The impact of unemployment on depression: combining the parametric g-formula and individual intercepts to adjust for time-varying confounding and unobserved selection

Maarten J. Bijlsma[a,*], *Ben Wilson*[b], *Lasse Tarkiainen*[c],

Mikko Myrskylä[a,c,d], *Pekka Martikainen*[a,c,e]

[a] Max Planck Institute for Demographic Research, Konrad-Zuse str. 1, 18057 Rostock, Germany

[b] Stockholm University Demography Department, Universitetsvägen 10 B, Stockholm, Sweden

[c] Department of Social Research, University of Helsinki, Unioninkatu 37 (P.O. Box 54), 00014 Helsinki, Finland

[d] London School of Economics & Political Science, Houghton St, London WC2A 2AE, United Kingdom

[e] Centre for Health Equity Studies (CHESS), Stockholm University and Karolinska Institutet, SE-106 91 Stockholm Sweden

* Corresponding author. E-mail address: bijlsma@demogr.mpg.de

Max Planck Institute for Demographic Research, Konrad-Zuse-Straße 1, Rostock, 18057, Germany. Tel. +49 (0)381 2081 211; Fax: +49 (0)381 2081-439.

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Abstract

The estimated effect of unemployment on depression may be biased by time-varying, intermediate, and time-constant confounding. To address this, we apply a g-formula with individual-level fixed-effect intercepts to estimate how antidepressant purchasing is affected by a hypothetical intervention that provides employment to the unemployed. We use sample of the Finnish adult population (n = 49,753). We compare estimates that adjust for various baseline confounders and time-varying socio-economic covariates (confounders and mediators) with estimates that also include individual-level fixed-effect intercepts. In the empirical data around 10% of person-years are unemployed. Setting these person-years to employed, the g-formula without individual intercepts found a 5% (95% CI: 2.5 to 7.4%) reduction in antidepressant purchasing at the population-level. However, when also adjusting for individual intercepts, we find no effect (-0.1%, 95% CI: -1.8 to 1.5%). The results indicate that the relationship between unemployment and depression is confounded by residual time-constant confounding (selection).

Introduction

Depression is a leading cause of disability in both men and women, and a major public health concern globally.[1-3] The worldwide prevalence of depression has increased in recent decades, and is expected to continue increasing.[4] One determinant of depression is unemployment.[5,6] Unemployment can result in loss of financial means, social contacts, and purposeful activity, all of which increase the risk of depression.[5-7] However, vice versa, depression is a risk factor for unemployment, as individuals suffering from depression may experience greater difficulty in finding and retaining employment.[8,9]

Due to the interrelationships between unemployment and depression, many methods will struggle to estimate an unbiased causal effect of unemployment on depression.[8,10] Given their time-dependent relationship, a longitudinal design is imperative. Furthermore, various determinants, such as physical health or partnership status, may affect both unemployment and depression, i.e. they may function as (time-varying) confounders. At the same time, such determinants may also be affected by unemployment or depression themselves. Confounders that are affected by prior exposures are also known as intermediate confounders.[11,12] Most traditional statistical techniques cannot account for time-varying and intermediate confounding.[13]

The g-formula is one method among very few that can be used to model complex longitudinal dependencies, including time-varying and intermediate confounding.[14-16] The g-formula has been used before to model the complex interrelationships between unemployment and antidepressant purchasing, an indicator of diagnosis of depression.[5] Bijlsma and colleagues found that among young adults entering the labor market for the first time, reducing unemployment indeed results in a reduction in antidepressant purchasing, especially for low educated men. However, the authors note that unmeasured time-constant confounding may affect their estimates despite a rich set of baseline controls.

A typical way to adjust for unmeasured time-constant confounding when using longitudinal data is to include individual-level fixed effect intercepts.[17] By including such individual intercepts, only exposures that change over time contribute to an estimated effect. As such, the influence of time-constant determinants, including unmeasured time-constant confounders, is eliminated. Although this method is relatively common across the quantitative social sciences, we are not aware of any previous research that combines the method with the parametric g-formula, despite the potential advantages of such an approach.

The aims of this study are therefore twofold. First, we aim to determine the population-level effect of eliminating unemployment on antidepressant purchases among a cohort of men and women in Finland who were aged 30-52 from 1995-2012. Second, we aim to demonstrate a new approach to causal inference that combines the parametric g-formula to account for time-varying confounders that are affected by prior exposures, with individual-level fixed-effects to account for unmeasured time-constant confounding.

Data and Methods

Study population

We study a closed cohort of Finnish men and women in calendar years 1995 to 2012. All individuals are aged 30-35 at the start of follow-up, and 47-52 at the end. The sample size is 49,753 individuals, with non-administrative right-censoring of 2,693 individuals. The study includes 826,526 person-years, with intermediate censoring of 4,743 person-years.

Data source

The data source for this study is an 11% random sample of the population permanently residing in Finland at the end of 1995, and is updated each calendar year. Statistics Finland constructed these data by linking individual-level census records, death records and labor market records to social care records, sickness absence allowance records and medication records maintained by the Social Insurance Institution of Finland (permission code TK-53-339-13).

Outcome variable

Our outcome is antidepressant purchasing (henceforth AD purchasing), an indicator variable measuring whether an individual has purchased an antidepressant (ATC N06A) or an antidepressant in combination with psycholeptics (ATC N06CA) in a calendar year.

Time varying exposures, mediators and confounders

All time-varying variables are measured annually and function simultaneously as exposures, mediators and confounders. The primary exposure of interest is employment status, categorized as employed, unemployed, retired, or other (containing student and other minor categories). In addition, we have time-varying information on household status, income, and other drug purchases. Household status is categorized as ‘Child living with parents’, ‘Single without children’, ‘Single with children’, ‘Cohabiting without children’, ‘Cohabiting with children’, ‘Married without children’, and ‘Married with children’. Income is measured using personal income subject to state taxation, and household disposable income including non-taxable income. Both income types are continuous variables measured in euros and corrected for inflation (2014 as reference year). Household disposable income was corrected by dividing it by the number of consumption units present in the household using the OECD-modified scale (OECD, 2013). Other drug purchases are measured as a set of 11 binomial variables registering the purchase of an antibacterial (ATC J01), opioid (N02A), antipyretic and analgesics other than opioids (N02B), psycholeptic (N05), psycholeptics other than antidepressants (N06, but not N06A or N06CA), sex hormones (G03), drugs for obstructive airway diseases (R03), antihistamines (R06), beta blockers (C07), renin-angiotensin agents (C09), and antiprotozoals (P01). We also adjusted for age, in 5-year categories (30-34, 35-39, 40-44, 45-49, and 50-52).

Time constant variables

Time constant variables are sex (female or not), language spoken at home (Finnish, Swedish, or other), and highest educational level attained in 4 categories (lower secondary, higher secondary, lower tertiary and higher tertiary - ISCED 2011 categories 2, 3-4, 5-6, 7-8, respectively).

Effect estimation

We estimate the effect of setting all unemployed person-years to employed throughout follow-up. We assume a set of cross-lagged relationships between the time-varying variables, allowing for mediation (Figure 1). Time-constant variables, when included in the analysis, are allowed to affect all time-varying variables at every time-point. To estimate the effect of our intervention, we apply the parametric g-formula using the following steps:[14,18]

1. Randomly draw individuals from the data with replacement (n = 49,753).
2. To the randomly drawn individuals (step 1), fit parametric models for covariates at time *t* as a function of covariate history at time *t*.
3. Take observations from the first year of follow-up (from the step 1 sample) and using the models (step 2), predict observations for the second year of follow-up. Then use those (predicted) observations to predict observations in the next year, etc. until the end of follow-up.
4. Save the predicted outcomes (from step 3) for AD purchasing and the other variables for all simulated years (these represent the 'natural course scenario').
5. Perform step 3 a second time, now setting all unemployed person-years at the first year of follow-up to employed. Whenever unemployment is predicted, set it to employed instead.
6. Save the predicted outcomes (step 5) for AD purchasing and the other variables for all simulated years (these represent the 'intervention scenario').
7. Calculate the difference in AD purchasing between the natural course and intervention scenarios, and save this estimate.
8. Perform the steps 1-7 500 times. The distribution of effect estimates (step 9) is used to derive the mean effect and the 2.5 and 97.5% quantiles are used to determine 95% confidence intervals for the effect.

Full details on the functional form of the models (step 2) are provided in the supplemental material. The pertinent details are as follows. We perform the g-formula estimation with 5 different covariate sets, (Table 1). Covariate sets 4 and 5 follow our directed acyclic graph (DAG), as they include time-varying covariates (Figure 1). For all covariate sets, the models in step 2 are linear regression models, i.e. linear probability models are assumed for nominal variables. Linear models allow for the inclusion (and extraction) of individual fixed intercepts in a computationally efficient manner, compared to a g-formula with individual intercepts and non-linear (i.e. generalized linear) models. Covariate sets 2-5 include interactions between employment status and sex, and between employment status and education. For binary and multinomial variables, the prediction steps (4 and 7) use predicted probabilities to draw values (0 or 1) from binomial and multinomial distributions, respectively. Note that the models with individual-level fixed effect intercepts have different effective sample sizes for each coefficient (Table 2). We produce population-averaged effect estimates by including the estimated individual-level fixed effect intercepts in the prediction steps (steps 4 and 7). Individual intercepts were estimated using the 'plm' package in R.[19]

Subgroup and sensitivity analyses

We perform additional analyses to gain further insight into our results.

Firstly, when performing the g-formula procedure as outlined above, we also save effect estimates by education (secondary and tertiary levels) and sex subgroups, because previous research has shown that effects can differ strongly by these subgroups.[5]

Secondly, we extract the estimated individual-level fixed effect intercepts from the model (covariate set 5) for AD purchasing and the model for unemployment. We then quantify the strength of their association with AD purchasing and unemployment, respectively, by comparing the 75% and 25% quantiles of these individual intercepts. To provide a comparison to a measured variables' strength, we also compare the 75% and 25% quantiles of personal income multiplied with the coefficient of personal income from the same models.

Thirdly, we extract the coefficient of employment on personal income from both modelling sets 4 and 5, in order to determine how introducing individual intercepts affects this coefficient's strength, given that a causal effect of employment on personal income is known to exist.

Finally, the estimation of all 5 covariate sets is also performed with hospitalization due to injuries and accidents (ICD-10 codes: S00-T79, T90-T98) taking the place of AD purchasing. This is performed because this outcome, compared to AD purchases, is likely less sensitive to differences in treatment seeking behavior between social strata.

Results

Descriptive findings

Of the study cohort, 18% has lower secondary as their highest attained educational level, 48% higher secondary, 24% lower tertiary, and9% higher tertiary (Table 2). Finnish native speakers account for 94% of the cohort, 4% Swedish, and 2% some other language. The percentage of men is 50%.

Antidepressants are purchased by 3% of cohort members in 1995, increasing over time (as individuals age) to 11% in 2012, with the average being 8%. In 1995, 16% of all individuals are registered as unemployed, decreasing to 6% at the end of follow-up, with the average being 10%. Around 11% of unemployment spells last 5 consecutive years or more. From 1995 to 2012, the percentage employed increases from 71% to 84%, with the discrepancy between the decline in unemployment and the rise in employment caused by changes in the other categories (retired or other). In 1995, average yearly taxable income (inflation corrected) is 22,090 euro, and rises to 35,600 euro in 2012.

There are many transitions within key variables, and thereby also the effective sample size for the estimation of the coefficients of those variables is high (Table 3). Noteworthy is that among those individuals that do not experience an employment transition, 95.7% are employed.

Unemployment coefficients

The coefficients of the multivariate model for AD purchasing that includes time-constant and time-varying covariates (Table 2) are similar to those that replace time-constant covariates with individual intercepts, though magnitudes differ. Conditional on the other covariates, both models show that unemployment in the previous year is associated with an increased probability of an

AD purchase (relative to employment), but in the model without individual intercepts the coefficient is three times larger (0.009 vs. 0.003). The results of all multivariate models can be found in the supplemental material.

G-formula results: no unemployment versus natural course

Our intervention sets all unemployed person-years (10.2% of all person-years) to employed. We use five covariate to estimate the effect of the no-unemployment scenario on AD purchases (Table 1). The g-formula's natural course scenario from the richest measured covariate set (set 4) appears to adequately approximate the empirical data (see supplemental material). Covariate sets that do not include individual-level fixed effect intercepts (sets 1, 2, and 4) all estimate some population-level reduction in annual person-years with AD purchases (Figure 2). For example, in the basic model without any covariates other than employment status (set 1), an 8.6% population-averaged reduction in AD purchasing is estimated. With the richest possible covariate set (set 4) that includes time constant (sex, language, and education) and time-varying covariates (income, household status, other drug purchases, and previous AD purchases) suggesting that the intervention reduces AD purchasing by 5%.

Covariate sets 3 and 5 adjust for unobserved time-constant individual characteristics by including intercepts into the models. These covariate sets did not find an effect, suggesting that reducing unemployment among those who have experienced unemployment may not reduce AD purchases. Including time-varying variables into the covariate set attenuates effect estimates both when added to the covariate set without individual intercepts (set 2 to set 4) and to the covariate set with individual intercepts (set 3 to set 5).

Subgroup and sensitivity analyses

The differences found between the covariate sets largely persisted in our subgroup analysis, being present within each sex by education stratum (Table 4). In the covariate sets without individual intercepts (1, 2 and 4), effect estimates of the intervention are stronger for the low educated compared to the high educated, and are closer to a null effect for women than for men. Reflecting the overall analysis, null effects are found for all subgroups when including individual intercepts (sets 3 and 5).

Time-constant factors, as measured by comparing the 75% quantile of individual intercepts from the model for AD purchasing with the 25% quantile, are associated with a 3.3 percentage point increase in person-years with antidepressants. Comparing the same quantiles using individual intercepts from the model for unemployment showed that they are associated with a 7.8 percentage point increase. For comparison, the 75% and 25% quantiles for personal income are associated with a 0.2 percentage point increase in AD purchasing and a 1 percentage point increase in unemployment.

Comparing the effect of employment on personal income from a model without individual intercepts (set 4) with a model that includes individual intercepts (set 5), we find that the coefficient of unemployment on income is 30% smaller in the model with individual intercepts (see supplemental material).

Finally, findings for the effect of a no-unemployment scenario on person-years with at least one hospitalization due to injury or accident are similar to those with AD purchasing as an outcome. The no-unemployment effect on hospitalization due to injury or accidents is stronger than for AD purchasing, but the sets including individual-level fixed effects (3 and 5) also do not find an effect despite high precision (Figure 3).

Discussion

The estimated effect of unemployment on depression may be biased by time-varying, intermediate, and time-constant confounding. The parametric g-formula is one of the few methods that can account for these sources of bias, but has previously required that all relevant confounders are measured. For the first time, we combine the g-formula with methods to adjust for unmeasured time-constant confounding. We estimate the effect of a hypothetical intervention which sets all unemployed person-years (10.2% of all person-years) to employed on antidepressant purchasing. The covariate sets that do not include individual-level fixed effect intercepts estimate a reduction in the number of person-years with antidepressant purchasing, when compared to the natural course. The reduction is estimated to be 5 percentage points (95% CI: 2.5 to 7.4%), population-averaged, in the covariate set that includes time-varying covariates and which most closely follows our assumed DAG. However, when including individual-level fixed-effect intercepts, to remove unmeasured time-constant confounding, no effect is found. It is estimated as -0.1 percentage points (95% CI: -1.8 to 1.5%) for the covariate set that also includes time-varying covariates.

Strengths & limitations

We use an 11% random sample from high quality Finnish register data. Since missingness on covariates is very small (< 1%) we do not use missing data imputation methods. The exception is employment status (employed, unemployed, retired, or other), which has 4.6% missingness. Using a multiple imputation procedure for this variable, including all time-constant and time-varying covariates, does not substantially alter the findings of this study. Because our study follows a closed cohort of individuals (aged 30-35 at the start of follow-up), and we include age as a categorical variable in the study, we do not also include calendar time as a covariate. Furthermore, our natural course scenario closely approximates empirical antidepressant purchases, and all other time-varying covariates, which indicates that our models are not grossly misspecified.[5,16]

Antidepressant purchases do not perfectly indicate the presence of depression, but rather a diagnosis of depression. Individuals that become employed may receive access to occupational health services, which increases the probability of a depression diagnosis. This would negatively bias the estimates provided in Figure 2. Thereby, it would in part explain why the point estimates of the models with individual intercepts (sets 3 and 5) suggest an increase in antidepressant purchases (Figure 2), while not doing so in the sensitivity analysis where hospitalization due to injuries and accidents replaces antidepressant purchasing as an outcome (Figure 3).

The causal claims of this study rely on three fundamental assumptions: consistency, positivity, and no unmeasured confounding.[20-22] The consistency assumption requires that there are no different versions of the exposure that have different effects on the outcome. Strictly speaking, different types of employment may have different effects on mental health, which affects the generalizability of our study. We reflect on this in later paragraphs. The positivity assumption requires that observed treatment levels vary within confounder strata. In our empirical data, employment status varies within the strata of all measured covariates. Importantly, although some source of time-varying confounding may remain unobserved, our study adjusts for unmeasured time-constant confounding using individual-level fixed effect intercepts as well as observed time-varying confounding. To the best of our knowledge, we are the first to do so using the parametric g-formula.

Unemployment and antidepressant purchasing

When not adjusting for all time-constant confounding, i.e. by not including individual-level fixed effect intercepts, we estimate that employment is associated with a reduction in antidepressant purchases. The multivariate model with time-varying covariates estimates a 0.9 reduction in antidepressant purchasing, but this estimate is conditional on holding constant potential intermediate confounders, such as income and household status. Allowing for mediation in the g-formula, we find a 5% population-averaged reduction in antidepressant purchasing.

In the subgroup analysis, the intervention effect is somewhat stronger among the low educated. This finding is corroborated by other studies, and may be caused by loss of self-esteem and workplace social contacts more strongly affecting the lower educated.[5,23,24] Similarly, the association being stronger for men than women aligns with other studies, and may be explained by differences in gender roles, with men experiencing more psychological pressure to be employed.[5-25-28]

Unfortunately, the findings reported in this paragraph may overestimate the effect of unemployment on antidepressant purchases and depression, due to the presence of unmeasured time-constant confounders, such as problem behavior.

Unmeasured time-constant confounding

Our findings indicate the presence strong time-constant factors that determine both unemployment and antidepressant purchasing. As measured through the fixed effect intercepts, the relationship between unmeasured time-constant factors and both antidepressant purchasing and unemployment is very strong when compared to the coefficients of all other covariates in the multivariate models. When including these individual intercepts, we find that the effect estimate moves towards the null. As indicated by our subgroup analysis, the null effect is also found across educational and sex strata.

The validity of our approach was supported by an assessment of the impact of including individual-level intercepts on the association between employment status and income. It is well known that unemployment results in loss of personal income. Therefore, the effect on income should be captured in both the models with and without individual-level fixed effect intercepts. Indeed, in contrast to our findings regarding unemployment and antidepressant purchases, including individual intercepts only reduced the coefficient of unemployment on income by 30%.

In the sensitivity analysis where we replace antidepressant purchasing with injuries and accidents as the outcome variable, conclusions reflect those of the main analysis. Not adjusting for individual intercepts results in an intervention effect that reduces injuries and accidents, but adjusting for individual-level intercepts results in a null estimate. This finding is important because unemployment and hospitalization due to injuries and accidents are likely to be partly affected by time-constant factors similar to those that also affect unemployment and depression, such as problem behavior.[29,30] At the same time hospitalization due to injuries and accidents as an outcome is less sensitive to selection through care-seeking behavior, compared to antidepressant purchasing. Individuals with a lower socio-economic status are less to likely to seek treatment for mental health problems or have poorer access to good medical care, which decreases the probability of a diagnosis and thereby an antidepressant purchase.[31] Our subgroup analysis implies that socio-economic differences in care-seeking do not explain our results.

The unemployment effect

The association between employment status and antidepressant purchasing appears to be explained by time-constant factors that make individuals both more prone to be unemployed and depressed. The findings of our study corroborate those of other studies that found no effects of unemployment on mental health when including individual intercepts to adjust for time-constant confounding.[32-33] A third study using individual intercepts found only weak effects of unemployment on health, and large selection into unemployment and poor health.[34] However, it is important to note that adding individual intercepts to the modelling procedure also changes the meaning of the coefficients in the multivariate models, and thereby the results of a g-formula procedure that uses these coefficients. When including individual-level fixed effect intercepts, the only observations that contribute to the estimation of relevant coefficients are those where the exposure varies over time.[17] In our study, on average 10.2% of person-years were unemployed, and roughly half of all individuals were continuously employed throughout the study. Individuals in the age-range 30-55 that spent a year unemployed are likely to be qualitatively different from individuals that have not spent any time unemployed (as measured annually). The type of employment that they can obtain may also differ qualitatively. Individuals that switch regularly between unemployment and employment are more likely to experience precarious employment. Various studies have found that those in precarious employment, such as temporary employment or employment with weak social protections, and those transferring to such jobs, have higher mental health risks than those in non-precarious employment.[35-38] This is not to imply that the estimates of the covariate sets with individual intercepts should be disregarded. Some employment interventions may result in less fulfilling and more precarious forms of employment and may therefore be better approximated by the g-formula with individual intercepts. Therefore, at the very least, when the aim of an employment intervention is to improve mental health, consideration should be given to the exact nature of the kind of job that is created.

Conclusion

This is the first study – of any exposure or outcome – to combine individual-level fixed effect estimation with the parametric g-formula in order to adjust for unobserved time-constant confounding. We use this method to study the impact of unemployment on depression. At the population-level, without fixed effects, we find that in a scenario where everyone is employed (10.2% employed person-years set to 0%), there is a substantial reduction in antidepressant purchasing. However, when we include individual-level fixed effect intercepts, we estimate a null effect. We argue that this null effect not only arises due to the adjustment for time-constant confounding, but also due to a change in the meaning and generalizability of the effect of employment in fixed effects models.

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	Included covariates		
Covariate set	*Time constant*	*Time varying*	*Individual Intercepts*
Set 1			
Set 2	**X**		
Set 3			**X**
Set 4	**X**	**X**	
Set 5		**X**	**X**

Table 1. Covariates included in the 5 different covariate sets (model 1 only includes the primary exposure: unemployment status).

Variables	% Person-years in category	Model without individual intercepts		Model with individual intercepts	
		Estimate (log OR)	**95% CI**	**Estimate (log OR)**	**95% CI**
Time constant variables					
Sex (female)	50%	0.010	0.009 to 0.011		
Education					
Lower Secondary	18%	0.000	-0.001 to 0.002		
Higher Secondary	48%	-0.002	-0.003 to -0.001		
Lower Tertiary	24%	-	-		
Higher Tertiary	9%	0.004	0.002 to 0.006		
Time varying variables (not lagged)					
Age					
Age 30-34	24%	-		-	-
Age 35-39	23%	0.006	0.004 to 0.008	0.011	0.009 to 0.013
Age 40-44	21%	0.015	0.013 to 0.017	0.026	0.024 to 0.028
Age 45-49	20%	0.017	0.015 to 0.019	0.038	0.036 to 0.040
Age 50-52	13%	0.010	0.008 to 0.012	0.038	0.036 to 0.041
Time varying variables (1 year lagged)					
Employment Status					
Unemployed	10%	0.009	0.005 to 0.013	0.003	-0.002 to 0.007
Employed	81%	-	-	-	-
Other	2%	0.004	-0.004 to 0.011	-0.006	-0.013 to 0.002
Retired	4%	0.039	0.032 to 0.047	-0.008	-0.019 to 0.003

Household Status					
With Parents	4%	-0.009	-0.011 to -0.006	0.003	-0.001 to 0.007
Single	18%	-	-	-	-
Cohabiting without Children	6%	-0.002	-0.005 to 0.001	0.002	-0.001 to 0.004
Cohabiting with Children	9%	-0.004	-0.007 to -0.002	0.001	-0.001 to 0.004
Married without Children	8%	-0.003	-0.006 to 0.000	0.004	0.001 to 0.006
Married with Children	54%	-0.005	-0.007 to -0.003	0.005	0.003 to 0.007
Income (per 100,000 euro)					
Personal Income		-0.012	-0.012 to -0.012	-0.010	-0.010 to -0.010
Household Income		-0.009	-0.009 to -0.009	0.006	0.006 to 0.006
Antidepressant Purchase	8%	0.659	0.657 to 0.660	0.402	0.400 to 0.404

Table 2. Partial table of coefficients from covariate sets 4 and 5 (see supplemental material for full tables).

Variable	Individuals	Person-years
Antidepressant purchase	28.7%	4.4%
Employment status	50.9%	10.8%
Household status	65.4%	7.8%
Income	99.6%	99.3%

Table 3. Transitions in key variables. Percentage of individuals (total = 49,753) with at least one transition, and number of person-years (total = 826,526) representing a transition.

Men				
	Low educated		**High educated**	
Covariate set	*% Reduction*	*95% CI*	*% Reduction*	*95% CI*
Set 1	8.7%	5.8% to 11.5%	7.8%	2.8% to 12.6%
Set 2	21.6%	18.1% to 24.9%	10.5%	4.1% to 16.8%
Set 3	0.2%	-2.3% to 2.7%	-0.3%	-4.4% to 3.7%
Set 4	9.9%	5.4% to 14.2%	2.9%	-5.6% to 11.0%
Set 5	1.0%	-2.3% to 4.0%	0.3%	-5.5% to 5.8%

Women				
	Low educated		**High educated**	
Covariate set	*% Reduction*	*95% CI*	*% Reduction*	*95% CI*
Set 1	9.0%	5.9% to 12.0%	8.2%	4.3% to 12.3%
Set 2	9.8%	6.8% to 12.7%	4.3%	0.4% to 8.1%
Set 3	-1.6%	-3.6% to 0.3%	-1.0%	-3.8% to 1.7%
Set 4	4.4%	0.7% to 8.0%	0.8%	-4.5% to 5.8%
Set 5	-0.9%	-3.5% to 1.5%	-0.5%	-3.9% to 2.9%

Table 4. The effect of making all unemployed person-years employed on person-years of antidepressant purchasing (negative values indicate an increase) by subgroup.

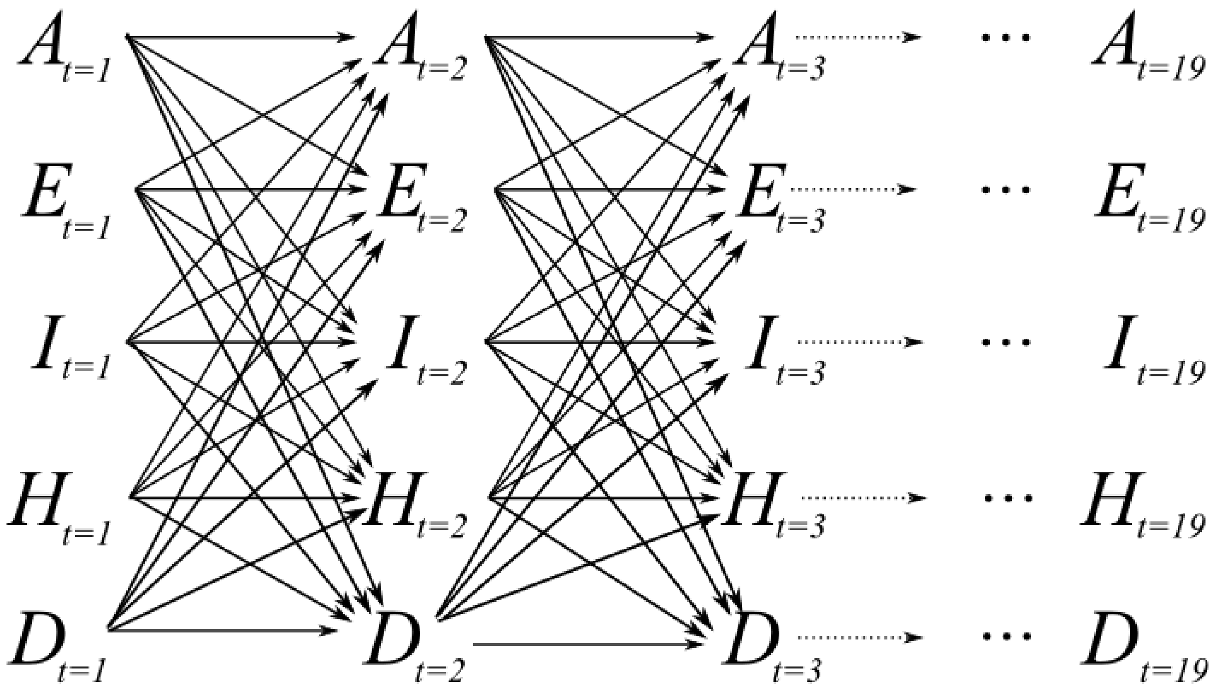

Figure 1. Assumed causal directed acyclic graph (DAG). A, E, I, H and D represent antidepressant purchasing, employment status, income, household status, and (other) drug purchases, respectively. Time-constant variables (not shown) were allowed to affect all time-varying variables.

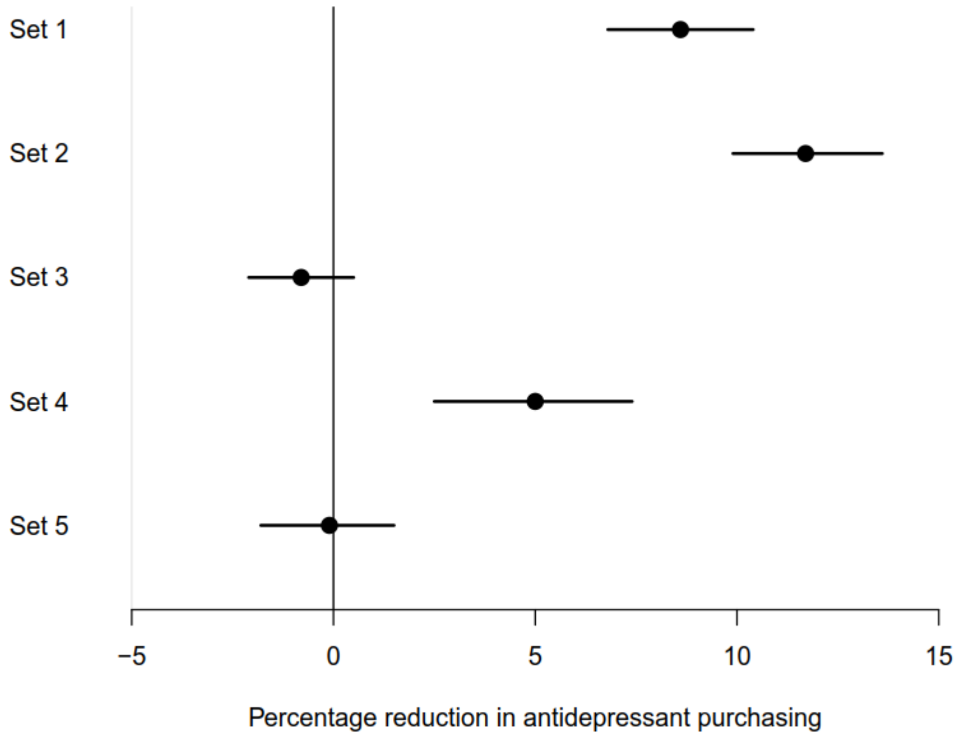

Figure 2. Forest plot of the population-averaged effect of making all unemployed person-years employed on person-years of antidepressant purchasing (negative values indicate an increase).

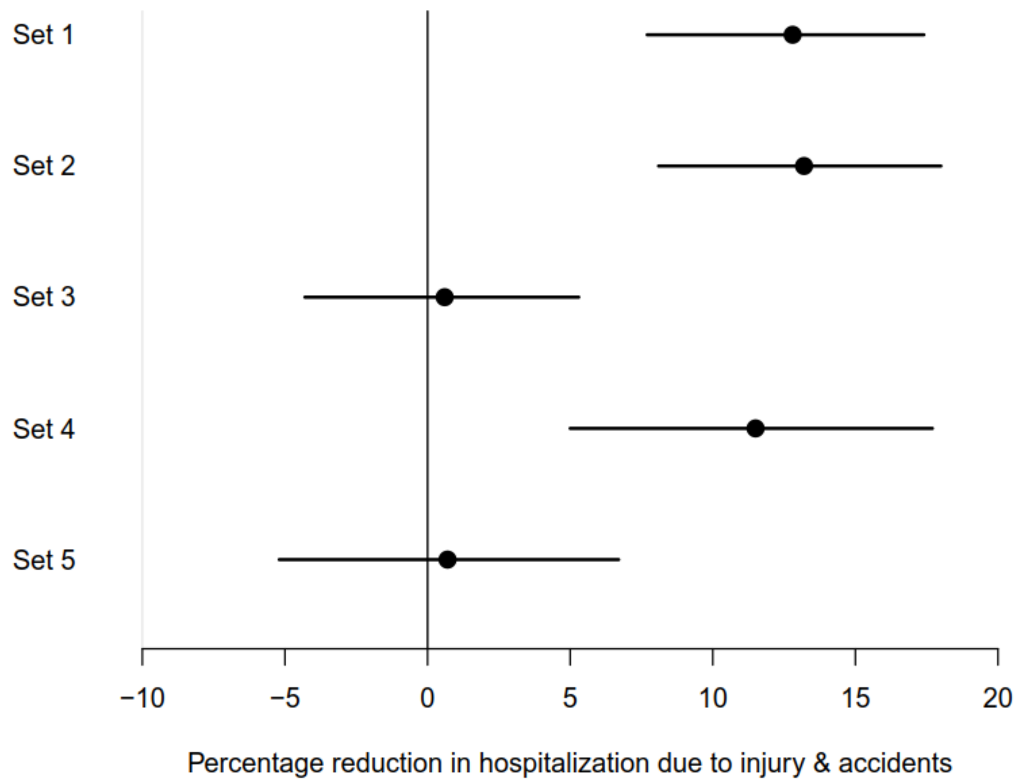

Figure 3. The population-averaged effect of making all unemployed person-years employed on annual person-years with hospitalization due to injury or accident (negative values indicate an increase).