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Prenatal exposure to the German food crisis 1944–1948 and health after 65 years

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Abstract:

Using data on 90% of the German population, we investigate the long-term relationship between intra-uterine exposure to the German food crisis 1944–1948 and 16 doctordiagnosed health conditions at age 60 to 70. We find elevated risks of being diagnosed with a wide range of conditions, including diabetes, depression, lung disease, and back pain. In terms of critical periods, malnutrition in the first trimester of pregnancy appears to have the strongest negative correlation with health at older ages.

Zusammenfassung:

Wir nutzen Daten von 90% der deutschen Bevölkerung um den langfristigen Zusammenhang zwischen intrauteriner Mangelernährung nach dem Zweiten Weltkrieg und 16 ärztlich diagnostizierten Krankheiten im Alter von 60 bis 70 Jahren zu untersuchen. Dabei stellen wir ein erhöhtes Risiko in Bezug auf die Diagnose einer Vielzahl von Erkrankungen, einschließlich Diabetes, Depressionen, Lungenerkrankungen und Rückenschmerzen fest. Die kritischste Phase bezüglich der negativen Auswirkungen scheint das erste Schwangerschaftsdrittel zu sein.

Keywords:

Fetal origins, Nutrition, Health, Aging

JEL Classification:

I15, N34

Prenatal exposure to the German food crisis 1944–1948 and health after 65 years

Hendrik Jürges * & Thomas Kopetsch†

2 Nov 2018

Abstract

Using data on 90% of the German population, we investigate the long-term relationship between intra-uterine exposure to the German food crisis 1944–1948 and 16 doctor-diagnosed health conditions at age 60 to 70. We find elevated risks of being diagnosed with a wide range of conditions, including diabetes, depression, lung disease, and back pain. In terms of critical periods, malnutrition in the first trimester of pregnancy appears to have the strongest negative correlation with health at older ages.

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1 Introduction

This paper provides empirical evidence on the link between intrauterine malnutrition and later-life outcomes by studying the post-World War II food crisis 1944–1948 in Germany. It aims at documenting long-term associations of being born during this period with health outcomes measured 65 years later, thereby contributing to the large medical literature on the developmental origins of conditions such as cardiovascular disease, diabetes, or depression (see Lumey et al. (2011) for a comprehensive overview), and on to an emerging economic literature on non-health outcomes such as educational attainment or income. Recent contributions include Chen and Zhou (2007) studying the Chinese famine 1959–1961, Neelsen and Stratmann (2011) studying Greece during the German occupation in World War II, or Scholte et al. (2015) studying the Dutch famine 1944–45, also due to the German occupation.

Compared to other war-related famines, in particular the Dutch famine, the Leningrad siege, or the Chinese famine, the German food crises is not much studied to date. Earlier work has demonstrated that prenatal exposure to the food crisis was associated with impaired socio-economic outcomes, such as lower educational achievement, lower occupational status, and lower income (Jürges; 2013). Our contribution to the literature is threefold. First, to the best of our knowledge no systematic analyses have been conducted linking exposure to the German food crisis and health outcomes in general or morbidity rates for specific conditions in particular. Thus we add an independent study population to the existing literature. Second, we use the same data and methodology to study the link between 16 ICD-coded doctor diagnosed conditions and the prenatal environment, providing the most comprehensive study to date in terms of the range of diagnoses. Most previous studies concentrate on single conditions. While on the one hand, this allows a thorough discussion of possible biological pathways, it precludes a broader understanding of the possible effects of intrauterine malnutrition. Our choice of conditions under study was largely guided by the literature, especially the overview given by Lumey et al. (2011), and includes diabetes, coronary heart disease, depression, and cancer. However, we also included some conditions that have not been studied before and for which biological pathways have not yet been discussed, such as lower back pain. Third, we used

a large administrative data set, covering 90 percent of the German population. This is the largest data set ever used to study the link between intrauterine malnutrition and long-term health outcomes. Its analysis allows us to provide statistically more robust evidence on such associations than the existing literature.

The German food crisis after the Second World War lasted from late 1944 to early 1948.[1] It was most severe shortly after the end of the war. The main reasons were the loss of agricultural areas in the former Eastern provinces, immediate war consequences such as destruction of machinery, transport infrastructure, and the inflow of some 12 million refugees from the Eastern provinces (Pomerania, Silesia, East Prussia) and other East European countries (e.g., Sudetenland). The contemporary medical literature has described quantitative and qualitative (particularly protein) malnutrition, low birth weight, high infant mortality, growth problems, and an increased susceptibility to infections as the main medical problems caused by shortage of food after World War II (Droese and Rominger; 1949).

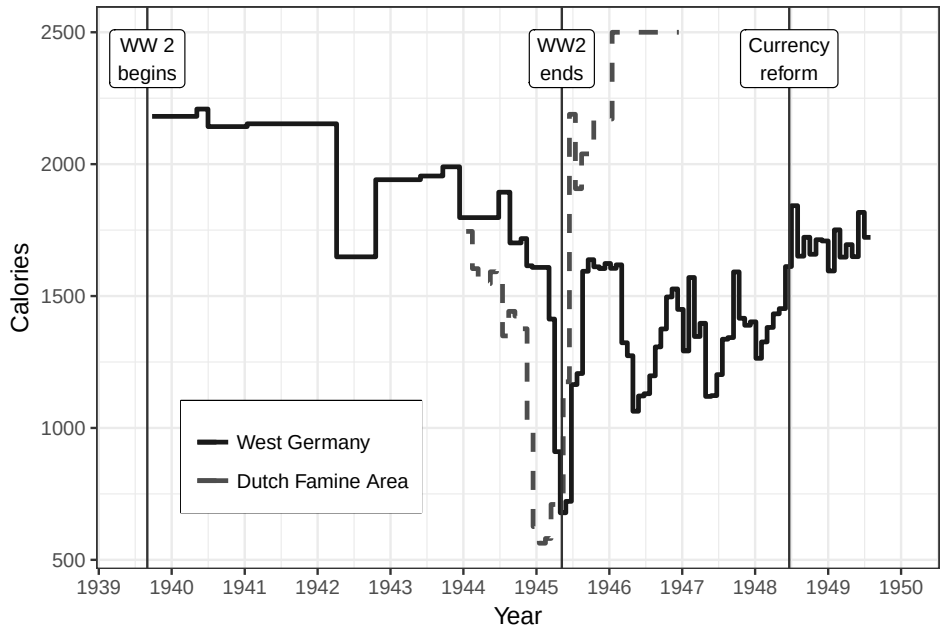

Figure 1: Average daily allowances according to food ration cards. Data are for Wuppertal (September 1939 to August 1944, allocation periods 1 to 65), Düsseldorf and Wuppertal (September 1944 to May 1947, allocation periods 66 to 101), Düsseldorf (June 1947 to November 1947, allocation periods 102 to 107) and Northrhine-Westphalia (December 1947 to August 1949, allocation periods 108 to 129). *Sources:* Sons; 1983, Table 11, Schön; 1947, Stein et al.; 1975 (Netherlands).

[1]Here we give a brief introduction. More detailed accounts can be found in Jürges (2013) or Kesternich et al. (2015).

Figure 1 illustrates the timing and extent of the food crisis compared to the well-studied Dutch famine (also an immediate consequence of the war). It shows average daily calories according to food ration cards from 1939 to 1950 in a specific region of Germany. Food was rationed throughout the war, but on a fairly high level. Food supply began to fall dramatically by the end of 1944, and reached its minimum in April – July 1945 when according to food ration cards, less than 800 calories per day were allocated to each adult on average. The situation improved quickly in the fall of 1945 but deteriorated again each following spring for the next three years. The key insight is that – as already acknowledged by contemporary research – "difficulties of ordinary life, particularly shopping for food, [...] reached their most serious point in 1945, at the end of the war, and immediately after it" (Dean; 1951, p. 371).

2 Data and Methods

Our main data source is the universe of 2009 ambulatory care health insurance claims in the German statutory health insurance. These data were supplied by the National Association of Statutory Health Insurance Physicians (KBV). We use the claims of all statutorily insured German citizens born between 1930 and 1959 with at least one claim in 2009 ($N = 23.6m$).[2] Comparison with population statistics (Statistisches Bundesamt (Destatis); 2017) shows that the 2009 claims data cover 97.6% of all statutorily insured women and 92.0% of all statutorily insured men in these cohorts. Each claim contains information on primary and secondary diagnoses pertinent to that claim in ICD-10 format. Strictly speaking, our data reflect the probability of generating a claim to the statutory health insurance related to a specific ICD-10 code rather than one-year or even lifetime prevalence. Thus we will generally speak of morbidity rates. We aggregated individual claims into grouped data time series with the number of individuals having a condition on record, and the total number of individuals, for each year and month of birth, starting in January 1930 and ending in December 1959. As noted in the

[2] In Germany the account for the outpatient treatment of statutorily insured patients is initially settled between the office-based doctor carrying out the treatment and the local association of statutory health insurance physicians (Kassenärztliche Vereinigung – KV), membership of which is compulsory for all office-based doctors in that region. The basis for the doctor's account is a document recording the treatment data, including information about the patient, the diagnoses and the services performed. A copy of this document is sent to the National Association of Statutory Health Insurance Physicians (Kassenärztliche Bundesvereinigung – KBV), the original being forwarded to the patient's statutory health insurance organisation for payment.

introduction, the choice of diseases was largely guided by the existing literature. The second data source contains average daily caloric and nutrient intake in (Western) Germany between 1939 and 1949, which was derived from monthly food rations for adults (Schön; 1947; Sons; 1983), see Figure 1.

Our analysis consists of two steps. First, we study whether individuals born in certain months during the observation window have substantially (and significantly) higher morbidity rates than predicted by a smooth general cohort (or equivalently, age) trend and by season-of-birth. Essentially this is a straightforward time-series decomposition, where our primary object of interest is the remainder or prediction error. While there are several different ways of decomposing time-series data, we have chosen a log-binomial parametric regression approach:[3]

$$\ln(\pi_{y,c}) = f(c) + \mu_{m\times c} + \beta_x \mathbb{I}(c = x) + \varepsilon_c \tag{1}$$

where $\pi_{y,c}$ denotes the proportion of individuals in month-of-birth cohort c diagnosed with condition y. $f(c)$ is a global non-linear birth cohort trend (modeled as a higher-order polynomial, where the order was chosen by leave-one-out cross-validation). $\mu_{m\times c}$ is a set of month-of-year dummy variables m (January, February, ..., December) and a linear interaction of each month-of-year dummy m with c, which captures general seasonal fluctuations and their possible changes over time. $\mathbb{I}(c = x)$ is an indicator variable for one specific month of birth cohort x and ε_c is the error term. $\exp(\beta_x)$ gives the morbidity rate ratio of diagnosis y among individuals of month-of-birth cohort $c = x$ compared to the long-term (higher-order polynomial) trend and general season-of-birth fluctuations. We compute $\exp(\beta_x)$ for each month-of-birth cohort in our data, estimating equation (1) 360 times. This procedure allows us to compute point estimates and confidence intervals for the morbidity rate ratio $\exp(\beta_x)$ for each cohort c essentially from a leave-one-out specification.

The second step of our analysis is to study possible critical periods in terms of intrauterine malnutrition. We match month-of-birth cohorts to the availability of calories at different

[3]One alternative is seasonal decomposition of time series by loess, or STL (Cleveland et al.; 1990), which in our case leads to similar results. However, computing standard errors and confidence intervals for the remainder of the time series is more straightforward in the context of our approach. STL results can be found in the Appendix, Figures A.6 and A.5.

phases of pregnancy. We restrict this analysis to births within the period January 1942 to December 1949 because only in this period there is sufficient variation in the rationing of food (see Figure 1). We then estimate similar models as above, replacing $\mathbb{I}(c = x)$ by X_{c-t}, which measures the availability of nutrients X in month $c - t$, where t indicates the time lag between the assessed exposure and birth in months.:

$$\ln(\pi_{y,c}) = f(c) + \mu_{m \times c} + \gamma_t X_{c-t} + \varepsilon_c \tag{2}$$

To ease the interpretation, X_{c-t} is defined as the difference in available calories between January 1942 (when food supply was still sufficient) and month $c - t$. In words, γ_t estimates the partial association (controlling for long-term trends and seasonal influences) of the *lack of macronutrients* in different months of pregnancy with the excess morbidity in later life. We show the different coefficients $\gamma_t, t = 0, \ldots, 9$ to provide evidence regarding the importance of deprivation in early compared to late pregnancy.

3 Results

Figure 2 shows the number of observations in our data, i.e. the number of German citizens with at least on statutory health insurance claim in 2009, in each month-year-cohort, separately for men and women. The numbers clearly reflect the influence of historical events and World War II on fertility and infant mortality. Following a period of low fertility in the early 1930s during the Great Depression, the late 1930s were characterized by comparatively high fertility, spurred by a pro-natalist Nazi ideology. The peak number of observations is found among those born early 1940 and thus conceived before the war. The run-up to and the beginning of the war in the East in June 1941 appears to have caused a significant drop in the number of births. In contrast to the brief periods of fighting following the attacks on Poland and France, the fighting in the USSR proved to be long and fierce and eventually led to a large number of casualties. The smallest number of observations can be found among those born between April 1945 and February 1946. In terms of the time when these individuals were conceived, this corresponds to the period between the Allied invasion in Normandy and the German capitulation, i.e. when

German men were fighting on two fronts. Moreover, especially in the final months of the war, infant mortality was very high. A great number of children born in that period may thus not have survived. In January/February 1946, i.e. exactly nine months after the German capitulation, the number of observations rises steeply. This increase is obviously related to the great number of men returning home from the war.[4]

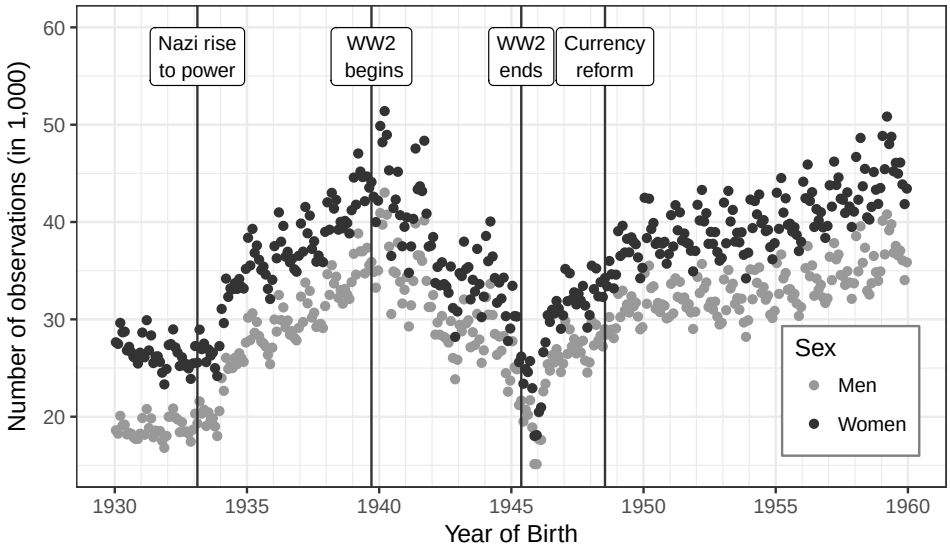

Figure 2: Number of observations, by sex and birth-month cohort. *Source:* own computation based on KBV claims data.

ICD-coded diagnoses and their raw morbidity rates for the entire sample as estimated from the claims data are shown in Table 1. Morbidity rates are of the same order of magnitude in women and men (also see Table 1), but there are also exceptions: Ischemic heart disease is about twice as prevalent among men, whereas depression is more than twice as prevalent and urogenital conditions are about 60% more prevalent among women.

The analyses described above produce very large amounts of output. They are run for each sex and condition, which yields a total of $2 \times 16 \times 3$ sets of output (raw data, morbidity rate ratios, correlation structure with lagged nutrition). All results are shown graphically. To alleviate concerns of multiple testing, we show a Manhattan plot of all p-values of the predictions errors obtained from equation 1.

[4]The US began to release their approximately 3 million German prisoners of war as early as mid May 1945.

Table 1: Diagnoses and Morbidity Rates in Percent, by sex*

ICD-10	Diagnosis	Men	Women
I10-I15	Hypertension	57.4	55.4
I20-I25	Ischemic heart disease	19.4	10.7
I60-I69	Cerebrovascular Disease	8.9	6.7
C00-C97	Malignant neoplasms	11.8	10.0
E10-E15	Diabetes mellitus	23.7	17.7
E66	Obesity	13.2	16.5
E78	Disorders of lipoprotein metabolism	40.0	37.6
J40-J47	Chronic lower respiratory diseases	19.9	19.0
F30-F39	Depression	10.9	21.6
F00-F03	Dementia	2.0	1.9
F20-F29	Schizophrenia	1.2	1.7
F70-F79	Mental retardation	0.6	0.5
M00-M99	Diseases of the musculoskeletal system	65.0	72.1
M54	Low back pain	33.4	39.8
N00-N99	Diseases of the genitourinary system	35.0	56.5
K00-K93	Diseases of the digestive system	42.1	41.2

* Numerator contains only those with at least one claim. *Source:* own computation based on KBV claims data.

3.1 Results for Women

Figure 3 shows the raw morbidity rates calculated for 16 (groups of) conditions in 2009, by year and month of birth. Grey lines (not always visible) show the long-term trends estimated from high-order polynomials. Most conditions show morbidity rates that are monotonically increasing in age (decreasing in year of birth). One important exception are urogenital disorders, which are decreasing in age. Some conditions, including depression, back pain, lung disease, and obesity show non-monotonic age trends. This finding points to the fact that morbidity rates, as measured in our data, do not equal life-time prevalence but rather reflects being treated for a disorder in a specific year. For instance, conditions like back pain or depression are possibly more likely diagnosed and treated when individuals are still in the labor market. The sudden decrease in the percentage treated for lower back pain or depression for women born before 1950 possibly reflects a "retirement effect". Back pain and depression are among the most important drivers of early retirement (on disability pensions) in Germany (Börsch-Supan and Jürges; 2011), but to become eligible for disability pensions, a certified diagnosis is mandatory. In 2009, most working women could draw an old-age pension at age 60, so that retirement was possible without being diagnosed.

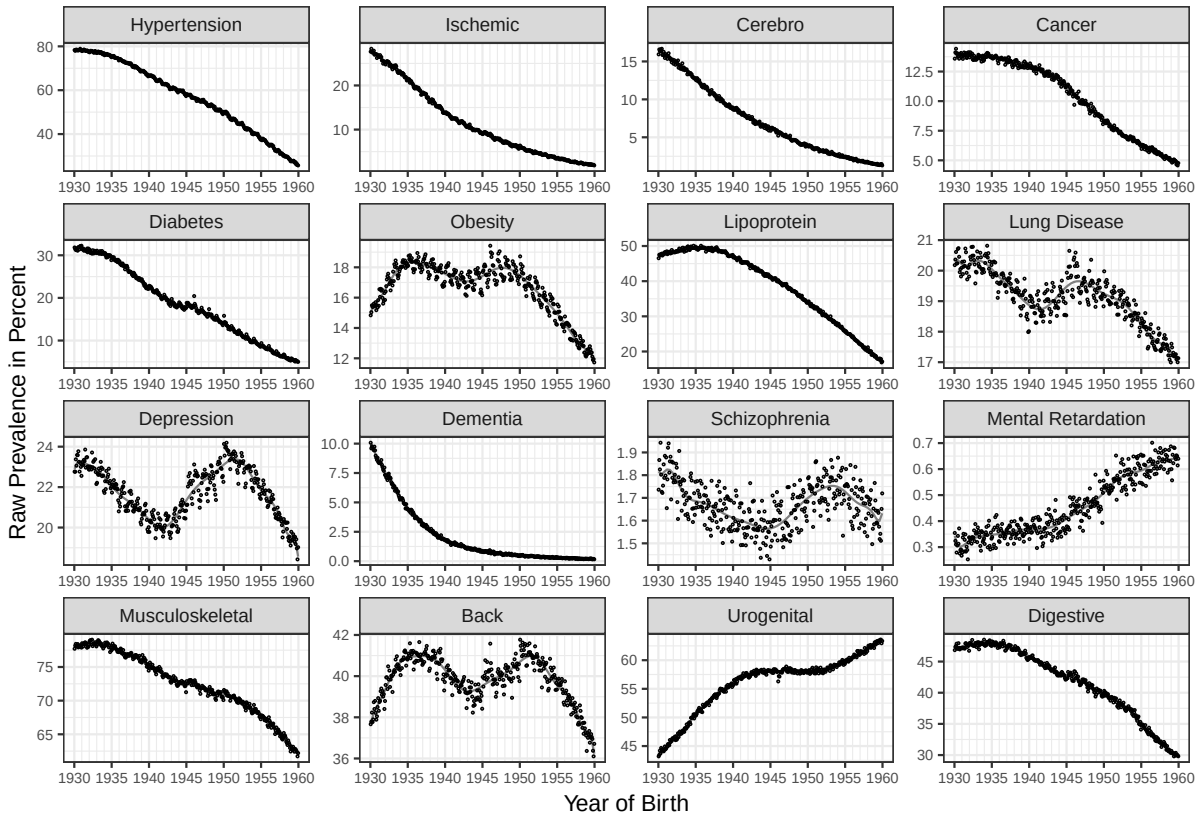

Figure 3: Raw morbidity rates by year and month of birth, women, 2009. *Source:* own computation based on KBV claims data.

Our main interest, however, does not lie in long-term trends, which may be subject to many different influences. Rather, we are interested in short-term deviations from those long-term trends. They are estimated from Equation (1) and shown in Figure 4. To avoid clutter, we show 95% and 99% confidence intervals only for those months of births where the morbidity rate ratio is significantly different from one at the 1% level. Even without prior knowledge about the food crisis, inspection of Figure 4 clearly suggests that cohorts born in 1945 and shortly after are exceptional. We find particularly high morbidity rate ratios for diabetes (1.11), obesity (1.07), lung disease (1.06), depression (1.07), dementia (1.26) and lower back pain (1.04), and exceptionally *low* morbidity rate ratios for cancers (0.93) and urogenital disorders (0.97).

Closer inspection of the months with the highest morbidity rate ratios reveals an astonishing congruence: for four of the 16 disorders shown in Figure 3, the peak month of birth in terms of morbidity rate ratios is January 1946 (diabetes, obesity, depression, lower back pain), and for seven disorders (the four just mentioned plus lung disease, musculoskeletal disorders

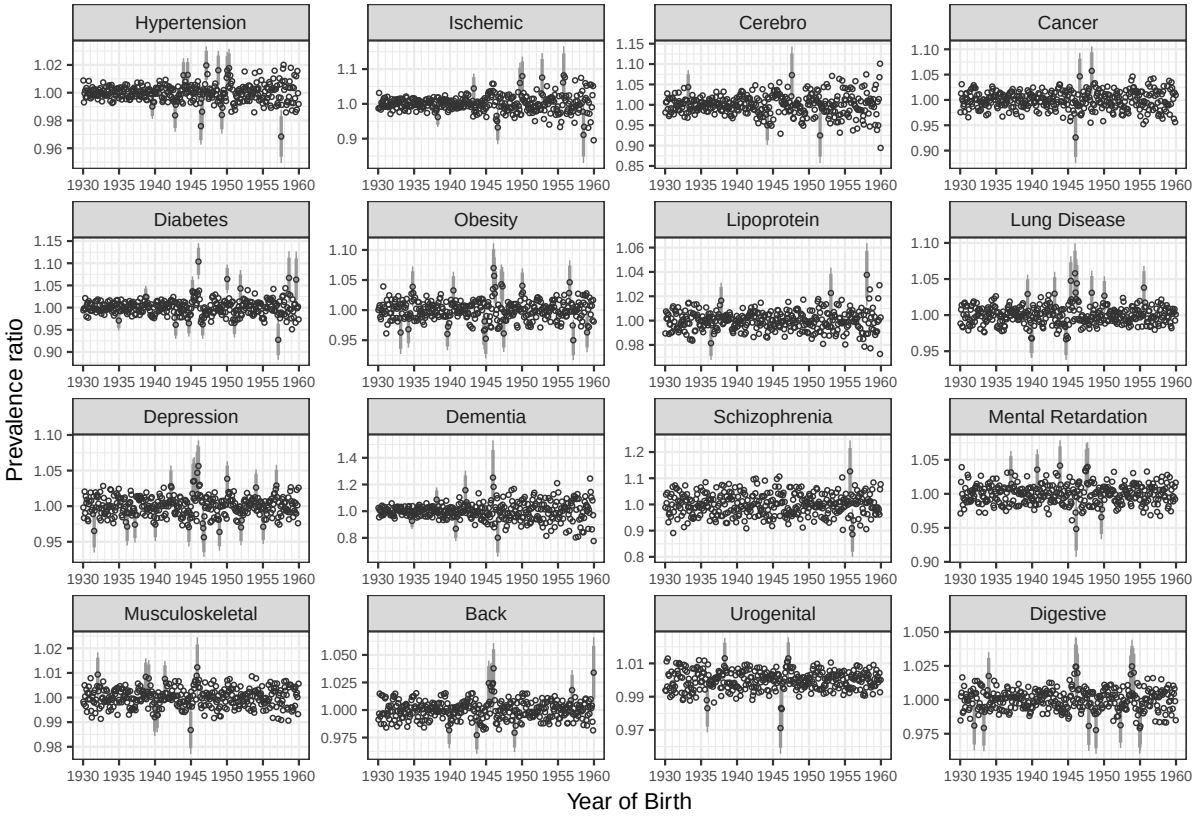

Figure 4: Excess morbidity rates, by year and month of birth; women 2009. Error bars indicate 95% (thick) and 99% (thin) confidence intervals only if estimated excess morbidity rates are significant at the 1% level. *Source:* own computation based on KBV claims data.

and dementia it is the period November 1945 to January 1946. For schizophrenia and digestive disorders, November 1945 and January 1946, respectively are the birth months with the second largest morbidity rate ratios.

We now bring together our finding that women born November 1945 to January 1946 have the highest morbidity rate ratios for many disorders and the data on available calories shown in Figure 1, which have their lowest values in May–July 1945. The time difference between the trough in calories and the peak in excess morbidity suggests that it is intrauterine malnutrition in the *first* few months of pregnancy that is of particular importance.

Figure 5 shows the partial associations, net of general trends and month of birth effects, between lack of calories 0 to 9 months before birth and the likelihood of having some condition, as estimated from Equation (2). Thick error bars indicate ±1 standard error and thin error bars indicate ±2 standard errors, respectively. Calories were scaled for convenience so that the plotted associations show the morbidity rate ratio associated with a 500 calorie reduction. As an example, consider the morbidity rate ratio for ischemic heart disease of 1.03, six months before birth. This means that each 500 calories reduction in available food in the fourth month of pregnancy is associated with a (significant) increase in the morbidity rate of ischemic heart disease of 3 percent.

This more systematic analysis of the data clearly shows that for cardiovascular conditions such as hypertension and ischemic heart disease, for metabolic diseases such as diabetes, for mental health problems such as depression and even for musculoskeletal disease in general and lower back pain in particular, the strongest links can be found for lack of available food five to eight months prior to birth. This strongly supports the notion that the first trimester or first half of pregnancy might be the most critical period with respect to the developmental origins of disease. This also holds for cancer and urogenital disease but in the opposite direction. Here, reduced availability of calories at the beginning of pregnancy is linked with lower morbidity rates. We can also identify a third group of conditions, where both early and late pregnancy nutrition seem to matter, but in different directions. This pattern is most prominent for obesity, where we find almost equally strong but opposite associations in early and late

pregnancy: reduced food availability in early pregnancy is linked with higher morbidity rates, whereas reduced food availability in late pregnancy is linked with lower morbidity rates.

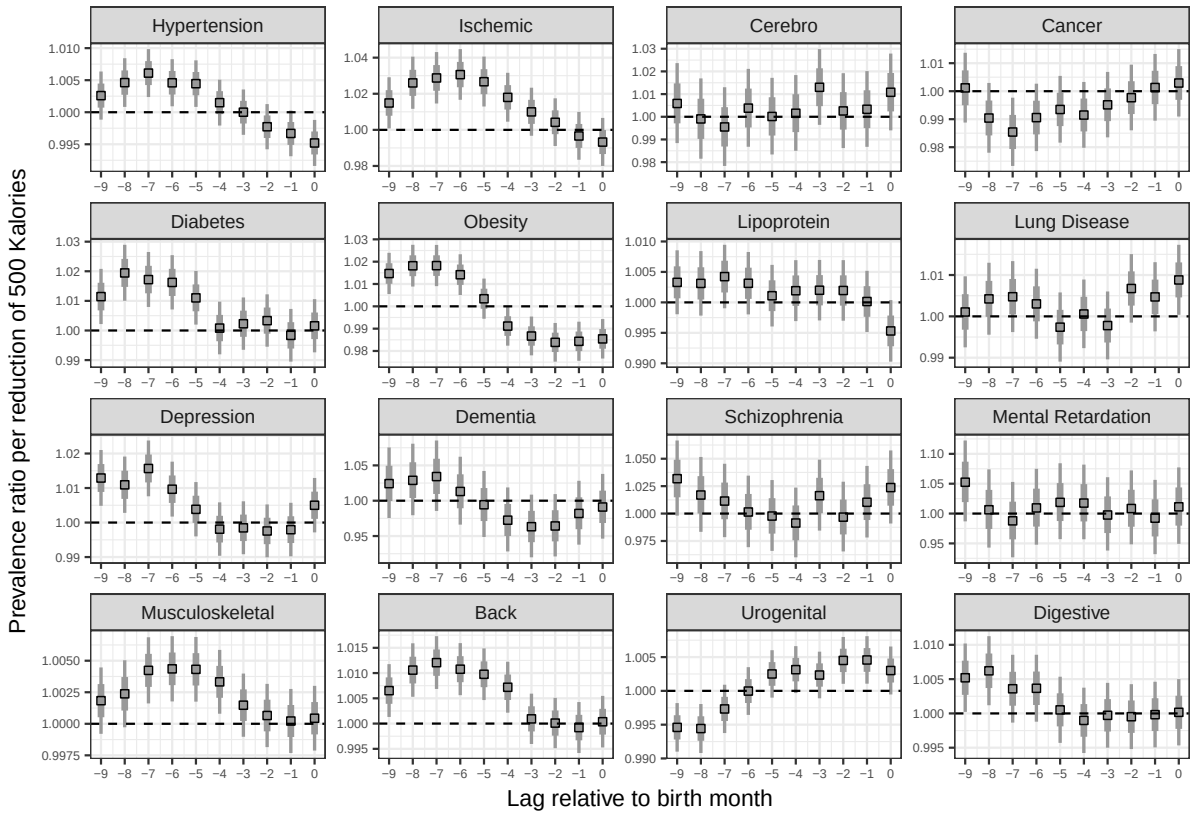

Figure 5: Link between lack of calories during pregnancy and later life health; women 2009; birth cohorts January 1942 to December 1949; Each point shows the morbidity rate ratio associated with a reduction of 500 calories. Error bars indicate ±1 (thick) and ±2 (thin) standard errors. *Source:* own computation based on KBV claims data and nutrition data shown in Figure 1.

3.2 Results for Men

Next, we discuss the results for men. Raw morbidity rates are shown in Figure 6. Broad comparisons of morbidity rates and their development across birth cohorts between men and women reveal similarities for most of the conditions under study. The most striking difference is the trend in the morbidity rate of urogenital conditions, which is increasing in age among men but decreasing among women.

As for women, the long-term trends are only reported for reference. We do not seek to explain these trends but rather the short-term deviations from these trends, which are depicted in Figure 7. Again, significant peaks in morbidity rate ratios can be found for men born in – or close to – January 1946 (Diabetes, Lung Disease, Depression: January 1946; ischemic Heart

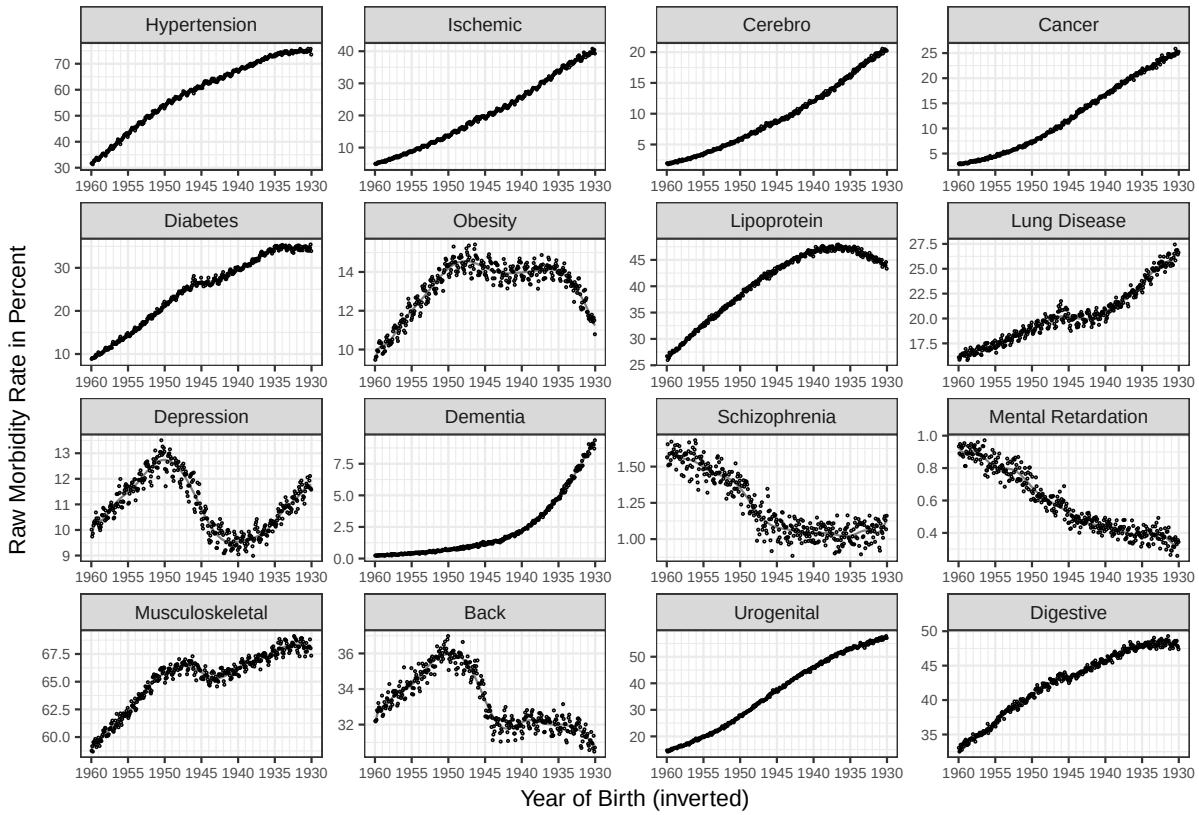

Figure 6: Morbidity rates by year and month of birth, men, 2009. *Source:* own computation based on KBV claims data.

Disease, Musculoskelatal Conditions: November 1945; Schizophrenia: April 1946). Although not significantly different from one at the 1% level, morbidity rate ratios for several other conditions bulge upward for men born around this time: diseases of the digestive system, back pain, mental retardation, back pain, and cerebrovascular disease. The only remarkable difference to women can be found with respect to urogenital conditions. Morbidity rate ratios are high especially among those born in mid 1945, at the end of the war, whereas women born a few months later had particularly low morbidity rate ratios. Obviously this can be the result of the mixture of sex-specific conditions that are bunched together in this broad ICD category.

Our final set of results is shown in Figure 8. Here we show again the (lagged) time-series correlations between being diagnosed with one of the 16 conditions and nutrition available during specific months of pregnancy. We find less systematic evidence for men than for women (confidence intervals are generally wider), but the qualitative results are again quite similar. For most conditions, lack of nutrients in early pregnancy appears to be more relevant than lack of nutrients in late pregnancy. This holds specifically for diabetes, lung disease, depression, and

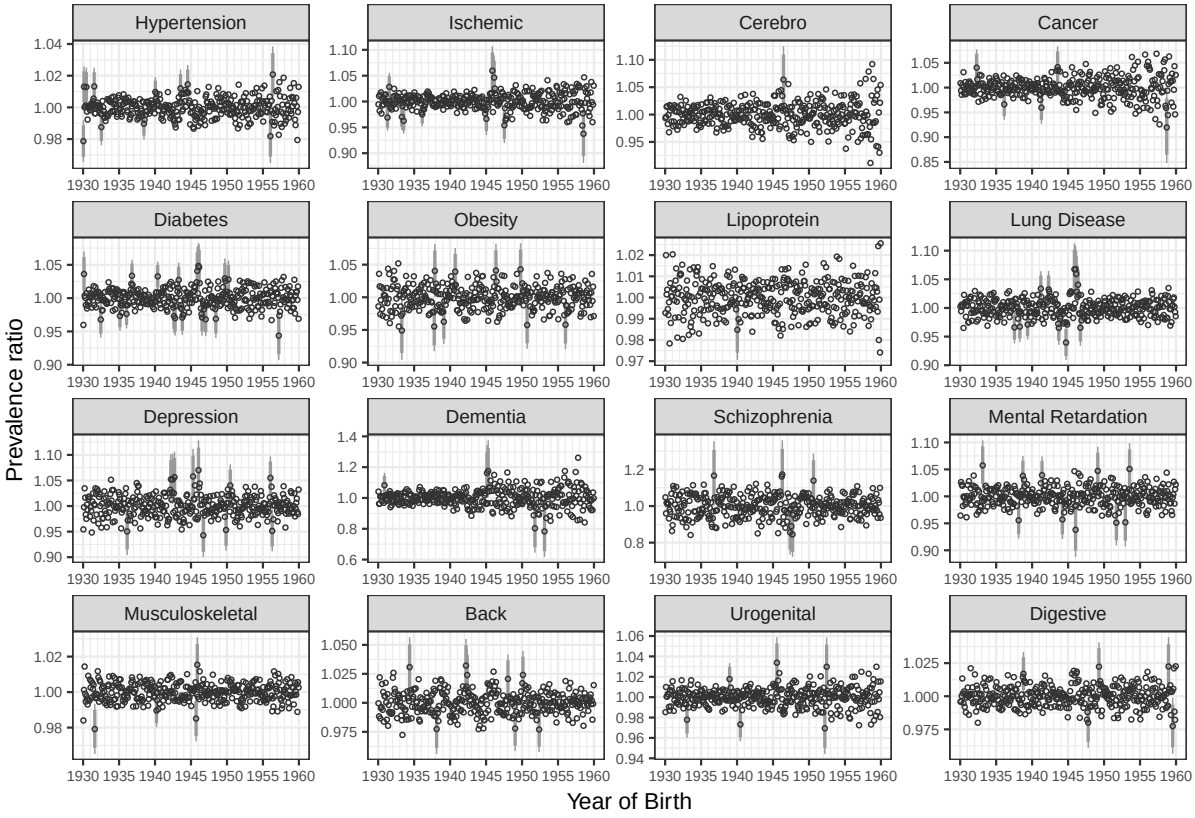

Figure 7: Excess morbidity by year and month of birth, men, 2009. Error bars indicate 95% (thick) and 99% (thin) confidence intervals only if estimated excess morbidity is significant at the 1% level. *Source:* own computation based on KBV claims data.

digestive disorders. For cancer, however, we find the opposite result. Malnutrition in early pregnancy appears to be *negatively* linked with the prevalence of cancer.

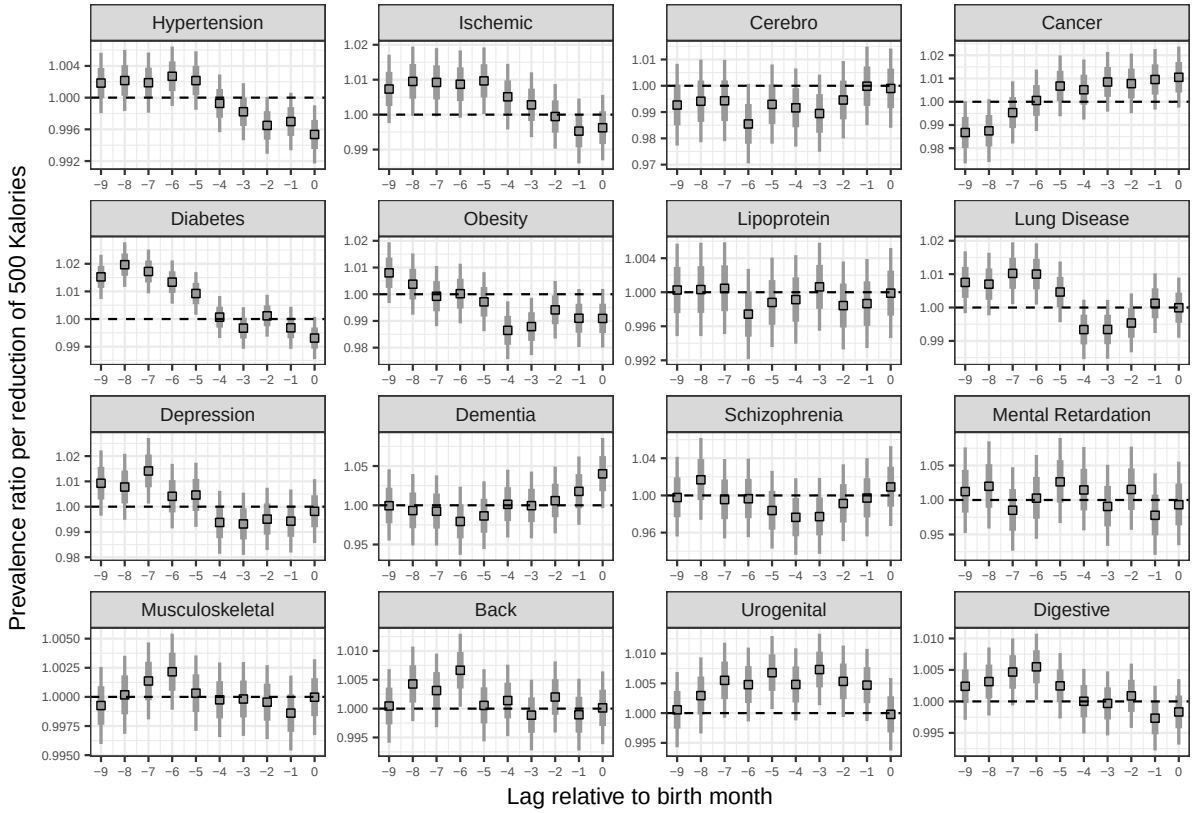

Figure 8: Link between lack of calories during pregnancy and later life health; men 2009; birth cohorts January 1942 to December 1949; Each point shows the morbidity rate ratio associated with a reduction of 500 calories. Error bars indicate ±1 (thick) and ±2 (thin) standard errors. *Source:* own computation based on KBV claims data and nutrition data shown in Figure 1.

3.3 Summarizing 11,520 regressions

One concern might be that our prediction error's p-values might be adjusted for multiple testing across months of births, sexes, and conditions. Overall, we have estimated 11,520 regressions and thus conducted 11,520 tests. Procedures that control for multiple testing usually assume independence, which is clearly violated in our case: some of the conditions we study are correlated due to patterns of co-morbidity, and morbidity rate ratios can be serially correlated because adjacent months of birth share similar environments. Ignoring this complication, we computed the p-values corresponding to the Benjamini-Hochberg false discovery rate (FDR) at 5% and 10% levels.

We plotted every computed p-value (on a log scale) by month of birth, separately for positive and negative morbidity risk ratios, that is 16 conditions times 2 sexes = 32 p-values per month of birth. This plot closely resembles the Manhattan plots used in genome wide association studies, see Figure 9. We also show the threshold p-values corresponding to Benjamini-Hochberg false discovery rates of 5% and 10% as vertical lines. Our Manhattan plots clearly show that there are a substantial number of p-values above those lines for individuals born around the beginning of the year 1946. It is particularly impressive to see those p-values mounting up at this period. Another, yet unnoticed, data is January 1950. An unusual number of women born January 1950 suffer from diabetes, high blood pressure, or cardiovascular disease.

Overall, Figure 9 shows that our test results regarding increased morbiditiy risk ratios for those born end of 1945 to beginning of 1946 hold up to controlling for worries that may arise from multiple testing.

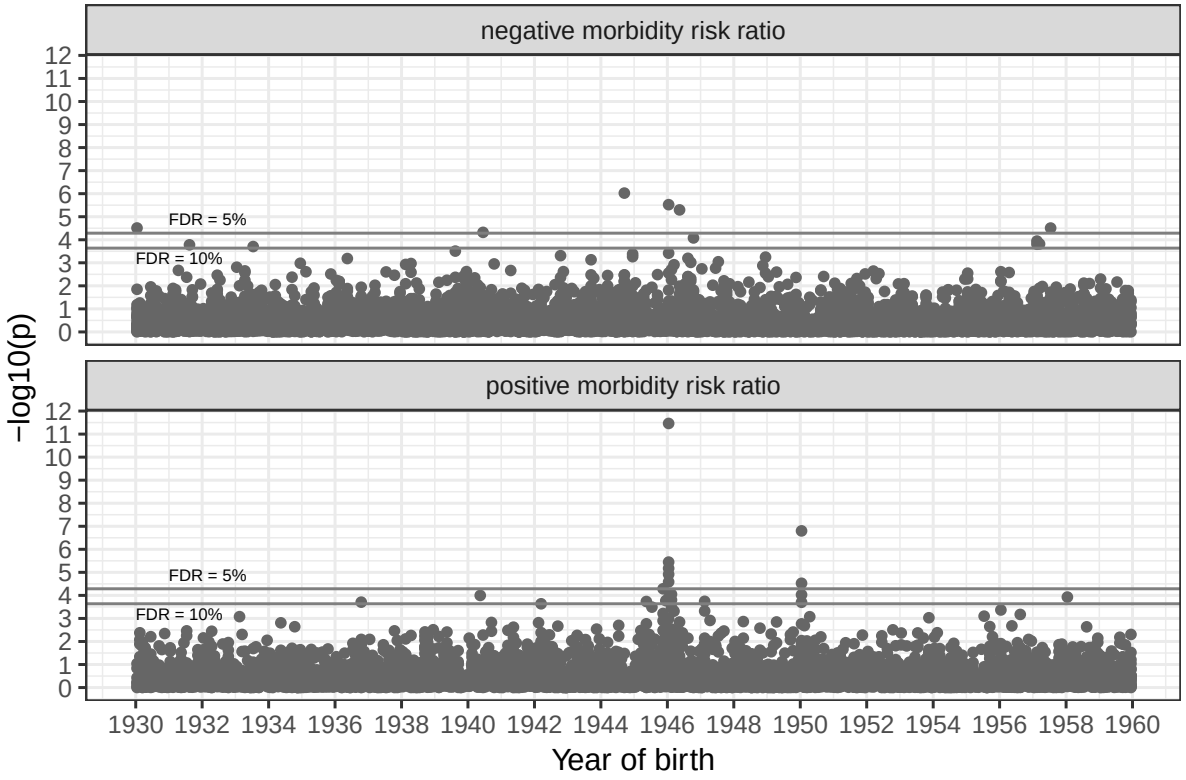

Figure 9: Manhattan plot of p-values of prediction errors (on a log scale), separately for positive and negative morbidity risk ratios. The horizontal lines mark p-values corresponding to Benjamini-Hochberg false discovery rates of 5% and 10%, respectively. *Source:* own computation based on KBV claims data.

4 Discussion

Ambulatory care health insurance claims data clearly show that German cohorts born shortly after the end of World War II are at higher risks of developing metabolic diseases, depression or back pain. At the same time, women in these cohorts are at lower risk of developing cancer of urogenital conditions. To the best of our knowledge, we are the first to document such findings for Germany. They complement earlier analyses that have shown lower educational attainment and worse labor market outcomes among the very same cohorts. Our preferred explanation for these findings is intrauterine malnutrition, in line with the fetal origins of disease hypothesis (Barker; 1995). We support this interpretation of the data by showing the partial association of the availability of food in different months before birth with the morbidity rate of specific conditions. For most of the conditions under study, we find that lack of food in the first half of pregnancy is more strongly related to later life health problems than lack of food in the second half of pregnancy.

Our study is unique in several ways: first, our estimates are based on more than 10 million observations per sex. In the month of birth cohorts most affected by the food crisis (where fertility was low) we have at least 15,000 to 20,000 observations. This allows us to estimate morbidity rate ratios for individuals born in single months of birth with unprecedented precision. Many earlier studies, especially the Dutch famine studies, have suffered from small sample sizes, which may partly explain inconsistent findings described in the earlier literature. Second, our estimates of morbidity rate ratios are based on claims data, which avoids problems of reporting errors typical to self-reports of doctor diagnoses (Datta Gupta and Jürges; 2012). Third, this is the most comprehensive study to date, covering a larger number of different conditions applying the exact same methodology than any single study before.

Our findings generally confirm those found in earlier studies, but the morbidity rate ratios are usually smaller, for two reasons. First, our large data set allows us to detect smaller effects than before. Effects of the sizes we find might not have passed the statistical significance filter in earlier studies. Second, as discussed in detail below, our data and methodology likely

yield underestimates of true effects. Thus it can be argued that the estimates are lower bounds for the effects of prenatal exposure to famine on later-life health.

We now go through all of our examined conditions and place the results in context. Perhaps the chronic condition most studied in relation with prenatal malnutrition is *diabetes*. Increased morbidity rates of diabetes mellitus among those exposed to famine in utero has been documented in Austria (Thurner et al.; 2013), China (Li et al.; 2010), the Netherlands, Nigeria (Hult et al.; 2010), and Ukraine (de Rooij et al.; 2014). We find statistically significant morbidity rate ratios of 1.1 (women) and 1.05 (men) among those born in January 1946 – eight months after the end of the war – and elevated morbidity rate ratios among those born a couple of months earlier or later. In contrast to early pregnancy exposure, late pregnancy exposure showed no association with diabetes morbidity.

Increased *body weight and BMI* at older ages after prenatal exposure to famine have been documented for women but not men in the Netherlands and in China (Lumey et al.; 2011). We have no information on BMI or body weight but diagnosed obesity in our data. We find morbidity rate ratios of 1.07 for women and 1.03 for men born January 1946 and somewhat smaller adverse effects in the months before and after. This period generally appears to stand out more among women. For the Netherlands, Ravelli et al. (1999) showed that higher BMI was associated with malnutrition in early-pregnancy but not in mid- or late-pregnancy. Point estimates for mid- and late-pregnancy exposure were actually negative. Our analysis of critical periods confirms this and even suggests that late-pregnancy exposure to undernutrition might be negatively linked with obesity in older adults.

To date, the evidence regarding the link between intrauterine malnutrition and later-life *blood pressure* is fairly weak and unsystematic (Roseboom, van der Meulen, van Montfrans, Ravelli, Osmond, Barker and Bleker; 2001). While earlier studies may have suffered from small sample sizes, our much larger data base confirms that the link is at best unclear. We find morbidity rate ratios significantly different from one for several birth months during and after the war, but they appear to go both ways and the timing does generally not seem in line with other conditions studied here, i.e. being in utero during the immediate post-war period is not particularly salient. However, the time series correlation between lack of available calories

and hypertension suggests there may be some link especially in the first half or trimester of pregnancy, so effects of the food crisis on hypertension cannot be rule out entirely.

Increases in cholesterol and triglyceride levels have been documented among individuals affected by the Dutch famine, but findings were mostly confined to women, and statistical significance could not always be ascertained (Lumey et al.; 2011). Our results on diagnosed hypercholesterolaemia or hyperglyceridaemia clearly support skepticism that may arise due to this lack of robustness. We find no link between adult lipid outcomes and intrauterine malnutrition in any of our analyses.

High blood pressure, overweight and obesity, as well as high cholesterol and triglyceride levels are known risk factors for *cardiovascular and cerebrovascular diseases* such as angina pectoris, myocardial infarction, or stroke. Given the weak evidence on those risk factors obtained from the Dutch Famine studies, it is not surprising that the evidence on cardiovascular outcomes – although pointing towards an effect of prenatal exposure – also remained largely inconclusive (Lumey et al.; 2011), in particular in light of the small numbers of observations. Our results are mixed as well. We find elevated morbidity of cardiovascular and cerebrovascular disease among men who were born in early 1946 and thus conceived around the end of the war. Among women the picture is less clear. One the one hand, peak morbidity rate ratios generally do not match with the historical events we study, but on the other hand the time series correlation of food availability with morbidity rate ratios suggests that early- to mid-pregnancy is a critical period in terms of cardiovascular disease.

In our data, results related to *depression* as an important *mental health* outcome are relatively strong and consistent across men and women. Again early pregnancy exposure appears to be more critical than late pregnancy exposure. This confirms earlier suggestive evidence from the Dutch famine studies (Brown et al.; 1995). Another often studied mental health outcome is schizophrenia, and we find some evidence that intrauterine malnutrition is indeed associated with the risk of schizophrenia among men but not among women.

Studies using Dutch famine cohorts have found little systematic evidence that prenatal malnutrition affects on *cognitive ability*. For instance, Stein et al. (1975) report no differences in intelligence measured in conscripts. However, de Rooij et al. (2010) recently reported weaker

performance in selective attention tasks among those exposed to malnutrition during the first part of pregnancy, which could be first signs of accelerated mental decline. Our results on dementia partly support this finding. We find elevated morbidity rate ratios of diagnosed dementia among women born in December 1945–January 1946. Among men, however, the peak is in May 1945, which suggest that late pregnancy exposure might be more important. Since the prevalence of dementia exponentially increases in age, we have repeated our analyses for diagnoses of dementia with claims data from 2015, i.e. when cohorts are six years older than in 2009. The results – shown in Figures A.1 and A.2 in the Appendix – show patterns of high rates of dementia for the *entire* birth cohorts 1944 and 1945 but also low rates among those born in the summer of 1946. Taken together, these findings suggest that intrauterine as well as early childhood malnutrition might contribute to an earlier onset of dementia, but further study is necessary to establish the exact nature of this link.

For several of the conditions not yet discussed here, systematic evidence from other study populations is mostly lacking. Most studies surveyed in Lumey et al. (2011) are based on the Dutch famine cohorts and usually suffer from very small sample sizes. The evidence shown in our study, high morbidity rates in musculoskeletal disorders, especially lower back pain, and digestive disorders – is new. Importantly, peak morbidity rates can be found exactly among those month-of-birth cohorts that suffer from higher morbidity rates of other conditions that have been studied in several independent populations and that have been linked with intrauterine malnutrition. Whether the effect of malnutrition on the musculoskeletal disorders is independent of those other conditions is unclear. Overweight and obesity are likely to cause such problems themselves. In any case, our finding thus suggest that larger samples may be needed in other populations, too, to detect these effects.

Similar to previous studies, our results point to the importance of malnutrition in early pregnancy rather than late pregnancy. This also holds a lesson regarding birth weight as a marker for the development of chronic conditions later in life. The obvious advantage of birth weight is that it is available in medical records and can thus be linked directly with later-life outcomes. However, as evidence from the Dutch famine suggests, low birth weight is correlated with undernutrition especially in the last trimester of pregnancy (Stein et al.; 1975; Roseboom,

van der Meulen, Ravelli, Osmond, Barker and Bleker; 2001). Thus it may well be possible that correlations between birth and later-life outcomes understate the true correlation between intrauterine malnutrition and later-life health.

Some limitations of our study are related to the data we use. Broadly, these limitations can be classified into those leading to an underestimation and those leading to an overestimation of the true effect of prenatal malnutrition on later-life health. We begin by discussing two factors that might be lead to an overestimation: other war- or post-war related stress and selective fertility.

One obvious concern is that the immediate post-war period in Germany was characterized by unusual circumstances in many different respects, so that intrauterine malnutrition is only one possible candidate explanation among many others, as for instance prenatal or early childhood war-related stress due to Allied bombings, absent fathers, or political oppression. Generally, at least with respect to some important conditions like diabetes, increased morbidity rates in response to malnutrition in utero could be documented for other countries, historical times and circumstances, which supports the notion that intrauterine malnutrition is the main driver of excess risks.

Jürges (2013) includes a thorough discussion of alternative explanations for adverse non-health outcomes such as lower educational attainment among those conceived and born in Germany immediately after the Second World War, such as (additional) detrimental effects of flight and expulsion from the Eastern Provinces and Eastern European countries and selective fertility. We briefly reiterate this discussion here. When the Red Army reached the German border on January 12, 1945, most ethnic Germans fled from the Eastern Provinces. Those who did not leave voluntarily, were expulsed after the war. Flight and expulsion happened under very harsh conditions that also affected children in utero and newborns (Jochims and Doerks; 1947). Intrauterine stress due to flight and expulsion in addition to malnutrition may thus have *added* to the detrimental effect of the food crisis. Indeed, Jürges (2013) finds stronger affects (on education) among those whose mothers fled from the Eastern Provinces, but importantly, this does not affect the results for non-refugees. The data used in the present study do not allow the distinction between children of refugee mothers and others, but we in light of these earlier

findings, we are confident that the results are not only driven by intrauterine stress of children of refugees.

Selective fertility with regard to socio-economic status (SES) might be another concern. If parents of higher SES were less likely to conceive children in the final war months or the first post-war months, the average child born nine months after would be of lower SES as well. To the extent that childhood SES affects later-life health (Brandt et al.; 2012), our findings could also be explained by such selective fertility. Again, we are not able to test this directly, because our data do not contain information on parental SES. But using German survey data, Jürges (2013) shows that the cohorts born November 1945 to April 1946 were neither positively nor negatively selected with respect to parental education.

Limitations that could lead to an underestimate of the true effect of prenatal famine on adult health are related to measurement error regarding the exposure. In contrast to the Dutch famine, there are no clear-cut start and end points of the food crisis. Thus there are no clearly identifiable pre- or post-famine cohorts that could be used as control groups providing credible counterfactual outcomes. We believe that our identification strategy – estimating counterfactual morbidity rates by a long-term trend plus a seasonal component – is reasonably credible, but the actual implementation is subject to a number of specification choices. For instance, we determined the "optimal" order of the polynomial to estimate long-term trends by cross-validation. While cross-validation generally safeguards against over-fitting a model, it is an entirely data-driven approach and does not account for any prior knowledge. However, inspection of the raw morbidity rates and their development as shown in Figure 3 and 6 suggests that while there may be significant hikes in morbidity rate ratios for single month-of-birth cohorts, especially January 1946, the actual effect of post-war food crisis on later life health might have been larger and might have affected more cohorts. If several month-of-birth cohorts born around January 1946 are affected as well by the food crisis but not as strongly, they will pull the estimated trend curve in the post-war year slightly upwards and hence reduce our estimate of the morbidity rate ratio. In other words, morbidity rate ratios are estimated conservatively. Hence they cannot be interpreted as "the effect" of the food crisis. The true additional burden of disease might well be higher and affecting more month-of-birth cohorts. This could be the case for instance for

diabetes, lung disease, or musculoskeletal disorders. One ad hoc robustness check is to arbitrarily omit entire year-of-birth cohorts (e.g., 1945 and 1946) from estimating the long-term trend, so that the trend estimate is not affected by anything specific that might have happened during those years. We have done this and the results were as expected: for some (but not all) of the conditions under study the morbidity rate ratios for birth years 1945 and 1946 were higher than before and significant estimates are spread out over a longer period (see Figures A.3 and A.4 in the Appendix).

Another source of measurement error is the lack of information on immigrant status. We are not able to identify immigrants who were not exposed to the German food crisis, but who were born during the critical period. The proportion of immigrants born 1945 to 1948 is nearly 9 percent (Statistisches Bundesamt (Destatis); 2017). In this group, the excess morbidity rate should be lower than the morbidity rate among the same German month-of-birth cohorts. Under the assumption of no effect among immigrants, dropping immigrants from the sample would roughly yield about 10 percent larger morbidity rate ratios than shown above. Another potential advantage of identifying immigrants in our data could have been to use them as an additional control group to increase the credibility of our findings.

Recent studies have used information on regional variation in food availability to further the identification of causal effects of undernutrition in post-war Germany (Kesternich et al.; 2015) or elsewhere (Lumey et al.; 2015). For obvious reasons, rural areas such as Schleswig-Holstein were less affected by the food crisis than urban areas such as the Ruhr area. Our data contain place of residence and treatment, but not place of birth. Thus even if we linked individuals with data on food availability in their region of residence, internal migration – possibly selective – would affect our estimates, most likely introduce a bias towards no effect. Thurner et al. (2013) demonstrate that accounting for internal migration amplifies estimates of excess risk of diabetes among Austrians affected by three food crises during the 20th century by about 20%. In future research, we will take regional differences into account. We also expect that this improvement will increase the estimated effects.

Since we observe individuals in 2009, selective mortality in the decades leading to our observation period might as well contribute to an underestimate of the effect of the food crisis

(Bozzoli et al.; 2009). Lindeboom and van Ewijk (2015) show, for several European countries that were occupied by Germany, that life expectancy at birth is greatly reduced among cohorts prenatally exposed to World War II. However, this reduction is almost exclusively due to perinatal and infant mortality. If especially "frail" infants perish, the selection of surviving infants might on average be "stronger" and thus inherently less likely to develop any of the conditions we study in our paper. Indeed, Van Ewijk and Lindeboom (2016) provide some suggestive evidence that older people who had been exposed to World War II are in better health. In Germany, infant mortality rates in the last year of war and first post-war year were extremely high. Official figures for the whole of Germany are not available, but local estimates indicate that infant mortality rates peaked locally at 20% to 30% in March, April, and May 1945 (Droese and Rominger; 1949; Plotz; 1950; Weber; 1949). Hence it is possible that selective infant mortality has driven down the observed detrimental effects of intrauterine malnutrition we find today among the survivors.

Finally, one potential drawback of using claims data is that some diagnoses may be over-reported due to financial incentives (Bauhoff et al.; 2017). Although this may be the case in general, so that morbidity rates are somewhat exaggerated across the board, it seems highly unlikely that morbidity rates are exaggerated to a greater extent among the cohorts that were born just after the Second World War and thus exposed to the food crisis.

5 Conclusion

Overall, the strengths of our study outweigh its limitations. Hence our analysis provides important new evidence on a (causal) link between prenatal exposure to malnutrition and later-life health. First, most of the results of the Dutch famine studies and from other contexts have been confirmed. Strong and robust effects that were documented in the earlier literature can also be found in our data. Effect sizes in our study are often smaller, however. This is likely due to the fact that our approach to identification is very conservative and almost certainly yields an underestimate of the true effect. Moreover, measurement error in exposure to undernutrition, the most important limitation of our study, likely biases the estimates toward finding no effect.

Inconclusive evidence in the literature also often turns out inconclusive in our study. Perhaps the most important contribution of the study is that we find evidence for effects of the German food crisis on conditions that have not been studied before, such as on lower back pain, urogenital conditions or digestive disorders, among *exactly the same birth dates* that have elevated morbidity rates in conditions studied in the existing literature. Together with the large sample size on which these findings are based, this clearly suggest that such findings are not just statistical flukes. Rather they indicate that there is large scope for future research to replicate these finding on independent study populations and to deeper understand the mechanisms by which prenatal exposure to malnutrition affects many different outcomes later in life.

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A Supplementary Tables and Figures

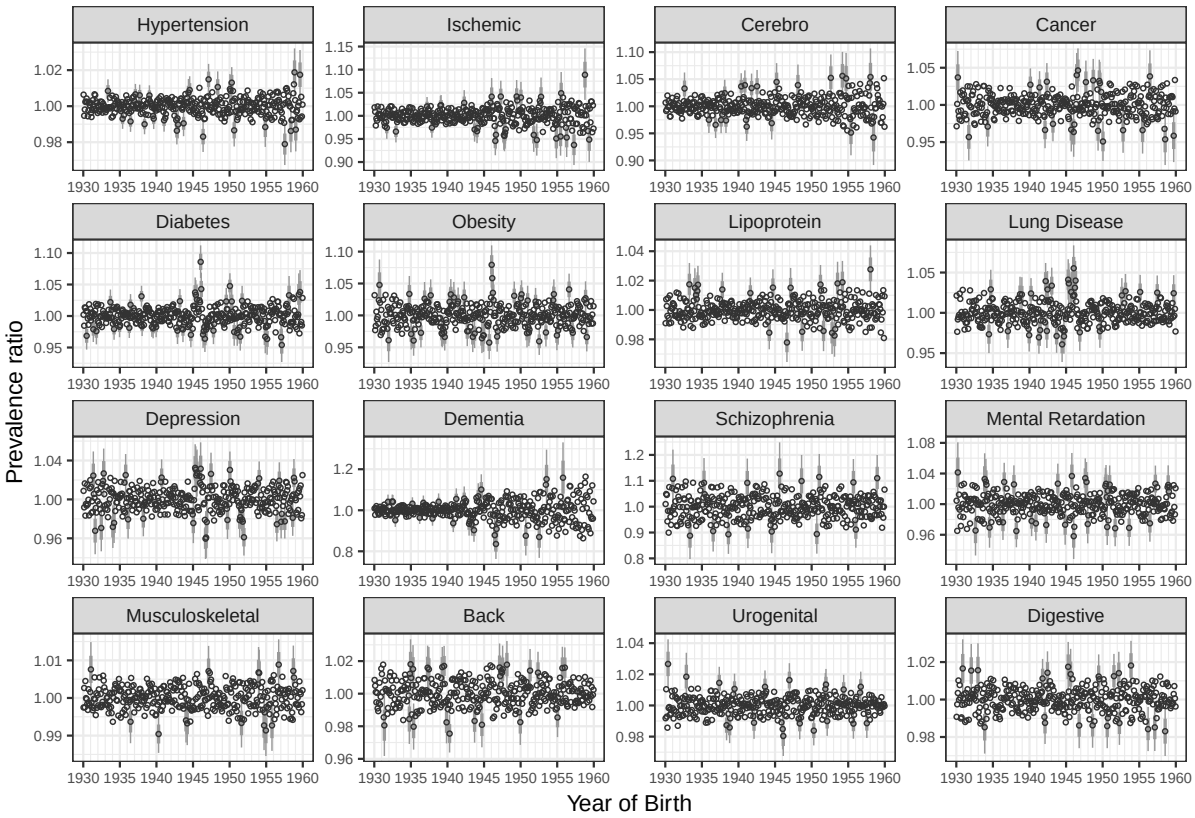

Figure A.1: Excess morbidity rates by year and month of birth, women, 2015. *Source:* own computation based on KBV claims data.

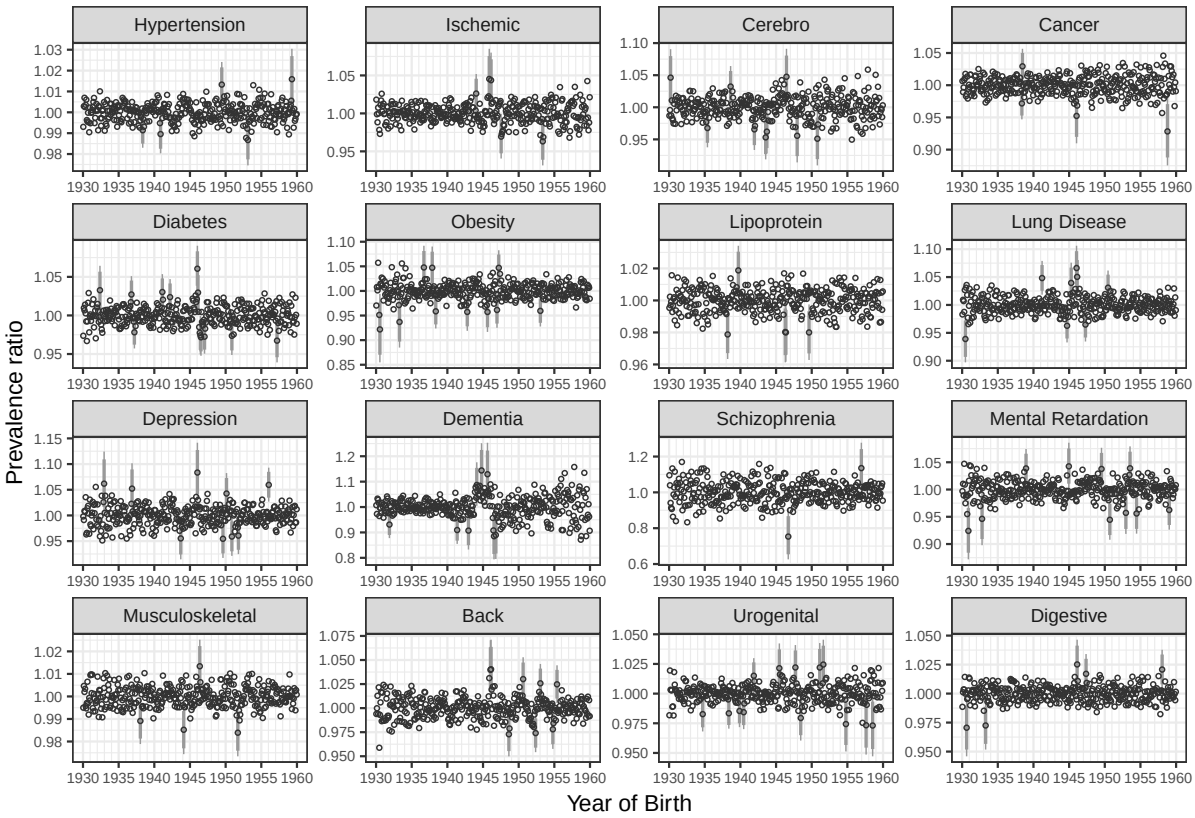

Figure A.2: Excess morbidity rates by year and month of birth, men, 2015. *Source:* own computation based on KBV claims data.

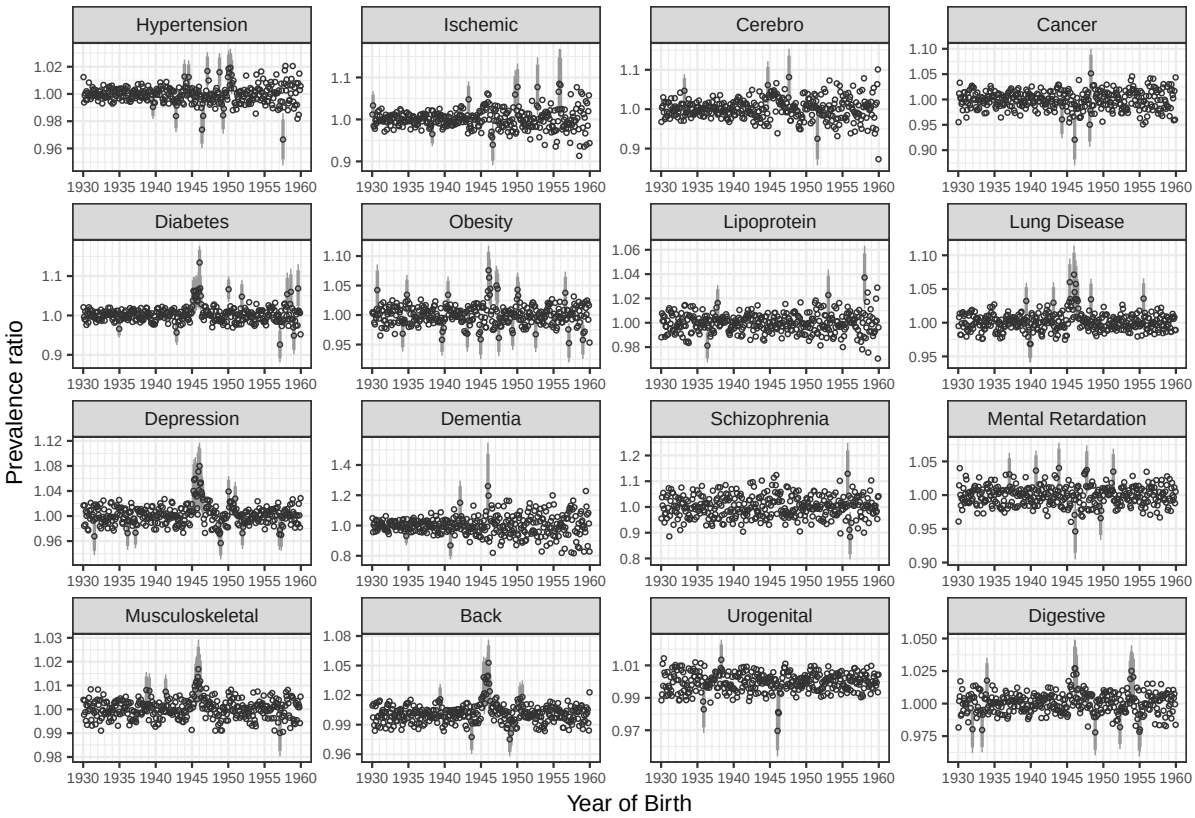

Figure A.3: Excess morbidity rates by year and month of birth; women 2009; long-term trend estimated excluding birth years 1945 and 1946. *Source:* own computation based on KBV claims data.

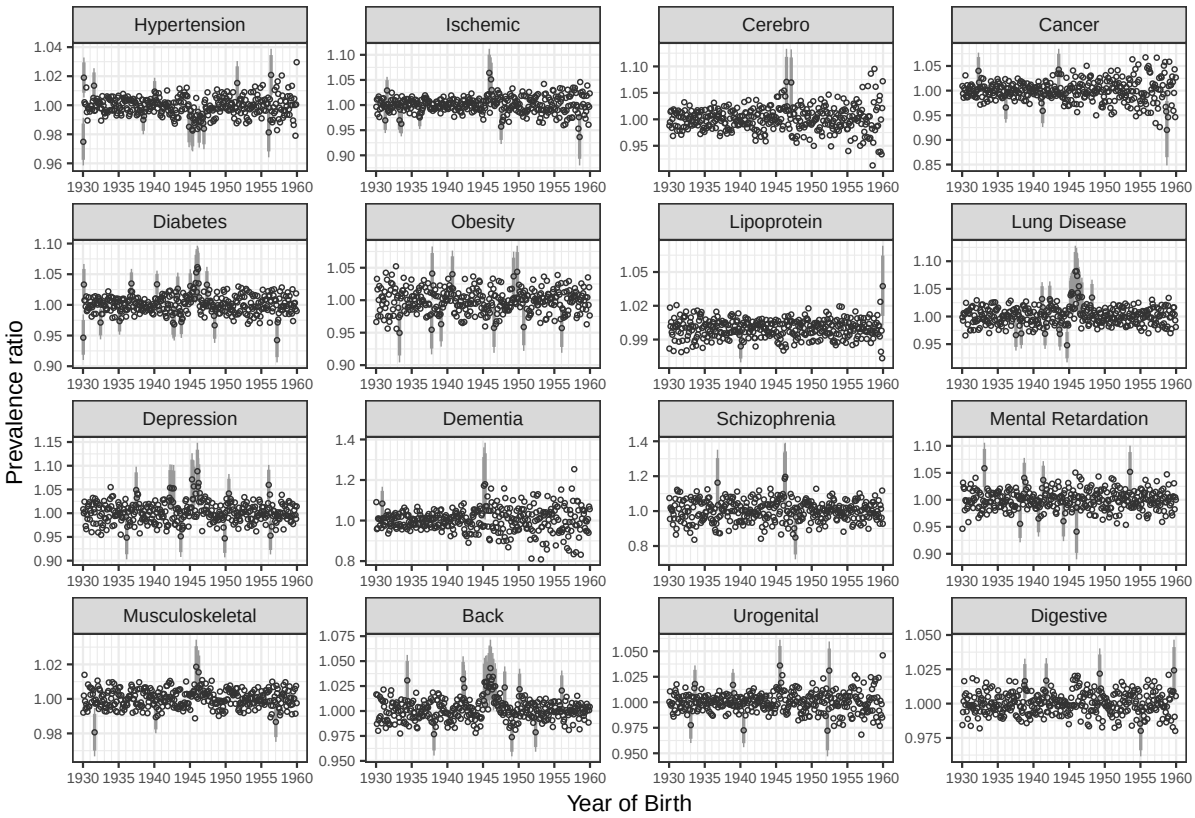

Figure A.4: Excess morbidity rates by year and month of birth; men 2009; long-term trend estimated excluding birth years 1945 and 1946. *Source:* own computation based on KBV claims data.

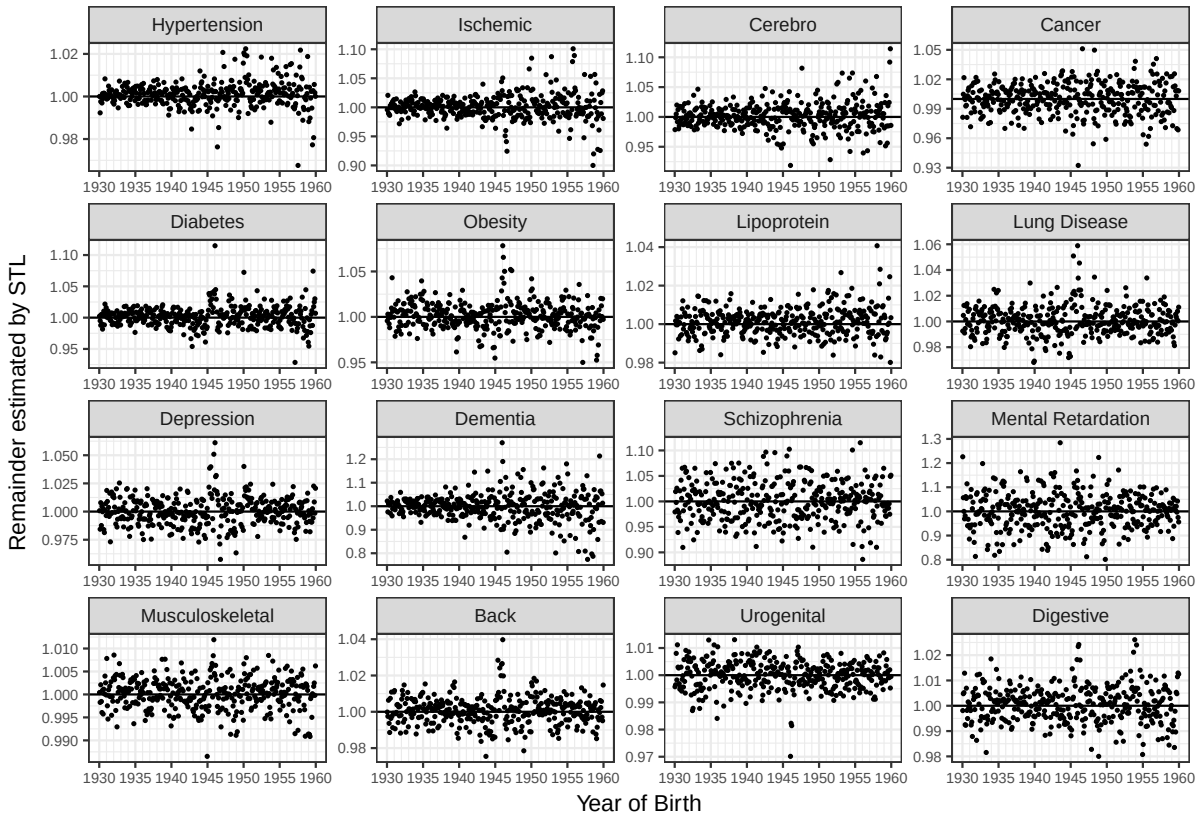

Figure A.5: Excess morbidity rates by year and month of birth; women 2009; estimated by STL. *Source:* own computation based on KBV claims data.

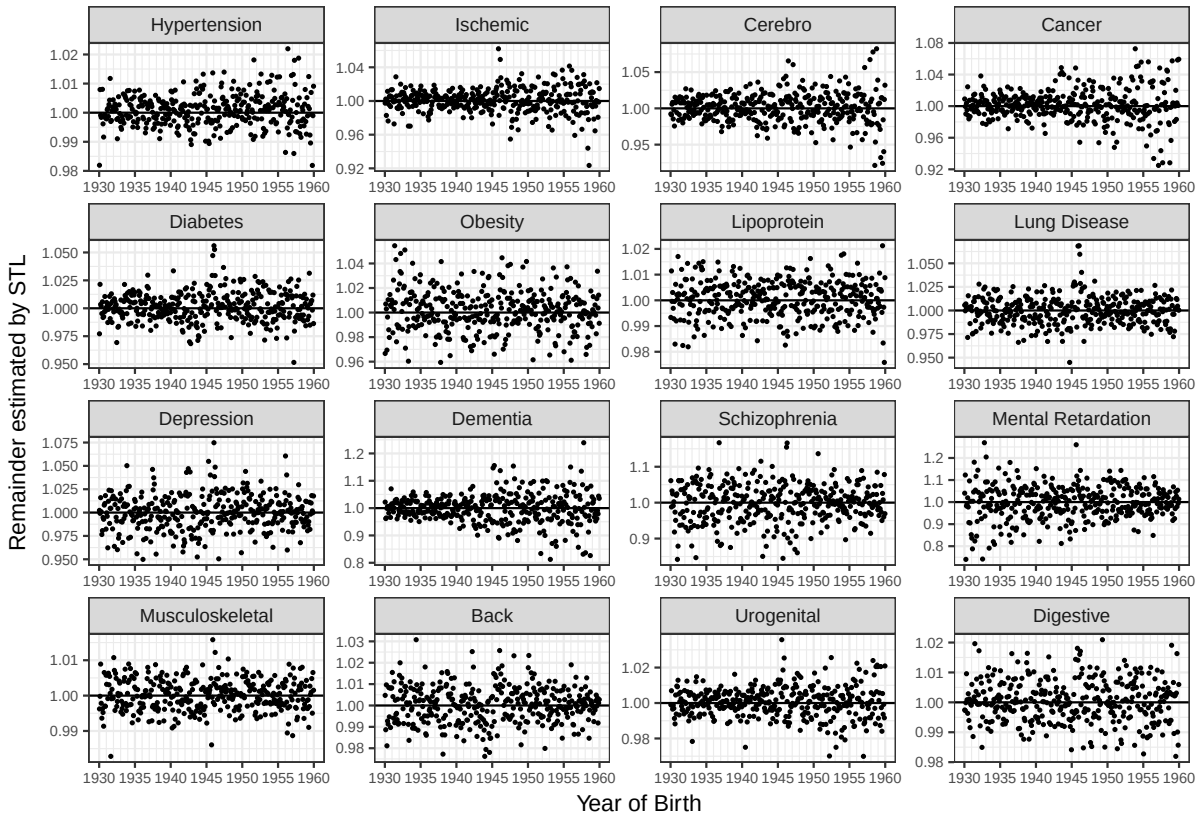

Figure A.6: Excess morbidity rates by year and month of birth; men 2009; estimated by STL. *Source:* own computation based on KBV claims data.