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ABSTRACT

Multigenerational Effects of Smallpox Vaccination

Can the effect of a positive health shock, such as childhood vaccination, transmit across three generations? To answer this question, we estimate the impact of smallpox vaccination in childhood on the longevity and occupational achievements of three generations using unique individual-level data from Sweden, covering the last 250 years. We apply different estimation strategies based on linear and non-linear probability models. To address endogeneity concerns, we construct a shift-share instrumental variable, utilizing the fact that vaccination in Sweden was administered by the low-skilled clergy, who otherwise did not perform public health duties. Overall, our results show that a positive shock to the health of the first generation, such as smallpox vaccination, operating through various channels, enhances both health and socio-economic outcomes for at least two more generations.

JEL Classification: I18, J24, J62

Keywords: intergenerational transmission of health, smallpox vaccination, shift-share instrumental-variables

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1. Introduction

Vaccines save lives, benefiting approximately four million people annually (Patel et al. 2022). Live vaccines may also protect against unrelated diseases, with childhood vaccination enhancing the immune system through epigenetic and metabolic changes (for reviews see Benn et al. 2023, de Bree et al. 2018). Recent randomized control trials confirm these "non-specific" positive effects of vaccines on health during childhood (Schaltz-Buchholzer et al. 2021; Lund et al. 2015; Kleinnijenhuis et al. 2014; Aaby et al. 2010). Inspired by epidemiological findings, economic studies have explored childhood vaccination's impact on adult labor market outcomes in a human capital framework (Atwood 2022; Bütikofer and Salvanes 2020; Serratos-Sotelo, Bengtsson, and Nilsson 2019). However, the overall effects of vaccination remain underestimated, as such effects persist in health and economic outcomes across one's lifetime and generations (Collado, Ortuño-Ortín, and Stuhler 2023; Lee and Conine 2022).

In this study we estimate the impact of smallpox vaccination on longevity and economic wellbeing of three generations, exploring smallpox vaccination campaign in Sweden as a quasi-experiment. Vaccination against smallpox was the first known vaccination globally and was considered by the Swedish reformers as "among the greatest inventions ever, which—when it has increased in confidence—will be the supreme happiness of the human race and the triumph of medicine." (Hedin 1802). Historically, anecdotal records suggest that the smallpox vaccine produced "non-specific" health effects (Mayr 2004). To capture the causal effects of vaccination, we apply a shift-share instrumental-variables approach in both linear and hazard models and use unique individual-level data covering multiple generations from 1790 until 2016. Given the extensive historical data available, we investigate the entire lives of three generations to assess their health, behavioral, and socio-economic outcomes, including disability, literacy, and occupational scores.

We find that smallpox vaccination in early childhood enhances both longevity and occupational achievements of the first generation (those vaccinated in childhood, generation 1 thereafter) as well as of their children (generation 2) and grandchildren (generation 3). Smallpox vaccination adds 11 years of life to the first generation and 2 and 1 years to the second and third generations. To put such results in perspective, vaccination in childhood in historical Sweden produces similar effects for longevity as quitting smoking in today's context (Shaw, Mitchell, and Dorling 2000). All three generations that we study died primarily from causes other than smallpox, but we also establish explicit "non-specific" vaccination effects: while mortality from smallpox is reduced the most, there are negative effects on mortality from other causes. We also

find that vaccination improves economic outcomes across generations—in terms of disability and occupational achievements, with these effects with a reduced magnitude being transmitted to subsequent generations. Around the half of the transmitted effects are driven by nurture, as vaccinated individuals are more likely to vaccinate their children across generations; epigenetic inheritance likely drives another half.

In addition to being the first to establish vaccination effects across multiple generations, our paper contributes to two strands of economic literature. Firstly, our knowledge on whether health shocks for one generation determine the outcomes of the subsequent generations causally is extremely scarce. There are several studies that attempt to derive the causal impacts of health transmission by relying on environmental shocks as a source of exogenous variation (East et al. 2023 for Medicaid; Mazumder, Rosales-Rueda, and Triyana 2023 and Lundborg, Nilsson, and Rooth 2014 for the school reform; Cook, Fletcher, and Forgues 2019 for Spanish flu; Nilsson 2017 for the abolishment of alcohol ban). We contribute to this literature by tracing the effects of a positive health shock over the full life cycles of three generations.

Secondly, while there exists an extensive body of literature on the long-term health and economic effects of recent interventions, there is a smaller, yet steadily expanding, literature focused on interventions that occurred further back in history. Based on causal designs, economists have recently studied the establishment of epidemical and modern hospitals (Hollingsworth et al. 2022; Lazuka Forthcoming; Lazuka, Quaranta, and Bengtsson 2016), the impacts of licensed midwifery (Kotsadam, Lind, and Modalsli 2022; Anderson et al. 2020; Lazuka 2018), of tuberculosis dispensaries (Egedesø, Hansen, and Jensen 2020; Clay et al. 2020; Anderson et al. 2019), and of mid-twentieth-century vaccinations (Atwood 2022; Bütikofer and Salvanes 2020; Serratos-Sotelo, Bengtsson, and Nilsson 2019). The focus on historical interventions has helped us better understand their effects on individuals. We contribute to this literature by examining the vaccination campaign, which is the world's first documented public health initiative and an intervention that has received limited attention in previous research.

2. The Context of Smallpox Vaccination in Sweden

2.1 Introduction of Smallpox Vaccination

In 1798, Edward Jenner published a book outlining his successful smallpox vaccination method, where he initially vaccinated a boy with cowpox. After an eight-week interval, he administered smallpox to the same boy without any adverse effects, confirming the vaccine's efficacy (Baxby 1985). Vaccination against smallpox reached Sweden a few years later and was

first mentioned on 7 December 1801 by the Medical Board of Sweden (Riksarkivet 1802-1812). The first vaccinations in Sweden were carried out at the end of 1801, and starting from 1803, the Inoculation House of Stockholm maintained a fresh vaccine available to facilitate nationwide vaccination efforts.

Before the introduction of vaccination, inoculation—a deliberate infection with smallpox (rather than cowpox) via the skin—was used as a preventive measure against smallpox. Even though inoculation was introduced in Britain in 1721, it was not until 1756 that it was first used in Sweden. The historical narrative suggests that inoculation never gained wide acceptance because of, for instance, the risk of dying from the procedure (Pettersson 1912). Both the country records on the number of inoculations and our data confirm that inoculation had low uptake in Sweden: less than 0.01 percent of parishioners were inoculated between 1769 and 1800 (Riksarkivet 1769-1801).

The introduction of vaccination in Sweden in the 1801 had several remarkable features that we exploited in our empirical design. First, vaccination efforts primarily focused on children, typically aged around 2 years old (Riksarkivet 1802-1812). Starting in March 1816, parents were required to have their children under the age of 2 vaccinated, with fines imposed for non-compliance. If parents were unable to pay the fine, they would be subject to imprisonment and would receive only a diet of water and bread.

Second, vaccination was nearly free of charge. Vaccinators were not permitted to charge parents for vaccinating children. Local solutions for compensation included the salary from the parish, small fees charged from the wealthiest parents, a payment from poor relief, or medals (Sköld 2000). Naturally, there were no discernible differences in the practice of vaccination in Sweden based on social class (Dribe and Nystedt 2003).

Finally, in 1804 every parish was instructed to appoint a vaccinator. The state authorities did not allow local physicians to monopolize the vaccination process, fearing the low uptake and voluntary fee charges. However, the vaccine could be safely administered by non-medical individuals — "anyone, without prior experience but with good interpersonal skills, common sense, and the ability to read and write, who would simply need to acquire a few skills" (Ekelund 1804). As a solution, starting in 1805, low-skilled church personnel, commonly with no prior involvement in health or epidemic matters, were obliged to attain the skill of vaccination. Data from the 1810s indicate that over 60% of those administering vaccinations were church assistants or church musicians, followed by clergy members (12%), upper-class women (10%), and

midwives, physicians, and other people (each accounting for 5%) (Sköld 1996a). In contrast to the local demographic and cultural factors, the availability and employment of church personnel emerges as the sole factor highly correlated with vaccination uptake (Sköld 1996b).

2.2 Disease Environment and Vaccine Uptake

Smallpox was the main disease and cause of death among children in the pre-vaccination era. In Sweden, an ordinary, *Variola major* was widespread, a highly contagious type, spread through the air, which affected children or persons lacking natural immunity against smallpox. The virus remained unchanged throughout history, causing a two-week period of suffering characterized by symptoms such as headache, fever, backache, vomiting, and diarrhea, followed by the development of pustules (Fenner et al. 1988). Case fatality rate reaches 20% among all infected persons and 55% among children below age 2 (Sköld 1996b). Survivors often bore life-long pitted scars (pockmarks) and could experience various complications, such as blindness, baldness, limb deformities, infertility, and conditions in respiratory, gastrointestinal, and central nervous system.

There is no effective treatment against smallpox due to the virus's resistance to temperatures below 60 degrees and its independence from nutrition, leading to losses regardless of access to food or other family conditions (Lunn 1991). Pregnant women transmit infection, rather than protective antibodies, to fetuses, leading to premature neonatal death (Hassett 2003). Therefore, the children must eventually develop their own immunity or receive vaccination to achieve protection. Vaccination, including earlier iterations, offers approximately 95% effectiveness (Fenner et al. 1988).

The age pattern of smallpox mortality in Sweden has changed dramatically with introduction of vaccination in 1801, as shown in Figure 1. We calculated the rates based on population counts for the regions we further analyze; these numbers are similar to those for the entire country (Pettersson 1912). Even though among causes of death the proportion of unknown cases is significant, the symptoms of the primary infectious diseases were recognizable to death registrars (i.e., priests and doctors); consequently, in relative terms, the age pattern of smallpox deaths has a high degree of accuracy (Bengtsson and Lindstrom 2000). Between 1790 and 1800, smallpox mortality followed an *L*-shaped pattern, with approximately 3% of children under the age of three succumbing to the disease (16% of all causes), a decreasing rate among older children, and relatively few deaths among adults. This pattern is indicative of a society where older individuals acquired natural immunity but did not pass it on to their children. In a few decades after 1801,

in a scale with the previous decades, age pattern has almost flattened. During this period, less than 0.2 percent of children died due to smallpox.

[Figure 1 about here]

Figure 2 shows the share of the cohort vaccinated by age two for the nineteenth-century Sweden, encompassing all the generations explored in this study. Vaccine uptake was gradual for the first few decades after 1801 and then stabilized at 85 percent. Mandatory vaccination in 1816 only resulted in a modest increase in uptake among small children, suggesting that most of the uptake is associated with other factors, suggestively the number of vaccinators, rather than the mandatory law. No one died from smallpox in the 1890s, causing the vaccination rate to decline. The mortality and vaccination patterns are similar to development presented by Sköld (1996b) for the whole of Sweden.

[Figure 2 about here]

A question that naturally arises is why vaccination rates did not reach 100% since vaccination was mandatory. The historical narrative suggests that the compulsory vaccination law was a threat, which made most parents comply with vaccination (Pettersson 1912). Yet, it is very difficult to find historical examples of fines being executed. Anti-vaccination opposition was very low in Sweden compared to other European countries, with the first known petition presented a half a century after the start of the vaccination. Nevertheless, some people were spreading the message that smallpox was a religious sin, and the local authorities were reluctant to bring in the policy and start a conflict with people who had religious reasons for refusing to vaccinate their children (Sköld 1996b). Another source of vaccine hesitance was that (false) stories about the negative consequences from vaccines were spread by vagabonds and beggars. Regarding parents who did not vaccinate their children, one local doctor classified cases as follows: laziness, pleasure from defying the law, and fears of the consequences of vaccination (Landsarkivet i Lund 1805-1827).

2.3 Non-Specific Vaccination Effects in the Historical Narrative

Many contemporaries of smallpox vaccination believed that little would be gained by the elimination of smallpox since other diseases would take over (Hofsten and Lundström 1976). But the historical narrative for Sweden and other countries suggests the opposite — the vaccine combated both smallpox and other infectious diseases, known in the current literature as "non-specific" health effects of vaccination. Mayr (2004) cites circumstantial evidence from German and Austrian vaccinators, who reported, for example, that "eye and ear disorders not only

improved but also disappeared, and that chronic diseases vanished amongst the vaccinees." He also notes that, as found, vaccinated persons are less susceptible to infectious diseases such as measles, scarlet fever, whooping cough, and even syphilis, than non-vaccinated persons. For Sweden, we searched in the annual reports from provincial and city doctors from different regions and found several indications of a close association between high vaccination rates and less infectious disease, not just smallpox (Riksarkivet 1796-1820).

Moreover, the lifetime gains for the vaccinated children may emerge from the improved disease environment. About one percent of smallpox survivors develop vivid life-long complications, such as blindness, limb deformities, infertility, and conditions in respiratory, gastrointestinal, and central nervous system (Sköld 1996b). But smallpox can affect much larger fractions of population, as confirmed by extensive empirical literature findings that being born in epidemic years reduces longevity and labor-market performance (Almond, Currie, and Duque 2018). Respiratory infections in childhood are causing atopy, reversible airway obstruction, chronic mucus hypersecretion, and irreversible airflow obstruction, affecting working capacity (Kuh, Ben-Shlomo, and Ezra 2004). Early exposure to infectious diseases may prime the immune system to remain chronically alert, leading to chronic inflammation, which in turn increases the risk of various chronic diseases (Finch and Crimmins 2004). Today, the marker of chronic inflammation, C-reactive protein, is a well-established risk factor in the clinical assessment of cardiovascular disease, and it is also associated with diabetes, mental health issues, atherosclerosis, and the disability uptake (Arnett et al. 2019).

3. Data

3.1 Microdata for Three Generations

We aim to investigate if vaccinating generation 1 against smallpox positively affects their lifelong well-being, as well as the well-being of generation 2 and generation 3. To do this, we use high-quality data spanning a long time and age range, with connections across multiple generations.

Our data come from unique register-based datasets containing health, demographic, and socio-economic information on residents from 79 different parishes in Sweden, spanning from the 18th to the 21st centuries, including their descendants. We accessed the data from two sources: for northern and central Sweden, we obtained them from the Demographic Data Base (CEDAR 2021; CEDAR 2022), and for southern Sweden, from the Scanian Economic-Demographic Database (Bengtsson et al. 2021). Both sources share essential features for our

study: The parishes selected into the datasets are built on high-quality archival records and represent geographically compact areas, which reduces biases stemming from regional differences. These datasets represent the reconstructed life and family histories of parish residents. Moreover, the data are homogeneous in terms of sources and structure, providing variables at the individual level in the same metrics across cohorts. The quality of data has been confirmed by over 250 articles that rely on it (Dribe and Quaranta 2020; Edvinsson and Engberg 2020).

Out of the datasets, we chose parishes that contained both pre- and post-vaccination cohorts. Figure A1 in Appendix A presents the parishes used in the analysis. The analytic sample for generation 1 includes individuals born in between 1790 and 1820, a period roughly equivalent to the general definition of generation – the mean age difference between parents and children. In the succeeding generations, we adhered to the same definition, with the latest cohort for the descendants corresponding to the last reproductive age of the latest born mother. Specifically, generation 2 includes the children of generation 1, born between 1805 and 1865 (with mothers in reproductive ages 15-45 years), and generation 3 includes the grandchildren of generation 1, born between 1820 and 1910. In total, we tracked the full life cycles of three generations, which amounts to 141,067 individuals, up until their death, out-migration, or reaching the age of 100.

The datasets collectively represent the economic and health development of Sweden well (Lazuka 2017; Dribe and Quaranta 2020; Edvinsson and Engberg 2020). For our analytic sample, Figure A2 in Appendix A presents below-10 mortality rates by the cause of death aggregated into smallpox, other infectious, and non-infectious groups from 1790 to 1920. In the data, the causes of deaths are available as codes of the tenth version of the international classification of diseases, which is based on the encoding of historical causes of death performed by medical experts. As shown in the figure, the influence of smallpox declined with the inception of vaccination, but perhaps surprisingly, child mortality reduced only slightly. This observation, namely, led economic historians to argue for the absence of vivid vaccination effects. However, the potential gain in survival for children becomes apparent when looking at the cohort life expectancy at age two. After a period of no improvement, life expectancy surged by 14 years for cohorts born between 1801–1820 as compared to 1790–1800, and it continued to grow for the succeeding generations.

3.2 Individual Vaccination

Our key treatment variable is whether an individual belonging to generation 1 was vaccinated against smallpox by the age of 2 years. From the microdata, we observed that the first years of life are the most common vaccination age for cohorts born after 1801, with the median age among those eventually vaccinated being 2.04 years. We did not opt for the continuous measure of the vaccination date because it could be somewhat imprecise. For instance, Dribe and Nystedt (2003) have suggested that the changing frequency of vaccinated children in the first post-vaccination years, which we also observe in the data, might indicate inaccuracy in the exact age of vaccination.

The control group includes individuals who were never vaccinated. This group includes individuals who obtained natural immunity (i.e., recovered from smallpox and are alive by the age of 2 years) or had neither vaccination nor immunity. Smallpox vaccination status is available in the data as a mark and a date of the mark, recorded by the priests in the church books during censuses and on many occasions, such as at birth, baptism, vaccination, in- and out-migration. Later ages of vaccination may therefore be associated with the period of the family's absence from the parish rather than the first vaccination date. This observation reinforces our prior decision to exclude migrant families from the estimation sample, and we additionally exclude children vaccinated after the age of 2 from the control group. A few vaccination cases mention natural immunity, but they are rare and unsystematic to constitute a separate control group.

We conducted two checks to assess measurement errors in vaccination status. First, we compared the number of vaccinated children in the microdata with the aggregated parish censuses (The Demographic Data Base 2022). Local doctor reports often mention that the aggregated parish records of vaccinees, which were reported by the priests to the state during census years, provide the most accurate counts (Riksarkivet 1796-1820). While our microdata also include linked census data, it is possible that some parish books, which serve as the foundation for family reconstitutions, have been lost, leading to the underutilization of the available census data. We found that the counts between the datasets matched nearly perfectly. Second, for our final sample – individuals vaccinated by age 2 and never vaccinated – we checked statistical differences in the means across seasons of birth – the common markers of data inaccuracy. As Table A1 in Appendix A shows, we find no evidence of inaccuracy.

3.3 Lifetime Outcomes

The data provide information on the time of an individual's death or outmigration from the studied area. For southern Sweden, records have been linked to the Swedish Death Index, which includes most deaths in Sweden (Släktforskarförbund 2019). For central and northern Sweden, we have information on death dates for around two-thirds of the sample. Our preferred indicator of longevity is a linear count of the number of years lived after the age of two (i.e., after the smallpox vaccination). This measure also indicates the latest point in time individuals are observed within the area for a portion of the sample. As we demonstrate in the results section, our findings remain similar even when these observations are treated as censored.

We used rich information on occupation from the datasets, employing it as an outcome measure, a control variable, and in construction of the instrumental variables. The original sources contributing to the occupational information in the microdata are rich and include church books, poll-tax, and examination registers, facilitating cross-checking and complementarity. Information on the occupations of individuals and household heads is available in the form of annual records and is coded into historical social stratification, represented as an occupational score on a continuous scale (Lambert et al. 2013; van Leeuwen and Maas 2011). This classification enables systematic comparisons across different cohorts. For the instrument, we selected specific occupations, such as church assistants and church musicians, and augmented the microdata with parish and county annual examination records that report the counts of clergy in these roles (The Demographic Data Base 2022).

We had access to two additional socio-economic outcomes, which are unique for such distant cohorts as we study. For the data from northern and central Sweden, we employ a variable indicating an onset of disability, such as blidness, deafness, mental and behavioral disorders (insanity, epilepsy, and speech disorder), and general weakness ("crippleness"). The variable is derived from the church records and encoded to ensure consistency across different cohorts (Wisselgren and Vikström 2023). For the northern parishes, we have also obtained an individual's literacy (for generation 1). Such data are registered annually as a test on the catechism and on reading ability, on a categorical scale.

4. Empirical Strategy

4.1 Selection into Vaccination

We begin with the analysis of selection for vaccination against smallpox by the age of two for generation 1. From the microdata, we obtained various background characteristics of the

individual, measuring parental wealth (occupational score and marital status), literacy, parenting style (survival history of the family and death of a sibling due to an external cause), as well as the year and parish of birth. Figure A3 in Appendix A presents the OLS estimates for these variables. The results show that most variables measuring family conditions correlate weakly or not at all with the probability of children being vaccinated. For instance, paternal literacy and church attendance does not influence the probability, and a one-standard deviation change in paternal occupation score increases the probability by only 0.012 percentage points. These results align well with the fact that vaccination was free for parents and did not face opposition in Sweden.

The results also indicate that differences in a child's vaccination status primarily stem from the parental parish of residence in the first years of the child's life. The differences across parishes in the proportion of children vaccinated by the age of two vary between -1.1 to 0.16 percentage points compared to the baseline. Previous research has shown that the availability of vaccinators, such as the ratio of clergy, church assistants, and church musicians per population, explains such geographical differences (Sköld 1996b). Another significant factor is the year of birth, as vaccination was first introduced in 1801, and the vaccination rate steadily rose in the subsequent years. The findings therefore suggest that the factors driving vaccination of a child by the age of two appear at the regional and cohort level.

4.2 Shift-Share Instrumental-Variables Approach

Even with no indication of selection into vaccination at the family level based on observables, selection could still appear from unobservable factors. For instance, parishes with a higher share of vaccinated children may also be characterized by higher levels of trust to authorities, which, in turn, are eager to implement health policies that benefit parishes' residents, such as employ licensed midwives or practice isolation of sick residents before it became a widespread health measure. On the individual level, families that decide to vaccinate their own child may also be more cooperative and such social norms could affect the child's future outcomes and the outcomes of the next generations regardless of initial vaccination (Lazuka and Elwert 2023; Acemoglu and Jackson 2015; Guiso, Sapienza, and Zingales 2011). To address selection into treatment, we apply a shift-share instrumental-variables approach.

We consider the first- and second-stage equations:

$$(1)\ Y_{iprt} = \beta Vaccinated_{iprt} + \boldsymbol{X}_{i(p)t}\Gamma + \eta_t + \gamma_p + \delta_{rt} + \nu_{irpt},$$

$$(2)\ Vaccinated_{iprt} = \alpha\,(C_{p(t-1)} \times C_{rt}) + \boldsymbol{X}_{i(p)t}\Gamma + \eta_t + \gamma_p + \delta_{rt} + \varepsilon_{irpt}.$$

Equation (1) is the second stage of our 2SLS system and equation (2) is the first stage. The index *i* denotes individuals, *r* denotes six geographic regions (counties), *p* denotes parishes, and *t* is cohort. For generation 1, we analyze a panel of 31 cohorts, born between 1790 and 1820, for 70 parishes. For the subsequent generations, we will describe the transformation of the instrumental-variables approach after we present results for generation 1.

The dependent variable, $Y_{iprt,}$ is an individual's outcome, such as years lived (after the age of two), disability-free years lived, literacy, and occupational score. $Vaccinated_{iprt}$ is the endogenous variable of interest, an individual's vaccination status by the age of two (vaccinated or not), who belongs to a particular cohort and was born in a known region and parish. $\boldsymbol{X}_{i(p)t}$ is a vector of individual-level variables and parish of birth-level variables interacted with cohort dummies that we discuss in section 4.3. η_t is cohort (i.e., year of birth) fixed effects. γ_p is parish fixed effects. γ_p denotes region-by-cohort fixed effects.

The instrument, $C_{p(t-1)}$ x $C_{rt,}$ is based on the interacted number of church assistants and church musicians at the parish and county levels. $C_{p(t-1)}$ denotes the number of church assistants for each parish in the previous year (cohort). C_{rt} represents the ratio of church assistants and musicians in the region compared to the previous year (cohort), calculated for the entire region, encompassing both participating and non-participating parishes in the estimation sample. The interaction term resembles the logic of the shift-share instrumental-variables method applied for the case of panel data, where $C_{p(t-1)}$ serves as shares and C_{rt} as regional shifts (shocks). Recent methodological literature demonstrates that, when shares are "incomplete" (observe that in Eq.2 the sum of $C_{p(t-1)}$ is "incomplete" because it does not equal one), omitted variable bias is still present and must be addressed by adjusting for the sum of shares or the expected value of the instrument (Borusyak, Hull, and Jaravel 2022). However, in our case, the need for adjusting the formula has been eliminated since we have already included parish and cohort-by-county fixed effects among the exogenous variables in Eq. 1 and Eq. 2.

Methodological literature on shift-share instruments recommends to use the instrument's formula that best describes the impact of the shock (Borusyak and Hull 2023; Borusyak, Hull, and Jaravel 2022). In constructing the interaction term, we use the ratio of church assistants and church musicians instead of the growth rates, more frequently used in the literature. In the preliminary analysis, we found that the levels or growth rates of church assistants are weakly identified in the first-stage equations. We also prefer regional over national shocks because of the large differences in the policies in Sweden in the eighteenth century. The county was governed by a county governor with sole responsibility, with a chancellery under him who gave

an annual report of activities and accounts. The governor was independent in the decisions for the social and healthcare issues, including the control of vagrants and hospitals, and the stipulation of the mandatory employment of church assistants as vaccinators according to the law of 1804 (Skold 1998). However, we also ran the estimates with national shocks in church assistants instead of regional shocks and found results very similar to what we further present in the paper.

In terms of interpretation, the first-stage estimates will compare the vaccination rates in the parishes that prior to vaccination had a large stock of church assistants to the parishes that had a low stock, in years (cohorts) following large regional employment influx of church assistants relative to years (cohorts) following lower influx of church assistants. The reduced-form estimates make a similar comparison but with lifetime outcomes as the dependent variables. Clearly, the estimate for α should be positive in both first- and second-stage equations, because parishes with a small stock of church assistants should vaccinate more and benefit more from regional shocks in church assistants.

We present the interacted instrumental variable by cohort and region of birth in Figure 3. Across all regions, the series exhibit a distinct change around 1805, corresponding to the introduction of state directives mandating the employment of church assistants and musicians for smallpox vaccination efforts. However, there is significant variation in law adoption, as the series demonstrate. In central Sweden (Östergötland county), where the number of church assistants was already relatively high before the law, more than two assistants were, on average, employed after 1804. In southern Sweden (Malmöhus county), the uptake was notably low, with not every parish employing a church assistant. In the four northern regions, the series display varying levels and dynamics. For instance, Jämtland county exhibited high uptake, while Norrbotten county had a lower uptake. The overall ranking of regions based on this instrument's quantity perfectly aligns with the county ranking observed across the entire country (Sköld 1996b).

[Figure 3 about here]

4.3 Identifying Assumptions

Interpretation of the effect of interacted instrumental variable as causal requires an exclusion restriction: Conditional on controls the interaction between the lagged number of church assistants in the parish and the regional shocks in church assistants only affects individuals' lifetime outcomes through vaccination. The exclusion is violated in two instances: (1) if there is a direct effect of the instrument on the outcomes; (2) there are (omitted) common factors affecting

both the instrument and the outcome. To address (1), we chose to focus on church assistants and church musicians as the only subgroup of vaccinators. Historical sources highlight that Church workers were trustworthy and literate yet lacking knowledge on medicine (Sköld 1996b). The law of 1804 stipulated that each parish must employ a church assistant or musician for vaccination, thereby blocking the potential monopolization of the process by doctors. Vaccinations were easy to learn, following the instructions distributed by the state and short training by the priest (Banggaard 2002).

As an illustration, a church musician who assisted at choirs became the first vaccinator in Kävlinge, one of the parishes in southern Sweden, and vaccinated against smallpox as his second part-time job; he did not participate in other health-related matters (Landsarkivet i Lund 1805-1827). In the neighboring parish, initially, a licensed midwife vaccinated children (Landsarkivet i Lund 1785-1857). Although the means of preventing disease were very limited in the beginning of the 19th century, some were practiced by doctors, such as cause-of-death counting and isolation of the sick (Lazuka, Quaranta, and Bengtsson 2016), or by midwives, such as proper assistance at labour (Lorentzon and Pettersson-Lidbom 2021). In these two parishes, our instrument will capture the vaccination efforts of a church musician but not of a midwife.

Type (2) violation implies the presence of common factors that affect both the instrument and the outcomes. In our case, the series of lagged church assistants and musicians in the parish along with the shocks in current church assistants and musicians in the region (which constitute two components of the interacted instrumental variable) are likely to be correlated with both fixed and varying characteristics of the parish (region), such as wealth or religiosity, for instance, which influence the outcomes too. In practice, this is not a serious problem for our estimates for several reasons. Parish fixed effects in the baseline specification control for all permanent factors at the parish level affecting the employment of church assistants and musicians. We also introduce families' characteristics affecting families' decision to vaccinate children interacted with cohort dummies (as in section 4.1), which account for the parish shocks related to the changing parish residents' behavior and outcomes. To identify any unobserved time-varying parish shocks, we examine pre-trends and find none, as we further elaborate on in Section 5.2.2.

In relation to the regional shocks, they similarly can reflect regional health policies, other than vaccination. The region-year of birth fixed effects in our baseline specification account for any such effects, observed an unobserved. Our analysis also introduces interactions between cohort (i.e., year of birth) dummies and local (i.e., for the group of parishes) measures of wealth, religiosity, and health policies, which capture differential responses of regions to the mandatory

vaccination campaign. In particular, we include the number of midwives (interacted with cohort dummies) that will control for development of healthcare and composition of the vaccinators' group in the area; smallpox death rate will control for demographic and disease conditions; the share of urban population and university students per capita will control for the urbanization and progressivity; the number of priests will difference out the effects of religiosity; and the price of rye will control for economic development. Finally, to account for the mutual correlation of the local shocks, we cluster standard errors at the parish level.

Finally, we relax an assumption of the constant treatment effects. Under the presence of heterogeneous treatment effects, as discussed in Borusyak, Hull, and Jaravel (2022), a causally interpretable instrumental-variables estimand is guaranteed as long as the treatment (i.e., individual vaccination) is correctly specified, shares are non-negative, and the true effects of shocks on each treatment are monotone (i.e., there are no "defiers"). We have already discussed that the error in the treatment variable is unlikely in Section 3.2. The shares cannot be negative by construction. Finally, we have searched the local vaccination reports (Riksarkivet 1796-1820) to identify the possibility of "defiers", i.e., cases in which parishes *reduce* the vaccination rate when there is a positive regional employment influx of church assistants and church musicians, and increase it when the influx is negative; we have not found any such cases.

Our shift-share instrumental-variables estimates hence reflect the average effect for the observations that comply with the instrument, i.e., a local average treatment effect (Angrist, Imbens, and Rubin 1996). In our setting, compliers are parishes that vaccinate a larger proportion of children following a response to the regional employment influx of church assistants and church musicians. Those parishes that did not respond to the instrument do not contribute to the estimate.

5. Results for Generation 1

5.1 Descriptive Analysis

We begin the analysis with the relationships between the interacted instrumental variable and the probability of being vaccinated by the age of two (first-stage) and the lifetime outcomes (reduced-form). We aggregate the estimation sample by the birth cohort and plot the observations and the fitted line, weighted by the number of individuals in each cohort. The first-stage relationship is shown on Figure 4. The results show a strong positive association: one unit change in the interacted instrument increases the share of vaccinated children by 20%.

[Figure 4 about here]

The reduced-form relationships are shown on Figure 5, for each lifetime outcome separately. All outcomes are positively associated with the instrument. One more church assistant in the year of birth is associated with 0.69 more years lived and 0.51 more disability-free years lived after the age of two. The relationship with economic outcomes in adult ages is also strong: the share of individuals with good literacy skills increases by 4% and occupation score by 0.74 units, as a result of one unit change in the instrument. The figures are rough approximations of the first-stage and reduced-form estimates, because they do not consider control variables, important for the identification of the causal effects.

[Figure 5 about here]

We continue the analysis by reporting the OLS estimates of Eq. 1, which are presented in Panel A Table 1. The results show positive and statistically significant effects (at a 1 percent level) for all lifetime outcomes. Being vaccinated by the age of two is associated with 12 more years of life. The relationship between vaccination and disability-free remaining years lived, which measures the time until individuals develop a disability, shows a similar pattern. There are also strong effects on economic outcomes: Vaccination by the age of two is associated with a 19 percentage points increase in the share of people who possess good literacy skills and a 2-unit larger occupational score after the age of 15. The effects are robust to the inclusion of additional family and parish controls accounting for time-varying shocks.

[Table 1 about here]

5.2 Linear Shift-Share Instrumental-Variables Estimates

5.2.1 Reduced-form and 2SLS estimates

We turn to the instrumental-variables estimates of the impact of vaccination by the age of two on lifetime outcomes in later ages. First, since the instrument is available only for a subsample of parishes in the dataset, we run the OLS estimates according to Eq. 1 on a restricted sample and show them in Panel A.2, Table 1. Such controlling-for-observables estimates are more modest compared to the full sample but remain similar in statistical terms.

In Panel B, Table 1, we present the results from the instrumental-variables estimations. For all outcomes and specifications, a Kleibergen-Paap F-statistic, which is robust to heteroskedasticity and clustering in errors, in the first stage is close to 50, meaning that the interacted instrumental variable yields a strong impact on the probability of being vaccinated in the first ages of life (Keane and Neal 2023). The first-stage results imply that a unit change in the interacted instrument increases the probability of being vaccinated by the age of two by 0.4%,

when considering a sample of individuals for years lived as an outcome, for instance. The instrument values range from 0 to 89, hence at most the instrument increases the vaccination uptake by 32% (0.36% x 89).

The 2SLS estimates are shown in Panel B.1 and reduced-form estimates are in Panel B.2, Table 1. Regarding the impact on the outcomes, the 2SLS estimates show a positive and statistically significant impact of vaccination on health variables and an occupational score. Here the reduced-form estimates are also strong. The Anderson-Rubin 2SLS test statistic draws a similar conclusion about the impact of vaccination as the 2SLS *t*-statistic, indicating that the latter is unbiased (Keane and Neal 2023). Regarding the reduced-form effects, a one unit increase in the instrument increases the number of years lived by 0.039 years and the number of disability-free years by 0.04 years. The 2SLS estimate for the impact of vaccination on years lived and disability-free years lived is 11 and 12 years, respectively.

Turning to economic outcomes, the reduced-form impact of the instrument is 0.013 units of occupational score in adult ages in terms of standard deviations, and the 2SLS impact of vaccination is 3 units, which is statistically significant at the 5 percent level. For literacy, the 2SLS impact of vaccination loses statistical significance but remains in a similar magnitude, with a 4-percentage-point increase in the probability of having good literacy skills in adult ages. For this outcome, our 2SLS estimates are thus not informative about the causal vaccination effect, which, however, does not imply that there is no such effect.

We observe that our results are robust to the inclusion of additional parish- and time-varying controls, but the estimates become less precise when more controls are added. This happens because many controls in the extended model are also strongly correlated with the vaccination variable, so adding these controls reduces variation in the vaccination variable induced by the instrument and increases standard errors. The point estimate of the vaccination effect is smaller in the instrumental-variables compared to the controlling-for-observables estimations but remains similar in statistical terms. However, even the lowest, a 10-year increase in years lived due to smallpox vaccination in the 2SLS estimations is large enough to account for most of the cohort improvements in life expectancy after the age of two.

5.2.2 Parallel Pre-Trends

It is possible to validate the shift-share instrument (essentially, type (2) exclusion restriction violation) by examining whether observations with different exposure shares exhibit parallel trends prior to the shock (Borusyak, Hull, and Jaravel Forthcoming). This follows from

that linear instrumental-variables with shift-share as an instrument varying by year of birth and parish of birth are analogous to the difference-in-differences with continuous treatment, with underlying "parallel trends" restrictions. Any evidence for significant pre-trends would signal that a set of cohorts in particular parishes that had a low stock of church assistants/musicians and are affected by an influx of church assistants/musicians would have evolved differently from the other cohorts and parishes with a low stock even in the absence of the influx. The parallel development should similarly apply to various levels of the influx.

To assess the plausibility of the parallel trends, we create the leads of the instrument and estimate the reduced-form effects with these leads instead of the instrument. The results for the models with two sets of covariates (as in Table 1) are presented on Figure B1 Appendix B. Overall, there is no evidence of significant pre-trends in mortality, disability, and literacy. For occupational score, there is a significant coefficient for the first lead in the baseline model, but it becomes null in the model with all controls, suggesting that the addition of the covariates partial out any time-varying shocks from the instrument's estimate.

5.3 Nonlinear Shift-Share Instrumental-Variables Estimates on Mortality and Disability Risks

5.3.1 2SRI Estimates

In this section, we investigate at which ages the health benefits of smallpox vaccination materialize for generation 1 and whether they emerge due to non-specific vaccination effects. Answering these questions requires the utilization of nonlinear instrumental-variables models because an individual's risk of dying changes over lifetime (usually following a *U*-shaped pattern), and death from a particular cause competes with other alternatives. Moreover, unlike linear models, nonlinear (duration) models for health outcomes account for censoring due to outmigration and serve as a good check for our previous results.

We follow the same logic as with linear shift-share instrumental-variables models: first, we run a model that controls for observables, and then we estimate an instrumental-variables model. To fit nonlinear shift-share instrumental-variables, we apply a control function approach, more specifically a two-stage residual inclusion model, 2SRI (Palmer 2024; Wooldridge 2015; Terza, Basu, and Rathouz 2008). The second equation estimated is as follows:

$$(3)\ ln(h_{iprt}) = \beta Vaccinated_{iprt} + \boldsymbol{X}_{i(p)t}\Gamma + \eta_t + \gamma_p + \delta_{rt} + \widehat{\varepsilon_{irpt}} + \nu_{irpt},$$

where $ln(h_{iprt})$ is a natural logarithm of the hazard of death (disability) and other terms are defined as before. We follow Tchetgen Tchetgen (2014) and fit the first stage (i.e., Equation 2) with a logistic regression, because the second stage requires the residual from the a location shift model for a binary treatment. We fit a logistic model (a generalized linear model) and save Anscombe residuals instead of raw residuals because this approach produces the least biased estimates of average treatment effects (Basu and Coe 2017). In the second stage, we add the individuals' residual from the first stage, $\widehat{\varepsilon_{irpt}}$, and estimate a proportional hazard model. A proportional hazard model is preferred because it can effectively incorporate a control-function residual: in this model the effects of covariates multiply the baseline hazard function, leaving it unspecified (Palmer 2024). Both a survival function and age-specific life expectancy can be derived as post-estimation results.

We present the estimates for the risk of death and disability in ages between 2 and 100 years from the controlling-for-observables and 2SRI in Table 2. For the 2SRI estimations, we run the estimations on a reduced sample, in which there is variation in the outcome in the first stage for each control variable. The controlling-for-observables results show a lower risk of mortality for individuals who were vaccinated before the age of two–by 80%. The 2SRI estimate indicates that vaccination reduces mortality risk by 68%. The first-stage residual is less than 1 albeit unsignificant in statistical terms, suggesting that omitted variables may lead to the overestimation of the effects in controlling-for-observables regression. In this regard, our results resemble those in the linear models. In terms of disability risk, the 2SRI estimates indicate that vaccination reduces this risk by 73-80%.

[Table 2 about here]

Based on the 2SRI models, we obtain the average survival function and life expectancy (total and disability-free) after the age of two for the whole life and at different ages and present them in Figure 6. To calculate the average life expectancy, we first estimate the baseline cumulative hazard function, calculate the scenario-specific hazard contributions and the survival function (i.e., at different combinations of the control variables), and then compute the integral of the latter in the ages of interest, as suggested by (Finkelstein and Vaupel 2009). As Panel A shows, vaccination improves the probability of survival at all ages. For total life expectancy, vaccination in childhood adds 0.06 years for each survived year between ages 2 and 15, 0.15 years between ages 15 and 70, and afterwards the contribution declines, giving an average of 0.08 years. In total, vaccination adds 11.6 years to life expectancy ate the age of 2 (51.8 years versus 40.2 years

for vaccinated versus never-vaccinated individuals), which is the number similar to our 2SLS result from linear models.

[Figure 6 about here]

For disability, when we obtain survivor functions and life expectancies based on the estimates from Table 2, their shapes look very similar to those for mortality, resulting in a total of 12.5 disability-free years of life. Perhaps of prime interest would be to know how many years of disability net of mortality is saved by vaccination. We, therefore, estimate the models with a disability onset as the only failure and calculate survivor functions and life expectancies. As Panel B in Figure 9 shows, vaccination increases disability-free life expectancy primarily after the age of 20 years, resulting in a total of 2.8 additional years.

5.3.2 Cause-Specific Mortality and Disability

We further assess the vaccination effect on the hazards of death and disability by cause. An ideal way to obtain such effects is to model cause-specific hazards by treating events due to competing causes as censored observations. Therefore, we apply an approach by Lunn and McNeil (1995): stack the events with as many rows as there were causes of death (disability) and fit a 2SRI model (i.e., with controls and a first-stage residual) stratified by cause. The controls and the first-stage model are the same as in section 5.3.1.

Table 3 shows the results for cause-specific mortality and disability. Vaccination reduces the risk of death from smallpox to almost null, implying high efficiency of the historical vaccine. But it also reduces the mortality risk from other causes by 79%. This finding for mortality suggests the presence of "non-specific" vaccination effects. For disability, we distinguish two causes—those known as a consequence of smallpox infection (blindness, mental retardation, and general weakness) and other causes (deafness and mixed causes). Our results show that smallpox primarily reduces the risk of disability due to smallpox-related causes (by 42%), linking smallpox to the individual's ability to learn and physical fitness.

[Table 3 about here]

5.3.3 Bounds Test

Nonlinear instrumental-variables estimations rely on the same assumptions as linear instrumental-variables do, and the primary assumption to emphasize is the requirement for an exclusion restriction. As with linear instrumental variables, we foresee that there might be two type of exclusion restriction violations, the direct effects of the instrument on the outcome and

the common factors between the instrument and the outcome. Regarding the first type, our reasoning for the linear models applies for nonlinear models too. To avoid violation of the second type, our models included an extended set of controls. We additionally conduct a bounds test. In the controlling-for-observables model, the duration models also assume random censoring. This additional assumption is relaxed in the nonlinear instrumental-variables model (MacKenzie, Martinez-Camblor, and O'Malley 2021).

In the context of duration models, we compute a so-called *e*-value that shows how robust the effect to potential unmeasured selection, without assuming any particular form of the relationship between the treatment, unobservable, and the outcome (VanderWeele and Ding 2017). Figure B2 in Appendix B shows the *e*-value and its lower 95% confidence interval for the vaccination effect of generation 1 across the life cycle. These two measures suggest that any potential selection effects should be linked to both vaccination and survival with a hazard ratio of at least 5.3 (5.1) to nullify the vaccination effect. Such an effect would be considered unlikely to diminish the vaccination's impact in a modern context, but it should be evaluated in the context of nineteenth-century Sweden.

To benchmark the effects, we estimate the effects of family conditions, in particular those associated with misery, neglect and poor prospects in life–being born out of wedlock or born to family with a high proportion of children dying (Edvinsson et al. 2005). Table B1 in Appendix B reports the estimates. Indeed, illegitimate children and children whose older siblings died prior to their birth carry a disadvantage in terms of survival throughout their lifetime. However, the strength of these associations amounts to not more than 1.3 on a hazard-ratio scale, which is four times lower than the ratio suggested by the sensitivity analysis. None of the other individual-level covariates indicate strong effects in childhood, nor do they suggest any lasting consequences. We also show the estimates for the parishes of birth, among which the largest hazard ratio amounts to 2.7 (for the parish of Gällivare). Therefore, in our context, any unmeasured factors could not eliminate the impact of vaccination.

5.4 Additional Robustness Analyses

5.4.1 Mother Fixed-Effects Estimates

An alternative approach to account for unobservable selection into smallpox vaccination involves introducing mother fixed-effects into Equation 1. Mother fixed effects allow us to compare biological siblings, one of whom received the treatment while the other did not. This effectively removes all fixed, unobservable family-related factors that may affect both the

treatment and long-term outcomes in life. We maintain the same set of controls as in the previous specifications to effectively control for time-varying factors at the family and area levels, such as changes in parish of residence, local health policies, or family-specific disease events. Vaccination here can be treated as a positive external shock to one sibling but not the other, occurred because at that time family resided in the parish where vaccination was provided or the child was born when vaccine became available, even though the family decisions were orthogonal to the decision to vaccinate both of their children.

The results of the mother fixed-effects estimations are presented in Table 4. These results reveal positive and statistically significant effects of smallpox vaccination in childhood on both health and economic lifetime outcomes. Vaccination by age two increases the number of years lived and disability-free years lived by 16 years, raises the probability of possessing good literacy skills by 4 percentage points, and improves occupational scores by 2.7 units. The effects increase in the models with more controls.

[Table 4 about here]

To account for the influence of unobservable variables at the family level, we also introduce mother fixed effects into Equation 1 on the hazards as an outcome. When estimating a large number of incidental parameters for mothers, duration models can produce an "incidental parameter problem" and bias the estimates. We therefore implement a common solution to solve the problem—apply a stratified partial likelihood model, in which a set of baseline hazards, separate for each mother (strata), get absorbed into the unspecified function of age. The results for the duration mother fixed-effects models are presented in Table B4 of Appendix B. They show an even larger negative impact of vaccination on mortality and disability, compared to the controlling-for-observables models.

Mother fixed-effects produce the local average treatment effects of vaccination for families that have a varying treatment status of their children (Miller, Shenhav, and Grosz 2023). To analyze a mothers' complier population, in Figure B3 Appendix B, we assess the differences between the families with and without varying vaccination status of their children. Mothers who choose to vaccinate some children but not all have a higher proportion of children who die and husbands who are illiterate. However, a more significant difference emerges based on the child's year of birth. This suggests that, for mothers with varying vaccination status of their children, smallpox vaccination varies due to the unavailability of the vaccine for children born before 1801, not due to family factors.

5.4.2 Influence of Other Interventions

The institutional context of the vaccination campaign suggests that no significant interventions took place in parallel. Medicine was underdeveloped at that time, and the knowledge of isolating infectious diseases through epidemiological hospitals was realized much later (Lazuka, Quaranta, and Bengtsson 2016). One potential intervention to consider was the practice of midwives—they improved maternal survival and could influence infant health, with long-term health consequences. However, previous research has found no effects on infant health prior to the acceptance of the germ theory of disease and re-education of midwives at the late nineteenth century (Lorentzon and Pettersson-Lidbom 2021; Lazuka 2018). Another intervention to contemplate is the introduction of potatoes around 1805. Around this time, farmers began growing potatoes in arable fields, which increased the production of nutritious food, potentially benefiting the growth and health of the population (Lazuka, Bengtsson, and Svensson 2023; Floud et al. 2011).

We assess the influence of other interventions on vaccination against smallpox and lifetime outcomes by introducing an interaction of the number of midwives and the quantity of potato seeds (observed at the parish level) with a vaccination dummy into Equation 1. Table B4 in Appendix B reports the results. The estimates for the vaccination effects on all outcomes remain almost unchanged after accounting for the interaction with co-interventions. For midwives, the absence of the interaction effect aligns with the observation that midwives or doctors did not serve as the primary group of vaccinators. Regarding potatoes, the results reinforce the notion that smallpox is a disease with a low correlation to nutritional intake, and there are no complementary effects in areas with both high potato productivity and high smallpox vaccination rates on the health of children born in these areas.

6. Results for Generation 2 and Generation 3

6.1 The Effects on Health and Occupational Score

In this section, we examine whether vaccination status of generation 1 improves the lifetime outcomes of their children (generation 2) and grandchildren (generation 3). In distant relationships such as intergenerational ones, it is hard to believe that omitted variables are orthogonal to the offspring's outcomes. Therefore, we rely strictly on instrumental variables with an interacted instrument, $C_{p(t-1)}$ x C_{rt}, which allows us to omit the influence of unobservable selection for the mother and the father (generation 1). Covariates are measured and defined for generation 1, including both a baseline and an extended set. We implement the instrumental

variables using the 2SRI approach because it eases interpretation and enables the application of causal mediation analysis. For linear outcomes (i.e., linear first and second stages), the 2SRI approach is analogous to the 2SLS (Wooldridge 2015; Terza, Basu, and Rathouz 2008), so our strategy resembles the one we used to estimate the vaccination's effects for generation 1. We stack individual observations for the sample of mothers and fathers (grandmothers and grandfathers from the mother's and father's side) because, as we find, the effects are similar regardless of the parent's (grandparent's) gender.

Generation 2 consists of biological children of generation 1 (and who are born between 1805 and 1865), and generation 3 consists of biological grandchildren of generation 1 (and who are born between 1820 and 1910). Only half of generation 1 individuals are linked to their children and thus included in the subsequent generation's estimation samples. In Figure E1 Appendix E, we illustrate differences in the observable characteristics of generation 1 between those linked and those not linked to the next generation. Notably, this linkage is uncorrelated with individuals' socio-economic traits, such as family occupational scores, literacy, or maternal marital status, suggesting that we do not observe the healthier children. The association with the year of birth is also marginally statistically significant. Substantial disparities are observed among parishes, yet identifying their sources proves challenging, as they are not linked to geographic factors like the south-north or urban-rural divide. Perhaps more important is that merged individuals are present across all 70 parishes and 31 cohorts studied in generation 1. The outcomes available for the offsping' cohorts include life expectancy, disability-free life expectancy, and occupational score. We refrain from estimating the effects for literacy rates, as the offsprings' literacy is almost perfectly (positively) collinear with the vaccination status of parents.

Table 5 presents the 2SRI results for the outcomes of generation 2 and 3 in Panels A and B. Smallpox vaccination of generation 1 improves the health lifetime outcomes of both generation 2 and 3, and the effects are statistically significant at least at the 5% level. If to rely on the magnitude with a more extended set of controls, life expectancy at birth increases by 2.2 years for generation 2 and 1.1 years for generation 3. Regarding occupational score, we find the marginally statistically significant effect for generation 2 only, with a 1-point increase on a continuous scale, while generation 3 does not benefit from grandparents' vaccination status. The relative magnitudes of the effects on life expectancy and occupational score are around 20% and 10% for generation 2 and 3, when compared to the effects observed in generation 1. The increase in disability-free life expectancy—a measure of morbidity—is even more substantial, with gains

of 8 years for generation 2 and 4.3 years for generation 3, which is more than a half of disability gain for generation 1.

[Table 5 about here]

Narrowing the birth cohorts to individuals born close to 1845 and 1890, with these years serving as the median for generation 2 and 3, does not alter the results. Our findings regarding the health of succeeding generations therefore suggest potential mediation (i.e., reinforcement) by other influential factors, such as health interventions against infectious disease implemented from the 1880s, for instance. The absence of transmission of socio-economic relationship to the distant generations is consistent with increased social mobility among cohorts born around the 1890s in early industrializing Sweden. We further explore these possibilities in the causal mediation analysis.

6.2 Mechanisms of Intergenerational Transmission

In the last section, we conduct a causal mediation analysis of the impact of generation 1 vaccination on the outcomes of subsequent generations. While there are numerous potential mediators in these long-term relationships, our primary focus is to distinguish between factors related to nature and nurture. Specifically, we aim to determine whether smallpox vaccination induces people to transmit knowledge through nurturing or if there is a direct biological transmission of past environments (i.e., epigenetic inheritance) (Collado, Ortuño-Ortín, and Stuhler 2023; Lee and Conine 2022; Vågerö et al. 2018). Among the mediators that measure nurture, we analyze childhood smallpox vaccination status of generation 2 (generation 3), whether the child was assisted by a midwife at birth, and the parental occupational score. The effects of nature are represented by the residual total effects, which are the direct effects of smallpox vaccination status of generation 1.

To perform the causal mediation analysis, we follow the causal inference literature, which proposes to decompose the total effect into the natural direct effect and natural indirect effect (Heckman, Pinto, and Savelyev 2013; Imai, Keele, and Tingley 2010). In our case, the natural direct effect is comparing $Vaccinated_{iprt}$ at 1 and 0 intervening to fix the level of mediator to 0, and the natural indirect effect is comparing the effects at different levels of mediator, intervening to fix $Vaccinated_{iprt}$ at 1. Both effects are identified under the assumptions of no unmeasured confounders between the combinations of treatment, outcome, and mediator, given a set of observables. To improve the plausibility of these assumptions, we perform the analysis on a set of covariates that we used in a 2SRI model.

We follow Imai, Keele, and Yamamoto (2010) and estimate the direct and indirect natural effects by fitting a parametric regression model for the outcome of generation 2 (generation 3) and a parametric regression model for mediator in the following ways:

$$(4)\ Y^{2(3)}_{iprt} = \beta Vaccinated_{iprt} + \mu_1 M^{2(3)}_{iprt} + \mu_2 M^{2(3)}_{iprt} X Vaccinated_{iprt} + \boldsymbol{X}_{i(p)t}\Gamma + \eta_t + \gamma_p + \delta_{rt} + \widehat{\varepsilon_{irpt}} + \nu_{irpt},$$

$$(5)\ M^{2(3)}_{iprt} = \beta Vaccinated_{iprt} + \boldsymbol{X}_{i(p)t}\Gamma + \eta_t + \gamma_p + \delta_{rt} + \widehat{\varepsilon_{irpt}} + \epsilon_{irpt},$$

where $Y^{2(3)}$ is the outcome for generation 2 (generation 3), and $M^{2(3)}$ is the mediator for generation 2 (generation 3). The term $M^{2(3)}_{iprt}\ X\ Vaccinated_{iprt}$ denotes an interaction between smallpox vaccination status of generation 1 and the mediator. All other terms are defined as before. After fitting the models *(4)* and *(5)*, the method then uses simulations to calculate natural direct and natural indirect effects. Robust standard errors are clustered at parish of birth of generation 1 and retrieved by bootstrapping.

Table 6 displays the results for direct and mediated effects on offspring's life expectancy, disability, and occupational score. For the health outcomes, the propensity of parents to vaccinate their children against smallpox emerges as a significant, reinforcing mediator. Because parents (grandparents) were vaccinated against smallpox before age two and vaccinated their children, generation 2 and 3 experience gains of 1 and 0.8 years of life, as well as 2.8 and 2.5 disability-free years, respectively. The impact of other mediators, like parental occupational score and assistance at birth by a licensed midwife, is low or marginally statistically significant. Dependent on the outcome, around 40-60% of the years gained due to smallpox vaccination for generation 1 remain unexplained by mediators. This translates to 0.8 years and 4.1 disability-free years of life for generation 2, and 0.7 years and 2.7 disability-free years of life for generation 3. These unexplained effects might be attributed to other (unobserved) mediators or epigenetic inheritance, including the genetic transmission of improved health, acquired through smallpox vaccination by the age of two, to subsequent generations.

[Table 6 about here]

For the occupational scores of subsequent generations, the mediated results show a different pattern. Occupational score of generation 2 increases by 2.2 units due to parental smallpox vaccination directly. However, the natural indirect effect of parental occupational scores amounts to 0.07 per unit and is statistically significant at the 5% level. With a range of parental occupational scores of 61.8 units, the maximum mediated effect amounts to 4.5 units (61.8 x 0.072), which is even larger than the direct effect. Previously, we did not find any significant total effects of grandparental smallpox vaccination on the occupational scores of generation 3.

We now observe a substantial indirect effect through parental occupational scores: individuals belonging to generation 3, whose grandparents were vaccinated against smallpox by age two, receive a gain of 0.09 per unit of their own occupational score, or 5.4 units at the maximum (61.8 x 0.087).

Overall, a positive shock to health of generation 1, such as smallpox vaccination, operating through various channels, enhances both health and socio-economic outcomes for at least two more generations.

7. Conclusions

In this study, we investigated whether smallpox vaccination in early childhood enabled individuals to live longer and become prosperous as adults, and whether such vaccination effects were transmitted to their two consecutive generations. To obtain the causal effects of smallpox vaccination, we applied a shift-share instrumental-variables approach, using the fact that vaccination in Sweden was carried out by low-skilled clergy who otherwise did not perform public health duties. We leveraged unique historical microdata from different areas across Sweden, covering the full lifespans of three generations.

Our study leads us to draw several important conclusions. First, we find evidence consistent with both specific and non-specific vaccination effects. Smallpox vaccination increases the total and disability-free life expectancy of generation 1 by 11 years and enhances their occupational achievements by 10%. Such effects emerged due to decreases in mortality from smallpox and other causes, but also appear to have reduced disability associated with ailments that could hinder human capital accumulation. Second, these effects persist across generations. Smallpox vaccination of generation 1 increases the life expectancy of generation 2 by 2 years and of generation 3 by 1 year, as well as improving their occupational scores. Around half of the transmitted effects are driven by nurture, as vaccinated individuals are more likely to vaccinate their children across generations; epigenetic inheritance likely drives the other half. Finally, we obtain similar results when utilizing different causal strategies, such as linear and non-linear shift-share instrumental-variables, and mother fixed-effects. The results withstand a large number of robustness checks.

Our findings are potentially important for policy as they underscore the power of vaccination. The evidence that smallpox vaccination offers protection not only against smallpox but also against other diseases makes vaccination a powerful health intervention. Our findings, which highlight very long-term, intergenerational health and economic benefits from

vaccination, suggest that the total benefits of smallpox vaccination were much larger than the existing literature suggests. Whether these findings are applicable to other vaccines is beyond the scope of this paper but remains an important topic for future research.

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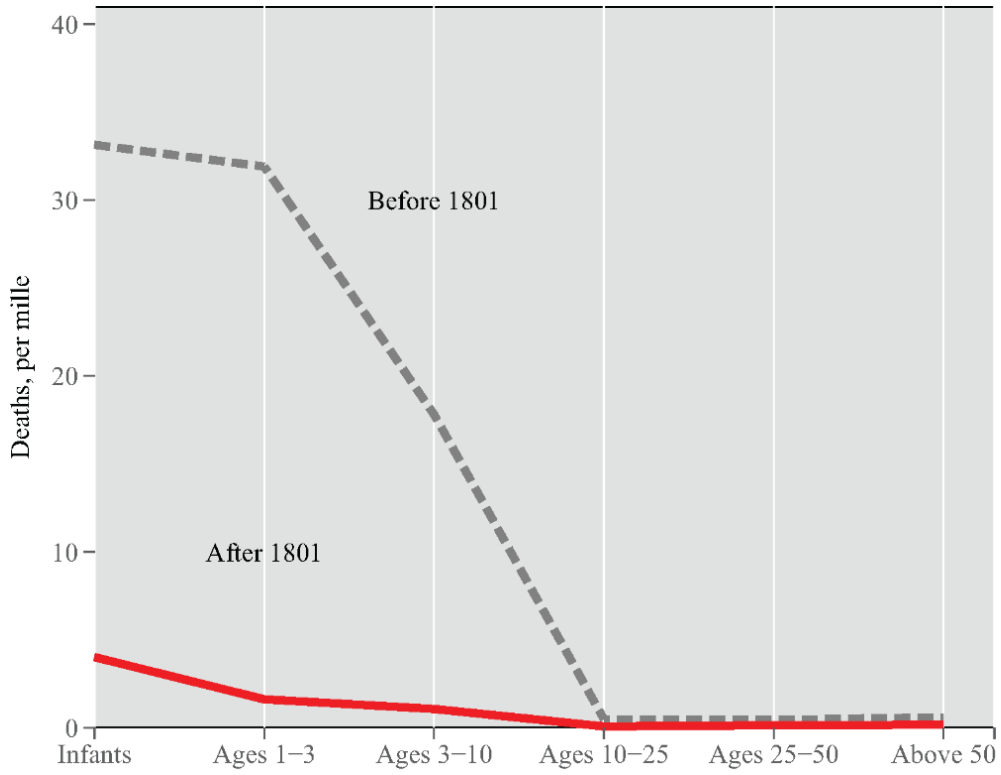

Figure 1 – Age pattern of smallpox mortality before and after the introduction of vaccination, 1790–1820.

Source: own calculations based on the estimation sample.

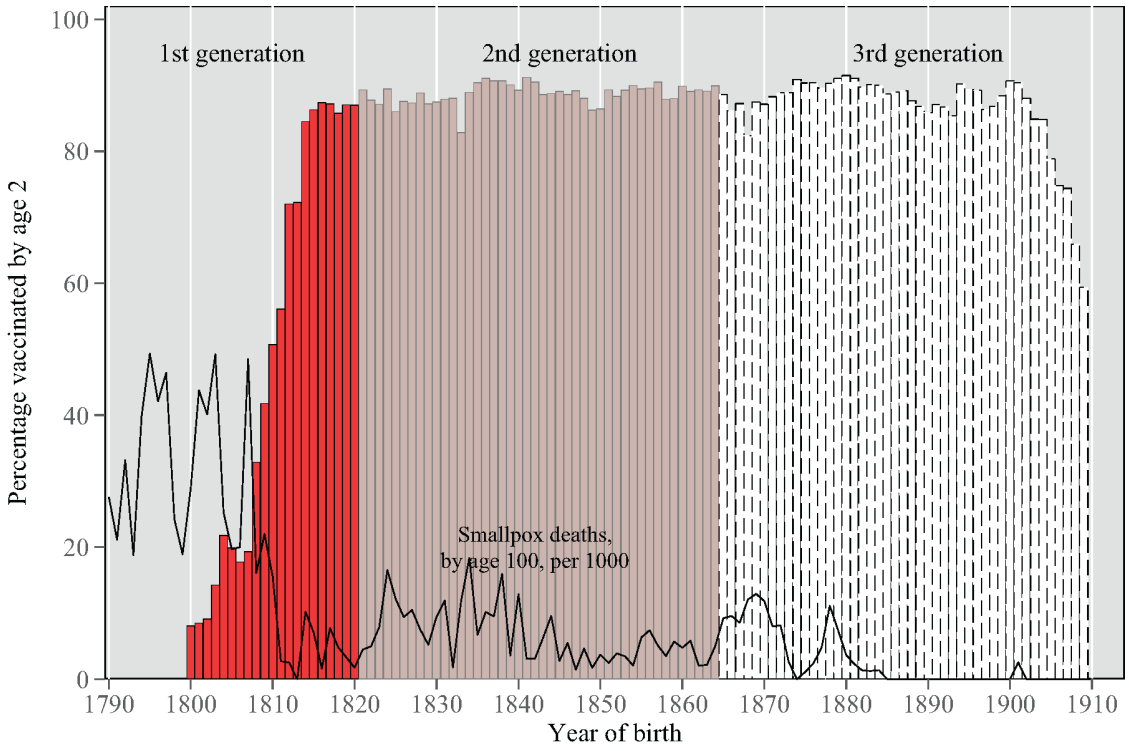

Figure 2 – Share of vaccinated by the age of 2 and of dying from smallpox by age 100, cohorts 1790–1910

Source: own calculations based on the estimation sample.

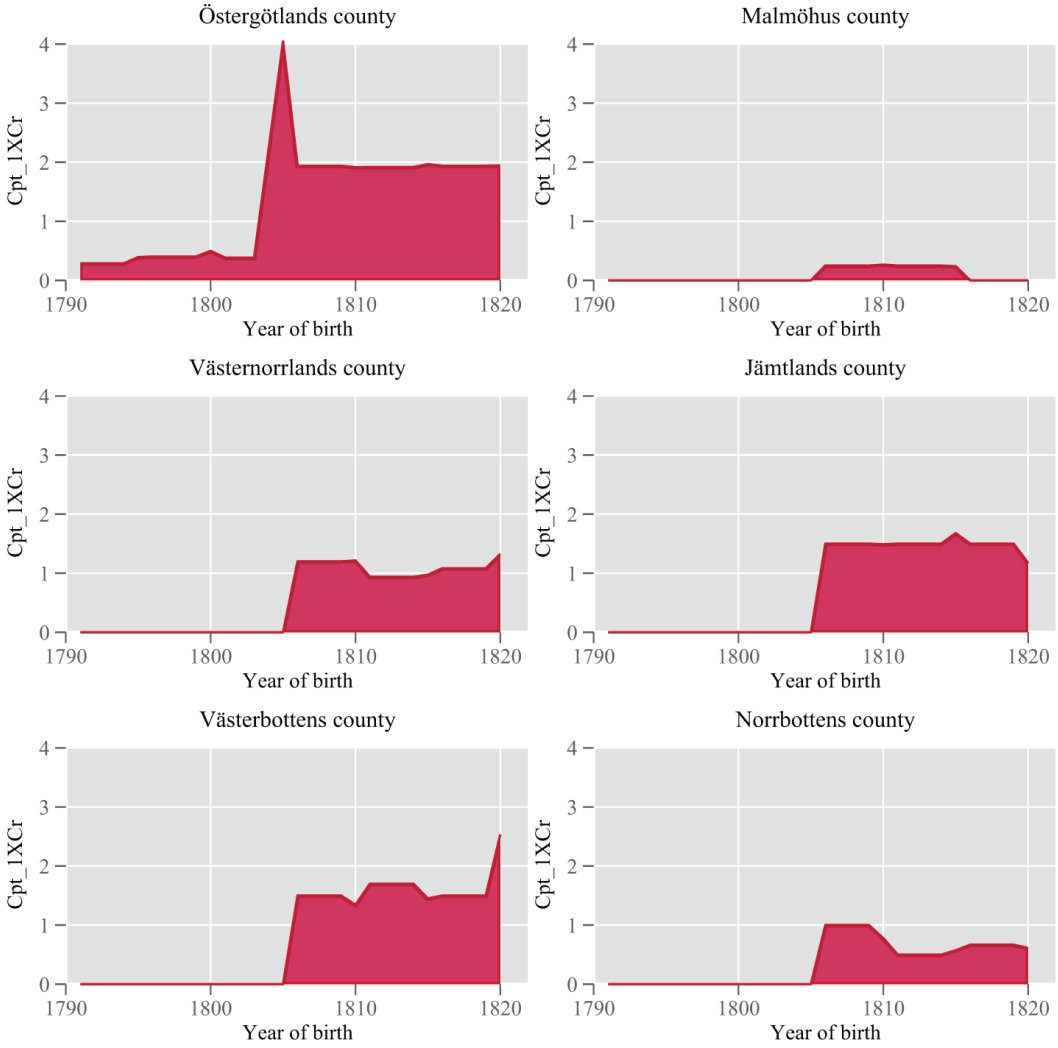

Figure 3 – Interacted instrumental variable ($C_{p(t-1)}$ x C_{rt}), average by birth cohort and region of birth.

Source: own calculations from the estimation sample.

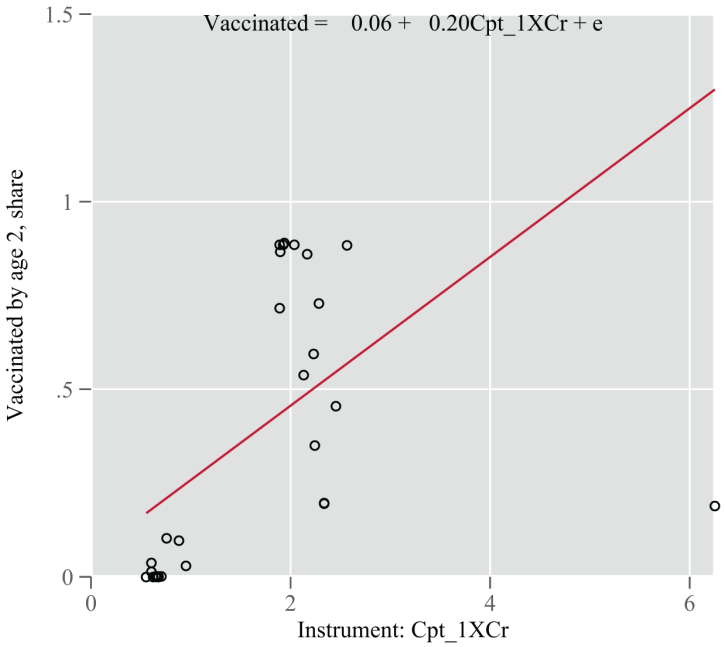

Figure 4 – Interacted instrumental variable ($C_{p(t-1)}$ x C_{rt}) and the share vaccinated by age 2, average by birth cohort weighted by the number of individuals.

Source: own calculations from the estimation sample.

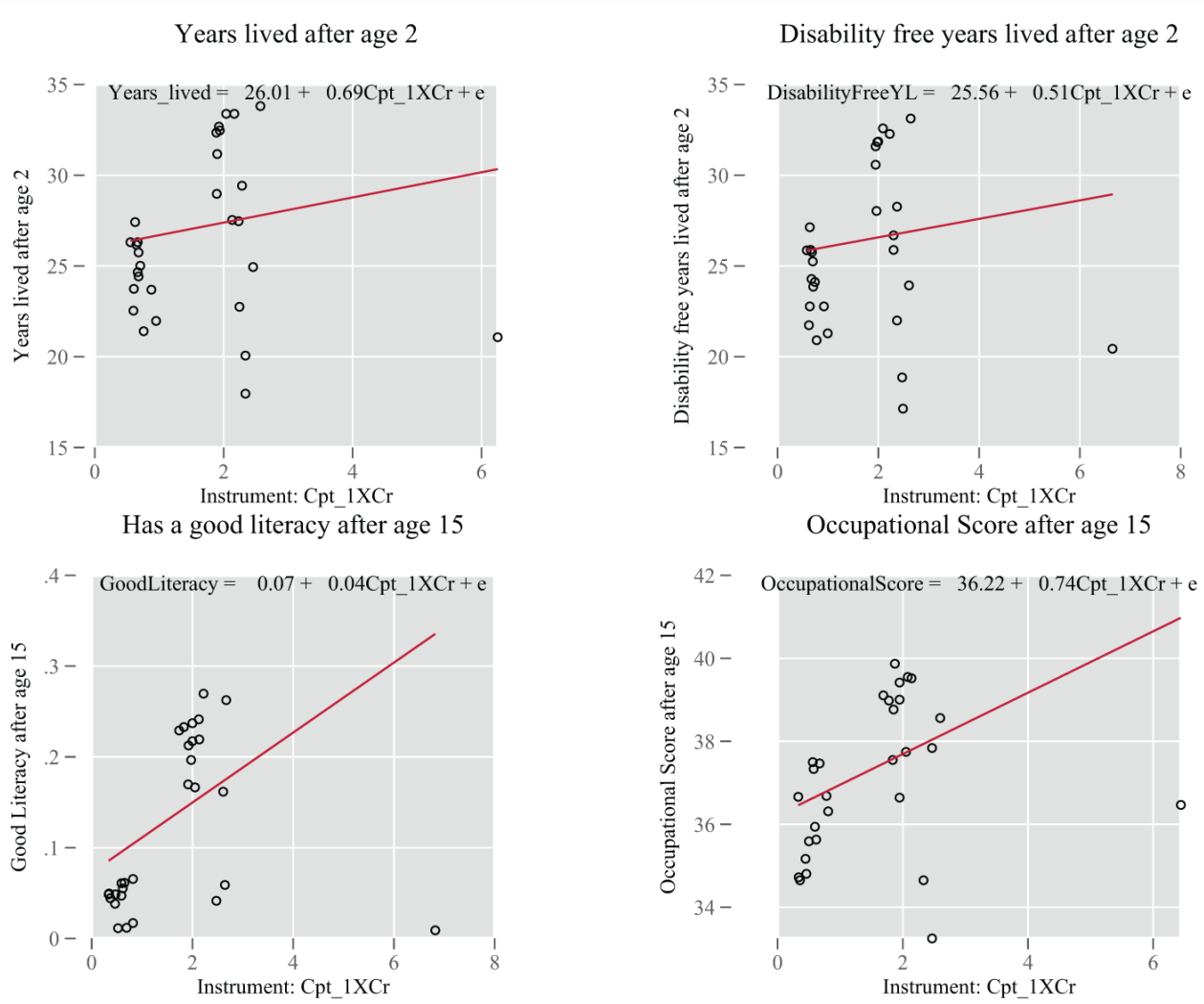

Figure 5 – Interacted instrumental variable ($C_{p(t-1)}$ x C_{rt}) and the individuals' lifetime outcomes, average by birth cohort weighted by the number of individuals.

Source: own calculations from the estimation sample.

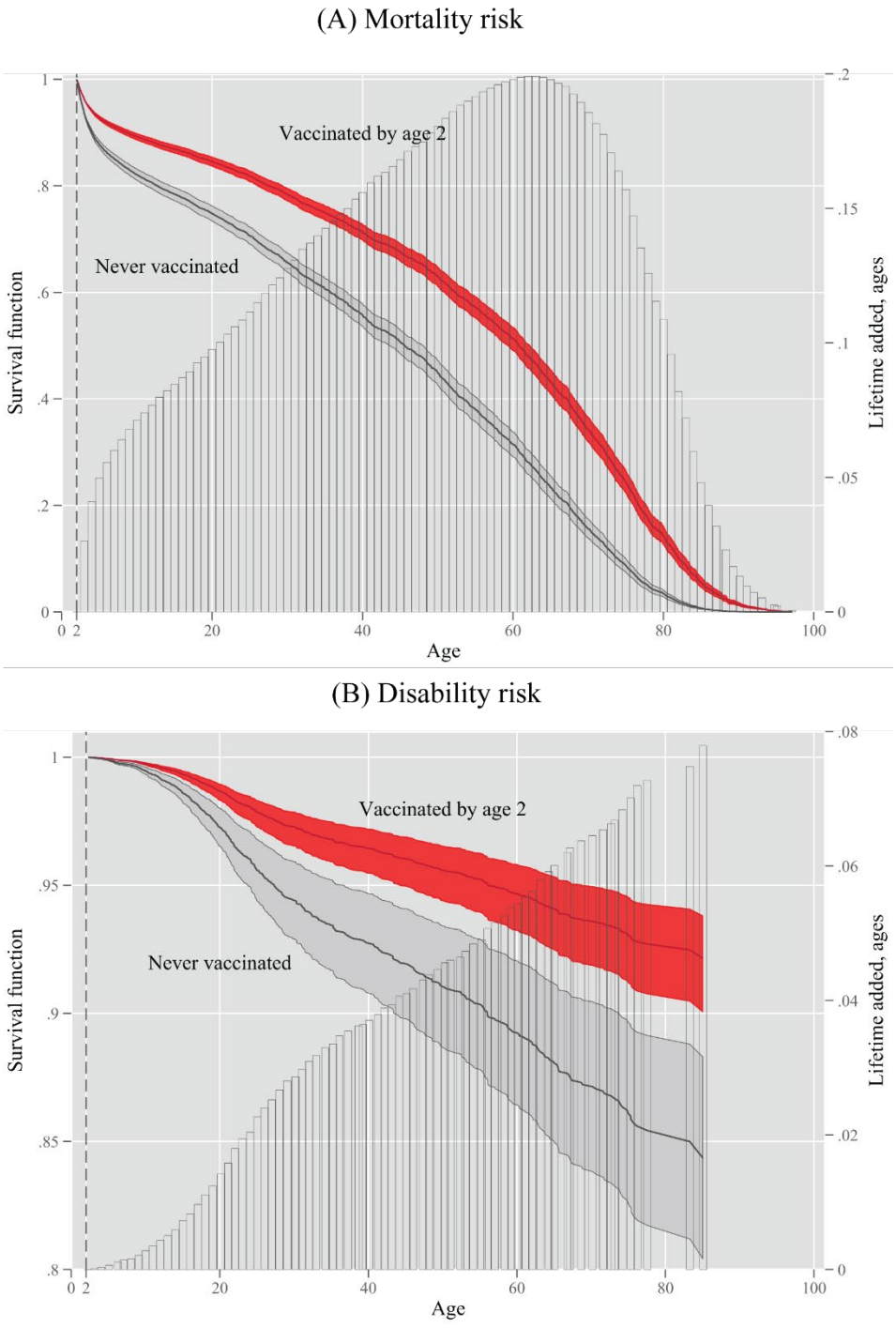

Figure 6 – Survivor functions and lifetime added due to vaccination for mortality and disability.

Source: Estimates are based on the estimations from the 2SRI models. Lines denote point estimates for survivor functions and their 95-% confidence intervals. Bars denote point estimates for the added lifetime in ages.

Table 1 – The effect of smallpox vaccination on the lifetime outcomes of generation 1: Controlling-for-observables

	Remaining years lived at age 2			Disability-free years lived at age 2			Good literacy, after age 15			Occupational score, max in ages 15-100		
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Panel A: OLS estimates on the full sample												
Vaccinated	11.697***	17.322***	17.338***	11.152***	17.109***	17.650***	0.188***	0.0386***	0.0382***	2.291***	4.941***	4.948***
	(1.624)	(1.825)	(1.825)	(1.882)	(1.966)	(1.986)	(0.0321)	(0.0123)	(0.0122)	(0.234)	(0.201)	(0.212)
R sq	0.0740	0.172	0.182	0.0708	0.163	0.183	0.0617	0.428	0.438	0.00550	0.0871	0.239
Observations	43,450	43,450	43,450	42,025	42,025	42,025	29,786	29,786	29,786	30,806	30,806	30,806
Panel B: OLS estimates on the IV sample												
Vaccinated	12.171***	16.694***	17.001***	11.766***	16.425***	16.818***	0.194***	0.0286**	0.0276***	2.436***	5.036***	5.994***
	(1.911)	(1.993)	(1.970)	(2.232)	(2.166)	(2.140)	(0.0443)	(0.0125)	(0.0125)	(0.201)	(0.258)	(0.267)
R sq	0.0859	0.159	0.167	0.0854	0.149	0.162	0.0806	0.351	0.0125	0.00430	0.0645	0.218
Observations	32,120	32,120	32,120	30,930	30,930	30,930	21,990	21,990	21,990	22,823	22,823	22,823
Parish of birth FEs	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Year of birth FEs	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Region of birth x Year of birth FEs	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Families' *Xs* x Year of birth FEs	No	No	Yes	No	No	Yes	No	No	Yes	No	No	Yes
Parish of birth *Xs* x Year of birth FEs	No	No	Yes	No	No	Yes	No	No	Yes	No	No	Yes

Note: Observations are individuals. The controls included are indicated in the table by Yes and No. "Families' Xs" include child characteristics at birth: sex, paternal occupational score, maternal occupational score, paternal literacy, maternal literacy, proportion of non-surviving children in the family, maternal marital status, the presence of siblings deceased due to external or unknown causes. "Parish Xs" include time-varying parish of birth characteristics: the number of midwives, the number of priests, smallpox death rate, university students per capita, price of rye, and the share of urban population. Standard errors are clustered at the parish level.

*** p<0.001, ** p<0.01, * p<0.05

Table 2 – The effect of smallpox vaccination on the lifetime outcomes of generation 1: Linear (2SLS) instrumental-variables with $C_{p(t-1)}$ x C_{rt} as an instrument

	Remaining years lived at age 2		**Disability-free years lived at age 2**		**Good literacy, after age 15**		**Occupational score, max in ages 15-100**	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A: 2SLS Estimates								
Vaccinated	10.912***	11.592**	11.467**	11.999**	0.0408	0.0315	3.262**	5.049**
	(4.044)	(4.144)	(4.155)	(4.374)	(0.0491)	(0.418)	(1.520)	(2.191)
R sq	0.153	0.161	0.145	0.158	0.330	0.348	0.235	0.186
Panel B: Reduced-Form Estimates								
$C_{p(t-1)}$ x C_{rt}	0.0393**	0.0465**	0.0400**	0.0448**	0.000216	0.000222	0.0131**	0.0155**
	(0.0149)	(0.0177)	(0.0143)	(0.0170)	(0.000278)	(0.000312)	(0.00516)	(0.00672)
R sq	0.112	0.120	0.103	0.116	0.330	0.347	0.289	0.210
Panel C: First-Stage Estimates (on **Vaccinated by age 2**)								
$C_{p(t-1)}$ x C_{rt}	0.00361***	0.00402***	0.00348***	0.00373***	0.00529***	0.00704***	0.00402***	0.00397***
	(0.000723)	(0.000700)	(0.000719)	(0.000674)	(0.00153)	(0.00133)	(0.00103)	(0.00101)
Kleibergen-Paap F-statistic	51.999	52.999	48.001	48.999	45.999	45.999	52.001	52.999
Anderson-Rubin F-statistic	6.940	3.290	7.530	6.860	0.600	0.850	6.450	4.352
Observations	32,120	32,120	30,930	30,930	21,990	21,990	22,823	22,823
Parish of birth FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year of birth FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Region of birth x Year of birth FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Families' *Xs* x Year of birth FEs	No	Yes	No	Yes	No	Yes	No	Yes
Parish of birth *Xs* x Year of birth FEs	No	Yes	No	Yes	No	Yes	No	Yes

Note: Observations are individuals. The controls included are indicated in the table by Yes and No. "Families' Xs" include child characteristics at birth: sex, paternal occupational score, maternal occupational score, paternal literacy, maternal literacy, proportion of non-surviving children in the family, maternal marital status, the presence of siblings deceased due to external or unknown causes. "Parish Xs" include time-varying parish of birth characteristics: the number of midwives, the number of priests, smallpox death rate, university students per capita, price of rye, and the share of urban population. Standard errors are clustered at the parish level.

*** p<0.001, ** p<0.01, * p<0.05

Table 3 – The effect of smallpox vaccination on the hazard of death and disability of generation 1: Nonlinear (2SRI) instrumental-variables with $C_{p(t-1)}$ x C_{rt} as an instrument

	Mortality risk		**Disability risk**	
Panel A: 2SRI Estimates				
Vaccinated	0.320**	0.319**	0.273***	0.201***
	(0.113)	(0.119)	(0.0875)	(0.0543)
First-stage residual	0.858	0.853	0.857	0.806
	(0.0997)	(0.104)	(0.0869)	(0.212)
Log pseudolikelihood	-53,952	-53,926	-52,040	-52,005
Observations	94,061	94,061	91,463	91,463
Panel B: First-stage ML estimates (on **Vaccinated by age 2**)				
$C_{p(t-1)}$ x C_{rt}	0.0141***	0.0154***	0.0137***	0.0138***
	(0.00382)	(0.00399)	(0.00381)	(0.00395)
Kleibergen-Paap F-statistic	51.999	52.999	48.001	48.999
Anderson-Rubin F-statistic	6.940	3.290	7.530	6.860
Observations	23,802	23,802	22,965	22,228
Parish of birth FEs	Yes	Yes	Yes	Yes
Year of birth FEs	Yes	Yes	Yes	Yes
Region of birth x Year of birth FEs	Yes	Yes	Yes	Yes
Families' *Xs* x Year of birth FEs	No	Yes	No	Yes
Parish of birth *Xs* x Year of birth FEs	No	Yes	No	Yes

Note: Observations are time spells for all individuals. Time splits exist for those individuals who migrated in and out of the parishes. ML denotes maximum likelihood. The estimates for Panel A and Panel B.1 are exponentiated, represent hazard ratios. The estimates for Panel B.2 are from generalized linear models with a logistic link. The controls included are indicated in the table by Yes and No. "Families' Xs" include child characteristics at birth: sex, paternal occupational score, maternal occupational score, paternal literacy, maternal literacy, proportion of non-surviving children in the family, maternal marital status, the presence of siblings deceased due to external or unknown causes. "Parish Xs" include time-varying parish of birth characteristics: the number of midwives, the number of priests, smallpox death rate, university students per capita, price of rye, and the share of urban population. Standard errors are clustered at the parish level.

*** p<0.001, ** p<0.01, * p<0.05

Table 3 – The effect of smallpox vaccination on mortality and disability by cause for generation 1: Nonlinear (2SRI) instrumental-variables with $C_{p(t-1)}$ x C_{rt} as an instrument

	Mortality risk		**Disability risk**	
	(1)	(2)	(3)	(4)
Vaccinated X Death due to smallpox	0.0261***	0.0193***		
	(0.0178)	(0.0123)		
Vaccinated X Other cause of death	0.334**	0.244***		
	(0.117)	(0.0774)		
Vaccinated X Smallpox-related causes			0.571**	0.506***
			(0.113)	(0.0963)
Vaccinated X Other cause of disability			0.781	0.744
			(0.145)	(0.189)
First-stage residual	0.857	0.868	1.0375	1.0284
	(0.0991)	(0.260)	(0.0337)	(0.0447)
Log pseudolikelihood	-53,889	-53,886	-2,779	-2,125
Observations	189,334	189,334	183,022	183,022
Parish of birth FEs	Yes	Yes	Yes	Yes
Year of birth FEs	Yes	Yes	Yes	Yes
Region of birth x Year of birth FEs	Yes	Yes	Yes	Yes
Families' *Xs* x Year of birth FEs	No	Yes	No	Yes
Parish of birth *Xs* x Year of birth FEs	No	Yes	No	Yes

Note: Observations are time spells for all individuals. Time splits exist for those individuals who migrated in and out of the parishes. First-stage estimates are the same as in Table 4. The estimates for Panel A and Panel B.1 are exponentiated. The controls included are indicated in the table by Yes and No. "Families' Xs" include child characteristics at birth: sex, paternal occupational score, maternal occupational score, paternal literacy, maternal literacy, proportion of non-surviving children in the family, maternal marital status, the presence of siblings deceased due to external or unknown causes. "Parish Xs" include time-varying parish of birth characteristics: the number of midwives, the number of priests, smallpox death rate, university students per capita, price of rye, and the share of urban population. Standard errors are clustered at the parish level.

*** p<0.001, ** p<0.01, * p<0.05

Table 4 – The effect of smallpox vaccination on the lifetime outcomes of generation 1: Mother fixed effects

	Remaining years lived at age 2			Disability-free years lived at age 2			Good literacy, after age 15			Occupational score, max in ages 15-100		
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Vaccinated	16.559***	19.762***	19.863***	15.996***	19.839***	19.568***	0.0421***	0.0343**	0.0311**	2.691***	4.714**	4.741**
	(0.477)	(0.586)	(0.594)	(0.575)	(0.580)	(0.589)	(0.0105)	(0.0140)	(0.0145)	(0.815)	(0.357)	(0.323)
R sq	0.107	0.0607	0.0276	0.119	0.0123	0.0209	0.0424	0.0121	0.0109	0.0790	0.0871	0.0666
Observations	35,904	35,904	35,904	35,350	35,350	35,350	22,896	22,896	22,896	20,247	20,247	20,247
Parish of birth FEs	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Year of birth FEs	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Region of birth x Year of birth FEs	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Families' Xs x Year of birth FEs	No	No	Yes	No	No	Yes	No	No	Yes	No	No	Yes
Parish of birth Xs x Year of birth FEs	No	No	Yes	No	No	Yes	No	No	Yes	No	No	Yes

Note: Observations are individuals. The controls included are indicated in the table by Yes and No. "Families' Xs" include child characteristics at birth: sex, paternal occupational score, maternal occupational score, paternal literacy, maternal literacy, proportion of non-surviving children in the family, maternal marital status, the presence of siblings deceased due to external or unknown causes. "Parish Xs" include time-varying parish of birth characteristics: the number of midwives, the number of priests, smallpox death rate, university students per capita, price of rye, and the share of urban population.

*** p<0.001, ** p<0.01, * p<0.05

Table 5 – The effect of smallpox vaccination of generation 1 on the lifetime outcomes of generation 2 and 3: Instrumental-variables (2SRI) with $C_{p(t-1)}$ x C_{rt} as an instrument for generation 1

	Remaining years lived at birth		**Disability-free years lived at birth**		**Occupational score, max in ages 20-100**	
	(1)	(2)	(3)	(4)	(5)	(6)
(A) Generation 2						
Parent Vaccinated	1.171**	2.204***	6.836***	8.015***	1.531**	1.099*
	(0.401)	(0.652)	(1.517)	(2.008)	(0.599)	(0.656)
First-stage residual	0.0893	-1.475	-6.899**	-9.176***	0.0813	0.717
(from parental equation)	(0.0741)	(0.799)	(2.0391)	(2.678)	(0.797)	(0.873)
R sq	0.0564	0.0689	0.00610	0.0455	0.126	0.178
Observations	109,112	109,112	29,748	29,748	90,294	90,294
(B) Generation 3						
Grandparent Vaccinated	1.236***	1.057**	4.503***	4.262**	-1.0278	-0.715
	(0.361)	(0.497)	(0.916)	(1.886)	(0.836)	(0.445)
First-stage residual	-0.0694	-0.505	0.0999	-1.690	1.982	0.341
(from grandparental equation)	(0.0651)	(0.638)	(0.151)	(2.283)	(1.236)	(0.644)
R sq	0.116	0.187	0.00830	0.0316	0.0831	0.0846
Observations	116,544	116,544	40,324	40,324	70,920	70,920
Parish of birth FEs	Yes	Yes	Yes	Yes	Yes	Yes
Year of birth FEs	Yes	Yes	Yes	Yes	Yes	Yes
Region of birth x Year of birth FEs	Yes	Yes	Yes	Yes	Yes	Yes
Families' *Xs* x Year of birth FEs	No	Yes	No	Yes	No	Yes
Parish of birth *Xs* x Year of birth FEs	No	Yes	No	Yes	No	Yes

Note: Observations are stacked individuals (54,506 unique individuals for generation 2 and 58,272 unique individuals for generation 3 in total). First-stage regression is the same as in Table 1. The controls included are indicated in the table by Yes and No. "Families' Xs" include child characteristics at birth: sex, paternal occupational score, maternal occupational score, paternal literacy, maternal literacy, proportion of non-surviving children in the family, maternal marital status, the presence of siblings deceased due to external or unknown causes. "Parish Xs" include time-varying parish of birth characteristics: the number of midwives, the number of priests, smallpox death rate, university students per capita, price of rye, and the share of urban population. Standard errors are clustered at the parish level. *** p<0.001, ** p<0.01, * p<0.05

Table 6 – Direct and mediated effects of smallpox vaccination of generation 1 on the lifetime outcomes of generation 2 and 3: Instrumental-variables (2SRI) with $C_{p(t-1)}$ x C_{rt} as an instrument for generation 1

	Years lived			**Disability-free years lived**			**Occupational score**		
	Mediator:			*Mediator:*			*Mediator:*		
	Vaccinated	Parental occupation	Midwife-assisted	Vaccinated	Parental occupation	Midwife-assisted	Vaccinated	Parental occupation	Midwife-assisted
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
(A) Generation 2									
Parent Vaccinated (natural direct effect)	0.772**	1.743***	1.994***	4.097***	6.854***	6.571***	1.752***	2.161***	2.291***
	(0.303)	(0.316)	(0.338)	(1.469)	(1.517)	(1.139)	(0.381)	(0.595)	(0.594)
Mediated Effect (natural indirect effect)	1.042***	-0.00587*	-0.00788***	2.749***	-0.00266	-0.00585*	0.0636**	0.0720**	0.000279
	(0.0881)	(0.00342)	(0.00171)	(0.405)	(0.00993)	(0.0328)	(0.0255)	(0.0289)	(0.00346)
Observations	109,112	109,112	109,112	29,748	29,748	29,748	90,294	90,294	90,294
(B) Generation 3									
Grandparent Vaccinated (natural direct effect)	0.691	1.469***	1.307***	2.690**	5.161***	5.185***	0.0819	0.0334	0.0925
	(0.426)	(0.440)	(0.441)	(1.0781)	(1.124)	(1.126)	(0.332)	(0.331)	(0.332)
Mediated Effect (natural indirect effect)	0.838***	-000684	-0.00209	2.504***	0.00561	-0.00501	0.0308**	0.0866***	0.0161
	(0.124)	(0.00535)	(0.0139)	(0.363)	(0.0114)	(0.0530)	(0.0148)	(0.0309)	(0.0137)
Observations	116,544	116,544	116,544	40,324	40,324	40,324	70,920	70,920	70,920
Parish of birth FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year of birth FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Region of birth x Year of birth FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Note: Observations are stacked individuals (54,506 unique individuals for generation 2 and 58,272 unique individuals for generation 3 in total). First-stage regression is the same as in Table 1. The effects are estimated for each mediator separately. Bootstrapped standard errors clustered at the parish level are in parentheses.

*** p<0.001, ** p<0.01, * p<0.05

Online Appendices

to the paper "Multigenerational Effects of Smallpox Vaccination"

by Volha Lazuka and Peter S Jensen

Appendix A – Selection and data inaccuracy in data for generation 1

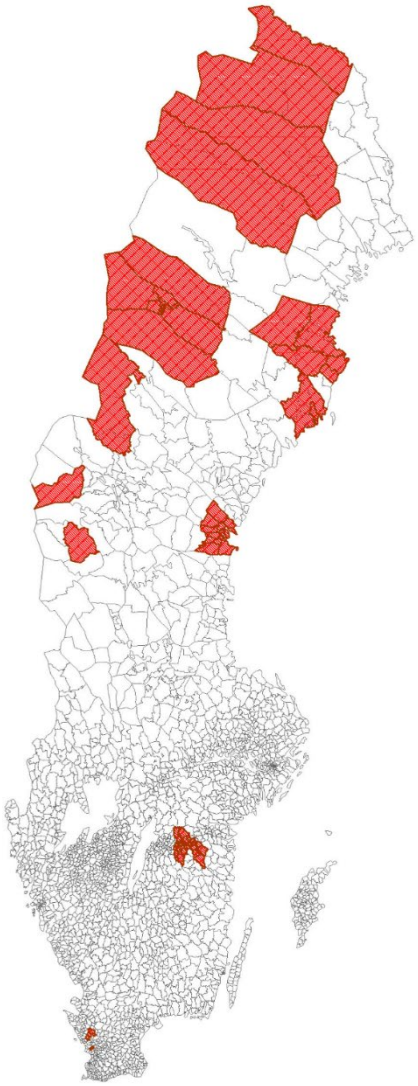

Figure A1 – Parishes under analysis, a snapshot of Sweden in 1820

Source: Based on the estimation sample and administrative boundaries from Riksarkivet (2016).

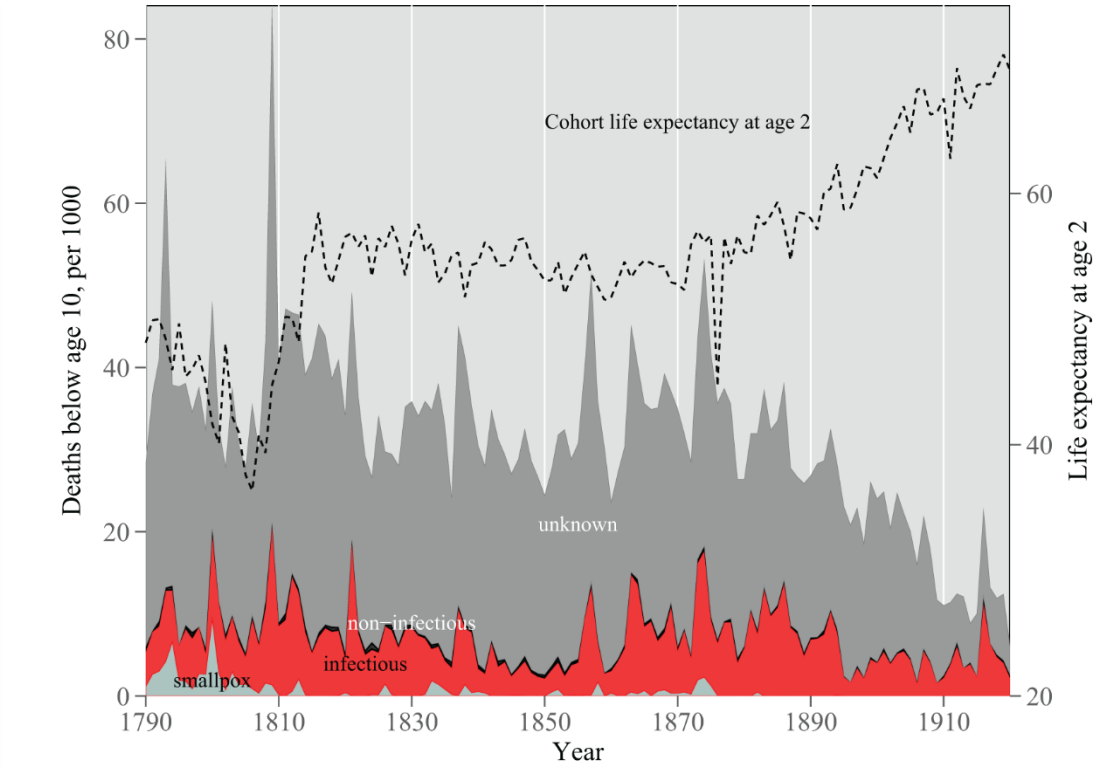

Figure A2 – Mortality rate below age 10 by cause and cohort life expectancy at age 2, 1790–1920

Source: own calculations based on the estimation sample.

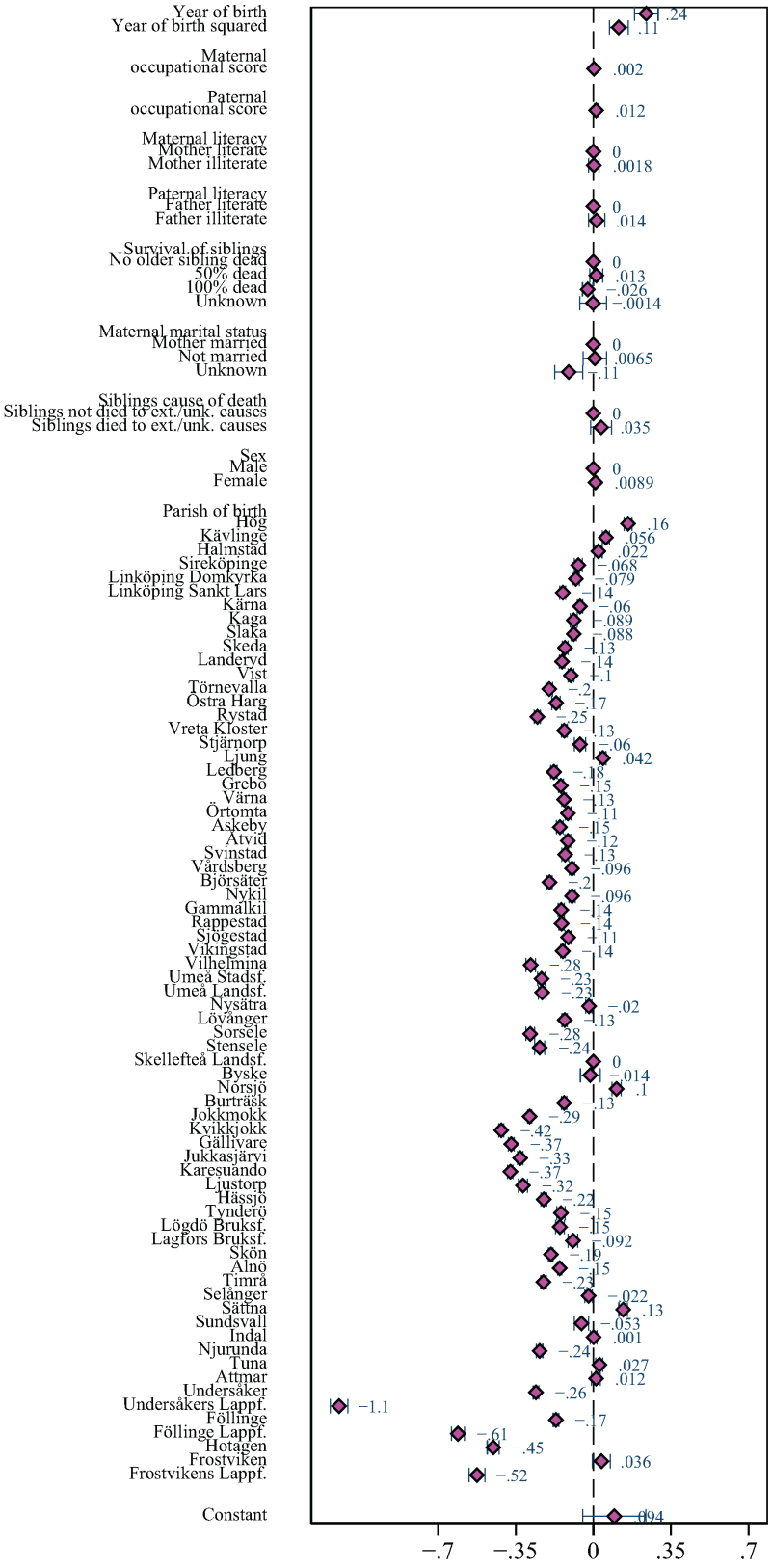

Figure A3 – Selection into vaccination status by the age of 2 for generation 1

Note: The estimates are obtained from an OLS multivariate regression with a vaccination by age 2 as an outcome, cohorts born in 1790-1820. Point estimates and 95% confidence intervals. Robust standard errors are clustered at the parish of birth. Continuous variables (year of birth, year of birth squared, maternal and paternal occupational scores) are divided by their standard deviation.

Table A1 – Check for the date inaccuracy

	Vaccinated by age 2
Spring	ref
Summer	0.007*
	(0.004)
Autumn	0.007
	(0.004)
Winter	0.007*
	(0.004)
Constant	0.130***
	(0.005)
Individuals	43,466
R-squared	0.670

Note: OLS regression estimates with parish and year of birth fixed effects for the first generation. Robust standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Appendix B – Robustness analysis

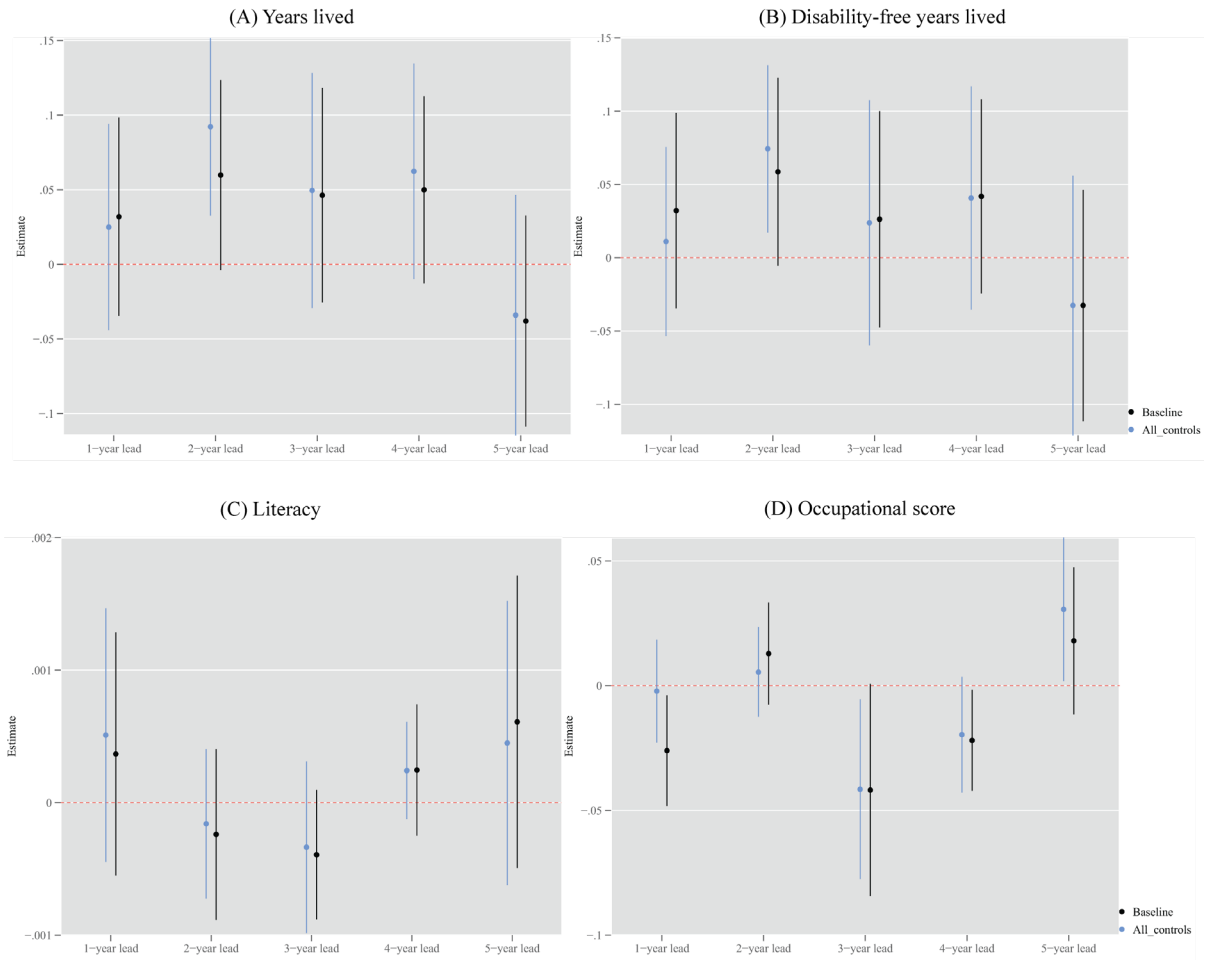

Figure B1 – 2SLS estimates of the leads of the interacted instrumental variable for all outcomes.

Note: 2SLS point estimates and 95% confidence intrevals. We estimate the models with all 30 leads (the year of 1790 is the reference) but report the first five estimates, which is conventional in the difference-in-differences literature (Roth et al. 2023). "Baseline" controls include year of birth fixed effects, arish of birth fixed effects, and county of birth-by-year of birth fixed effects. "All controls" addditionaly include interactions between year of birth and child characteristics at birth (sex, paternal occupational score, maternal occupational score, paternal literacy, maternal literacy, proportion of non-surviving children in the family, maternal marital status, the presence of siblings deceased due to external or unknown causes) and interactions between year of birth and parish of birth characteristics (the number of midwives, the number of priests, smallpox death rate, university students per capita, price of rye, and the share of urban population). Standard errors are clustered at the parish level.

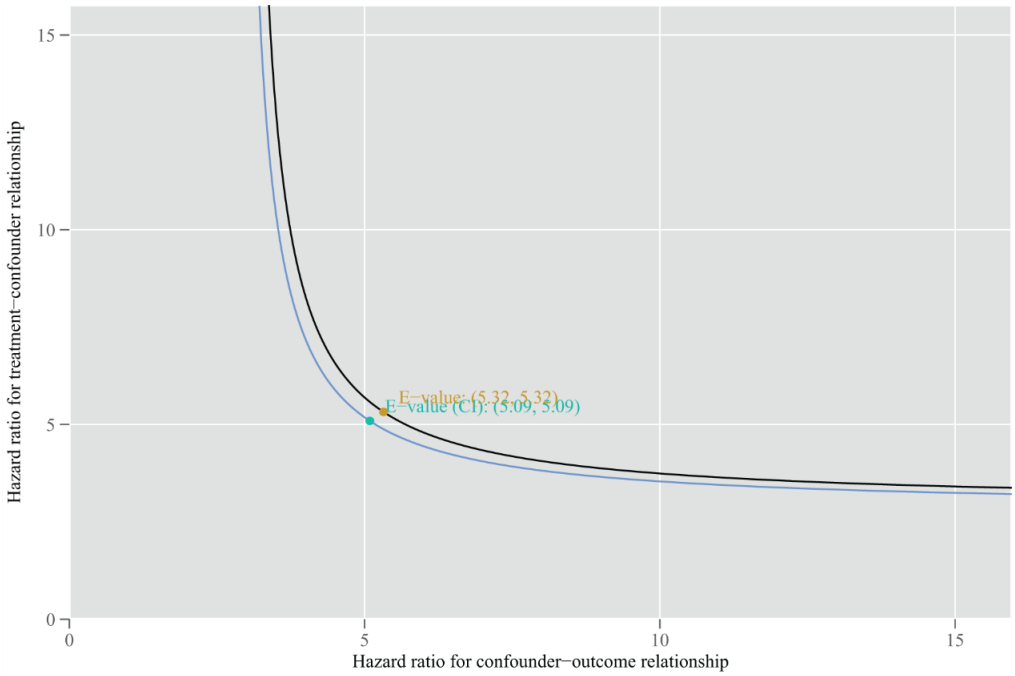

Figure B2 – E-value for the effect of smallpox vaccination by age 2 across the life cycle, generation 1

Note: E-value and lower 95%-CI are presented.

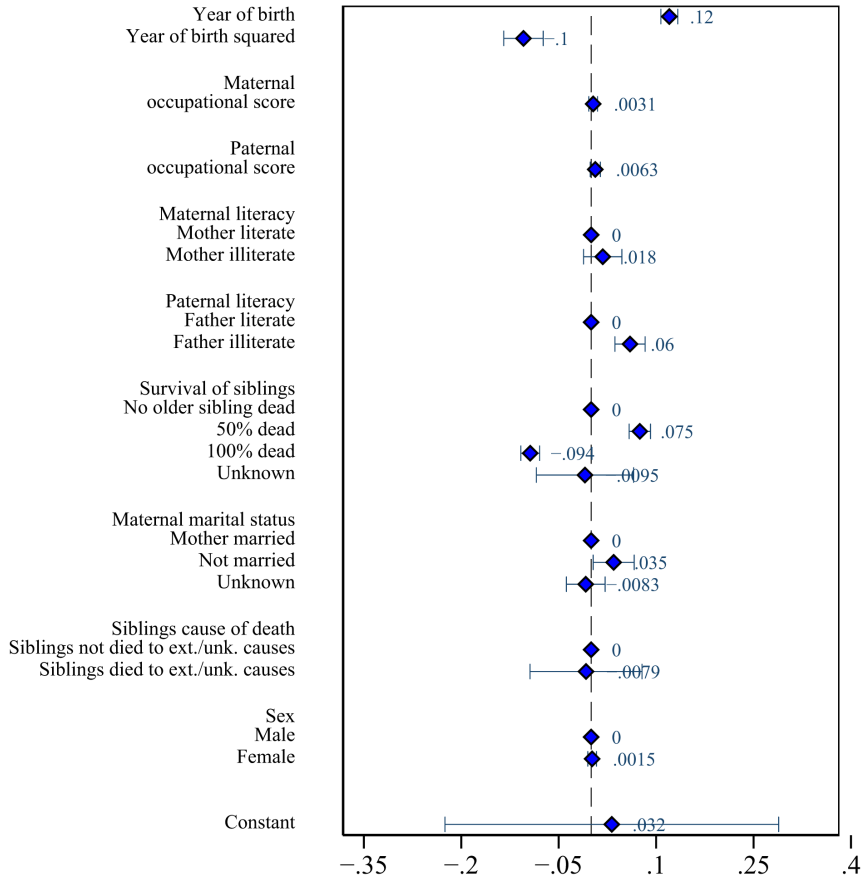

Figure B3 – Differences in the share of mothers with varying vaccination status of their children across children's observable characteristics (versus mothers with unvarying status).

Note: 17.6% of mothers have both vaccinated and not-vaccinated children.

Table B1 – The effect of smallpox vaccination on the hazard of death and disability of generation 1: Controlling-for-observables

	Mortality risk			**Disability risk**		
	(1)	(2)	(3)	(4)	(5)	(6)
Panel A: ML Estimates on Full Sample						
Vaccinated	0.477***	0.205***	0.199***	0.456***	0.184***	0.172**
	(0.0494)	(0.0359)	(0.0367)	(0.0485)	(0.0302)	(0.0314)
Log pseudolikelihood	-81,671	-80,418	-80,225	-79,230	-80,118	-79,855
Observations	122,528	122,528	122,528	122,098	122,098	122,098
Panel B: ML Estimates on the IV Sample						
Vaccinated	0.451***	0.208***	0.205***	0.417***	0.176***	0.164***
	(0.0483)	(0.0471)	(0.0455)	(0.0487)	(0.0367)	(0.0373)
Log pseudolikelihood	-54,770	-53,954	-53,928	-52,831	-52,042	-52,006
Observations	94,061	94,061	94,061	91,463	91,463	91,463
Parish of birth Fes	No	Yes	Yes	No	Yes	Yes
Year of birth Fes	No	Yes	Yes	No	Yes	Yes
Region of birth x Year of birth Fes	No	Yes	Yes	No	Yes	Yes
Families' *Xs* x Year of birth Fes	No	No	Yes	No	No	Yes
Parish of birth *Xs* x Year of birth Fes	No	No	Yes	No	No	Yes

Note: Observations are time spells for all individuals. Time splits exist for those individuals who migrated in and out of the parishes. ML denotes maximum likelihood. The estimates for Panel A and Panel B.1 are exponentiated, represent hazard ratios. The estimates for Panel B.2 are from generalized linear models with a logistic link. The controls included are indicated in the table by Yes and No. "Families' Xs" include child characteristics at birth: sex, paternal occupational score, maternal occupational score, paternal literacy, maternal literacy, proportion of non-surviving children in the family, maternal marital status, the presence of siblings deceased due to external or unknown causes. "Parish Xs" include time-varying parish of birth characteristics: the number of midwives, the number of priests, smallpox death rate, university students per capita, price of rye, and the share of urban population. Standard errors are clustered at the parish level.

*** p<0.001, ** p<0.01, * p<0.05

Table B2 – The Cox proportional hazard model estimates for individual-level covariates, generation 1.

	Mortality risk
Mother married	(ref)
Mother unmarried	1.222*
	(0.132)
No siblings dead	(ref)
50% dead	0.902
	(0.0927)
100% dead	1.313***
	(0.137)
Sibling died due to other cause	(ref)
Siblings died to external/unknown causes	1.279
	(0.378)
Unknown	1.071**
	(0.0306)
Male	(ref)
Female	0.926***
	(0.0271)
Mother literate	(ref)
Mother illiterate	1.046
	(0.0729)
Father literate	(ref)
Father illiterate	0.994
	(0.0811)
Father: Higher-skilled managers	(ref)
Lower managers, professionals, clerical	1.133
	(0.110)
Foremen, medium skilled workers	1.294**
	(0.151)
Farmers, fishermen	1.228**
	(0.112)
Lower skilled workers, farm workers	1.131
	(0.119)
Unskilled workers, farm workers	1.279**
	(0.146)
Hög	(ref)
Kävlinge	1.060
	(0.0614)
Halmstad	1.236***
	(0.0648)
Sireköpinge	0.979
	(0.0474)
Linköping Domkyrka	1.490
	(0.372)
Linköping Sankt Lars	1.380
	(0.342)
Kärna	1.309
	(0.324)
Kaga	1.231
	(0.298)
Slaka	1.349
	(0.333)
Skeda	1.030
	(0.255)
Landeryd	1.087
	(0.269)
Vist	1.074
	(0.267)
Törnevalla	0.834
	(0.207)
Östra Harg	1.617*
	(0.399)
Rystad	1.485
	(0.366)
Vreta Kloster	1.114
	(0.275)
Stjärnorp	0.868
	(0.212)
Ljung	0.830
	(0.206)
Ledberg	1.655**
	(0.406)
Grebo	0.860
	(0.211)
Värna	1.096
	(0.269)
Örtomta	0.850
	(0.208)
Askeby	0.907
	(0.224)
Åtvid	0.883
	(0.221)
Svinstad	0.949
	(0.235)
Vårdsberg	1.323
	(0.329)
Björsäter	0.974
	(0.242)
Nykil	1.114
	(0.277)
Gammalkil	0.920
	(0.226)
Rappestad	1.128
	(0.274)
Sjögestad	1.333
	(0.330)
Vikingstad	1.337
	(0.328)

Vilhelmina	0.898
	(0.202)
Umeå Stadsf.	1.332
	(0.930)
Umeå Landsf.	1.223**
	(0.505)
Nysätra	0.978
	(0.222)
Lövänger	0.974
	(0.242)
Sorsele	0.777
	(0.180)
Stensele	0.429***
	(0.104)
Skellefteå Landsf.	1.035
	(0.235)
Byske	0.135
	(0)
Norsjö	1.228
	(0.278)
Burträsk	0.995
	(0.238)
Jokkmokk	2.207***
	(0.622)
Kvikkjokk	1.226
	(0.365)
Gällivare	2.763***
	(0.813)
Jukkasjärvi	1.406
	(0.396)
Karesuando	1.608*
	(0.455)
Ljustorp	0.948
	(0.277)
Hässjö	0.870
	(0.302)
Tynderö	1.153
	(0.320)
Lögdö Bruksf.	0.840
	(0.242)
Lagfors Bruksf.	2.169**
	(0.735)
Skön	1.059
	(0.335)
Alnö	1.271
	(0.394)
Timrö	1.856*
	(0.593)
Selänger	0.908
	(0.290)
Sättna	0.612*
	(0.178)
Sundsvall	1.862
	(0.720)
Indal	0.657
	(0.194)
Njurunda	1.116
	(0.369)
Tuna	1.016
	(0.298)
Attmar	0.769
	(0.218)
Undersäker	0.773
	(0.319)
Undersäkers Lappf.	1.281***
	(0.318)
Föllinge	0.735
	(0.250)
Föllinge Lappf.	1.077
	(0.479)
Hotagen	0.840
	(0.380)
Frostviken	0.607
	(0.226)
Frostvikens Lappf.	0.803
	(0.358)
Log pseudolikelihood	-81,217
Observations	122,528
Parish of birth Fes	Yes
Year of birth Fes	Yes
Region of birth x Year of birth Fes	Yes

Note: Observations are time spells for all individuals. Time splits exist for those individuals who migrated in and out of the parishes. The estimates for Panel A and Panel B.1 are exponentiated. The controls included are indicated in the table by Yes and No. "Families' Xs" include child characteristics at birth: sex, paternal occupational score, maternal occupational score, paternal literacy, maternal literacy, proportion of non-surviving children in the family, maternal marital status, the presence of siblings deceased due to external or unknown causes. "Parish Xs" include time-varying parish of birth characteristics: the number of midwives, the number of priests, smallpox death rate, university students per capita, price of rye, and the share of urban population. Standard errors are clustered at the parish level. *** p<0.001, ** p<0.01, * p<0.05

Table B3 – The effect of smallpox vaccination on mortality and disability by cause: Controlling-for-observables (Cox proportional hazards model) estimates

	Mortality risk			Disability risk		
	(1)	(2)	(3)	(4)	(5)	(6)
Panel A: Controlling-for-observables on the full sample						
Vaccinated X Smallpox death	0.0207***	0.0207***	0.0206***			
	(0.00941)	(0.00941)	(0.00939)			
Vaccinated X Other cause death	0.211***	0.211***	0.209***			
	(0.0389)	(0.0389)	(0.0381)			
Vaccinated X Smallpox-related causes				0.489***	0.489***	0.352***
				(0.0953)	(0.0953)	(0.0712)
Vaccinated X Other cause disability				0.647**	0.647**	0.602***
				(0.0922)	(0.0922)	(0.0959)
Log pseudolikelihood	-80,353	-80,353	-80,311	-2,534	-2,534	-2,412
Observations	246,556	246,556	246,556	244,196	244,196	244,196
Panel A: Controlling-for-observables on the IV sample						
Vaccinated X Smallpox death	0.0207***	0.0207***	0.0206***			
	(0.00941)	(0.00941)	(0.00939)			
Vaccinated X Other cause death	0.211***	0.211***	0.209***			
	(0.0389)	(0.0389)	(0.0381)			
Vaccinated X Smallpox-related causes				0.489***	0.489***	0.352***
				(0.0953)	(0.0953)	(0.0712)
Vaccinated X Other cause disability				0.647**	0.647**	0.602***
				(0.0922)	(0.0922)	(0.0959)
Log pseudolikelihood	-80,353	-80,353	-80,311	-2,534	-2,534	-2,412
Observations	246,556	246,556	246,556	244,196	244,196	244,196
Parish of birth FEs	No	Yes	Yes	No	Yes	Yes
Year of birth FEs	No	Yes	Yes	No	Yes	Yes
Region of birth x Year of birth FEs	No	Yes	Yes	No	Yes	Yes
Families' *Xs* x Year of birth FEs	No	No	Yes	No	No	Yes
Parish of birth *Xs* x Year of birth FEs	No	No	Yes	No	No	Yes

Note: Observations are time spells for all individuals. Time splits exist for those individuals who migrated in and out of the parishes. First-stage estimates are the same as in Table 4. The estimates for Panel A and Panel B.1 are exponentiated. The controls included are indicated in the table by Yes and No. "Families' Xs" include child characteristics at birth: sex, paternal occupational score, maternal occupational score, paternal literacy, maternal literacy, proportion of non-surviving children in the family, maternal marital status, the presence of siblings deceased due to external or unknown causes. "Parish Xs" include time-varying parish of birth characteristics: the number of midwives, the number of priests, smallpox death rate, university students per capita, price of rye, and the share of urban population. Standard errors are clustered at the parish level.

*** p<0.001, ** p<0.01, * p<0.05

Table B4 – The effect of smallpox vaccination on the hazard of death and disability of generation 1: Mother fixed-effects (Cox proportional hazards model) estimates

	Mortality risk			**Disability risk**		
	(1)	(2)	(3)	(4)	(5)	(6)
Vaccinated	0.114***	0.0939***	0.0962***	0.119***	0.0924***	0.0971***
	(0.0309)	(0.00955)	(0.00986)	(0.0323)	(0.00978)	(0.0103)
Log pseudolikelihood	-3,509	-6,989	-6,980	-3,512	-3,444	-3,411
Observations	108,749	108,749	108,749	106,899	106,899	106,899
Parish of birth FEs	No	Yes	Yes	No	Yes	Yes
Year of birth FEs	No	Yes	Yes	No	Yes	Yes
Region of birth x Year of birth FEs	No	Yes	Yes	No	Yes	Yes
Families' *Xs* x Year of birth FEs	No	No	Yes	No	No	Yes
Parish of birth *Xs* x Year of birth FEs	No	No	Yes	No	No	Yes

Note: Observations are time spells for all individuals. Time splits exist for those individuals who migrated in and out of the parishes. ML denotes maximum likelihood. The estimates for Panel A and Panel B.1 are exponentiated. The controls included are indicated in the table by Yes and No. "Families' Xs" include child characteristics at birth: sex, paternal occupational score, maternal occupational score, paternal literacy, maternal literacy, proportion of non-surviving children in the family, maternal marital status, the presence of siblings deceased due to external or unknown causes. "Parish Xs" include time-varying parish of birth characteristics: the number of midwives, the number of priests, smallpox death rate, university students per capita, price of rye, and the share of urban population. Standard errors are clustered at the parish level.

*** p<0.001, ** p<0.01, * p<0.05

Table B5 – The interaction effects of vaccination with cointerventions, generation 1.

	Remaining years lived at age 2		**Disability-free years lived at age 2**		**Good literacy, after age 15**		**Occupational score, max in ages 15-100**	
	Midwives	Potatoes	Midwives	Potatoes	Midwives	Potatoes	Midwives	Potatoes
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Vaccinated	17.453***	17.664***	17.237***	17.567***	0.0481***	0.0543**	4.987***	5.215***
	(1.781)	(1.398)	(1.914)	(1.546)	(0.0134)	(0.0212)	(0.215)	(0.215)
Vaccinated X Cointervention	-0.305	-0.00809	-0.283	-0.0105	-0.0248*	-0.000368	0.702	-0.0159*
	(0.507)	(0.0215)	(0.568)	(0.0222)	(0.0129)	(0.000291)	(0.515)	(0.00843)
R sq	0.173	0.172	0.164	0.163	0.429	0.428	0.191	0.192
Observations	43,450	43,450	42,023	42,023	29,786	29,786	30,806	30,806
Parish of birth FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year of birth FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Region of birth x Year of birth FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Note: Observations are individuals. The controls included are indicated in the table by Yes and No. For the "Midwives" model, there is a basline impact for the impact of midwives, not reported in the table. Fo the "Potatoes" model, the basline estimate for the potatoes is missing because potato seed data are available only for the year 1805.

*** p<0.001, ** p<0.01, * p<0.05

Appendix C – The analysis of the outcomes of generation 2 and 3.

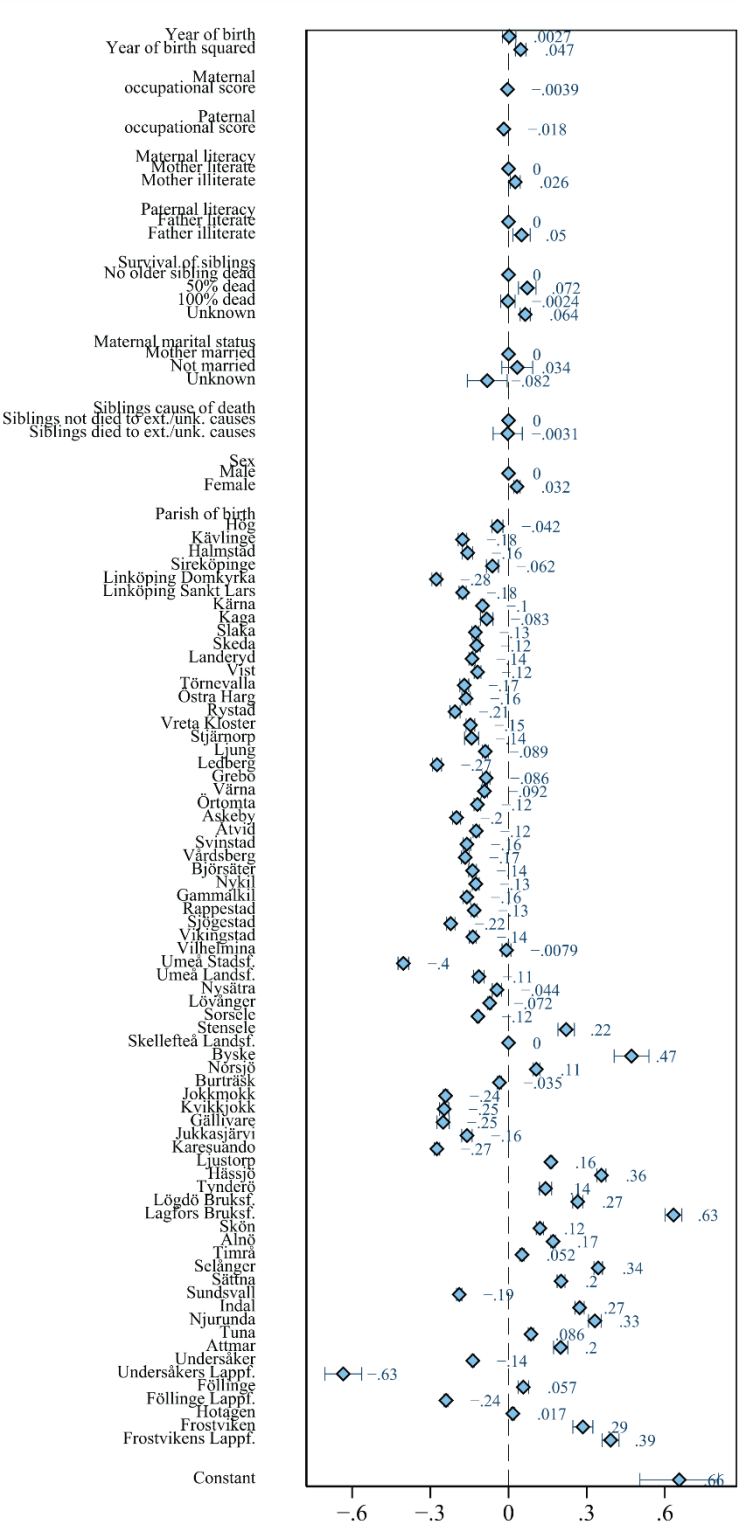

Figure C1 – Differences in the observable characteristics between individuals belonging to generation 1, linked and not-linked to generation 2 and 3.

References (in Appendices)

Riksarkivet (2016): Historiska GIS-Kartor (Information om Territoriella Indelningar i Sverige från 1500-Talets Slut till 1900-Talets Slut) [Historical GIS Maps (Information on Territorial Divisions in Sweden from the 1500s to the 1900s)]. Shape-file.

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