Progress in reaching unvaccinated (zero-dose) children in India, 1992–2016: a multilevel, geospatial analysis of repeated cross-sectional surveys

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Summary

Background Reaching zero-dose children (infants who receive no routine vaccinations) is a global strategic priority. We studied zero-dose children in India over 24 years to clarify aggregate trends and the contribution of large-scale social, economic, and geographical inequalities to these.

Methods We did a multilevel, geospatial analysis of repeated cross-sectional surveys of all four rounds (1992–2016) of India's National Family Health Survey to study the prevalence, distribution, and drivers of zero-dose (no first dose of diphtheria, tetanus, and pertussis) vaccination status. We included all children born to participating women who were aged 12–23 months at the time of the survey, as this is the standard age at which immunisation data are assessed. Children who died before the survey and those missing data on key outcomes or correlates were excluded. The outcome was child zero-dose vaccination status. We also compared the prevalence of nutritional deficits among zero-dose versus vaccinated children. For the most recent survey, we produced geospatial estimates identifying the prevalence of zero-dose children across states and districts and used these to project head count.

Findings We examined 393 167 children for eligibility. 72 848 children were included in the final analytic data set. The proportion of zero-dose children in India declined from 33·4% (95% CI 32·5–34·2) in 1992 to 10·1% (9·8–10·4) in 2016. Progress notwithstanding, in 2016, zero-dose children remained concentrated among disadvantaged groups (prevalence in the bottom wealth quintile 15·3%, 95% CI 14·6–16·0; prevalence among mothers with no education 16·8%, 16·1–17·4). Compared with vaccinated children, zero-dose children were more likely to suffer from malnutrition in all survey rounds (prevalence of severe stunting in 1992: zero dose 41·3%, 95% CI 39·2–43·8 *vs* vaccinated 28·5%, 27·2–29·7; 2016: zero dose 24·9%, 23·6–26·2 *vs* vaccinated 18·7%, 18·3–19·1). In 2016, there were an estimated 2·88 (95% CI 2·86–2·89) million zero-dose children in India, concentrated in less developed states and districts and several urban areas.

Interpretation Over a 24-year period in India, child zero-dose status was shaped by large-scale social inequalities and remained a consistent marker of generalised vulnerability. Interventions that address this cycle of intergenerational inequities should be prioritised.

Funding None.

Lancet Glob Health 2021; 9: e1697–706

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For the French translation of the abstract see **Online** for appendix 1

For the Spanish translation of the abstract see **Online** for appendix 2

For the Hindi translation of the abstract see **Online** for appendix 3

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Introduction

From 2000 to 2019, substantial increases in vaccination coverage in 98 low-income and middle-income countries substantially reduced mortality.[1] Yet, in 2019, approximately 14 million infants (aged <1 year) did not receive even a single dose of vaccine containing antigens against diphtheria, tetanus, and pertussis (DTP),[2] a crucial marker of access to routine immunisation.[3] These zero-dose infants are believed to be among the world's most vulnerable children.[4] The Immunization Agenda 2030 (IA2030), a new global strategy co-developed by WHO, countries, and partners and endorsed by the World Health Assembly in May, 2021, aims to reach zero-dose children and bring them sustainably into the routine immunisation system.[3]

The IA2030 strategic focus on zero-dose children raises new learning challenges. Emerging evidence suggests that zero-dose children belong to households and communities suffering from multiple, synergistic sources of disadvantage,[4] including social, political, economic, geographical, and health systems factors reflective of entrenched inequalities.[4] Causes could be highly heterogeneous, requiring a deep understanding of national and subnational contexts.[4]

India has the world's largest birth cohort and the second largest number of zero-dose children after Nigeria.[2] We analysed the situation of zero-dose children (aged <1 year) in India over two and a half decades to study overall trends and to elucidate how large-scale social, economic, and geographical inequalities

Research in context

Evidence before this study

We adopted a two-stage approach to identify published systematic reviews and primary research studies with quantitative information relevant to child non-vaccination, including its prevalence, risk factors, and characteristics. On Jan 26, 2020 (updated June 9, 2021), we searched three electronic databases (PubMed, LILACS, and Cochrane Library or Cochrane Database of Systematic Reviews) using structured combinations of keywords to identify candidate studies. For example, we searched PubMed using a combination the key terms: ("vaccin*"[MeSH Terms] OR "immuniz*"[MeSH Terms]) AND ("systematic review"[Publication Type]) AND ("incomplete" OR "non-vaccination" OR "under-vaccination" OR "under*" OR "unreached" OR "unvaccinated" OR "zero-dose" OR "zero"). The search was limited to systematic reviews; no date or language restrictions were applied. Database searches identified 452 records; three articles were suggested by experts. After eliminating 67 duplicates, 388 unique candidate systematic reviews were screened for relevance based on titles and abstracts. Of the 14 reviews retained for full-text screening, eight were excluded as they did not contain information about unvaccinated children. In total, six systematic reviews with information about unvaccinated children were included. We searched the bibliographies of the included systematic reviews to identify 26 primary studies. Experts and targeted database searching contributed an additional six primary studies. In total, we identified 38 published articles (six systematic reviews and 32 primary studies) with quantitative information about unvaccinated children. Unvaccinated children have been little studied. Most primary research studies described the prevalence of non-vaccination in a given sample. A multilevel analysis of risk factors for non-vaccination in India highlighted the multiple risks shaping zero-dose status. An analysis of the immunisation cascade in 92 low-income and middle-income countries based on household survey data showed the importance of reaching zero-dose children with immunisation, as those reached with the first vaccine are highly likely also to receive remaining vaccines.

Added value of this study

To our knowledge, this is the first study to trace aggregate patterns in the situation of zero-dose children over time globally and in India. Over the 24-year analysis timeframe, the proportion of zero dose-children in India declined by 23·3% in absolute terms, with more rapid reductions among the worst off. Despite impressive progress, zero-dose children continue to be concentrated among socially disadvantaged groups, including rural households, poorer households, Muslims, mothers with less education, and mothers with inadequate patterns of health services use during pregnancy. In multilevel regression analyses, child zero-dose status was associated with multiple, overlapping markers of household, maternal, and child disadvantage. Gender-related factors, including low maternal education and low utilisation of key maternal health services, remained salient determinants throughout the analysis timeframe. Zero-dose children were more likely to experience early childhood nutritional failures linked to poor growth trajectories and outcomes over the life course. In 2015–16, there were an estimated 2·88 million zero-dose children in India, concentrated in lagging states and districts. Their highly heterogeneous spatial distribution, with substantial variations across urban and rural settings, states, and districts, underscores the need for subnational prioritisation and tailored responses.

Implications of all the available evidence

Evidence from India suggests that child zero-dose vaccination status is an important marker of generalised vulnerability; further research should be done in other settings. Interventions that address the complex causes of disadvantage faced by zero-dose children could disrupt the cycle of intergenerational inequities and should be prioritised.

contribute to child zero-dose status.[5] Specifically, we did repeated cross-sectional analyses using four waves of nationally representative microdata to study aggregate trends in the prevalence, distribution, and drivers of zero-dose vaccination status and investigated potential differences in nutritional deficits for zero-dose versus vaccinated children indicative of cumulative disadvantage across the life course. For the most recent survey round, we produced geospatial estimates of the prevalence and headcount of zero-dose children across Indian states and districts to inform tailored policy actions.

See Online for appendix 4

Methods

Study design and participants

We did a multilevel, geospatial analysis of repeated cross-sectional surveys of all four waves of India's National Family Health Survey (NFHS) covering a 24-year timeframe from 1992 to 2016. This study is based on publicly available, anonymised data and was considered exempt from the requirement for research ethics review by the Comité d'éthique de la recherche en sciences et en santé (CERSES), Université de Montréal. Mothers participating in the NFHS surveys provided written informed consent.

Part of the Demographic and Health Surveys (DHS) programme, the NFHS surveys employ a multi-stage, stratified cluster-sampling design (appendix 4 p 2). Microdata from four survey rounds are currently available through the DHS and were used in this study. All four NFHS surveys covered geographical areas comprising more than 99% of India's population. District-level representation was first achieved in the NFHS-4 (2015–16), which derived a representative sample for all 640 districts within India's 29 states and seven union territories.[6] Due to substantial differences in the design and methods, and the much finer degree of representation achieved, the NFHS-4 survey is not strictly comparable to the earlier survey rounds.[6]

We constructed an analysis sample from the four NFHS survey rounds. We included all children born to participating women who were aged 12–23 months at the time of the survey, as this is the standard age at which immunisation data are assessed. We excluded children who died before the survey was done and those missing data on key outcomes or correlates. Appendix 4 (pp 4–5) describes the construction of the analytic samples used to study trends in the prevalence, distribution, and drivers of zero-dose status, and nutritional outcomes, respectively.

Outcomes

The outcome was child zero-dose vaccination status. IA2030 defines zero-dose children as those who lack access to or are never reached by routine immunisation services.[3] We defined the main study outcome as a binary variable using the proposed IA2030 monitoring definition, which deems all surviving children aged 12–23 months who did not receive the first dose of DTP-containing vaccine (DTP1) as zero dose, and those who receive DTP1 are considered as vaccinated.[7]

The NFHS surveys collected vaccination data through a standardised procedure implemented by trained field personnel. The child's primary caregiver (usually the mother) was interviewed and requested to provide the child's vaccination record. If available, vaccination data were transcribed from the card. If the card was not available at the time of the interview, vaccination data were taken by caregiver report, ignoring the child's age at vaccination. Vaccination information was collected for the last two (NFHS-2) or three (NFHS-1, NFHS-3, NFHS-4) children born within a defined window period and alive at the time of the interview.[6,8–10]

Correlates

Variables of interest were identified through the scientific literature,[11] including relevant systematic reviews[12,13] and organised following a conceptual framework describing the socioeconomic determinants of child health equity (appendix 4 p 6).[14] We retained all candidate variables with a low proportion of missing data across all or most NFHS rounds.

Household area of residence was categorised as urban or rural according to the national census for the relevant survey round. All NFHS surveys include asset quintiles as a proxy for economic status; we used these variables in our analysis. As done in recent NFHS reports, we constructed a variable for mother's education from self-reported years of schooling grouped into categories.[6,10] Social group was based on maternal self-report and presented following classifications used by the Government of India to promote the development of historically disadvantaged communities. There were three socially or educationally disadvantaged groups (scheduled tribes, scheduled castes, and other backwards castes), and one residual group (other) comprising individuals with no disadvantaging characteristics. Religion was reported by the household head and classified into three categories: Hindu, Muslim, and any other religion. Use of antenatal care services and place of delivery were ascertained through maternal self-reporting.

Anthropometry data were collected by trained interviewers using standard procedures.[15] Age was taken from the birth history reported by the mother or from another knowledgeable adult. Height (recumbent length in children aged <24 months) was measured to the nearest 0·1 cm using a measuring board. Weight was measured using a UNICEF Uniscale (Unicef Supply Division, Denmark) for NFHS-1 to NFHS-3 or a Seca digital scale (Seca, Germany) for NFHS-4, accurate to within 100 grams.[6,8–10] We classified children as moderately stunted, underweight, or wasted if the relevant Z score (height for age, weight for age, and weight for height, respectively) was less than –2 SD (severely so if <–3 SD) from the WHO Multicenter Growth Reference Study population for children of their age and sex.[15]

Statistical analysis

We did repeated cross-sectional analyses covering all four survey rounds to examine aggregate trends; and geospatial analyses focusing on the most recent (NFHS-4) survey to identify high-burden districts. A repeated cross-sectional design was chosen due to the substantial variations in survey size, design, and sampling approach across the four NFHS rounds. Geospatial analyses focused on the NFHS-4 as it is the most recent survey and is representative at the district level (appendix 4 pp 2–3).[6]

Repeated cross-sectional analyses

For each survey round, we estimated the prevalence of zero-dose children as a percentage of all children in the population. We also estimated zero-dose prevalence according to selected sociodemographic and health service delivery characteristics. All prevalence estimates were weighted, and error terms adjusted for the complex survey design. For the same set of characteristics, we compared the distribution of zero-dose children with all children, applying weights to account for the sampling design. To examine absolute trends in zero-dose prevalence, we computed the percentage change between surveys divided by the number of years between surveys. To examine relative trends, we calculated the average annualised rate of decline (AARD) using the equation:[16]

$$AARD\ (\%) = ln\left(\frac{initial\ (NFHS-1) prevalence}{final\ (NFHS-4) prevalence}\right) * 100 * \left(\frac{1}{number\ of\ years\ between\ surveys}\right)$$

To assess whether India is on track to meet the IA2030 zero-dose target of a 50% reduction in 2030 zero-dose prevalence from 2019 levels, we used the equation:[16]

$$2030 \text{ prevalence } (\%) = \textit{final } (NFHS-4) \textit{ prevalence} * [1-(0\cdot01*AARD)]^n$$

Where n represents the number of years between the NFHS-4 survey and 2030.

To define the drivers of zero-dose status, we fit random effects regression models to estimate the relationship between a set of explanatory variables and a binary response variable representing child zero-dose status. Multilevel models were used due to the nested (non-independent) data structure. For each survey round, we examined correlates individually and implemented a full model including all explanatory variables. We explored possible interactions between area of residence and each of the other explanatory variables. Each model included all main effects and a single interaction term; these models were dropped due to multicollinearity. To account efficiently for the hierarchical data structure specific to each survey, for the first three NFHS rounds, we included random intercepts for primary sampling

	NFHS-1 (1992–93)			NFHS-2 (1998–99)			NFHS-3 (2005–06)			NFHS-4 (2015–16)		
	Survey sample (N)	Zero dose (national)*		Survey sample (N)	Zero dose (national)*		Survey sample (N)	Zero dose (national)*		Survey sample (N)	Zero dose (national)*	
		%	95% CI		%	95% CI		%	95% CI		%	95% CI
All children	11 489	33·4%	32·5–34·2	9201	26·4%	25·5–27·3	8457	23·9%	22·9–24·7	43 701	10·1%	9·8–10·4
Place of residence												
Urban	3147	19·4%	17·9–20·7	2486	12·5%	11·4–13·9	3233	15·4%	14·0–16·5	10 558	9·3%	8·7–9·8
Rural	8342	37·5%	36·5–38·6	6715	30·5%	29·4–31·6	5224	26·8%	24·8–27·2	33 143	10·4%	10·1–10·7
Wealth quintile												
WQ5 (top)	2223	9·4%)	8·2–10·7	1813	4·9%	4·0–6·0	1855	6·0%	4·6–6·8	6227	6·4%	5·7–7·0
WQ1 (bottom)	2123	51·0%	48·9–53·2	1612	43·1%	40·2–45·0	1488	39·8%	36·6–41·7	11 303	15·3%	14·6–16·0
WQ2	2057	43·2%	41·1–45·3	1753	38·0%	35·7–40·2	1563	29·3%	26·2–30·8	9920	11·1%	10·4–11·7
WQ3	3401	34·7%	32·8–36·6	1953	24·4%	22·5–26·3	1697	20·8%	18·5–22·4	8826	8·5%	7·9–9·1
WQ4	2685	21·1%	19·5–22·6	2070	14·2%	14·7–15·7	1854	13·3%	11·6–14·7	7425	6·8%	6·2–7·3
Mother's education												
≥12 years complete	438	1·9%	0·6–3·1	457	1·8%	0·6–3·1	718	3·1%	1·8–4·3	4644	5·0%	0·4–5·6
No schooling	6688	45·3%	44·1–46·4	4502	40·5%	38·9–41·7	3276	38·5%	35·9–39·3	12 542	16·8%	16·1–17·4
<5 years complete	1533	19·9%	17·9–21·9	1416	19·5%	17·4–21·5	1170	18·5%	16·2–20·7	6145	10·1%	9·3–10·8
5–9 years complete	2449	11·0%	9·7–12·2	2405	8·7%	7·6–9·8	2677	8·6%	7·5–9·6	15 799	7·8%	7·3–8·1
10–11 years complete	381	3·3%	1·4–5·0	421	3·7%	1·9–5·5	616	3·7%	2·2–5·2	4571	6·5%	5·7–7·1
Child's sex												
Male	5877	31·3%	30·2–32·6	4805	24·9%	23·7–26·1	4509	21·5%	20·3–22·7	22 943	10·1%	9·7–10·4
Female	5612	35·5%	34·2–36·7	4396	27·9%	26·6–29·2	3948	26·6%	25·2–27·9	20 758	10·1%	9·7–10·5
Social group												
Other	8597	30·4%	29·4–31·4	3470	20·9%	19·5–22·2	2734	17·3%	15·8–18·6	8219	10·4%	9·7–11·1
Other backwards castes	..	..	..	2604	25·4%	23·6–26·9	2789	25·4%	23·7–26·9	17 895	9·9%	9·4–10·2
Schedule castes	1413	41·3%	38·6–43·8	1750	29·9%	27·7–32·0	1500	25·7%	23·5–27·9	8521	9·2%	8·5–9·7
Schedule tribes	1479	46·8%	44·4–49·5	1377	42·7%	39·7–44·9	1434	33·4%	30·9–35·8	9066	12·6%	11·8–13·3
Religion												
Hindu	8732	32·0%	31·0–33·0	6825	26·1%	25·0–27·0	5966	22·2%	21·1–23·2	32 296	8·9%	8·6–9·2
Muslim	1519	44·9%	42·4–47·3	1293	33·0%	30·5–36·6	1259	34·5%	31·8–37·1	5967	16·8%	15·8–17·7
Any other	1238	20·7%	18·6–23·2	1083	13·4%	11·3–15·3	1232	16·7%	14·6–18·8	5438	8·6%	7·8–9·3
≥4 antenatal care visits												
Yes	3558	9·2%	8·2–10·1	3162	6·3%	5·4–7·1	3742	7·0%	6·2–7·8	20 325	6·1%	5·7–6·4
No	7931	43·0%	41·9–44·0	6039	31·2%	34·9–37·3	4715	33·4%	32·1–34·8	23 376	14·3%	13·8–14·7
Institutional birth												
Yes	3283	11·1%	9·9–12·1	3426	9·1%	8·2–10·1	3941	9·2%	8·3–10·1	34 447	7·8%	7·5–8·1
No	8206	41·4%	40·3–42·4	5775	36·5%	35·2–37·7	4516	33·8%	32·4–35·2	9254	20·8%	20·0–21·6

Data are n, %, or 95% CI. NFHS=National Family Health Survey. *Nationally representative estimates of zero-dose prevalence computed from the survey sample.

Table 1: **Prevalence of zero-dose children (aged 12–23 months) by selected sociodemographic and health service delivery characteristics, India, 1992–2016**

	NFHS-1 (1992–93)		NFHS-2 (1998–99)		NFHS-3 (2005–06)		NFHS-4 (2015–16)	
	Zero dose	Population proportion	Zero dose	Population proportion	Zero dose	Population proportion	Zero dose	Population proportion
Place of residence								
Urban	13·3%	22·9%	11·0%	76·9%	16·9%	26·2%	25·9%	28·3%
Rural	86·7%	77·1%	89·0%	23·1%	83·1%	73·8%	74·1%	71·7%
Wealth quintile								
WQ5 (top)	4·4%	15·5%	3·0%	16·1%	3·9%	15·6%	9·5%	15·1%
WQ1 (bottom)	33·9%	22·2%	36·1%	22·1%	41·8%	25·1%	37·4%	24·7%
WQ2	26·5%	20·5%	31·5%	21·9%	27·4%	22·3%	12·4%	21·4%
WQ3	22·3%	21·5%	19·0%	20·6%	17·2%	19·7%	17·0%	20·2%
WQ4	12·8%	20·3%	10·4%	19·3%	9·7%	17·3%	12·6%	18·7%
Mother's education								
≥12 years complete	0·2%	3·1%	0·4%	4·3%	0·7%	5·7%	5·8%	11·7%
No schooling	86·2%	63·6%	79·9%	52·1%	78·4%	48·6%	46·1%	27·8%
<5 years complete	7·3%	12·1%	11·2%	15·1%	10·4%	13·4%	13·7%	13·8%
5–9 years complete	6·1%	18·3%	7·9%	24·0%	9·7%	26·9%	27·5%	35·9%
10–11 years complete	0·3%	2·9%	0·6%	4·5%	0·8%	5·3%	6·9%	10·8%
Child sex								
Male	47·9%	51·1%	48·1%	51·0%	48·7%	53·9%	52·4%	52·5%
Female	52·1%	48·9%	51·9%	49·0%	51·3%	46·1%	47·6%	47·5%
Social group								
Other	70·8%	77·6%	29·5%	37·2%	21·1%	29·1%	21·9%	21·2%
Other backward castes	..	..	31·2%	32·3%	42·8%	40·3%	44·7%	45·9%
Schedule castes	16·2%	13·1%	23·6%	20·8%	22·6%	20·9%	20·1%	22·2%
Schedule tribes	13·1%	9·3%	15·8%	9·8%	13·6%	9·7%	13·3%	10·7%
Religion								
Hindu	76·6%	79·9%	78·5%	79·5%	73·8%	79·4%	70·8%	80·1%
Muslim	20·1%	14·9%	14·9%	15·0%	22·8%	15·8%	25·1%	15·1%
Any other	3·3%	5·2%	5·6%	5·5%	3·4%	4·8%	4·1%	4·8%
≥4 antenatal care visits								
Yes	7·8%	28·3%	8·0%	33·2%	10·7%	36·2%	30·4%	50·7%
No	92·2%	71·7%	92·0%	66·8%	89·3%	63·8%	69·6%	49·3%
Institutional birth								
Yes	8·7%	26·3%	12·8%	36·8%	15·5%	40·4%	63·6%	82·3%
No	91·3%	73·7%	87·2%	63·2%	84·5%	59·6%	36·4%	17·7%

Data are %. NFHS=National Family Health Survey.

Table 2: **Distribution of zero-dose children (aged 12–23 months) by selected sociodemographic and health service delivery characteristics, India, 1992–2016**

unit (PSU) and state. For the NFHS-4 model, we included random intercepts for PSU, district, and state. The estimated odds ratios (ORs) and 95% CIs account for survey weights and survey design characteristics, including geographical clustering of respondents.

To identify nutritional deficiencies among zero-dose versus vaccinated children, for each survey round, we estimated the prevalence of stunting, underweight, and wasting among zero-dose versus vaccinated children overall, and within strata defined by area of residence (urban or rural) and child sex (boy or girl). Analyses were done separately for moderate and severe nutritional deficiencies. All prevalence estimates were weighted using the state household weight to adjust for the complex survey design.

Geospatial analyses

For the most recently available survey (NFHS-4) round, we generated crude estimates of mean child zero-dose prevalence by district and their standard errors. Models to estimate district-level prevalence were fit for a binary outcome on a sample of children aged 12–23 months. Survey weights were applied to adjust for the multistage survey design. To compute the absolute headcount of zero-dose children for a given district, we multiplied the mean district prevalence ratio by the total child population 12–23 months in that district. To derive the population of children aged 12–23 months by district, we calculated the district proportion of children in this age group from the 2015–16 NFHS-4 survey[6] and applied it to the 2016 district-level population estimates of children

	NFHS-1 (1992–93)		NFHS-2 (1998–99)		NFHS-3 (2005–06)		NFHS-4 (2015–16)	
	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI
Place of residence								
Urban*	1·00	··	1·00	··	1·00	··	1·00	··
Rural	1·14	0·98–1·32	1·18	0·99–1·41	1·50†	1·23–1·82	1·22†	1·11–1·35
Wealth quintile								
WQ5 (top)*	1·00	··	1·00	··	1·00	··	1·00	··
WQ1 (bottom)	2·90†	2·30–3·65	3·67†	2·70–4·97	2·55†	1·80–3·61	2·03†	1·71–2·41
WQ2	2·60†	2·08–3·25	3·17†	2·37–4·24	1·92†	1·38–2·68	1·50†	1·28–1·77
WQ3	1·99†	1·60–2·46	2·15†	1·63–2·84	1·48†	1·08–2·03	1·30†	1·11–1·52
WQ4	1·41†	1·15–1·72	1·60†	1·23–2·09	1·24†	0·92–1·68	1·13†	0·96–1·32
Mother's education								
≥12 years complete*	1·00	··	1·00	··	1·00	··	1·00	··
No schooling	6·30†	3·24–12·27	7·49†	3·34–16·83	6·09†	3·24–11·44	1·84†	1·55–2·19
<5 years complete	3·77†	1·93–7·37	5·29†	2·35–11·92	4·39†	2·32–8·30	1·33†	1·11–1·59
5–9 years complete	2·81†	1·45–5·46	3·80†	1·70–8·49	2·73†	1·47–5·07	1·22‡	1·03–1·43
10–11 years complete	1·44	0·64–3·23	2·35	0·94–5·88	1·86†	0·91–3·79	1·05	0·86–1·27
Child's sex								
Male*	1·00	··	1·00	··	1·00	··	1·00	··
Female	1·30†	1·19–1·42	1·15‡	1·03–1·28	1·16†	1·01–1·32	1·01	0·94–1·07
Social group								
Other*	1·00	··	1·00	··	1·00	··	1·00	··
Schedule caste	1·28†	1·12–1·47	1·07	0·90–1·27	1·01	0·81–1·28	0·89	0·79–1·00
Schedule tribe	1·45†	1·22–1·71	1·56†	1·27–1·91	1·56†	1·20–2·02	1·07	0·95–1·22
Other backward castes	··	··	0·91	0·78–1·07	1·13	0·92–1·38	0·94	0·85–1·04
Religion								
Hindu*	1·00	··	1·00	··	1·00	··	1·00	··
Muslim	2·15†	1·86–2·48	1·59†	1·33–1·90	1·93†	1·58–2·37	1·72†	1·57–1·89
Any other	0·98	0·77–1·24	0·81	0·62–1·07	1·24	0·92–1·67	1·13	0·96–1·34
≥4 antenatal visits								
Yes*	1·00	··	1·00	··	1·00	··	1·00	··
No	2·48†	2·16–2·84	2·13†	1·80–2·53	2·07†	1·71–2·49	1·89†	1·75–2·05
Institutional birth								
Yes*	1·00	··	1·00	··	1·00	··	1·00	··
No	1·51†	1·31–1·75	1·35†	1·16–1·57	1·61†	1·34–1·93	2·07†	1·92–2·22

Data are aOR or 95% CI. aORs from 3-level (NFHS 1, 2, and 3) multilevel logistic regression models adjusted for state-level and PSU-level random effects, and 4-level (NFHS-4) multilevel logistic regression models adjusted for state, district, and PSU level random effects. To derive aORs, models were simultaneously adjusted for all correlates in the table. aOR=adjusted odds ratio. NFHS=National Family Health Survey. PSU=primary sampling unit. *Reference category. †p<0·001. ‡p<0·01.

Table 3: **Sociodemographic and health systems drivers of zero-dose status among children (aged 12–23 months), India, 1992–2016**

aged 0–48 months from the DHS spatial data repository.[17] The total number of districts as per DHS 2016 was 674, and the contemporaneous NFHS-4, based on the earlier census 2011 framework, consisted of 640 districts. To harmonise the district information, the 34 districts newly formed between 2011 and 2016 were merged with their respective parent districts.[18] We computed CIs for the mean using SEs.

As the new IA2030 definition of zero-dose children based on non-receipt of DTP1 vaccine is a proxy primarily designed for monitoring and cross-country comparisons,[7] we did a sensitivity analysis to assess the robustness of our findings. We repeated all analyses using a more precise definition of children who receive no routine vaccinations tailored to the Indian context (appendix 4 p 7). We also re-estimated prevalence using a wider (12 months to the maximum available) child age range.

Analyses were done and validated by two authors (SR and MJ). All analyses were done on a complete case dataset within the Stata (version 16) statistical software environment.[19] Missing values were not imputed. Multilevel modelling was done using the MLwiN 2.28 software programme[20] accessed via Stata's runmlwin command.[21]

Role of the funding source

There was no funding source for this study.

Results

We examined 393 167 children (aged <5 years) for eligibility; the final analytic data set for zero-dose prevalence, trends, and drivers included 72 848 children over the four cross-sectional survey rounds (appendix 4 p 4). Participation rates for the NFHS surveys typically exceeded 95%, ranging from 95·6% (NFHS-1) to 97·7% (NFHS-3) for households, and 94·5% (NFHS-3) to 96·7% (NFHS-4) for individual or women respondents.[6,8–10]

The weighted prevalence of zero-dose children declined by 23·3% over the four survey rounds, from 33·4% (95% CI 32·5–34·2) in 1992 to 10·1% (9·8–10·4) in 2016 (table 1). The AARD was 1·0% (absolute) and 5·2% (relative; appendix 4 p 8). If this trend continues, India is on track to meet its IA2030 zero-dose target.

In 1992, for all characteristics studied, the prevalence of zero-dose children was markedly higher among disadvantaged subgroups. Over the next three survey rounds, zero-dose prevalence declined in absolute terms according to all characteristics; the most rapid declines occurred among the worst off. Relative social disparities persisted over the four rounds but were substantially attenuated. Progress notwithstanding, in 2016, the prevalence of zero-dose children remained higher among households in the bottom wealth quintile, mothers in lowest educational category, scheduled tribes, Muslims, women with incomplete antenatal care, and women giving birth outside a health facility.

Zero-dose children were strongly concentrated among the most disadvantaged in all survey rounds (table 2). For example, in 2016, 37·4% of zero-dose children belonged to the bottom wealth quintile (as compared with 9·5% in the top quintile), and 46·1% had mothers with no schooling (whereas 5·8% had mothers with more than 12 years of schooling).

We used random effects models to examine the sociodemographic and health systems drivers of zero-dose

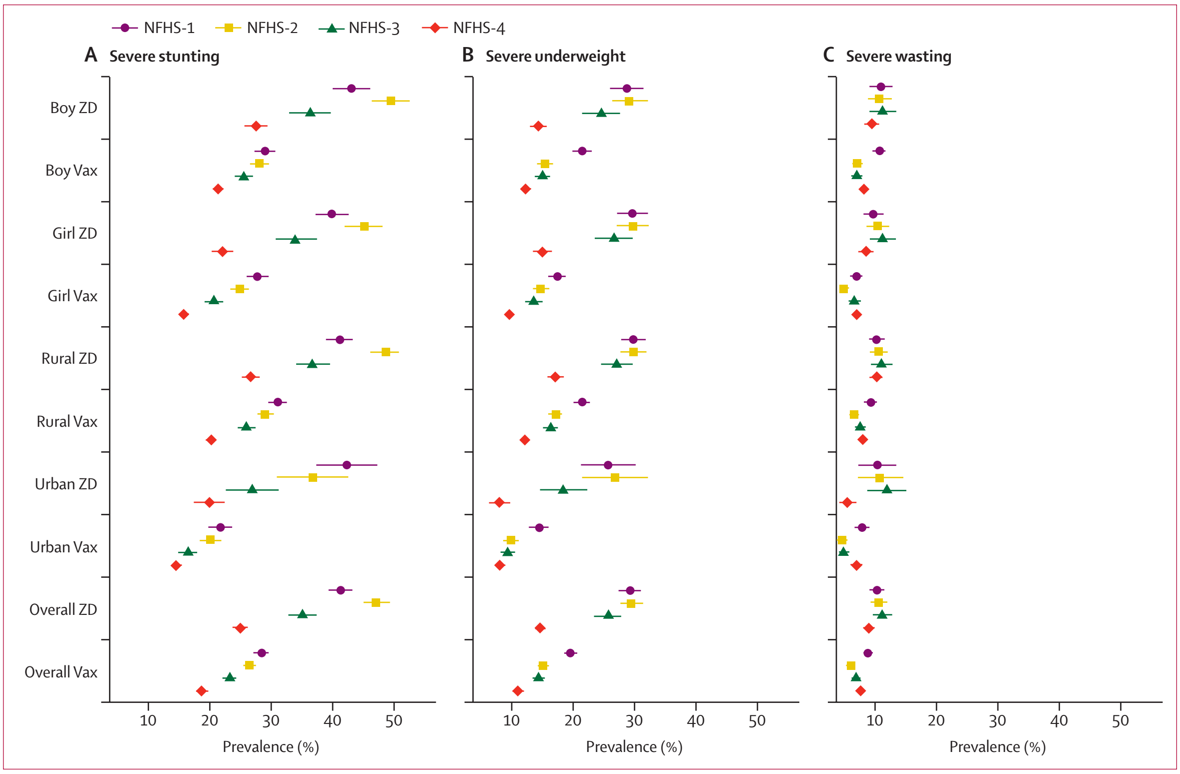

Figure 1: **Prevalence of severe stunting, severe underweight, and severe wasting among zero-dose versus vaccinated children (aged 12–23 months), overall, by child sex, and by area of residence, India, 1992–2016**

The lines represent 95% CIs. Severe stunting height-for-age Z score <–3 SD of the WHO Child Growth Standards median;[15] severe underweight weight-for-age Z score <–3 SD of the WHO Child Growth Standards median;[15] severe wasting weight-for-height Z score <–3 SD of the WHO Child Growth Standards median.[15] NFHS=National Family Health Survey. ZD=zero dose. Vax=vaccinated.

status from 1992 to 2016. In crude models (appendix 4 pp 9–10), all correlates were initially associated with zero-dose status. Children of mothers with no schooling had the highest odds of zero-dose status in all survey rounds; effect sizes decreased substantially over the analysis timeframe. Table 3 presents findings from four fully adjusted multivariable random effects logistic regression models. Adjusted models for NFHS-1 and NFHS-2 showed that all correlates were associated with zero-dose status, except for place of residence. For the NFHS-3 model, all correlates were linked to zero-dose status. The NFHS-4 model found that all correlates were associated with zero-dose status, except for social group and child sex. Patterns across all surveys revealed a persistent negative risk gradient within levels of maternal education and wealth, which were attenuated by survey round four. Notably, there was little attenuation in the adjusted odds of child zero-dose status for Muslims (as compared with Hindus). The adjusted odds of zero-dose status associated with health services factors (incomplete antenatal care or non-institutional delivery) were important in all survey rounds.

Figure 1 depicts the prevalence of severe nutritional deficiencies among zero-dose versus vaccinated children. The prevalence of severe stunting (appendix 4 p 11) was higher for zero-dose than for vaccinated children in all rounds (NFHS-1: zero dose 41·3%, 95% CI 39·2–43·8 *vs* vaccinated 28·5%, 27·2–29·7; NFHS-2: zero dose 46·7%, 44·5–48·8 *vs* vaccinated 26·7%, 25·6–27·8; NFHS-3: zero dose 35·1%, 32·7–37·4 *vs* vaccinated 23·3%, 22·2–24·4; and NFHS-4: zero dose 24·9%, 23·6–26·2 *vs* vaccinated 18·7%, 18·3–19·1). Within strata of urban children, rural children, boys, and girls, the prevalence of severe stunting was higher among zero-dose than vaccinated children in all survey rounds. The prevalence of severe underweight was higher for zero-dose than for vaccinated children in all four rounds; the patterning of disparities was similar to that for severe stunting. Patterns for moderate malnutrition (appendix 4 p 12) were similar to those for severe malnutrition.

In 2015–16, there were an estimated 2·88 (95% CI 2·86–2·89) million zero-dose children in India, concentrated in lagging states and districts (appendix 4 pp 13–43). More than 80% of India's zero-dose children lived in just eight states: Uttar Pradesh (29·2%), Bihar (12·0%), Maharashtra (11·2%), Rajasthan (8·0%), Madhya Pradesh (6·2%), Gujarat (5·5%), Assam (4·2%), and Karnataka (3·9%), with distinct patterns of urban and rural location (appendix 4 pp 44–45). Figure 2 illustrates the spatial distribution of zero-dose children across Indian districts, revealing substantial variability.

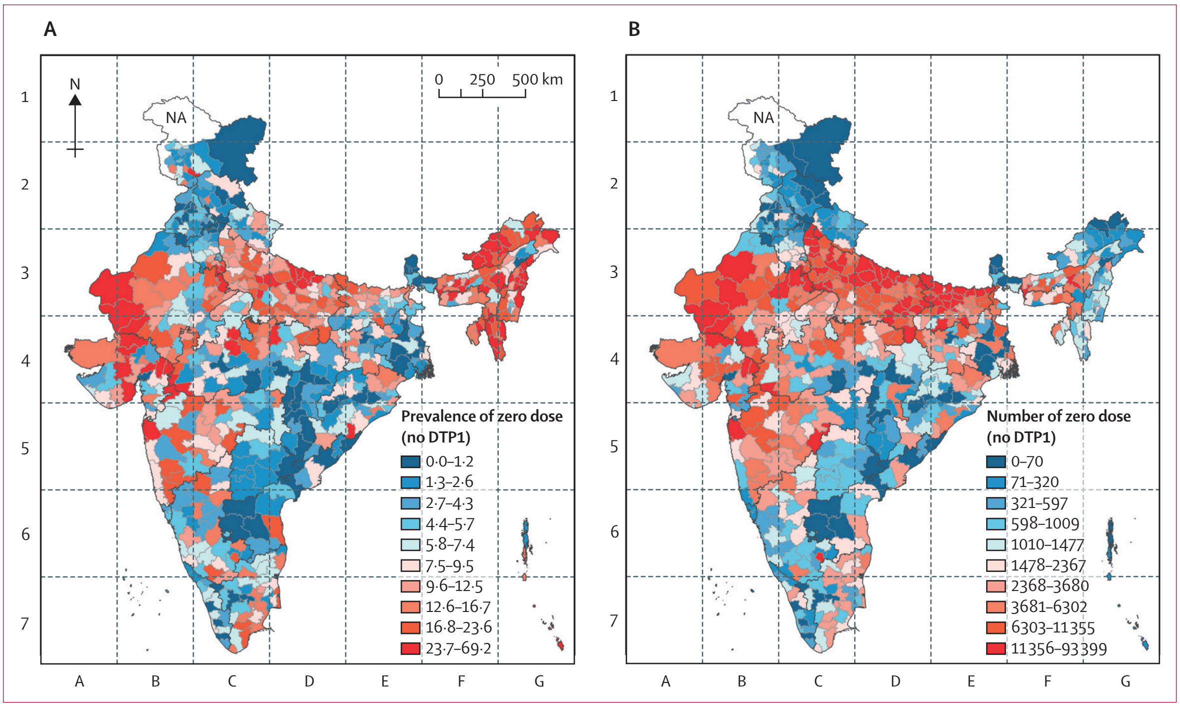

Figure 2: **Prevalence and numbers of zero-dose children (aged 12–23 months) by district, India, 2015–16**
Estimates based on the 2015–16 National Family Health Survey (NFHS-4). Legend colours represent (A) prevalence deciles and (B) number deciles. DTP1=first dose of diphtheria, pertussis, and tetanus.

Sensitivity analyses implementing an alternative outcome definition (appendix 4 pp 46–50) yielded qualitatively similar conclusions to those obtained using the IA2030 definition.

Discussion

To our knowledge, this is the first study to trace aggregate patterns in the numbers of zero-dose children over time globally and in India. We highlight four salient findings. First, India has made tremendous progress in reaching children with routine immunisation and is likely to achieve its IA2030 zero-dose target. Over the 24-year analysis timeframe, the proportion of zero-dose children in India declined by 23·3% in absolute terms, with more rapid reductions generally seen among the worst off. Differentials in zero-dose prevalence related to child sex and caste were eliminated. The urban advantage was virtually eliminated. The rate of decline was particularly rapid between the NFHS-3 and NFHS-4 rounds, concomitant with major health system reforms in 2005 introducing India's National Rural Health Mission. Second, progress notwithstanding, in the most recent survey (NFHS-4), zero-dose children continue to be concentrated among socially disadvantaged groups, including rural households, mothers with less education, and households in lower wealth quintiles. Moreover, although most relative inequalities were attenuated over the four survey rounds, we found little reduction in the likelihood of zero-dose status for Muslim children. Gender-related factors, including low maternal education and low utilisation of key health services by women, remained salient determinants of child zero-dose status throughout the analysis timeframe. Third, compared with vaccinated children, zero-dose children were more likely to have moderate and severe malnutrition in early childhood for all three indicators (stunting, underweight, and wasting) studied. For moderate and severe stunting and underweight, in all survey rounds, this relative disadvantage persisted within strata of urban children, rural children, boys, and girls. Collectively, these analyses expose the cumulative effects of intersecting axes of disadvantage.[22] Fourth, there remains a substantial number of zero-dose children in India. Their spatial distribution is highly heterogeneous, with a higher prevalence in geographies facing large-scale development challenges (notably, parts of Bihar, Uttar Pradesh, Madhya Pradesh, Rajasthan, and Assam), and urban areas including large populations of migrant or informal sector workers (for example, in Maharastra, Karnataka, and Gujarat). Many of these areas were prioritised in recent government immunisation strategies.[23]

Several limitations should be acknowledged. First, household surveys might not include all zero-dose children (appendix 4 pp 2–3).[24] Although each NFHS round used the most recent national census as a sampling frame, these data were at times outdated for survey planning.[24] Moreover, although geographical coverage of the NFHS series is excellent, some areas, including conflict-affected, or small, low-density settings, were excluded from the NFHS-1, NFHS-2, and NFHS-3 surveys.[24] In addition, populations with unstable housing are less likely to be surveyed, even in included geographical areas.[24] Most crucially, children who died before the survey date are not considered when immunisation coverage is assessed—a survivorship bias likely to undercount zero-dose children. Second, we were unable to consider some relevant variables (paternal education, maternal tetanus vaccination, and geographical accessibility of health services)[11] due to inconsistencies in data collection across NFHS survey rounds or substantial missing data. Third, a substantial proportion of vaccination data was based on caregiver recall (appendix 4 p 3), whose validity is unknown.[25] Fourth, child zero-dose status is a new policy focus and definitions are debated. We adopted the IA2030 monitoring definition but implemented an alternative definition specific to India in the sensitivity analyses. Findings were similar, suggesting that the monitoring definition is robust. Fifth, repeated cross-sectional designs trace aggregate population changes over time; however, they do not elucidate causal mechanisms. Sixth, our results are based on survey data available only up to 2015–16. In the interim, India implemented Mission Indradhanush and Intensified Mission Indradhanush—large-scale national initiatives that have markedly improved immunisation coverage[23] and have helped to reduce the number of zero-dose children substantially based on provisional estimates.[26] Adding complexity to the picture, since March, 2020, the COVID-19 pandemic has disrupted immunisation delivery worldwide, with service breeches augmenting the numbers of zero-dose and undervaccinated children, especially in South Asia.[27] Furthermore, India's most recent available census dates from 2011[28] and interim demographic shifts contribute to unclear population denominators. There is hence considerable uncertainty about the current state of play in India; fresh data are eagerly anticipated. Seventh, our analysis of India's progress towards IA2030 goals assumes a linear rate of progress; however, diminishing returns are common. Finally, the extent to which these findings are generalisable to other countries is unknown.

Despite limitations, our study offers enduring insights. The results highlight useful policy entry points to further India's exceptional progress in improving immunisation coverage.[23] The Janani Suraksha Yojana, a conditional cash transfer programme launched in 2005, aimed to promote safe motherhood in India by improving antenatal and postnatal care and increasing births in health facilities;[29] these improvements are corroborated by our findings. Analyses of administrative and survey data to highlight households who do not receive complete antenatal care or deliver in institutions could help to identify those at elevated risk of zero-dose status. India's polio programme illustrates scalable strategies to achieve high coverage in Muslim communities based on genuine partnerships. Moreover, our results clarify what is required to intervene effectively for zero-dose children. We found that, over a 24-year period in India, despite considerable social and economic progress, child zero-dose status was a consistent marker of generalised vulnerability. Zero-dose status was linked to multiple, overlapping sources of disadvantage, and zero-dose children were in turn more likely to experience early childhood nutritional failures linked to high risk of morbidity and mortality in childhood, poor growth trajectories, and poor health outcomes over the lifecourse.[22] Zero-dose immunisation status, therefore signals structural vulnerability at a crucial juncture where life opportunities can be lost or reshaped by effective interventions.

These findings lend strength and urgency to the IA2030 policy orientations.[3,4] Reaching zero-dose children with immunisation is a crucial first step.[30] Holistic strategies offering a range of essential services are urgently needed to enable children to achieve their full potential. In addition to immunisation and other high-impact interventions targeting proximal determinants of health, transformative approaches that attend to the broader social, economic, and environmental determinants that structure life opportunities will be required to disrupt the cycle of intergenerational inequities.[22,31]

Contributors

MJ conceptualised and validated the study, and wrote the original draft of manuscript. MJ (support) and SR (lead) were responsible for the formal analysis. SVS conceptualised the study and provided supervision. MJ and SR verified the underlying data. All authors were responsible for reviewing and editing the manuscript. All authors confirm that they had full access to all the data in the study and accept responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

This study is based on publicly available data from India's National Family Health Survey. The datasets that support the findings of this study are available for download through the Demographic and Health Surveys programme's data distribution system. All analysis files and logs required to reproduce study results are available at https://osf.io/9wbre/files/.

For the **Demographic and Health Surveys programme** see www.dhsprogram.com

Acknowledgments

The authors are grateful to four anonymous reviewers for their very constructive and insightful comments, and to Weiyu Wang (Geographic Insights Lab, Harvard Center for Population and Development Studies, Cambridge, MA, USA) for assistance in developing the maps.

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