Early life exposure to measles and later-life outcomes: Evidence from the introduction of a vaccine

Gerard J. van den Berg[1] Stephanie von Hinke[2] Nicolai Vitt[3]

[1]University of Groningen, University Medical Center Groningen, IFAU, IZA, ZEW, CEPR and CESIfo

[2]University of Bristol, Erasmus University Rotterdam, Institute for Fiscal Studies

[3]University of Bristol.

EEA Conference, August 2022

This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme, Grant agreement No. 851725.

Motivation

- Developmental origins of later life outcomes
- Main focus among childhood illnesses: severe disease such as tuberculosis (Bütikofer and Salvanes, 2020) and pneumonia (Bhalotra and Venkataramani, 2015)
  - Exception: recent research on long-term effects of measles vaccination in US & Mexico (Atwood, 2022; Atwood and Pearlman, 2022; Barteska et al., 2022; Chuard et al., 2022)
- Less severe illnesses may still divert resources away from child development and disrupt schooling
- Measles:
  - low fatality (during period of interest)
  - high prevalence
  - recent evidence of detrimental effects on immune system (Gadroen et al., 2018; Mina et al., 2019, 2015; Petrova et al., 2019)

Our paper in a nutshell

- **Research question:** What are the long-term human capital and health effects of the introduction of the measles vaccine in the UK?
  - Gene-environment interactions (GxE): Are there complementarities between public health investments in early life and genetic endowments?

- **Identification approaches:**
  - Nationwide introduction of the vaccine in 1968: treatment intensity captured by district-level infection rates prior to vaccination
  - Local vaccination trials in 1966: comparison of trial and control districts

- **Findings:**
  - No impact on educational attainment
  - Positive impact on adult height among those with high genetic predisposition

Literature

- **Developmental origins of later life human capital and health** - specifically in context of early-life exposure to infectious disease:
  - e.g. Almond (2006); Bütikofer and Salvanes (2020); Daysal et al. (2021); Kelly (2011); Mosca et al. (2022)
  - Measles:
    - Atwood (2022); Barteska et al. (2022); Chuard et al. (2022): show long-term effects on education, health and labour market outcomes in US
    - Atwood and Pearlman (2022): larger labour market effects in Mexico

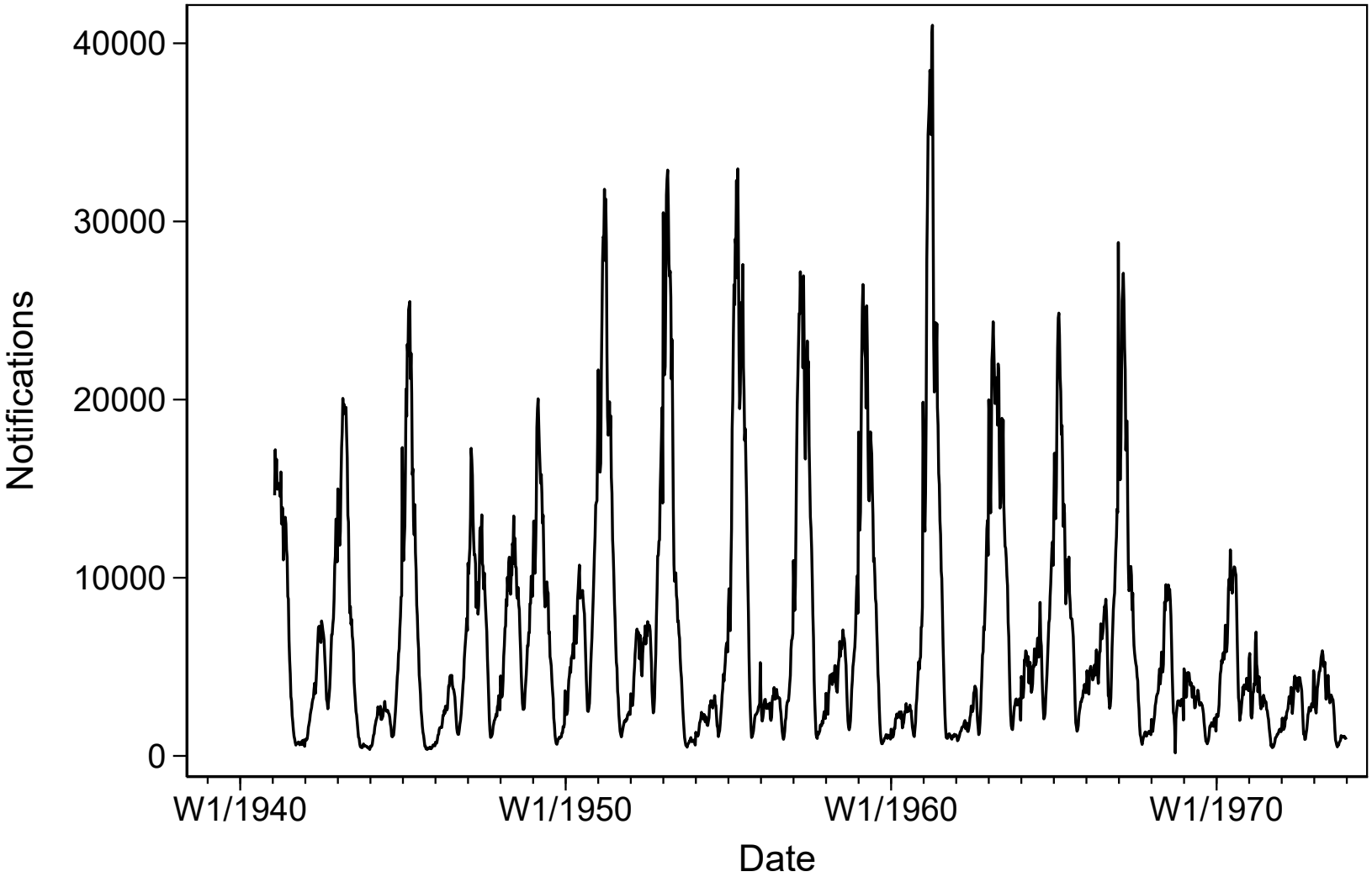
- **Gene-environment interplay** ($G \times E$) in shaping individuals' outcomes - accounting for endogeneity of E
  - e.g. Muslimova et al. (2020); Pereira et al. (2020); van den Berg et al. (2021)

- **Human capital formation** (e.g.: Becker and Tomes, 1986; Cunha and Heckman, 2007): complementarity between endowments and investments
  - Muslimova et al. (2020) explore the complementarity between genetic endowments and parental investments

Measles

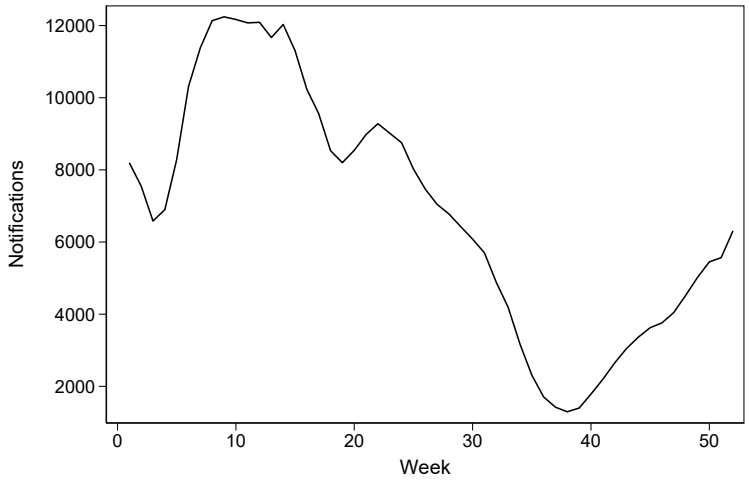
- highly-infectious viral illness
- spreads through water droplets in the air and direct contact
- symptoms:
  - initially: cold-like symptoms
  - later: red blotchy skin rash
- possible serious complications: infections of lung (pneumonia) and brain (encephalitis), severe diarrhoea
- low mortality rate in post-war UK
- age profile of measles in the UK (prior to the vaccine):
  - majority of cases occurred in children aged 1 to 6 years (General Register Office, 1973a; Woods, 2000)

Measles in the UK

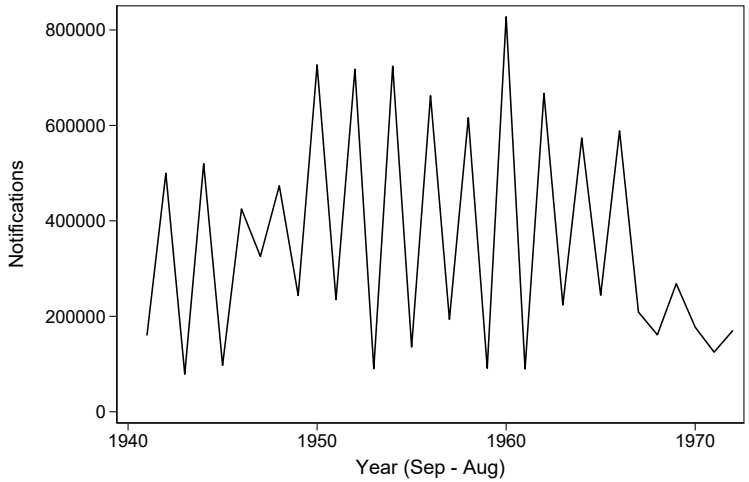


Measles in the UK

- Drivers of measles epidemics:
  - susceptible population: births vs infections / vaccinations
  - mixing of children: epidemic cycles follow school year
  - population density and family size



- Timeline:
  - 1945-50:
    - annual pattern (baby boom)
  - 1950-68:
    - bi-annual pattern
  - 1966:
    - MRC blanketing vaccine trial in 8 areas
  - 1968:
    - full roll-out of vaccine



Data

- **UK Biobank - UKB (Sudlow et al., 2015):**
  - approx. 500,000 participants born between 1934 and 1971
  - detailed survey data (demographics, lifestyle, medical history)
  - cognitive tests
  - physiological measurements
  - genetic data
  - hospitalisation data, GP records and death records

- **Measles exposure rates** merged with UKB data based on participants' place of birth (BIO-HGIS disease data for England and Wales; Baker, 2021):
  - capture district-level variation in number and severity of measles cases (due to under-reporting)

▸ BIO-HGIS disease data ▸ Descriptive Statistics

Data

- **Sample restrictions:**
  - Born Sep 1949 - Aug 1969 in England or Wales
  - Can identify district of birth
  - European ancestry (for genetic analysis)

- **Outcomes:**
  - Years of education (derived from completed qualifications)
    - measure of human capital
  - Height in cm (measured)
    - measure of childhood health

▶ Descriptive Statistics

Empirical approach

- Nationwide introduction of a measles vaccine in the UK in 1968
- Exploit two sources of variation:
  1. Temporal (cohort-level) variation in exposure to the vaccination programme
  2. Geographical (district-level) variation in the benefits from the vaccination programme
     - treatment intensity captured by pre-vaccination disease rates
     - benefits of the vaccine introduction were stronger for districts with previously high rates of measles
- Similar approach used in: e.g. Bleakley (2007), Bhalotra and Venkataramani (2015) and Bütikofer and Salvanes (2020), Atwood (2022)

Empirical approach

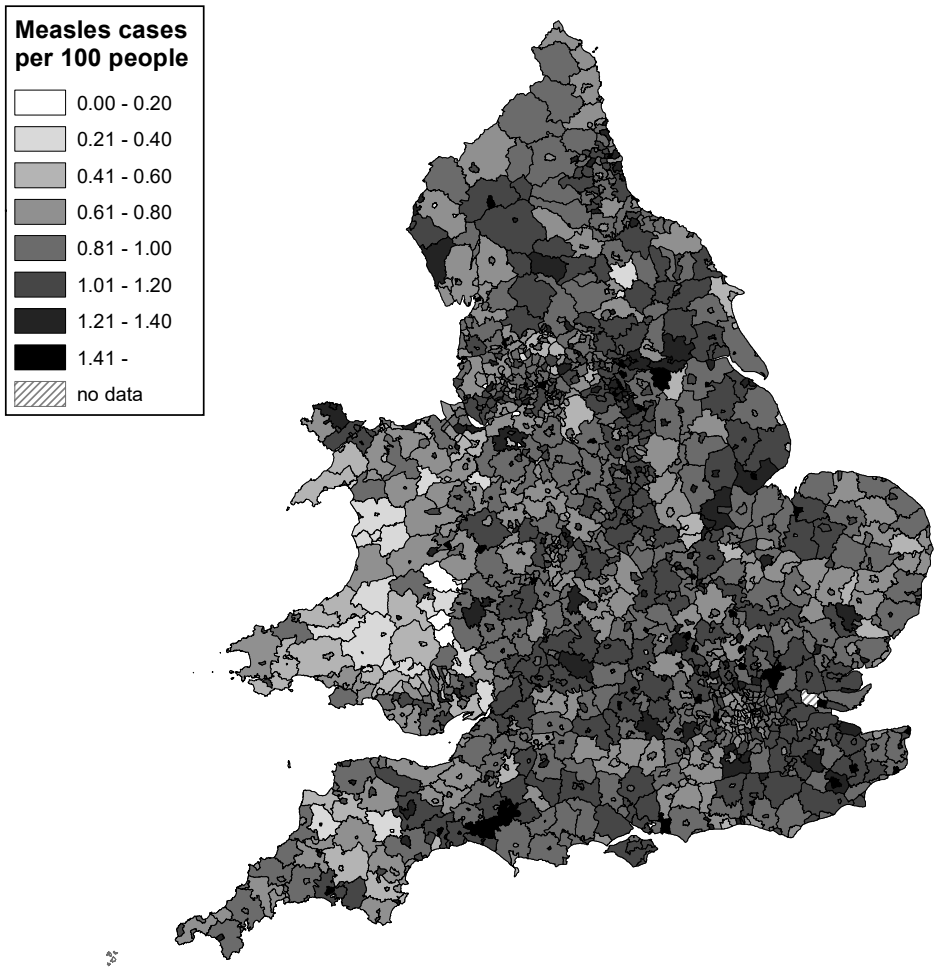
$$Y_{idc} = \alpha + \sum_{a} \beta_a Post_{age_i=a} \times PreRate_d + \mathbf{X_i'}\psi + \gamma_d + \lambda_c + u_{idc} \quad (1)$$

- Y_{idc}: outcome of interest
- $Post_{age_i=a}$: measure of exposure to the post-vaccination period at age(s) a
- $PreRate_d$: average measles rate in district d prior to vaccination (1950-1960)
- $\mathbf{X_i}$: individual-level controls (e.g. gender and month of birth fixed effects)
- γ_d: district fixed effects
- λ_c: cohort fixed effects
- u_{idc}: error term

▸ Descriptive Statistics ▸ Additional Figures

Empirical approach

Pre-vaccination measles rates across England and Wales

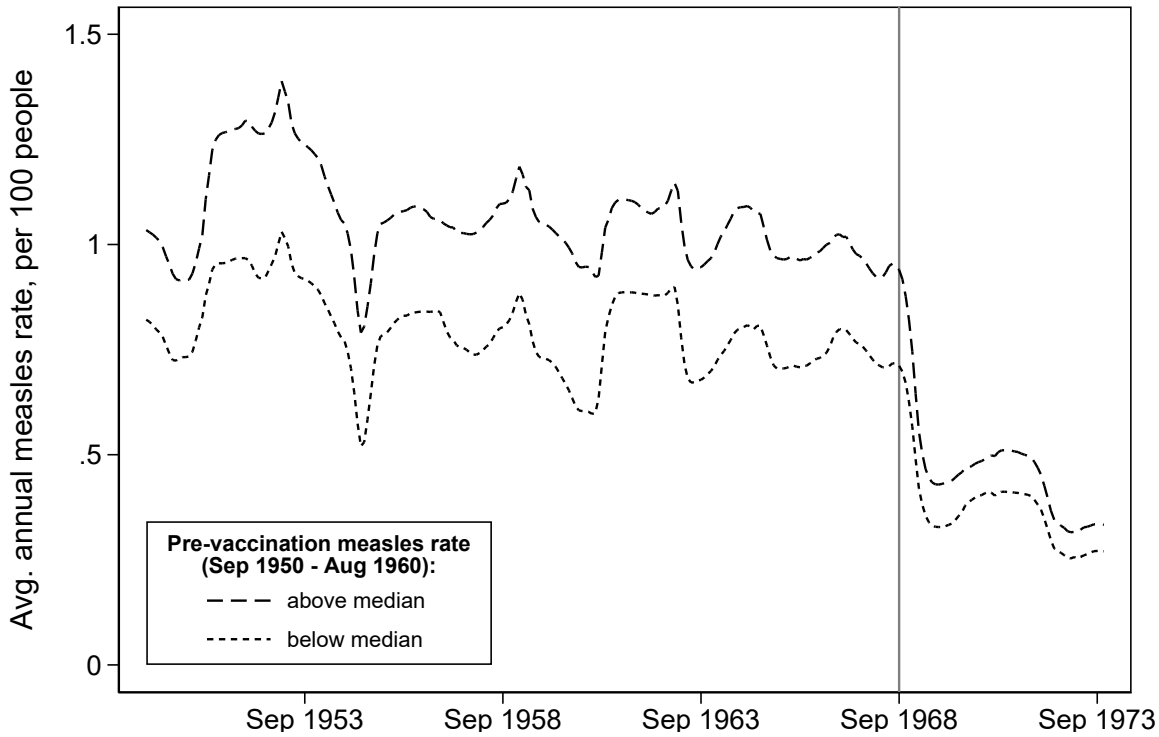


Note: The maps shows the average district-level annual measles rate between September 1950 and August 1960, in cases per 100 people.

▸ Descriptive Statistics ▸ Additional Figures

Empirical approach

Average annual measles rates in districts with high and low pre-vaccination rates



Note: The grey vertical line represents the beginning of the vaccine roll-out in September 1968. Each monthly observation corresponds to the average annual measles rate (per 100 people) over the preceding 24 months. 11 out of 1472 districts were excluded due to (partially) missing data on measles cases or population size. Districts participating in the 1966 trial are excluded from the figure.

▸ Descriptive Statistics ▸ Additional Figures

Results

Long-term effects of the measles vaccine introduction

	Years of education				Height in cm			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A:								
Post-vaccine share 1 to 6 × Pre-vacc. measles	0.227***	0.191***	0.031	−0.027	2.002***	1.969***	0.453*	0.090
	(0.029)	(0.023)	(0.102)	(0.105)	(0.073)	(0.063)	(0.271)	(0.256)
Panel B:								
Post-vaccine share 1 to 2 × Pre-vacc. measles	0.044	0.027	−0.039	−0.056	0.428***	0.325***	0.402	0.304
	(0.041)	(0.034)	(0.092)	(0.093)	(0.115)	(0.111)	(0.325)	(0.320)
Post-vaccine share 3 to 4 × Pre-vacc. measles	0.082**	0.062	−0.009	−0.027	−0.039	−0.052	−0.150	−0.215
	(0.039)	(0.038)	(0.090)	(0.091)	(0.110)	(0.110)	(0.277)	(0.282)
Post-vaccine share 5 to 6 × Pre-vacc. measles	0.088***	0.087***	0.060	0.037	1.388***	1.427***	0.286	0.105
	(0.029)	(0.027)	(0.083)	(0.082)	(0.076)	(0.075)	(0.245)	(0.237)
Controls for:								
Gender	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Month of birth FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
District of birth FE	No	Yes	Yes	Yes	No	Yes	Yes	Yes
School year of birth FE	No	No	Yes	Yes	No	No	Yes	Yes
County-specific birthdate trend	No	No	No	Yes	No	No	No	Yes
Compulsory schooling 16	Yes	Yes	No	No	No	No	No	No
Compulsory schooling 16 × Pre-vacc. measles	Yes	Yes	Yes	Yes	No	No	No	No
N	170,802	170,778	170,778	170,778	171,395	171,370	171,370	171,370

Note: The explanatory variables of interest are the share of the given age periods during which the individual was exposed to the vaccination program, interacted with the measles cases per 100 people prior to the vaccination program. Individuals born in districts that participated in the 1966 trial are excluded from the sample. Standard errors clustered at the district of birth level are shown in parentheses. Significance levels are indicated as follows: * $p<0.1$, ** $p<0.05$, *** $p<0.01$

Gene-environment interactions (GxE)

- Heterogeneity of the effects of the measles vaccine introduction by genetic predisposition for the outcome of interest
  - Are there complementarities between public health investments in early life and genetic endowments?

- **Measures of genetic predisposition:**
  - Polygenic indices (PGI) for educational attainment and height
  - not purely biological or non-modifiable
  - depend on context in which the PGI is derived

- **PGI data sources:**
  - Summary statistics from EA3 excl. UKB (Lee et al., 2018) and GIANT (Wood et al., 2014)
    - Incremental R^2: 8.56% for education, 21.21% for height
  - PGI repository (Becker et al., 2021)
    - Incremental R^2: 9.75% for education, 32.40% for height

▸ Descriptive Statistics ▸ Background: Genetics

GxE Results

Gene-environment interplay using EA3 / GIANT PGIs (Lee et al., 2018; Wood et al., 2014)

	Years of education				Height in cm			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Post-vaccine share 1 to 6 × Pre-vacc. measles	0.233***	0.209***	0.090	0.040	2.010***	2.007***	0.302	0.017
	(0.024)	(0.021)	(0.094)	(0.096)	(0.061)	(0.053)	(0.235)	(0.223)
PGI	0.676***	0.616***	0.617***	0.616***	3.248***	3.217***	3.222***	3.221***
	(0.009)	(0.009)	(0.009)	(0.009)	(0.016)	(0.016)	(0.016)	(0.016)
Post-vacc. share 1 to 6 × Pre-vacc. measles × PGI	−0.005	−0.012	−0.013	−0.012	0.079	0.091*	0.082	0.089*
	(0.018)	(0.017)	(0.017)	(0.017)	(0.052)	(0.051)	(0.052)	(0.051)
Controls for:								
Gender	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Month of birth FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
District of birth FE	No	Yes	Yes	Yes	No	Yes	Yes	Yes
School year of birth FE	No	No	Yes	Yes	No	No	Yes	Yes
County-specific birthdate trend	No	No	No	Yes	No	No	No	Yes
Compulsory schooling 16	Yes	Yes	No	No	No	No	No	No
Compulsory schooling 16 × Pre-vacc. measles	Yes	Yes	Yes	Yes	No	No	No	No
Comp. schooling 16 × Pre-vacc. measles × PGI	Yes	Yes	Yes	Yes	No	No	No	No
Principal components 1-20	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	170,158	170,134	170,134	170,134	170,750	170,725	170,725	170,725

Note: The explanatory variable of interest is the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program, interacted with the measles cases per 100 people prior to the vaccination program. This measure of treatment intensity for the vaccine introduction is furthermore interacted with the polygenic index (PGI) for education (columns 1-4) / height (columns 5-8). The measure of genetic propensity for education is based on summary statistics from Lee et al. (2018), the measure for height is based on summary statistics from Wood et al. (2014). Individuals born in districts that participated in the 1966 trial are excluded from the samples. Standard errors clustered at the district of birth level are shown in parentheses. Significance levels are indicated as follows: * $p<0.1$, ** $p<0.05$, *** $p<0.01$

Additional results

- Sibling GxE analysis:
  - Exogenous G: deviation of PGI from sibling mean
  - Effects in same direction (and larger for height)

▸ Sibling GxE Analysis

- Alternative identification approach: local MRC blanketing trials of the measles vaccine in 1966/67
  - Comparison of trial districts with similar "control" districts
  - Similar results for main effects (small sample for GxE)

▸ Blanketing Trial

- Heterogeneity by gender:
  - GxE effects on height driven by female sub-sample

▸ Heterogeneity by gender

Additional results

- Robustness checks:
  - binary measures of treatment intensity and of exposure to the post-vaccination period
  - alternative GxE models: median-split, different PGIs
  - control for other pre-vaccination disease rates and socio-economic measures interacted with post-vaccination exposure
  - different time windows for pre-vaccination rates
  - different levels of standard error clustering
  - differential trends at administrative county or district level
  - measles rates using estimated population size aged 1-6 (based on birth records)
  - omitting rural districts from sample

▸ Robustness checks

Conclusion

- Study of long-term effects of exposure to measles in early childhood on human capital and health in adulthood
- Use quasi-experimental variation in exposure to measles:
  - nationwide introduction of measles vaccine
  - local large-scale trials of measles vaccine
- No impact on educational attainment
- Evidence of GxE interactions for height: positive impact of vaccination among those with high genetic propensity
  - complementarity between public health investment in early life and genetic health endowment

References

Almond, D. (2006). Is the 1918 influenza pandemic over? Long-term effects of in utero influenza exposure in the post-1940 US population. *Journal of Political Economy*, *114*(4), 672–712.

Atwood, A. (2022). The Long-Term Effects of Measles Vaccination on Earnings and Employment. *American Economic Journal: Economic Policy*, *14*(2), 34–60.

Atwood, A., and Pearlman, S. (2022). Measles, Mexico and labor markets. *NBER SI*.

Baker, S. (2021). *The Biobank Historical Geographic Information System (BIO-HGIS)*.

Barteska, P., Dobkowitz, S., Olkkola, M., and Rieser, M. (2022). Mass vaccination and educational attainment: Evidence from the 1967–68 measles eradication campaign. *Available at SSRN 4060966*.

Becker, G. S., and Tomes, N. (1986). Human capital and the rise and fall of families. *Journal of labor economics*, *4*(3, Part 2), S1–S39.

Becker, J., Burik, C. A. P., Goldman, G., Wang, N., Jayashankar, H., Bennett, M., ... Okbay, A. (2021). Resource profile and user guide of the Polygenic Index Repository. *Nature Human Behaviour*, *5*, 1744–1758. doi: 10.1038/s41562-021-01119-3

Bhalotra, S. R., and Venkataramani, A. (2015). Shadows of the Captain of the Men of Death: Health Interventions, Human Capital Investments, and Institutions. *SSRN*, *1940725*. doi: 10.2139/ssrn.1940725

References

Bleakley, H. (2007). Disease and development: Evidence from hookworm eradication in the American South. *Quarterly Journal of Economics*, *122*(1), 73–117. doi: 10.1162/qjec.121.1.73

Bütikofer, A., and Salvanes, K. G. (2020). Disease control and inequality reduction: Evidence from a tuberculosis testing and vaccination campaign. *Review of Economic Studies*, *87*(5), 2087–2125. doi: 10.1093/restud/rdaa022

Chuard, C., Schwandt, H., Becker, A. D., and Haraguchi, M. (2022). *Economic vs. epidemiological approaches to measuring the human capital impacts of infectious disease elimination* (Tech. Rep.). National Bureau of Economic Research.

Cunha, F., and Heckman, J. (2007). The technology of skill formation. *American Economic Review*, *97*(2), 31–47. doi: 10.1257/aer.97.2.31

Daysal, N. M., Ding, H., Rossin-Slater, M., and Schwandt, H. (2021). *Germs in the family: The long-term consequences of intra-household endemic respiratory disease spread* (Tech. Rep.). National Bureau of Economic Research.

Gadroen, K., Dodd, C. N., Masclee, G. M. C., De Ridder, M. A. J., Weibel, D., Mina, M. J., ... De Swart, R. L. (2018). Impact and longevity of measles-associated immune suppression: A matched cohort study using data from the THIN general practice database in the UK. *BMJ Open*, *8*(11), e021465. doi: 10.1136/bmjopen-2017-021465

References

General Register Office. (1973a). *The Registrar General's Statistical Review of England and Wales for the Years 1941-1973, Part 1 Medical*. London: Her Majesty's Stationery Office. Retrieved from `https://lse-atom.arkivum.net/uklse-dl1eh01002`

General Register Office. (1973b). *The Registrar General's Weekly Returns for England and Wales, 1941-1973*. London: Her Majesty's Stationery Office.

Kelly, E. (2011). The scourge of asian flu in utero exposure to pandemic influenza and the development of a cohort of british children. *Journal of Human resources*, *46*(4), 669–694.

Lee, J. J., Wedow, R., Okbay, A., Kong, E., Maghzian, O., Zacher, M., ... Cesarini, D. (2018). Gene discovery and polygenic prediction from a genome-wide association study of educational attainment in 1.1 million individuals. *Nature Genetics*, *50*(8), 1112–1121. doi: 10.1038/s41588-018-0147-3

Mina, M. J., Kula, T., Leng, Y., Li, M., De Vries, R. D., Knip, M., ... Elledge, S. J. (2019). Measles virus infection diminishes preexisting antibodies that offer protection from other pathogens. *Science*, *366*(6465), 599–606. doi: 10.1126/science.aay6485

Mina, M. J., Metacalf, C. J. E., de Swart, R. L., Osterhaus, A. D. M. E., and Grenfell, B. T. (2015). Long-term measles-induced immunomodulation increases overall childhood infectious disease mortality. *Science*, *348*(6235), 694–700.

References

Mosca, I., Nolan, A., et al. (2022). *The long-term effects of in-utero exposure to rubella* (Tech. Rep.). Department of Economics, National University of Ireland-Maynooth.

Muslimova, D., van Kippersluis, H., Rietveld, C. A., von Hinke, S., and Meddens, F. (2020). Dynamic complementarity in skill production: Evidence from genetic endowments and birth order. *Tinbergen Institute Discussion Paper, TI 2020-08*.

Pereira, R. D., Biroli, P., Galama, T., von Hinke, S., van Kippersluis, H., Rietveld, C. A., and Thom, K. (2022). Gene-Environment Interplay in the Social Sciences. *arXiv*. Retrieved from `http://arxiv.org/abs/2203.02198`

Pereira, R. D., Rietveld, C. A., and van Kippersluis, H. (2020). The interplay between maternal smoking and genes in offspring birth weight. *MedRxiv*.

Petrova, V. N., Sawatsky, B., Han, A. X., Laksono, B. M., Walz, L., Parker, E., ... Russell, C. A. (2019). Incomplete genetic reconstitution of B cell pools contributes to prolonged immunosuppression after measles. *Science Immunology*, *4*(41), eaay6125. doi: 10.1126/sciimmunol.aay6125

Public Health England. (2014). *Completed primary courses at 2 years of age: England and Wales.* Retrieved 2022-06-20, from `https://www.gov.uk/government/publications/completed-primary-courses-at-2-years-of-age-england-and-wales`

References

Sudlow, C., Gallacher, J., Allen, N., Beral, V., Burton, P., Danesh, J., ... Collins, R. (2015). UK Biobank: An Open Access Resource for Identifying the Causes of a Wide Range of Complex Diseases of Middle and Old Age. *PLoS Medicine*, *12*(3), e1001779. doi: 10.1371/journal.pmed.1001779

van den Berg, G. J., von Hinke, S., and Wang, R. A. H. (2021). Prenatal sugar consumption and late-life health: Analyses based on post-wartime ratinoing and polygenic scores. *Mimeo, University of Bristol*.

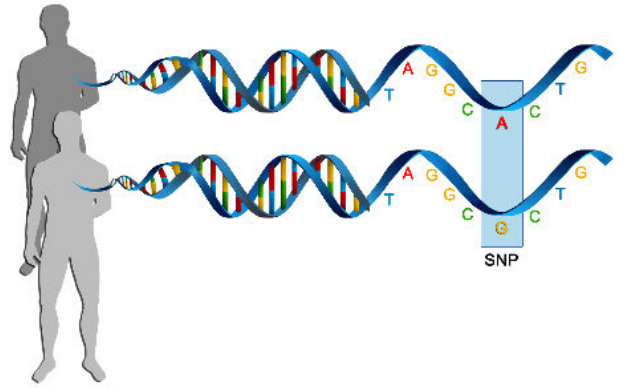
Wood, A. R., Esko, T., Yang, J., Vedantam, S., Pers, T. H., Gustafsson, S., ... Frayling, T. M. (2014). Defining the role of common variation in the genomic and biological architecture of adult human height. *Nature Genetics*, *46*(11), 1173–1186. doi: 10.1038/ng.3097

Woods, R. (2000). *The Demography of Victorian England and Wales* (Vol. 35). Cambridge University Press.

Appendix: Introduction to genetics and polygenic indices

The human genome:

- 23 pairs of chromosomes
  - one each from biological father and mother
  - each is a "random" mix of sections inherited from the respective grandfather and grandmother
- Each chromosome:
  - two intertwined strands of DNA made up of base pairs
  - possible pairs of nucleotides:
    - A (adenine) & T (thymine)
    - C (cytosine) & G (guanine)
- Genes:
  - sections of base pairs that code for a specific protein
  - varying lengths
  - approx. 20,000-25,000 genes

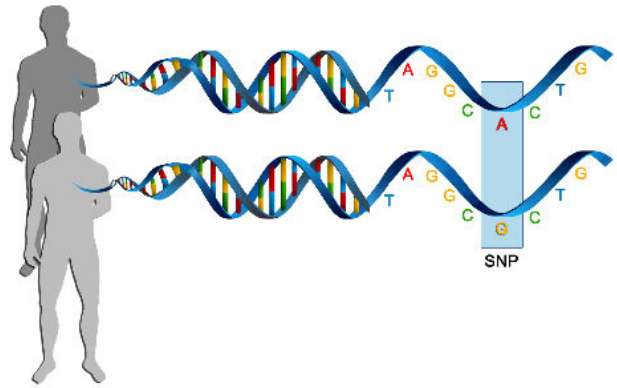


Source: Pereira et al. (2022)

Back - GxE interactions

Appendix: Introduction to genetics and polygenic indices

- 3 million base pairs in human genome
- any two humans typically share >99% of their genetic sequence
- the remaining <1% differ between individuals (polymorphism)
- most common form of genetic variation: SNP (single nucleotide polymorphism)
  - A location on the genome where two different nucleotides (alleles) can be observed in the population
  - Can code individuals genotype at a SNP as 0, 1 or 2 of a given allele



Source: Pereira et al. (2022)

Back - GxE interactions

Appendix: Introduction to genetics and polygenic indices

- Genome-wide association studies (GWAS):
  - Hypothesis-free approach to identify SNPs associated with a particular outcome
  - Univariate regressions for each SNP
  - genome-wide significance: $p < 5 \times 10^{-8}$
- Most complex human traits are polygenic
  - Single SNPs typically explain less than 0.02% of the variance in a trait
  - Increase predictive power by aggregating many SNPs into a combined measure of genetic predisposition / propensity

Back - GxE interactions

Appendix: Introduction to genetics and polygenic indices

- Polygenic (risk) score (PGS/PRS) or polygenic index (PGI):

$$PGI_i = \sum_{j=1}^{J} \beta_j x_{ij}$$

  - x_{ij}: count of effect alleles (0, 1 or 2) at SNP j
  - β_j: effect size for SNP j derived from an independent GWAS and adjusted for correlation between SNPs (linkage disequilibrium)

- Interpretation:
  - best linear genetic predictor of trait
  - not purely biological or non-modifiable
  - depends on context in which the score is derived

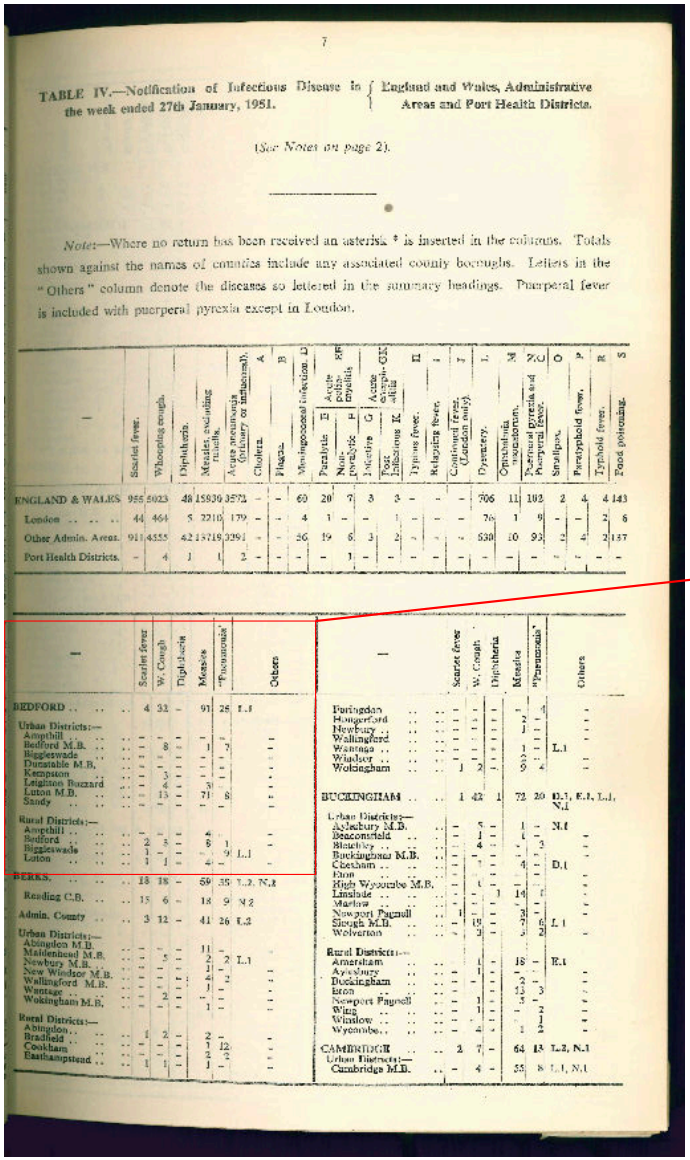
◂ Back - GxE interactions

BIO-HGIS

Biobank Historical Geographic Information System (BIO-HGIS) disease data for England and Wales (Baker, 2021):

- weekly number of disease notifications at the district level from Registrar General's Weekly Reports (General Register Office, 1973b)
  - measles: 1941-1973
- annual district-level population from Registrar General's Statistical Review of England and Wales (General Register Office, 1973a)
- measles exposure rates merged with UKB data based on participants' place and date of birth
  - measles notifications were subject to substantial under-reporting
  - measles rates therefore capture district-level variation in number and severity of measles cases

Back - Data



7

TABLE IV.—Notification of Infectious Disease in the week ended 27th January, 1951. { England and Wales, Administrative Areas and Port Health Districts.

(*See Notes on page 2*).

Note:—Where no return has been received an asterisk * is inserted in the columns. Totals shown against the names of counties include any associated county boroughs. Letters in the "Others" column denote the diseases so lettered in the summary headings. Puerperal fever is included with puerperal pyrexia except in London.

—	Scarlet fever.	Whooping cough.	Diphtheria.	Measles, excluding rubella.	Acute pneumonia (primary or influenzal).	Cholera.	Plague.	Meningococcal infection.	Acute poliomyelitis: Paralytic.	Acute poliomyelitis: Non-paralytic.	Dysentery.	Encephalitis lethargica.	Infective hepatitis.	Food infections.	Typhus fever.	Relapsing fever.	Continued fever. (London only).	Dysentery.	Ophthalmia neonatorum.	Puerperal pyrexia and Puerperal fever.	Smallpox.	Paratyphoid fever.	Typhoid fever.	Food poisoning.
ENGLAND & WALES	955	5023	48	15839	3572	–	–	60	20	7	3	3	–	–	–	–	706	11	102	2	4	4	143
London	44	464	5	2210	179	–	–	4	1	–	–	1	–	–	–	–	76	1	9	–	–	2	8
Other Admin. Areas.	911	4555	42	13719	3391	–	–	56	19	6	3	2	–	–	–	–	630	10	93	2	4	2	137
Port Health Districts.	–	4	1	1	2	–	–	–	–	1	–	–	–	–	–	–	–	–	–	–	–	–	–

—	Scarlet fever	W. Cough	Diphtheria	Measles	"Pneumonia"	Others
BEDFORD	4	32	–	91	25	L.1
Urban Districts:—						
Ampthill	–	–	–	–	–	
Bedford M.B.	–	8	–	1	7	
Biggleswade	–	–	–	–	–	
Dunstable M.B. ..	–	–	–	–	–	
Kempston	–	3	–	–	–	
Leighton Buzzard ..	–	4	–	3	–	
Luton M.B.	–	13	–	71	8	
Sandy	–	–	–	–	–	
Rural Districts:—						
Ampthill	–	–	–	4	–	
Bedford	2	3	–	8	1	
Biggleswade	1	–	–	–	9	L.1
Luton	1	1	–	4	–	

—	Scarlet fever	W. Cough	Diphtheria	Measles	"Pneumonia"	Others
Faringdon	–	–	–	–	4	–
Hungerford	–	–	–	2	–	–
Newbury	–	–	–	1	–	–
Wallingford	–	–	–	–	–	–
Wantage	–	1	–	1	–	L.1
Windsor	–	–	–	–	–	–
Wokingham	1	2	–	9	4	–
BUCKINGHAM	1	42	1	72	20	E.1, L.1, N.1
Urban Districts:—						
Aylesbury M.B.	–	5	–	1	–	N.1
Beaconsfield	–	1	–	–	–	–
Buckingham M.B. ..	–	4	–	3	–	–
Chesham	–	–	–	4	–	D.1
Eton	–	–	–	–	–	–
High Wycombe M.B. ..	–	1	–	14	1	–
Marlow	–	–	–	–	–	–
Newport Pagnell ..	1	–	–	32	–	–
Slough M.B.	–	15	–	76	1	L.1
Wolverton	–	3	–	3	2	–
Rural Districts:—						
Amersham	–	1	–	18	–	E.1
Aylesbury	–	1	–	–	–	–
Buckingham	–	–	–	2	–	–
Eton	–	–	–	13	3	–
Newport Pagnell	–	1	–	3	–	–
Wing	–	1	–	–	2	–
Winslow	–	–	–	1	–	–
Wycombe	–	4	–	1	–	–
CAMBRIDGE	2	7	–	64	13	L.2, N.1
Urban Districts:—						
Cambridge M.B. ..	–	4	–	55	8	L.1, N.1

—	Scarlet fever	W. Cough	Diphtheria	Measles	"Pneumonia"	Others
BEDFORD	4	32	–	91	25	L.1
Urban Districts:—						
Ampthill	–	–	–	–	–	
Bedford M.B.	–	8	–	1	7	
Biggleswade	–	–	–	–	–	
Dunstable M.B. ..	–	–	–	–	–	
Kempston	–	3	–	–	–	
Leighton Buzzard ..	–	4	–	3	–	
Luton M.B.	–	13	–	71	8	
Sandy	–	–	–	–	–	
Rural Districts:—						
Ampthill	–	–	–	4	–	
Bedford	2	3	–	8	1	
Biggleswade	1	–	–	–	9	L.1
Luton	1	1	–	4	–	

◂ Back - Data

Appendix: Descriptive statistics

Descriptive statistics

	Mean	SD	Min	Max	N
Measles rates (annual avg. per 100 people):					
- Age 1 to 6	0.86	0.25	0.00	5.48	176,067
- Age 1 to 2	0.89	0.36	0.00	13.56	187,045
- Age 3 to 4	0.83	0.37	0.00	13.82	185,592
- Age 5 to 6	0.80	0.37	0.00	13.63	176,163
- pre-vaccination (Sep 1950 - Aug 1960)	0.96	0.19	0.02	2.71	187,078
Outcomes:					
- years of education	13.38	2.22	10.00	16.00	186,104
- any qualification	0.91	0.29	0.00	1.00	186,104
- upper secondary qualification	0.72	0.45	0.00	1.00	186,104
- degree qualification	0.35	0.48	0.00	1.00	186,104
- height in cm	169.62	9.24	118.00	209.00	186,766
Demographic characteristics:					
- female	0.55	0.50	0.00	1.00	187,078
- year of birth	1957.54	5.44	1949.00	1969.00	187,078

◂ Back - Data ◂ Back - Empirical Approach

Appendix: Descriptive statistics

Descriptive statistics for districts with above- and below-median measles infection rates prior to vaccination

	Pre-vaccination measles rate (Sep 1950 - Aug 1960)	
	below median	above median
Social class:		
- class 1 (professional)	0.037	0.030
- class 2 (intermediate)	0.156	0.135
- class 3 (skilled)	0.526	0.532
- class 4 (partly skilled)	0.160	0.163
- class 5 (unskilled)	0.122	0.140
Housing density:		
- 0 to 1 persons per room	0.749	0.731
- 1 to 1.5 persons per room	0.168	0.177
- 1.5 to 2 persons per room	0.064	0.068
- 2 to 3 persons per room	0.017	0.020
- 3+ persons per room	0.003	0.004
Age left education:		
- 0 to 14 years	0.738	0.770
- 15 years	0.104	0.101
- 16 years	0.081	0.072
- 17 to 19 years	0.051	0.037
- 20+ years	0.026	0.020

Note: Data on social class, housing density and age left education is obtained from the 1951 UK Census.

◂ Back - Data ◂ Back - Empirical Approach

Appendix: Descriptive statistics

Mapping between highest reported qualification and derived years of education

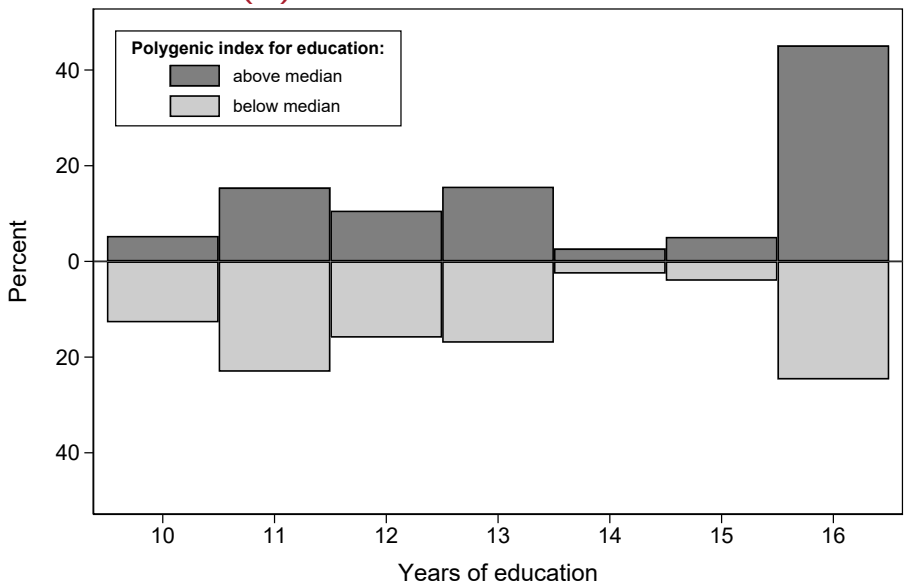
Highest qualification(s)	Derived years of education
College or university degree	16
Combination of: Other professional qualifications eg: nursing, teaching *and* A levels/AS levels or equivalent	15
Combination of: NVQ or HND or HNC or equivalent *and* A levels/AS levels or equivalent	14
Other professional qualifications eg: nursing, teaching	13
A levels/AS levels or equivalent	13
NVQ or HND or HNC or equivalent	12
CSEs or equivalent	11
O levels/GCSEs or equivalent	11
None of the above	10
Prefer not to answer	–

◂ Back - Data ◂ Back - Empirical Approach

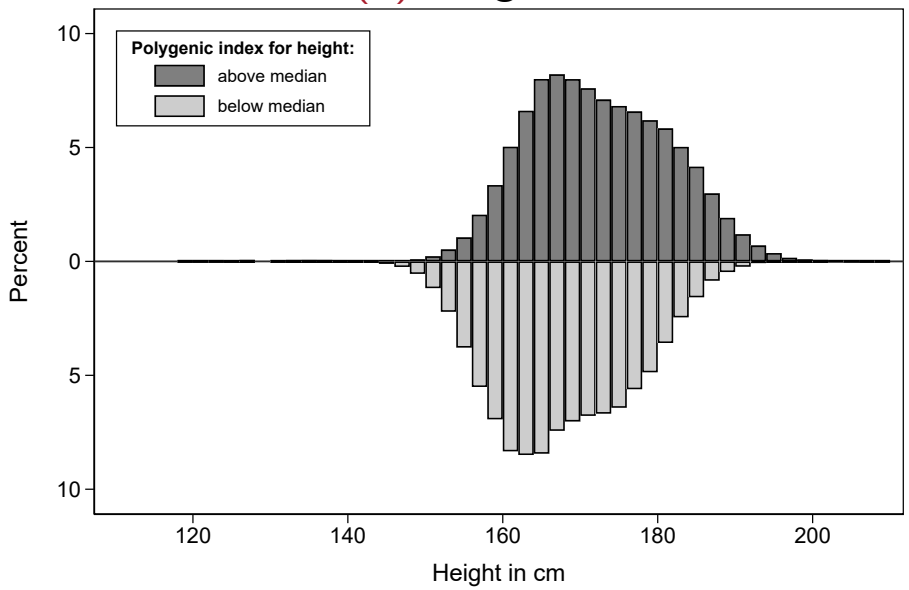
Appendix: Descriptive statistics for PGIs

Average years of education and height, by genetic propensity
Measures: EA3 (Lee et al., 2018) / GIANT (Wood et al., 2014) PGIs

(a) Years of education



(b) Height



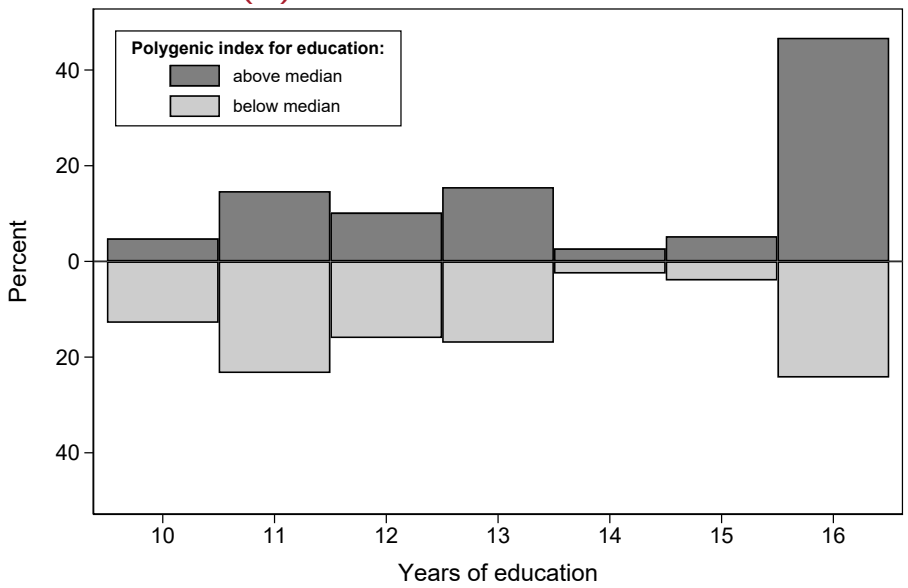
Note: The figures show the distributions of years of education and height in centimetres in the sub-samples with above- / below-median genetic propensity for the respective trait.

◂ Back - Data ◂ Back - Empirical Approach

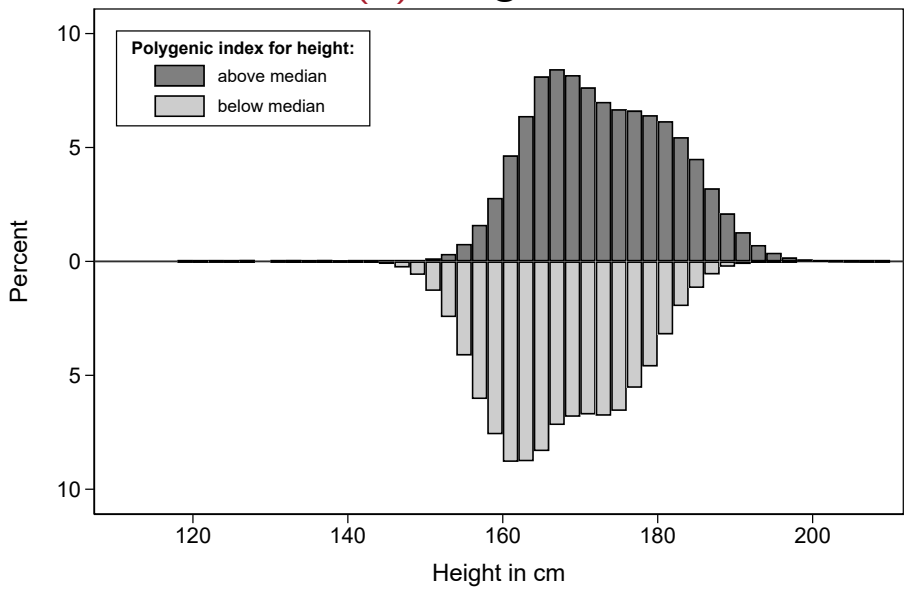
Appendix: Descriptive statistics for PGIs

Average years of education and height, by genetic propensity
Measures: repository PGIs Becker et al. (2021)

(a) Years of education



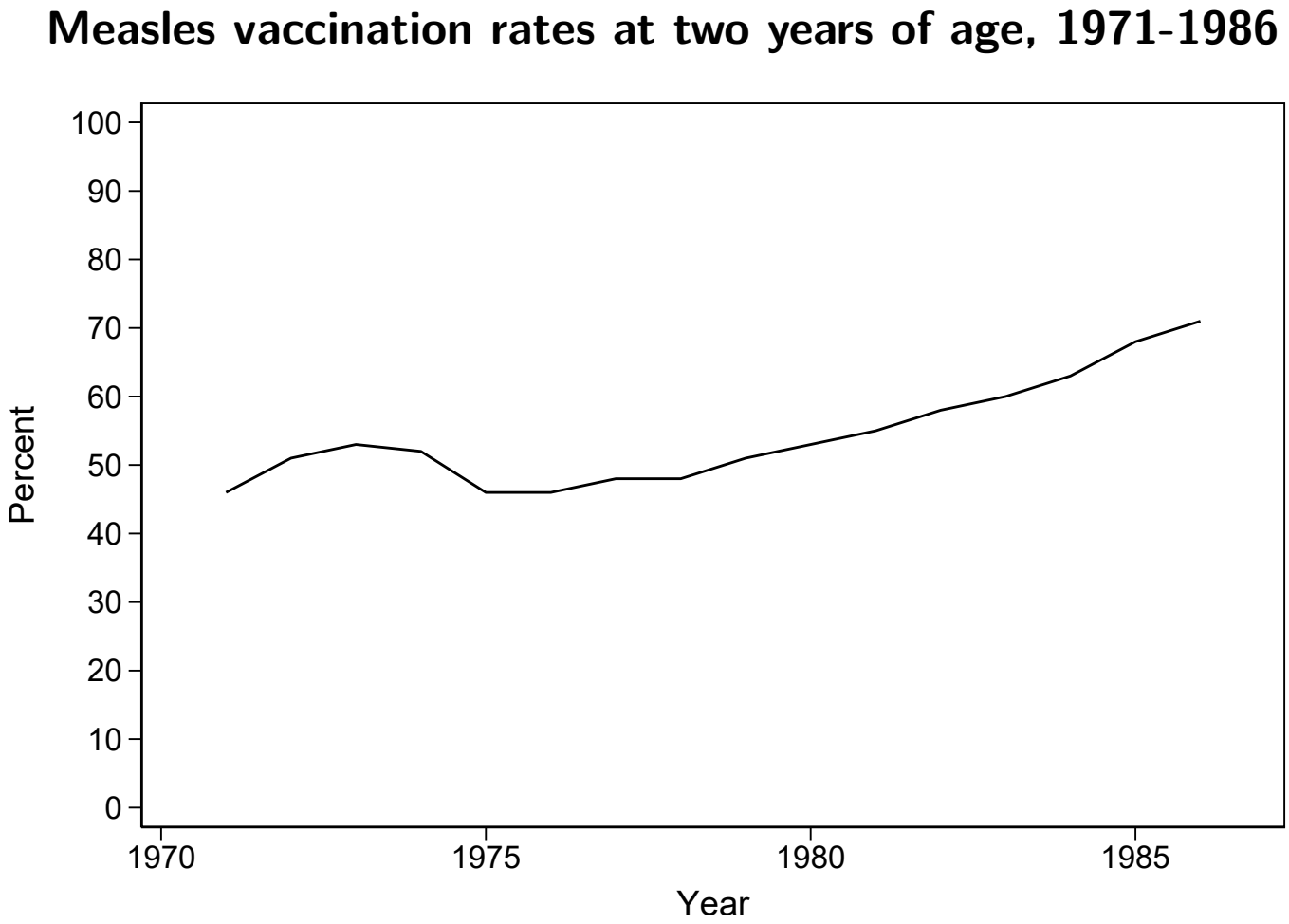
(b) Height



Note: The figures show the distributions of years of education and height in centimetres in the sub-samples with above- / below-median genetic propensity for the respective trait.

◂ Back - Data ◂ Back - Empirical Approach

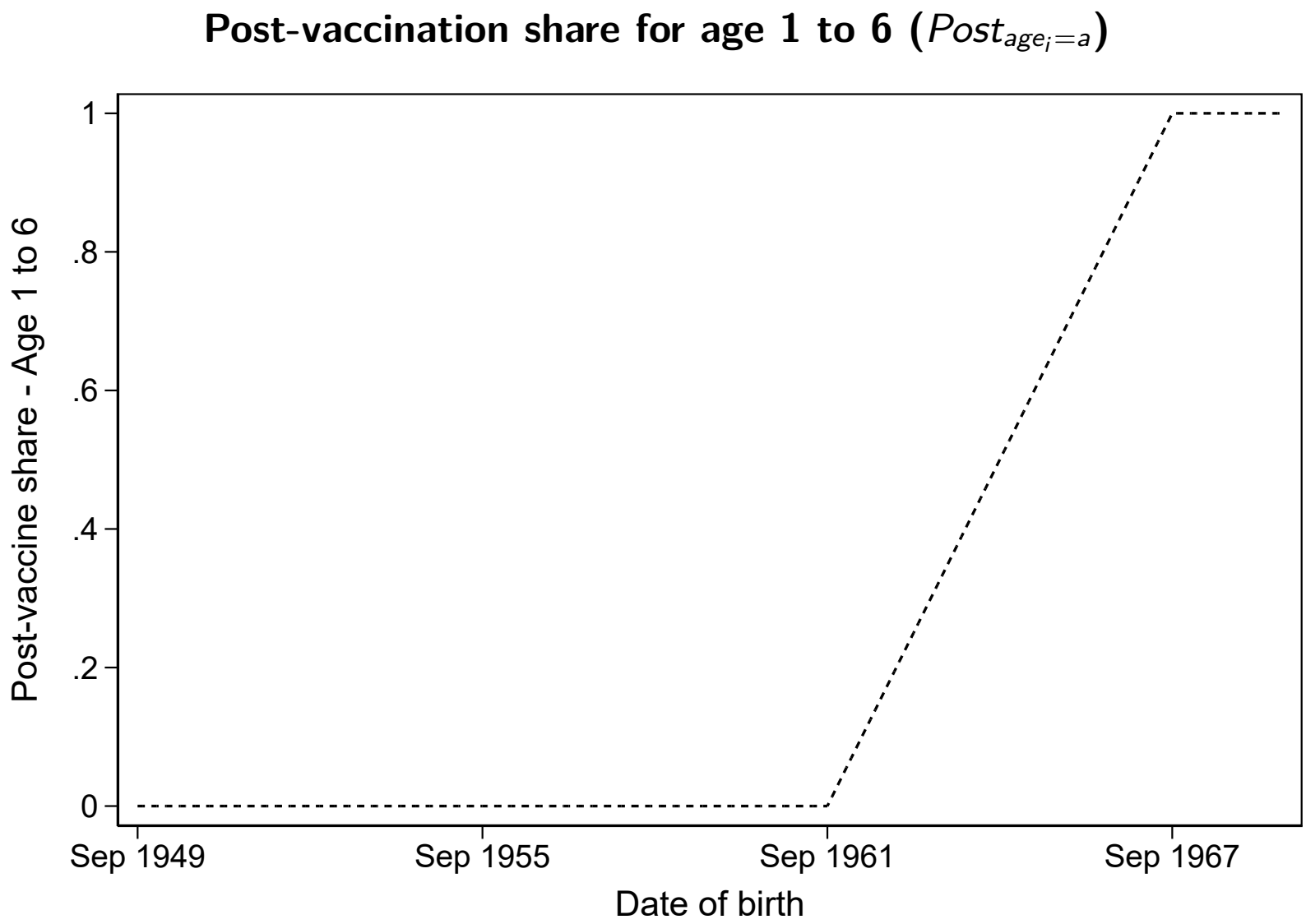
Appendix: Empirical approach - Additional figures



Note: The figure shows the rate of children aged two years who had completed the primary course of the measles vaccination by the end of the given year. Data source: Public Health England (2014).

Back

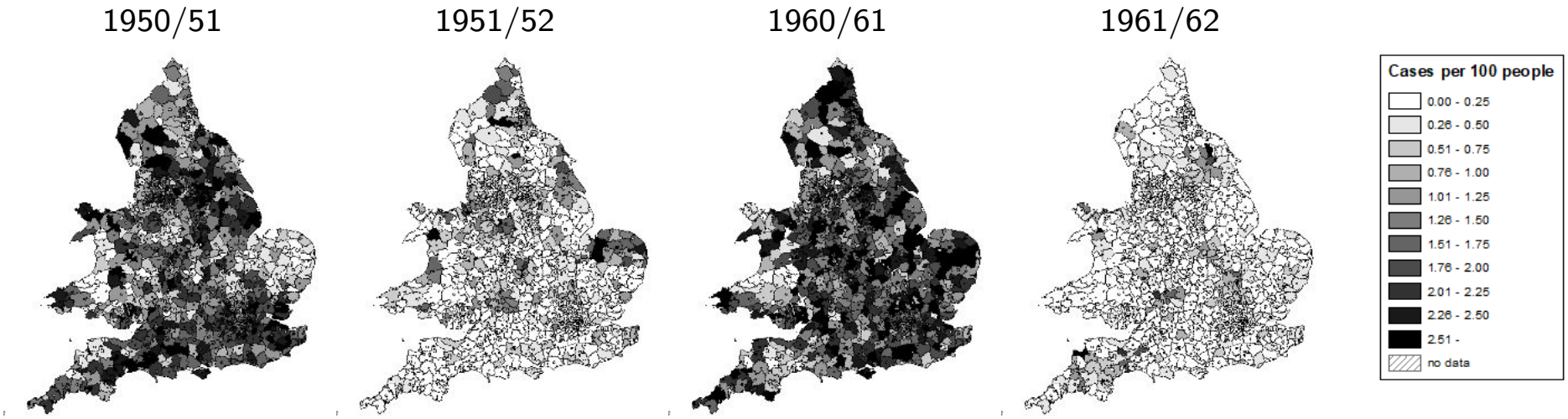
Appendix: Empirical approach - Additional figures



Back

Appendix: Empirical approach - Additional figures

Measles rates across England and Wales

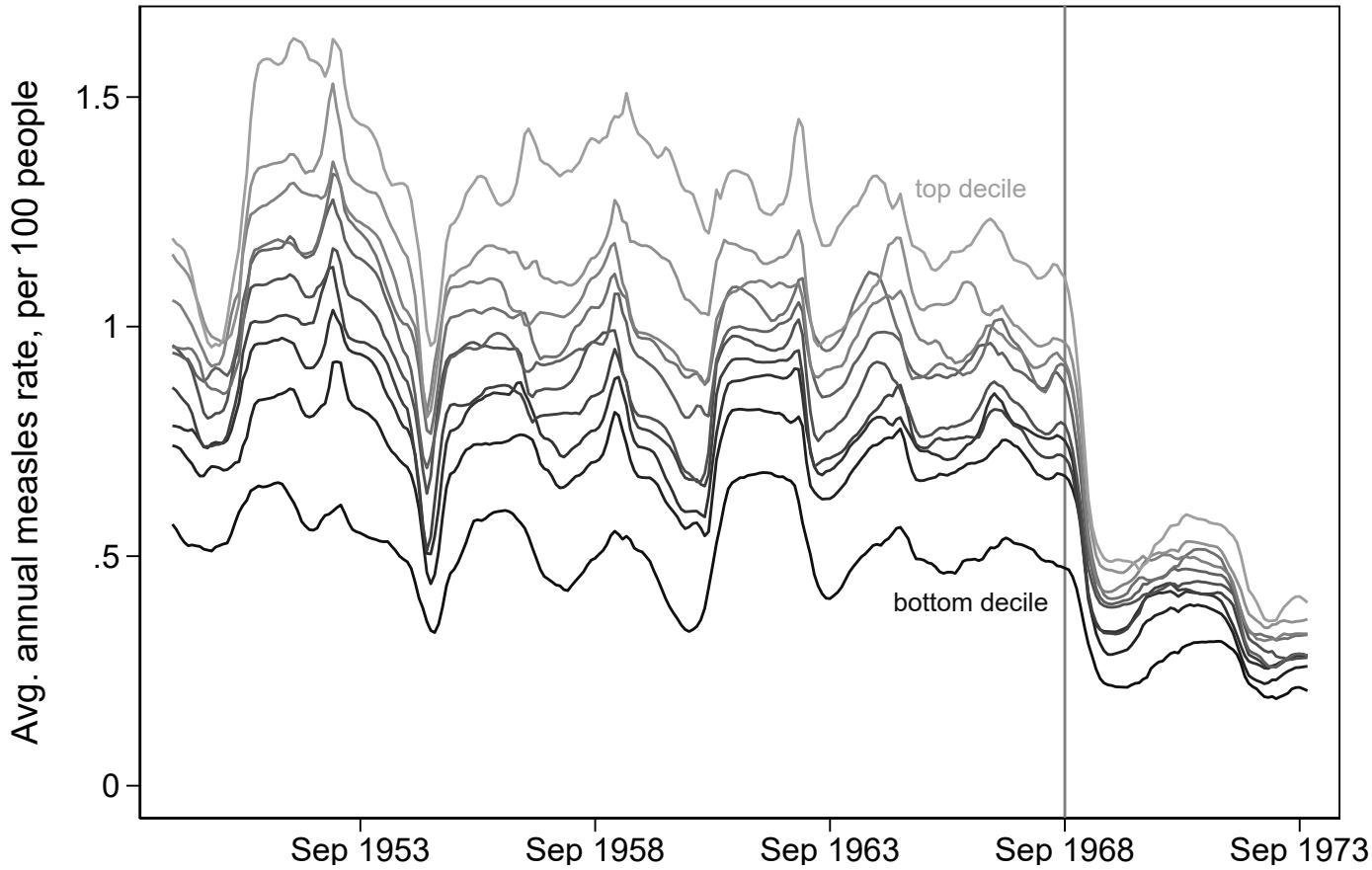


Note: The maps shows the district-level measles rates in cases per 100 population for school years running from September to August.

Back

Appendix: Empirical approach - Additional figures

Average annual measles rates for deciles of the pre-vaccination rate distribution

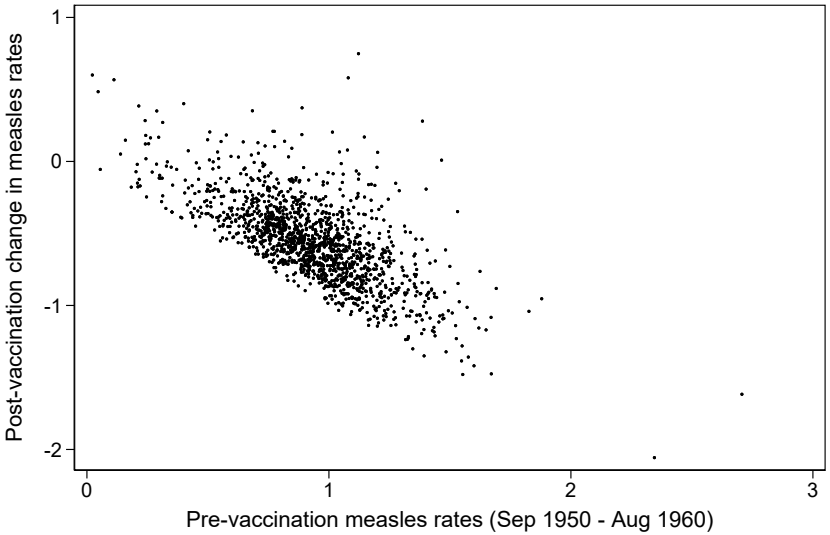


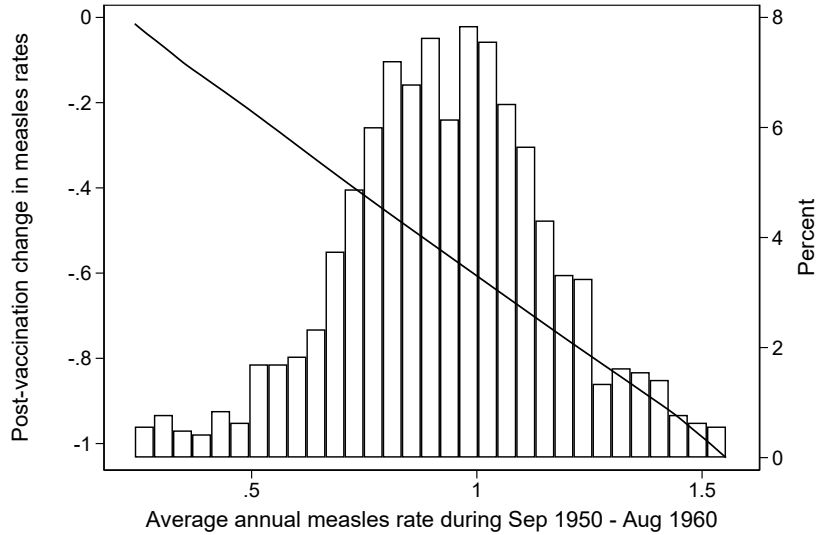
Note: The grey vertical line represents the beginning of the vaccine roll-out in September 1968. Each monthly observation corresponds to the average annual measles rate (per 100 people) over the preceding 24 months. 11 out of 1472 districts were excluded due to (partially) missing data on measles cases or population size. Districts participating in the 1966 trial are excluded from the figure.

Back

Appendix: Empirical approach - Additional figures

Pre-vaccination measles rates and the post-vaccination change in measles rates





Note: The horizontal axis measures the average annual measles rate between September 1950 and August 1960, in cases per 100 people. The vertical axis measures the change in the average annual measles rate following the introduction of the measles vaccine, comparing the post-vaccination period between September 1968 and August 1972 with the pre-vaccination period between September 1950 and August 1960. In the left panel, each data point corresponds to a district, excluding any districts that participated in the 1966 trial. In the panel on the right, the histogram shows the distribution of district-level measles rates during the pre-vaccination period. The solid line represents the conditional mean change in district measles rates between 1950-60 and 1968-72 from a local linear regression on the districts' pre-vaccination rates (bandwidth: 0.25 cases per 100 people). Districts in the top and bottom 1% of the pre-vaccination measles rate distribution and districts participating in the 1966 trial are excluded from this graph.

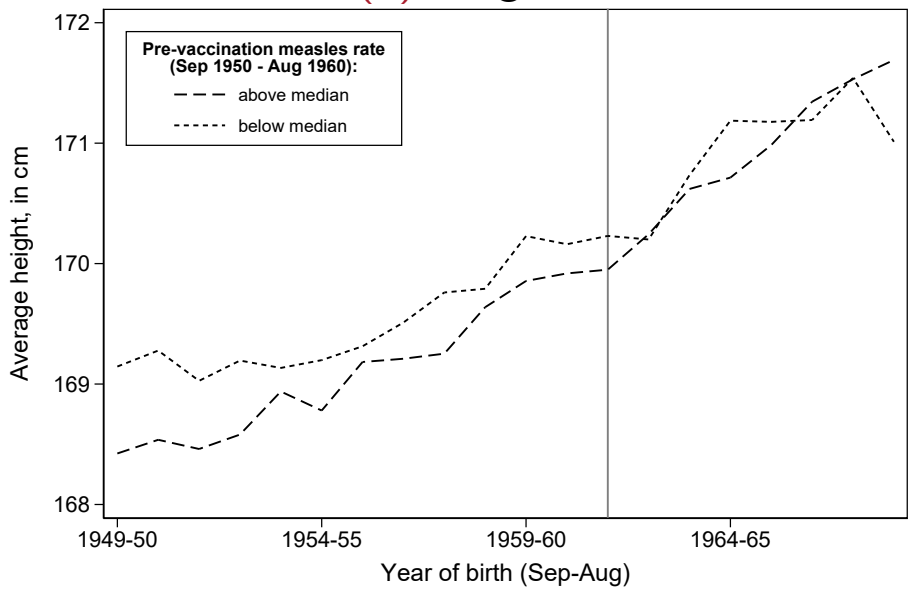
Back

Appendix: Empirical approach - Additional figures

Average years of education and height in districts with high and low pre-vaccination measles rates

(a) Years of education

(b) Height



Note: Years of education and height in centimetres are averaged across schoolyears of birth (September to August). E.g. the 1949-1950 period covers the cohorts born between September 1949 and August 1950. The grey vertical line represents the last cohort likely unaffected by the vaccine introduction, namely those born between September 1961 and August 1962. Districts participating in the 1966 trial are excluded from the figures.

Back

Appendix: Empirical approach - Additional figures

Qualification completion in districts with high and low pre-vaccination measles rates

(a) Any qualification

(b) Upper secondary qualification

(c) Degree qualification

Note: Qualification shares are averaged across schoolyears of birth (September to August). E.g. the 1949-1950 period covers the cohorts born between September 1949 and August 1950. The grey vertical lines represents the last cohort likely unaffected by the vaccine introduction, namely those born between September 1961 and August 1962. Districts participating in the 1966 trial are excluded from the figures.

Back

Appendix: Sibling GxE analysis

Gene-environment interplay using EA3 / GIANT PGIs (Lee et al., 2018; Wood et al., 2014) in the sibling sample

	Years of education				Height in cm			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Post-vaccine share 1 to 6 × Pre-vacc. measles	0.228***	0.189**	0.189	0.124	1.882***	2.165***	2.490**	2.190*
	(0.084)	(0.085)	(0.416)	(0.434)	(0.219)	(0.215)	(1.081)	(1.259)
PGI	0.652***	0.594***	0.592***	0.592***	3.275***	3.278***	3.280***	3.270***
	(0.030)	(0.033)	(0.032)	(0.033)	(0.077)	(0.081)	(0.081)	(0.082)
Post-vacc. share 1 to 6 × Pre-vacc. measles × PGI	0.000	−0.018	−0.013	−0.013	0.120	0.138	0.120	0.163
	(0.086)	(0.090)	(0.091)	(0.093)	(0.245)	(0.265)	(0.267)	(0.272)
Controls for:								
Gender	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Month of birth FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
District of birth FE	No	Yes	Yes	Yes	No	Yes	Yes	Yes
School year of birth FE	No	No	Yes	Yes	No	No	Yes	Yes
County-specific birthdate trend	No	No	No	Yes	No	No	No	Yes
Compulsory schooling 16	Yes	Yes	No	No	No	No	No	No
Compulsory schooling 16 × Pre-vacc. measles	Yes	Yes	Yes	Yes	No	No	No	No
Comp. schooling 16 × Pre-vacc. measles × PGI	Yes	Yes	Yes	Yes	No	No	No	No
Principal components 1-20	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	10,763	10,553	10,553	10,553	10,803	10,592	10,592	10,592

Note: The sample was restricted to full siblings - identified based on genetic relatedness. The explanatory variable of interest is the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program, interacted with the measles cases per 100 people prior to the vaccination program. This measure of treatment intensity for the vaccine introduction is furthermore interacted with the polygenic index (PGI) for education or height. The measure of genetic propensity for education is based on summary statistics from Lee et al. (2018), the measure for height is based on summary statistics from Wood et al. (2014). Individuals born in districts that participated in the 1966 trial are excluded from the samples. Standard errors clustered at the district of birth level are shown in parentheses. Significance levels are indicated as follows: * $p<0.1$, ** $p<0.05$, *** $p<0.01$

◂ Back

Appendix: Sibling GxE analysis

Gene-environment interplay using within-sibling difference in EA3 / GIANT PGIs (Lee et al., 2018; Wood et al., 2014)

	Years of education				Height in cm			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Post-vaccine share 1 to 6 × Pre-vacc. measles	0.238***	0.205**	0.074	0.003	1.967***	2.227***	2.982**	2.181
	(0.091)	(0.091)	(0.425)	(0.443)	(0.267)	(0.268)	(1.250)	(1.433)
PGI sibling mean deviation (PGI-SMD)	0.379***	0.388***	0.386***	0.388***	2.723***	2.736***	2.747***	2.726***
	(0.056)	(0.053)	(0.054)	(0.055)	(0.110)	(0.109)	(0.108)	(0.107)
Post-vacc. share 1 to 6 × Pre-vacc. measles × PGI-SMD	−0.085	−0.125	−0.123	−0.143	0.498	0.449	0.380	0.446
	(0.179)	(0.178)	(0.180)	(0.179)	(0.475)	(0.477)	(0.464)	(0.463)
Controls for:								
Gender	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Month of birth FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
District of birth FE	No	Yes	Yes	Yes	No	Yes	Yes	Yes
School year of birth FE	No	No	Yes	Yes	No	No	Yes	Yes
County-specific birthdate trend	No	No	No	Yes	No	No	No	Yes
Compulsory schooling 16	Yes	Yes	No	No	No	No	No	No
Compulsory schooling 16 × Pre-vacc. measles	Yes	Yes	Yes	Yes	No	No	No	No
Comp. schooling 16 × Pre-vacc. measles × PGI-SMD	Yes	Yes	Yes	Yes	No	No	No	No
Principal components 1-20	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	10,748	10,538	10,538	10,538	10,788	10,577	10,577	10,577

Note: The sample was restricted to full siblings - identified based on genetic relatedness. The explanatory variable of interest is the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program, interacted with the measles cases per 100 people prior to the vaccination program. This measure of treatment intensity for the vaccine introduction is furthermore interacted with the deviation of the polygenic index (PGI) for education or height from the sibling mean. The measure of genetic propensity for education is based on summary statistics from Lee et al. (2018), the measure for height is based on summary statistics from Wood et al. (2014). Individuals born in districts that participated in the 1966 trial are excluded from the samples. Standard errors clustered at the district of birth level are shown in parentheses. Significance levels are indicated as follows: * $p<0.1$, ** $p<0.05$, *** $p<0.01$

Back

Appendix: Blanketing trial

- Medical Research Council (MRC) blanketing trial in 1966/67
- Vaccination offered to eligible susceptible children in some districts, but not in others
- Focus on four trial districts offering vaccination between 10/18 months and 10/12 years: Bedford, Kingston upon Hull, Newcastle upon Tyne and Oxford
- Difference-in-difference specification comparing trial district with "control" districts
  - trial districts mainly urban
  - control districts: districts with population density (1961-64) within 1 SD of trial district mean

Back

Appendix: Blanketing trial

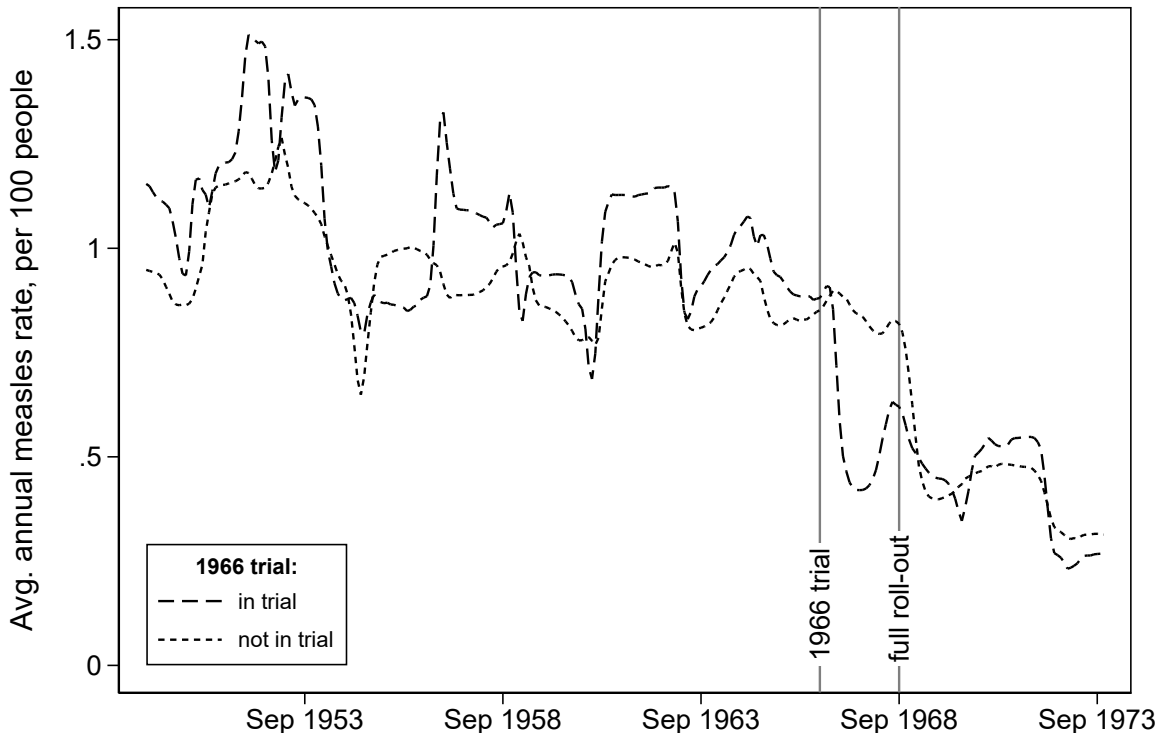
$$Y_{idc} = \eta + \pi_a \, TrialYears_{age_i=a} + \sum_a \theta_a \, TrialYears_{age_i=a} \times TrialDistrict_d + \mathbf{X_i'}\psi + \gamma_d + \lambda_c + u_{idc} \quad (2)$$

- Y_{idc}: outcome of interest
- $TrialYears_{age_i=a}$: years of exposure to the trial period at age(s) a
- $TrialDistrict_d$: indicator for district of birth participating in blanketing trial
- $\mathbf{X_i}$: individual-level controls (e.g. gender and month of birth fixed effects)
- γ_d: district fixed effects
- λ_c: cohort fixed effects
- u_{idc}: error term

Back

Appendix: Blanketing trial

Average annual measles rates in districts participating in the 1966/67 trial and control districts



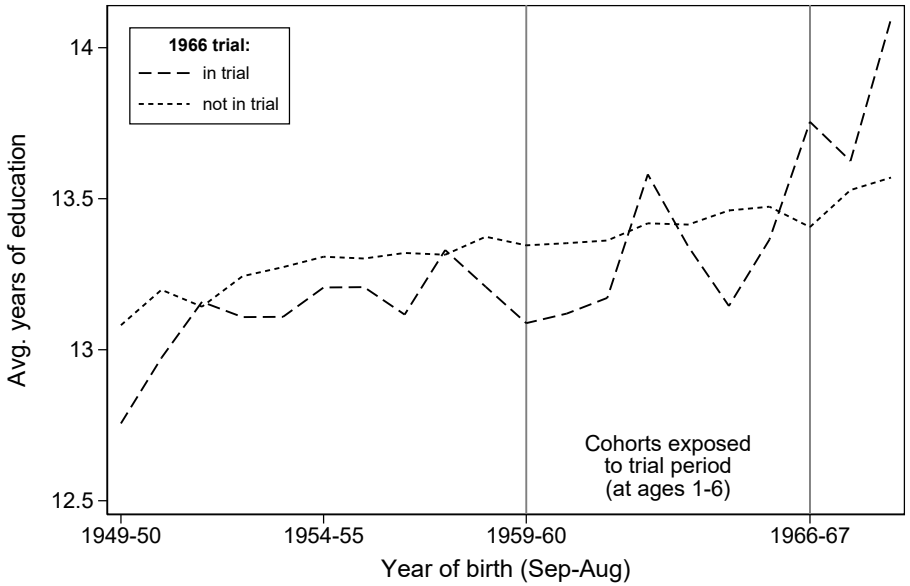
Note: We focus here on the trial targeting susceptible children up to age 10 or 12. Districts with trials targeting children up to age 2 are excluded from the graph. The sample was furthermore restricted to control districts with a population density within one standard deviation of the mean among the trial districts. Each monthly observation corresponds to the average annual measles rate (per 100 people) over the preceding 24 months. 11 out of 1472 districts were excluded due to (partially) missing data on measles cases or population size.

Back

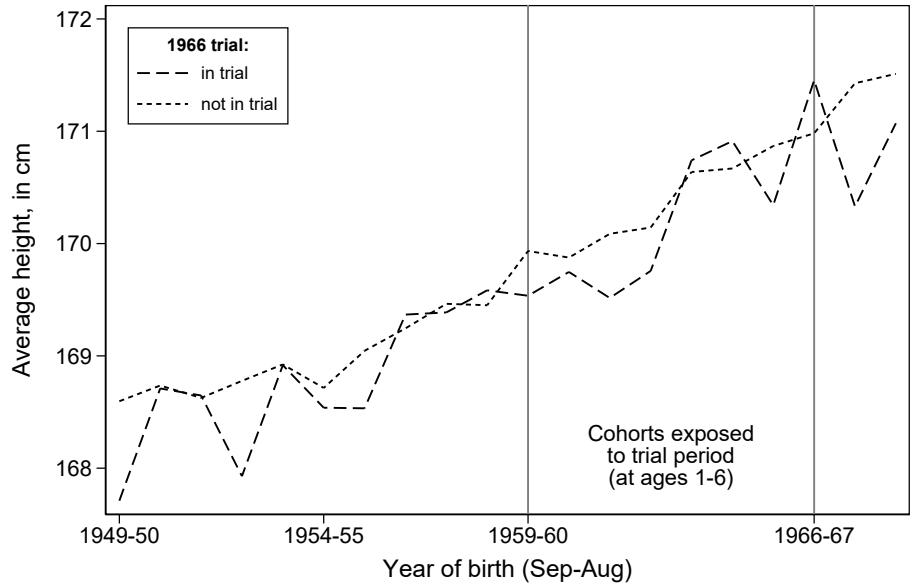
Appendix: Blanketing trial

Average years of education and height in districts participating in the 1966/67 trial and control districts

(a) Years of education



(b) Height



Note: We focus here on the trial targeting susceptible children up to age 10 or 12. Districts with trials targeting children up to age 2 are excluded from the graph. The sample was furthermore restricted to control districts with a population density within one standard deviation of the mean among the trial districts. Years of education and height in centimetres are averaged across schoolyears of birth (September to August). E.g. the 1949-1950 period covers the cohorts born between September 1949 and August 1950. The grey vertical lines represent the first and last cohorts (partially) exposed to the period of the vaccine trial at age 1 to 6.

Back

Appendix: Blanketing trial

Long-term effects of the 1966 measles vaccine trial

	Years of education		Height in cm	
	(1)	(2)	(3)	(4)
Panel A:				
Trial district × Trial period exposure - Age 1 to 6	−0.000	−0.003	0.134	0.116
	(0.029)	(0.029)	(0.106)	(0.107)
Trial period exposure - Age 1 to 6	0.083***	0.099**	0.615***	0.002
	(0.011)	(0.049)	(0.032)	(0.201)
Panel B:				
Trial district × Trial period exposure - Age 1 to 2	−0.031	−0.033	0.383**	0.374**
	(0.034)	(0.034)	(0.162)	(0.158)
Trial district × Trial period exposure - Age 3 to 4	0.024	0.023	0.058	0.037
	(0.040)	(0.040)	(0.133)	(0.140)
Trial district × Trial period exposure - Age 5 to 6	−0.003	−0.007	0.025	−0.005
	(0.066)	(0.066)	(0.108)	(0.106)
Trial period exposure - Age 1 to 2	0.125***	0.104	0.898***	0.027
	(0.019)	(0.063)	(0.057)	(0.248)
Trial period exposure - Age 3 to 4	0.062***	0.012	0.540***	−0.121
	(0.019)	(0.079)	(0.053)	(0.247)
Trial period exposure - Age 5 to 6	0.072***	0.096	0.457***	−0.023
	(0.017)	(0.062)	(0.052)	(0.214)
Controls for:				
Gender	Yes	Yes	Yes	Yes
Month of birth FE	Yes	Yes	Yes	Yes
District of birth FE	Yes	Yes	Yes	Yes
School year of birth FE	No	Yes	No	Yes
N	95,774	95,774	96,148	96,148

Note: The explanatory variable of interest is an indicator for districts participating in the trial, interacted with the period of exposure (in years) to the vaccine trial period during the given age periods. We focus here on the trial targeting susceptible children up to age 10 or 12. Individuals born in trial districts targeting children up to age 2 are excluded from the sample. The sample was furthermore restricted to individuals born in a district with a population density within one standard deviation of the mean among the trial districts. Standard errors clustered at the district of birth level are shown in parentheses. Significance levels are indicated as follows: * $p<0.1$, ** $p<0.05$, *** $p<0.01$

◂ Back

Appendix: Heterogeneity by gender

Heterogeneity by gender: Long-term effects of the measles vaccine introduction

	Years of education				Height in cm			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A - Women:								
Post-vaccine share 1 to 6 × Pre-vacc. measles	0.271***	0.242***	0.045	−0.023	2.012***	1.990***	0.544*	−0.086
	(0.036)	(0.032)	(0.140)	(0.143)	(0.093)	(0.080)	(0.322)	(0.336)
N	94,380	94,346	94,346	94,346	94,715	94,682	94,682	94,682
Panel B - Men:								
Post-vaccine share 1 to 6 × Pre-vacc. measles	0.182***	0.138***	0.002	−0.048	1.990***	1.934***	0.227	0.165
	(0.035)	(0.029)	(0.130)	(0.138)	(0.094)	(0.093)	(0.424)	(0.391)
N	76,422	76,348	76,348	76,348	76,680	76,606	76,606	76,606
Controls for:								
Month of birth FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
District of birth FE	No	Yes	Yes	Yes	No	Yes	Yes	Yes
School year of birth FE	No	No	Yes	Yes	No	No	Yes	Yes
County-specific birthdate trend	No	No	No	Yes	No	No	No	Yes
Compulsory schooling 16	Yes	Yes	No	No	No	No	No	No
Compulsory schooling 16 × Pre-vacc. measles	Yes	Yes	Yes	Yes	No	No	No	No

Note: The explanatory variable of interest is the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program, interacted with the measles cases per 100 people prior to the vaccination program. Individuals born in districts that participated in the 1966 trial are excluded from the samples. Standard errors clustered at the district of birth level are shown in parentheses. Significance levels are indicated as follows: * $p<0.1$, ** $p<0.05$, *** $p<0.01$

Back

Appendix: Heterogeneity by gender

Heterogeneity of gene-environment interplay by gender: Long-term effects of the measles vaccine introduction

	Years of education				Height in cm			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A - Women:								
Post-vaccine share 1 to 6 × Pre-vacc. measles	0.289***	0.264***	0.132	0.072	2.027***	2.027***	0.331	−0.171
	(0.032)	(0.029)	(0.128)	(0.133)	(0.081)	(0.072)	(0.284)	(0.296)
PGI	0.677***	0.617***	0.618***	0.617***	3.129***	3.096***	3.100***	3.098***
	(0.012)	(0.011)	(0.011)	(0.010)	(0.020)	(0.020)	(0.020)	(0.020)
Post-vacc. share 1 to 6 × Pre-vacc. measles × PGI	0.016	0.008	0.007	0.008	0.105	0.127*	0.116*	0.119*
	(0.025)	(0.025)	(0.025)	(0.025)	(0.069)	(0.069)	(0.070)	(0.069)
N	94,066	94,032	94,032	94,032	94,399	94,366	94,366	94,366
Panel B - Men:								
Post-vaccine share 1 to 6 × Pre-vacc. measles	0.173***	0.149***	0.038	−0.066	1.992***	1.975***	0.177	0.132
	(0.030)	(0.027)	(0.123)	(0.132)	(0.073)	(0.070)	(0.343)	(0.330)
PGI	0.675***	0.613***	0.613***	0.613***	3.398***	3.368***	3.375***	3.374***
	(0.011)	(0.012)	(0.012)	(0.012)	(0.026)	(0.026)	(0.026)	(0.026)
Post-vacc. share 1 to 6 × Pre-vacc. measles × PGI	−0.032	−0.039	−0.040	−0.039	0.036	0.037	0.029	0.042
	(0.028)	(0.027)	(0.027)	(0.027)	(0.073)	(0.073)	(0.073)	(0.074)
N	76,092	76,018	76,018	76,018	76,351	76,277	76,277	76,277
Controls for:								
Month of birth FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
District of birth FE	No	Yes	Yes	Yes	No	Yes	Yes	Yes
School year of birth FE	No	No	Yes	Yes	No	No	Yes	Yes
County-specific birthdate trend	No	No	No	Yes	No	No	No	Yes
Compulsory schooling 16	Yes	Yes	No	No	No	No	No	No
Compulsory schooling 16 × Pre-vacc. measles	Yes	Yes	Yes	Yes	No	No	No	No
Comp. schooling 16 × Pre-vacc. measles × PGI	Yes	Yes	Yes	Yes	No	No	No	No
Principal components 1-20	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Note: The explanatory variable of interest is the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program, interacted with the measles cases per 100 people prior to the vaccination program. This measure of treatment intensity for the vaccine introduction is furthermore interacted with the polygenic index (PGI) for education (columns 1-4) / height (columns 5-8). The measure of genetic propensity for education is based on summary statistics from Lee et al. (2018), the measure for height is based on summary statistics from Wood et al. (2014). Individuals born in districts that participated in the 1966 trial are excluded from the samples. Standard errors clustered at the district of birth level are shown in parentheses. Significance levels are indicated as follows: * $p<0.1$, ** $p<0.05$, *** $p<0.01$

Back

Appendix: Robustness checks

Long-term effects of the measles vaccine introduction – Binary intensity measure

	Years of education				Height in cm			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A:								
Post-vacc. share 1 to 6 × High pre-vacc. measles	0.262***	0.208***	0.040	0.024	1.772***	2.059***	0.258**	0.115
	(0.035)	(0.029)	(0.048)	(0.046)	(0.090)	(0.077)	(0.121)	(0.123)
Panel B:								
Post-vacc. share 1 to 2 × High pre-vacc. measles	0.030	0.009	−0.042	−0.053	0.557***	0.475***	0.400*	0.348*
	(0.055)	(0.046)	(0.062)	(0.061)	(0.147)	(0.150)	(0.205)	(0.203)
Post-vacc. share 3 to 4 × High pre-vacc. measles	0.096*	0.066	0.005	0.004	−0.065	−0.205	−0.373*	−0.359*
	(0.050)	(0.049)	(0.065)	(0.065)	(0.153)	(0.149)	(0.205)	(0.205)
Post-vacc. share 5 to 6 × High pre-vacc. measles	0.112***	0.108***	0.054	0.048	1.150***	1.556***	0.330**	0.235*
	(0.036)	(0.035)	(0.049)	(0.049)	(0.116)	(0.101)	(0.137)	(0.136)
Controls for:								
Gender	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Month of birth FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
District of birth FE	No	Yes	Yes	Yes	No	Yes	Yes	Yes
School year of birth FE	No	No	Yes	Yes	No	No	Yes	Yes
County-specific birthdate trend	No	No	No	Yes	No	No	No	Yes
Compulsory schooling 16	Yes	Yes	No	No	No	No	No	No
Comp. schooling 16 × High pre-vacc. measles	Yes	Yes	Yes	Yes	No	No	No	No
N	170,802	170,778	170,778	170,778	171,395	171,370	171,370	171,370

Note: The explanatory variables of interest are the share of the given age periods during which the individual was exposed to the vaccination program, interacted with an indicator for above-median measles cases (per 100 people) prior to the vaccination program. Individuals born in districts that participated in the 1966 trial are excluded from the sample. Standard errors clustered at the district of birth level are shown in parentheses. Significance levels are indicated as follows: * $p<0.1$, ** $p<0.05$, *** $p<0.01$

Back

Appendix: Robustness checks

Gene-environment interplay: Long-term effects of the measles vaccine introduction – Sample split by PGI

	Years of education				Height in cm			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A - High PGI:								
Post-vaccine share 1 to 6 × Pre-vacc. measles	0.270***	0.229***	0.090	0.026	2.066***	2.069***	0.680**	0.462
	(0.033)	(0.030)	(0.140)	(0.133)	(0.083)	(0.075)	(0.334)	(0.347)
N	81,013	80,958	80,958	80,958	90,175	90,129	90,129	90,129
Panel B - Low PGI:								
Post-vacc. share 1 to 6 × Pre-vacc. measles	0.207***	0.179***	0.125	0.072	2.021***	2.003***	0.100	−0.352
	(0.035)	(0.031)	(0.145)	(0.150)	(0.084)	(0.077)	(0.354)	(0.329)
N	89,145	89,091	89,091	89,091	80,575	80,527	80,527	80,527
Controls for:								
Gender	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Month of birth FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
District of birth FE	No	Yes	Yes	Yes	No	Yes	Yes	Yes
School year of birth FE	No	No	Yes	Yes	No	No	Yes	Yes
County-specific birthdate trend	No	No	No	Yes	No	No	No	Yes
Compulsory schooling 16	Yes	Yes	No	No	No	No	No	No
Comp. schooling 16 × Pre-vacc. measles	Yes	Yes	Yes	Yes	No	No	No	No

Note: The explanatory variable of interest is the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program, interacted with the measles cases per 100 people prior to the vaccination program. Panel A is for the sub-sample with an above-median genetic propensity for education (columns 1-4) / height (columns 5-8), Panel B for the sub-sample with a below-median propensity. The measure of genetic propensity for education is based on summary statistics from Lee et al. (2018), the measure for height is based on summary statistics from Wood et al. (2014). Individuals born in districts that participated in the 1966 trial are excluded from the samples. Standard errors clustered at the district of birth level are shown in parentheses. Significance levels are indicated as follows: * $p<0.1$, ** $p<0.05$, *** $p<0.01$

Back

Appendix: Robustness checks

Gene-environment interplay: Long-term effects of the measles vaccine introduction – Sample split based on alternative PGI measures

	Years of education				Height in cm			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A - High PGI:								
Post-vaccine share 1 to 6 × Pre-vacc. measles	0.231***	0.198***	0.183	0.103	2.154***	2.156***	0.896***	0.684**
	(0.034)	(0.031)	(0.135)	(0.134)	(0.083)	(0.074)	(0.321)	(0.334)
N	81,091	81,044	81,044	81,044	87,246	87,201	87,201	87,201
Panel B - Low PGI:								
Post-vaccine share 1 to 6 × Pre-vacc. measles	0.225***	0.192***	0.015	−0.033	1.987***	1.950***	0.277	−0.122
	(0.033)	(0.029)	(0.138)	(0.140)	(0.079)	(0.073)	(0.324)	(0.303)
N	88,954	88,892	88,892	88,892	83,391	83,327	83,327	83,327
Controls for:								
Gender	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Month of birth FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
District of birth FE	No	Yes	Yes	Yes	No	Yes	Yes	Yes
School year of birth FE	No	No	Yes	Yes	No	No	Yes	Yes
County-specific birthdate trend	No	No	No	Yes	No	No	No	Yes
Compulsory schooling 16	Yes	Yes	No	No	No	No	No	No
Compulsory schooling 16 × Pre-vacc. measles	Yes	Yes	Yes	Yes	No	No	No	No

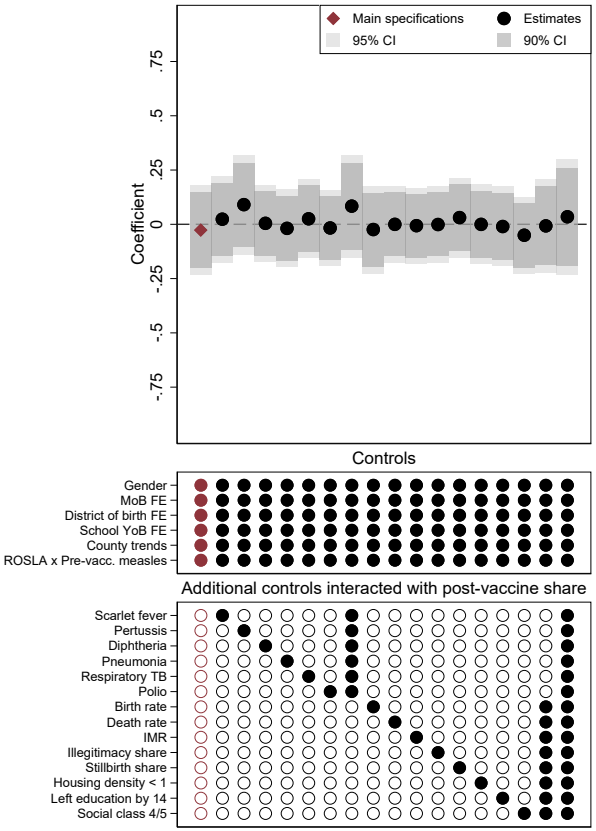
Note: The explanatory variable of interest is the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program, interacted with the measles cases per 100 people prior to the vaccination program. Panel A is for the sub-sample with an above-median genetic propensity for education (columns 1-4) / height (columns 5-8), Panel B for the sub-sample with a below-median propensity. The measures of genetic propensity are from Becker et al. (2021). Individuals born in districts that participated in the 1966 trial are excluded from the samples. Standard errors clustered at the district of birth level are shown in parentheses. Significance levels are indicated as follows: * $p<0.1$, ** $p<0.05$, *** $p<0.01$

Back

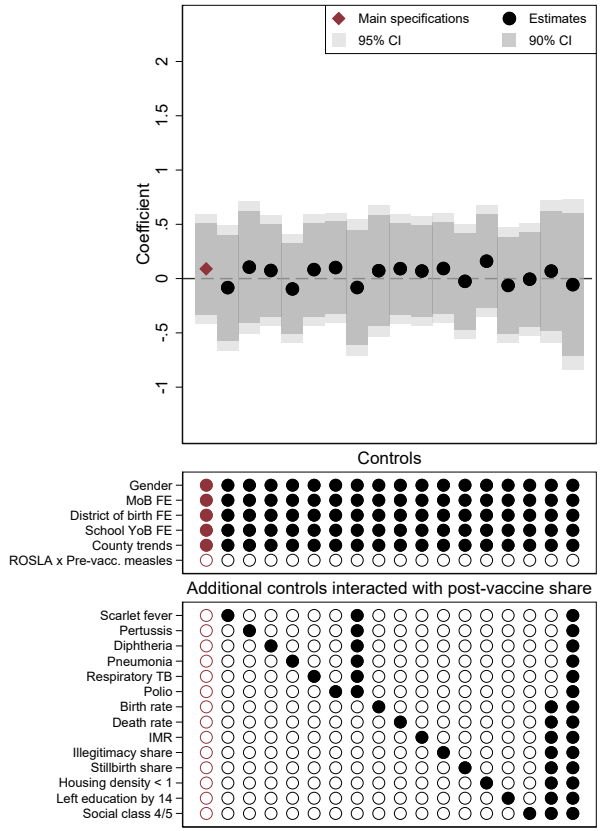
Appendix: Robustness checks

Robustness of results to inclusion of other pre-vaccination disease rates and socio-economic measures interacted with the post-vaccine share

(a) Years of education



(b) Height



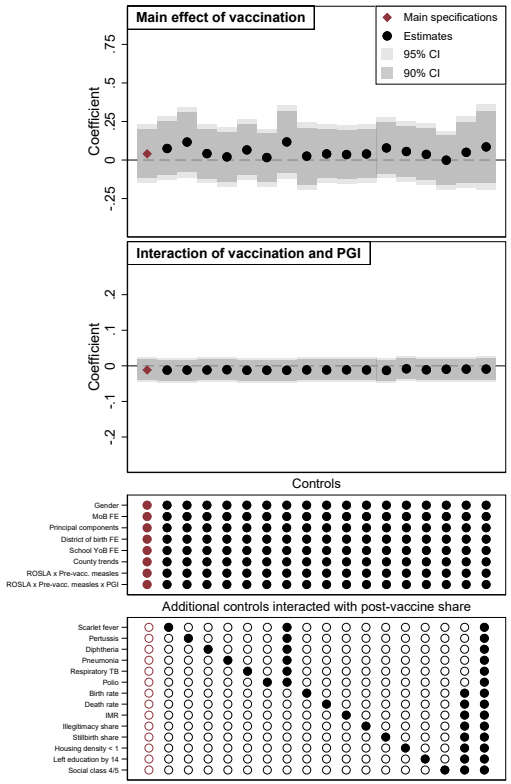
Note: The figure plots the estimated coefficient for the explanatory variable of interest, i.e. for the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program interacted with the measles cases per 100 people prior to the vaccination program. We focus on specifications (4) and (8) in our main results and include several pre-vaccination disease rates and socio-economic measures, all interacted with the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program.

Back

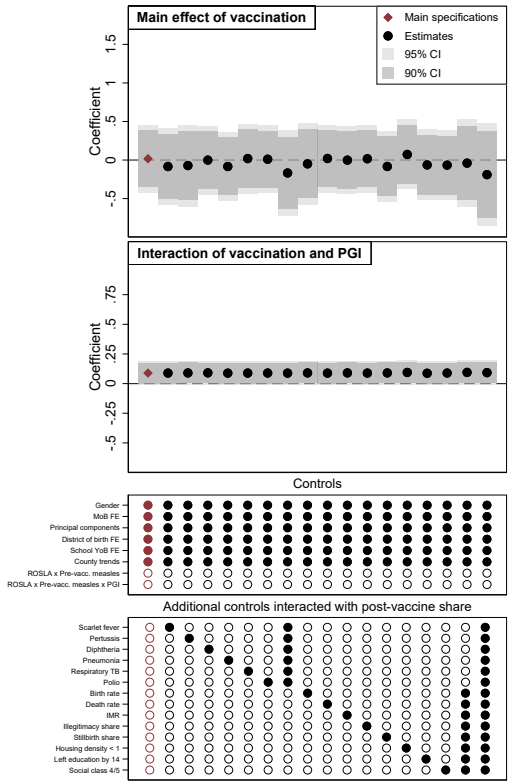
Appendix: Robustness checks

Robustness of GxE results to inclusion of other pre-vaccination disease rates and socio-economic measures interacted with the post-vaccine share

(a) Years of education



(b) Height



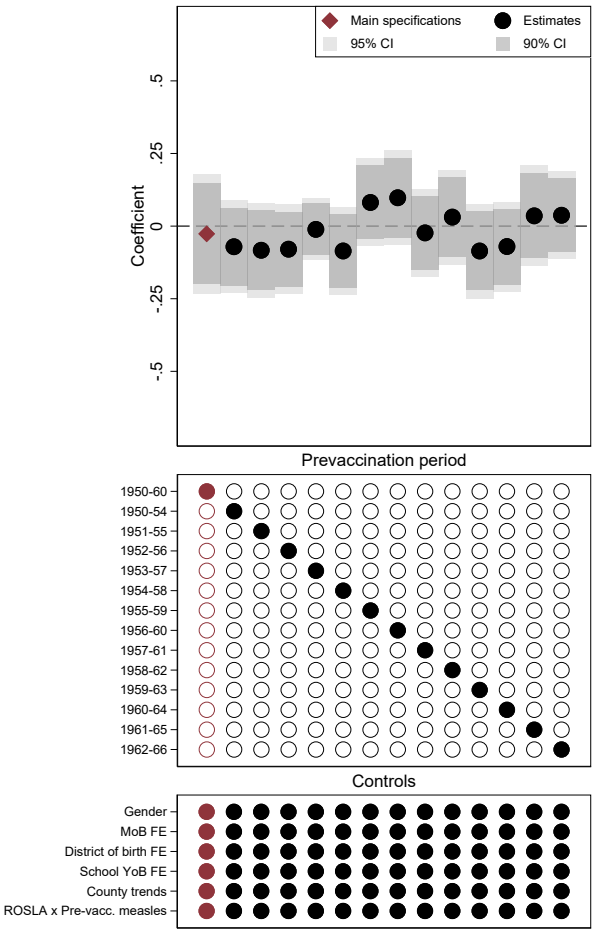
Note: The figure plots the estimated coefficients for the explanatory variables of interest, i.e. for the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program interacted with the measles cases per 100 people prior to the vaccination program and for its interaction with the PGI. We focus on specifications (4) and (8) in our main results and include several pre-vaccination disease rates and socio-economic measures, all interacted with the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program.

Back

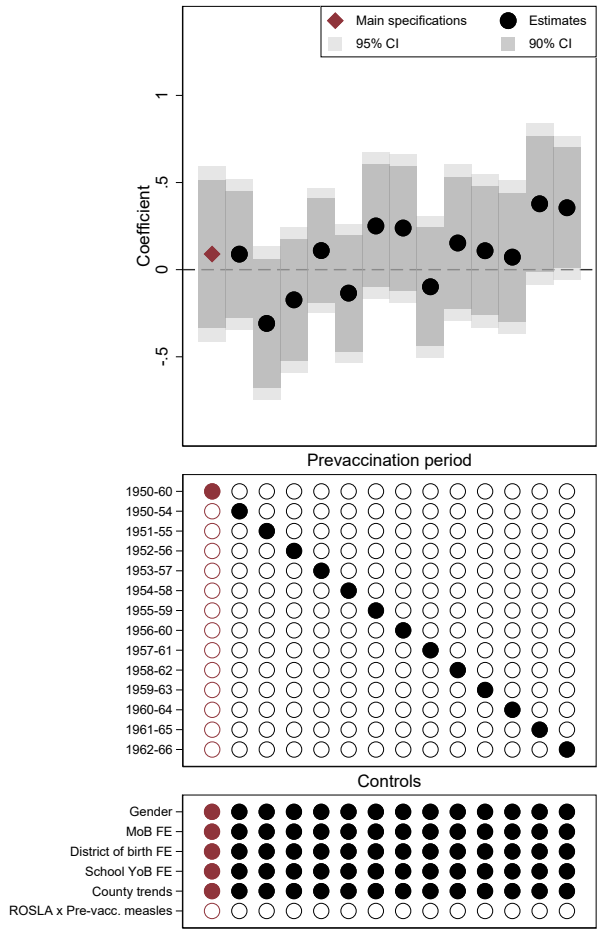
Appendix: Robustness checks

Robustness of results to the use of alternative pre-vaccination time windows

(a) Years of education



(b) Height



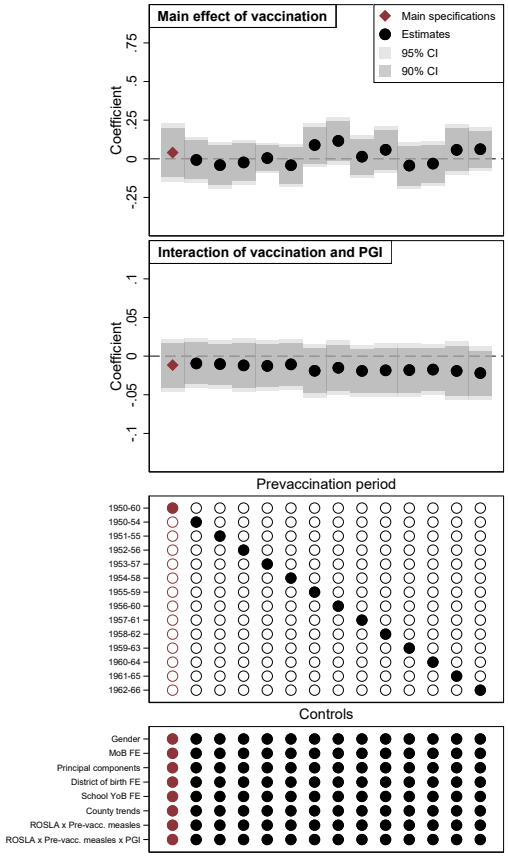
Note: The figure plots the estimated coefficient for the explanatory variable of interest, i.e. for the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program interacted with the measles cases per 100 people prior to the vaccination program. We focus on specifications (4) and (8) in our main results and use different time windows for the pre-vaccination measles rates.

Back

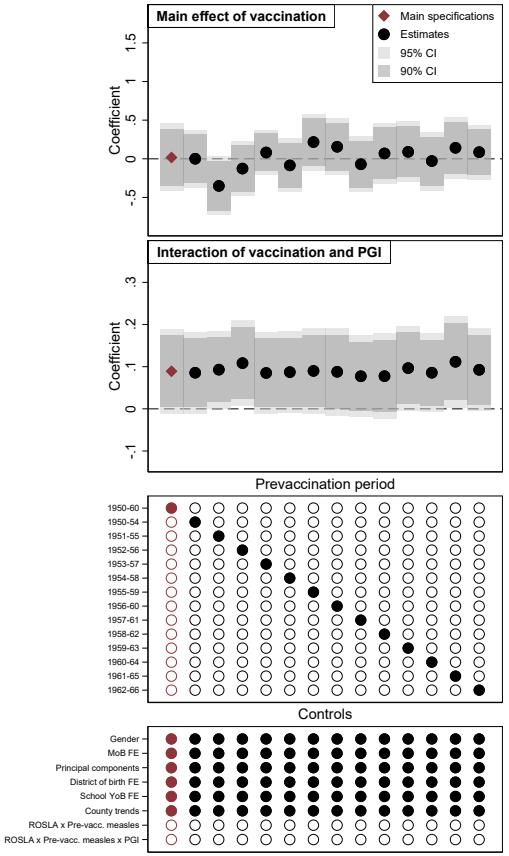
Appendix: Robustness checks

Robustness of GxE results to the use of alternative pre-vaccination time windows

(a) Years of education



(b) Height



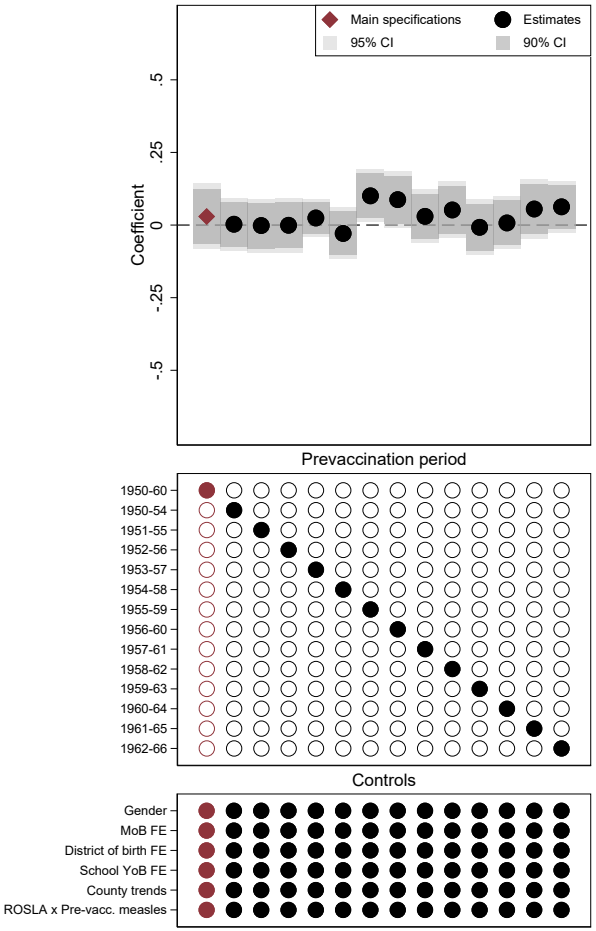
Note: The figure plots the estimated coefficients for the explanatory variables of interest, i.e. for the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program interacted with the measles cases per 100 people prior to the vaccination program and for its interaction with the PGI. We focus on specifications (4) and (8) in our main results and use different time windows for the pre-vaccination measles rates.

Back

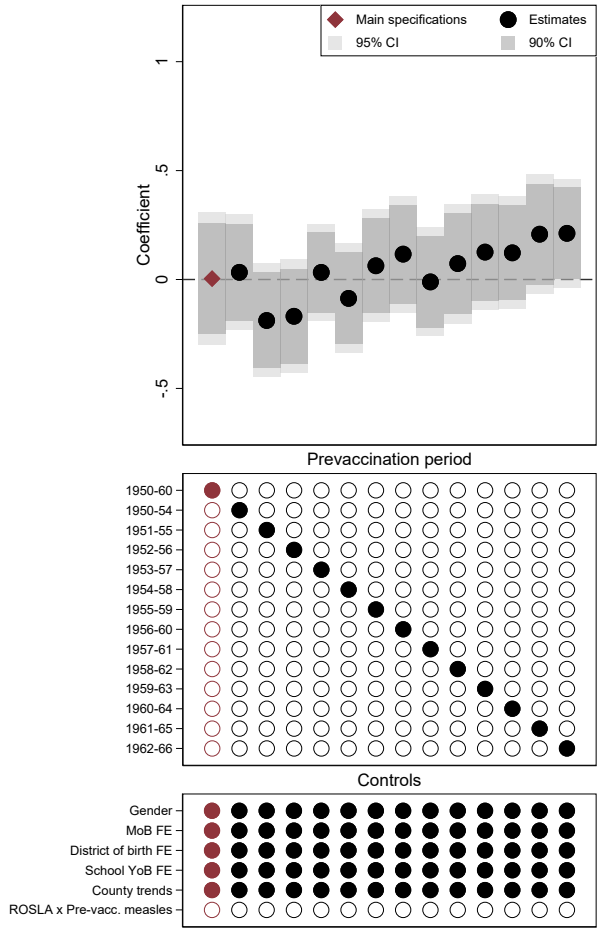
Appendix: Robustness checks

Robustness of results to the use of a binary measure of vaccine exposure

(a) Years of education



(b) Height



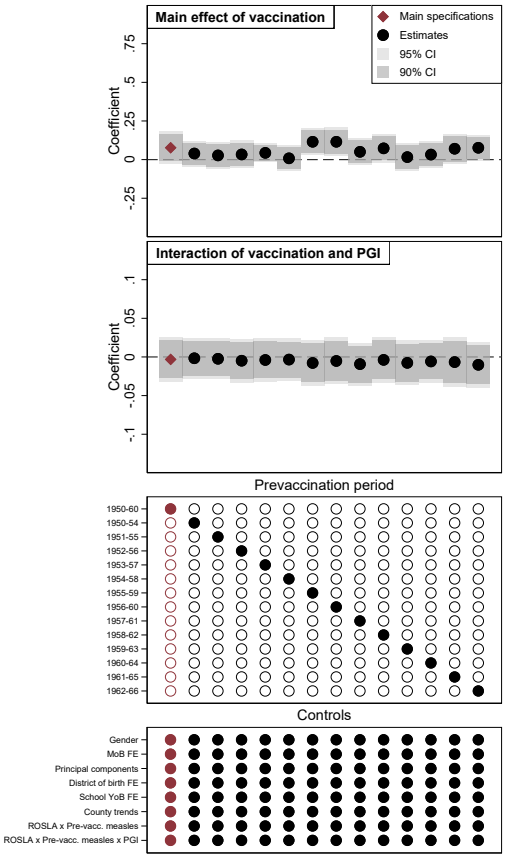
Note: The figure plots the estimated coefficient for an alternative variable of interest. Instead of the exposure share, we use a binary indicator for any exposure (of at least 1 month) to the vaccination program during ages 1 to 6 years, interacted with the measles cases per 100 people prior to the vaccination program. We focus on the equivalent of specifications (4) and (8) in our main results and explore different time windows for the pre-vaccination measles rates.

Back

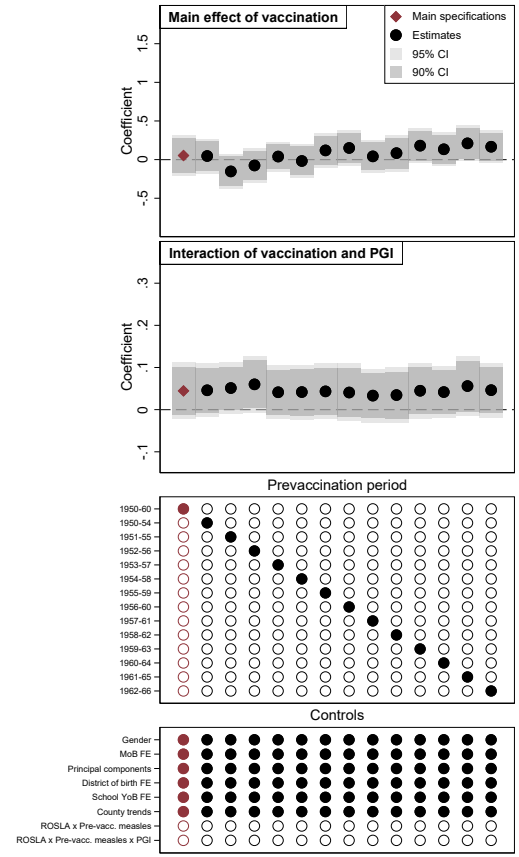
Appendix: Robustness checks

Robustness of GxE results to the use of a binary measure of vaccine exposure

(a) Years of education



(b) Height

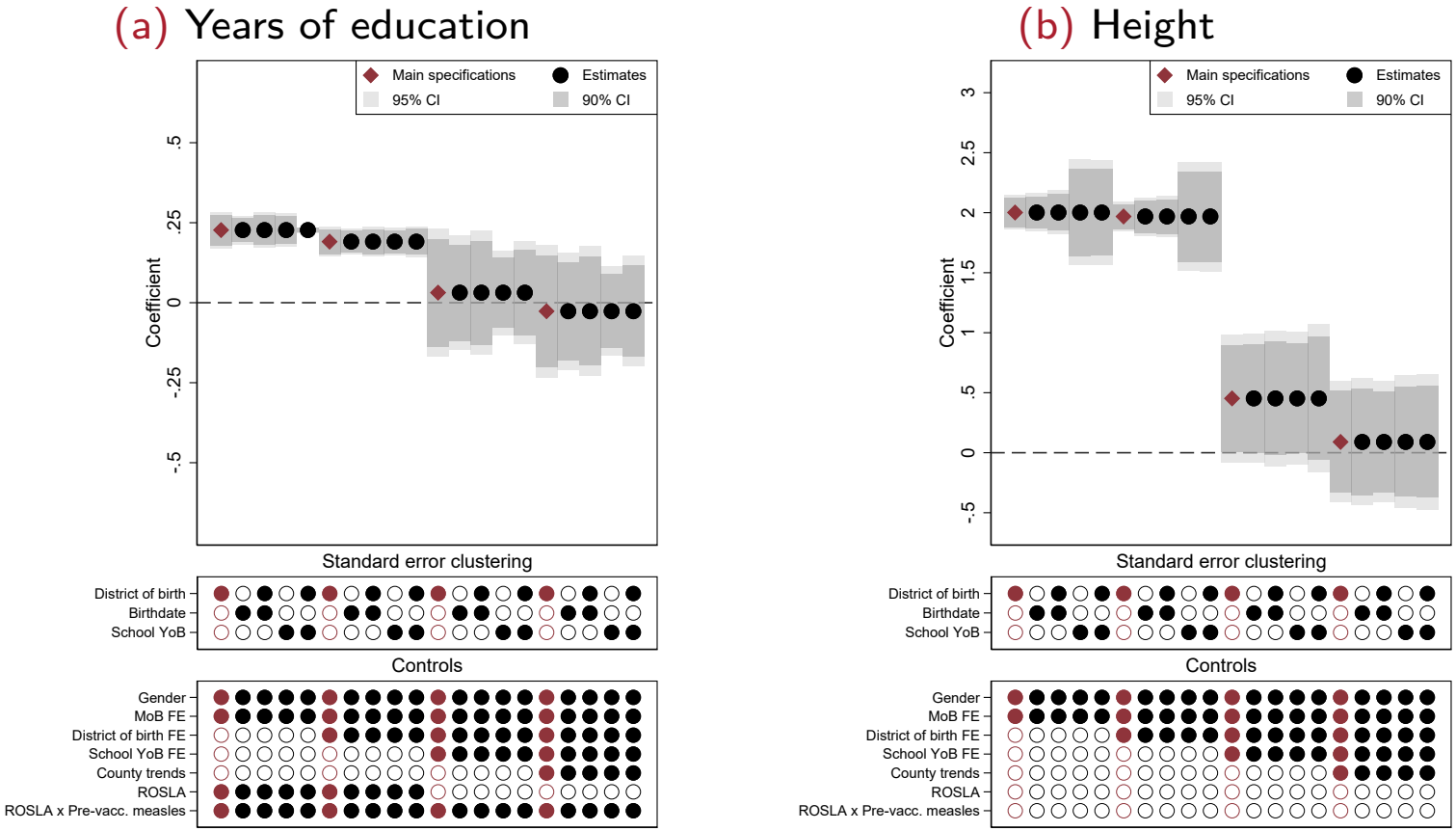


Note: The figure plots the estimated coefficients of interest for an alternative measure of exposure to the post-vaccination period. Instead of the exposure share, we use a binary indicator for any exposure (of at least 1 month) to the vaccination program during ages 1 to 6 years, interacted with the measles cases per 100 people prior to the vaccination program. This exposure measure is furthermore interacted with the PGI. We focus on the equivalent of specifications (4) and (8) in our main results and explore different time windows for the pre-vaccination measles rates.

Back

Appendix: Robustness checks

Robustness of results to different levels of standard error clustering



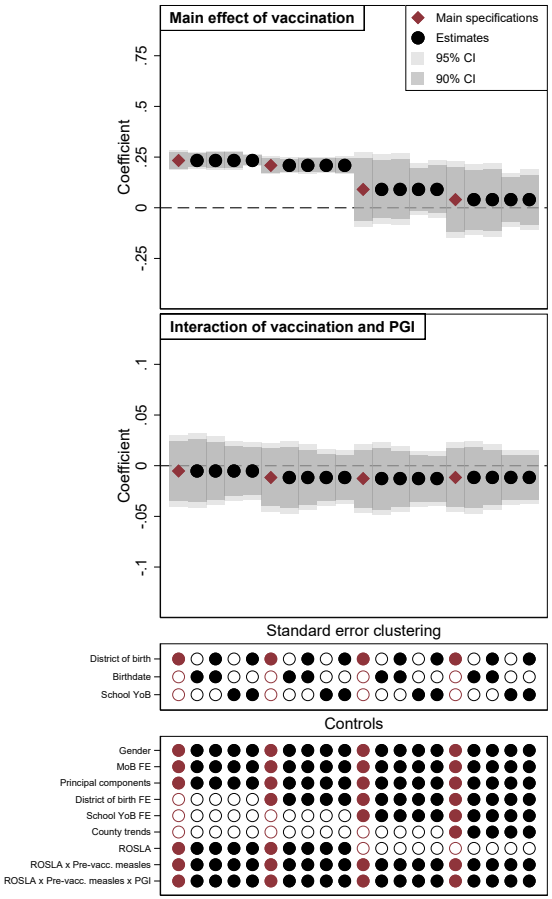
Note: The figure plots the estimated coefficient for the explanatory variable of interest, i.e. for the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program interacted with the measles cases per 100 people prior to the vaccination program.

Back

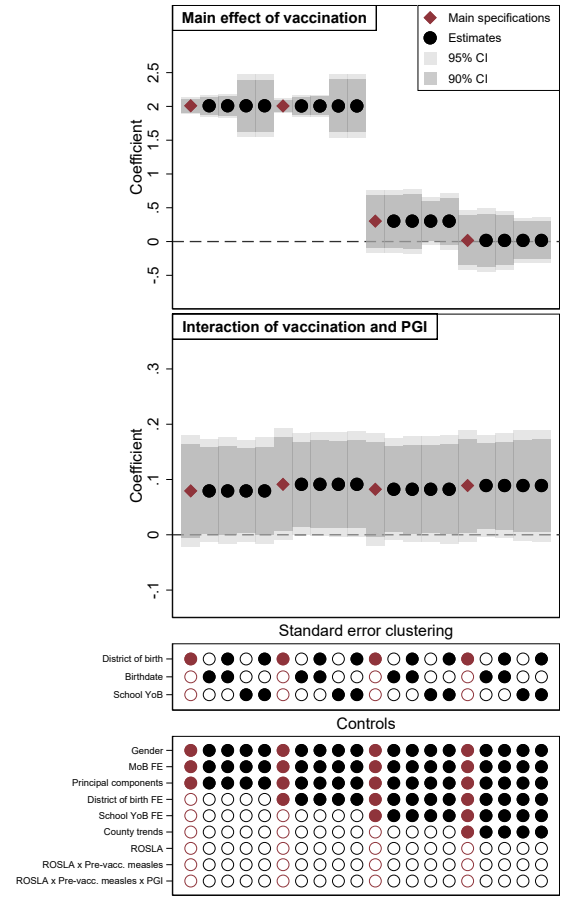
Appendix: Robustness checks

Robustness of GxE results to different levels of standard error clustering

(a) Years of education



(b) Height



Note: The figure plots the estimated coefficients for the explanatory variables of interest, i.e. for the share of the age period from 1 to 6 years during which the individual was exposed to the vaccination program interacted with the measles cases per 100 people prior to the vaccination program and for its interaction with the PGI.

Back