MULTIGENERATIONAL EFFECTS OF SMALLPOX VACCINATION

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Summary

We explore the multigenerational effects of smallpox vaccination on mortality over two centuries. Unique individual level data of high quality from Sweden covering 1760 to 1960 allow us to investigate whether and how vaccination affected the first generation of vaccinated and whether these effects persisted to the second and third generation. We apply several methods of causal inference, such as the instrumental-variables and sibling fixed-effects methods, to high-quality longitudinal individual-level data for 49 parishes and find similar effects across methods. Our results show that smallpox vaccination improved survival of the first generation by 10.5 years, and that these effects, with a reduced magnitude, persisted to the second and third generation.

Purpose and research questions

This study investigates whether acquired immunity to smallpox and the rollout of smallpox vaccination in early life enable individuals to live longer, be wealthy as adults, and whether their consecutive generations were better off. We will be able to trace the effects of smallpox vaccination for at least three generations. Our two main research questions are to investigate:

(i) whether acquired immunity to smallpox and smallpox vaccination in early life determined survival of the individuals, their children and grandchildren throughout their life cycle, and to explore the dynamics of these effects.

(ii) through what mechanisms, biological and/or socio-economic, these effects evolve.

Contributions

Our paper contributes to three strands of literature. First, economic historians have suggested that either resistance (through better nutrition and wealth) or exposure to disease (through changes in pathogens or public health measures) might underlie the general mortality decline.[1] We contribute to this literature by showing that acquired immunity to smallpox and smallpox vaccination are the important determinants of longevity. Second, a rapidly growing literature in economic history and applied economics has recently shown that medical interventions in early life have large causal impacts on later-life health and earnings.[2] We study the long-term effects of a vaccination campaign that is an intervention with limited coverage in previous research. Finally, our knowledge on whether health shocks for one generation determine the outcomes of the next generation is extremely scarce.[3] This study is the first ever to trace the effects of the positive health shock over three generations.

Data and empirical strategy

Our data come from two individual-level register-based datasets that are homogenous in terms of data sources, data collection and structure, and cover all parts of Sweden.[4] The overlapping time-depth of the data is 1760–1960, and registration lasts until 2019 for southern Sweden, which allows us to analyze the effects through the life cycle, until death or outmigration, of three generations. Among the core variables, the data contain smallpox vaccination and infection status, demographic events and population at risk (death, cause of death in ICD-10, births, and marriages), and socio-economic status (HISCLASS). Our estimation sample includes individuals born in 1760–1850 and their offsrpings (around 65,000 individuals), out of which 45% were vaccinated against smallpox by the age of 2. To account for a high share of censored cases, we use survival models, in particular flexible parametric survival models that in addition are capable

to model the dynamic long-term effects efficiently.[5]

To build our empirical strategy, we rely on several features of the smallpox vaccination campaign in Sweden.

(1) Smallpox vaccination started in 1801, focused on small children, and it became compulsory to vaccinate children below age 2 in 1816. This feature makes this campaign a nearly perfect early-life experiment and allows us to focus on children below age 2 as the core treatment group, but also consider their older siblings and unvaccinated children as potential counterfactuals. Consistently, our data shows that the share of vaccinated below age 2 by cohort increases since 1799 reaching around 70% after 1814.

(2) From 1804, every parish had to appoint a vaccinator, commonly a church assistant. This feature allows us to use the number of vaccinators in each parish as the instrument for an individual-level smallpox vaccination status. We obtain the parish-by-year number of church assistants directly from the data due to the availability of information on occupation for the parish residents. To validate these series, we use parish vaccination reports 1802–1850 collected by the state health board, Collegium Medicum. We use a two-stage residual-inclusion method as that analogous to the instrumental-variables approach in the context of survival models.[6]

The equations to be estimated are the following:

(Second stage): $\ln[H(t/\mathbf{x})] = s\,[\ln(t)/\gamma_0, \mathbf{k}_0] + s\,[\ln(t)/\gamma_1, \mathbf{k}_1]$ vaccinated by age $2_i + \eta \text{residual}_i + \mathbf{x}_i\beta$,

(First stage): vaccinated by age $2_{ipt} = \alpha + \delta$n church assistants$_{pt} + \mathbf{x}_i\beta + v_i$

where **xi** denotes parish of birth, SES at birth, year of birth FEs, number of siblings, survival status of older siblings, maternal marital status, and sex.

(3) Fees for vaccination were very low or not charged at all, and vaccination was free for the poor. This feature of the campaign, supported with observations in our data, implies that any effects of smallpox vaccination are likely to be underestimated, due to the larger share of poorer individuals among the treated that likely have worse long-term outcomes. In the baseline models, in addition to year of birth fixed effects and demographic basics, we include parental socio-economic information. Consistently, we find that the broadening of the set of controls enlarges the estimates of smallpox vaccination.

Findings (preliminary)

Our results show that smallpox vaccination reduces mortality risk by remarkable 56%. It adds ~10.5 years in terms of a cohort expectation of life (from the age of 2 until the age of 100), and these effects are similar across models that control for observable and unobservable factors.[7] Cohort expectation of life is larger due to smallpox vaccination by 3.5 years of the second generation (currently followed until the age of 75), and by 0.9 years for the third generation (currently followed until the age of 40). Regarding the dynamics, consistently with the early-life theoretical predictions (i.e., critical periods), we find the beneficial effects in childhood and then appearing throughout adulthood and old age.

Regarding the mechanisms, we find that smallpox vaccination positively affected not only health but also socio-economic status, marriage and fertility of individuals. The dynamics of health effects for individuals infected with smallpox (“natural smallpox”) are similar to the effects of smallpox vaccination, although the latter are larger.This points to both inflammation and immunity biological mechanisms behind the early-life effects. We further perform a causal mediation analysis to estimate the extents to which the effects for children and grandchildren can be attributed to biological and socio-economic mechanisms.

[1] One of the recent reviews in Floud, Fogel, Harris, and Hong, 2011. *The Changing Body: Health, Nutrition, and Human Development in the Western World since 1700.* NBER Books. Cambridge: Cambridge University Press.
[2] One of the recent review in Almond, Currie, and Duque, 2018. Childhood Circumstances and Adult Outcomes: Act II, *Journal of Economic Literature*, 56(4): 1360–1446.
[3] To our knowledge, Cook, Fletcher and Forgues (2019) is the only study that shows in a causal framework that exposure to the 1918 influenza pandemic in early life influences the outcomes of the children and grandchildren of those affected ("Multigenerational Effects of Early-Life Health Shocks". *Demography*, 56: 1855–1874).
[4] Data for residents of 4 parishes in southern Sweden comes from the Scanian Economic Demographic Database (Dribe and Quaranta, 2020 (Lund University, CED) *Historical Life Course Studies*, 11(2)). Data for residents of 45 parishes in northern and central Sweden comes from the Demographic Data Base (Edvinsson and Engberg, 2020. (Umeå University, CEDAR) *Historical Life Course Studies*. 10(1)).
[5] Royston and Parmar, 2002. Flexible parametric proportional-hazards and proportional-odds models for censored survival data, with application to prognostic modelling and estimation of treatment effects, *Statistics in Medicine*, 2002 (21): 2175–2197.
[6] The method is discussed, in relation to survival models, in Terza, Basu, and Rathouz, 2008. Two-stage residual inclusion estimation: Addressing endogeneity in health econometric modelling. *Journal of Health Economics* 27, 531–543.
[7] Two-stage residual inclusion method uses the number of church assistants (conditional on covariates) as an instrument for the individual treatment status (F-stat = 2177.7, the estimate for δ is 0.030 (0.000) implying that one standard deviation change in the number of church assistants increases the share of vaccinated by 16.8 percentage points). The effects with sibling fixed effects, estimated with Cox proportional hazard models, are similar.