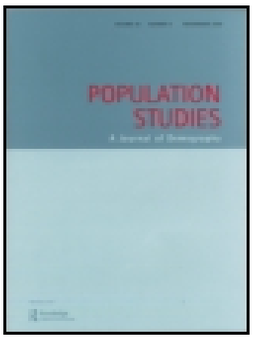

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Did smallpox cause stillbirths? Maternal smallpox infection, vaccination, and stillbirths in Sweden, 1780–1839

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While there is strong evidence that maternal smallpox infection can cause foetal loss, it is not clear whether smallpox infections were a demographically important cause of stillbirths historically. In this paper, we use parish-level data from the Swedish Tabellverket data set for 1780–1839 to test the effect of smallpox on stillbirths quantitatively, analysing periods before and after the introduction of vaccination in 1802. We find that smallpox infection was not a major cause of stillbirths before 1820, because most women contracted smallpox as children and were therefore not susceptible during pregnancy. We do find a small, statistically significant effect of smallpox on stillbirths from 1820 to 1839, when waning immunity from vaccination put a greater share of pregnant women at risk of contracting smallpox. However, the reduced prevalence of smallpox in this period limited its impact on stillbirths. Thus, smallpox was not an important driver of historical stillbirth trends.

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Keywords: stillbirth; foetal death; smallpox; vaccination; historical demography

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Introduction

Exposure to infectious diseases during pregnancy can lead to a number of adverse birth outcomes. The recent outbreak of Zika virus, which caused substantial cases of microcephaly, raised this issue once again, but a number of infectious diseases including rubella, chickenpox, and smallpox are known to lead to congenital malformations and foetal loss (Nishiura 2006; Silasi et al. 2015; Racicot and Mor 2017). In addition, a growing literature has shown that exposure to infectious disease in utero leads to worse health in later life and poorer human capital outcomes. For instance, cohorts exposed to the 1918 flu pandemic in utero experienced slower physical growth and also had lower educational attainment and income (Almond 2006; Mazumder et al. 2010; Ogasawara 2017), although some of these results have recently been disputed (Helgertz and Bengtsson 2019; Beach et al. 2022). Given the importance of infectious disease for health across the life course, the eradication of infectious diseases in the nineteenth and twentieth centuries may have led to significant improvements in foetal health and cohort health more generally.

This paper explores the consequences of smallpox—historically, a particularly virulent and prevalent disease—for stillbirths, using parish-level data from Sweden in the eighteenth and nineteenth centuries. Woods first argued, using a mixture of evidence from medical case books and back-of-the-envelope estimations, that maternal smallpox infections were an important cause of stillbirths in the eighteenth and nineteenth centuries (Woods 2009, pp. 231–2). Given the decline in smallpox mortality across the nineteenth century due to vaccination, if smallpox were a major driver of stillbirth rates then the changing epidemiology of smallpox would have had an important effect on trends in stillbirth rates over time. There is strong historical evidence from the nineteenth and twentieth centuries that smallpox could lead to foetal deaths (Nishiura 2006; Woods

2009, pp. 219–21), but these studies tended to be drawn from smallpox epidemics occurring long after vaccination was introduced. To date, no one has been able to quantify how important smallpox infections in pregnancy were as a cause of stillbirths before, during, and after the introduction of vaccination.

The importance of smallpox for stillbirths is dependent on two factors: the share of women of childbearing age who are susceptible to smallpox and the overall prevalence of smallpox in the population. We can see these factors at play in the eighteenth and nineteenth centuries. In the north of England and Sweden before vaccination began, the vast majority of smallpox deaths occurred among children, indicating that most adults were immune (Sköld 1996a). Thus, although smallpox prevalence was high, smallpox infections in pregnancy were likely rare. However, Woods argued, based on a small case study from eighteenth-century England, that adult smallpox mortality was more common (Woods 2009, p. 224), and a more recent and extensive study of smallpox in England found that the majority of smallpox deaths in southern England in the eighteenth century occurred among adults (Davenport et al. 2018). This age pattern was different because inoculation (the practice of introducing smallpox material into an individual's skin to produce a milder infection and confer immunity) and isolation of smallpox cases in pesthouses helped to reduce smallpox prevalence in the population.

After the introduction of vaccination c. 1800, smallpox prevalence fell dramatically because take up of vaccination was far greater than for inoculation. Vaccination with cowpox and, later, vaccinia was safer than inoculation because there was no chance that someone would contract smallpox from vaccination. However, unlike for inoculation, individual immunity from vaccination diminishes with time, leaving adults at risk of contracting the disease. Thus, the prevalence of smallpox among adults likely increased, as suggested by the tenfold increase in the smallpox age-specific mortality rate for adults aged 25–49 in Sweden between 1790 and 1850 (Sköld 1996a, pp. 579, 588). Therefore, there were women of childbearing age who were susceptible to smallpox and could have been at risk of smallpox-related stillbirths. However, the overall prevalence of smallpox was far lower in the post-vaccination era, perhaps counteracting the increased susceptibility of pregnant women.

This paper tests the net impact of these factors in 1780–1839 using parish-level data from Sweden, where smallpox deaths and stillbirths were registered from the eighteenth century onward. We analyse a panel data set of 622 parishes (with consistent boundaries) from the Tabellverket Database constructed by the Umeå Demographic Data Base team. We use several empirical strategies to test whether the effect of smallpox on stillbirths changed before and after the introduction of vaccination and to isolate exogenous variation in smallpox prevalence. We start by presenting the historical background on the causes of and trends in stillbirths, the changes in smallpox epidemiology over time, and existing theories of how smallpox might have caused stillbirths. The following sections present the Tabellverket data set and our two empirical strategies for estimating the causal effect of smallpox on stillbirths. Next, we present the results and then extend these Swedish results to other time periods and places, before concluding.

Background

Historical trends in and causes of stillbirths

Compiling long-run data on stillbirth rates is a particular challenge because stillbirths were often not registered in the same way as other vital events and because definitions of stillbirth changed over time and between countries. Scandinavian countries and Zeeland, a province of the Netherlands, were the first to register stillbirths. Sweden and Norway's registration practices seem to have been good from the early days (Woods 2009, pp. 56–7; Sommerseth 2021), but in Denmark, neonatal deaths in the first 24 hours were considered stillbirths until 1861, after which all neonatal deaths were meant to be excluded from stillbirth registration (Løkke 2018a). In Zeeland, stillbirths were defined as children who died before registration (which was required within three days of birth). Thus, it is likely that very early neonatal deaths were also included in the Zeeland series (van Poppel 2018). Roman Catholic countries tended to see relatively few stillbirths registered, as families sought to baptize stillborn children, making stillbirth registration for countries such as France, Spain, and Italy unreliable until the twentieth century (Woods 2009, pp. 77–82). More recently, changes in the age threshold between miscarriages and stillbirths have affected data series, but these age differences are not thought to be an important bias in stillbirths historically.

Woods et al. (2006) presented intriguing trends in late-foetal mortality for three Northern European

countries and one province (Sweden, Denmark, Norway, and Zeeland) across the nineteenth and twentieth centuries (reproduced and updated in Figure 1). Series for England and Wales, France, and the Netherlands are included from when stillbirth registration became reasonably comprehensive and accurate. Woods (2009, p. 59) argued that the rises in stillbirths across all countries from the early to mid-nineteenth century may have been due partly to improving registration practices, and the subsequent decline was in part driven by the removal of neonatal deaths in the first 24 hours from the series. However, the uniformity of the trend across all contexts and its presence in Sweden and Norway, which did not record early neonatal deaths as stillbirths, suggests that registration practices alone were not driving the pattern (Løkke 2018a, p. 91).

Explanations for the nineteenth-century trends are somewhat limited, especially when considering the increasing stillbirth rate in the first half of the nineteenth century. This could be related to smallpox, as discussed shortly, but might also be the consequence of improvements in obstetric care. Løkke (2018b) argued that the successful implementation of invasive intrapartum procedures that prevented children from being stuck in the uterus led to fewer maternal deaths where the child was undelivered. The dissemination of these techniques in the early nineteenth century may explain some of the increase in stillbirth rates across countries, as children who had previously not been registered at all were added to the ranks of stillbirths. The decline in stillbirth rates in the second half of the nineteenth century has been attributed to further dissemination of best-practice maternal care and especially the use of antiseptics from the 1870s onward (Högberg and Wall 1986; Högberg 2004; Woods et al. 2006; Løkke 2018b).

Stillbirth rates were relatively stable from the 1880s until the late 1930s, when all countries experienced sharp declines. Woods ascribed this to sulfa drugs, antibiotics, and better-quality maternal care but did not understand the precise mechanisms

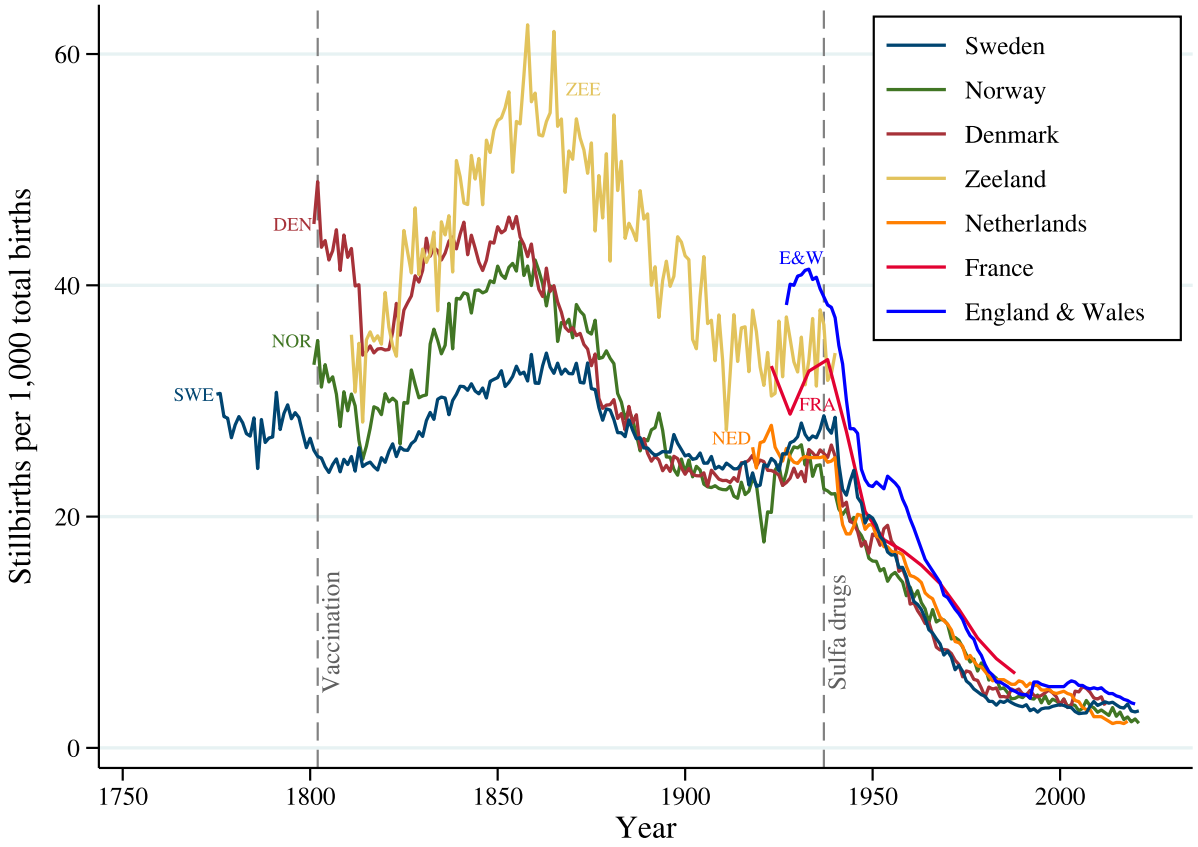

Figure 1 Time series of stillbirth rates in selected European countries

Source: Adapted from Woods et al. (2006). Sweden: Statistics Sweden (n.d.); Norway: Statistics Norway (n.d.); Denmark: Anne Løkke, personal communication (2022); Zeeland: Frans van Poppel, personal communication (2022); Netherlands: Statistics Netherlands (n.d.); France: Macfarlane et al. (2000), pp. 664–5; England and Wales: ONS (n.d.). These data are compiled and archived in Schneider (2022) as the European stillbirth rate time series dataset.

through which these medical innovations would have affected stillbirths (Woods 2009, pp. 82–5). Løkke (2012) provided a potential explanation for the effects of sulfa drugs and antibiotics on stillbirths by studying births at the National Hospital in Copenhagen: once doctors could treat puerperal fever with these drugs, they were much more likely to perform invasive surgeries to save the child when there were intrapartum complications. These interventions, along with the declining incidence of maternal syphilis, can explain a large share of the decrease in the stillbirth rate after 1940 (Schneider 2017).

The existing explanations for changing stillbirth rates over time tend to emphasize foremost the importance of obstetric care, with underlying maternal and foetal health being secondary causes of changes in stillbirths. Thus, more research is needed on other factors, such as disease, that might have influenced stillbirths historically.

Smallpox in Sweden

Smallpox was a leading cause of death in late-eighteenth-century Sweden and was responsible for 8–14 per cent of total deaths. In the second half of the eighteenth century, smallpox mortality was concentrated among children (Table 1), and there were severe epidemics at least once per decade, killing thousands of people (Figure 2). There was spatial variation in these epidemics, which recurred at the local level every 3–25 years except in Stockholm, where smallpox was endemic (Sköld 1996b, pp. 248–9). Although inoculation was growing in popularity in eighteenth-century England and seemingly affecting the epidemiology of smallpox there (Davenport et al. 2018), Sköld (1996b) argued that inoculation was largely ineffective in Sweden, because it was costly, there was concern about the health risks and lack of confidence in the

Table 1 Period age-specific smallpox mortality rates per 100,000 population, Sweden, 1788–92 to 1850–54

	Age-specific smallpox mortality rate per 100,000 population						
Period	0	1–2	3–4	5–9	10–24	25–49	50+
1788–92	2,471	1,339	820	293	40	2	1
1806–10	765	486	289	119	15	1	1
1831–35	410	81	39	15	10	15	1
1850–54	404	68	n/a	19	20	23	6

Source: Sköld (1996b, pp. 579–88) and Ager et al. (2018).

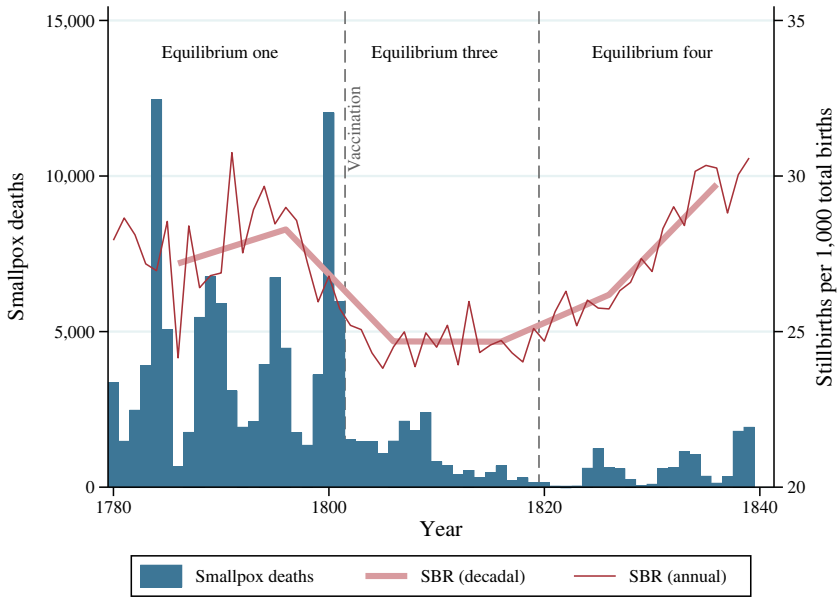

Figure 2 Smallpox deaths and stillbirth rates in Sweden, 1780–1839
Note: SBR is the stillbirth rate (per 1,000 total births).
Source: Smallpox deaths from Sköld (1996b, p. 52); SBR (decadal) from Statistiska Centralbyrån (1969, p. 108); SBR (annual) from Statistics Sweden (n.d.).

procedure, and the Department of Health monopolized inoculation, preventing its diffusion. Thus, smallpox mortality rates remained high in Sweden throughout the late eighteenth century.

The situation changed with the introduction of the smallpox vaccine, following the publication of Jenner's findings in 1798 (Crosby 1993). It took a few years for vaccination to be practised in Sweden, with the first vaccination administered in late November 1801 (Sköld 1996a, p. 371). Vaccination uptake increased very rapidly, from 0 to 60 per cent between 1800 and 1820, although with substantial regional variation. Vaccination was targeted at young children and became compulsory in 1816 (Sköld 1996b). It led to a sharp reduction in smallpox mortality (see Figure 2), with smallpox never again reaching its late-eighteenth-century zenith despite a resurgence in the mid-nineteenth century (Sköld 1996b; Ager et al. 2018).

In the early days of vaccination, there was little understanding of waning immunity over time. Swedish doctors expected vaccination to provide the same lifelong immunity as a previous infection (Sköld 1996a, pp. 480–2). However, with time it became clear that the vaccine provided only limited immunity, and there was a resurgence of smallpox beginning in the 1820s. The Swedish Medical Board eventually recognized the need for revaccination and allowed physicians to revaccinate individuals, beginning in 1839. However, aside from Swedish military recruits, revaccination was never a requirement, nor widespread in Sweden. Instead, revaccination was practised during smallpox epidemics to contain the spread of the disease (Sköld 1996a, pp. 482–4). Vaccination and waning immunity from vaccination changed the age pattern of smallpox mortality (Table 1). Age-specific mortality rates at young ages dropped dramatically after vaccination was introduced, as fewer young children contracted the disease. However, age-specific mortality rates for individuals aged 25+ increased, because having escaped smallpox in childhood through vaccination, adults in that age group were now more susceptible to smallpox than they had been in the eighteenth century. These changes in smallpox epidemiology in eighteenth- and nineteenth-century Sweden provide fertile ground for testing the effect of smallpox on stillbirths.

Smallpox and stillbirths

There are three mechanisms through which smallpox infection could have affected stillbirths in the eighteenth and nineteenth centuries in Sweden. The first mechanism is perhaps the most straightforward. If smallpox were present in a parish, and a susceptible pregnant woman contracted smallpox, then she would be at risk of stillbirth from the smallpox infection. There is ample historical evidence that smallpox could be passed from the mother to the foetus and that this could lead to miscarriage and stillbirth (Nishiura 2006; Woods 2009, pp. 218–23). A meta-analysis estimate of the foetal death rate among women who contracted smallpox in pregnancy was 39.9 per cent (Nishiura 2006), suggesting that this direct mechanism could have led to substantial foetal losses among infected pregnant women.

Second, smallpox could also have caused stillbirths directly if subclinical smallpox infection was possible among women who had already contracted smallpox. To be clear, there is no medical evidence that this was possible. The modern literature on smallpox is clear that smallpox infection granted lifelong immunity and that the smallpox virus did not persist in the body after infection (Fenner et al. 1988, pp. 144–7; Breman and Henderson 2002; Petersen et al. 2014). Fenner et al. (1988, p. 147) suggested that less than one in 1,000 pockmarked individuals experienced a second smallpox infection, making secondary infections extremely rare and epidemiologically unimportant. However, we do not rule out this possibility, because the smallpox virus has evolved over time and may have been different in the eighteenth century: a more lethal strain of smallpox emerged globally in the sixteenth or seventeenth century (Carmichael and Silverstein 1987; Harper 2021, pp. 362–3), and a less lethal form, variola minor, appeared in the late nineteenth century (Fenner et al. 1988, pp. 242–3).

The third and final mechanism through which smallpox epidemics could have affected stillbirth rates is an indirect mechanism: smallpox epidemics could have disrupted economic and social systems and increased stress among pregnant women, increasing the likelihood of stillbirths. Discussing the smallpox epidemics in the Americas following the Columbian Exchange, Jones (2003) argued that the large share of people who were sick during epidemics would have prevented normal economic activities (e.g. harvesting, planting, and trade) from being conducted and could have had large consequences for mortality from causes unrelated to the epidemics. However, there is no reason to assume that this disruption was similar in Sweden, given that smallpox epidemics there were relatively frequent and familiar occurrences and led to morbidity and mortality mainly among children, who were less

critical to economic activity. Still, a smallpox epidemic may have increased stress levels for pregnant women, and stress has been shown to increase the risk of stillbirth (Wisborg et al. 2008).

The importance of these mechanisms depends on the two factors highlighted in the Introduction: the share of pregnant women who are susceptible to smallpox and the prevalence of smallpox. We can combine these two factors in a simple two-by-two matrix to understand the different equilibria that would have been present at different points in Swedish history (Figure 3). In equilibrium one, smallpox prevalence is high because there is little to no control of smallpox, and therefore most people contract smallpox as children, leaving very few pregnant women susceptible. This equilibrium reflects the situation in Sweden in the eighteenth century before the introduction of vaccination. As shown in Table 1, smallpox mortality in Sweden was highly concentrated among children before vaccination began, so it is unclear whether enough pregnant women were still susceptible to smallpox infections during pregnancy for this to matter. However, given the high mortality of foetuses exposed to smallpox, if even a small proportion of women were still susceptible to smallpox during pregnancy, there could have been a substantial impact on stillbirths. Likewise, if subclinical infection were possible, then we would expect to see an effect during this period. Finally, if smallpox disruption contributed to stillbirths through a stress channel, then we might expect this indirect path to have mattered most when smallpox prevalence was high.

Immediately after vaccination was introduced, Sweden would have moved to equilibrium three. Smallpox prevalence would have fallen substantially, but most adult women would still have had immunity from smallpox based on infections in childhood. Given that the share of women susceptible to smallpox was low, we might again expect to find only a small effect in this period, but the first two mechanisms should still have mattered even if smallpox prevalence was lower.

Equilibrium four arises from the changing nature of smallpox epidemiology following the introduction of vaccination. Vaccination on its own will lead to an increase in age at infection, since lower prevalence will delay infection among the unvaccinated. However, in the mid-nineteenth century, waning

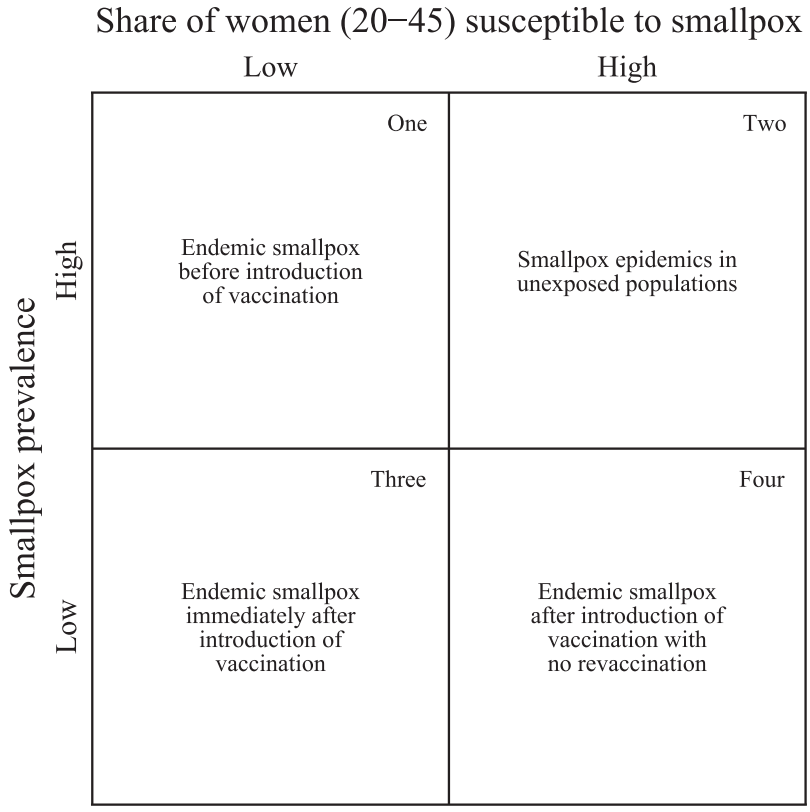

Figure 3 Equilibria of smallpox prevalence in relation to stillbirths
Source: Authors' own.

immunity from vaccination would also have left a greater share of pregnant women susceptible to smallpox than there had been in the eighteenth century, as reflected in age-specific mortality rates (see Table 1). Determining precisely how long immunity from vaccination would have lasted in early-nineteenth-century Sweden is difficult, because most studies of waning immunity have been conducted with more developed and effective vaccines. However, in summarizing the state of knowledge in 1988, Fenner et al. (1988, p. 42) suggested that vaccination was highly protective if it occurred within five years of smallpox exposure. Some immunity could last up to 20 or 30 years, but immunity from vaccines certainly became less effective after five years. Evidence from the 1878 smallpox epidemic in Philadelphia shows that both vaccinated and unvaccinated pregnant women contracted smallpox and experienced foetal deaths (Welch 1878; Nishiura 2006). Thus, it might be possible that smallpox mortality was more important in driving stillbirth rates after vaccination was introduced than when smallpox was far more prevalent and deadly in the eighteenth century. Revaccination would have blunted this effect somewhat, but the focus of revaccination on areas already experiencing smallpox outbreaks may have limited the effectiveness of revaccination for preventing smallpox among pregnant women.

We do not observe equilibrium two—high smallpox prevalence and high susceptibility among pregnant women—as smallpox was endemic in Sweden throughout our study period, but we discuss how our findings can be extended to this equilibrium in the Implications section.

Keeping the mechanisms and equilibria in mind, we can reinterpret the national time series evidence for stillbirths in Figure 2 in relation to the prevalence of smallpox and the equilibria presented in Figure 3. The sharp decline in stillbirth rates at the beginning of the nineteenth century, especially in the decadal data available to previous authors, seems to suggest that the introduction of vaccination and the decline in smallpox prevalence reduced stillbirths accordingly. Thus, perhaps smallpox was virulent enough to foetuses that even a few cases among pregnant women before the introduction of vaccination were contributing to the stillbirth rate. These lower stillbirth rates persisted for 20 years, but in the 1820s stillbirths began to increase again. This increase in stillbirths could have been caused by a greater share of women becoming susceptible to smallpox in pregnancy, even though smallpox prevalence was far lower in the mid-nineteenth century. Testing whether these trends in the national time series were driven by the epidemiology of smallpox is the key objective of this paper.

Data

We use a panel of Swedish parishes to test the effect of smallpox on stillbirths from 1780 to 1839. The data are drawn from the SHiPS database, which itself is based on the Tabellverk records kept by Swedish clergy and reported to the state during the eighteenth and nineteenth centuries (Tabellverket Database 2015). Clergy kept meticulous records of births, marriages, deaths, and migration in their parish and reported their figures to the Swedish state at regular intervals (Jeub 1993; Sköld 2004). They also recorded stillbirths and deaths from smallpox in their parish each year. As noted earlier, changes in stillbirth registration practices were not as pronounced in Sweden as they were in other parts of Scandinavia. Still, there are likely to be inconsistencies in registration over time, even if they are not as clearly spelled out for Sweden as for other countries. The most important registration issue we face is a temporary change between 1802 and 1821, from reporting the number of stillbirths to reporting the number of women experiencing stillbirths. This is discussed at length in Appendix A (sections A.1 and A.2, supplementary material) and does not seem to produce any major error in our data.

In analysing smallpox and stillbirths, we use 622 parishes which form a balanced panel between 1780 and 1839. These are parishes that are linked explicitly in the SHiPS database, suggesting that there were no or only very minor border changes over time. However, this is a subset of all parishes: there were around 1,900 in total in our study period. To judge whether our balanced panel is representative of all parishes, Figure A4 in the supplementary material (section A.3) compares parishes included and excluded from our balanced panel in terms of the stillbirth rate, smallpox mortality rate, maternal mortality rate, infant mortality rate, population, and births. The balanced and unbalanced parishes are remarkably similar in both level and trend for rates of stillbirths, smallpox mortality, maternal mortality, and infant mortality; however, the balanced panel parishes were larger on average by about 200–300 people, and consequently there were more births in the balanced panel parishes each year as well. While we prefer the balanced panel for econometric rigour, we also reproduce our empirical results using the whole (unbalanced) Tabellverket data (Appendix B, supplementary material), and the

interpretation of the results is the same. Table 2 presents descriptive statistics for our key variables of interest for the three periods/equilibria in our data.

Methods

We use two empirical strategies to test the mechanisms presented earlier, as outlined next.

Dynamic panel regressions

First, we use dynamic panel regressions to test whether the presence or severity of smallpox in a parish leads to an instantaneous increase in stillbirth rates. We estimate the following model using ordinary least squares (OLS) regression:

$$SBR_{i,t} = \alpha + \beta SBR_{i,t-1} + \gamma Pox_{i,t} + \rho_i + \phi_t + \varepsilon_{i,t}, \quad (1)$$

where the dependent variable ($SBR_{i,t}$) is the stillbirth rate in parish i in year t. The main independent variable of interest ($Pox_{i,t}$) takes two forms: either the smallpox mortality rate in parish i in year t or a binary indicator variable equal to one in years in which any smallpox deaths are recorded in the parish. We would expect smallpox to have an instantaneous effect on stillbirths, since smallpox infections develop within a couple of weeks of exposure and any foetal deaths would occur during the worst of the infection, within four weeks of exposure (Woods 2009, pp. 218–22). There may be spatial spillovers in the smallpox variable, so we also ran specifications that clustered the standard errors at the county level and found nearly identical results (not shown).

We include parish fixed effects (ρ_i) to control for time-invariant parish characteristics that could confound the relationship between smallpox and stillbirths: for example, geographical features, population density, settlement type, and the placement of a parish in the transport network. We include time fixed effects (ϕ_t) to capture common shocks to all parishes by year: for example, national smallpox epidemics, changes in national registration policies regarding stillbirths, greater integration of the transport network over time (Bergenfeldt et al. 2013), and general improvements in medical knowledge and care. Finally, we include the lagged dependent variable ($SBR_{i,t-1}$) to capture dynamic spillovers in the quality of medical care from year to year. These effects are likely greater for stillbirths, since skilled midwives may have helped to reduce intrapartum deaths, but are less clear for smallpox, since smallpox occurred as epidemics in most parishes. The results were nearly identical when we excluded the lagged dependent variable from the regressions (not shown).

We estimate the models for our entire period, 1780–1839, and for three subperiods. The first period, 1780–1801, captures the relationship during equilibrium one, when smallpox mortality was high before vaccination began in earnest in Sweden. The second period, 1802–19, captures equilibrium three, when vaccination reached high levels, causing smallpox prevalence to fall dramatically. The final period, 1820–39, measures the relationship in equilibrium four, when waning immunity from vaccination would have first increased the susceptibility of women of childbearing age to smallpox: the first cohorts vaccinated in the 1800s and 1810s would have been giving birth in the 1820s and 1830s. We end the third period in 1839 when revaccination was officially endorsed. Thus, these subperiods allow us to understand the relationship between smallpox and stillbirths in three of the possible equilibria. We would expect the effects to differ across the equilibria, so being able to test this directly is important.

Table 2 Descriptive statistics of key variables, Sweden, by time period

	Equilibrium one 1780–1801		Equilibrium three 1802–19		Equilibrium four 1820–39	
	Mean	SD	Mean	SD	Mean	SD
Stillbirth rate per 1,000 total births	31.2	41.0	27.3	42.0	30.7	35.3
Smallpox mortality rate per 1,000 population	1.81	3.88	0.42	1.54	0.17	0.75
Proportion of parish-years with smallpox deaths (binary)	0.35	–	0.15	–	0.10	–
Number of parishes	622		622		622	
Number of years	22		18		20	
Number of observations	13,684		11,196		12,440	

Note: SD is the standard deviation.
Source: Tabellverket data set.

Although this empirical strategy does not rely on any quasi-experimental variation in smallpox mortality, we argue that after conditioning on our controls, annual smallpox mortality was as if randomly assigned. The only potential source of endogeneity in our setting is omitted variable bias, because reverse causality and attenuation bias are not major problems in this historical context. There is no mechanism to explain why stillbirths would have led to smallpox mortality, and substantial measurement error in the smallpox mortality variable is unlikely because the symptoms of smallpox were so distinctive that misdiagnosis in cause of death was unlikely (Sköld 1997). Although it is impossible to rule out all confounders, the causes of stillbirths and smallpox mortality are disparate enough that it is difficult to think of omitted confounders. For instance, although stillbirths may be sensitive to income shocks, smallpox mortality is not related to nutritional status (Riley 2010), which means that localized famines would not be confounders, at least not through that pathway. Given our controls, omitted confounders would need to be time-varying, localized effects that could have influenced both the stillbirth rate and smallpox mortality: for instance, a localized famine that increased stillbirths and also increased labour mobility, leading to smallpox epidemics. Bengtsson (1999) and Bengtsson and Quaranta (2017) showed that high food prices were associated with greater smallpox mortality in southern Sweden, likely because of greater labour mobility, but given that grain markets were relatively well integrated in eighteenth-century Sweden, much of the effect of these price shocks would have been national rather than local and would therefore be captured by our year fixed effects (Bengtsson and Jörberg 1975). We could also consider parish-specific time trends in the variables, but these would be captured largely by the lagged dependent variable. Breaking the analysis into subperiods also reduces the possibility that long-run trends might bias our results.

Difference-in-differences strategy

Although we believe that the scope for endogeneity in our panel regressions is minimal, we also exploit exogenous variation in smallpox mortality in a continuous treatment difference-in-differences framework. We use the introduction of vaccination in 1802 as an exogenous shock to smallpox mortality (treatment) that varied in intensity in relation to the pre-vaccination level of smallpox in each parish. This tests whether a reduction in smallpox prevalence affected stillbirths, holding the share of pregnant women susceptible to smallpox constant: the introduction of vaccination did not change the susceptibility of pregnant women of childbearing age because these women had lifelong acquired immunity from smallpox infections in childhood. Essentially, this tests the impact on stillbirths of moving from equilibrium one to equilibrium three (see Figure 3). The empirical specification takes the following form, estimated by OLS:

$$SBR_{i,t} = \alpha + \beta SBR_{i,t-1} + \theta Pox_{1780-1801} \times post_t + \rho_i + \phi_t + \varepsilon_{i,t}, \quad (2)$$

where the dependent variable ($SBR_{i,t}$) is again the stillbirth rate in parish i and year t. The main coefficient of interest is θ, which is the effect of the interaction of smallpox prevalence in the period 1780–1801 before vaccination was introduced ($Pox_{1780-1801}$), and $post_t$, a binary indicator variable equal to one in years following the start of vaccination in 1802. We measure pre-vaccination-era smallpox prevalence in two ways: as the mean smallpox mortality rate in a parish between 1780 and 1801 and as the number of years with smallpox deaths in a parish in the same period. These measures capture the intensity and frequency of smallpox deaths, both of which would have affected the prevalence of smallpox. While these two indicators are positively correlated ($r = 0.38$), the correlation is low enough that we feel they are capturing different aspects of smallpox prevalence. We use an indicator variable ($post_t$) as the vaccination shock variable, because vaccination rates may have been endogenous to local, time-varying confounders that would bias the relationship of interest, and vaccination rates were only recorded at county level anyway, preventing us from exploring parish-level variation. Again, we include the lagged dependent variable and parish and year fixed effects as controls. As before, excluding the lagged dependent variable did not change the key results (not shown). Thus, this empirical strategy tests whether parishes with higher levels of smallpox mortality in the pre-vaccination era experienced lower stillbirth rates following the introduction of vaccination in 1802. Most immediately, this can be seen as a test of the extent to which pregnant women were contracting smallpox before vaccination began.

Recent econometric work on continuous treatment difference-in-differences has highlighted two key assumptions for identification: that the

treatment cannot be anticipated and that the average causal response must be homogenous across all dosage levels of the treatment (Callaway et al. 2021). On the first assumption, given that vaccination was only practised in Sweden from the end of 1801, it is very difficult to see how the treatment could have been anticipated, especially since there were very few things that women in this period could do to cause or prevent stillbirths. Inoculation could have partially anticipated vaccination, but it was never widespread in Sweden (Sköld 1996b). On the second assumption, there is no reason to believe that a one-unit decrease in smallpox prevalence (from vaccination) would have yielded different changes in stillbirths for parishes with high or low pre-vaccination-era smallpox prevalence. The concern is that there could have been selection on unobservables based on the treatment dosage that would have affected the average causal response between dosage groups. The treatment effect of smallpox on stillbirths is a largely biological causal path that should not vary according to whether women were living in areas with high or low pre-vaccination-era smallpox prevalence. Given that medical doctors could not treat smallpox at the time and could not prevent stillbirths caused by smallpox, it is difficult to see how the causal response would have varied based on the treatment dosage.

We analyse the period 1780–1819 for a number of reasons. First, we begin our analysis in 1780 because smallpox and measles mortality were reported together until 1774 (Ager et al. 2018). Starting from 1780 ensures that this change was fully implemented before our analysis begins. Second, we also want to capture the long-run average level of smallpox in a parish in the pre-vaccination era so that our pre-treatment smallpox prevalence variables are not biased by short-run shocks or periods without smallpox epidemics. Finally, we include a large number of post-vaccination years in order to explore dynamic treatment effects across that period.

Results

The results of the dynamic panel regressions are presented in Table 3. These show the instantaneous effect of a smallpox epidemic on the stillbirth rate controlling for parish and year fixed effects and the lagged stillbirth rate. We first test the effect for the entire period from 1780 to 1839 in specifications (1) and (2). Whether we measure smallpox through the smallpox mortality rate or through a binary indicator variable equal to one when there was a smallpox death in a parish, the coefficients are statistically insignificant and close to zero.

We next break the analysis into the three subperiods reflecting the three equilibria. Before vaccination was introduced, again the effect is statistically insignificant and close to zero, which suggests that in the pre-vaccination era when smallpox prevalence was high, very few women of childbearing age contracted smallpox. This also suggests that subclinical smallpox cases were not a source of foetal deaths and likely did not exist. In the period immediately after vaccination began (1802–19), the coefficients are also statistically insignificant, but the coefficient for the smallpox mortality rate increases somewhat in specification (5). This suggests that a growing share of pregnant women were becoming susceptible, most likely because smallpox prevalence had fallen and they had escaped childhood infection rather than because of waning immunity from vaccination.

In the final period, 1820–39, when women who had been vaccinated as children were reaching childbearing age, we see positive and statistically significant coefficients for both smallpox mortality variables. Smallpox did contribute to the stillbirth rate in this period (equilibrium four). However, the size of the effect is still relatively small. A one-standard-deviation (SD) increase in smallpox mortality in specification (7) increases the stillbirth rate by 0.6 and the presence of a smallpox death in a parish in specification (8) increases the stillbirth rate by 1.3. These magnitudes are small relative to the variation in the stillbirth rate across parishes and years in the 1820–39 period (SD = 35.3) and can explain only a fraction of the increase in the national stillbirth rate in the first half of the nineteenth century. Thus, although more pregnant women were susceptible to smallpox in the final period and smallpox did influence stillbirths, the prevalence of smallpox was likely low enough that the impact of smallpox on stillbirths was relatively small.

We also test whether vaccination affected the stillbirth rate by drastically reducing the prevalence of smallpox in the population. Table 4 presents the results from the difference-in-differences empirical strategy. We interact the pre-vaccination smallpox measures with two periods after the introduction of vaccination to determine whether there were dynamic treatment effects. The key period of interest is the period immediately after vaccination began, 1802–10, when smallpox prevalence fell sharply but women of childbearing age would still have had immunity from prior smallpox infections. We also include the period 1811–19 to understand whether the stillbirth effects are clearer once vaccination became widespread.

Table 3 Instantaneous effect of smallpox on stillbirths in Sweden, 1780–1839: dynamic panel regression results

	All periods 1780–1839		Equilibrim one 1780–1801		Equilibrium three 1802–19		Equilibrium four 1820–39	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Smallpox mortality rate	0.003 [−0.1411, 0.1472]	–	−0.026 [−0.1734, 0.1212]	–	0.186 [−0.1584, 0.5307]	–	0.807** [0.1305, 1.4835]	–
Binary smallpox dummy	–	0.295 [−0.5052, 1.0951]	–	0.121 [−1.0537, 1.2959]	–	0.181 [−1.2355, 1.5976]	–	1.338* [−0.2395, 2.9158]
Lagged dependent variable	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Parish fixed effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Time effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	36,698	36,698	13,062	13,062	11,196	11,196	12,440	12,440

*$p < 0.1$, * $p < 0.05$, ***$p < 0.01$.
Notes: Table shows OLS regression estimates from equation (1). The 95 per cent confidence intervals are given in square brackets; these are calculated using standard errors that are clustered on the running variable (CRV). Binary smallpox dummy is equal to one in years where a smallpox death is recorded in a parish and zero otherwise. The analysis is conducted on a balanced panel of 622 parishes.
Source: As for Table 2.

When looking at mean smallpox mortality rates before vaccination started, the coefficients are positive. This is the opposite sign to what we would expect if smallpox were behaving as outlined earlier: parishes with higher smallpox prevalence before the introduction of vaccination should have experienced greater declines in stillbirths. One possible explanation for this pattern is that before the introduction of vaccination, women in parishes with low smallpox prevalence were more likely to escape smallpox infection in childhood than women in parishes with high smallpox prevalence. This left women in parishes with low smallpox prevalence vulnerable to smallpox infection during pregnancy. Thus, with the decline in smallpox prevalence after the introduction of vaccination, women in low-smallpox-prevalence parishes experienced a reduction in stillbirths, whereas the reduction of smallpox prevalence did not affect stillbirths in high-smallpox-prevalence parishes. This could explain this positive coefficient.

However, the coefficients are small in magnitude. A one-SD increase in pre-vaccination-era smallpox mortality rates (0.66 smallpox deaths per 1,000) leads to an increase in the stillbirth rate of 0.90 when considering

Table 4 The effect of reduction in smallpox prevalence (due to vaccination) on stillbirth rates in Sweden, 1780–1819: difference-in-differences results

	(1)	(2)	(3)
Pre-vacc smallpox rate × Post	1.352* (0.816)	–	–
Pre-vacc smallpox rate × 1802–10	–	0.910 (0.899)	–
Pre-vacc smallpox rate × 1811–19	–	1.793* (0.971)	–
Pre-vacc smallpox count × 1802–10	–	–	−0.343 (0.328)
Pre-vacc smallpox count × 1811–19	–	–	−0.501 (0.504)
Lag dependent variable	Yes	Yes	Yes
Parish fixed effects	Yes	Yes	Yes
Time fixed effects	Yes	Yes	Yes
N	24,258	24,258	24,258

*$p < 0.1$, * $p < 0.05$, ***$p < 0.01$.
Notes: Table shows OLS regression estimates from equation (2). Smallpox rate is the mean smallpox mortality rate per 1,000 in 1780–1801 (pre-vaccination era) and smallpox count is the number of years with smallpox deaths in the same period. Post is a binary variable equal to one after vaccination began in 1802 and zero otherwise. Standard errors based on the CRV estimator are shown in parentheses. The analysis is conducted on a balanced panel of 622 parishes.
Source: As for Table 2.

the entire post-vaccination period 1802–19 (specification (1)). When interacting the two post-vaccination periods with the pre-vaccination-era smallpox rate, a one-SD increase in smallpox rates leads to increases of 0.60 and 1.19, respectively, in the stillbirth rate (specification (2)). These figures should be compared against an SD of the stillbirth rate of 42.03 in the post-vaccination period.

The results are similar when we use the number of years with smallpox deaths before vaccination began as our treatment variable (specification (3)). Here the coefficients are negative: high frequency of smallpox epidemics in the pre-vaccination era led to lower stillbirth rates after vaccination started, as we would expect, but again the magnitude of the coefficient is very small. These results confirm that the exogenous drop in smallpox prevalence driven by vaccination did not influence stillbirth rates. This suggests that there were very few women who contracted smallpox while pregnant in the pre-vaccination era. It also suggests that the decline in national stillbirth rates in Sweden, Norway, and Denmark at the beginning of the nineteenth century was not related to a decline in smallpox prevalence as we might have guessed.

Implications for other populations and contexts

Overall, in this paper we find that smallpox was not an important cause of stillbirths in the past. Figure 4 restates our findings by placing them in the framework of the four equilibria. Before vaccination was introduced (equilibrium one) and immediately following this (equilibrium three), smallpox epidemics did not affect stillbirth rates. The most likely explanation for this null result is that very few women were still susceptible to smallpox by the time they reached childbearing ages, because they had contracted smallpox as children. This explanation is confirmed by our difference-in-differences analysis. If pregnancies were affected by smallpox before vaccination began, then an exogenous and large reduction in smallpox prevalence should have led to a decrease in stillbirth rates. However, this was not the case. We do find an instantaneous effect of smallpox on stillbirths from the 1820s onwards, as women of childbearing ages who had been vaccinated as children became susceptible because of waning vaccine immunity (equilibrium four). This effect is very small though and cannot account for

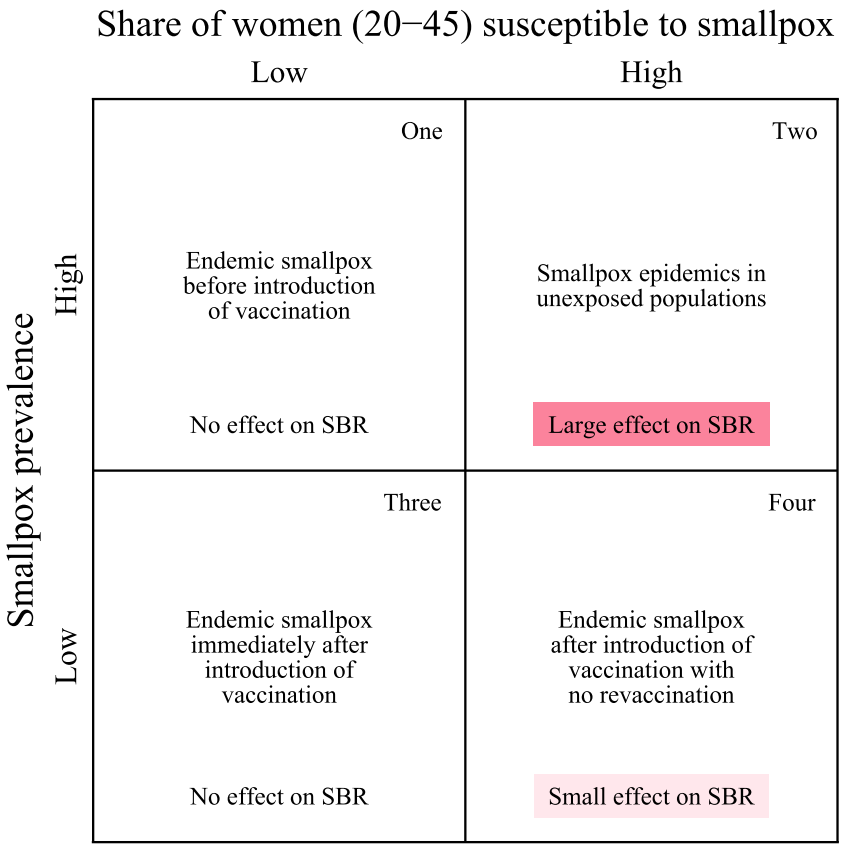

Figure 4 Equilibria of smallpox prevalence in relation to stillbirths, showing the effect of smallpox on stillbirths in each equilibrium
Note: SBR is the stillbirth rate.
Source: As for Figure 3.

the substantial increase in stillbirth rates from the early to mid-nineteenth century.

Although this paper focuses explicitly on Sweden between 1780 and 1839, the results can tentatively be extended to other time periods and places. To make inferences about other contexts, it is helpful to consider where a particular population would sit in the two-by-two matrix of equilibria (Figure 4). For countries starting at equilibrium one, the pattern related to vaccination seems clear. Vaccination, if it proceeded quickly enough, would shift the population from equilibrium one to equilibrium three in the short run, but as soon as waning immunity from vaccination became an important feature of smallpox epidemiology, the population would shift to equilibrium four. The rise of revaccination in Sweden and elsewhere may have shifted populations back to equilibrium three, as fewer women were susceptible to smallpox in pregnancy. Alternatively, measures such as efficient notification and isolation of cases, alongside universal child vaccination, could also have worked to keep smallpox prevalence low enough that few pregnant women were infected despite their continued susceptibility to smallpox (Hardy 1993, pp. 147–50). Thus, in the typical trajectory of the disease, it seems that smallpox was likely not an important driver of stillbirth rates.

It is also worth considering the case of southern England, where inoculation and isolation of smallpox cases in pesthouses may have prevented smallpox from becoming endemic even before vaccination was introduced (Davenport et al. 2018). While inoculation did reduce smallpox prevalence, it was not widespread enough to shift southern England to equilibrium three: the high share of smallpox deaths occurring in people aged 15+ suggests that pregnant women were at risk of contracting smallpox. Thus, it is possible that southern England was in equilibrium four in the eighteenth century in the absence of vaccination. What this means for stillbirths is difficult to establish precisely. Waning immunity should not have been a problem with inoculation, since it involved infecting people with the actual smallpox virus. Thus, inoculated women would not have been susceptible to smallpox infections in the same way that vaccinated women were in the mid-nineteenth century. However, inoculation was never as widespread as vaccination, so there would still have been a large number of women at risk. The effect of smallpox on stillbirths was dependent largely on smallpox prevalence. In epidemics, smallpox could have caused some stillbirths, but it seems likely that the average effect was small.

Of course, some subpopulations may have been at greater risk. Rural migrants to London, where smallpox remained endemic in the pre-vaccination era, would have been at higher risk of smallpox-induced stillbirths than women born in London. However, it is not clear whether these migrants would have had a demographically meaningful effect on the population stillbirth rate. Migrants tended to be unmarried and young. In addition, migrant women would have been at risk of smallpox-induced stillbirths only if they became pregnant before contracting smallpox. There is also growing evidence that London-bound migrants were inoculated before leaving the countryside (Davenport et al. 2016) and many had likely contracted smallpox in childhood anyway. Thus, it is not clear that migrant women experienced substantially higher rates of stillbirths caused by smallpox infections.

There are, however, contexts where smallpox would likely have been an important driver of stillbirths, as reflected by equilibrium two in Figure 4. If smallpox occurred in an epidemic form and attacked a population without prior acquired immunity to the disease, then very high rates of stillbirths would be possible. The most obvious example of this is the smallpox epidemics that occurred among indigenous Americans as part of the Columbian Exchange (Riley 2010, p. 274). These epidemics led to mortality on a very large scale, but as several authors have suggested, a decrease in the birth rate may also be important in explaining depopulation (Jones 2003, p. 721; Livi-Bacci 2006). If 40 per cent of pregnant women infected with smallpox experienced stillbirths, then the smallpox epidemics would have affected both births and deaths directly, with important implications for population growth. Of course, populations would have suffered these massive consequences only when large shares of adults had no acquired immunity to smallpox. This could have occurred when smallpox was first introduced to a population or in repeated epidemics where population size and density were low enough to prevent smallpox from becoming endemic. As smallpox became endemic, populations would have shifted to equilibrium one.

Conclusion

In conclusion, our paper has shown that smallpox is unlikely to have been an important cause of stillbirths in the past except for very specific and short-run instances, such as the smallpox epidemics during the Columbian Exchange. Our findings contradict earlier arguments by Woods (2009), mainly because

there were simply too few women who were still susceptible to smallpox in pregnancy for smallpox to matter. Thus, other factors, such as obstetric practice and maternal health, must have been more important in driving trends in stillbirth rates in the eighteenth and nineteenth centuries (Woods et al. 2006), despite the intriguing trends that made smallpox appear to be a potentially important factor.

This also means that changes in smallpox exposure in utero did not have a strong influence on cohort health in the eighteenth and nineteenth centuries. We could have imagined that the decline in smallpox prevalence after vaccination was introduced would have been associated with a reduction in foetal scarring, which could also have influenced adult mortality (cf. Quaranta 2013). However, in the pre-vaccination era, smallpox affected very few births, because the vast majority of women had contracted smallpox in childhood. It is possible that smallpox produced scarring effects among children in the mid-nineteenth century (as in equilibrium four), but this group of children would likely have been small enough that this would not have had a strong influence on population health.

Although this paper has focused on stillbirths, our findings can also be extended to maternal mortality. Like foetuses, pregnant women are also at high risk of dying from smallpox (Nishiura 2006), but given that very few pregnant women appear to have been infected with smallpox, it seems very unlikely that declines in smallpox prevalence can explain the declining maternal mortality rates in England and Sweden in the eighteenth and early nineteenth centuries (Högberg and Wall 1986; Wrigley et al. 1997, p. 313). Large smallpox epidemics among a vaccinated or susceptible population could lead to smallpox cases among pregnant women, producing the evidence Nishiura (2006) used to estimate the effects of smallpox, but these were rare, at least in Sweden, and likely did not influence population rates.

Finally, the paper has highlighted how vaccination drastically changes both the epidemiology of a disease and its potential to cause in utero shocks to health. While vaccination reduces the prevalence of a disease, it may also make pregnant women more vulnerable to the disease through two mechanisms. First, vaccination leads to an increase in mean age of infection, as lower prevalence allows the unvaccinated to delay infection, potentially increasing infections among pregnant women. And second, waning immunity from vaccination may leave women at greater risk of infection in adulthood. While this paper has focused on smallpox, the same mechanisms could be at play for rubella or chickenpox. The extent of foetal exposure depends on whether the prevalence of the disease is great enough to infect pregnant women. When prevalence is low, few pregnant women are likely to be infected, but during epidemics the risk of infection could increase substantially. Thus, our results have highlighted yet again the importance of repeated vaccination to keep the prevalence of disease at low levels and protect pregnant women from infection.

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