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What is the case fatality rate of smallpox?

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What is the case fatality rate of smallpox?[1]

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Abstract:

This paper uses population smallpox mortality rates in eighteenth-century Sweden and the death toll from the 1707-9 smallpox epidemic in Iceland to estimate plausible ranges for the case fatality rate (CFR) of the deadly form of smallpox, *Variola major*, in both its endemic (Sweden) and epidemic (Iceland) form. We find that smallpox CFRs could be extremely high (40-53%) when smallpox was epidemic and attacked a population where both children and adults were susceptible as in Iceland. However, where smallpox was endemic and therefore a disease of childhood, as in Sweden, a better estimate of the CFR is 8-10%. This is far lower than the consensus CFR of 20% to 30%. Part of the differences between the CFRs studied here could be due to differences in the inherent virulence of smallpox in the two contexts. However, we argue that social factors are more likely to explain the differences. Where both adults and children were susceptible to smallpox, smallpox epidemics fundamentally disrupted household tasks such as fetching water and food preparation and prevented parents from nursing their sick children, dramatically increasing the CFR. Thus, when historians and epidemiologists give CFRs of smallpox, they should consider the population and context rather than relying on an implausible intrinsic CFR of 20% to 30%.

Keywords: smallpox, epidemics, case fatality rate, historical demography

JEL Codes: N30, I14, J10

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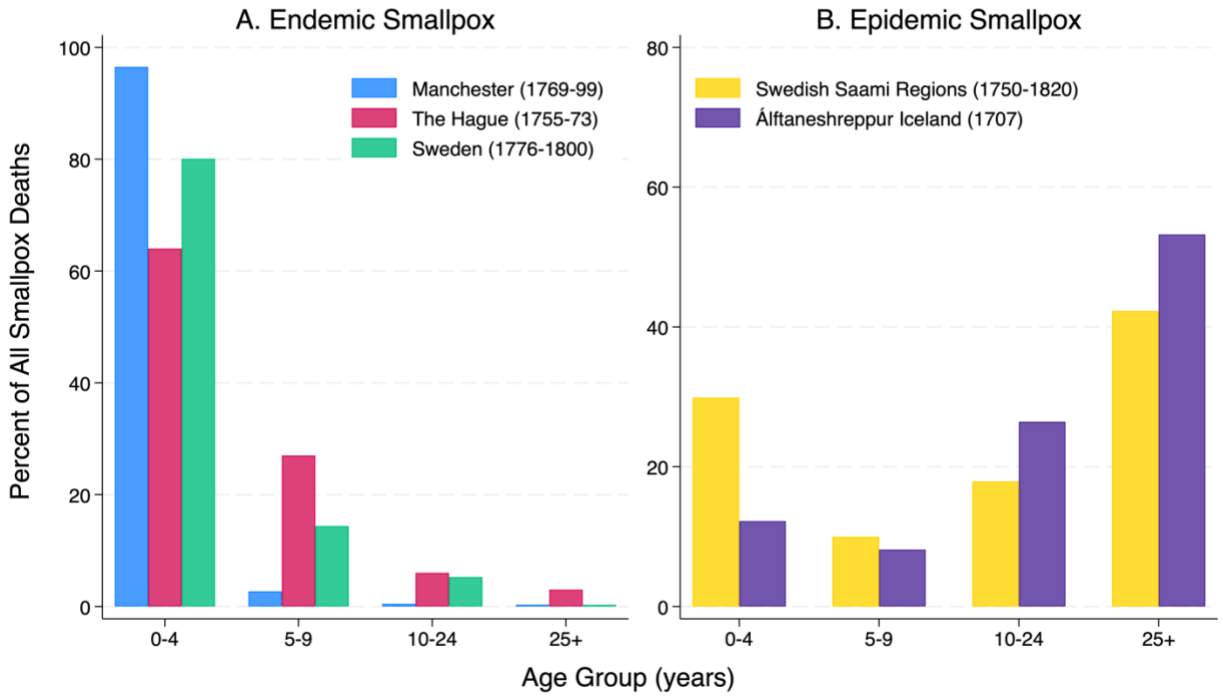
I. Introduction

Smallpox was one of the most virulent pathogens to infect humanity. According to paleogenomic studies, smallpox diverged from its most recent ancestor approximately 1,700 years ago and experienced important mutations over time that changed the virulence of the disease (Harper 2021, p. 195). For instance, a new, more deadly form of smallpox appears to have emerged in the sixteenth and seventeenth centuries, which is now known as *Variola major* (Carmichael and Silverstein 1987). Periodic epidemics of *Variola major* were a key component of the massive population losses of indigenous Americans after the arrival of Columbus in the 'New World' (Livi-Bacci 2006; McNeill 2022, pp. 147-53). However, *Variola major* also circulated in Eurasia and Africa and became an endemic disease where the population was large enough to sustain it. Where endemic, *Variola major* became a disease of childhood (see Figure 1). For instance, only about 5 per cent of smallpox victims were aged 10 years or more in Sweden in the period 1788-92 (Sköld 1996a, p. 580). The age structure of smallpox mortality was similar before 1800 in Finland, the Netherlands and Northern England (Davenport et al. 2018; Mielke et al. 1984; Rutten 1997, p. 45). However, where smallpox was epidemic, as in Iceland or in the northern-most regions of Sweden where the Saami population lived, a higher proportion of smallpox deaths occurred among adults. The epidemiological picture in Europe changed dramatically after the discovery/invention of smallpox vaccination by Jenner in 1796. Within a few years, vaccination had spread throughout the continent and later to other parts of the world (Bowers 1981) and led to dramatic reductions in smallpox cases and deaths (Edwardes 1902; Fenner et al. 1988; Mercer 1990). A relatively mild form of the virus, *Variola minor*, emerged in the late nineteenth century, and phylogenetic analyses suggest that *V. major* and *V. minor* underwent substantial evolution and radiation in the twentieth century (Duggan et al. 2016). In 1977, after 175 years of sustained primary vaccination efforts alongside other interventions such as isolating cases and revaccination around outbreaks, smallpox became the only human disease to be eradicated (Henderson 2009, p. 11).

Given the importance of smallpox as a major human pathogen, it is important to understand how deadly the disease actually was, but assessing the case fatality rate (CFR) of smallpox is more complicated than one might think (Fenn 2001, p. 20). Even when focussing solely on the period before vaccination, when strain diversity was low and resistance was not complicated by vaccination, reported CFRs varied dramatically. Where they have been estimated for the eighteenth century, for example, they vary from 9.1% in Deal, England in 1725-26 (Razzell 2003, p. 173) to 36.4% in Uxbridge, England in 1727 (Razzell 2003, p.174) to 15.6% in Prussian towns in 1796 (Riley 2010, p. 451). CFRs in the nineteenth and twentieth centuries, after the introduction of vaccination, could be higher still, ranging from 9% to over 40% in unvaccinated cases (Edwardes 1902, p. 99, 105, pp.114-18; Fenner et al. 1988, p.

175). Despite these very large variations in reported CFRs, there seems to be consensus among epidemiologists and medical historians that the CFR of *Variola major* was 20-30% and the CFR of *Variola minor* was closer to 1% (Bhattacharya et al. 2005, p. 2; Campbell 2002, p. 33; Carmichael and Silverstein 1987, p. 149; Crosby 1993, p. 1008; Fenner et al. 1988, p. 208; Grant 2019, p. 6; Hays 2005, p. 152; Henderson 2009, p. 33; Hopkins 1983, pp. 5-6; Kotar and Gessler 2013, p. 4; Oldstone 2010, p. 54; Penschow 2022, p. 1; Petersen et al. 2014, p. 503).

Figure 1: Percentage of Total Smallpox Deaths by Age Category



Notes: The underlying data has been aggregated so that the age categories match for all samples. For the Icelandic case, some deaths where exact age was not available had to be allocated to specific age categories. Where exact age was not reported, it was clear whether the individual was a child or an adult, so it will not alter the large percentages of adult smallpox deaths in Iceland. Note also that the specific community of Álftaneshreppur in Iceland seems to have avoided the previous smallpox epidemic on the island in 1670-72, so everyone under age fifty was susceptible.

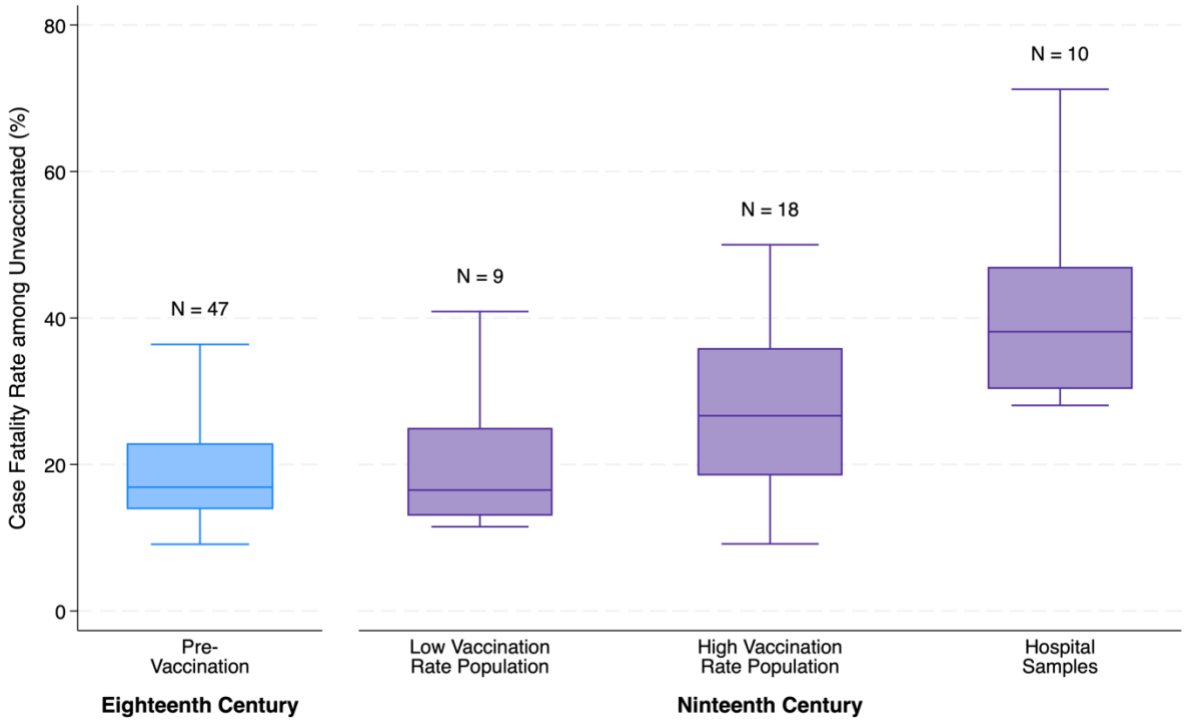
Sources: Manchester – Davenport et al. (2016, p. 195); The Hague – Rutten (1997, p. 45); Sweden – Pettersson (1913, p. 175); Swedish Saami Regions – Sköld (1997, p. 12); Álftaneshreppur Iceland – Steffensen (1977, p. 53).

However, this consensus is built on shakier evidence than it might first appear: sampling biases and measurement errors in the deaths and cases have large effects on estimates of smallpox CFRs. Beginning with the denominator (cases), getting accurate counts of smallpox cases was notoriously difficult even though smallpox had easily identifiable symptoms and had no asymptomatic carrier state (Fenner 1982). During the 'intensified smallpox eradication campaign' of 1967-80, reported numbers of smallpox cases often peaked shortly before smallpox was eliminated because better surveillance ensured that fewer cases were missed (Fenner et al. 1988, p. 174). Careful estimates of the completeness of case detection in this period ranged from 1% to 83 % (Fenner et al, 1988, p. 175, 824). Although there may have been under-recording of smallpox deaths, death registration was likely far more complete than case registration. Additionally, many of the smallpox CFR estimates from the twentieth century were drawn from hospital populations. Koplan et al. (1978) show that the extremely high CFR of 51% in a hospital in Dacca, Bangladesh in 1972-73 relative to a CFR of 21% in a neighbouring rural area was most likely driven by selection of the most severe cases into the hospital, thus inflating the CFR. Selection into vaccination could have also biassed death rates (Dribe and Nystedt 2003; Rutten 2011; p. 188; Theilmann et al. 2023). As Koplan et al. (1978, p. 358) argue, 'smallpox in Dacca was primarily a disease of transients, traders, unemployed males searching for work, and widows with dependent children searching for food'. Although smallpox virulence was likely not influenced by malnutrition (Riley 2010, p. 466), if those remaining unvaccinated (or not revaccinating) were more prone to receiving high viral loads or were less likely to have access to nursing care once sick, then these social factors might also inflate the CFR relative to what would have been experienced in a population before vaccination.

Figure 2 illustrates some of these issues. It compares smallpox CFRs reported in eighteenth century communities with nineteenth century CFRs drawn from three contexts: populations that rejected vaccination; populations with high levels of vaccination, and hospital settings. Populations that rejected vaccination include the ethnic minority community of Lippowaner in Bukovina and the Calvinist community on Urk in the Netherlands (Rutten 2011, p. 188); poorly vaccinated populations such as Norwich 1819, Verona 1810-38, France 1816-41 (Del Panta 1980, p. 70; Edwardes 1902, pp. 85-6; Royal Commission 1889, pp. 73-4); and English towns that embraced conscientious objection, most notably Gloucester and Leicester (Royal Commission 1986, appendix VII p. 8). All CFRs refer to groups considered unprotected (unvaccinated or, in the eighteenth century, uninoculated). As expected, CFRs reported for hospital cases were highest, with a median CFR of 40%. CFRs were also higher in populations with high vaccination rates compared with those that rejected or pre-dated vaccination, consistent with negative selection of unvaccinated cases in populations in which the vaccine was available. Finally, CFRs were similar and relatively low (medians of

17.1 and 16.5) in eighteenth and nineteenth century populations with low or zero rates of vaccination, which suggests, albeit on the basis of a small sample, that there was no major change in the virulence of *Variola major* over this period. This contrasts with very marked geographical heterogeneity in CFRs in the mid-twentieth century consistent with the circulation of *V. major* in Asia and parts of Europe and *V. minor* in the Americas and parts of Europe including the United Kingdom, and evidence of intermediate CFRs especially in eastern and southern Africa (Fenner et al. 1988, chap. 8, 12-23; Hedrich 1936).

Figure 2: Smallpox case fatality rates in eighteenth and nineteenth century European and American populations.



Notes: 'Pre-Vaccination' refers to eighteenth century populations; the other samples refer to nineteenth century samples. 'Low Vaccination Rate Population' refers to populations with low levels of vaccination (<70% where stated, otherwise as indicated by religious preference, by contemporaries, or by unusually high ratios of unvaccinated to vaccinated cases). 'High Vaccination Rate Population' refers to populations with high levels of vaccination (>=70% or presumed to be such); 'Hospital Samples' refers to evidence drawn from hospital registers.

Sources: See Appendix Table A4.

More broadly, smallpox case-fatality rates also depended on the age distribution of victims. Smallpox CFRs varied with age with a reverse J-shaped distribution similar to but shallower than all-cause mortality (see Figure 4, below). Thus, the age composition of cases could mechanically influence the overall CFR. Where smallpox struck frequently then a larger share of cases would be young children and CFRs would be higher (Riley, 2010, p. 251). Vaccination tended to drive up the average age at infection, which would have acted to lower or to raise the overall CFR depending on the age distribution of those left vulnerable. And vaccination did not afford complete protection. The immunity conferred by vaccination waned over time and varied depending on the quality of the vaccination and on individual characteristics. Even where observers reported CFRs by vaccination status, that status was not straightforward to determine. In general, it seems likely that CFR estimates after vaccination may be biased upward both by biases in the numerator and undercounting of cases in the denominator of the CFR.

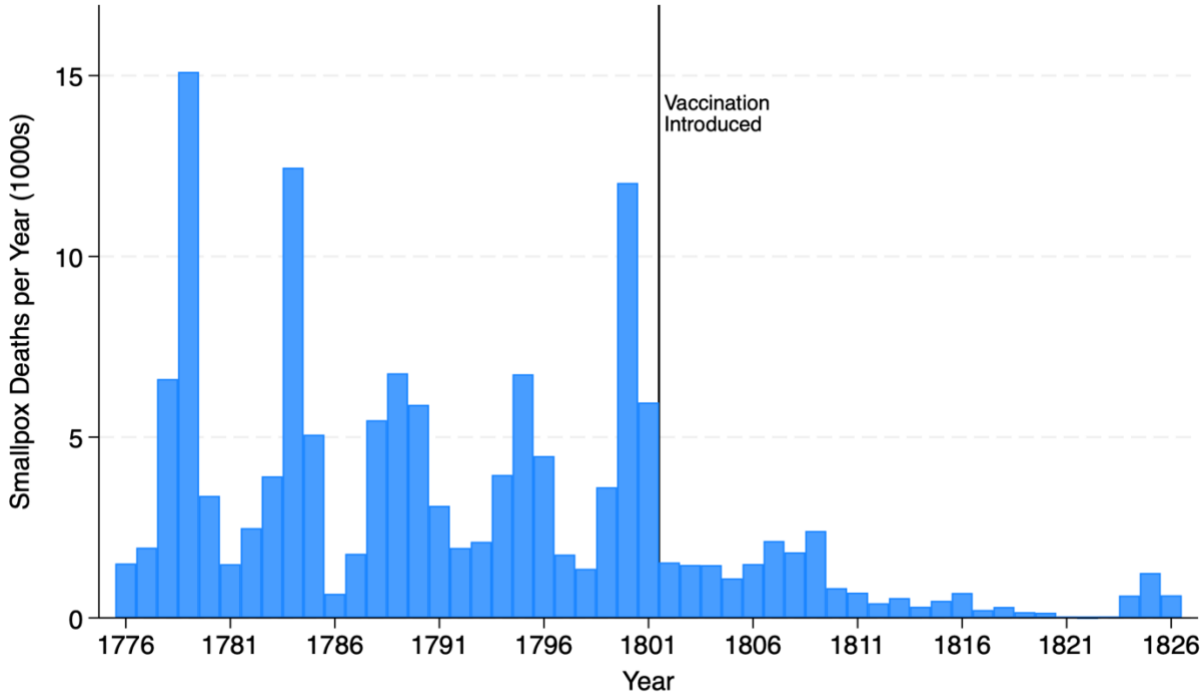
Rather than trying to estimate CFRs directly, this paper starts with population-level age-specific smallpox mortality rates (or total smallpox deaths) and then uses reasonable assumptions about the age-pattern of cases and susceptibility across age groups to estimate CFRs for *Variola major*. We draw on two case studies from the eighteenth century: Sweden 1776-1800 and Iceland 1707-9. Focussing on the eighteenth century is helpful because it predates vaccination,[2] as well as the diversification of smallpox lineages in the late nineteenth and twentieth centuries. In addition, inoculation, the practice of introducing smallpox material under an individual's skin to induce a mild smallpox infection and confer immunity, was not practised widely in Sweden or Iceland in the eighteenth century and would therefore not affect our estimates of incidence and case fatality rates (Sköld 1996b, p. 250). Studying both Sweden and Iceland allows us to estimate CFRs for smallpox in both its endemic (Sweden) and epidemic (Iceland) states in populations with high-quality mortality data related to smallpox. These populations therefore provide reasonable estimates of what the CFR of smallpox could have been on the eve of vaccination.

[2] Vaccination was introduced to Sweden in October 1801 and in Iceland in March 1802 (Sköld 1996b, p. 253; Steffensen 1977 p. 55).

II. Endemic Smallpox: Sweden 1776-1800

Beginning with Sweden, Figure 3 presents the total annual deaths from smallpox in Sweden between 1776 and 1826 and shows clearly that vaccination drastically reduced mortality from smallpox in Sweden after 1801. Smallpox deaths were reported by age group nationally and by county and indicate that only about 5 per cent of smallpox victims were aged 10 years or more in Sweden in the period 1776-1800 (Figure 1). Since smallpox could be deadly for adults as well as children, the rarity of adult victims implies that almost all of adults had acquired immunity, i.e. almost all the Swedish population was exposed to smallpox in childhood. The apparent ubiquity of smallpox in Sweden poses a conundrum – could smallpox really have infected almost everyone *and* have killed 30 per cent of all those infected (Rutten 1997; 2011)?

Figure 3: Number of Deaths from Smallpox in Sweden from 1775 to 1825



Source: Sköld (1996a, p. 52).

IIa. Data and Methods

For understanding the population-level epidemiology of smallpox in Sweden, we draw on two main demographic sources. Pettersson (1913, p. 175) reports the number of deaths from

smallpox by age from 1776 to 1800. We convert these to age-specific mortality rates using the age-specific population counts from the Human Mortality Database (Human Mortality Database 2025). In addition, we use the period life tables for Sweden in the Human Mortality Database to understand the overall mortality from other causes (Human Mortality Database 2025). We combine the age-specific smallpox mortality rates and the period life tables to create period multiple decrement life tables. We use multiple decrement life tables to account for people who died of other causes before they could contract smallpox. We used standard methods to create the life table with one minor adjustment for smallpox. Since infants born to mothers who had already survived smallpox infection had some immunity from smallpox in the first five or six months of life, we assume that the average age at death (a_x) among infants contracting smallpox was 0.75 years (Davenport et al. 2016, p. 202).[3] The life table is presented in the supplementary materials (Appendix Table A1). These methods allow us to predict a cohort death rate from smallpox, i.e. the share of the whole synthetic cohort that died from smallpox.

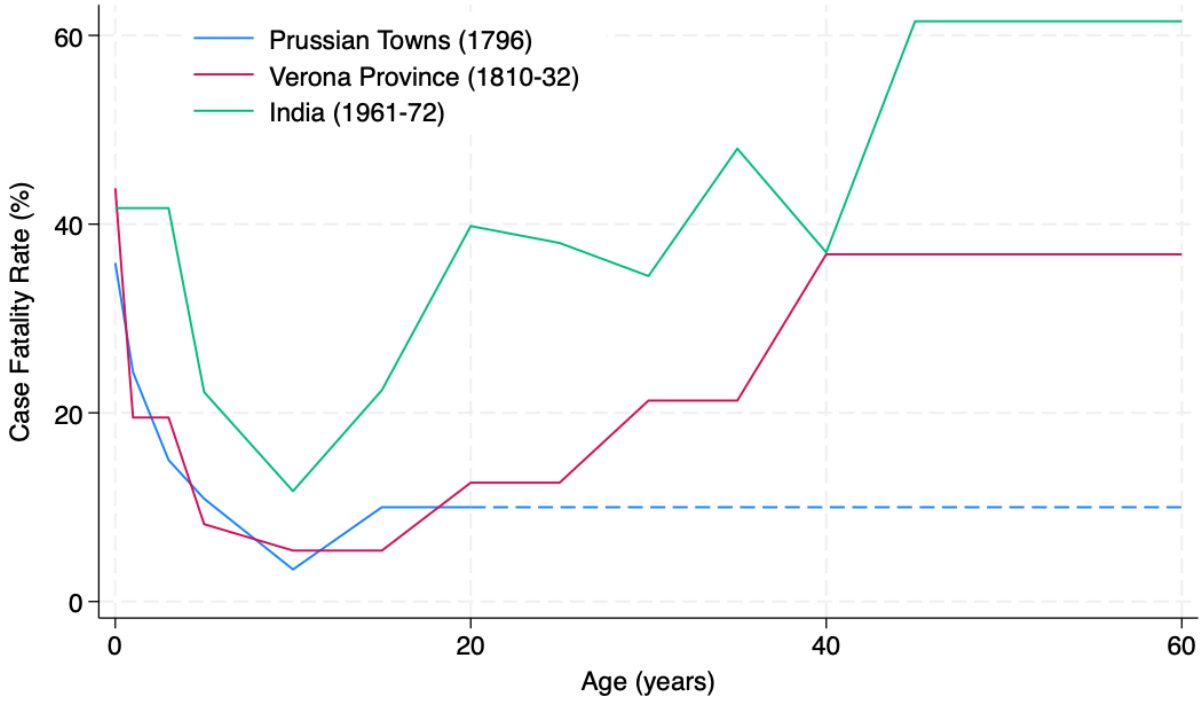
In addition to the mortality data from Sweden, we use estimates of age-specific CFRs of smallpox from three sources (Figure 4). The first, our preferred source, is derived from a smallpox epidemic in three Prussian towns in 1796 (Riley 2010, p. 452; Kübler 1901, p. 97). This estimate is particularly helpful because it provides data from before the start of vaccination. It also provides CFRs for single year age groups under the age of ten. In this outbreak there were no cases or deaths above the age of 20, which limits our understanding of the dynamics in adulthood. However, there were very few smallpox deaths above age 20 in eighteenth-century Sweden, so this does not influence our results. The second set of age-specific CFRs are drawn from unvaccinated individuals in the province of Verona between 1810 and 1832 (Rutten 1997, p. 52). Finally, to get a sense of the pattern from a reportedly highly lethal setting, we also use the CFRs reported by Rao (1972, p. 137) for India for the period 1961-72 in the run-up to smallpox eradication. The CFRs in India are higher at all ages but also show a somewhat different relative relationship between CFRs at different ages. Our results are robust to whichever of these series is used.

We combine our multiple decrement life tables with the historical age-specific CFRs from smallpox to estimate the share of susceptible individuals remaining alive at each age: Appendix Table A2 provides a worked example of these calculations for the Verona CFRs. We estimate the number of cases at each age by dividing the deaths by the CFR. Then we subtract the smallpox deaths from the cases to get the surviving immunes for each age group. We then subject the surviving immunes in an age group and immunes from previous

[3] Smallpox was a childhood disease in the second half of the 18th century in Sweden, and so we assume that all mothers were immune and conferred maternally-acquired immunity on their infants (Sköld 1996a, p. 87).

age groups to the non-smallpox death probabilities to model the build-up of immune individuals in the population. We subtract the immunes at each age from the total surviving at each age (l_x) to compute the number susceptible at each age. Dividing the susceptibles by the surviving total population at each age yields the share of individuals alive who are susceptible. This is a fairly straightforward application of Bournoulli's epidemiological model (Dietz and Heesterbeek 2002).

Figure 4: Smallpox Case Fatality Rates by Age



Notes: There were no cases above the age of 20 in the Prussian Towns, so the case fatality rate was held at 10% for those age groups (dashed line). There were so few adult smallpox deaths in eighteenth century Sweden that this does not influence our results.

Sources: Prussia - Kübler (1901, p. 97); Verona – Rutten (1997, p. 52); India – Rao (1972, p. 137).

In conducting this exercise, however, it became clear that the age-specific CFRs drawn from the Prussian towns, Verona and India were too high to explain the age patterns of smallpox deaths observed in Sweden. That is, the numbers of cases predicted by the CFRs formed a relatively small fraction of the cohort surviving at each age, leaving far too many uninfected, non-immune individuals surviving at older ages where we know that smallpox deaths were

very low. Therefore, we proportionally adjusted the age-specific CFRs for each series upward and downward to understand how changing the overall CFR would affect the age distribution of susceptibles in the synthetic cohorts. Overall CFRs were varied at one percentage point intervals from 4% to 35%. We excluded models that predicted greater than 100% incidence of smallpox in the synthetic cohort.

IIb. Results

The multiple decrement life period for the period 1776 to 1800 (Appendix Table A1) shows that the lifetime risk of dying from smallpox was 6.9% in the synthetic cohort, close to the 8.3 % of all deaths recorded in the actual population in this period (Sköld 1996a, pp. 549-50).

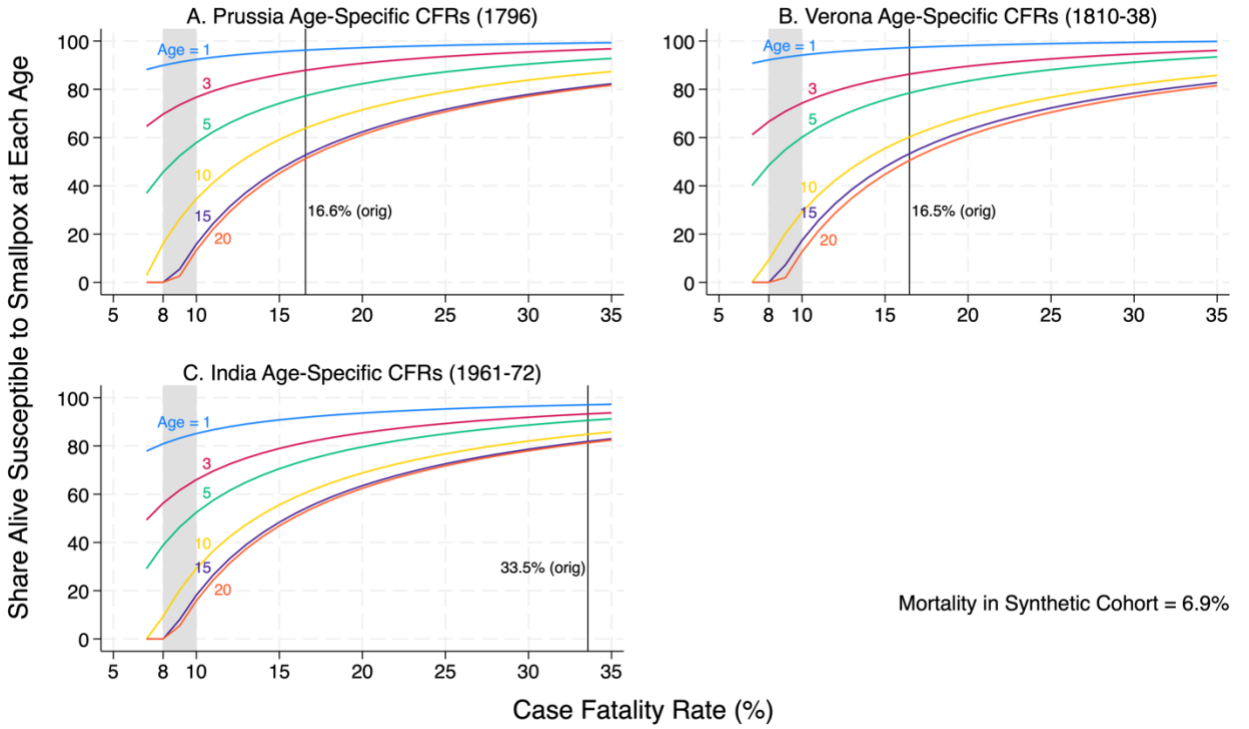
Figure 5 below shows the results from varying the overall case fatality rate assuming that the Swedish smallpox mortality rates are correct and the pattern of age-specific CFRs come from any of the three known patterns. These graphs display how changing the case fatality rate alters what proportion of people are susceptible to smallpox at different ages. For instance, Figure 5A shows the results with the Prussian age-pattern of CFRs. Assuming a case fatality rate of 8% implies that 89.9% of individuals surviving to age 1 were still susceptible to smallpox. The percentage surviving that were susceptible to smallpox for individuals surviving to ages 3, 5, 10, and 15 was 69.7%, 45.7%, 16.1%, and 0% respectively. Thus, if the case fatality rate of smallpox were 8%, there should not be any smallpox deaths or cases for individuals over the age of 15. On the other hand, if we assume a case fatality rate of smallpox of 30%, the share of the synthetic cohort susceptible at ages, 1, 3, 5, 10 and 15 would be 98.9%, 95.5%, 90.5%, 83.8% and 77.9% respectively. With such a high share of the cohort still susceptible to smallpox at age 15, one would expect to see considerable numbers of smallpox cases and deaths above age 15. These age patterns change somewhat when assuming different age-patterns of CFRs (Figures 5B and 5C). However, the overall picture is largely the same.

Starting with the claim that case fatality rates of *Variola major* were 25-30%, we can see that it is not possible that the Swedish population had such high case fatality rates as is commonly assumed. With case fatality rates above 25%, more than 70% of 20-year-olds would have been susceptible to smallpox. This is implausible given that there were so few deaths from smallpox above the age of 20: the synthetic cohort experienced only 62 smallpox deaths above the age of 20, out of 6,911 total smallpox deaths in an initial population of 100,000. Thus, assuming that the smallpox mortality figures are correct, we

can rule out CFRs in the range 25 – 30 % at the population level in eighteenth-century Sweden.

We can also see that the overall CFRs predicted from applying the unadjusted age-specific CFRs from Prussia and Verona are also implausible. These are the vertical lines in Figure 5 labelled '(orig)', and they imply that half of 20-year-olds would still be susceptible to smallpox. The extremely high overall CFR from the unadjusted India CFRs would imply that 81.3% of 20-year-olds were susceptible to smallpox.

Figure 5: Age Pattern of Susceptibles for Varying Overall Case Fatality Rates using Different Patterns of Age-Specific Case Fatality Rates



Notes: Shaded grey area denotes the CFR range of 8% to 10% that is most consistent with the age pattern of smallpox deaths reported in Figure 1.

Source: Pettersson (1913, p. 175) and Human Mortality Database (2025). See Figure 4 for sources of CFRs.

Instead, case fatality rates of 8-10%, the grey shaded areas in the graphs of Figure 5, seem to be the most realistic. These lead to shares of susceptibles at age 15 which are compatible with smallpox cases at these ages being low, and shares of susceptibles at age 20 that suggest smallpox cases above 20 should be extremely rare. This requires reducing the age-

specific CFRs from the Prussian towns and province of Verona by approximately 40% and those from India by approximately 70%.

III. Epidemic Smallpox: Iceland 1707-9

If case fatality rates of 8-10% were typical of smallpox where it was endemic, very different CFRs may have prevailed where the disease was not endemic and a wide range of age groups in the population were susceptible when the epidemic struck.[4] The best documented epidemic of this nature before the vaccination era was the 1707-9 smallpox epidemic in Iceland (Hays 2005, pp. 131-33; McNeil 2023, p. 154-55). Iceland's population was not large enough to sustain endemic smallpox infection in the sixteenth and seventeenth centuries: when smallpox was introduced to the island, it quickly burned through the susceptible population leaving too few susceptible individuals to sustain continuing infections. This meant that the island was subject to smallpox epidemics every 15 to 30 years when smallpox was re-introduced from the outside. The 1707 smallpox epidemic in Iceland began in June 1707 when the clothes of a smallpox victim who had died at sea returning from Denmark were returned to his family in Iceland. Over the next two years, the epidemic killed an estimated 26.4% of the population. The epidemic was well-documented because the Danish government had sent a delegation to report on the state of the economy of Iceland after a series of famines in the 1690s. For this reason, they produced a census of the population in 1703 and kept track of smallpox deaths in many areas of the country during the epidemic. Steffensen (1977) collated this evidence, estimating the 26.4% total mortality rate. He also found interesting age patterns of mortality in the data. While it was not possible to analyse narrow age groups, he found clear evidence that the mortality rates were substantially lower for individuals old enough to have been exposed to the previous two smallpox epidemics in 1670-72 and 1655-58, i.e. individuals over age 35 in 1707.

Given that we have a good estimate of the overall death toll from the epidemic, we can use the reported age structure of the Icelandic population from the 1703 census (Tomasson 1977) and assumptions about the susceptible population at different ages and the share of the population infected to create plausible ranges of case fatality rates in this epidemic. We create a lower and upper bound estimate of the population susceptible to smallpox. In both

[4] Note that we deliberately avoid using the term 'virgin-soil epidemics' because this term is controversial (Jones 2002) and tends to be used to discuss theorised innate immunological deficiencies of populations isolated from Old World diseases for millennia, i.e. indigenous Americans and Pacific Islanders (Crosby 1976; Diamond 1997). However, this does not apply to Iceland, which was settled by Europeans in the ninth century and was connected to Europe through trade and immigration throughout its history. The Icelandic population suffered 20 smallpox epidemics between 1240 and 1800, which makes it hard to argue that it was 'virgin soil' for smallpox in any meaningful sense (Steffensen 1977).

scenarios, we assume that the full population under the age of 35 was susceptible to smallpox since they were not alive during one of the previous epidemics. We also assume that all people without a reported age in the census were susceptible (0.7% of the total population). For the lower bound of the susceptible population, we assume that 20% of 35–49-year-olds were still susceptible but 0% of the population over the age of 50 were susceptible since they had been exposed to two smallpox epidemics. For the upper bound estimate, we assume that 40% of the 35–45-year-olds were still susceptible and 20% of the 50+ population were still susceptible. The upper bound estimate accounts for the age-pattern of susceptibility based on the timing of prior epidemics but also accounts for the fact that prior epidemics likely did not strike the entire island or affect all individuals, leaving some in older age groups susceptible (Steffensen 1977, p. 54). We also make different assumptions about the share of susceptibles infected to estimate the number of cases for the case fatality rate. We assume either that 75% or 90% of the susceptible population contracted smallpox. The full calculations are presented in Appendix Table A3.

Table 1 presents the results and shows that the estimated case fatality rates for the 1707-9 Iceland smallpox epidemic vary from 39.7% in the case of 90% incidence and the upper bound estimate of the population susceptible to 53.2% if assuming 75% incidence and the lower bound estimate of the population susceptible. Obviously, these rates are far higher than the 8%-10% found for endemic smallpox in Sweden.

Table 1: Estimates of the case fatality rate of smallpox in the 1707-9 Iceland smallpox epidemic

Incidence	Lower Bound Susceptibility	Upper Bound Susceptibility
90%	44.3%	39.7%
75%	53.2%	47.7%

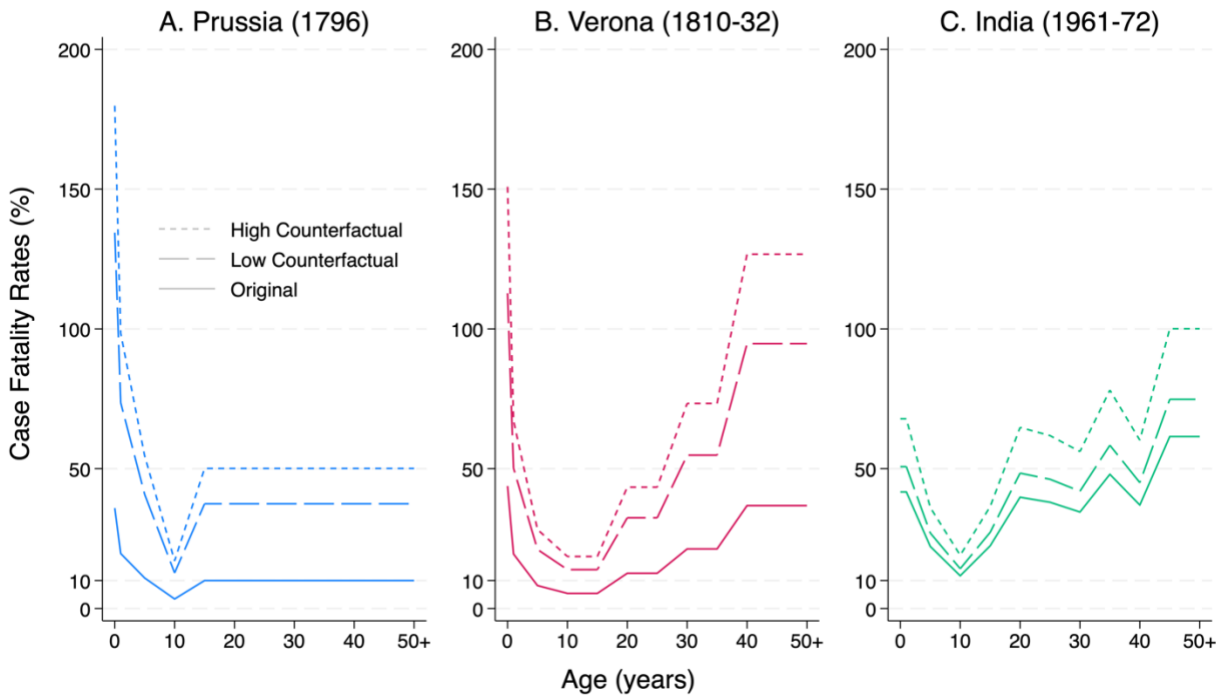
Notes: See Appendix Table A3 for full calculations.

Source: Steffensen (1977); Tomasson (1977, p. 419).

In fact, these rates are so high that it is impossible that the age-specific pattern of case fatality rates found in Prussia or Verona could have held. Figure 6 shows the counterfactual age-specific CFRs necessary to predict the highest CFR (53.2%) and lowest CFR (39.7%) in Table 1. For the pattern of CFRs reported from both Prussia and Verona, the counterfactual CFR for infants is greater than 100%, and the counterfactual CFRs at older ages also

approach or exceed 100% using the Verona or India CFRs. Thus, it is also likely that during smallpox epidemics where a wide range of ages were affected, the age pattern of CFRs became flatter.

Figure 6: Counterfactual Age-Specific CFRs Necessary to Replicate the Estimated Iceland CFRs



Notes: High counterfactual refers to the Iceland CFR with 75% incidence and the lower bound figure on the population susceptible, a CFR of 53.2%. The low counterfactual refers to the Iceland CFR with 90% incidence and the upper bound figure on the population susceptible, a CFR of 39.7%. Note that the inflation for the India CFRs is smaller because the original age-specific CFRs are higher in the India case.

Source: See Figure 2 for CFR sources.

IV. Discussion

Our two eighteenth-century case studies yield very different estimates of the smallpox CFR. Where smallpox was endemic in Sweden, we estimate that the CFR was between 8% and 10%. These rates are lower than other estimates of smallpox CFRs in low vaccination rate populations in the eighteenth century and in the nineteenth century (Figure 2), but it is worth noting that these are still high CFRs relative to other human pathogens. This finding confirms

earlier work by Rutten (1997; 2011) which showed that there is a fundamental incompatibility between endemic smallpox being highly lethal with case fatality rates of 25-30% and smallpox having high incidence rates that would ensure that nearly all of the surviving population was immune by adulthood. We build on Rutten's theoretical work by placing bounds on the CFR using population-level data in our two historical contexts. On the other hand, where smallpox was epidemic and affected both children and adults as in Iceland in 1707-9, CFRs from 40% to 53% were plausible. What explains these differences in the CFR?

First, it is important to consider whether these differences are due to data limitations. Starting with Sweden, Sköld, the leading expert on Swedish smallpox, suggests that the smallpox mortality rates are reliable. Deaths by cause were not reported for a few dioceses in a small number of years, but these were nearly all before 1776, the start of our period (Sköld 1996a, pp. 53-54). While smallpox and measles deaths were reported together until 1774 in Sweden, there is no reason to believe that these diseases were being substantially confused across the time periods analysed (Sköld 1996a, p. 50). Smallpox was a much-feared and lethal disease that recurred regularly all over Sweden. Its symptoms are easy to recognize and distinguish from other diseases (Fenner 1982). The main diagnostic confusion was with chickenpox, which was rarely lethal. Thus, it seems unlikely that smallpox deaths were severely under-registered, except possibly in infancy, where severe infection may have been lethal before the characteristic eruption of pustules. Note also that in order to produce an overall case fatality rate of 30% and an age-pattern of susceptibility that matches the age-pattern of deaths, the smallpox age-specific mortality rates would have to be three times larger. This scale of under-registration of smallpox deaths is extremely unlikely.

The Iceland data also seem broadly reliable. The 1703 census appears to have been complete, with negligible age heaping and plausible sex ratios(Tomasson 1977, p. 418), although there may have been an undercount of infants.[5] Records of smallpox deaths during the epidemic only cover 59% of the population of Iceland, but Steffensen (1977, pp. 49-50) argues that there is no reason to believe that conditions in the unobserved areas would be

[5] Adjusting for potential under-enumeration of infants does not substantially affect our results. The Icelandic population did not have a stable age structure in 1703 and there were smaller numbers of children aged under 10 and of reproductive-age adults (ages 25-39) than would be expected in a stable population. Given the near-completeness of reporting of exact age, sex and household status, variations in the size of age classes seems more likely to reflect historical fluctuations in fertility and age-specific mortality rates than selective under-enumeration. The 1690s were marked by a series of famines (Steffensen 1977, p. 46), which could have both depressed fertility and raised child mortality. If children were under-enumerated, this would push our CFR estimates downward, but the maximum downward bias would be 3 percentage points, which does not qualitatively alter our arguments about the CFR in Iceland.

different. He also cites a letter from a contemporary that estimated the death toll at 25%, very similar to the 26.4% death toll in observed regions.

Given that our results are not figments of the data, there are two possible explanations for the differences in the CFRs. First, it is possible that the strain of smallpox that affected Iceland in 1707-9 was more virulent than the one that was endemic in Sweden half a century later. When smallpox next affected Iceland 32 years later in 1741-43, it was 'mild' without the dramatic death toll seen in 1707-9. Later epidemics in 1761-64 and 1785-87 were also not as deadly: smallpox deaths were again recorded in the 1785-87 epidemic, which only killed 3.4% of the population (Steffensen 1977, p. 55). Paleogenomic evidence is lacking for the eighteenth century, and while there is no evidence for rapid viral evolution in this period, it is possible that the 1707-9 smallpox strain was more virulent. However, there is no evidence that smallpox in 1706 in Copenhagen, which sparked the Icelandic epidemic, was particularly deadly (Johansen 2002, pp. 60-2). In addition, if such virulent strains of smallpox were circulating in Europe at the time, it seems likely that there would have been more records of epidemics of this scale.

A second explanation could be that epidemics where both adults and children were susceptible had higher CFRs. Part of this effect would be mechanical since CFRs were higher for older adults than for children and adolescents. There is also strong evidence that pregnant women suffered higher CFRs from smallpox and experienced stillbirths as a result of smallpox (Nishiura 2006; Schneider et al. 2024; Steffensen 1977, p. 47; Woods 2009, pp. 218–23). However, social and economic factors are likely to have mattered as well. While smallpox virulence does not appear to be exacerbated by poor nutritional status (Riley 2010, p. 466), parents infected with smallpox would not have been able to do even the bare minimum of caring for their children such as fetching water and cooking food. Contemporary accounts of the period provide vivid evidence of the disruptive effects of the epidemic on caring roles and on economic activities:

> At that time [1707], so many people were infected with smallpox in Snæfellssýsla that the healthy could not tend to the sick, and I am certain that many died due to a lack of care, who might otherwise have lived. (Þorsteinsson et al. 1922, p. 715)
>
> This illness spread so swiftly in Árnessþing that livestock could not be milked in several places, and so both cows and sheep wandered the pastures bawling and bleating, and their milk dried up, but the farms were deserted.' (Þorsteinsson et al. 1922, p. 708)

These social factors could have led to smallpox deaths among cases that would have survived when a smaller share of the population was infected and when parents could care for their children, i.e. the conditions where smallpox was endemic. This may also explain the

likely flattening of the age-gradient in smallpox CFRs in the 1707-9 epidemic. Interestingly, Steffensen (1977, p. 49) shows that in addition to the smallpox deaths in 1707, 10.8% of the population of Iceland appears to have died from causes other than smallpox, again emphasising the breakdown of social and economic processes that could have ameliorated the disease. Thus, the breakdown of caring may have as much to do with the high CFRs in 1707-9 as the virulence of the smallpox strain itself.[6]

V. Conclusion

So what is the case fatality rate of smallpox? This paper shows that social factors may be just as important as the intrinsic and age-specific virulence of smallpox in determining smallpox CFRs in particular contexts. How historians and epidemiologists describe the CFR should therefore reflect those contexts. Where smallpox was endemic before vaccination, it is unlikely that the CFR was greater than 10%. In fact, it was probably far lower in populations that actively practiced deliberate smallpox infection via inoculation such as eighteenth-century Massachusetts and Southern England (Blake 1959, p. 245; Davenport et al. 2018).[7] After vaccination, CFRs among the unvaccinated became a reflection of both the virulence of smallpox and the selection of those who remained unvaccinated. In contexts where the unvaccinated were likely to face higher viral loads or suffer from lack of care during their illness, CFRs would be higher. Still, given the evidence from Sweden, it is hard to believe that *average* CFRs after vaccination were as high as 30%. Finally, when smallpox epidemics struck populations where both adults and children were susceptible, extremely high CFRs of 40% to 50% were possible. The social disruption, particularly to water collection, food preparation and nursing care caused by the epidemic magnified the virulence of smallpox. This explains the extreme death tolls observed in Iceland in 1707-9 but is also relevant to the extremely high mortality of indigenous Americans following the Columbian Exchange (Livi-Bacci and Maeder 2004, p. 210). The death toll in Iceland suggests that theories of indigenous Americans having innately weak immunity from lack of exposure to Old World diseases, the virgin soils hypothesis, are not necessary to explain mass mortality there (Crosby 1976; Diamond 1997; Jones 2002). The mass mortality observed in Iceland occurred in a European-descended population that experienced regular smallpox epidemics during its history.

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[6] The importance of the age pattern of susceptibles is also highlighted by the relatively mild smallpox epidemic of 1670-72 in Iceland, which came only twelve years after the previous epidemic of 1655-58 (Steffensen 1977, p. 45).

[7] Blake (1959, p. 245) shows that the total CFR for smallpox, including both natural and inoculated smallpox cases and deaths, declined from 14.3% in 1721 to 3.0% in 1792. Between the two epidemics the share of smallpox cases that were initiated by inoculation rose from 2.2% to 97.2%.

This paper highlights the need to move away from rigid understandings of the CFR of *Variola major*, i.e. the 20-30% consensus, and consider context more carefully. Realistically, for endemic smallpox, average CFRs of 8% to 10% are most plausible given the population-level evidence, at least before the twentieth century. It is possible that CFRs showed a greater range in the twentieth century with the genetic diversification of *Variola major* strains. However, claims for very high average CFRs remain subject to the caveats outlined in this paper: under-reporting of cases, positive selection into vaccination and selection of severe cases into hospital samples all likely bias CFRs upward. In terms of individual risk, CFRs could vary widely depending on age, health status and the context of the smallpox outbreak.

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Web Appendix: What is the case fatality rate of smallpox?

Table A1: Multiple Decrement Period Life Table for Smallpox and non-Smallpox Deaths in Sweden, 1776-1800

x	n	${}_nM_x$(s)	a_x	${}_nq_x$(s)	${}_nq_x$(ns)	${}_nq_x$(all)	l_x	${}_nd_x$(s)	${}_nd_x$(ns)	${}_nd_x$(all)
0	1	0.02066	0.75000	0.02055	0.17627	0.19682	100000	2055	17627	19682
1	2	0.01310	0.38175	0.02579	0.07334	0.09912	80318	2071	5890	7961
3	2	0.00908	0.38175	0.01795	0.03326	0.05121	72356	1299	2406	3706
5	5	0.00317	0.37938	0.01569	0.04319	0.05887	68651	1077	2965	4042
10	5	0.00077	0.50426	0.00385	0.02706	0.03091	64609	249	1748	1997
15	5	0.00031	0.50141	0.00155	0.03001	0.03156	62612	97	1879	1976
20	5	0.00013	0.52100	0.00063	0.03873	0.03936	60636	38	2349	2387
25	5	0.00004	0.50298	0.00020	0.04641	0.04661	58249	12	2703	2715
30	5	0.00002	0.50895	0.00009	0.05388	0.05397	55534	5	2992	2997
35	5	0.00001	0.49998	0.00005	0.05660	0.05665	52537	3	2973	2976
40	5	0.00000	0.51817	0.00002	0.07232	0.07234	49561	1	3584	3585
45	5	0.00000	0.49636	0.00001	0.08026	0.08027	45976	1	3690	3691
50	5	0.00000	0.51787	0.00001	0.09975	0.09976	42285	0	4218	4218
55	5	0.00000	0.50788	0.00002	0.12355	0.12357	38067	1	4703	4704
60	+	0.00001	0.52680	0.00005	0.99995	1.00000	33363	2	33361	33363

Notes: Life table functions with "(s)" afterward refer to functions related to smallpox, i.e. ${}_nq_x$(s) is the probability of dying of smallpox between exact age x and $x+n$. Functions with "(ns)" afterward refer to functions related to non-smallpox mortality. All is the combination of the two. We computed the all-cause age-specific death probabilities (${}_nq_x$(all)) by creating the abridged q_x values to match the age groups of smallpox deaths reported by Pettersson using the annual Swedish complete period life tables in the Human Mortality Database. We then took a weighted average of the q_x and a_x values by age group for the annual period life tables from 1776 to 1800 weighting by the population in each age group in each year. The a_x for smallpox at exact age 0 is set to 0.75 because mothers who have survived smallpox pass on immunity to their children in the first six months of life (Davenport et al. 2016, p. 202).

Sources: Pettersson (1913, p. 175) provides counts of smallpox deaths by age from 1776 to 1800; and the Human Mortality Database (2025) provided population by age for the same period to compute the age-specific mortality rates from smallpox (${}_nM_x$(s)) and all-cause age-specific death probabilities (${}_nq_x$(all)).

Table A2: Worked example of computing the percentage of the population susceptible to smallpox at each age

						1	2	3	4	5	6	7
x	n	Verona CFR	${}_nd_x$(s)	${}_nq_x$(ns)	l_x	Cases	Cases Surviving Smallpox	Non-Smallpox Deaths of Surviving Cases	Surviving Immunes	Non-Smallpox Deaths of Immunes	Susceptibles Alive	% Alive Susceptible at Age X
0	1	0.438	2055	0.17627	100000	4692	2637	465	0	0	100000	100.0
1	2	0.195	2071	0.07334	80318	10622	8551	627	2172	159	78145	97.3
3	2	0.195	1299	0.03326	72356	6662	5363	178	9937	330	62419	86.3
5	5	0.082	1077	0.04319	68651	13133	12056	521	14791	639	53859	78.5
10	5	0.054	249	0.02706	64609	4609	4360	118	25688	695	38922	60.2
15	5	0.054	97	0.03001	62612	1801	1704	51	29234	877	33378	53.3
20	5	0.126	38	0.03873	60636	303	265	10	30010	1162	30626	50.5
25	5	0.126	12	0.04641	58249	94	83	4	29102	1351	29148	50.0
30	5	0.213	5	0.05388	55534	23	18	1	27830	1500	27704	49.9
35	5	0.213	3	0.05660	52537	12	10	1	26347	1491	26189	49.8
40	5	0.368	1	0.07232	49561	3	2	0	24865	1798	24695	49.8
45	5	0.368	1	0.08026	45976	2	1	0	23069	1852	22907	49.8
50	5	0.368	0	0.09975	42285	1	1	0	21218	2117	21067	49.8
55	5	0.368	1	0.12355	38067	2	1	0	19102	2360	18964	49.8
60	+	0.368	2	0.99995	33363	5	3	3	16743	16743	16620	49.8

Notes: The computations in this table are based on the life table functions ${}_nd_x$(s), ${}_nq_x$(ns) and l_x from the multiple decrement life table for Sweden presented in Table A1, re-reported here for ease. Here we assume that the age-specific CFRs in Verona were correct, an overall CFR of 16.5%. To produce age patterns of susceptibles for different overall CFRs, we adjust the age-specific CFRS proportionally upward and downward. We compute the share of the population susceptible at each using the following steps: Column 1 is ${}_nd_x$(s) divided by the Verona CFR. Column 2 is Column 1 minus ${}_nd_x$(s). Column 3 is Column 2 multiplied by ${}_nq_x$(ns). Column 4 is zero at age 0 because no children have been exposed to smallpox. Afterward, Column 4 is Column 2 minus Column 3 plus Column 4 minus Column 5 for the previous age group. Column 5 is Column 4 multiplied by ${}_nq_x$(ns). Column 6 is l_x minus Column 4 for the previous age group. Column 7 is Column 6 divided by l_x multiplied by 100 to produce a percentage. Note that numbers have been rounded to the nearest whole unit in the table, but they have not been rounded in the computations.

Table A3: Estimation of Ranges of CFRs for Iceland Smallpox Epidemic of 1707-9

x	n	Population 1703	Susceptible Share Low	Susceptible Share High	Pop Susc. Low	Pop Susc. High
0	1	433	1	1	433	433
1	4	3295	1	1	3295	3295
5	5	4611	1	1	4611	4611
10	5	5101	1	1	5101	5101
15	5	5372	1	1	5372	5372
20	5	4839	1	1	4839	4839
25	5	3485	1	1	3485	3485
30	5	3728	1	1	3728	3728
35	5	3692	0.2	0.4	738	1477
40	5	3910	0.2	0.4	782	1564
45	5	3037	0.2	0.4	607	1215
50	5	2702	0	0.2	0	540
55	5	2075	0	0.2	0	415
60	5	1365	0	0.2	0	273
65	5	845	0	0.2	0	169
70	5	665	0	0.2	0	133
75	5	397	0	0.2	0	79
80	5	274	0	0.2	0	55
85	5	123	0	0.2	0	25
90	5	36	0	0.2	0	7
95	5	16	0	0.2	0	3
not reported		357	1	1	357	357

Total Population	50,358	Population Susceptible	33,349	37,176
Death Rate	0.264	High Incidence (90%)	44.3%	39.7%
Total Deaths	13,295	Low Incidence (75%)	53.2%	47.7%

Notes: See explanation in text. The range of CFRs are in the bottom right corner shaded in grey. The CFRs vary based on assumptions about lower and upper bound levels of the population at risk and lower and upper bounds on the incidence, the share of susceptibles that contract smallpox.

Sources: Age breakdown of the 1703 population from the 1703 census (Tomasson 1977, p. 419). Assumptions about the share of individuals susceptible and the death rate of 26.4% from Steffensen (1977).

Table A4: Smallpox case fatality rates in eighteenth and nineteenth century European and American populations.

Population	*Period*	*CFR (unvaccinated)*	*CFR (vaccinated)*	*Source*
Eighteenth century (pre-vaccination				
Boston, USA	1721	14.6		Blake 1959, p. 244
Halifax, UK	1721-22	15.9	-	Razzell 2003, p. 172
Leeds, UK	1721-22	23.8	-	Razzell 2003, p. 172
Rochdale, UK	1721-22	21.4	-	Razzell 2003, p. 172
Ashton under Lyme, UK	1722	20.0	-	Razzell 2003, p. 172
Barstand, Ripponden, Scorby, Halifax rural, UK	1722	16.5	-	Razzell 2003, p. 173
Bradford, UK	1722	27.9	-	Razzell 2003, p. 172
Chichester, UK	1722	16.9	-	Razzell 2003, p. 173
Halifax, UK	1722	15.4	-	Razzell 2003, p. 172
Hatherfield, UK	1722	11.0	-	Razzell 2003, p. 173
Haverfordwest, UK	1722	22.9	-	Razzell 2003, p. 173
Macclesfield, UK	1722	12.2	-	Razzell 2003, p. 172
Stockport, UK	1722	25.4	-	Razzell 2003, p. 173
Wakefield, UK	1722	13.6	-	Razzell 2003, p. 172
Bedford, UK	1723	18.4	-	Razzell 2003, p. 173
Bolton, UK	1723	21.6	-	Razzell 2003, p. 173
Havant, UK	1723	23.1	-	Razzell 2003, p. 172
Romsey, Hertfordshire UK	1723	15.6	-	Razzell 2003, p. 173
Salisbury, UK	1723	13.2	-	Razzell 2003, p. 173
Ware, UK	1723	11.7	-	Razzell 2003, p. 173
Aynho, UK	1723-24	18.8	-	Razzell 2003, p. 173
Bolton-le Moor, UK	1724	18.8	-	Razzell 2003, p. 173
Cobham, UK	1724	19.0	-	Razzell 2003, p. 173
Dedham, Essex, UK	1724	31.3	-	Razzell 2003, p. 173
Plymouth, UK	1724	17.2	-	Razzell 2003, p. 173
Shaftesbury, UK	1724	15.1	-	Razzell 2003, p. 173
Stratford on Avon	1724	15.8	-	Razzell 2003, p. 173
Deal, UK	1725-26	9.1	-	Razzell 2003, p. 173
Dover, UK	1725-26	12.1	-	Razzell 2003, p. 172
Kempsey, UK	1726	20.5	-	Razzell 2003, p. 174
Uxbridge, UK	1727	36.4	-	Razzell 2003, p. 174
Boston, USA	1730	13.9	-	Blake 1959, p. 244
Northampton, UK	1740	14.5	-	Razzell 2003, p. 177
Northampton, UK	1747	15.5	-	Razzell 2003, p. 177
Boston, USA	1752	9.7	-	Blake 1959, p. 244
Chelmsford, UK	1753	33.0	-	Razzell 2003, p. 177
Salisbury, UK	1753	13.0	-	Razzell 2003, p. 177
Boston, USA	1764	17.7	-	Blake 1959, p. 244
Chester, UK	1774	14.5	-	Razzell 2003, p. 177
Boston, USA	1776	9.5	-	Blake 1959, p. 244
Leeds, UK	1781	28.0	-	Razzell 2003, p. 177
Huddersfield, UK	1783	22.5	-	Razzell 2003, p. 177

Population	*Period*	*CFR (unvaccinated)*	*CFR (vaccinated)*	*Source*
Carnock, Fife, UK	1787	33.0	-	Brunton 1992, p. 407
Boston, USA	1788	32.8		Blake 1959, p. 244
Boston, USA	1792	29.7		Blake 1959, p. 244
Prussian towns	1796	15.6		Riley 2010, p. 451
Nineteenth century populations with low vaccination rates				
Verona, Italy	1810-38	11.5	5.6	Del Panta 1980, p. 70
France	1816-41	16.5	1.0	Royal Commission 1889, p. 74
Norwich, UK	1819	23.0	0.0	Royal Commission 1889, p. 73
Marseilles, France	1828	25.0	1.0	Royal Commission 1889, p. 74
Urk, Netherlands	1844-45	13.0	-	Rutten 2011, p.188
Dewsbury, UK	1893-94	25.1	2.6	Royal Commission 1896, Appendix VII, p. 8
Leicester, UK	1893-94	12.0	1.0	Royal Commission 1896, Appendix VII, p. 8
Gloucester, UK	1893-94	40.9	9.9	Royal Commission 1896, Appendix VII, p. 8
Lippowaner, Austro-Hungary	1898	13.5	-	Rutten 2011, p.188
Nineteenth century populations with high vaccination rates				
Canton Vaud, Switzerland	1825-29	24.0	2.0	Royal Commission 1889, p. 74
Darkehmen, Prussia	1825-29	18.5	0	Royal Commission 1889, p. 74
Milan, Italy	1830-43	36.1	9.4	Del Panta 1980, p. 71
Wirtemberg	1831-35	27.5	7.1	Royal Commission 1889, p. 74
Corinthia, Greece		14.5	0.5	Royal Commission 1889, p. 74
Carmola, Genoa	1834-35	16.5	4.8	Royal Commission 1889, p. 74
Adriatic	1835	15.2	2.8	Royal Commission 1889, p. 74
Lower Austria	1835	25.8	11.3	Royal Commission 1889, p. 74
Dalmatia	1836	19.5	8.3	Royal Commission 1889, p. 74
Galicia, Spain	1836	23.5	5.8	Royal Commission 1889, p. 74
Kiel, German Confederation	1852-53	32	6	Royal Commission 1889, p. 74
Chemnitz, German Confederation	1870-71	9.2	0.7	Edwardes 1902, p. 99
Leipsig district, German Confederation	1870-72	36.4	8.8	Edwardes 1902, p. 101
Sheffield	1887-88	49.6	4.8	Edwardes 1902, pp. 117-8
London	1892-93	35.9	1.4	Edwardes 1902, p. 105
London	1892-93	50.0	2.3	Edwardes 1902, p. 105

Population	*Period*	*CFR (unvaccinated)*	*CFR (vaccinated)*	*Source*
Warrington	1892-93	35.3	6.4	Edwardes 1902, p. 105, 118, 123
Nineteenth century hospital samples				
Vienna hospital, Austria	1834	51.3	12.5	Royal Commission 1889, p. 74
London Smallpox Hospital	1836-56	33	7	Royal Commission 1889, p. 74
Vienna Hospital, Austria	1837-56	30	5	Royal Commission 1889, p. 74
Leipsig city hospitals, German Confederation	1870-72	71.2	7.7	Edwardes 1902, p. 102
London Smallpox Hospital	1870-86	32.1	8.7	Royal Commission 1891, p. 204
Homerton Hospital, London	1873-84	43.2	10.6	Royal Commission 1896, p. 59
London Hampstead Hospital	1876-78	47.0	9.1	Royal Commission 1891, p. 205
Fulham Hospital, London	1880-85	46.1	11.8	Royal Commission 1896, p. 59

Notes. 'CFR (vaccinated)' includes individuals identified as vaccinated by verbal report or by vaccination scar. 'CFR (unvaccinated)' refers to individuals identified as unvaccinated (or not inoculated in eighteenth century samples). Populations were classified as having low levels of vaccination if <70% were vaccinated, where stated, or if described as abjuring vaccination for religious reasons by contemporaries, or if they demonstrated unusually high ratios of unvaccinated to vaccinated cases. Populations were classified as having high levels of vaccination if 70% or more of the population was vaccinated, or where vaccination levels were unknown. Hospital samples were drawn from hospital registers.