Social Science & Medicine 194 (2017) 142–150

Contents lists available at ScienceDirect

Social Science & Medicine

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

Unemployment and subsequent depression: A mediation analysis using the parametric G-formula

Maarten J. Bijlsma[a,*], Lasse Tarkiainen[b], Mikko Myrskylä[a,b,c], Pekka Martikainen[a,b,d]

[a] Max Planck Institute for Demographic Research, Konrad-Zuse str. 1, 18057 Rostock, Germany
[b] Department of Social Research, University of Helsinki, Unioninkatu 37 (P.O. Box 54), 00014 Helsinki, Finland
[c] London School of Economics & Political Science, Houghton St, London WC2A 2AE, United Kingdom
[d] Centre for Health Equity Studies (CHESS), Stockholm University and Karolinska Institutet, SE-106 91 Stockholm Sweden

ARTICLE INFO

Keywords:
Unemployment
Mental health
Depression
Young adults
Life course
Causal inference
g-formula

ABSTRACT

The effects of unemployment on depression are difficult to establish because of confounding and limited understanding of the mechanisms at the population level. In particular, due to longitudinal interdependencies between exposures, mediators and outcomes, intermediate confounding is an obstacle for mediation analyses. Using longitudinal Finnish register data on socio-economic characteristics and medication purchases, we extracted individuals who entered the labor market between ages 16 and 25 in the period 1996 to 2001 and followed them until the year 2007 (n = 42,172). With the parametric G-formula we estimated the population-averaged effect on first antidepressant purchase of a simulated intervention which set all unemployed person-years to employed. In the data, 74% of person-years were employed and 8% unemployed, the rest belonging to studying or other status. In the intervention scenario, employment rose to 85% and the hazard of first antidepressant purchase decreased by 7.6%. Of this reduction 61% was mediated, operating primarily through changes in income and household status, while mediation through other health conditions was negligible. These effects were negligible for women and particularly prominent among less educated men. By taking complex interdependencies into account in a framework of observed repeated measures data, we found that eradicating unemployment raises income levels, promotes family formation, and thereby reduces antidepressant consumption at the population-level.

1. Introduction

Depression is a leading contributor to the global burden of disease, having a lifetime prevalence of 10–15% worldwide (Lépine and Briley, 2011). For individuals suffering from it, depression extends far beyond its direct symptoms, to large increased risks of suicide and possibly to cardiac death (Lépine and Briley, 2011; Whooley et al., 2008; Bell and Blanchflower, 2011). At the societal level, this results in a large economic burden, for example estimated to be $98.9 billion in the US in the year 2010 alone (Greenberg et al., 2015). Unemployment is an important determinant of depression (Egan et al., 2016; Jefferis et al., 2011). Unemployment results in economic uncertainty, loss of workplace social contacts, time structures and purposeful activity (Jefferis et al., 2011; Paul and Moser, 2009). However, *vice versa*, depression may also lead to unemployment. Individuals with poor (mental) health have more difficulty in both finding and retaining employment, also known as healthy hire and healthy worker survivor effects, respectively (Egan et al., 2016; Buckley et al., 2015; Wagenaar et al., 2012). While a problem at all ages, unemployment especially affects young people; for every 1% increase in adult unemployment rates, youth unemployment (aged 16 to 24) rises by 1.8%, and can result in adverse employment and mental health prospects much later in life (Bell and Blanchflower, 2011; Martikainen and Ferrie, 2008; Mroz and Savage, 2006; Strandh et al., 2014).

Various methodological problems must be overcome to disentangle the relationship between depression and unemployment (Bell and Blanchflower, 2011). When causal pathways are of interest, a longitudinal approach is vital as both variables will affect each other over time (Steele et al., 2013). Furthermore, it has been shown that in many settings it will be difficult or even impossible to use ordinary regression approaches to prevent confounding and colliding bias (Buckley et al., 2015; Picciotto and Hertz-Picciotto, 2015). For example, in mediation analysis, the methodology used to determine through what pathway(s) an intervention operates, the issue of intermediate confounding arises;

* Corresponding author. Max Planck Institute for Demographic Research, Konrad-Zuse-Straße 1, Rostock, 18057, Germany.
E-mail addresses: bijlsma@demogr.mpg.de (M.J. Bijlsma), lasse.tarkiainen@helsinki.fi (L. Tarkiainen), myrskyla@demogr.mpg.de (M. Myrskylä), pekka.martikainen@helsinki.fi (P. Martikainen).

http://dx.doi.org/10.1016/j.socscimed.2017.10.011
Received 31 May 2017; Received in revised form 22 September 2017; Accepted 12 October 2017
Available online 22 October 2017

this occurs when a mediator of interest is also a confounder of the relationship between another mediator (or another exposure) and the outcome (De Stavola et al., 2015; VanderWeele et al., 2014). For example, unemployment may affect mental health partly through physical health, but physical health may also affect subsequent unemployment and mental health (and therefore confounds their relationship). Among other problems, this creates the basic dilemma that controlling for the confounder will also 'block' mediation via this variable (VanderWeele et al., 2014). Unfortunately, methods to deal with these issues appropriately have not yet been widely adopted, and therefore intermediate confounding has so-far often been ignored.

The G-formula is a method that can account for these potentially biasing influences in health and unemployment settings (Buckley et al., 2015; Chevrier et al., 2012). The G-formula is firmly grounded in the counterfactual causal inference approach (Keil et al., 2014; Pearl, 2002). This results in clear interpretations of causal effects (independent of the statistical tests with which they are estimated), clear separation of individual-level (conditional) and population-level (population-averaged) effects, and more flexible statistical modelling. Greater flexibility makes it easier to adjust for various sources of bias and allows the modelling of outcomes and mediators of any type, distribution and functional form (Imai et al., 2010; Richiardi et al., 2013). Importantly, the G-formula can be used to account for measured time-varying confounders that are also affected by prior exposures (i.e. intermediate confounders) (Keil et al., 2014; Daniel et al., 2013).

Several studies have found links between unemployment and income loss, between income and depression, and have found marital status to attenuate the effect of unemployment on depression (Lorant et al., 2003, 2007; Sareen et al., 2011; Dooley et al., 2000). These variables are therefore of interest as potential mediators of the unemployment effect; unemployment may have direct effects on mental health, but also indirect effects through material consequences (e.g. loss of income), psychological consequences (e.g. in part through inhibiting household formation and related social support), and health consequences. However, to the best of our knowledge there has been no study that investigated the effects of unemployment on antidepressant purchasing as mediated by income, household status (denoting marital status, cohabitation or singleness, with or without children) and other health conditions simultaneously and dynamically. Our primary research question (Q1) that we address by using the parametric G-formula that accounts for both time varying intermediate confounding and reverse causality is: What is the population-level effect of eliminating youth unemployment on first antidepressant purchases in Finland in the period 1996 to 2007?

In addition to analyzing the effects at the total population level (research question Q1), we focus on key sub-populations. Studies find that associations between unemployment and depression have strong socio-economic differentials (Chazelle et al., 2011; Melchior et al., 2015; Lee et al., 2015), and differ by gender (Artazcoz et al., 2004; Hollander et al., 2013; Strömberg et al., 2011). In particular, the effects of unemployment on major depression are more strongly associated with low education level and financial strain (Chazelle et al., 2011). The association between unemployment and substance abuse, an indicator of mental health, is also stronger in young adults with low educational attainment (Melchior et al., 2015) and in those with a low socio-economic background (Lee et al., 2015). Unemployment more strongly affects the mental health of men than women, which is attributed to differences in household responsibilities (Artazcoz et al., 2004), social roles and social support (Ensminger and Celentano, 1990). These studies indicate that both the overall effects as well as the mediating mechanisms may operate differently for these subgroups. We analyze to what extent the no-unemployment effect operates via changes in income, household status (i.e. partnership and parenthood), and health conditions (Q2); and to what extent the no-unemployment effect differs by gender and educational status (Q3). Questions 2 and 3 will help discern the causal mechanisms by which a no-unemployment effect on first antidepressant purchases operates and how these might differ by gender and educational groups.

2. Data and methods

2.1. Setting and study population

We studied individuals of both genders in the period 1996 to 2007 in Finland. We extracted individuals who were 14–24 years old and entered the labor market in the calendar period 1996–2001 and followed them annually until the end of 2007. Entering the labor market was defined as entering status 'employed' or status 'unemployed' from any other status. After inclusion, individuals that returned to non-labor market statuses (such as studying) were allowed to remain in the study. Individuals that purchased an antidepressant prior to entering the labor market were excluded from the study. We identified 42172 individuals who met these criteria. Non-administrative right-censoring occurred to 914 individuals (2% of total n), and intermediate censoring to 660 person-years (0.2% of total person-years), which could occur if the individual out-migrated, died or was institutionalized.

2.2. Data source

Our data are an 11% random sample of the population permanently residing in Finland at the end of any of the years in the period 1996–2007. The data were constructed from register data by Statistics Finland (permission TK-53-339-13), and contains individual-level linked information on labor market records, census records and death records, with a further linkage to social care records, medication records and sickness absence allowance records maintained by the Social Insurance Institution of Finland.

2.3. Outcome variable

The outcome variable of interest is time from entering the labor market to first antidepressant purchase (WHO anatomical-therapeutical-chemical (ATC) code N06A and N06CA; the categories 'Antidepressants' and 'Antidepressants in combination with psycholeptics' respectively). Time was measured in calendar years.

2.4. Primary exposure

The primary (time-varying) exposure is employment status. Employment status is a categorical (multinomial) variable which indicates if an individual is employed, unemployed, student, or other (includes pensioners and conscripts). Employment status was measured once per calendar year.

2.5. Time varying (confounding) mediators

Variables that may mediate the effect of unemployment on antidepressant consumption are income, household status, physical health and mental health, and education. These time-varying variables are measured once per calendar year. Two separate income variables are used, and are both continuous and inflation corrected; personal income subject to state taxation in euros, and household combined disposable income including non-taxable income transfers and excluding paid taxes. Household combined disposable income was additionally corrected by dividing income by the consumption units present in the household using the OECD-modified scale (OECD, 2013). Household status is a categorical variable with the categories 'Child living with parents', 'Single without children', 'Single with children', 'Cohabiting without children', 'Cohabiting with children', 'Married without children', and 'Married with children'. Physical health and mental health were measured using pharmacy dispensing records. It was included in the analysis as a set of binary variables, each representing whether a drug from a particular major drug category was dispensed to the individual in a particular year. The drug categories are based on level 1 ATC codes. Categories included in the analysis are A, B, C, D, G, H, L, M, N, P, R, S, and V. Psycholeptics and psychoanaleptics (ATC N05 and N06), and anti-addiction drugs (N07B) were excluded from category N due to their association with antidepressant use. Education was measured as highest completed degree, it goes from lower secondary to higher tertiary level in four categories (ISCED 2011 categories: 2–4, 5, 6, 7–8). Because these mediators may also affect later unemployment, they are potential mediating confounders.

2.6. Control variables

Parental income, language, gender, age and year are treated as controls. Parental income is inflation-corrected household income subject to state taxation when the individual was still living with parents and not in the labor market. This variable was included in the analysis both uncorrected and corrected for the number of consumption units present in the household (OECD, 2013). Language is a categorical variable, measured as being a first language speaker of Finnish, Swedish or other language. Age and calendar time are both measured in years and treated as continuous variables.

2.7. Causal mediation analysis

Our causal mediation analysis was performed in four steps. First, we formulated a causal DAG. Secondly, we fit multivariate models to the data following the DAG. Thirdly, we chose mediation definitions and corresponding intervention scenarios. Fourthly, using the multivariate models in the G-formula we simulated these scenarios.

2.7.1. Causal DAG and multivariate models

We fitted multivariate regression models following our causal DAG (Fig. 1). Time-varying variables in year *k* were allowed to be affected by all control variables and, to limit assumptions on causality within a calendar year, by all time-varying variables in year *k-1*. Categorical variables were modeled with sets of logistic regressions (in the G-formula procedure operating together as a multinomial logistic regression model) and continuous variables with linear regression models. Continuous variables were included in models as ordinary, squared, and natural logged versions, thereby allowing for diminishing effects of income on other covariates. Model pruning, using a likelihood-ratio based backward selection procedure ($p < 0.05$), resulted in some variables not being included in some multivariate models (see Appendix 1 for all models).

2.7.2. Total effect estimation

To determine what would have happened to first antidepressant purchases if all unemployed individuals in our study population had instead been employed, we contrasted a no-unemployment scenario (the intervention scenario) with a scenario in which all observations were as empirically observed (the natural course scenario). This was done by in the simulation step of the G-formula, including a 500 iteration bootstrap to produce confidence intervals (Keil et al., 2014; Hernán and Robins, 2013; Efron and Tibshirani, 1994). In each iteration of the bootstrap we randomly drew individuals with replacement from the data and re-estimated the earlier specified multivariate models on these data. Then, using the first observations of these individuals and the estimates from the multivariate models we predicted their observations in the second year; for binomial variables these predictions were drawn stochastically from a binomial distribution with the predicted mean based on the corresponding multivariate model, and for continuous variables this was done likewise using a Gaussian distribution (with variance based on the prediction model's residual variance). These predictions then served to predict those in the third year, and so on, until predicted antidepressant purchase, censoring, or until the simulated year 2007 (Keil et al., 2014). This estimated Y_x (Table 1, Eq. (0)). The estimates of Y_{x^*} were produced similarly, but whenever unemployment was predicted, it was set to employed instead. The difference between Y_x and Y_{x^*} is known as the total effect (TE).

2.7.3. Mediation

The TE was decomposed into the stochastic controlled direct effect (CDE) and the proportion eliminated (PE) (Wang and Arah, 2015). The proportion eliminated represents the total of the indirect effects of unemployment via income (personal and household), household status,

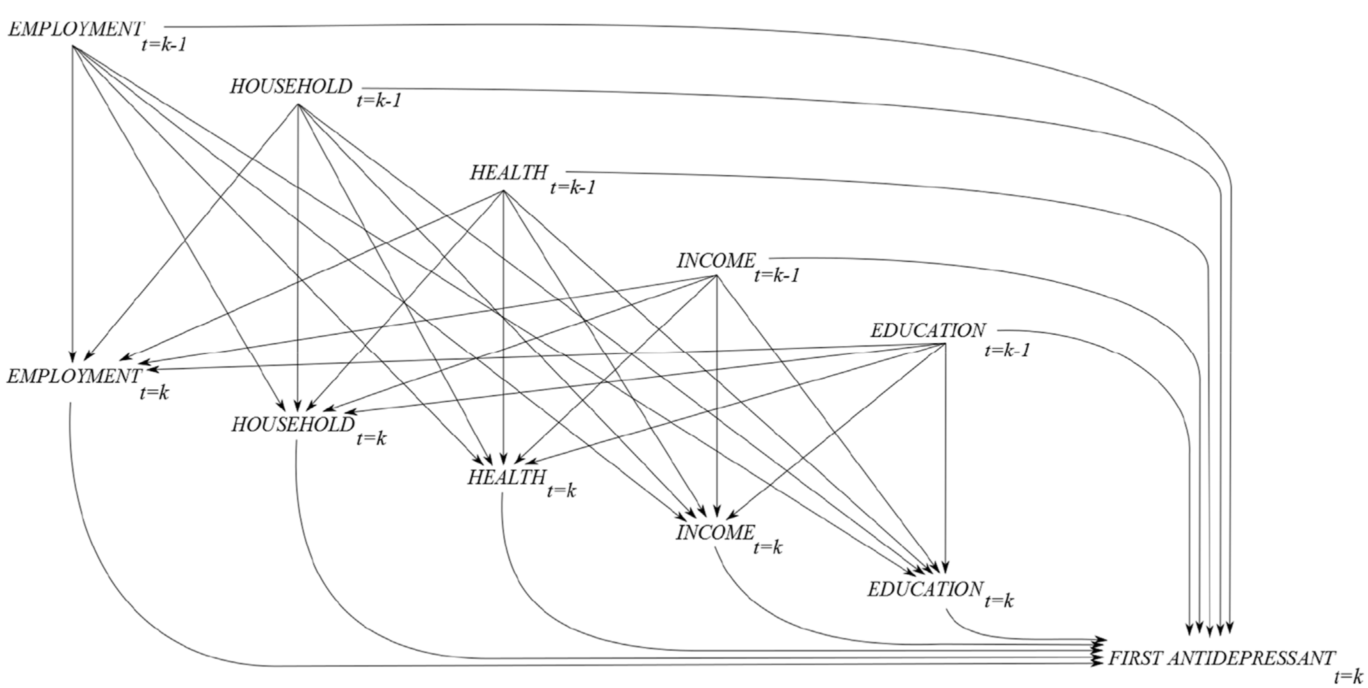

Fig. 1. Causal DAG of the time-varying variables in the study.
Control variables (not shown) were allowed to affect all time-varying variables.

Table 1
Definitions used in the mediation analysis.

Equation	Definitions used[a]	To quantify
(0)	$E[Y_x - Y_{x^*}]$	Total employment effect
(1)	$E[Y_{xI'S'H'} - Y_{x^*I'S'H'}]$[a,b]	Stochastic controlled direct employment effect
(2)	$E[Y_{xI'S'H'} - Y_{x^*I_{x^*}S'H'}]$	As 1) + indirect employment effect via income
(3)	$E[Y_{xI'S'H'} - Y_{x^*I'S_{x^*}H'}]$	As 1) + indirect employment effect via household
(4)	$E[Y_{xI'S'H'} - Y_{x^*I'S'H_{x^*}}]$	As 1) + indirect employment effect via health
(5)	$E[Y_x - Y_{x^*}]$[c]	Total employment effect without mediator control

[a] Y represents here the log hazard of first antidepressant purchase, X employment, I income, S household and H health.
[b] Since x is drawn stochastically from the values of X in the natural course data we have: $I' \approx I_x, \quad S' \approx S_x, \quad H' \approx H_x$.
[c] In equation (5) Y_{x^*} is estimated using models for employment and first antidepressant purchase which do not include the mediators I, S and H.

and health. To perform this mediation analysis, we stochastically drew mediator values from the distribution of the respective mediators in the natural course scenario data, so that their values are independent of the intervention on unemployment (Wang and Arah, 2015). This produced $Y_{x^*I'S'H'}$ (Table 1. Eq. (1)). Because we draw mediator values stochastically from the natural course distribution, our estimate of the CDE may be close to the natural direct effect estimate. In all scenarios, education was predicted instead of drawn stochastically, and its effect is thereby included in the CDE. Scenarios were contrasted using Cox regression with only a scenario indicator as a covariate, thereby producing population averaged estimates (Keil et al., 2014).

To additionally get insight into the direction and degree of mediation by each individual mediator, we performed analyses where we included the mediators, one by one, in the CDE (Table 1, Eqs. (2)–(4)). These additional analyses diverge from standard definitions and their estimates are not additive (Wang and Arah, 2015). Finally, to get insight into the role of intermediate confounding, we re-estimated the total effect using multivariate models which did not include the mediators (Table 1, Eq. (5)). In Appendix 2, we included results from a more traditional mediation analysis method (adding mediators successively to the logistic model).

2.7.4. Subgroup analysis: gender and educational level

We performed additional analysis within gender and educational groups to determine if causal mechanisms operate differently within these subgroups. For this subgroup analysis, we entered interaction terms between gender and employment, and education and employment, in the G-formula estimation model for antidepressant purchasing. In each iteration of the simulation step of the G-formula, we calculated TE, CDE and PE by comparing individuals by gender and by their highest attained educational status (secondary level or higher than secondary level) in the natural course scenario with those same individuals in the intervention scenario.

2.7.5. Population attributable fraction

To compare the population-averaged TE and CDE with a more traditional analysis, we also calculated the population attributable fraction of unemployment (PAF) (Laaksonen et al., 2010). The CDE was compared with the PAF calculated from the unemployment coefficient produced by the multivariate model for antidepressant purchase used in the G-formula and which contained the mediators as covariates. The TE was compared with a PAF based on the unemployment coefficient from a logistic regression model with only (non-lagged) employment status variables (unemployed, student, other, and employment as a reference) included.

Table 2
Characteristics (averages over all person-years in the study sample) of 42172 study participants aged 16–32 years and who have entered the labor market during follow-up, Finnish register data, calendar years 1996–2007.

Characteristics	
Employment status	
Employed	74.0%
Unemployed	8.3%
Studying	11.8%
Other	5.9%
Income	
Personal income (SD)	€ 19210 (13740)
Household income (SD)	€ 21000 (9440)
Household status	
Living with parents	24.5%
Single without child(ren)	25.5%
Single with child(ren)	0.4%
Cohabiting without child(ren)	22.7%
Cohabiting with child(ren)	7.2%
Married without child(ren)	6.2%
Married with child(ren)	13.5%
Health	
ATC A (Alimentary tract and metabolism)	4.4%
ATC B (Blood and blood forming organs)	0.3%
ATC C (Cardiovascular system)	1.7%
ATC D (Dermatologicals)	7.3%
ATC G (Genitu-urinary system)	4.9%
ATC H (Systemic hormonal preparations)	1.8%
ATC L (Antineoplastic and immunomodulating agents)	0.5%
ATC M (Musculo-skeletal system)	15.2%
ATC N (Nervous system)	4.7%
ATC P (Antiparastics)	0.7%
ATC R (Respiratory system)	15.1%
ATC S (Sensory organs)	2.5%
ATC V (Various)	0.0%
Education	
Secondary	73.9%
Lowest tertiary	9.7%
Low tertiary	10.3%
Higher tertiary	6.1%
Controls	
Sex (female)	47.6%[a]
Parental household income (SD)	€ 36950 (16790)
Language spoken at home	
Finnish	93.6%
Swedish	5.2%
Other	1.2%

Values are % of total person-years in the study unless otherwise specified.
SD is standard deviation.
[a] Percentage reported in text was calculated at baseline and therefore differs.

3. Results

3.1. Time constant characteristics (controls)

We followed 42172 individuals over 12 years. In the data, 49% of individuals were female. Ca. 93% spoke the Finnish language as a native language, 6% Swedish and 1% other (Table 2). The average annual parental household income when still living at home was ca. 36,850 Euro, with 90% of observations between 12,300 and 73,300 Euro.

3.2. Time-varying characteristics

In the empirical data, at the first year of follow-up, 77% of individuals were employed and 23% were unemployed (start to follow-up required either employment or unemployment). In the first year, the modal age was 18 years (15% of all individuals). At this time 57% of individuals were living in with their parents, 20% living by themselves and 18% cohabiting and 4% were married. At this point, 70% had secondary education as highest education. These characteristics

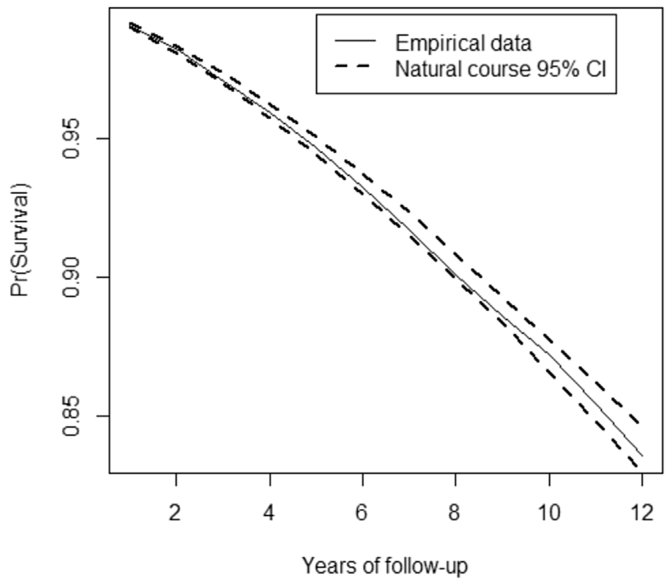

Fig. 2. Survival function (Kaplan-Meier) from entering the labor market to receiving a first antidepressant in the observed data together with 95% confidence intervals from the 'Natural Course' (no intervention) G-formula scenario.

diversified during follow-up. Over the entire study-period, 74% of observed person-years were employed, 8% being unemployed, 12% studying, and 6% of 'other' status. The number of individuals in our closed cohort that received a first anti-depressant during the follow-up was 5286, or 12.5% of all individuals (see also Fig. 2). These time-varying characteristics were closely matched by the natural-course scenario, indicating that the G-formula adequately modeled the joint distribution in the empirical data (see Appendix 1 Table A).

3.3. Multivariate model for first antidepressant purchase

The multivariate logistic regression model for first antidepressant purchase shows the model where we allowed all relations as shown by the arrows entering 'first antidepressant' as shown in the DAG (Fig. 1). It shows that being unemployed, compared to other statuses, increases the odds of first antidepressant purchase by 40%, controlling for all the other covariates (Appendix 1, Table B). Older individuals are more likely to receive a first antidepressant (1.7% increase per year of age). Women have a higher odds (39% increase) of receiving an antidepressant compared to men. Over time, the odds of a first antidepressant purchase increases (8% increase per calendar year). Compared to living alone, all other categories had a lower risk of antidepressant purchase, with especially the presence of children lowering the risk of a first antidepressant purchase (ca. 60% reduction for both categories with children). The lagged versions of household statuses however do show an increase compared to lagged being single, though together with their non-lagged versions the non-single household statuses are still protective. Education higher than secondary is associated with lower risk of antidepressant purchase, though not with a clear trend. Other health conditions, as indicated by the utilization of various drugs are generally associated with an increased risk of antidepressant purchase. The estimates of all other multivariate models can be found in Appendix 1.

3.4. No unemployment versus natural course

In the no-unemployment scenario, actual employment increased by 11 percentage points compared to the natural course data (see Appendix 1 Table A), as it also resulted in small decreases in the number of individuals in categories 'studying' and 'other'. Median

Table 3
Change in the population-averaged hazard of first antidepressant purchase in the natural course scenario with scenario's where we did not allow unemployment.

Equation	Effect type	Change in hazard	95% CI
0	Total effect	−7.6%	−11.9%, −2.8%
1	Controlled direct effect	−2.9%	−6.0%, 0.6%
	Proportion eliminated	−4.7%	
2	Income into CDE	−7.4%	−11.0%, −4.1%
3	Household into CDE	−6.5%	−11.4%, −1.3%
4	Health into CDE	0.3%	−2.8%, 3.6%
5	Total effect confounded	−6.6%	−9.9%, −6.4%

personal income increased by 4400 euro and median household income by 1900 euro. The number of respondents living at home with parents decreased by 4 percentage points, while the number of single individuals living by themselves and the number of individuals cohabiting or married increased by roughly 1 percentage point each. On the absolute scale there were no noticeable changes in drug utilization for other health conditions.

3.5. Mediation: TE, CDE and PAF

Using the multivariate models in the G-formula, we contrasted the natural course scenario with the no-unemployment scenario. We found that the total effect (TE) of this intervention was a hazard ratio of 0.924 (95% CI 0.881 to 0.972), which translates to a 7.6% decrease in the population-averaged hazard of antidepressant purchase (Table 3). The controlled direct effect of the intervention (i.e. the intervention effect not via income, household status, and other health conditions) was a hazard ratio of 0.971 (95% CI 0.940 to 1.006), indicating a 2.9% decrease in the hazard of antidepressant purchase. The proportion eliminated (PE = TE − CDE) is therefore 4.5%, and CDE and PE therefore account for 39% and 61% of the TE, respectively. Entering each of the mediators into the CDE one at a time, showed strong positive effects for income and household status, but a potentially damaging pathway via other health conditions if it is not allowed to affect the other two mediators (Table 3). The PAF equivalent of the TE, assuming 8 percentage point increase in employment, is a 5% reduction, and the PAF equivalent of the CDE is a 3.1% reduction (see Appendix 1). The PAF equivalent of the TE assuming 11% percentage point increase in employment is 6.7%, and of the CDE is 4.2%. The former value is similar to the TE value from equation (5) (Table 3; 6.5%, 95% CI 2.6%–9.9%), which did not include the mediators and therefore did not control for intermediate confounding.

3.6. Subgroup analysis: gender and educational level

Subgroup analyses for the total effect of the no-unemployment scenario show a strong reduction (25.1%) in first antidepressant purchase for men with secondary education as their highest attained educational level, and weaker effects for men with tertiary level education (Table 4). For women, gradients are in the same direction but effects are much weaker or even positive. Effects within the tertiary educational levels (lowest, low and higher tertiary educational levels) for both genders were very similar and therefore collapsed to one tertiary level for this subgroup analysis. Decomposing the total effect into the controlled direct effect and the proportion eliminated shows that direct effects for men and women with secondary level education are about the same (ca. 7%–9% reduction), and similarly for men and women in tertiary level education (ca. 6%–9% increase). The difference between men and women in the no-unemployment effect on first antidepressant purchasing therefore operates largely indirectly via changes in income, household status and health.

Table 4
Subgroup analysis by gender and educational status: change in the population-averaged hazard comparing the natural course with the no-unemployment scenario.

Gender	% Unemployed person-years	Educational level	Effect type	Change in hazard	95% CI
Men	9.5%	Secondary	Total effect	−25.1%	−33.0%, −17.8%
			Controlled direct effect	−9.3%	−17.2%, −1.8%
			Proportion eliminated	−15.8%	
Men	4.1%	Tertiary +	Total effect	−11.1%	−24.9%, 1.8%
			Controlled direct effect	5.6%	−7.0%, 19.4%
			Proportion eliminated	−16.7%	
Women	10.6%	Secondary	Total effect	−3.1%	−10.2%, 3.0%
			Controlled direct effect	−6.6%	−12.4%, −0.6%
			Proportion eliminated	3.5%	
Women	4.5%	Tertiary +	Total effect	12.0%	1.7%, 25.2%
			Controlled direct effect	9.2%	−4.1%, 21.2%
			Proportion eliminated	2.8%	

4. Discussion

The primary research question (Q1) of this study is “What is the population-level effect of eliminating youth unemployment on first antidepressant purchases in Finland in the period 1996 to 2007?”. We found that the total effect of the no-unemployment intervention on first antidepressant purchase was 0.924 (95% CI 0.881 to 0.972), indicating a 7.6% population averaged reduction in first antidepressant purchases. The second research question (Q2) was “To what extent does the no-unemployment effect operate via changes in income, household status and health conditions?”. We found that the direct effect of the intervention was a hazard ratio of 0.971, which indicates that 39% of the total effect is a direct effect, and 61% operated via the mediators. Of these mediators, its effects via income and household status were clearly positive, but its effect via other health conditions was less clear. Finally, we the third research question (Q3) was “To what extent does the no-unemployment effect differ by gender and educational status?”. Subgroup analysis indicated that the no-unemployment effect had strong reductive effects on first antidepressant purchases for men with secondary level educational status as their highest attained status, and less strong effects for women of secondary level education and men and women of tertiary level education. Importantly, the differences between men and women are largely caused by women having negligible indirect effects.

4.1. Evaluation of data and methods

The total effect of an exposure on an outcome via mediators can be decomposed in various ways (Wang and Arah, 2015). In our analysis, the primary exposure and its mediators were time-varying variables which also mediated their own effect; i.e. unemployment at time t can affect unemployment at time $t+1$ and onwards. Decomposition of the total effect into the controlled direct effect and proportion eliminated allowed us to simulate an intervention on unemployment at all time points (all person-years). An additional advantage of controlled (in) direct effect over the natural (in)direct effect decomposition is that it has less stringent identification assumptions, however our operationalization of the stochastic controlled direct effect is close to that of the natural direct effect (Lin et al., 2017; VanderWeele, 2011).

For our analysis, we used an 11% random sample from high quality Finnish register data. Missingness on the covariates was small (< 3%), and therefore we chose not to use missing data imputation methods. The study outcome is subject to competing risks, but its effect is likely negligible given that only 2% of individuals were censored. While our G-formula modeling procedure was complex, we adequately approximated the marginal distribution in the data, as indicated by the values of time-varying covariates generated in the natural course scenario having nearly identical values to those found in the empirical data. Income was somewhat underestimated, but this property was present in both the natural course and intervention simulations, thereby capturing the shift in income caused by the no-unemployment intervention.

To model the joint distribution, assumptions were made regarding the real-world data generating mechanism. By using lagged variables in the multivariate models we are more certain about the direction of causality as the temporal order is established; only ‘anticipation effects’ might bias such relations (Steele et al., 2013; Ferrie et al., 1995). By controlling for parental household income when leaving the parental home, plus potential mediating confounders (previous household status and income), we account for indirect selection effects (Steele et al., 2013). Nevertheless, residual unobserved heterogeneity may be present through other factors that predispose individuals both to unemployment and antidepressant consumption, or affect both a mediator and antidepressant consumption (i.e. mediator-outcome confounding) (VanderWeele et al., 2014). Such factors, such as behavioral problems, are likely to affect unemployment and antidepressant purchasing positively and therefore the no-unemployment intervention effect may be overestimated. We suggest that unmeasured confounding of such (time-constant) nature could be accounted for by applying an individual-level fixed effects approach or similar methodology (Fitzmaurice et al., 2004). Literature combining such methodology with the G-formula is currently lacking.

When interpreting our results, it is important to note that first antidepressant purchase is an imperfect indicator of the presence of depression, and instead more so an indicator of depression diagnosis. The hazard of first antidepressant purchase increases when the hazard of receiving care (or care seeking) increases. Thus becoming employed may increase this hazard through access to occupational health services. Similarly, income, partnership status and health (the mediators) are tied to risk of diagnosis and antidepressant purchases: wealthier individuals may have a lower thresholds to seeking care and have access to higher quality healthcare, individuals with partners are more likely to receive care (e.g. through the partner and their lay referral network), and our health variable is itself constructed using purchases for other drugs and is therefore an indicator of contact with a prescriber. Given that in our study, becoming employed, increasing income, and partnership decreased the risk of a first antidepressant purchase, we believe that the true protective effect of employment and the mediators on depression is underestimated.

Overall, our causal estimates are dependent on our causal model and the observed data that underlie the estimation of this model. We believe that it is a particular advantage that we can analyze a cohort of young Finns as they enter the labor market and have annual data for the follow-up. These data allow us to identify the temporal sequence of the experience of unemployment with depression and our observed mediators. However, our register based data does not allow us to observe and control for all possible confounders; such as personality traits or substance use. Causal interpretation of our results thus need to be drawn cautiously.

4.2. The G-formula and PAF

The marginal effect of an exposure can be different from its stratum-specific effects, a phenomenon known as non-collapsibility. It is caused by, for example, conditioning on mediators in non-linear settings. The G-formula solves this through population-averaging (Keil et al., 2014; Greenland et al., 1999). The population-attributable fraction (PAF) weights effects by the proportion of the population at risk of that effect, and therefore produces estimates which are roughly comparable with G-formula estimates. However, the PAF is 'naïve' in the sense that it does not capture the dynamism between exposure, mediators and outcome; it therefore does not approximate the causal effect of an intervention except in simple scenarios. The PAF equivalent of the total effect in our study, 5% reduction, is lower than the G-formula estimate of 7.6% by 2.6 percentage points. This is in part caused by assuming that setting the 8% unemployed person-years to 0% results in an equivalent 8 percentage point increase in employment, while actually implementing this intervention resulted in an 11 percentage point increase in employment. However, a PAF estimate of the total effect assuming an 11 percentage point increase in employment would still be lower, namely 6.7%. The remaining difference may be caused by intermediate confounding: standard PAF calculations are based on models that either include mediating confounders (thereby blocking mediation) or do not (thereby risking confounding) and therefore risk bias either way. When we estimated the total effect using the G-formula without including the mediators in the estimation step, the estimate was a 6.5% reduction, close to the PAF total effect equivalent which assumed an 11 percentage point increase in employment. By determining the total effect this way, effects via mediators become part of the direct effect of unemployment, but confounding is not controlled. These findings indicate that the measured mediators (especially income and household status) positively mediate the effect of the employment on antidepressant purchasing, but also negatively confound the relationship between employment and antidepressant purchasing.

4.3. Pathways of the no-unemployment intervention effect

The total effect estimate in our study indicates that if Finnish individuals aged 14 to 35 who were unemployed in the period 1996 to 2007 had instead been employed, the risk of a first antidepressant purchase would have been lower. Decomposing this effect estimate into the direct effect, and the effect mediated by income, household status and health conditions other than depression, we find that especially the mediated effect on first antidepressant purchasing was strong, accounting for 61% of the total effect. This is largely due to increases in income and changing household status.

The effect via household status was especially a reduction in the number of individuals living with their parents, and increases in other categories. Others have described that both unemployment and income are indeed factors that affect duration of residence at the parental home (Aassve et al., 2002; Jacob and Kleinert, 2008). Furthermore, establishing and maintaining relationships may be more difficult under the psychological strain of unemployment (Ekert-Jaffe and Solaz, 2001). In our analysis, especially the presence of children in the household, which saw a small increase, appears to strongly reduce the risk of antidepressant purchasing. Increases in income represent material factors; previous research has also shown the link between material conditions and health (Martikainen et al., 2003), and has shown income change to be an important mediator for the effect of unemployment on depression (Chazelle et al., 2011; Elwell-Sutton et al., 2017).

The scenarios where we added each mediator individually to the controlled direct effect provided additional information. The controlled direct effects with income or household status added (equations (2) and (3)) had large positive estimates, indicating that most of the indirect effect likely goes through these two mediators. The large size of these estimates relative to the total effect may in part be because the total effect is roughly an average of the positive effects via income and household status, and the negative effect via health. However, these are rough comparisons; in these scenarios the effects of the intervention can affect only one mediator at a time, and therefore does not allow mediators to affect each other, and take place in a nonlinear setting. Therefore, the distributions of the one mediator that is free to change will not be identical to the same mediator's distribution in the total effect scenario. When simulating the total effect the pathway via health was negligible, as there were no noticeable changes in drug utilization in that scenario compared to the natural course (see Appendix 1). This was our expected finding, given that health problems are rare at young ages and the effect sizes are population-averaged.

The direct effect of unemployment, i.e. the effect not mediated by income, household status and other health conditions, accounted for 39% of the total effect (95% CI: 0–76%). Because of the modeled causal structure (which includes the effect of employment status on subsequent employment status), the 'direct' effect is not necessarily manifested directly after the onset of unemployment. As described previously, the intervention effect via income largely represents material factors, and the effect via household status possibly represents psychological factors. We speculate that the direct effect may also be of a psychological nature; e.g. being or becoming unemployed has been associated with loss of self-esteem and loss of workplace social contacts (Bell and Blanchflower, 2011; Stronks et al., 1997).

4.4. Gender and education differentials

The total effect of our intervention of no-unemployment on first antidepressant purchase was stronger for men than for women, which is in line with other studies (Artazcoz et al., 2004; Simon, 2002). Because the proportion of unemployed person-years was similar among men and women, the intervention affects roughly the same number of person-years in both groups. The difference in the no-unemployment effect is therefore caused instead by the intervention's mechanism of action operating differently for men than for women. Men and women had similar direct effects, but the intervention had virtually no indirect effects (via income, household status, and other health) for women, whereas it had strong indirect effects for men. The stronger total effect among men was thus driven by much stronger mediated effects.

Despite the Nordic countries being forerunners in gender equality, the explanation for stronger mediated effects for men may be found in gender roles. For example, Finnish women report spending more time on housework and care related non-paid work (Lammi-Taskula, 2008; Melkas, 2005; Niemi and Pääkkönen, 2001), and have lower wages (Pulkkinen, 2005). On the population-level, becoming employed therefore has a less strong effect on female income than male income, and reduces the 'free' time a woman has, competing with the time that she is socially expected to spend taking care of the household (Lehman Schlozman et al., 1999). Furthermore, given that women leave the parental home earlier than men (e.g. to live with a partner), an intervention on unemployment has less opportunity to affect subsequent female than subsequent male household formation (Billari and Liefbroer, 2007). Other studies have also linked employment status to household status (Ekert-Jaffe and Solaz, 2001), and report that household status has different effects on mental health for men and women (Artazcoz et al., 2004; Simon, 2002). Unfortunately, we were unable to find studies of mental health that separate the effects of income (except poverty) from those of employment, by gender. However, one study that looked at general health in this manner also reported stronger effect of income for men than for women (Stronks et al., 1997). Finally, the positive direct effects of employment for tertiary educated men and women are perhaps explained by increases in the probability of diagnosis (such as gaining access to occupational health services), though none of these effects were statistically significant.

In line with other studies, our results show that the full employment intervention more strongly affected those with secondary education as their highest achieved educational level, compared to those with higher education (Chazelle et al., 2011; Melchior et al., 2015; Lee et al., 2015). In our study estimates are population-averaged, and therefore part of the effect is explained by a larger proportion of person-years being unemployed in the secondary education group. This means that the intervention affects more person-years in the secondary education group. Decomposing the total effect, we see that the controlled direct effect reduces the hazard of antidepressant purchase for those with secondary education, but may increase it for those in the tertiary education group. This indicates there are also difference in the mechanisms of the intervention between educational groups. An explanation may be differences in psychological effects; loss of self-esteem and loss of workplace social contacts appear to more strongly affect those with secondary educational attainment as opposed to those with a higher educational attainment (Bell and Blanchflower, 2011; Stronks et al., 1997). These findings are in line with studies showing that individuals with a higher educational attainment have stronger social networks outside work than those with low educational attainment (Weyers et al., 2008).

5. Conclusion

Our work adds evidence about the pathways of the unemployment-mental health relation at young ages. Intervening on unemployment appears to reduce antidepressant consumption primarily through increases in income and changes in household status. It is widely acknowledged that health and unemployment interact in complex ways across the life course. The G-formula can be used to model these processes, simulate policy interventions, and thereby generate information on population-level intervention effects and the pathways through which these interventions operate.

Acknowledgements

The study has been funded by the Strategic Research Council of the Academy of Finland (#303615, Lasse Tarkiainen & Pekka Martikainen), and European Research Council grant #336475 (Mikko Myrskylä).

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.socscimed.2017.10.011.

References

Aassve, A., Billari, F.C., Mazzuco, S., Ongaro, F., 2002. Leaving home: a comparative analysis of ECHP data. J. Eur. Soc. Policy 12 (4), 259–275.
Artazcoz, L., Benach, J., Borrell, C., Cortès, I., 2004. Unemployment and mental health: understanding the interactions among gender, family roles, and social class. Am. J. Public Health 94 (1), 82–88.
Bell, D.N.F., Blanchflower, D.G., 2011. Young people and the great recession. Oxf. Rev. Econ. Policy 27 (2), 241–267.
Billari, F.C., Liefbroer, A.C., 2007. Should I stay or should I go? the impact of age norms on leaving home. Demography 44, 181–198.
Buckley, J.P., Keil, A.P., McGrath, L.J., Edwards, J.K., 2015. Evolving methods for inference in the presence of healthy worker survivor bias. Epidemiology 26 (2), 204–212.
Chazelle, E., Lemogne, C., Morgan, K., Kelleher, C.C., Chastang, J.F., Niedhammer, I., 2011. Explanations of educational differences in major depression and generalised anxiety disorder in the Irish population. J. Affect Disord. 134 (1–3), 304–314.
Chevrier, J., Picciotto, S., Eisen, E.A., 2012. A comparison of standard methods with g-estimation of accelerated failure-time models to address the healthy-worker survivor effect: application in a cohort of autoworkers exposed to metalworking fluids. Epidemiology 23 (2), 212–219.
Daniel, R.M., Cousens, S.N., De Stavola, B.L., Kenward, M.G., Sterne, J.A., 2013. Methods for dealing with time-dependent confounding. Stat. Med. 32 (9), 1584–1618 30.
De Stavola, B.L., Daniel, R.M., Ploubidis, G.B., Micali, N., 2015. Mediation analysis with intermediate confounding: structural equation modeling viewed through the causal inference lens. Am. J. Epidemiol. 181 (1), 64–80.
Dooley, D., Prause, J., Ham-Rowbottom, K.A., 2000. Underemployment and depression: longitudinal relationships. J. Health Soc. Behav. 41 (4), 421–436.
Efron, B., Tibshirani, R.J., 1994. An Introduction to the Bootstrap. CRC Press, Boca Raton.
Egan, M., Daly, M., Delaney, L., 2016. Adolescent psychological distress, unemployment, and the Great Recession: evidence from the national longitudinal study of young 1997. Soc. Sci. Med. 156, 98–105.
Ekert-Jaffe, O., Solaz, A., 2001. Unemployment, marriage, and cohabitation in France. J. Socio-Economics 30 (1), 75–98.
Elwell-Sutton, T., Folb, N., Clark, A., Fairall, L.R., Lund, C., Bachmann, M.O., 2017. Socioeconomic position and depression in South African adults with long-term health conditions: a longitudinal study of causal pathways. Epidemiol. Psychiatr. Sci. 1–11.
Ensminger, M.E., Celentano, D.D., 1990. Gender differences in the effect of unemployment on psychological distress. Soc. Sci. Med. 30 (4), 469–477.
Ferrie, J.E., Shipley, M.J., Marmot, M.G., Stansfeld, S., Smith, G.D., 1995. Health effects of anticipation of job change and non-employment: longitudinal data from the Whitehall II study. BMJ 311 (7015), 1264–1269.
Fitzmaurice, G.M., Laird, N.M., Ware, J.H., 2004. Applied Longitudinal Analysis. John Wiley & Sons, Hoboken.
Greenberg, P.E., Fournier, A.A., Sisitsky, T., Pike, C.T., Kessler, R.C., 2015. The economic burden of adults with major depressive disorder in the United States (2005 and 2010). J. Clin. Psychiatry. 76 (2), 155–162.
Greenland, S., Robins, J.M., Pearl, J., 1999. Confounding and collapsibility in causal inference. Stat. Sci. 14 (1), 29–46.
Hernán, M.A., Robins, J.M., 2013. Causal Inference. Fla: Chapman & Hall/CRC, Boca Raton.
Hollander, A.C., Bruce, D., Ekberg, J., Burström, B., Ekblad, S., 2013. Hospitalisation for depressive disorder following unemployment–differentials by gender and immigrant status: a population-based cohort study in Sweden. J. Epidemiol. Community Health. 67 (10), 875–881.
Imai, K., Keele, L., Tingley, D., 2010. A general approach to causal mediation analysis. Psychol. Methods 15, 309–334.
Jacob, M., Kleinert, C., 2008. Does unemployment help or hinder becoming independent? the role of employment status for leaving the parental home. Eur. Sociol. Rev. 24 (2), 141–153.
Jefferis, B.J., Nazareth, I., Marston, L., Moreno-Kustner, B., Bellón, J.Á., Svab, I., Rotar, D., Geerlings, M.I., Xavier, M., Goncalves-Pereira, M., Vicente, B., Saldivia, S., Aluoja, A., Kalda, R., King, M., 2011. Associations between unemployment and major depressive disorder: evidence from an international, prospective study (the predict cohort). Soc. Sci. Med. 73 (11), 1627–1634.
Keil, A.P., Edwards, J.K., Richardson, D.B., Naimi, A.I., Cole, S.R., 2014. The parametric g-formula for time-to-event data: intuition and a worked example. Epidemiology 25 (6), 889–897.
Laaksonen, M.A., Knekt, P., Härkänen, T., Virtala, E., Oja, H., 2010. Estimation of the population attributable fraction for mortality in a cohort study using a piecewise constant hazards model. Am. J. Epidemiol. 171 (7), 837–847.
Lammi-Taskula, J., 2008. Doing fatherhood: understanding the gendered use of parental leave in Finland. Fathering 6 (2), 133–148.
Lee, J.O., Hill, K.G., Hartigan, L.A., Boden, J.M., Guttmannova, K., Kosterman, R., Bailey, J.A., Catalano, R.F., 2015. Unemployment and substance use problems among young adults: does childhood low socioeconomic status exacerbate the effect? Soc. Sci. Med. 143, 36–44.
Lehman Schlozman, K., Burns, N., Verba, S., 1999. "What happened at work today?": a multistage model of gender, employment, and political participation. J. Polit. 61 (1), 29–53.
Lépine, J.P., Briley, M., 2011. The increasing burden of depression. Neuropsychiatr. Dis. Treat. 7 (Suppl. 1), 3–7.
Lin, S.H., Young, J., Logan, R., Tchetgen Tchetgen, E.J., VanderWeele, T.J., 2017. Parametric mediational g-formula approach to mediation analysis with time-varying exposures, mediators, and confounders. Epidemiology 28 (2), 266–274.
Lorant, V., Deliège, D., Eaton, W., Robert, A., Philippot, P., Ansseau, M., 2003. Socioeconomic inequalities in depression: a meta-analysis. Am. J. Epidemiol. 157 (2), 98–112.
Lorant, V., Croux, C., Weich, S., Deliège, D., Mackenbach, J., Ansseau, M., 2007. Depression and socio-economic risk factors: 7-year longitudinal population study. Br. J. Psychiatry 190, 293–298.
Martikainen, P., Adda, J., Ferrie, J.E., Davey Smith, G., Marmot, M., 2003. The effects of income and wealth on GHQ depression and poor self-rated health in white-collar women and men in the Whitehall II Study. J. Epidemiol. Community Health 57 (9), 718–723.
Martikainen, P., Ferrie, J., 2008. Populations at special health risk: unemployed: unemployment and job insecurity. In: Heggenhougen, K., Quah, S. (Eds.), International Encyclopedia of Public Health. Elsevier, pp. 268–276.
Melchior, M., Chollet, A., Elidemir, G., Galéra, C., Younès, N., 2015. Unemployment and substance use in young adults: does educational attainment modify the association? Eur. Addict. Res. 21 (3), 115–123.
Melkas, T., 2005. Gender Equality Barometer 2004. Ministry of Social Affairs and Health, Helsinki.
Mroz, T.A., Savage, T.H., 2006. The long-term effects of youth unemployment. J. Hum. Resour. 41 (2), 259–293.
Niemi, I., Pääkkönen, H., 2001. [Changes in time-use in the 1990s]Statistics Finland, Helsinki.
OECD, 2013. OECD Framework for Statistics on the Distribution of Household Income, Consumption and Wealth [Internet]. OECD Available from: http://www.oecd.org/statistics/OECD-ICW-Framework-Chapter8.pdf.
Paul, K.I., Moser, K., 2009. Unemployment impairs mental health: meta-analyses. J. Vocat. Behav. 74 (3), 264–282.
Pearl, J., 2002. Causality: Models, Reasoning, and Inference. Cambridge University Press, Cambridge.
Pulkkinen, P., 2005. Gender Equality in Finland 2004. Statistics Finland, Helsinki.

Picciotto, S., Hertz-Picciotto, I., 2015. Commentary: healthy worker survivor bias: a still-evolving concept. Epidemiology 26 (2), 213–215.
Richiardi, L., Belloco, R., Zugna, D., 2013. Mediation analysis in epidemiology: methods, interpretation and bias. Int. J. Epidemiol. 42 (5), 1511–1519.
Sareen, J., Afifi, T.O., McMillan, K.A., Asmundson, G.J., 2011. Relationship between household income and mental disorders: findings from a population-based longitudinal study. JAMA Psychiatry 68 (4), 419–427.
Simon, R.W., 2002. Revisiting the relationships among gender, marital status, and mental health. Am. J. Sociol. 107 (4), 1065–1096.
Stronks, K., van de Mheen, H., van den Bos, J., Mackenbach, J.P., 1997. The interrelationship between income, health and employment status. Int. J. Epidemiol. 26 (3), 592–600.
Steele, F., French, R., Bartley, M., 2013. Adjusting for selection bias in longitudinal analyses using simultaneous equations modeling: the relationship between employment transitions and mental health. Epidemiology 24 (5), 703–711.
Strandh, M., Winefield, A., Nilsson, K., Hammarström, A., 2014. Unemployment and mental health scarring during the life course. Eur. J. Public Health 24 (3), 440–445.
Strömberg, R., Backlund, L.G., Löfvander, M., 2011. Psychosocial stressors and depression at a Swedish primary health care centre. A gender perspective study. BMC Fam. Pract. 12, 120.
VanderWeele, T.J., Vansteelandt, S., Robins, J.M., 2014. Effect decomposition in the presence of an exposure-induced mediator-outcome confounder. Epidemiology 25 (2), 300–306.
VanderWeele, T.J., 2011. Controlled direct and mediated effects: definition, identification and bounds. Scand. Stat. Theory Appl. 38 (3), 551–563.
Wagenaar, A.F., Kompier, M.A., Houtman, I.L., van den Bossche, S.N., Taris, T.W., 2012. Employment contracts and health selection: unhealthy employees out and healthy employees in? J. Occup. Environ. Med. 54 (10), 1192–1200.
Wang, A., Arah, O.A., 2015. G-computation demonstration in causal mediation analysis. Eur. J. Epidemiol. 30 (10), 1119–1127.
Weyers, S., Dragano, N., Möbus, S., Beck, E.M., Stang, A., Möhlenkamp, S., Jöckel, K.H., Erbel, R., Siegrist, J., 2008. Low socio-economic position is associated with poor social networks and social support: results from the Heinz Nixdorf Recall Study. Int. J. Equity Health. 7, 13.
Whooley, M.A., de Jonge, P., Vittinghoff, E., Otte, C., Moos, R., Carney, R.M., Ali, S., Dowray, S., Na, B., Feldman, M.D., Schiller, N.B., Browner, W.S., 2008. Depressive symptoms, health behaviors, and risk of cardiovascular events in patients with coronary heart disease. JAMA 300 (20), 2379–2388.