Addictive Behaviors 157 (2024) 108078

Contents lists available at ScienceDirect

Addictive Behaviors

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

The effect of heavy smoking on retirement risk: A mendelian randomisation analysis

Alessio Gaggero [a], Olesya Ajnakina [b,c], Eugenio Zucchelli [d,e,f], Ruth A. Hackett [g,*]

[a] Department of Quantitative Methods for Economics and Business, Universidad de Granada (UGR), Spain
[b] Department of Biostatistics & Health Informatics, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[c] Department of Behavioural Science and Health, Institute of Epidemiology and Health Care, University College London, London, UK
[d] Department of Economic Analysis: Economic Theory and Economic History, Universidad Autónoma de Madrid (UAM), Spain
[e] Division of Health Research, Faculty of Health & Medicine, Lancaster University, Lancaster, UK
[f] Institute of Labor Economics (IZA), Bonn, Germany
[g] Health Psychology Section, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

ARTICLE INFO

Keywords:
Smoking
Retirement risk
Polygenic Risk Scores
Mendelian Randomisation

ABSTRACT

Background and aims: The extent to which heavy smoking and retirement risk are causally related remains to be determined. To overcome the endogeneity of heavy smoking behaviour, we employed a novel approach by exploiting the genetic predisposition to heavy smoking, as measured with a polygenic risk score (PGS), in a Mendelian Randomisation approach.

Methods: 8164 participants (mean age 68.86 years) from the English Longitudinal Study of Ageing had complete data on smoking behaviour, employment and a heavy smoking PGS. Heavy smoking was indexed as smoking at least 20 cigarettes a day. A time-to-event Mendelian Randomization (MR) analysis, using a complementary log–log (cloglog) link function, was employed to model the retirement risk.

Results: Our results show that being a heavy smoker significantly increases the risk of retirement ($\beta = 1.324$, standard error $= 0.622$, $p < 0.05$). Results were robust to a battery of checks and a placebo analysis considering the never-smokers.

Conclusions: Overall, our findings support a causal pathway from heavy smoking to earlier retirement.

1. Introduction

Smoking is a preventable cause of morbidity and mortality (ASH, 2020). Heavy smokers have a particularly elevated risk of negative health outcomes (Murray, 2014) while smokers are less likely to be economically active than non-smokers (Office for National Statistics, 2020). Early retirement represents an economic challenge as governments pursue policies to extend working lives to improve the financial sustainability of pensions (OECD, 2019). As smoking is potentially modifiable (Hackett et al., 2018; West et al., 2015), it is crucial to understand how it influences early retirement.

Longitudinal evidence suggests smoking may be a predictor of early retirement. Occupational cohort data indicates there is a dose–response relationship between the number of cigarettes smoked daily and early disability retirement (Claessen et al., 2010; Rothenbacher et al., 1998). Evidence from Scandinavian population cohorts suggests that smoking is associated with increased risk of receiving a disability pension (Haukenes et al., 2013; Husemoen et al., 2004; Lallukka et al., 2015). Heavy smoking was the strongest predictor of disability retirement in one study (Lallukka et al., 2015) but similar associations were only seen in those aged under 60 (Husemoen et al., 2004) and in women (Haukenes et al., 2013) in others. However, data from 11 European countries found no association between smoking and disability retirement (Robroek et al., 2013).

Although these studies assessed smoking and subsequent retirement, the possibility of reverse causality, whereby retirement could influence smoking, cannot be ruled out. A review of 14 longitudinal studies investigating the impact of retirement on smoking presented mixed findings, with decreased smoking and no effect on smoking mainly reported (Xue et al., 2020). Yet, two studies found that retirement was

* Corresponding author at: Health Psychology Section, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK.
E-mail addresses: alessiogaggero@ugr.es (A. Gaggero), olesya.ajnakina@kcl.ac.uk, Olesya.ajnakina@ucl.ac.uk (O. Ajnakina), eugenio.zucchelli@uam.es (E. Zucchelli), ruth.hackett@kcl.ac.uk (R.A. Hackett).

https://doi.org/10.1016/j.addbeh.2024.108078
Received 2 February 2024; Received in revised form 30 May 2024; Accepted 1 June 2024
Available online 17 June 2024

associated with increased smoking (Xue et al., 2020), including an analysis of ~ 12,000 US-based adults (Ayyagari, 2016).

Such studies could also be subject to residual confounding by socio-economic status, as some results are attenuated by the inclusion of education and occupation (Bengtsson & Nilsson, 2018; Haukenes et al., 2013; Husemoen et al., 2004; Lallukka et al., 2015). However, income was not accounted for meaning this omitted variable may have contributed to the potential confounding. Another possibility is confounding by other health behaviours as behaviours tend to cluster (Mawditt et al., 2016). Previous studies (Eriksen et al., 1998; Lallukka et al., 2015) found that smoking was only predictive of disability pension in those who were physically inactive. This may suggest that smoking is an indicator of other health-related factors that increase the likelihood of labour market exit, rather than a causal predictor of retirement in itself.

Genetic approaches can help resolve these issues, as genetic factors influence smoking behaviour (Liu et al., 2019). Sibling and twin pair designs try account for unobserved factors related to family background. One study estimated the impact of smoking on disability retirement in 80,000 sisters (Bengtsson & Nilsson, 2018), finding a significant association when accounting for sibling effects. Significant associations between heavy smoking and disability retirement were also observed when accounting for sibling effects but reverted towards the null when education and occupation were considered. Studies of men and women from the Finnish Twins Cohort have been more able to account for the influence of genetic and shared environmental factors in the smoking-disability retirement relationship (Korhonen et al., 2015; Koskenvuo et al., 2011; Ropponen et al., 2013). One of these studies (Korhonen et al., 2015) with 22,000 participants found a dose–response relationship between the number of cigarettes smoked and the likelihood of receiving a disability pension.

Although studies using a familial design likely come closer to causal estimates of the impact of smoking on retirement, we cannot be certain all relevant factors have been accounted for (e.g., aspects of the home environment that might influence smoking or access/use of pension services). Furthermore, those who have a twin or siblings may differ from only children.

Genome-wide association studies (GWAS) have made it possible to investigate genetic variants across the genome for associations with traits measured in unrelated individuals (Dudbridge, 2013). Many complex traits are polygenic, implying their onset cannot be attributed to the independent contributions of individual genetic markers, but rather to the combined additive effects of multiple common genetic traits (So & Sham, 2017). Heavy smoking is one such 'polygenic' trait (Liu et al., 2019). This has led to the creation of polygenic scores (PGS), which reflect the aggregate of risk conferred by many genetic variants of small effect into a single continuous score that represents an individual load for the common variants associated with a particular trait.

PGS of robust genetic variants associated with heavy smoking have been developed in the English Longitudinal Study of Ageing (ELSA) (Ajnakina & Steptoe, 2019). This offers the possibility of a Mendelian Randomisation (MR) approach (Davey Smith & Hemani, 2014), whereby genetic predisposition to heavy smoking can be used an instrumental variable to test the inferred causality of heavy smoking on retirement risk.

The current study uses this approach, taking heavy smoking-related genetic variants (PGS) as an instrument for heavy smoking behaviour. As different smoking-associated genotypes are randomly allocated at conception, the associations of smoking-related variants with retirement risk should be free of confounding and reverse causation. In principle, this approach avoids the limitations of multivariable conditional correlational analyses (smoking predicting early retirement adjusting for confounders) and analyses accounting for familial effects. While it might be expected that heavy smoking influences retirement, we lack reliable estimates to quantify this. Therefore, we assessed whether heavy smoking is a causal factor leading to an earlier retirement, using PGS as an instrument.

2. Methods

2.1. Study cohort

We use data from ELSA, a longitudinal study of people aged ≥ 50 in England (Steptoe et al., 2013). Data collected started in 2002–03. Biennially, the sample is surveyed on health, social, and economic conditions. We pooled all available waves of data (waves 1–9). Ethical approval was obtained (MREC/01/02/91). Our full sample consists of 44,332 respondent-year-level observations. However, our analysis focuses specifically on smokers. Utilizing the wealth of information reported in ELSA, we were able to retrieve retrospective smoking behaviour data. This is crucial as it allows us to identify long-term smokers, namely those who smoked every day for at least 20 years (N = 8,164), and therefore provide a more comprehensive understanding of the cumulative effects of smoking over time.

2.2. Measures

2.2.1. Heavy smoking PGS

Participants of European ancestry were genotyped (2013–14), using Illumina HumanOmni2.5 Bead-Chips as described elsewhere (Ajnakina & Steptoe, 2019). Principal components analysis was performed to investigate population structure. Ten principal components were retained to account for differences in genetic ancestry (Price et al., 2006).

The heavy smoking PGS (2019) was calculated using summary statistics from the study that combined study-level summary association data from 1.2 million individuals of European ancestry (Liu et al., 2019). The calculation of this score is described elsewhere (Ajnakina et al., 2020; Ajnakina & Steptoe, 2019). Briefly, this PGS represents the weighted sum of cumulative genetic risk for heavy smoking, calculated by aggregating multiple individual loci associated with the number of cigarettes daily across the human genome and weighting them by their corresponding effects sizes derived from summary statistics. The resulting continuous PGS for number of cigarettes per day represents genetic predisposition towards heavy smoking. To ease interpretation, the PGS was standardised.

2.2.2. Heavy smoking

Heavy smoking was derived using the World Health Organisation cut point for heavy smoking (1 = ≥ 20 cigarettes, 0 = <20 cigarettes per day).

2.2.3. Retirement

Retirement was coded as a sequential binary variable taking the value of 1 when the individual transitions from employment to retirement and 0 otherwise.

2.2.4. Covariates

Age (years) was included (as a continuous variable) to account for the influence of age on retirement. Gender was coded as male/female. Education was coded as higher education qualification (yes/no). Marital status was coded as married vs divorced/separated/widowed/never married. Household size, measured as the number of people in the household, was included to account for potential economic and caregiving impacts, which may influence retirement decisions. Household income was measured using the log-yearly equivalised disposable real household income deflated using the Consumer Price Index with baseline 2005 = 100. To adjust for the 2010 change in state pension age (SPA), which standardized the SPA at 65 for both men and women (previously 65 for men and 60 for women), we included a binary variable into the model, set to 1 for waves post-reform and 0 otherwise, along with an interaction term with the gender dummy, reflecting its

impact on this specific category. Finally, we incorporated dummy variables for daily alcohol consumption (coded as 1) and sedentary behaviour (coded as 1), to address their potential impact on health and, consequently, retirement decisions.

2.2.5. Statistical analysis

To obtain casual estimates of the heavy smoking-retirement risk relationship we employ a two-stage time-to-event Mendelian Randomization (MR) analysis, using a complementary log–log (*cloglog*) link function (He et al., 2018; Teleka et al., 2020; Tadros et al., 2021). The main threat to the validity of MR is pleiotropy (i.e., if the same genetic variants associated with heavy smoking have a direct effect on retirement risk or influence other lifestyle/psychosocial factors that can, impact the decision to retire early). To address this concern, we ran a series of models of PGS on lifestyle/psychosocial factors that could be linked to early retirement (Supplementary Table 1). There were no significant associations suggesting that the heavy smoking genetic variants (indexed by the PGS) should only affect heavy smoking behaviour, and no other lifestyle/psychosocial factors assessed here.

For the time-to-event MR analyses, we adopted a two-stage regression approach utilizing the control function method. Specifically, we first fitted the following linear regression model, which estimates the effect of the PGS, denoted P_i, on the probability of being a heavy smoker, denoted H_i:

$$H_i = \mu + \pi P_i + \boldsymbol{X}_i'\Omega + \upsilon_i \quad (1)$$

Here, υ_i is the random error term following a zero–mean normal distribution and $\boldsymbol{X}_i'$ represents other observed individual-specific covariates. From this regression, we retrieved residuals, denoted $\widehat{\upsilon}_i$, to be included in the second stage. In the second stage, we estimate the effect of being a heavy smoker on retirement risk, fitting the following complementary log–log (*cloglog*) function:

$$\log\left[-log(1-h(t|\boldsymbol{X}_{it}')\right] = \mu(t) + \beta H_i + \boldsymbol{X}_i'\gamma + \lambda\widehat{\upsilon}_i + \varepsilon_i \quad (2)$$

in which $h(t|\boldsymbol{X}_{it}')$ is the conditional hazard function for retirement evaluated at t, with $\mu(t)$ representing the baseline hazard and β the main term of interest, measuring the effect of heavy smoking on retirement risk. $\boldsymbol{X}_i'$ represents person-specific covariates that might affect retirement behaviour. We include regional and time fixed effects to account for regional differences in retirement and macroeconomic differences between waves, and 10 principal components, to account for genetic ancestry. ε_i and υ_i are random error terms uncorrelated with each other. We cluster the standard error (SE) at the individual level as some individuals may appear in the regression during multiple time periods. Results were consistent using different cluster types (data not shown). Analyses were performed in Stata (v15).

2.2.6. Sensitivity analyses

We assessed whether the results changed using different cut points for heavy smoking (12–20 cigarettes a day). We replaced the PGS for heavy smoking with the CHRNA3 rs10417309 allele carrier status as instrumental variables as a large genetic component of heavy smoking is attributed to this variant (Leung et al., 2015). Although only available for waves 2–5, we also included as a covariate respondents' total pension wealth. Finally, we conducted a placebo analysis, to ensure the instrumental variable analysis requirement of exclusion restriction was met (i.e., to test whether the heavy smoking PGS could influence retirement risk through channels other than smoking behaviour). We used a sample of never-smokers for this. For exclusion restriction to be satisfied, no effect of PGS on retirement risk should be observed in never-smokers.

3. Results

3.1. Participant characteristics

In our sample of long-term smokers, 70 % are retired (Table 1). The average age of retirement is about 60. 7 % were heavy smokers ($\geq$ 20 cigarettes per day), with an average of about 3 cigarettes smoked per day. The average age was 68.86 (SD = 9.43). 48 % of the sample were female and 62 % were married. Few participants (12 %) reported having achieved higher education. The (log-equivalised) household income was 5.54 (SD = 0.67). The average household size is around 2. 34 % of the sample was interviewed after the 2010 SPA reform. Finally, 27 % and 28 % report to be sedentary and to drink every day.

3.2. MR analysis

Table 2 and Supplementary Figure 1 show a strong and significant relationship between PGS and the probability of being a heavy smoker (first stage). The fully adjusted model (column 4) suggests that if an individual had a PGS one SD larger, the probability of being a heavy smoker would increase by 1.5 % ($\beta = 0.015$, SE = 0.005, $p < 0.001$). Table 2 highlights that the estimated coefficients remain stable across specifications.

Table 3 shows the time-to-event MR estimates and reports a strong effect of heavy smoking behaviour on the retirement risk. To produce meaningful interpretation of the parameters estimated, one can exponentiate the coefficients and to obtain the hazard ratios. In the fully adjusted model (column 4) the exponentiated coefficient of heavy smoker (exp (1.324) = 3.75) suggests heavy smokers have a retirement risk approximately four times higher than their counterpart. In Supplementary Table 2 we investigate sex differences in the observed effect and find a stronger effect for women. There are no prior studies directly assessing the influence of heavy smoking on retirement risk, so no direct comparisons with effect sizes from the literature are possible. Our estimate broadly aligns with those reported in studies of smoking's impact on retirement and receipt of disability pensions/benefits (Bengtsson & Nilsson, 2018; Korhonen et al., 2015).

To strengthen the interpretation of our results, in Table 4 we perform MR estimates considering as an outcome variable the specific transition from employment to disability-induced retirement (Column 1). Additionally, Columns 2 and 3 explore the role of health as a mediating factor. Within the MR framework, these columns assess the impact of heavy smoking on the likelihood of experiencing health problems that

Table 1
Summary statistics of participant characteristics.

	Mean	S.D.	Min	Max
Key Variables:				
Retired [0,1]	0.70	0.46	0	1
Age of Retirement	59.70	7.14	18	86
Cigarettes Smoked p/d	3.17	7.17	0	66
Heavy Smoker [0,1]	0.07	0.26	0	1
PGS for Heavy Smoking	10714.91	24.12	10,625	10,791
Standardised PGS for Heavy Smoking	0.07	1.00	−3	4
Socio-Demographics:				
Years of Age	68.86	9.43	40	99
Female [0,1]	0.48	0.50	0	1
Higher Education [0,1]	0.12	0.32	0	1
Married [0,1]	0.62	0.48	0	1
Household Size	1.90	0.80	0	8
Household Income	5.54	0.67	−4	9
SPA reform [0,1]	0.34	0.47	0	1
Sedentary [0,1]	0.27	0.44	0	1
Drinker [0,1]	0.28	0.45	−3	1
Observations	8164			

Source: English Longitudinal Study of Ageing (ELSA), Wave 1–9.
Note: The table reports summary statistics of the main variables of interest. Individuals aged below 50 are partners of main participants.

Table 2
First stage estimates: the effect of the polygenic score (PGS) on heavy smoking behaviour.

	(1)	(2)	(3)	(4)
PGS for Heavy Smoking	0.014***	0.015***	0.015***	0.015***
	(0.005)	(0.005)	(0.005)	(0.005)
Covariates:				
Years of Age	−0.005***	−0.005***	−0.004***	−0.004***
	(0.000)	(0.000)	(0.000)	(0.000)
Female [0,1]	0.029**	0.030***	0.031***	0.031***
	(0.012)	(0.012)	(0.012)	(0.012)
Higher Education [0,1]	−0.020*	−0.019*	−0.017	−0.016
	(0.011)	(0.011)	(0.011)	(0.011)
Married [0,1]	−0.020*	−0.021**	−0.021**	−0.022**
	(0.010)	(0.010)	(0.010)	(0.011)
Household Size	0.001	0.001	0.002	0.002
	(0.007)	(0.007)	(0.007)	(0.007)
Household Income	0.001	0.001	0.003	0.004
	(0.005)	(0.005)	(0.005)	(0.005)
SPA reform [0,1]	0.004	0.005	−0.012	−0.013
	(0.007)	(0.007)	(0.012)	(0.012)
SPA reform × Female	−0.019*	−0.018*	−0.018*	−0.019*
	(0.010)	(0.010)	(0.010)	(0.010)
Sedentary [0,1]	0.014**	0.013*	0.014**	0.014**
	(0.007)	(0.007)	(0.007)	(0.007)
Drinker [0,1]	0.010	0.011	0.009	0.010
	(0.007)	(0.007)	(0.007)	(0.007)
Principal Components		✓	✓	✓
Time FE			✓	✓
Region FE				✓
Observations	8164	8164	8164	8164

Source: English Longitudinal Study of Ageing (ELSA), Wave 1–9.
Note: The Table reports first stage estimates, namely the effect of the polygenic score (PGS) for heavy smoking on heavy smoking behaviour. In Column (1), we report the estimate with full set of covariates as described in the manuscript. In Column (2), we include the principal components to account for genetic ancestry. In Columns (3) and (4), we include, respectively, time and region fixed effects (FE). Standard errors are clustered at the individual level.
* $p < 0.1$ ** $p < 0.05$ *** $p < 0.01$.

Table 3
MR estimates: the effect of heavy smoking on retirement risk.

	(1)	(2)	(3)	(4)
Heavy Smoker [0,1]	1.471***	1.068**	1.458***	1.324**
	(0.463)	(0.490)	(0.496)	(0.622)
Covariates:				
Years of Age	0.122***	0.119***	0.124***	0.124***
	(0.005)	(0.006)	(0.005)	(0.006)
Female [0,1]	−0.025	−0.059	0.006	−0.015
	(0.058)	(0.063)	(0.066)	(0.074)
Higher Education [0,1]	0.181***	0.189***	0.194***	0.193***
	(0.070)	(0.067)	(0.068)	(0.069)
Married [0,1]	0.246***	0.227***	0.260***	0.265***
	(0.061)	(0.061)	(0.062)	(0.067)
Household Size	−0.266***	−0.256***	−0.277***	−0.275***
	(0.035)	(0.035)	(0.036)	(0.038)
Household Income	−0.148***	−0.155***	−0.181***	−0.189***
	(0.028)	(0.028)	(0.029)	(0.030)
SPA reform [0,1]	0.261***	0.254***	0.509***	0.531***
	(0.059)	(0.059)	(0.108)	(0.108)
SPA reform × Female	0.112	0.124	0.103	0.120
	(0.086)	(0.085)	(0.085)	(0.084)
Sedentary [0,1]	−0.013	0.015	−0.045	−0.039
	(0.059)	(0.062)	(0.065)	(0.072)
Drinker [0,1]	−0.203***	−0.206***	−0.201***	−0.206***
	(0.054)	(0.051)	(0.050)	(0.056)
Principal Components		✓	✓	✓
Time FE			✓	✓
Region FE				✓
Observations	8164	8164	8164	8160

Source: English Longitudinal Study of Ageing (ELSA), Wave 1–9.
Note: The Table reports MR estimates of the effect of heavy smoking behaviour on retirement risk. In Column (1), we report the estimate with full set of covariates as described in the manuscript. In Column (2), we include the principal components to account for genetic ancestry. In Columns (3) and (4), we include, respectively, time and region fixed effects (FE). Standard errors are clustered at the individual level. * $p < 0.1$ ** $p < 0.05$ *** $p < 0.01$.

restrict paid work and on the prevalence of long-standing illnesses, respectively. These findings substantiate the role of health status as an important mediator in the association between heavy smoking and risk retirement.

3.3. Sensitivity analyses

The results remained consistent accounting for potential non-linearities (Supplementary Table 3), following Burgess et al. (2023). To address potential collider bias and reinforce the robustness of our findings, we included an analysis of the full sample (Supplementary Table 4). This analysis, consistent with our main results, shows more pronounced effects when comparing heavy smokers to the entire non-smoking population, highlighting the significant impact of heavy smoking. In Table 5, Panel B, we replace the PGS with an individual genetic variant that have been linked to heavy smoking, namely the CHRNA3. The results were slightly attenuated but similar. In Panel C our results are consistent when accounting for respondents' total pension wealth. In Panel D we show no association between PGS and retirement behaviour in never-smokers suggesting that exclusion restriction criteria are satisfied and, importantly, indicating that it is the effect of smoking, rather than the genetic liability to smoking, that is relevant.

4. Discussion

To our knowledge, this is the first study to investigate the link between heavy smoking and retirement risk using a time-to-event MR approach. We used genetic predisposition to heavy smoking (indexed by a PGS) to test the inferred causality of heavy smoking on retirement risk. We found that heavy smokers have a significantly higher retirement risk than their light smoking counterparts, adjusting for a range of covariates. Sensitivity analyses accounting for non-linearities, the inclusion of individual variants related to heavy smoking behaviour, and the inclusion of total pension wealth did not change the pattern of results. Importantly, our placebo analysis shows no effect of PGS on retirement risk for the sample of never smokers, suggesting that the exclusion restriction criteria is satisfied and, indicating that it is the effect of smoking, rather than the genetic liability to smoking, that is relevant.

Our heavy smoking PGS met the assumptions required for an MR instrumental variable analysis.

The PGS was strongly and positively associated with heavy smoking behaviour and our outcome, retirement risk, cannot plausibly affect the allocation of smoking-related genetic variants. This meant our MR analysis was more protected from reverse causality than conventional correlational. The assumption of pleiotropy (i.e., except for its association with the risk factor, there is no other pathway linking the PGS with the outcome) was met, as our PGS was not associated with behaviours (e.g., alcohol consumption) or psychosocial factors (e.g., depressive symptoms) that could influence the decision to retire early. Finally, the exclusion restriction assumption was met as the heavy smoking PGS did not impact early retirement for never-smokers.

Our results add to observational evidence that has assessed whether smoking is a predictor of labour market exit. The majority (Claessen et al., 2010; Haukenes et al., 2013; Husemoen et al., 2004; Lallukka et al., 2015; Rothenbacher et al., 1998), but not all (Robroek et al., 2013) previous studies report a positive association between the number of cigarettes smoked daily and early exit from the labour force. However, these findings may be at least partially confounded by socio-economic status (Pietikäinen et al., 2011), as attenuation by education and occupation was commonly reported (Haukenes et al., 2013; Husemoen et al., 2004; Lallukka et al., 2015). Confounding by other health behaviours could be an issue, as two earlier studies(Eriksen et al., 1998;

Table 4
MR estimates: the effect of heavy smoking on health outcomes.

	(1)	(2)	(3)
	Retirement due to Disability	Health problems that limit paid work	Long-standing Illness
Heavy Smoker [0,1]	1.456*	2.502***	1.839***
	(0.789)	(0.830)	(0.623)
Covariates:			
Years of Age	0.011	0.015***	0.012***
	(0.007)	(0.004)	(0.003)
Female [0,1]	−0.284**	−0.092***	−0.037
	(0.114)	(0.031)	(0.026)
Higher Education [0,1]	−0.408***	−0.020	0.014
	(0.124)	(0.026)	(0.024)
Married [0,1]	−0.066	0.055	0.069**
	(0.091)	(0.036)	(0.030)
Household Size	−0.255***	−0.008	−0.012
	(0.065)	(0.016)	(0.014)
Household Income	−0.095**	−0.041**	−0.013
	(0.038)	(0.017)	(0.013)
SPA reform [0,1]	0.526***	−0.038	0.157***
	(0.162)	(0.039)	(0.038)
SPA reform × Female	−0.147	0.026	−0.043
	(0.129)	(0.036)	(0.031)
Sedentary [0,1]	0.507***	0.273***	0.169***
	(0.105)	(0.048)	(0.035)
Drinker [0,1]	−0.177**	−0.055***	−0.037**
	(0.082)	(0.020)	(0.016)
Principal Components	✓	✓	✓
Time FE	✓	✓	✓
Region FE	✓	✓	✓
Observations	7887	6951	8161

Source: English Longitudinal Study of Ageing (ELSA), Wave 1–9.
Note: The Table reports MR estimates of the effect of heavy smoking behaviour on health outcomes. Standard errors are clustered at the individual level. * $p < 0.1$ ** $p < 0.05$ *** $p < 0.01$.

Table 5
Sensitivity analysis.

	(1)
Panel A: Benchmark Heavy Smoker [0,1]	1.324**
	(0.622)
Observations	8160
Panel B: CHRNA3 Heavy Smoker [0,1]	3.033*
	(1.824)
Observations	8160
Panel C: Accounting for Pension Wealth Heavy Smoker [0,1]	1.656*
	(0.882)
Observations	4419
Panel D: Placebo Analysis PGS for Heavy Smoking	0.021
	(0.018)
Observations	9939

Source: English Longitudinal Study of Ageing (ELSA), Wave 1–9.
Note: The table reports the sensitivity analysis of the main findings of the study. In Panel A, we report the benchmark estimates. In Panel B, we replace the polygenic score with an individual genetic instruments that have been linked to heavy smoking, namely the CHRNA3. In Panel C, we account for respondent total pension wealth. Lastly, in Panel D we conduct a placebo analysis to show that the heavy smoking polygenic score has no effect on early retirement for the sample of never smokers. Standard errors are clustered at the individual level. * $p < 0.1$ ** $p < 0.05$ *** $p < 0.01$.

Lallukka et al., 2015) found smoking was only associated with disability pension risk in participants who were physically inactive. This might suggest that smoking is an indicator of other health-related factors (Mawditt et al., 2016), that increase the probability of early labour market exit, rather than a causal predictor in of itself. Our results are less likely to be influenced by such confounding due to our MR methodology. Further, our findings were robust to adjustment for education and household income and our instrumental variable (heavy smoking PGS) was only associated with retirement risk through smoking behaviour and was not associated with sedentary activity.

Several studies have assessed heavy smoking and retirement with a disability pension (Haukenes et al., 2013; Husemoen et al., 2004; Lallukka et al., 2015). A study of 6000 Finnish adults found that heavy smoking women and men (>15 or > 20 cigarettes per day, respectively) had an increased risk of disability retirement (Lallukka et al., 2015). However, in other heavy smoking studies similar associations were only observed in those aged under 60 (Husemoen et al., 2004) and in women alone(Haukenes et al., 2013). Our results were robust to adjustment for age and gender and are less likely to be impacted by this type of confounding due to our MR approach. Overall, our findings add to the observational literature by demonstrating that the association between heavy smoking behaviour and retirement risk is likely to be causal.

We are not the first study to use unobserved genetic factors in an attempt to improve understanding of the relationship between smoking and labour market exit. A Swedish study of 80,000 sisters(Bengtsson & Nilsson, 2018) found an association between heavy smoking and disability retirement. Significant associations were detected when accounting for sibling effects but reverted towards the null when education and occupation were considered. The authors suggest that socio-economic or marital status could have been influenced by smoking in their study. Our results are less likely to suffer from this issue, as the genetic variants for heavy smoking allocated at conception are unlikely to influence subsequent socio-economic or marital status. Another possibility is that an omitted variable (such as household income) may have contributed to the reported confounding. Our results were robust to adjustment for education, marital status, and household income, and were less likely to have been influenced by omitted variable bias due to our MR approach.

Our findings agree with work from the Finnish Twins Cohort where a dose–response relationship between the number of cigarettes smoked daily and the probability of receiving a disability pension was observed in 22,000 men and women (Korhonen et al., 2015). This result was replicated in analyses within twin pairs discordant for the outcome (i.e., one twin got the pension, the other did not), suggesting that heavy smoking is likely a causal contributor to disability retirement. Our results add to this casual evidence by demonstrating an association between heavy smoking and retirement risk in unrelated individuals.

Our study has several strengths. Firstly, studies examining smoking and retirement risk in the context of genetics are limited, so our results contribute to an important, yet sparse, literature. Secondly, MR is a powerful control for confounding and reverse causation, which often impede prospective observational studies. Thirdly, our results reflect lifelong exposure to heavy smoking genetic variants rather than the temporary effect of current light or heavy smoking captured in observational studies, based on the assumption that the association between genetic variations and the relative effect of heavy smoking does not change with age (Bengtsson & Nilsson, 2018; Dixon et al., 2020; Holmes & Smith, 2017).

Our results are likely policy-relevant as smoking is a leading cause of poor health (ASH, 2020; Murray, 2014) and together with early retirement represents an economic challenge for the financial sustainability of pension schemes (OECD, 2019). The rationale behind the increased statutory pension age is that longer life expectancy will enable people to extend their working lives (OECD, 2019). However, as poor health is a key predictor of labour market exit (Fisher et al., 2016; Round, 2017) there is a need to understand health-related determinants of early retirement. Our study provides novel evidence that heavy smoking is likely a causal factor influencing an earlier retirement. As smoking is potentially modifiable (Hackett et al., 2018; West et al., 2015), this suggests that policies targeting reductions in smoking could plausibly

reduce the risk of retirement.

Our findings reflect the average lifetime effects of heavy smoking (randomly determined at conception) rather than current smoking, allowing for the possibility that individuals could quit smoking as they age. Workers may be willing to change their health behaviours if they expect to retire later (Bertoni et al., 2018). Policy research on extending working lives recommends that health interventions be integrated in the workplace (Round, 2017). Most adults spend a large amount of time at work, and activities that start before workers are considering retirement may be particularly effective as they allow healthy habits to develop and be maintained (Loeppke et al., 2013). Our findings add justification for policymakers' attempts to reduce smoking through smoking bans or other policies such as raising taxes on tobacco.

This study is not without limitations. The generalisability of genetic studies across populations is limited (Martin et al., 2019) as the method for computing PGS depends on summary statistics focused almost exclusively on participants of European ancestry. PGSs do not capture other structural variants beyond common genetic markers of relatively small effects, such as rare variants, poorly tagged or multiple independent variants, gene-by-gene interactions and gene-environment correlation (Reynolds & Finkel, 2015). While the study suggests strong internal validity, wider generalizability should be approached with caution.

In summary, we adopted a time-to-event MR approach to examine the association between heavy smoking and retirement risk. Although our study does not provide a definitive answer to the complex smoking-early retirement relationship, it adds a novel component to emerging literature using genetically sensitive designs and suggests this relationship is likely causal.

Funding

The English Longitudinal Study of Ageing is funded by the National Institute on Aging (Grant: RO1AG7644) and by a consortium of UK government departments coordinated by the Economic and Social Research Council. EZ acknowledges support from the Tomas y Valiente Fellowship funded by the Madrid Institute for Advanced Study (MIAS), Universidad Autonoma de Madrid (UAM), Spain, and grant PID2022-137819NB-I00 funded by the Spanish government.

Code availability

Available upon reasonable request.

Ethics approval

London Multicentre Research and Ethics Committee (MREC/01/02/91).

Pre-registration

Analyses were not pre-registered, findings should be considered exploratory.

CRediT authorship contribution statement

Alessio Gaggero: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Olesya Ajnakina:** Writing – review & editing, Data curation. **Eugenio Zucchelli:** Writing – review & editing, Writing – original draft. **Ruth A. Hackett:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

ELSA data is freely available from the UK dataservice. Code is available on reasonable request.

ELSA data is freely available https://ukdataservice.ac.uk/.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.addbeh.2024.108078.

References

Ajnakina, O., Cadar, D., & Steptoe, A. (2020). Interplay between socioeconomic markers and polygenic predisposition on timing of dementia diagnosis. *Journal of the American Geriatrics Society, 68*(7), 1529–1536. https://doi.org/10.1111/jgs.16406

Ajnakina, O., & Steptoe, A. (2019). *The English Longitudinal Study of Ageing (ELSA) Polygenic Scores*. https://www.elsa-project.ac.uk/genetics.

ASH. (2020). *Action on Smoking and Health (ASH) Factsheet: Smoking Statistics*. https://ash.org.uk/wp-content/uploads/2019/10/SmokingStatistics.pdf.

Ayyagari, P. (2016). The impact of retirement on smoking behavior. *Eastern Economic Journal, 42*(2), 270–287. https://doi.org/10.1057/eej.2014.51

Bengtsson, T., & Nilsson, A. (2018). Smoking and early retirement due to chronic disability. *Economics and Human Biology, 29*, 31–41. https://doi.org/10.1016/j.ehb.2017.12.005

Bertoni, M., Brunello, G., & Mazzarella, G. (2018). Does postponing minimum retirement age improve healthy behaviors before retirement? Evidence from middle-aged Italian workers. *Journal of Health Economics, 58*, 215–227. https://doi.org/10.1016/j.jhealeco.2018.02.011

Burgess, S., Davey Smith, G., Davies, N. M., et al. (2023). (2023) Guidelines for performing Mendelian randomization investigations: Update for summer 2023. *Wellcome Open Res., 4*(4), 186.

Claessen, H., Arndt, V., Drath, C., & Brenner, H. (2010). Smoking habits and occupational disability: A cohort study of 14,483 construction workers. *Occupational and Environmental Medicine, 67*(2), 84–90. https://doi.org/10.1136/oem.2009.046318

Davey Smith, G., & Hemani, G. (2014). Mendelian randomization: Genetic anchors for causal inference in epidemiological studies. *Human Molecular Genetics, 23*(R1), R89–R98. https://doi.org/10.1093/hmg/ddu328

Dixon, P., Hollingworth, W., Harrison, S., Davies, N. M., & Davey Smith, G. (2020). Mendelian Randomization analysis of the causal effect of adiposity on hospital costs. *Journal of Health Economics, 70*, Article 102300. https://doi.org/10.1016/j.jhealeco.2020.102300

Dudbridge, F. (2013). Power and predictive accuracy of polygenic risk scores. *PLoS Genetics, 9*(3), e1003348.

Eriksen, W., Natvig, B., Rutle, O., & Bruusgaard, D. (1998). Smoking as a predictor of long-term work disability in physically active and inactive people. *Occupational Medicine (Oxford, England), 48*(5), 315–320. https://doi.org/10.1093/occmed/48.5.315

Fisher, G. G., Chaffee, D. S., & Sonnega, A. (2016). Retirement timing: A review and recommendations for future research. *Work, Aging and Retirement, 2*(2), 230–261. https://doi.org/10.1093/workar/waw001

Hackett, R. A., Moore, C., Steptoe, A., & Lassale, C. (2018). Health behaviour changes after type 2 diabetes diagnosis: Findings from the English Longitudinal Study of Ageing. *Scientific Reports, 8*(1). https://doi.org/10.1038/s41598-018-35238-1. Article 1.

Haukenes, I., Riise, T., Haug, K., Farbu, E., & Maeland, J. G. (2013). Smokers' increased risk for disability pension: Social confounding or health-mediated effects? Gender-specific analyses of the Hordaland Health Study cohort. *Journal of Epidemiology and Community Health, 67*(9), 758–764. https://doi.org/10.1136/jech-2012-202182

He, L., Culminskaya, I., Loika, Y., et al. (2018). Causal effects of cardiovascular risk factors on onset of major age-related diseases: A time-to-event Mendelian randomization study. *Experimental Gerontology, 107*, 74–86.

Holmes, M. V., & Smith, G. D. (2017). Revealing the effect of CETP inhibition in cardiovascular disease. *Nature Reviews Cardiology, 14*(11), 635–636. https://doi.org/10.1038/nrcardio.2017.156

Husemoen, L. L. N., Osler, M., Godtfredsen, N. S., & Prescott, E. (2004). Smoking and subsequent risk of early retirement due to permanent disability. *European Journal of Public Health, 14*(1), 86–92. https://doi.org/10.1093/eurpub/14.1.86

Korhonen, T., Smeds, E., Silventoinen, K., Heikkilä, K., & Kaprio, J. (2015). Cigarette smoking and alcohol use as predictors of disability retirement: A population-based cohort study. *Drug and Alcohol Dependence, 155*, 260–266. https://doi.org/10.1016/j.drugalcdep.2015.06.047

Koskenvuo, K., Broms, U., Korhonen, T., Laitinen, L. A., Huunan-Seppälä, A., Keistinen, T., Autti-Rämö, I., Kaprio, J., & Koskenvuo, M. (2011). Smoking strongly predicts disability retirement due to COPD: The Finnish Twin Cohort Study. *The European Respiratory Journal, 37*(1), 26–31. https://doi.org/10.1183/09031936.00008910

Lallukka, T., Rahkonen, O., Lahelma, E., & Lahti, J. (2015). Joint associations of smoking and physical activity with disability retirement: A register-linked cohort study. *BMJ Open, 5*(7), e006988.

Leung, T., Bergen, A., Munafò, M. R., De Ruyck, K., Selby, P., & De Luca, V. (2015). Effect of the rs1051730–rs16969968 variant and smoking cessation treatment: A meta-analysis. *Pharmacogenomics, 16*(7), 713–720. https://doi.org/10.2217/pgs.15.34

Liu, M., Jiang, Y., Wedow, R., et al. (2019). Association studies of up to 1.2 million individuals yield new insights into the genetic etiology of tobacco and alcohol use. *Nature Genetics, 51*(2), 237–244. https://doi.org/10.1038/s41588-018-0307-5

Loeppke, R. R., Schill, A. L., Chosewood, L. C., Grosch, J. W., Allweiss, P., Burton, W. N., Barnes-Farrell, J. L., Goetzel, R. Z., Heinen, L., Hudson, T. W., Hymel, P., Merchant, J., Edington, D. W., Konicki, D. L., & Larson, P. W. (2013). Advancing workplace health protection and promotion for an aging workforce. *Journal of Occupational and Environmental Medicine, 55*(5), 500–506. https://doi.org/10.1097/JOM.0b013e31829613a4

Martin, A. R., Kanai, M., Kamatani, Y., Okada, Y., Neale, B. M., & Daly, M. J. (2019). Clinical use of current polygenic risk scores may exacerbate health disparities. *Nature Genetics, 51*(4), 584–591. https://doi.org/10.1038/s41588-019-0379-x

Mawditt, C., Sacker, A., Britton, A., Kelly, Y., & Cable, N. (2016). The clustering of health-related behaviours in a British population sample: Testing for cohort differences. *Preventive Medicine, 88*, 95–107. https://doi.org/10.1016/j.ypmed.2016.03.003

Murray, R. (2014). *The role of smoking in the progressive decline of the body's major systems*. Public Health England. https://www.gov.uk/government/publications/smoking-progressive-decline-of-the-bodys-major-systems.

OECD. (2019). *Pensions at a Glance 2019: OECD and G20 Indicators*. OECD Publishing. https://doi.org/10.1787/b6d3dcfc-en.

Office for National Statistics. (2020). *Adult Smoking Habits in the UK*. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthandlifeexpectancies/bulletins/adultsmokinghabitsingreatbritain/2019.

Pietikäinen, S., Silventoinen, K., Svedberg, P., Alexanderson, K., Huunan-Seppälä, A., Koskenvuo, K., Koskenvuo, M., Kaprio, J., & Ropponen, A. (2011). Health-related and sociodemographic risk factors for disability pension due to low back disorders: A 30-year prospective Finnish Twin Cohort Study. *Journal of Occupational and Environmental Medicine, 53*(5), 488–496. https://doi.org/10.1097/JOM.0b013e31821576dd

Price, A. L., Patterson, N. J., Plenge, R. M., Weinblatt, M. E., Shadick, N. A., & Reich, D. (2006). Principal components analysis corrects for stratification in genome-wide association studies. *Nature Genetics, 38*(8), 904–909. https://doi.org/10.1038/ng1847

Reynolds, C. A., & Finkel, D. (2015). A meta-analysis of heritability of cognitive aging: Minding the "Missing Heritability" Gap. *Neuropsychology Review, 25*(1), 97–112. https://doi.org/10.1007/s11065-015-9280-2

Robroek, S. J. W., Schuring, M., Croezen, S., Stattin, M., & Burdorf, A. (2013). Poor health, unhealthy behaviors, and unfavorable work characteristics influence pathways of exit from paid employment among older workers in Europe: A four year follow-up study. *Scandinavian Journal of Work, Environment & Health, 39*(2), 125–133. https://doi.org/10.5271/sjweh.3319

Ropponen, A., Korhonen, T., Svedberg, P., Koskenvuo, M., Silventoinen, K., & Kaprio, J. (2013). Persistent smoking as a predictor of disability pension due to musculoskeletal diagnoses: A 23year prospective study of Finnish twins. *Preventive Medicine, 57*(6), 889–893. https://doi.org/10.1016/j.ypmed.2013.10.001

Rothenbacher, D., Arndt, V., Fraisse, E., Zschenderlein, B., Fliedner, T. M., & Brenner, H. (1998). Early retirement due to permanent disability in relation to smoking in workers of the construction industry. *Journal of Occupational and Environmental Medicine, 40*(1), 63–68. https://doi.org/10.1097/00043764-199801000-00012

Round, A. (2017). *Extending working lives: A devolved, lifecourse approach to enabling work beyond state pension age*. Institute for Public Policy Research (IPPR) North.

So, H.-C., & Sham, P. C. (2017). Improving polygenic risk prediction from summary statistics by an empirical Bayes approach. *Scientific Reports, 7*(1), 1–11. https://doi.org/10.1038/srep41262

Steptoe, A., Breeze, E., Banks, J., & Nazroo, J. (2013). Cohort profile: The english longitudinal study of ageing. *International Journal of Epidemiology, 42*(6), 1640–1648. https://doi.org/10.1093/ije/dys168

Tadros, R., Francis, C., Xu, X., et al. (2021). Shared genetic pathways contribute to risk of hypertrophic and dilated cardiomyopathies with opposite directions of effect. *Nature Genetics, 53*, 128–134.

Teleka, S., Hindy, G., Drake, I., Poveda, A., Melander, O., et al. (2020). Blood pressure and bladder cancer risk in men by use of survival analysis and in interaction with NAT2 genotype, and by Mendelian randomization analysis. *PLoS One1, 15*(11), e0241711.

West, R., Raw, M., McNeill, A., Stead, L., Aveyard, P., Bitton, J., Stapleton, J., McRobbie, H., Pokhrel, S., Lester-George, A., & Borland, R. (2015). Health-care interventions to promote and assist tobacco cessation: A review of efficacy, effectiveness and affordability for use in national guideline development. *Addiction (Abingdon, England), 110*(9), 1388–1403. https://doi.org/10.1111/add.12998

Xue, B., Head, J., & McMunn, A. (2020). The impact of retirement on cardiovascular disease and its risk factors: A systematic review of longitudinal studies. *The Gerontologist, 60*(5), e367–e377. https://doi.org/10.1093/geront/gnz062