Multigenerational Effects of Smallpox Vaccination

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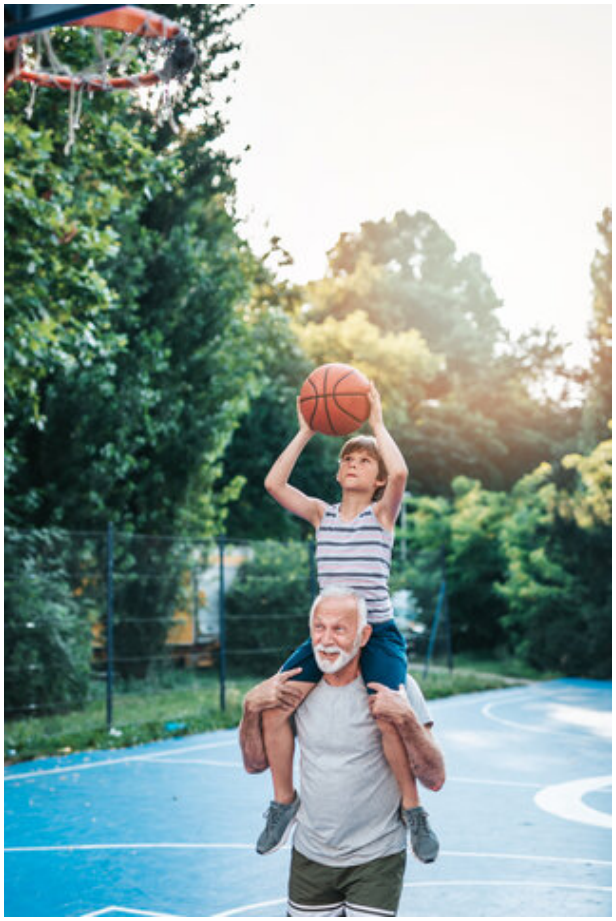
Motivation

1. Intergenerational health transmission is a significant barrier to overall socioeconomic mobility Björkegren et al. 2022, Halliday 2019.

2. Recent studies have shown that interventions can effectively reduce health persistence East et al. 2023, Mazumder et al. 2023.

3. Vaccination has the potential to benefit future generations due to *non-specific* vaccine effects Benn et al. 2023.



Our Contribution

- **How does childhood vaccination impact longevity and occupational status across three generations?**

- We explore **a smallpox vaccination campaign** in Sweden in 1801, applying an IV design with a shift-share formula as an instrument.

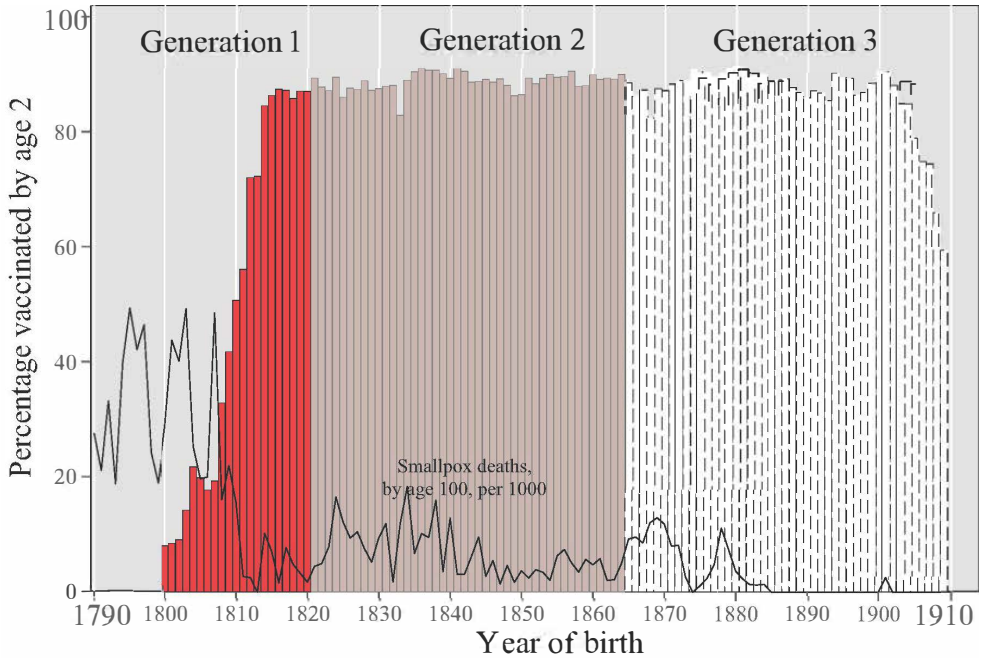
- **Results** indicate that the vaccine's positive effects persist through the third generation, driven equally by a higher likelihood of personal vaccination and epigenetic factors.

Smallpox Vaccination in Sweden

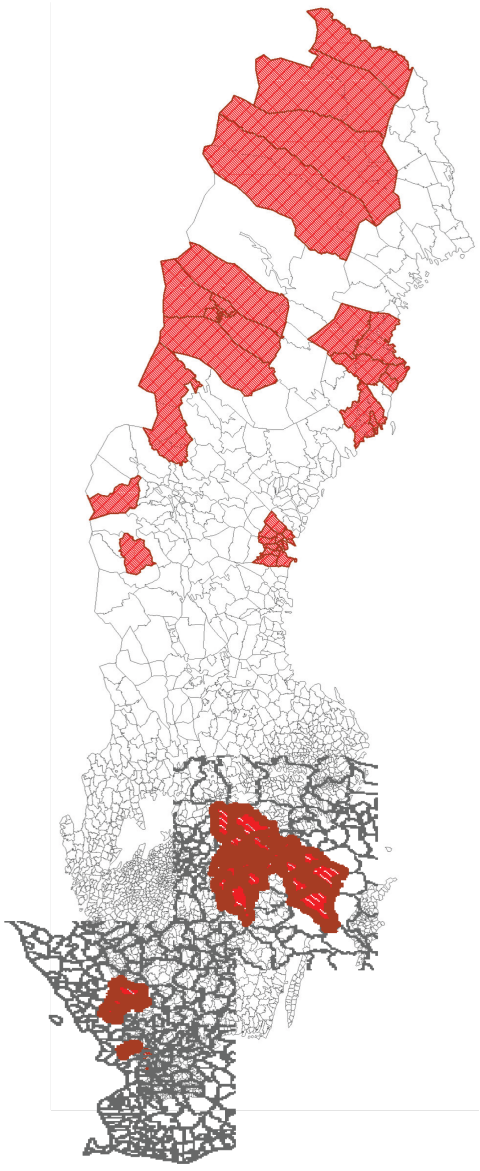
1. *Variola major* had a case fatality rate of 55% among children and caused lifelong complications (e.g., blindness and CNS problems).

2. **1801**: Free vaccination began across Sweden, targeting children under age 2.

3. **Church musicians and church assistants** who were not typically involved in public health duties administered the vaccinations.



Methodology and Data



1. Our sample includes $141,067$ individuals born in 1790-1910 across 70 parishes, followed until death, outmigration, or age 100 CEDAR 2022, SEDD 2021.

2. We use a shift-share IV approach Borusyak & Hull 2023, Borusyak et al. 2022.

   2SLS for Generation 1:

$$\mathtt{Vaccine_i} = \alpha \mathtt{C_{p(t-1)xC_{rt}}} + \eta_\mathtt{t} + \gamma_\mathtt{p} + \delta_\mathtt{rt} + \mathtt{X_{i(p)t}} + \epsilon_\mathtt{i}$$

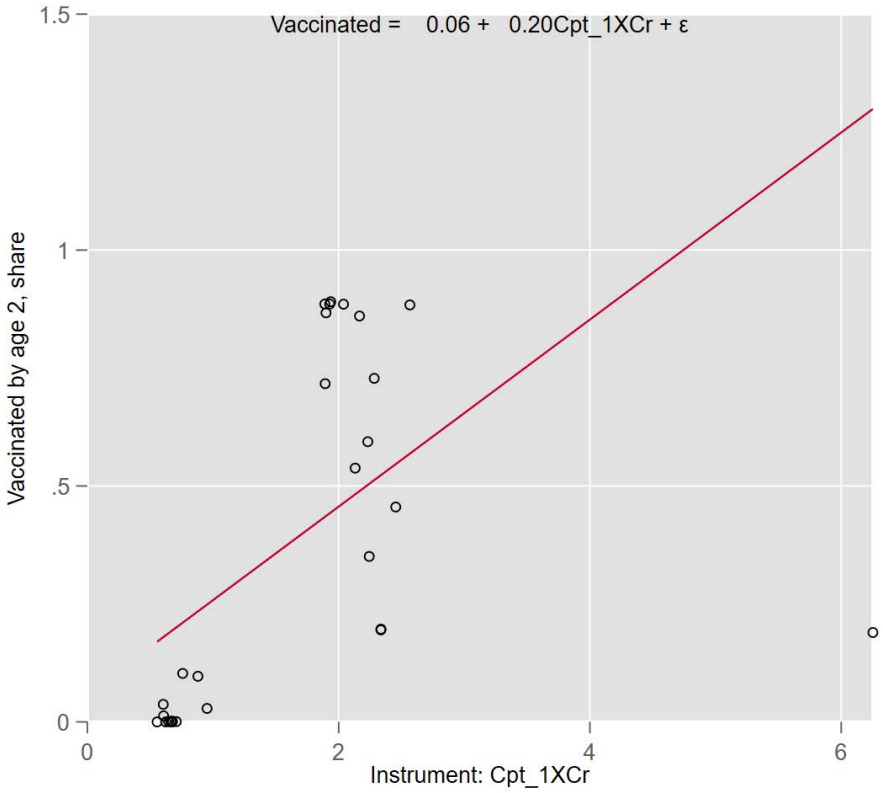
$$\mathtt{Y_i^{G1}} = \beta^{\mathtt{G1}} \widehat{\mathtt{Vaccine}}_\mathtt{i} + \eta_\mathtt{t} + \gamma_\mathtt{p} + \delta_\mathtt{rt} + \mathtt{X_{i(p)t}} + \nu_\mathtt{i}$$

   2SLS for Generations 2 and 3:

$$\mathtt{Y_{ji}^{G2(G3)}} = \beta^{\mathtt{G2(G3)}} \widehat{\mathtt{Parent(Grandparent)}} \mathtt{Vaccine_{ji}} + \eta_\mathtt{it} + \gamma_\mathtt{ip} + \delta_\mathtt{irt} + \mathtt{X_{i(p)t}} + \xi_\mathtt{ji}$$

   where $\mathtt{C_{p(t-1)xC_{rt}}}$ is a shift-share formula: $\mathtt{C}$ is the number (ratio) of church musicians/assistants.

First-stage estimates



	Vaccine
$C_{p(t-1)} \times C_{rt}$	0.129***
	(0.0224)
Kleibergen-Paap F-statistic	52.999
Anderson-Rubin F-statistic	3.290
Individuals	32,120
Parish of birth FEs	Yes
Year of birth FEs	Yes
Region of birth x Year of birth FEs	Yes
Families' Xs x Year of birth FEs	Yes
Parish of birth Xs x Year of birth FEs	Yes

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

Generation 1: OLS estimates

	Remaining years lived at age 2	Disability-free years lived at age 2	Occupational score, max after age 15
Vaccine	12.171***	11.766***	2.436***
	(1.911)	(2.232)	(0.201)
R sq	0.086	0.085	0.044
Individuals	32,120	30,930	22,823

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

Generation 1: 2SLS estimates

	Remaining years lived at age 2	Disability-free years lived at age 2	Occupational score, max after age 15
Vaccine	11.592**	11.999**	5.049**
	(4.144)	(4.374)	(2.191)
R sq	0.161	0.158	0.186
Individuals	32,120	30,930	22,823
Parish of birth FEs	Yes	Yes	Yes
Year of birth FEs	Yes	Yes	Yes
Region of birth x Year of birth FEs	Yes	Yes	Yes
Families' Xs x Year of birth FEs	Yes	Yes	Yes
Parish of birth Xs x Year of birth FEs	Yes	Yes	Yes

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

Generations 2 and 3: 2SLS estimates

	Remaining years lived at birth	Disability-free years lived at birth	Occupational score, max after age 20
ParentVaccine	2.204***	8.015***	1.099*
	(0.652)	(2.008)	(0.656)
R sq	0.069	0.045	0.178
Individuals	109,112	29,748	90,294
GrandparentVaccine	1.057**	4.262**	-0.715
	(0.497)	(1.886)	(0.445)
R sq	0.187	0.031	0.084
Individuals	116,544	40,324	70,920
Parish of birth FEs	Yes	Yes	Yes
Year of birth FEs	Yes	Yes	Yes
Region of birth x Year of birth FEs	Yes	Yes	Yes
Families' Xs x Year of birth FEs	Yes	Yes	Yes
Parish of birth Xs x Year of birth FEs	Yes	Yes	Yes

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

Mechanisms

1. **Generation 1**: Impacts arise from both specific and non-specific effects of the vaccine.

2. **Generations 2 and 3**: Using causal mediation analysis (Imai et al 2010), we find that personal vaccination in childhood and epigenetic changes each contribute equally to the observed effects.

Robustness analyses

1. Exclusion restriction and monotonicity assumptions are likely to hold.
2. No impact from overlapping interventions.
3. Mother fixed-effects estimates support the results.
4. Bounds tests on smallpox vaccination and placebo treatments shows that unmeasured covariates are unlikely to eliminate the vaccine effects.

Conclusions

1. Childhood smallpox vaccination significantly boosts longevity and occupational achievements, and these benefits are partially transmitted to the next two generations.

2. Both non-specific effects of the vaccine and the health behaviors it promotes in parents are important mechanisms.

Thank you!

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