VACCINE DELIVERY RESEARCH DIGEST

UNIVERSITY OF WASHINGTON STRATEGIC ANALYSIS, RESEARCH & TRAINING (START) CENTER

REPORT TO THE BILL & MELINDA GATES FOUNDATION

PRODUCED BY: SUTTON, A. & SHARMA, M.

MAY 2024

Want the Vaccine Delivery Research Digest delivered directly to your inbox?

Subscribe on the Digest website: http://uwstartcenter.org/publication-digests/vaccine-digest

List of Articles

1 Progress in Access and Oral Polio Vaccine Coverage Among Children Aged <5 Years in Polio Campaigns After the Political Change in Afghanistan.

{Abstract & START Commentary} {Full Article}

- This article describes improvements in polio vaccination coverage in Afghanistan since August 2021.
- 2 Health impact and cost-effectiveness of expanding routine immunization coverage in India through Intensified Mission Indradhanush.

{Abstract & START Commentary} {Full Article}

- The cost-effectiveness of periodic intensification of routine immunization (PIRI) in India was evaluated.
- 3 Estimating averted illnesses from influenza vaccination for children and pregnant women El Salvador, Panama, and Peru, 2011-2018.

{Abstract & START Commentary} {Full Article}

- The burden of influenza illnesses averted by seasonal influenza vaccination in El Salvador, Panama, and Peru during 2011-2017 among children aged 6-23 months and pregnant women was estimated.
- 4 Feasibility, safety, and impact of the RTS,S/AS01E malaria vaccine when implemented through national immunisation programmes: evaluation of cluster-randomised introduction of the vaccine in Ghana, Kenya, and Malawi.

{Abstract & START Commentary} {Full Article}

- This prospective study found introduction of the RTS,S/AS01E vaccine was associated with substantial reductions in hospital admission with severe malaria and found no evidence of the safety signals that had been observed in the phase 3 trial.
- 5 Setting up a data system for monitoring malaria vaccine introduction readiness and uptake in 42 health districts in Cameroon.

{Abstract & START Commentary} {Full Article}

 The use of the World Health Organization's malaria vaccine readiness assessment tool to monitor the implementation of pre-introduction activities at the district and national levels in Cameroon is described. 6 Perspectives on the Performance of the Ethiopian Vaccine Supply Chain and Logistics System after the Last Mile Delivery Initiative: A Phenomenological Study.

{Abstract & START Commentary} {Full Article}

- The performance of the vaccine supply chain and logistics system in Ethiopia was assessed through the perspectives of key stakeholders.
- 7 Success in vaccination programming through community health workers: a qualitative analysis of interviews and focus group discussions from Nepal, Senegal and Zambia.

{Abstract & START Commentary} {Full Article}

- Community health worker organization, motivation and trust facilitates improvements in immunization coverage.
- 8 Estimating the Potential Public Health Value of BCG Revaccination.

{Abstract & START Commentary} {Full Article}

- BCG revaccination cost effectiveness was evaluated at different levels of prevention-ofdisease estimates.
- 9 Global vaccine coverage and childhood survival estimates: 1990-2019.

{Abstract & START Commentary} {Full Article}

- The association between reduction in child mortality and routine immunization across 204 countries and territories from 1990 to 2019 was evaluated.
- 10 Post-campaign coverage evaluation of a measles and rubella supplementary immunization activity in five districts in India, 2019-2020.

{Abstract & START Commentary} {Full Article}

- Awareness and factors associated with vaccination during a measles and rubella supplementary immunization activity in India were assessed.
- 11 Utilization of Mobile Reminders in Improving the Completeness and Timeliness of Routine Childhood Immunization in Kano Metropolis, Nigeria: A Randomized Controlled Trial.

{Abstract & START Commentary} {Full Article}

- The effectiveness of a mobile phone reminder intervention to improve the completeness and timeliness of routine immunizations for infants was assessed.
- 12 Low Measles Vaccination Coverage and Spatial Analysis of High Measles Vaccination Dropout in Ethiopia's Underprivileged Areas.

{Abstract & START Commentary} {Full Article}

- The coverage of measles vaccinations among eight underserved populations in Ethiopia were estimated and the spatial distribution of measles vaccination dropout was mapped.
- 13 Cost-effectiveness and public health impact of typhoid conjugate vaccine introduction strategies in Bangladesh.

{Abstract & START Commentary} {Full Article}

- Nationwide TCV introduction with a catch-up campaign is projected to be cost effective and reduce typhoid incidence in Bangladesh.
- 14 The status of immunization program and challenges in Ethiopia: A mixed method study. {Abstract & START Commentary} {Full Article}
 - The status of the immunization service and challenges in Ethiopia were assessed.

Appendix

Details of Articles

Progress in Access and Oral Polio Vaccine Coverage Among Children Aged <5 Years in Polio Campaigns After the Political Change in Afghanistan.

Sabawoon W, Seino S, Pason B, Momin N, Kanamori S, Bender C, et al.

J Infect Dis. 2024 Apr 10. PubMed ID: 38597896

ABSTRACT

BACKGROUND: Warfare has long impeded vaccination programs in polio-endemic Afghanistan. We aimed to describe progress in access to children under 5, oral polio vaccine (OPV) coverage among children under 5 in nationwide polio campaigns, and polio surveillance performance indicators after the Islamic Republic of Afghanistan collapsed to Taliban forces in August 2021.

METHODS: Trends in the number of wild poliovirus type 1 (WPV1) and circulating vaccine-derived poliovirus type 2 (cVDPV2) cases and surveillance indicators from 2015 to 2023, and trends in the OPV coverage in the November 2020-June 2022 polio campaigns, were described.

RESULTS: From 2015 to mid-July 2020, 74 of 126 (58.7%) WPV1 cases were reported from inaccessible areas. In November 2020, 34.1% of target children under 5 were inaccessible; in November 2021 (the first postchange polio campaign), all were accessible. From November 2020, under-5 OPV coverage of 69.9% rose steadily to 99.9% in the May 2022 campaign. The number of cVDPV cases fell from 308 (2020) to zero (2022). June 2022's house-to-house OPV coverage was 34.2% higher than non-house-to-house modalities. Nonpolio acute flaccid paralysis and stool adequacy rates rose from 18.5/100 000 and 92.6% in 2020 to 24.3/100 000 and 94.4% in 2022, respectively.

CONCLUSIONS: Children's inaccessibility no longer vitiates polio eradication; polio surveillance systems are less likely to miss any poliovirus circulation.

WEB: 10.1093/infdis/jiae129

IMPACT FACTOR: 6.4 CITED HALF-LIFE: 9.5

START COMMENTARY

In Table 2, Sabawoon et al. report differences in polio vaccination coverage following the political transition to Taliban government in Afghanistan. The percentage of recorded missed children due to

parent refusal in house-to-house polio vaccination campaigns decreased from ~1% prior to the political transition to ~0.6% after the political transition, a which equates to >15,000 children under 5 years receiving the vaccine. The denominator of ~10,000,000 children under 5 used to calculate rates in this study is an estimate as there has not been a census conducted in Afghanistan for more than half a century.

2. Health impact and cost-effectiveness of expanding routine immunization coverage in India through Intensified Mission Indradhanush.

Clarke-Deelder E, Suharlim C, Chatterjee S, Portnoy A, Brenzel L, Ray A, et al.

Health Policy Plan. 2024 Apr 09.

PubMed ID: 38590052

ABSTRACT

Many children do not receive a full schedule of childhood vaccines, yet there is limited evidence on the cost-effectiveness of strategies for improving vaccination coverage. Evidence is even scarcer on the cost-effectiveness of strategies for reaching "zero-dose children," who have not received any routine vaccines. We evaluated the cost-effectiveness of periodic intensification of routine immunization (PIRI), a widely applied strategy for increasing vaccination coverage. We focused on Intensified Mission Indradhanush (IMI), a large-scale PIRI intervention implemented in India in 2017-2018. In 40 sampled districts, we measured the incremental economic cost of IMI using primary data, and used controlled interrupted time-series regression to estimate incremental vaccination doses delivered. We estimated deaths and disability-adjusted life years (DALYs) averted using the Lives Saved Tool and reported cost-effectiveness from immunization program and societal perspectives. We found that, in sampled districts, IMI had an estimated incremental cost of 2021US\$13.7 (95% uncertainty interval: 10.6 to 17.4) million from an immunization program perspective and increased vaccine delivery by an estimated 2.2 (-0.5 to 4.8) million doses over a 12month period, averting an estimated 1,413 (-350 to 3,129) deaths. The incremental cost from a program perspective was \$6.21 per dose (\$2.80 to dominated), \$82.99 per zero-dose child reached (\$39.85 to dominated), \$327.63 (\$147.65 to dominated) per DALY averted, \$360.72 (\$162.56 to dominated) per life-year saved, and \$9,701.35 (\$4,372.01 to dominated) per under-five death averted. At a cost-effectiveness threshold of 1x per-capita GDP per DALY averted, IMI was estimated to be cost-effective with 90% probability. This evidence suggests IMI was both impactful and cost-effective for improving vaccination coverage, though there is a high degree of uncertainty in the results. As vaccination programs expand coverage, unit costs may increase due to the higher costs of reaching currently unvaccinated children.

WEB: 10.1093/heapol/czae024

IMPACT FACTOR: 3.2 CITED HALF-LIFE: 7.0

START COMMENTARY

The estimated cost per dose of vaccine delivered through Intensified Mission Indradhanush (IMI) varied considerably across districts (\$3 in Udaipur, Rajasthan to \$28 in Hapur, Uttar Pradesh per

incremental dose) and states (\$3 in Rajasthan to \$8 in Upper Pradesh per incremental dose). Districts with a higher vaccine coverage at baseline tended to have higher incremental cost effectiveness ratios (ICERs). Estimates of the incremental cost per zero-dose child reached at the district level ranged from \$22 in Patna, Bihar, to \$193 in Jaunpur, Uttar Pradesh. Cost-effectiveness acceptability curves for incremental cost per: 1) dose delivered, 2) zero-dose child reached, 3) life-year saved, 4) under-5 death averted, and 5) DALY averted are in Figure 3.

3. Estimating averted illnesses from influenza vaccination for children and pregnant women - El Salvador, Panama, and Peru, 2011-2018.

Chard A, Machingaidze C, Loayza S, Gharpure R, Nogareda F, González R, et al.

Vaccine. 2024 Apr 07.

PubMed ID: 38584055

ABSTRACT

BACKGROUND: Estimating the burden of disease averted by vaccination can assist policymakers to implement, adjust, and communicate the value of vaccination programs. Demonstrating the use of a newly available modeling tool, we estimated the burden of influenza illnesses averted by seasonal influenza vaccination in El Salvador, Panama, and Peru during 2011-2017 among two influenza vaccine target populations: children aged 6-23 months and pregnant women.

METHODS: We derived model inputs, including incidence, vaccine coverage, vaccine effectiveness, and multipliers from publicly available country-level influenza surveillance data and cohort studies. We also estimated changes in illnesses averted when countries' vaccine coverage was achieved using four different vaccine deployment strategies.

RESULTS: Among children aged 6-23 months, influenza vaccination averted an estimated cumulative 2,161 hospitalizations, 81,907 medically-attended illnesses, and 126,987 overall illnesses during the study period, with a prevented fraction ranging from 0.3 % to 12.5 %. Among pregnant women, influenza vaccination averted an estimated cumulative 173 hospitalizations, 6,122 medically attended illnesses, and 16,412 overall illnesses, with a prevented fraction ranging from 0.2 % to 10.9 %. Compared to an influenza vaccine campaign with equal vaccine distribution during March-June, scenarios in which total cumulative coverage was achieved in March and April consistently resulted in the greatest increase in averted illness (23 %-3,129 % increase among young children and 22 %-3,260 % increase among pregnant women).

DISCUSSION: Influenza vaccination campaigns in El Salvador, Panama, and Peru conducted between 2011 and 2018 prevented hundreds to thousands of influenza-associated hospitalizations and illnesses in young children and pregnant women. Existing vaccination programs could prevent additional illnesses, using the same number of vaccines, by achieving the highest possible coverage within the first two months of an influenza vaccine campaign.

WEB: 10.1016/j.vaccine.2024.04.007

IMPACT FACTOR: 5.5 CITED HALF-LIFE: 7.2

START COMMENTARY

Chard et al. provide insight into the need for data to accurately model the impact of influenza vaccination. They note that their study required the assumption that the incidence of influenza-associated hospitalizations in pregnant women in both Panama and El Salvador were similar to estimates observed among pregnant women in Peru. Additionally, the assumed that effectiveness for the influenza vaccine among young children in El Salvador and Panama was similar to vaccine effectiveness estimated for Northern Hemisphere vaccines in the United States of lack of regional data. They suggest filling gaps by setting up local systems to obtain primary data.

4. Feasibility, safety, and impact of the RTS,S/AS01E malaria vaccine when implemented through national immunisation programmes: evaluation of cluster-randomised introduction of the vaccine in Ghana, Kenya, and Malawi.

Asante K, Mathanga D, Milligan P, Akech S, Oduro A, Mwapasa V, et al.

Lancet. 2024 Apr 27;403(10437):1660-1670.

PubMed ID: 38583454

ABSTRACT

BACKGROUND: The RTS,S/AS01E malaria vaccine (RTS,S) was introduced by national immunisation programmes in Ghana, Kenya, and Malawi in 2019 in large-scale pilot schemes. We aimed to address questions about feasibility and impact, and to assess safety signals that had been observed in the phase 3 trial that included an excess of meningitis and cerebral malaria cases in RTS,S recipients, and the possibility of an excess of deaths among girls who received RTS,S than in controls, to inform decisions about wider use.

METHODS: In this prospective evaluation, 158 geographical clusters (66 districts in Ghana; 46 subcounties in Kenya; and 46 groups of immunisation clinic catchment areas in Malawi) were randomly assigned to early or delayed introduction of RTS,S, with three doses to be administered between the ages of 5 months and 9 months and a fourth dose at the age of approximately 2 years. Primary outcomes of the evaluation, planned over 4 years, were mortality from all causes except injury (impact), hospital admission with severe malaria (impact), hospital admission with meningitis or cerebral malaria (safety), deaths in girls compared with boys (safety), and vaccination coverage (feasibility). Mortality was monitored in children aged 1-59 months throughout the pilot areas. Surveillance for meningitis and severe malaria was established in eight sentinel hospitals in Ghana, six in Kenya, and four in Malawi. Vaccine uptake was measured in surveys of children aged 12-23 months about 18 months after vaccine introduction. We estimated that sufficient data would have accrued after 24 months to evaluate each of the safety signals and the impact on severe malaria in a pooled analysis of the data from the three countries. We estimated incidence rate ratios (IRRs) by comparing the ratio of the number of events in children age-eligible to have received at least one dose of the vaccine (for safety outcomes), or age-eligible to have received three doses (for impact outcomes), to that in non-eligible age groups in implementation areas with the equivalent ratio in comparison areas. To establish whether there was evidence of a difference between girls and boys in the vaccine's impact on mortality, the female-to-male mortality ratio in age groups eligible to receive the vaccine (relative to the ratio in non-eligible children) was compared between implementation and comparison areas. Preliminary findings contributed to WHO's recommendation in 2021 for widespread use of RTS,S in areas of moderate-to-high malaria transmission.

FINDINGS: By April 30, 2021, 652 673 children had received at least one dose of RTS,S and 494 745 children had received three doses. Coverage of the first dose was 76% in Ghana, 79% in Kenya, and 73% in Malawi, and coverage of the third dose was 66% in Ghana, 62% in Kenya, and 62% in Malawi. 26 285 children aged 1-59 months were admitted to sentinel hospitals and 13 198 deaths were reported through mortality surveillance. Among children eligible to have received at least one dose of RTS,S, there was no evidence of an excess of meningitis or cerebral malaria cases in implementation areas compared with comparison areas (hospital admission with meningitis: IRR 0-63 [95% CI 0-22-1-79]; hospital admission with cerebral malaria: IRR 1-03 [95% CI 0-61-1-74]). The impact of RTS,S introduction on mortality was similar for girls and boys (relative mortality ratio 1-03 [95% CI 0-88-1-21]). Among children eligible for three vaccine doses, RTS,S introduction was associated with a 32% reduction (95% CI 5-51%) in hospital admission with severe malaria, and a 9% reduction (95% CI 0-18%) in all-cause mortality (excluding injury).

INTERPRETATION: In the first 2 years of implementation of RTS,S, the three primary doses were effectively deployed through national immunisation programmes. There was no evidence of the safety signals that had been observed in the phase 3 trial, and introduction of the vaccine was associated with substantial reductions in hospital admission with severe malaria. Evaluation continues to assess the impact of four doses of RTS,S.

FUNDING: Gavi, the Vaccine Alliance; the Global Fund to Fight AIDS, Tuberculosis and Malaria; and Unitaid.

WEB: 10.1016/S0140-6736(24)00004-7

IMPACT FACTOR: 168.9 CITED HALF-LIFE: 6.9

START COMMENTARY

Vaccine uptake was similar in boys and girls in all three included countries (Ghana, Kenya, Malawi) (Table 1). Authors found no difference in vaccine uptake across wealth rankings, except in Kenya where children from households in the upper third were more likely to have received three doses of RTS,S than children from households in the lowest third. Those who slept under long-lasting insecticidal nets were ~20% more likely to have received three doses of RTS,S. Based on midline surveys, vaccine introduction in the implementation group was not associated with an increase in coverage of other vaccines, LLIN use, use of vitamin A, or care-seeking behavior for fever (Figure 2).

5. Setting up a data system for monitoring malaria vaccine introduction readiness and uptake in 42 health districts in Cameroon.

Mboussou F, Ndoula S, Nembot R, Baonga S, Njinkeu A, Njoh A, et al.

BMJ Glob Health. 2024 Apr 08;9(4).

PubMed ID: 38580377

ABSTRACT

Three months after the first shipment of RTS,S1/AS01 vaccines, Cameroon started, on 22 January 2024, to roll out malaria vaccines in 42 districts among the most at risk for malaria. Cameroon adopted and implemented the World Health Organization (WHO) malaria vaccine readiness assessment tool to monitor the implementation of preintroduction activities at the district and national levels. One week before the start of the vaccine rollout, overall readiness was estimated at 89% at a national level with two out of the five components of readiness assessment surpassing 95% of performance (vaccine, cold chain and logistics and training) and three components between 80% and 95% (planning, monitoring and supervision, and advocacy, social mobilisation and communication). 'Vaccine, cold chain and logistics' was the component with the highest number of districts recording below 80% readiness. The South-West and North-West, two regions with a high level of insecurity, were the regions with the highest number of districts that recorded a readiness performance below 80% in the five components. To monitor progress in vaccine rollout daily, Cameroon piloted a system for capturing immunisation data by vaccination session coupled with an interactive dashboard using the R Shiny platform. In addition to displaying data on vaccine uptake, this dashboard allows the generation of the monthly immunisation report for all antigens, ensuring linkage to the regular immunisation data system based on the end-of-month reporting through District Health Information Software 2. Such a hybrid system complies with the malaria vaccine rollout principle of full integration into routine immunisation coupled with strengthened management of operations.

WEB: 10.1136/bmjgh-2024-015312

IMPACT FACTOR: 8.1 CITED HALF-LIFE: 2.7

START COMMENTARY

Mboussou et al. summarize key takeaways from the experience of adopting the World Health Organization's (WHO) malaria vaccine readiness assessment tool in Cameroon. They highlight the importance of adapting the readiness assessment tool to the local context and beginning to track completion of readiness activities at least three months prior to the launch of malaria vaccine programs. They suggest creating data visualization tools such as a dashboard to track progress

toward readiness for malaria vaccine introduction (MVI) across districts, and using dashboard results as the basis for discussion within coordinating teams to help address readiness activities that have not yet been completed. They assert that daily progress monitoring of malaria vaccine uptake is critical to inform planning decisions and risk communication messaging, and suggest connecting the data system used for routine immunization with the system used for collecting immunization data for MVI.

6 Perspectives on the Performance of the Ethiopian Vaccine Supply Chain and Logistics
System after the Last Mile Delivery Initiative: A Phenomenological Study.

Gebremedhin S, Shiferie F, Tsegaye D, Alemayehu W, Wondie T, Zeleke S, et al.

Am J Trop Med Hyg. 2024 May 01;110(5):1029-1038.

PubMed ID: 38574549

ABSTRACT

Uninterrupted availability of vaccines requires a robust vaccine supply chain and logistics system (VSCLS). With special focus on remote and underserved settings, we assessed the reach and bottlenecks of the Ethiopian VSCLS after the initiation of the last mile transition. We explored the perspectives of key stakeholders using a qualitative phenomenological study. More than 300 indepth interviews and 22 focus group discussions were conducted. The study was sequentially implemented over two phases to understand the bottlenecks at national and regional (Phase I) and lower (Phase II) levels. After the transition, the Ethiopian Pharmaceutical Supply Service started supplying vaccines directly to health facilities, bypassing intermediaries. The transition reduced supply hiccups and enabled the health sector to focus on its core activities. However, in remote areas, achievements were modest, and health facilities have been receiving supplies indirectly through district health offices. By design, health posts collect vaccines from health centers, causing demotivation of health extension workers and frequent closure of health posts. Challenges of the VSCLS include artificial shortage due to ill forecasting and failure to request needs on time, lack of functional refrigerators secondary to scarcity of skilled technicians and spare parts, and absence of dependable backup power at health centers. Vaccine wastages owing to poor forecasts, negligence, and cold chain problems are common. The VSCLS has not yet sustainably embraced digital logistics solutions. The system is overstrained by frequent outbreak responses and introduction of new vaccines. We concluded that the transition has improved the VSCLS, but the reach remains suboptimal in remote areas.

WEB: 10.4269/ajtmh.23-0622

IMPACT FACTOR: 3.3 CITED HALF-LIFE: 9.8

START COMMENTARY

Themes from analysis include last mile delivery transition, supply chain hiccups, timely request for adequate vaccines, vaccine wastage, and challenges and success of the cold chain system. Themes, subthemes, and codes that emerged from interviews and focus group discussions can be found in Table 2. When discussing digital solutions to improve vaccine logistics, Gebremedhin et al. highlight a cell phone-based stock management tool that had been implemented at scale that was

simple to use, well accepted, and improved availability of vaccines at health centers. Unfortunately, the project was not sustained in part due to shortage of technicians and information technology supplies.

Success in vaccination programming through community health workers: a qualitative analysis of interviews and focus group discussions from Nepal, Senegal and Zambia.

Ogutu E, Ellis A, Hester K, Rodriguez K, Sakas Z, Jaishwal C, et al.

BMJ Open. 2024 Apr 05;14(4):e079358.

PubMed ID: 38569679

ABSTRACT

OBJECTIVES: Community health workers are essential to front-line health outreach throughout low-income and middle-income countries, including programming for early childhood immunisation. Understanding how community health workers are engaged for successful early childhood vaccination among countries who showed success in immunisation coverage would support evidence-based policy guidance across contexts.

DESIGN: We employed a multiple case study design using qualitative research methods.

SETTING: We conducted research in Nepal, Senegal and Zambia.

PARTICIPANTS: We conducted 207 interviews and 71 focus group discussions with 678 participants at the national, regional, district, health facility and community levels of the health systems of Nepal, Senegal and Zambia, from October 2019 to April 2021. We used thematic analysis to investigate contributing factors of community health worker programming that supported early childhood immunisation within each country and across contexts.

RESULTS: Implementation of vaccination programming relied principally on the (1) organisation, (2) motivation and (3) trust of community health workers. Organisation was accomplished by expanding cadres of community health workers to carry out their roles and responsibilities related to vaccination. Motivation was supported by intrinsic and extrinsic incentives. Trust was expressed by communities due to community health worker respect and value placed on their work.

CONCLUSION: Improvements in immunisation coverage was facilitated by community health worker organisation, motivation and trust. With the continued projection of health worker shortages, especially in low-income countries, community health workers bridged the equity gap in access to vaccination services by enabling wider reach to underserved populations. Although improvements in vaccination programming were seen in all three countries-including government commitment to addressing human resource deficits, training and remuneration; workload, inconsistency in compensation, training duration and scope, and supervision remain major challenges to immunisation programming. Health decision-makers should consider organisation, motivation and trust of community health workers to improve the implementation of immunisation programming.

WEB: 10.1136/bmjopen-2023-079358

IMPACT FACTOR: 2.9 CITED HALF-LIFE: 4.0

START COMMENTARY

In Table 3, Ogutu et al. provide an overview of various cadres of community health workers (CHWs) in Nepal, Senegal, and Zambia, highlighting similarities and differences among groups. These countries were chosen for their high vaccination coverage. Authors note that each country had CHW cadres focused specifically on vaccine program implementation. Motivating factors for CHWs in all three countries included: 1) recognition for their contributions to the community, 2) incentives such as money food, and uniforms, and 3) training to increase their knowledge.

8 Estimating the Potential Public Health Value of BCG Revaccination.

Clark R, Sumner T, Weerasuriya C, Bakker R, Scriba T, White R.

J Infect Dis. 2024 Apr 03. PubMed ID: 38568214

ABSTRACT

An upcoming trial may provide further evidence that adolescent/adult-targeted BCG revaccination prevents sustained Mycobacterium tuberculosis infection, but its public health value depends on its impact on overall tuberculosis morbidity and mortality, which will remain unknown. Using previously calibrated models for India and South Africa, we simulated BCG revaccination assuming 45% prevention-of-infection efficacy, and we evaluated scenarios varying additional prevention-of-disease efficacy between +50% (reducing risk) and -50% (increasing risk). Given the assumed prevention-of-infection efficacy and range in prevention-of-disease efficacy, BCG revaccination may have a positive health impact and be cost-effective. This may be useful when considering future evaluations and implementation of adolescent/adult BCG revaccination.

WEB: 10.1093/infdis/jiae089

IMPACT FACTOR: 6.4 CITED HALF-LIFE: 9.5

START COMMENTARY

BCG revaccination may impact tuberculosis morbidity and mortality directly by preventing sustained infection in those who would have developed disease if infected, designated as prevention of infection (POI); revaccination may reduce TB morbidity and mortality by lowering progressing to disease in those who become infected despite vaccination, designated as prevention of disease (POD). There is uncertainty regarding POD for BCG revaccination as there is conflicting evidence that indicates that BCG could be either protective against disease progression or may increase likelihood of disease progression. The potential public health impact of BCG revaccination was estimated when the effect of revaccination on POD varies from reducing disease risk by 50% to increasing disease risk by 50% among those who received the vaccine when they were uninfected and became infected, with POI estimated to be 45% based on past studies. Results India and South Africa indicate that the vaccine would remain cost-effective even if POD efficacy was -50% (Figure 2).

9. Global vaccine coverage and childhood survival estimates: 1990-2019.

Zhang H, Patenaude B, Zhang H, Jit M, Fang H.

Bull World Health Organ. 2024 Apr 03;102(4):276-287.

PubMed ID: 3856219938693941

ABSTRACT

OBJECTIVE: To quantify the association between reduction in child mortality and routine immunization across 204 countries and territories from 1990 to 2019.

METHODS: We used child mortality and vaccine coverage data from the Global Burden of Disease Study. We used a modified child survival framework and applied a mixed-effects regression model to estimate the reduction in deaths in children younger than 5 years associated with eight vaccines.

FINDINGS: Between 1990 and 2019, the diphtheria-tetanus-pertussis (DTP), measles, rotavirus and Haemophilus influenzae type b vaccines were significantly associated with an estimated 86.9 (95% confidence interval, CI: 57.2 to 132.4) million fewer deaths in children younger than 5 years worldwide. This decrease represented a 24.2% (95% CI: 19.8 to 28.9) reduction in deaths relative to a scenario without vaccines. The DTP and measles vaccines averted 46.7 (95% CI: 30.0 to 72.7) million and 37.9 (95% CI: 25.4 to 56.8) million deaths, respectively. Of the total reduction in child mortality associated with vaccines, 84.2% (95% CI: 83.0 to 85.1) occurred in 73 countries supported by Gavi, the Vaccine Alliance, with an estimated 45.4 (95% CI: 29.8 to 69.2) million fewer deaths from 2000 to 2019. The largest reductions in deaths associated with these four vaccines were in India, China, Ethiopia, Pakistan and Bangladesh (in order of the size of reduction).

CONCLUSION: Vaccines continue to reduce childhood mortality significantly, especially in Gavisupported countries, emphasizing the need for increased investment in routine immunization programmes.

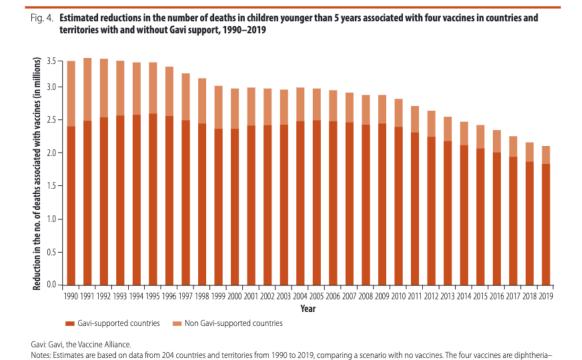
WEB: 10.2471/BLT.23.290129

IMPACT FACTOR: 11.1 CITED HALF-LIFE: 14.6

START COMMENTARY

Zhang et al. attribute the child mortality reduction in Gavi countries to both the rapid increases in coverage rates and the high mortality due to vaccine-preventable diseases. The DTP3 vaccine was associated with the largest reduction in child death in Gavi countries, with reductions in deaths in children <5 years across all time periods examined in this study. Measles, rotavirus, diphtheriatetanus-pertussis vaccine three doses (DTP3), and *Haemophilus influenzae* type B (Hib) vaccines

were responsible for a preventing 45.2 million infant deaths (11% decrease in infant mortality) from 1990 - 2019; the measles vaccine accounted for the largest decrease during this time. Figure 4 shows the estimated reduction in deaths in children <5 years for measles, rotavirus, DTP3, and Hib vaccines for Gavi and non-Gavi countries.



tetanus-pertussis vaccine three doses, Haemophilus influenzae type b vaccine three doses, measles vaccine one dose and rotavirus vaccine.

Return to List of Articles

20

10. Post-campaign coverage evaluation of a measles and rubella supplementary immunization activity in five districts in India, 2019-2020.

Thangaraj J, Prosperi C, Kumar M, Hasan A, Kumar V, Winter A, et al.

PLoS One. 2024 Apr 01;19(3):e0297385.

PubMed ID: 38551928

ABSTRACT

BACKGROUND: In alignment with the Measles and Rubella (MR) Strategic Elimination plan, India conducted a mass measles and rubella vaccination campaign across the country between 2017 and 2020 to provide a dose of MR containing vaccine to all children aged 9 months to 15 years. We estimated campaign vaccination coverage in five districts in India and assessed campaign awareness and factors associated with vaccination during the campaign to better understand reasons for not receiving the dose.

METHODS AND FINDINGS: Community-based cross-sectional serosurveys were conducted in five districts of India among children aged 9 months to 15 years after the vaccination campaign. Campaign coverage was estimated based on home-based immunization record or caregiver recall. Campaign coverage was stratified by child- and household-level risk factors and descriptive analyses were performed to assess reasons for not receiving the campaign dose. Three thousand three hundred and fifty-seven children aged 9 months to 15 years at the time of the campaign were enrolled. Campaign coverage among children aged 9 months to 5 years documented or by recall ranged from 74.2% in Kanpur Nagar District to 90.4% in Dibrugarh District, Assam. Similar coverage was observed for older children. Caregiver awareness of the campaign varied from 88.3% in Hoshiarpur District, Punjab to 97.6% in Dibrugarh District, Assam, although 8% of children whose caregivers were aware of the campaign were not vaccinated during the campaign. Failure to receive the campaign dose was associated with urban settings, low maternal education, and lack of school attendance although the associations varied by district.

CONCLUSION: Awareness of the MR vaccination campaign was high; however, campaign coverage varied by district and did not reach the elimination target of 95% coverage in any of the districts studied. Areas with lower coverage among younger children must be prioritized by strengthening the routine immunization programme and implementing strategies to identify and reach under-vaccinated children.

WEB: 10.1371/journal.pone.0297385

IMPACT FACTOR: 3.7 CITED HALF-LIFE: 7.3

START COMMENTARY

Results are from surveys conducted 3 to 16 months after the measles and rubella (MR) vaccine campaign in five districts in India (Dibrugarh District, Assam; Hoshiarpur District, Punjab; Palghar District, Maharashtra; Kanpur Nagar District, Uttar Pradesh; and Thiruvananthapuram District, Kerala), leading to concerns of recall bias particularly when asking about awareness of the vaccination campaign, source of information about the campaign, location of vaccination receipt, and reasons for not receiving the vaccine. The reason cited most often for non-receipt of the MR vaccine was lack of awareness of the location and time of the vaccination campaign. Among those who were aware of the campaign who did not have their child vaccinated, the primary reasons given were illness or fear of pain and side effects.

11 <u>Utilization of Mobile Reminders in Improving the Completeness and Timeliness of Routine Childhood Immunization in Kano Metropolis, Nigeria: A Randomized Controlled Trial.</u>

Yunusa U, Garba S, MacDonald S, Bello U, Ibrahim A, Abdulrashid I, et al.

J Pediatr Health Care. 2024 Mar 29.

PubMed ID: 38551537

ABSTRACT

INTRODUCTION: This study examined the effectiveness of mobile phone reminders in improving the completeness and timeliness of childhood immunization.

METHOD: We conducted a parallel arm cluster randomized controlled trial in four primary health care facilities in Nigeria. Reminders were sent to eligible participants in the intervention group at specific intervals when their children were scheduled to receive the vaccines administered at the sixth, 10, and 14 weeks after birth. Immunization records of all participants' children were then tracked to assess their immunization status.

RESULTS: The immunization status of the intervention (n = 275) and control (n = 261) arms was analyzed. Completeness and timeliness of the vaccine series were significantly higher (p < .001) among children of participants in the intervention (n = 169, 61.5% and n = 138, 50.2%) than those in the control group (n = 35, 13.4% and n = 13, 5%) arm.

DISCUSSION: Mobile phone reminders were established to be effective in increasing the completeness and timeliness of childhood immunization.

WEB: 10.1016/j.pedhc.2024.03.002

IMPACT FACTOR: 2.8 CITED HALF-LIFE: 6.5

START COMMENTARY

In this randomized controlled trial, participants in the intervention group received mobile phone reminders for routine childhood immunizations, with SMS reminders sent three days before each scheduled date for vaccines at six, ten, and fourteen weeks after birth. Participants also received a reminder phone call the day before the date of their child's immunization visit at six, ten, and fourteen weeks after birth. Control group participants received usual care without SMS or call reminders. Infants in the intervention group were statistically significantly more likely to receive vaccines on time at six weeks (71% vs 51%), ten weeks (64% vs 29%), and fourteen weeks (62% vs 17%) after birth (Table 3).

12. Low Measles Vaccination Coverage and Spatial Analysis of High Measles Vaccination Dropout in Ethiopia's Underprivileged Areas.

Shiferie F, Gebremedhin S, Andargie G, Tsegaye D, Alemayehu W, Fenta T.

Vaccines (Basel). 2024 Mar 31;12(3).

PubMed ID: 38543962

ABSTRACT

BACKGROUND: Measles remains a major cause of disease and death worldwide, especially in the World Health Organization African Region. This study aimed to estimate the coverage of measles vaccinations and map the spatial distribution of measles vaccination dropout in Ethiopia;

METHODS: A cross-sectional survey was conducted in Ethiopia's underprivileged areas. The study included 3646 mothers/caregivers of children. ArcGIS for the spatial analysis, Global Moran's I statistic for spatial autocorrelation, and Getis-Ord Gi* statistics for hot spot analysis were applied;

RESULTS: Overall, coverages of measles-containing-vaccine first- and second-doses were 67% and 35%, respectively. Developing regions had the lowest coverages of measles-containing-vaccine first- and second-doses, 46.4% and 21.2%, respectively. On average, the measles vaccination dropout estimate was 48.3%. Refugees had the highest measles vaccination dropout estimate (56.4%). The hot spot analysis detected the highest burden of measles vaccination dropout mainly in the northeastern parts of Ethiopia, such as the Afar Region's zones 1 and 5, the Amhara Region's North Gondar Zone, and peripheral areas in the Benishangul Gumuz Region's Assosa Zone;

CONCLUSIONS: The overall measles vaccination coverages were relatively low, and measles vaccination dropout estimates were high. Measles vaccination dropout hot spot areas were detected in the northeastern parts of Ethiopia.

WEB: 10.3390/vaccines12030328

IMPACT FACTOR: 7.8 CITED HALF-LIFE: 1.6

START COMMENTARY

The eight target population domains for this study conducted in Ethiopia are pastoral regions and populations, developing regions, newly established regions, conflict-afflicted areas, underserved urban slums, hard-to-reach areas in major regions, internally displaced populations, and refugees. Definitions for each target population can be found in Table 1, and their geographic location can be seen in Figure 1. Measles coverage among children living in underprivileged settings for dose one of

measles containing vaccine (MCV1) and dose two of measles containing vaccine (MCV2) are highest for those living in urban slums and lowest for those in developing regions (Figure 2).

Coverage of measles in underprivileged settings of Ethiopia 100 86.8 73.4 80 66.9 64.4 COVERAGE, % 58.2 54.1 60 46.4 45.1 39.4 36.5 34.9 40 29.4 25.4 23.7 21.2 20 0 Conflict-affected regions Newly established regions Hard-to-reach in agrarian regions Urban slums Pastoralist population Developing regions All **POPULATION DOMAIN** ■ MCV1, % ■ MCV2, %

Figure 2. MCV1 and MCV2 vaccination coverages in underserved settings of Ethiopia

13. Cost-effectiveness and public health impact of typhoid conjugate vaccine introduction strategies in Bangladesh.

Weyant C, Hooda Y, Munira S, Lo N, Ryckman T, Tanmoy A, et al.

Vaccine. 2024 Apr 16;42(11):2867-2876.

PubMed ID: 38531727

ABSTRACT

PURPOSE: Typhoid fever causes substantial morbidity and mortality in Bangladesh. The government of Bangladesh plans to introduce typhoid conjugate vaccines (TCV) in its expanded program on immunization (EPI) schedule. However, the optimal introduction strategy in addition to the costs and benefits of such a program are unclear.

METHODS: We extended an existing mathematical model of typhoid transmission to integrate cost data, clinical incidence data, and recently conducted serosurveys in urban, semi-urban, and rural areas. In our primary analysis, we evaluated the status quo (i.e., no vaccination) and eight vaccine introduction strategies including routine and 1-time campaign strategies, which differed by age groups targeted and geographic focus. Model outcomes included clinical incidence, seroincidence, deaths, costs, disability-adjusted life years (DALYs), and incremental cost-effectiveness ratios (ICERs) for each strategy. We adopted a societal perspective, 10-year model time horizon, and 3 % annual discount rate. We performed probabilistic, one-way, and scenario sensitivity analyses including adopting a healthcare perspective and alternate model time horizons.

RESULTS: We projected that all TCV strategies would be cost saving compared to the status quo. The preferred strategy was a nationwide introduction of TCV at 9-12 months of age with a single catch-up campaign for children ages 1-15, which was cost saving compared to all other strategies and the status quo. In the 10 years following implementation, we projected this strategy would avert 3.77 million cases (95 % Crl: 2.60 - 5.18), 11.31 thousand deaths (95 % Crl: 3.77 - 23.60), and save \$172.35 million (95 % Crl: -14.29 - 460.59) compared to the status quo. Our findings were broadly robust to changes in parameter values and willingness-to-pay thresholds.

CONCLUSIONS: We projected that nationwide TCV introduction with a catch-up campaign would substantially reduce typhoid incidence and very likely be cost saving in Bangladesh.

WEB: 10.1016/j.vaccine.2024.03.035

IMPACT FACTOR: 5.5 CITED HALF-LIFE: 7.2

START COMMENTARY

Figure 1 shows the model schematic, which considers seven typhoid statuses: susceptible, clinically infected, sub-clinically infected, recovered, carrier, vaccinated, and vaccinated with subclinical infection. The model projections for clinical typhoid cases, deaths, and societal costs over 10 years in Bangladesh without typhoid conjugate vaccine introduction are in Figure 2. Outcomes and costs under various vaccination strategies are in Figure 3. The projected cost of the most effective strategy was \$117 million for year 1 with cumulative vaccination costs across 10 years of \$176 million.

Return to List of Articles

14. The status of immunization program and challenges in Ethiopia: A mixed method study.

Nigatu T, Abraham L, Willems H, Tilaye M, Tiruneh F, Gebru F, et al.

SAGE Open Med. 2024 Mar 23;12:20503121241237115.

PubMed ID: 38516641

ABSTRACT

INTRODUCTION: Immunization helps reduce morbidity and mortality attributable to severe vaccine-preventable childhood illnesses. However, vaccination coverage and the quality of immunization data remain challenging in Ethiopia. This has led to poor planning, suboptimal vaccination coverage, and the resurgence of vaccine-preventable disease outbreaks in under-immunized pocket areas. The problem is further compounded by the occurrence of the COVID-19 pandemic and the disruption of the health information system due to recurrent conflict. This study assessed the current status of the immunization service and its challenges in Ethiopia.

METHODS: A mixed-methods study was conducted in three regions of Ethiopia from 21 to 31 May, 2023. A survey of administrative reports was done in a total of 69 health facilities in 14 woredas (districts). Nine KIIs were conducted at a district level among immunization coordinators selected from three regions to explore the challenges of the immunization program. Linear regression and descriptive statistics were used to analyze the quantitative data. Thematic analysis was applied to analyze the qualitative data. The findings from the qualitative data were triangulated to supplement the quantitative results.

RESULT: Two-thirds (66.4%) of the children were fully vaccinated, having received all vaccines, including the first dose of the MCV1, by 12 months of age, as reported through administrative reports collected from health facility records. Catchment area population size and region were significantly associated with the number of fully immunized children (p < 0.001 and p = 0.005, respectively). The vaccination dropout rates of the first to third dose of pentavalent vaccine and the first dose of pentavalent vaccine to the first dose of MCV1 were 8.6% and 7.4%, respectively. A considerable proportion of health facilities lack accurate data to calculate vaccination coverage, while most of them lack accurate data for dropout rates. Longer waiting time, interruptions in vaccine supply or shortage, inaccessibility of health facilities, internal conflict and displacement, power interruption and refrigerator breakdown, poor counseling practice, and caretakers' lack of awareness, fear of side effects, and forgetfulness were the reasons for the dropout rate and low coverage. The result also showed that internal conflict and displacement have significantly affected immunization coverage, with the worst effects seen on the most marginalized populations.

CONCLUSION: The study revealed low vaccination coverage, a high dropout rate, and poor quality of immunization data. Access and vaccination coverage among marginalized community groups (e.g., orphans and street children) were also low. Hence, interventions to address organizational, behavioral, technical, and contextual (conflict and the resulting internal displacement) bottlenecks affecting the immunization program should be addressed.

WEB: <u>10.1177/20503121241237115</u>

IMPACT FACTOR: 2.3 CITED HALF-LIFE: 3.5

START COMMENTARY

Across included sites in Ethiopia, coverage of dose one of pentavalent vaccine (penta1) was 77.4%, dose three of pentavalent vaccine (penta3) coverage was 70%, and first dose of measles containing vaccine (MCV1) coverage was 68.1%. Authors report data inconsistency and data quality issues. Information gathered through key informant interviews indicate that that reasons for data inaccuracy and inconsistency were lack of training, high client load, and high turnover of health care providers. Authors stress the importance of having good data quality to inform policy decisions.

Additional Articles of Interest

- 1 Spatial distribution of zero-dose children in Ethiopia: evidence for a targeted intervention from a large-scale cross-sectional evaluation survey. {Full Article}
- 2 Beyond constructs and principles: addressing gender-related barriers to high, equitable immunization coverage. {Full Article}
- 3 Influence of waning immunity on vaccination decision-making: A multi-strain epidemic model with an evolutionary approach analyzing cost and efficacy. {Full Article}
- 4 Challenges in capacity building of national immunization programs and emergency or pandemic vaccination responses in the Global Health Security Agenda member countries. {Full Article}
- 5 An Upsurge of Measles Cases in Mali-a Consequence of Pandemic-associated Disruption in Routine Immunization. {Full Article}
- 6 Etiology of diarrheal hospitalizations following rotavirus vaccine implementation and association of enteric pathogens with malnutrition among under-five children in India. {Full Article}
- 7 Implementation of an Innovative Learning Experience to Address Vaccine Hesitancy. {Full Article}
- 8 Early use of oral cholera vaccines as a prime control measure during outbreaks: Necessary but not sufficient. {Full Article}
- 9 Meaningful Media Experiences and Vaccination Message Communication: An Experimental Study with Vaccine-Hesitant Individuals. {Full Article}
- 10 Mass immunisation to eradicate Japanese encephalitis: Real-world evidence from Guizhou Province in 2005-2021. {Full Article}
- 11 Repeated vaccination with homologous influenza hemagglutinin broadens human antibody responses to unmatched flu viruses. {Full Article}
- 12 From single-cell cloning to high-yield influenza virus production implementing advanced technologies in vaccine process development. {Full Article}
- 13 Coverage of BCG Vaccination for children aged until 7 years old and its determinants in French Guiana. {Full Article}
- 14 Opportunities and challenges for human papillomavirus vaccination in China. [Full Article]
- 15 Costs of integrating hepatitis B screening and antiviral prophylaxis into routine antenatal care in Burkina Faso: Treat all versus targeted strategies. {Full Article}
- 16 An evaluation of the cost of human papilloma virus (HPV) vaccine delivery in Zambia. {Full Article}
- 17 Perceptions, attitudes, and willingness of healthcare and frontline workers to participate in an Ebola vaccine trial in Uganda. {Full Article}
- 18 Review of mathematical models of Neisseria gonorrhoeae vaccine impact: Implications for vaccine development. {Full Article}

- 19 Vaccine hesitancy under the lens: Nigeria's struggle against the worst diphtheria outbreak in decades. {Full Article}
- 20 A qualitative inquiry on drivers of COVID-19 vaccine hesitancy among adults in Kenya. {Full Article}
- 21 Optimizing Vaccine Trials for Enteric Diseases: The Enterics for Global Health (EFGH) Shigella Surveillance Study. {Full Article}
- 22 Reduced pertussis disease severity in infants following the introduction of pertussis vaccination of pregnant women in Spain, 2015-2019. {Full Article}
- 23 Leveraging seasonal influenza health worker vaccination programmes for COVID-19 vaccine Introduction: A global qualitative analysis. {Full Article}
- 24 Effects of Shock and Vibration on Product Quality during Last-Mile Transportation of Ebola Vaccine under Refrigerated Conditions1. {Full Article}
- 25 Child immunization status according to number of siblings and birth order in 85 low- and middle-income countries: a cross-sectional study. {Full Article}
- 26 Reverse engineering protection: A comprehensive survey of reverse vaccinology-based vaccines targeting viral pathogens. {Full Article}
- 27 Optimizing immunization services: A Data Envelopment Analysis (DEA) of child immunization facilities in Pakistan. {Full Article}
- 28 Simple economics of vaccination: public policies and incentives. {Full Article}
- 29 Expanded spectrum of varicella disease and the need for vaccination in India. (Full Article)
- 30 Prevalence and factors associated with hepatitis b vaccination uptake and completion among communities targeted for mass vaccination in gulu: a cross-sectional study. {Full Article}
- 31 Inequities and trends of polio immunisation among children aged 12-23 months in Ethiopia: a multilevel analysis of Ethiopian demographic and health survey. {Full Article}
- 32 Outcomes and Costs of the Transition From a Paper-Based Immunization System to a Digital Immunization System in Vietnam: Mixed Methods Study. {Full Article}
- 33 Translation and psychometric evaluation of an instrument to assess the health beliefs of Pakistani mothers regarding human papillomavirus vaccination. {Full Article}
- 34 How perceived coercion polarizes unvaccinated people: The mediating role of conspiracy beliefs. {Full Article}
- 35 Modelling the Public Health Burden of Herpes Zoster and the Impact of Adjuvanted Recombinant Zoster Vaccine in Five Selected Countries in Southeast Asia. {Full Article}
- 36 Circulating vaccine derived polio virus type 2 outbreak and response in Yemen, 2021-2022, a retrospective descriptive analysis. {Full Article}

Appendix

The literature search for the May 2024 Vaccine Delivery Research Digest was conducted on April 18, 2024. We searched English language articles indexed by the US National Library of Medicine and published between March 15, 2024 and April 14, 2024. The search resulted in 455 items.

SEARCH TERMS

(((((vaccine[tiab] OR vaccines[tiab] OR vaccination[tiab] OR immunization[tiab] OR immunisation[tiab] OR vaccine[mesh] OR immunization[mesh]) AND (logistics[tiab] OR supply[tiab] OR "supply chain"[tiab] OR implementation[tiab] OR expenditures[tiab] OR financing[tiab] OR economics[tiab] OR "Cost effectiveness"[tiab] OR coverage[tiab] OR attitudes[tiab] OR belief[tiab] OR beliefs[tiab] OR refusal[tiab] OR "Procurement"[tiab] OR timeliness[tiab] OR systems[tiab])) OR ("vaccine delivery"[tiab]) OR "vaccination refusal"[MeSH Terms] OR "immunization programs"[MeSH Terms] OR "zero dose"[tiab] OR "unvaccinated children"[tiab] OR "gavi"[tiab])) NOT ("in vitro"[tiab] OR "immune response"[tiab] OR gene[tiab] OR chemistry[tiab] OR genotox*[tiab] OR sequencing[tiab] OR nanoparticle*[tiab] OR bacteriophage[tiab] OR exome[tiab] OR exogenous[tiab] OR electropor*[tiab] OR "systems biology"[tiab] OR "animal model"[tiab] OR cattle[tiab] OR sheep[tiab] OR goat[tiab] OR rat[tiab] OR pig[tiab] OR mice[tiab] OR mouse[tiab] OR murine[tiab] OR porcine[tiab] OR ovine[tiab] OR rodent[tiab] OR fish[tiab])) AND (English[LA]) ("2024/15/03"[PDAT] : "2024/14/04"[PDAT]))