

Summary of Key Evidence Related to Zero Dose Indicators and Measurement

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Key Points:

- As of 2020, 17.1 million children are categorized as zero-dose, defined as never having received a single dose of life-saving DTP vaccine.
- The number of children at risk due to zero-dose status or under-vaccination has increased according to 2020 reports. Currently, it's estimated that 13.7 million (80%) of these zero-dose children are living in GAVI-eligible countries.
- Zero-dose children not only lack access to vaccines but lack access to other essential child health services. Prevalence is associated with poor or inadequate maternal healthcare.

As part of Gavi 5.0's ambitious agenda to "leave no one behind" on the path to achieving the 2030 SDGs, Gavi has commissioned the International Vaccine Access Center (IVAC) to produce evidence-based and policy-relevant knowledge products relevant to inform Gavi's equity approach in wider political and policy spaces. **This knowledge summary is the first in a series of six (6) documents which aim to provide a snapshot of recent key evidence related to a specific topic or area of interest. This document focuses on conceptualizing the burden of zero dose and estimating current levels and trends.** Presented here are the results from a search of published manuscripts and gray literature conducted through December 2021. Key findings and concepts are presented below in the format of an annotated bibliography.

How prevalent is zero-dose status?

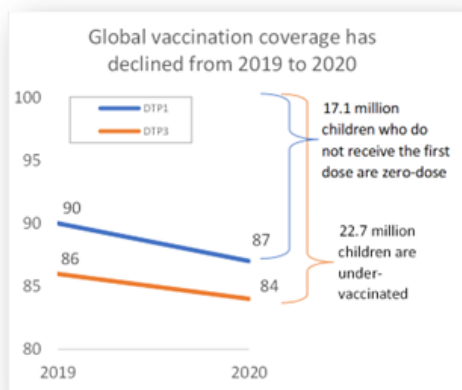
Globally in 2020, 17.1 million children did not receive the first DTP dose – an increase of 3.5 million children from 2019. An estimated 80% of these zero-dose children live in Gavi-eligible countries.

The COVID-19 pandemic has significantly impacted the global community and disrupted many health services and preventive interventions, including childhood immunizations.

The Centers for Disease Control and Prevention (CDC), World Health Organization, and UNICEF track yearly estimates of worldwide routine vaccination coverage. Vaccination status as either under- or un-vaccinated has been classified based upon diphtheria, tetanus, and pertussis (DTP) vaccine as a proxy indicator. Unvaccinated or **zero-dose children** are defined as those who have not received the first dose of DTP

vaccine (DTP1), indicating lack of access to immunizations, and **under-vaccinated children** are those who have not received the full course or third dose of DTP vaccine (DTP3), indicating weakness or gaps in immunization program performance.

Researchers estimated that vaccination coverage with DTP3 decreased from 86% in 2019 to 84% in 2020, leaving 22.7 million children under-vaccinated. Of these children, those who did not receive DTP1 by their first birthday accounted for 95% of the increase in under-vaccinated children. A similar decline in receipt of DTP1 was also observed from 90% in 2019 to 87% in 2020. This decline now means that an estimated 17.1 million children may be considered zero-dose.



After a decade of what was reported as “stagnant” immunization coverage from 2010 to 2019, the most recent declines (2019 to 2020) that saw considerable increases in the number of zero-dose and under-vaccinated children reached levels that had not been noted since 2006 and 2009. **These declines reflect the negative impact of both reduced immunization access and struggling program performance globally during the pandemic.**

13.7 million (80%) zero-dose children were identified in GAVI eligible countries, and of all zero-dose children, 65% were reported to be from 10 countries: Angola, Brazil, Democratic Republic of the Congo, Ethiopia, India, Indonesia, Mexico, Nigeria, Pakistan, and Philippines. Regionally, the lowest DTP1 and DTP3 coverage was observed in the WHO African Region – 79% and 72%, while the highest percent of DTP1 coverage (97%) was in the European Region. The only region that did not demonstrate a decrease in DTP3 coverage was in the Western Pacific region that remained 95%.

Similar declines were observed globally for coverage of other critical vaccines including a complete series of Hemophilus influenza type B (Hib) vaccine, rubella containing vaccine (RCV), three-dose hepatitis B vaccine series (HepB), and human papilloma virus (HPV) vaccine.

Although the influence of recall bias is a limitation of survey data, a small number of countries did not report 2020 immunization data, and statistical uncertainty is not included with the results, the downward trend observed in immunization coverage from 2019 to 2020 compared to the previously observed trends nonetheless highlights a pressing need to evaluate immunization access and programming to address the troubling increase in the proportion of zero-dose children.

Muhoza, P., Danovaro-Holliday, M. C., Diallo, M. S., Murphy, P., Sodha, S. V., Requejo, J. H., & Wallace, A. S. (2021). Routine Vaccination Coverage - Worldwide, 2020. MMWR. Morbidity and mortality weekly report, 70(43), 1495–1500. <https://doi.org/10.15585/mmwr.mm7043a1>

Are certain factors associated with increased risk or greater prevalence of zero-dose?

To estimate the prevalence and characterize groups of children at high risk of being zero-dose, researchers analyzed 92 countries using data from Demographic and Health Surveys (DHS) and Multiple Indicator Cluster Surveys (MICS) from 2010 - 2020. These nationally representative household surveys are conducted in low- and middle-income countries (LMIC) led by the United States Agency for International Development (USAID) and the United Nations Children's Fund (UNICEF). These surveys gather key information to understand health status including insight about vaccine coverage and sociodemographic indicators.

The objective of this study was to estimate prevalence and identify high-risk groups among the children surveyed who had not received any dose of four vaccines: Bacillus Calmette-Guérin (BCG), poliomyelitis (polio), diphtheria, tetanus, pertussis (DTP), and measles, which was applied to define zero-dose children in this study. Prevalence of zero-dose children in each country was estimated, and the highest prevalence of zero-dose children was further characterized based upon factors related to: (1) maternal tetanus immunization status, (2) antenatal care, and (3) place of delivery.

Zero-dose prevalence was 7.7% (95% CI 7.4–7.9%) with high variability across the sample (highest 57.6% in South Sudan and lowest 0% in Moldova).

The group characterized as the most deprived had 42%, the highest prevalence, of zero-dose children. This group represented children who were not born in a health facility, to a mother who did not receive a tetanus vaccine before or during pregnancy and reported no antenatal care visits. 24% of all zero-dose children and 4% of all surveyed children were in this highest risk group for zero-dose prevalence. Other indicators of inequality were examined and among this highest risk group, 47% were in the poorest wealth quintile, 89% lived in a rural area, and 81% had mothers with no education.

Zero-dose prevalence increased across all four groups, meaning that children were more likely to have missed a dose of any vaccine. Zero-dose prevalence was 6% in the group of children whose mother had received one dose of a tetanus vaccine before or during pregnancy and this group made up 90% of all surveyed children. Prevalence of zero-dose children was 11% in the group whose mother had not received a tetanus vaccine but had at least one antenatal care visit. Zero dose prevalence increased to 23% for the group of children who were born in a health facility, but their mother had no tetanus vaccine or antenatal care visit.

Overall, these results suggest that zero-dose children live in households, settings, and environments where they not only lack access to vaccines but access to other health services is crucially absent. Maternal indicators of antenatal care may be key to identifying and reaching zero-dose children. These findings cannot pinpoint cause but show an important association between the marked absence of vital maternal and child health services and the prevalence of zero-dose children.

This points toward systemic issues which may determine access and utilization of health services that may result in a growing burden of zero-dose children who are deprived of critical vaccines for essential health protection.

Santos, T. M., Cata-Preta, B. O., Victora, C. G., & Barros, A. (2021). *Finding Children with High Risk of Non-Vaccination in 92 Low- and Middle-Income Countries: A Decision Tree Approach*. *Vaccines*, 9(6), 646.
<https://doi.org/10.3390/vaccines9060646>

Children who receive just one vaccine are much more likely to receive other vaccines

From studying how children move from zero-dose to fully vaccinated and by determining the probability of a child receiving another vaccine after a previous one, immunization cascades can be created to examine patterns across low-resource settings, using the same DHS and MICS datasets. For 92 LMICs between 2010 and 2019, zero-dose was studied among children who were defined as those who had not received any of the four basic vaccines: BCG, polio, DPT and measles containing vaccines (MCV).

Zero-dose prevalence was higher for children in low-income countries and those in the poorest wealth quintile. An estimated 11.1% of children in low-income countries would be categorized as zero-dose, while prevalence dropped to 5.2% among upper-middle income countries. In terms of household wealth, across all countries, 12.5% of those in the poorest quintile were zero-dose while only 3.4% were zero-dose in the wealthiest quintile.

These results reveal an inverse relationship between the level of national income or household wealth and the prevalence of zero-dose children.

This analysis suggests that being zero-dose is more prevalent than children who receiving 1 or 2 vaccines. Polio was the predominant vaccine administered to “single-dose” children and was the most frequent vaccine administered among low-income countries and poor children in LMICs.

The immunization cascade demonstrated a J-shape pattern of prevalence: 8% of zero-dose, 3% single-dose or second-dose, 15% with at least 3 doses and 71% with all four vaccines. **Overall, 76.8% of children who received their initial vaccination went on to receive all four vaccines.** BCG, and polio1 had the highest rates of co-coverage, meaning children who received one dose of any of these vaccines were more likely to receive other vaccines and the cascades were similar for both genders which suggests that careseeking is similarly sparse for boys as well as girls.

Cata-Preta, B. O., Santos, T. M., Mengistu, T., Hogan, D. R., Barros, A., & Victora, C. G. (2021). *Zero-dose children and the immunisation cascade: Understanding immunisation pathways in low and middle-income countries*. *Vaccine*, 39(32), 4564–4570.
<https://doi.org/10.1016/j.vaccine.2021.02.072>

What approaches can be used to estimate the burden of zero-dose children?

Geospatial modeling has been used to map or locate zero-dose children before and after mass vaccination campaigns for measles and rubella. These models were

able to provide optimal locations for vaccinations sites by using fine-scale spatial mapping of zero-dose children. A measles and rubella vaccination campaign was conducted in Zambia in November 2020 and included a mop-up activity post campaign for any children who were initially missed. This prospective study obtained detailed household mapping of eligible zero-dose children and identified households that should be included in the vaccination campaign by relying on satellite imagery. Missing either DTP or measles as zero-dose was considered zero-dose status for this analysis.

Prior to the campaign, as estimated 17% of children younger than 9 months were DTP zero-dose children. For children between 9-60 months of age, 4.3% were measles zero-dose. The initial campaign was able to successfully immunize 73.3% of the targeted measles zero-dose children. The secondary mop up activity was able to reach another 25.6% children. Only about 1.1% remained unvaccinated in the catchment area.

The geospatial models revealed that both DTP and measles zero-dose prevalence increased as travel time to the nearest health facility increased. In addition to travel time, there was an increase in zero-dose status if children lived in households equidistant from two health facilities. These findings support earlier observations that a greater or increased burden of travel time to reach the nearest health facility is strongly associated with the zero-dose status of children.

The utilization of household-level zero-dose surveying before and after immunization campaigns may serve as a valuable framework to improve and increase the effectiveness of current campaign strategies.

Increased immunization activity during mop-up events suggests that access to healthcare is the main barrier for vaccine uptake and not vaccine refusal. The geospatial models were able to reveal fine-scale heterogeneity in vaccination status as well as predict the effect of adding new vaccinations sites in additional locations. Such innovative methods of modeling to guide program planning may become critical for campaign sites as they may provide critical information for micro planning and ultimately reaching children in underserved communities

Arambepola, R., Yang, Y., Hutchinson, K., Mwansa, F. D., Doherty, J. A., Bwalya, F., Ndubani, P., Musukwa, G., Moss, W. J., Wesolowski, A., & Mutembo, S. (2021). Using geospatial models to map zero-dose children: factors associated with zero-dose vaccination status before and after a mass measles and rubella vaccination campaign in Southern province, Zambia. *BMJ global health*, 6(12), e007479. <https://doi.org/10.1136/bmjgh-2021-007479>

Additional Resources

1. Portnoy, A., Jit, M., HELLERINGER, S., & Verguet, S. (2018). Impact of measles supplementary immunization activities on reaching children missed by routine programs. *Vaccine*, 36(1), 170–178. <https://doi.org/10.1016/j.vaccine.2017.10.080>
2. Dadari, I., Higgins-Steele, A., Sharkey, A., Charlet, D., Shahabuddin, A., Nandy, R., & Jackson, D. (2021). Pro-equity immunization and health systems strengthening strategies in select Gavi-supported countries. *Vaccine*, 39(17), 2434–2444. <https://doi.org/10.1016/j.vaccine.2021.03.044>