution to manuscript II

SP conceptualized the idea together with L. Schwettmann and W. Maier. SP conceptualized the analysis and managed project data. SP implemented the analysis under the supervision of P. Eibich and L. Schwettmann. SP wrote, edited and reviewed the manuscript. L. Schwettmann and P. Eibich contributed by editing the manuscript draft.

4.3. Contribution to manuscript III

SP conceptualized the idea together with C. Kurz and thereafter managed the project and the relative data. SP conceptualized and implemented the analysis. SP wrote, edited and reviewed the manuscript. C. Kurz, L. Schwettmann and M. Laxy contributed by editing the manuscript draft.

4.4. Contribution to manuscript IV (additional manuscript)

SP conceptualized the idea together with K. Emmert-Fees, L. Schwettmann and M. Laxy. SP and K. Emmert-Fees conceptualized, operationalized and carried out the research strategy and the evidence analysis and evaluation. SP wrote, edited and reviewed the manuscript draft. K. Emmert-Fees, L. Schwettmann and M. Laxy contributed by editing the manuscript.

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Affidavit

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I hereby declare, that the submitted thesis entitled:

"The two-way relation between socioeconomic status and risk factors for cardio-metabolic health: Implications for prevention and social policy"

is my own work. I have only used the sources indicated and have not made unauthorised use of services of a third party. Where the work of others has been quoted or reproduced, the source is always given.
I further declare that the submitted thesis or parts thereof have not been presented as part of an examination degree to any other university.

München, 21.09.2021 — Sara Pedron

place, date — Signature doctoral candidate

Confirmation of congruency

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I hereby declare, that the submitted thesis entitled:

“The two-way relation between socioeconomic status and risk factors for cardio-metabolic health: Implications for prevention and social policy”

is congruent with the printed version both in content and format.

München, 21.09.2021 — Sara Pedron

place, date — Signature doctoral candidate

Publication List

Pedron, S, Kurz, CF, Schwettmann, L & Laxy, M (2021). The effect of BMI and type 2 diabetes on socioeconomic status: a two-sample multivariable Mendelian randomization study. *Diabetes Care*, 44(3), 850-852.

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