

# VACCINE DELIVERY RESEARCH DIGEST

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# List of Articles

- 1 A shorter post-exposure prophylaxis regimen for rabies, Pakistan.  
{[Abstract & START Commentary](#)} {[Full Article](#)}
  - A study assessing the costs and effectiveness of two-site, 1-week, intradermal rabies post-exposure prophylaxis regimen.
- 2 Planning for supplemental immunization activities using the readiness assessment dashboard: Experience from 2017/2018 Measles vaccination campaign, Nigeria.  
{[Abstract & START Commentary](#)} {[Full Article](#)}
  - A retrospective review of a readiness assessment tool dashboard for measles which ensures that critical activities are completed before supplemental immunization activities.
- 3 Optimal human papillomavirus vaccination strategies to prevent cervical cancer in low-income and middle-income countries in the context of limited resources: a mathematical modelling analysis.  
{[Abstract & START Commentary](#)} {[Full Article](#)}
  - A mathematical modeling study of human papillomavirus vaccination strategies to determine the optimal use of vaccine supplies.
- 4 A realist systematic review of evidence from low- and middle-income countries of interventions to improve immunization data use.  
{[Abstract & START Commentary](#)} {[Full Article](#)}
  - A realist systematic review summarizing the evidence on effective interventions for improving immunization data use in decision-making.
- 5 Gender and intersectional analysis of livestock vaccine value chains in Kaffrine, Senegal.  
{[Abstract & START Commentary](#)} {[Full Article](#)}
  - A systematic review exploring the role of gender and social factors in the provision to and utilization of vaccines for livestock diseases.
- 6 The impact of rotavirus vaccination in the prevalence of gastroenteritis and comorbidities among children after suboptimal rotavirus vaccines implementation in Taiwan: A population-based study.  
{[Abstract & START Commentary](#)} {[Full Article](#)}

- A retrospective cohort analyzing the annual nationwide population-level trends in the prevalence of rotavirus related diseases.
- 7 Should countries switch to using five- or ten-dose rotavirus vaccines now that they are available?  
{[Abstract & START Commentary](#)} {[Full Article](#)}
- A modelling study simulating vaccine supply chains in the Republic of Benin, Mozambique, and Bihar state in India to evaluate operational and economic impacts of nine different vaccine preparations.
- 8 Effectiveness of a killed whole-cell oral cholera vaccine in Bangladesh: further follow-up of a cluster-randomised trial.  
{[Abstract & START Commentary](#)} {[Full Article](#)}
- A cluster-randomized controlled trial follow up study determining the long-term effectiveness of killed whole-cell oral cholera vaccine.
- 9 Optimized supply chain model reduces health system costs in DRC.  
{[Abstract & START Commentary](#)} {[Full Article](#)}
- A pre-post study comparing costs before and after the implementation of an optimized immunization supply chain.
- 10 The burden of hand, foot, and mouth disease among children under different vaccination scenarios in China: a dynamic modelling study.  
{[Abstract & START Commentary](#)} {[Full Article](#)}
- A modelling study predicting the burden of hand, foot, and mouth disease under several vaccination scenarios.

## [Appendix](#)

# Details of Articles

## 1. [A shorter post-exposure prophylaxis regimen for rabies, Pakistan.](#)

Salahuddin N, Ansari N, Gohar M.

*Bull World Health Organ.* 2021 Jul 13;99(7):506-513.

### ABSTRACT

**OBJECTIVE:** To assess the cost and effectiveness of the two-site, 1-week, intradermal rabies post-exposure prophylaxis regimen recommended by the World Health Organization (WHO) in 2018.

**METHODS:** We compared the number of rabies vaccine and rabies immunoglobulin ampoules consumed at The Indus Hospital in Karachi, Pakistan and their cost before and after implementing WHO's 2018 recommendations. In 2017, patients with suspected rabies-infected bites were treated using the two-site, 4-week, Thai Red Cross regimen, which involved administering four rabies vaccine doses intradermally over 4 weeks and infiltrating immunoglobulin into serious wounds, with the remainder injected into a distant muscle. In 2018, patients received three vaccine doses intradermally over 1 week, with a calculated amount of immunoglobulin infiltrated into wounds only. Remaining immunoglobulin was saved for other patients. The survival of patients bitten by apparently rabid dogs was used as a surrogate for effectiveness.

**FINDINGS:** Despite treating 8.5% more patients in 2018 (5,370 patients) than 2017 (4,948 patients), 140 fewer ampoules of rabies vaccine and 436 fewer ampoules of rabies immunoglobulin were used, at a cost saving of 4,202 United States dollars. Of 56 patients bitten by apparently rabid dogs, 50 were alive at 6-month follow-up. The remaining six patients could not be contacted but did not present to any hospital with rabies.

**CONCLUSION:** The new regimen was more economical than the two-site, 4-week regimen and was equally effective. This regimen is recommended for preventing rabies in countries where the disease is endemic and rabies vaccine and immunoglobulin are in short supply.

**WEB:** [10.2471/BLT.20.275453](https://doi.org/10.2471/BLT.20.275453)

**IMPACT FACTOR:** 6.360

**CITED HALF-LIFE:** 12.4

### START COMMENTARY

Salahuddin *et al.* assess the effectiveness and costs of a short post-exposure prophylaxis regimen (two-site, 1-week, intradermal with infiltration of rabies immunoglobulin into serious wounds

only) recommended by the World Health Organization (WHO) in 2018. Prior to the updated recommendations, patients were treated using the two-site, 4-week intradermal vaccine schedule with infiltration of immunoglobulin into the wounds and distant muscle. This study is important as it provides evidence about an effective and affordable regimen that could be implemented in other low- and middle-income countries (LMICs) where there are many dog bites and limited access to rabies vaccines and immunoglobulin. From January 2018, the Indus Hospital in Karachi, Pakistan implemented the new schedule following updated WHO Guidelines. Data was obtained from January 1<sup>st</sup> to December 31<sup>st</sup> in 2017 and 2018 and the authors reported descriptive statistics for all patients treated, including those bitten by a rabid dog. Since dogs were not tested for rabies virus, the authors defined a dog as rabid if five or more people were bit by the same dog on the same day without provocation. They also compared the cost of post-exposure prophylaxis and the differences in the number of ampoules of vaccine and immunoglobulin consumed.

Almost all patients with a category II (indicating moderate risk of exposure, only requiring vaccine) and category III (severe wound requiring vaccine and immunoglobulin) were given rabies vaccine (99% in 2017 and 98.3% in 2018). Further, 43-45.0% of category-III patients received immunoglobulin in 2017 and 2018, respectively. 71.8% of patients completed the 4-week regimen in 2017 and 78.5% completed the 1-week course in 2018, indicating high adherence. In terms of cost, 7,145 ampoules were used to treat 4,948 patients in 2017 for a total cost of \$40,537 USD and 7,035 ampoules were used in 2018 to treat 5,370 patients, resulting in a total cost of \$39,746 USD. Results indicated that 61 people were bitten by a rabid dog in 2017 and 56 people were bitten in 2018. In 2018, 89% (n=50) were alive at follow up and 11 could not be reached due to moving out of the area. Two notable limitations of this study included the lack of laboratory confirmed rabies infections in dogs and the loss to follow up of participants. Despite these limitations, this study demonstrates that the shorter regimen is noninferior and cost-effective, indicating it should be considered for implementation in other settings.

[Return to List of Articles](#)

## 2. [Planning for supplemental immunization activities using the readiness assessment dashboard: Experience from 2017/2018 Measles vaccination campaign, Nigeria.](#)

Terna Richard M, Taiwo L, Jean Baptiste A, Bawa S, Dieng B, Wiwa O, et al.

*Vaccine*. 2021 Jul 12.

### ABSTRACT

**INTRODUCTION:** Globally, supplemental immunization activities (SIAs) are known to be a major strategy for attainment of the global measles elimination goal of less than one measles case per million population within a geographic area by the year 2020. Adequate planning is critical to the success of a vaccination campaign. To achieve a quality SIA implementation for effective interruption of measles transmission, the World Health Organization introduced the SIA Readiness Assessment Tool, which includes the readiness dashboard. It is a strategic planning tool used to ensure critical activities are completed before SIAs. Nigeria implemented a phased measles SIA in 2017/2018 and used the readiness assessment tool in the planning for the campaign. In this article, we report the use of the readiness assessment dashboard in the 2017/2018 measles SIA, we also reviewed its contributions to the outcome of the campaign looking at the post campaign coverage survey results for the states.

**METHODS:** We conducted a retrospective review of the readiness assessment dashboard used during the 2017/2018 measles vaccination campaign in Nigeria. The readiness dashboard tool was designed using Microsoft Excel 2016. We reported results in frequencies and proportions using charts and tables.

**RESULTS:** The states with 100% readiness a week prior to the campaign scored a post campaign coverage survey result of 84.6 - 96.5% with just one out of the eight states in this category getting a score below 90%. In the same vein, of the eight states that their readiness score at one week to the campaign was below 85%, six had post campaign coverage survey score of less than 90% with the highest score in this category being 92.3%. Some states with good readiness scores also had poor post campaign coverage survey which has been attributed to other factors other than readiness.

**CONCLUSION:** The readiness assessment dashboard for the measles vaccination campaign provided a platform for tracking states readiness. It is our view that a link between readiness assessment and coverage should be examined in future studies.

**WEB:** [10.1016/j.vaccine.2021.06.070](https://doi.org/10.1016/j.vaccine.2021.06.070)

**IMPACT FACTOR:** 3.143

**CITED HALF-LIFE:** 7.3

## START COMMENTARY

Terna Richard *et al.* conducted a retrospective review of the supplemental immunization activities (SIA) Readiness Assessment Tool dashboard for measles, an excel-based strategic planning tool aimed at ensuring that critical activities are completed before SIAs in Nigeria. This article is impactful as it demonstrates the utility of setting up a dashboard to track performance in planning and readiness for public health interventions. The readiness dashboard includes 29 activities, which are used as indicators for readiness in the dashboard. Activities/indicators cover 7 thematic areas including coordination, planning, financing, cold chain and logistics, logistics, social mobilization and communication, adverse events following immunization (AEFI) surveillance, and monitoring and supervision (*Table 1*). The overall objectives of the readiness dashboard are to: monitor the status of weekly readiness at the national and state levels; identify challenges and address them at the service level; facilitate reporting of readiness data to higher-level authorities to aid in timely interventions; and ensure quality completion of pre-implementation activities at the state-level, with the aim of having a successful measles campaign. As such, the monitoring tracked readiness at all levels including the ward, local government area (LGA), state, and national level. Terna Richard *et al.* report frequencies and proportions based on the readiness dashboard.

Results indicated that all states used the dashboard in planning for the 2017/2018 measles vaccination campaign. One week before the campaign, 21 of 36 states had readiness between 85-99%, as shown in *Figure 2A*. Of these 21 states, 11 had post campaign coverage survey (PCCS) coverage of >90%, 7 had PCCS coverage of between 90-94.5%, and 3 had met the campaign target of PCCS coverage >95%. Among seven states that had 100% readiness, only one was shown to have PCCS coverage above 90%, however this was attributed to factors other than readiness. One limitation of note is that the data quality, although mentioned and assessed, was not reported in this study. The authors state that there is a possibility of data falsification and bias which may have played a role in the high readiness values observed. However, a weekly teleconference with state was conducted to validate this information and reduce potential bias. Overall, this study demonstrates the willingness of states to use this dashboard for monitoring weekly performance of pre-implementation activities. Such monitoring, planning, and readiness is critical to the success of vaccination campaigns and warrants future research.

[Return to List of Articles](#)

### 3. [Optimal human papillomavirus vaccination strategies to prevent cervical cancer in low-income and middle-income countries in the context of limited resources: a mathematical modelling analysis.](#)

Drolet M, Laprise J, Martin D, Jit M, Barnard J, Gingras G, et al.  
*Lancet Infect Dis.* 2021 Jul 10.

## ABSTRACT

**BACKGROUND:** Introduction of human papillomavirus (HPV) vaccination has been slow in low-income and middle-income countries (LMICs) because of resource constraints and worldwide shortage of vaccine supplies. To help inform WHO recommendations, we modelled various HPV vaccination strategies to examine the optimal use of limited vaccine supplies and best allocation of scarce resources in LMICs in the context of the WHO global call to eliminate cervical cancer as a public health problem.

**METHODS:** In this mathematical modelling analysis, we developed HPV-ADVISE LMIC, a transmission-dynamic model of HPV infection and diseases calibrated to four LMICs: India, Vietnam, Uganda, and Nigeria. For different vaccination strategies that encompassed use of a nine-valent vaccine (or a two-valent or four-valent vaccine assuming high cross-protection), we estimated three outcomes: reduction in the age-standardised rate of cervical cancer, number of doses needed to prevent one case of cervical cancer (NNV; as a measure of efficiency), and the incremental cost-effectiveness ratio (ICER; in 2017 international \$ per disability-adjusted life-year [DALY] averted). We examined different vaccination strategies by varying the ages of routine HPV vaccination and number of age cohorts vaccinated, the population targeted, and the number of doses used. In our base case, we assumed 100% lifetime protection against HPV-16, HPV-18, HPV-31, HPV-33, HPV-45, HPV-52, and HPV-58; vaccination coverage of 80%; and a time horizon of 100 years. For the cost-effectiveness analysis, we used a 3% discount rate. Elimination of cervical cancer was defined as an age-standardised incidence of less than four cases per 100,000 woman-years.

**FINDINGS:** We predicted that HPV vaccination could lead to cervical cancer elimination in Vietnam, India, and Nigeria, but not in Uganda. Compared with no vaccination, strategies that involved vaccinating girls aged 9-14 years with two doses were predicted to be the most efficient and cost-effective in all four LMICs. NNV ranged from 78 to 381 and ICER ranged from \$28 per DALY averted to \$1406 per DALY averted depending on the country. The most efficient and cost-effective strategies were routine vaccination of girls aged 14 years, with or without a later switch to routine vaccination of girls aged 9 years, and routine vaccination of girls aged 9 years with a 5-year extended interval between doses and a catch-up programme at age 14 years. Vaccinating boys (aged 9-14 years) or women aged 18 years or older resulted in substantially higher NNVs and ICERs.



**INTERPRETATION:** We identified two strategies that could maximise efforts to prevent cervical cancer in LMICs given constraints on vaccine supplies and costs and that would allow a maximum of LMICs to introduce HPV vaccination.

**FUNDING:** World Health Organization, Canadian Institute of Health Research, Fonds de recherche du Qu bec-Sant, Compute Canada, PATH, and The Bill & Melinda Gates Foundation.

**TRANSLATIONS:** For the French and Spanish translations of the abstract see Supplementary Materials section.

**WEB:** [10.1016/S1473-3099\(20\)30860-4](https://doi.org/10.1016/S1473-3099(20)30860-4)

**IMPACT FACTOR:** 24.446

**CITED HALF-LIFE:** 4.7

## START COMMENTARY

In this mathematical modelling study, Drolet *et al.* assess various human papillomavirus (HPV) vaccination strategies to determine the optimal use of vaccine supplies in LMICs. This article is impactful as it addresses scarce resources and limited supply of HPV vaccines globally, which are impediments to achieving the global elimination of cervical cancer. The authors developed HPV-ADVISE LMIC, a dynamic transmission model calibrated to India, Vietnam, Uganda, and Nigeria. The four countries were selected based on the differences in HPV prevalence, sexual behavior, and cervical cancer burden. The model is like previous versions of the HPV-ADVISE for high-income countries (HICs) with specific modifications for LMICs. The model includes four mutually exclusion levels of sexual activity ranging from marriage with one lifetime sexual partner to female sex workers and men who pay for sex. The model includes 18 HPV types individually and independently (i.e., assuming no competition or synergy). The authors compared seven HPV vaccination (including a nine-valent vaccine, or a two-valent or four-valent vaccine assuming high cross-protection) strategies with two doses and assumed 80% vaccine coverage. Outcomes included the absolute reduction in age-standardized cervical cancer, relative reduction in age-standardized incidence of cervical cancer, and prevalence of HPV-16 and HPV-18. The main cost outcome was the incremental cost-effectiveness ratio (ICER) in costs per disability-adjusted life-year (DALY) averted.

Results indicate that routine vaccination of girls alone at 80% coverage would result in substantial decreases in the incidence of cervical cancer in each country, shown in *Figure 1*. Specifically, routine vaccination of 9 year old girls would reduce age-standardized incidence from 19 to 3 per 100,000 in India, 9 to 1 per 100,000 in Vietnam, 57 to 12 per 100,000 in Uganda, and 34 to 7 per 100,000 in Nigeria. Similar results are shown across all vaccination strategies and illustrated in *Figure 2*. Vaccinating women up to age 25 was shown to be more efficient and cost-effective than adding vaccination of boys across countries. In strategies that vaccinated boys, the number of doses

needed to prevent one case of cervical cancer (NNV) were six to eight times higher than when vaccinating women up to 25 years of age. Overall, two strategies: 1) vaccination of girls aged 14 years with or without a switch to routine vaccination of girls aged 9, and 2) routine vaccination of girls aged 9 with extended time between doses (5 years) and a catch up program for girls aged 14 years were the most efficient and cost effective across countries. These produce NNVs between 78 and 351 and ICERS between \$28-1,149 per DALY averted across countries. These strategies could be employed in LMICs to reduce the impact of vaccine supply shortages and scarce resources to achieve gains in cervical cancer elimination.

[Return to List of Articles](#)

#### 4. [A realist systematic review of evidence from low- and middle-income countries of interventions to improve immunization data use.](#)

Osterman A, Shearer J, Salisbury N.

*BMC Health Serv Res.* 2021 Jul 12;21(1):672.

### ABSTRACT

**BACKGROUND:** The use of routine immunization data by health care professionals in low- and middle-income countries remains an underutilized resource in decision-making. Despite the significant resources invested in developing national health information systems, systematic reviews of the effectiveness of data use interventions are lacking. Applying a realist review methodology, this study synthesized evidence of effective interventions for improving data use in decision-making.

**METHODS:** We searched PubMed, POPLINE, Centre for Agriculture and Biosciences International Global Health, and African Journals Online for published literature. Grey literature was obtained from conference, implementer, and technical agency websites and requested from implementing organizations. Articles were included if they reported on an intervention designed to improve routine data use or reported outcomes related to data use, and targeted health care professionals as the principal data users. We developed a theory of change a priori for how we expect data use interventions to influence data use. Evidence was then synthesized according to data use intervention type and level of the health system targeted by the intervention.

**RESULTS:** The searches yielded 549 articles, of which 102 met our inclusion criteria, including 49 from peer-reviewed journals and 53 from grey literature. A total of 66 articles reported on immunization data use interventions and 36 articles reported on data use interventions for other health sectors. We categorized 68 articles as research evidence and 34 articles as promising strategies. We identified ten primary intervention categories, including electronic immunization registries, which were the most reported intervention type (n...=...14). Among the research evidence from the immunization sector, 32 articles reported intermediate outcomes related to data quality and availability, data analysis, synthesis, interpretation, and review. Seventeen articles reported data-informed decision-making as an intervention outcome, which could be explained by the lack of consensus around how to define and measure data use.

**CONCLUSIONS:** Few immunization data use interventions have been rigorously studied or evaluated. The review highlights gaps in the evidence base, which future research and better measures for assessing data use should attempt to address.

**WEB:** [10.1186/s12913-021-06633-8](https://doi.org/10.1186/s12913-021-06633-8)

**IMPACT FACTOR:** 1.987

**CITED HALF-LIFE:** 5.6

## START COMMENTARY

In this realist systematic review, Osterman *et al.* synthesize evidence on effective interventions for improving immunization data use in decision-making in LMICs. This study is important as data, although routinely collected, is underutilized. Peer-reviewed and grey literature was utilized for this analysis. The authors established a theory of change (TOC) for how data use interventions affect data use, shown in *Figure 1*. The TOC includes three behavioral drivers including motivation, opportunity, and capability, as mechanisms of data use interventions. Osterman *et al.* adopted the WHO definitions of data quality, which include four dimensions: completeness and timeliness, internal consistency of data, external consistency, and external comparisons to population data. WHO defines data-informed decision-making as the process by which health system data is converted to usable information to decide on actions. Based on prior literature, six key barriers to data use were identified, including demand, access/availability, skills, quality, structure and process, and communication. Articles were included based on the following inclusion criteria: 1) Focuses on routine health system data; 2) reports an intervention; 3) reports data use outcomes; 4) intervention targets data users.

A total of 102 articles met the inclusion criteria, including 49 articles from peer-reviewed journals and 53 articles from grey literature. Of these, 66 reported on immunization data use, and are mapped in *Figure 3*. In terms of intermediate outcomes, a total of 22 articles reported improvements in the availability, timeliness, and/or quality of data, and 23 reported evidence relating to data analysis, synthesis, interpretation, and review. In terms of data use outcomes, 21 articles reported evidence related to data use at the community/health facility level, 17 at the district level, and three at the national level. Overall, the authors concluded that the state of evidence on what works to improve data use is limited. The authors found more evidence of interventions aimed at improving intermediate outcomes (e.g., quality, analysis) rather than studies focused on data use, indicating there is a need for further research to improve data-informed decision-making.

[Return to List of Articles](#)

## 5. [Gender and intersectional analysis of livestock vaccine value chains in Kaffrine, Senegal.](#)

McKune S, Serra R, Tour A.

*PLoS One*. 2021 Jul 10;16(7):e0252045.

### ABSTRACT

Among livestock species, poultry and small ruminants are of particular importance to rural women in low- and middle-income countries, as means to generate income, provide nutritious food for the family, accumulate wealth, and confer social status. Newcastle disease (ND) and Peste des Petits Ruminants (PPR) are widespread livestock diseases of poultry and small ruminants, respectively. While both diseases are vaccine preventable, numerous constraints limit the availability of and access to livestock vaccines, especially among the most vulnerable populations in developing countries. The literature on equity and effectiveness of livestock vaccine distribution systems has emphasized many of these constraints, however a gendered analysis and deeper understanding of the vaccine system remain insufficient. This paper applies a gendered and intersectional transformational approach, or GITA, to highlight how gender and other social factors affect the provision and utilization of vaccines for ND and PPR diseases in the region of Kaffrine, Senegal. We first articulate and describe the vaccine value chains (VVCs) for these diseases in Kaffrine, and then analyze the gendered and intersectional dynamics at different nodes of the VVCs, including actors at the national level, through the regional and district levels, down to providers of animal health at community level and the livestock keepers themselves. Our findings indicate that actors' various experiences are shaped and defined mainly by rigid gender norms, location and remoteness, and to a lesser degree by other social stratifications of age, ethnicity, and livelihood. Given the significant role that gender norms play in the livestock vaccine value chains, differences according to the livestock species, regulation of vaccine administration, and vaccine distribution systems emerge as highly relevant for understanding barriers that women specifically face within the livestock vaccination system.

**WEB:** [10.1371/journal.pone.0252045](https://doi.org/10.1371/journal.pone.0252045)

**IMPACT FACTOR:** 2.704

**CITED HALF-LIFE:** 7.2

### START COMMENTARY

In this systematic review, McKune *et al.* apply a gendered and intersectional transformational approach (GITA) to understand how gender and social factors affect provision to and utilization of vaccines for livestock diseases in Kaffrine, Senegal. This research is important as it sheds light on gendered and social factors related to livestock vaccination, which are critically important given

livestock allows women to generate income, provide for their families, and confer social status across settings globally. This study focuses on Newcastle disease (ND) in poultry and Peste des Petites Ruminants (PPR) in small ruminants. McKune *et al.* describe vaccine value chains (VVCs) for these diseases and the various gendered and intersectional constraints within levels of the VVC. Methods included reviewing documents and conducting key informant interviews (KIIs), individual interviews (IIs) and focus group discussions (FGDs). Reviewed documents included peer-reviewed literature, institutional reports, and project reports. KIIs were conducted with 23 experts from the private and public sectors, government, and international donors. IIs were conducted with 30 actors at the community level (e.g., animal health workers, livestock keepers). Focus group discussions were conducted with 30 men and women to understand experiences at the community level.

The livestock value distribution system for ND and PPR involves several international actors (e.g., World Organization for Animal Health) and a national government agency (Ministry of Livestock and Animal Protection). Both vaccines for ND and PPR are distributed publicly and privately. *Figure 2* shows the private value chain which involves foreign labs and private actors as well as the public system which involves other parties such as the National Livestock and Veterinary Research Lab, the Departmental Service of Livestock and Animal Protection, veterinary posts, private veterinarians, and community animal health workers. McKune *et al.* describe key issues at each point of the value chain. At the highest level (nationally), key constraints included technical and logistical challenges such as disruptions in vaccine procurement. Gender was not explicitly noted, potentially due to the limited presence of women at this level. At the regional and departmental level, issues such as large catchment areas, a lack of cold chain, and limited female representation were noted. At the animal health provider level, themes that emerged included that women have less access to education and training, gender norms limit women's success as community animal workers, and there are fewer barriers for the ND VVC for women since poultry is widely regarded as more appropriate for women. At the livestock level, specific norms related to keeping livestock include that men typically keep cattle, horses/donkeys, and sheep whereas women typically keep poultry. Women noted that their ability to keep livestock is limited by their inability to travel at night to seek veterinarian assistance and locate animals that do not come home at night. As such, men seem to have greater power over vaccination use. McKune *et al.* found that the knowledge of vaccination is uneven, confidence in vaccine distribution is lacking, remoteness is a key barrier to vaccination, and that the vaccination system does not meet the needs of transhumant households.

[Return to List of Articles](#)

## 6. [The impact of rotavirus vaccination in the prevalence of gastroenteritis and comorbidities among children after suboptimal rotavirus vaccines implementation in Taiwan: A population-based study.](#)

Lu M, Shia B, Kao Y, Lin S, Wang C, Lin W, et al.  
*Medicine (Baltimore)*. 2021 Jul 01;100(25):e25925.

### ABSTRACT

In Taiwan, rotavirus vaccination was implemented in 2006 in the private sector. The population-based impact of rotavirus vaccination on gastroenteritis and comorbidities of children remains under-investigated. We analyzed the annual prevalence of rotavirus-related disease, including gastroenteritis, convulsions, epilepsy, type I diabetes mellitus, intussusception, and biliary atresia among children under 5 years of age. Data were collected from Taiwan's National Health Insurance Research Database, a nationwide population-based database. A 16-year retrospective cohort study was conducted between 2000 and 2015. Among children <5 years of age, the prevalence of gastroenteritis decreased after 2012 (44,259.69 per 100 thousands) and remained lower through 2015 (39,931.11 per 100 thousands,  $P < 0.001$ ). The prevalence of convulsions rose steadily and significantly from 2007 (775.90 per 100 thousands) to 2015 (962.17 per 100 thousands,  $P < 0.001$ ). The prevalence of epilepsy decreased significantly until reaching a nadir in 2013 (from 501.56 to 293.53 per 100 thousands,  $P < 0.001$ ). The prevalence of biliary atresia tended upward, and surged suddenly in 2007 with a peak in 2013 (18.74 per 100 thousands). Among infants (<1 year of age) from 2000 to 2015, the prevalence of gastroenteritis declined steadily, and more rapidly after 2007 (22,513 to 17,285 per 100 thousands). In Taiwan, after introducing rotavirus vaccination, gastroenteritis in young children decreased, especially in infancy. However, gastroenteritis is still common in children, given other emerging pathogens. Our results highlight the impact of rotavirus vaccines on children's health in Taiwan and provide indications for future preventive medicine and healthcare strategies in children.

**WEB:** [10.1097/MD.00000000000025925](https://doi.org/10.1097/MD.00000000000025925)

**IMPACT FACTOR:** 1.889

**CITED HALF-LIFE:** N/A

### START COMMENTARY

In this 16-year retrospective cohort study, Lu *et al.* analyzed the annual nationwide population-level trends in the prevalence of rotavirus-related disease including gastroenteritis, seizures, epilepsy, type 1 diabetes mellitus, biliary atresia, and intussusception in children under 5. Data for were extracted from the National Health Insurance Research Dataset (NHIRD), a comprehensive health care database for over 99% of the Taiwanese population (23 million enrollees from 2000-

2015), which is a key strength of this study. To determine the impact of rotavirus vaccine introduction, 2006 was used as a baseline year and compared to 2007-2015 (post rotavirus vaccine introduction).

Baseline prevalence of gastroenteritis in 2006 was 40,331 cases per 100,000 people among children. The prevalence was significantly higher in each of the following years except for 2009 ( $P < 0.001$ ). However, this changed in 2013-2015, when prevalence was significantly lower (39,931 per 100,000,  $P < 0.001$ ) than in 2006. Epilepsy followed a similar trend, with epilepsy decreasing significantly after vaccine introduction and reaching its lowest point in 2013 (292 per 100,000,  $P < 0.001$ ). Diabetes mellitus and intussusception among children under 5 remained steady over the study period with slight fluctuations. For biliary atresia, prevalence showed an upward trend with a prevalence surge in 2007 of 19 per 100,000. Detailed results are shown in *Table 3*. Among children under age 1 years, the prevalence of gastroenteritis and epilepsy steadily declined after rotavirus introduction ( $P < 0.001$ ). Convulsions and intussusception did not change after vaccine introduction whereas biliary atresia showed an upward trend. Overall, Lu *et al.* noted an overall reduction of gastroenteritis in children under age 1 year old, and a more delayed reduction in children under 5 after 2012 despite suboptimal vaccine coverage. These results underscore the importance of rotavirus vaccine introduction to reduce the burden of disease among young children.

[Return to List of Articles](#)



## 7. [Should countries switch to using five- or ten-dose rotavirus vaccines now that they are available?](#)

Wedlock P, Cox S, Bartsch S, Randall S, O'Shea K, Ferguson M, et al.  
*Vaccine*. 2021 Jul 06;39(31):4335-4342.

### ABSTRACT

**INTRODUCTION:** Single-dose rotavirus vaccines, which are used by a majority of countries, are some of the largest-sized vaccines in immunization programs, and have been shown to constrain supply chains and cause bottlenecks. Efforts have been made to reduce the size of the single-dose vaccines; however, with two-dose, five-dose and ten-dose options available, the question then is whether using multi-dose instead of single-dose rotavirus vaccines will improve vaccine availability.

**METHODS:** We used HERMES-generated simulation models of the vaccine supply chains of the Republic of Benin, Mozambique, and Bihar, a state in India, to evaluate the operational and economic impact of implementing each of the nine different rotavirus vaccine presentations.

**RESULTS:** Among single-dose rotavirus vaccines, using Rotarix RV1 MMP (multi-monodose presentation) led to the highest rotavirus vaccine availability (49-80%) and total vaccine availability (56-79%), and decreased total costs per dose administered (\$0.02-\$0.10) compared to using any other single-dose rotavirus vaccine. Using two-dose ROTASIIL decreased rotavirus vaccine availability by 3-6% across each supply chain compared to Rotarix RV1 MMP, the smallest single-dose vaccine. Using a five-dose rotavirus vaccine improved rotavirus vaccine availability (52-92%) and total vaccine availability (60-85%) compared to single-dose and two-dose vaccines. Further, using the ten-dose vaccine led to the highest rotavirus vaccine availability compared to all other rotavirus vaccines in both Benin and Bihar.

**CONCLUSION:** Our results show that countries that implement five-dose or ten-dose rotavirus vaccines consistently reduce cold chain constraints and achieve higher rotavirus and total vaccine availability compared to using either single-dose or two-dose rotavirus vaccines.

**WEB:** [10.1016/j.vaccine.2021.06.021](https://doi.org/10.1016/j.vaccine.2021.06.021)

**IMPACT FACTOR:** 3.143

**CITED HALF-LIFE:** 7.3

### START COMMENTARY

In this modelling study, Wedlock *et al.* use the Highly Extensible Resource for Modeling Supply Chains (HERMES) simulation model of vaccine supply chains of the Republic of Benin, Mozambique, and Bihar state in India to evaluate operational and economic impacts of each of the

nine different vaccine preparations. The HERMES simulation model includes human resources, storage facilities and devices, vehicles and routes, vaccines, supply chain policies and associated costs for each of the listed components. The model simulates each vial moving through the supply chain and provides outputs such as the number of vaccine doses administered, the location and magnitude of constraints for storage and transport and vaccine wastage over the course of one year. This model was fit to three locations (Benin, Mozambique, and Bihar, India) with differing vaccine supply chains (*Table 1*). Briefly, each location has 4 supply chain levels in the model. Bihar has the fewest vaccination locations in the model (161), compared to 637 in Benin and 1,797 in Mozambique. *Table 1* also describes the number of vaccines in each routine immunization program, the birth cohort population, and the range of total refrigerator and freezer storage volumes across all storage locations. The model includes nine rotavirus vaccine presentations which would work with existing cold chain capacity in each setting. These include five single-dose vaccines (Rotarix RV1, Rotarix RV1 multi-monodose presentation, single-dose Rotavac 5D, single-dose, lyophilized ROTASIIL RV5, and single-dose, liquid ROTASIIL RV5) and four multi-dose vaccines (two-dose, lyophilized ROTASIIL RV5, five-dose Rotavac, ten-dose Rotavac, and five-dose Rotavac 5D), described in *Table 2*.

Overall, Wedlock *et al.* found that five- and ten-dose vaccines achieved higher rotavirus and total vaccine availability compared to one- or two-dose vaccines (*Figure 1*). Total and component costs per dose administered across each scenario are shown in *Figure 3*. In each country, using Rotarix RV1 MMP led to the highest rotavirus vaccine availability (49-80%) and the total vaccine availability (56%-79%) compared to other single dose vaccines. The total cost per dose administered was between \$0.02 and \$0.10. In all three settings, using two-dose led to higher vaccine availability and total vaccine availability than using any single-dose vaccine. Further, it led to decreased utilization of transport capacity and refrigerator capacity when compared to four of the single-dose vaccines due to the smaller volume per fully-immunized-child. To cost per dose administered was shown to be between \$0.03 to \$0.20. For the five dose preparation, it was shown to increase rotavirus and total vaccine availability in all settings besides Mozambique, where single-dose Rotarix RV1 MMP had 1% higher vaccine availability. Despite the increase in vaccine wastage when compared to two-dose (13% vs. 6%, respectively), it still resulted in more efficient physical storage capacity utilization. The ten-dose Rotavac implementation led to the highest rotavirus and total vaccine availability in Bihar and Benin, but not in Mozambique (when compared to five dose vaccines). Similarly, it led to the lowest total cost per dose administered. One notable strength of this model is that it assumes a multi-dose vial will be opened regardless of vaccination session size (which is what is recommended by WHO). The simulation model determines wastage rates based on the number of doses per vial, how long the vial can remain open, and the number of children that arrive to be vaccinated each day, rather than relying on one estimate of vaccine wastage. Overall,

this study demonstrates the importance of considering the whole supply chain when making decisions on which vaccines to use.

[Return to List of Articles](#)

## 8. [Effectiveness of a killed whole-cell oral cholera vaccine in Bangladesh: further follow-up of a cluster-randomised trial.](#)

Ali M, Qadri F, Kim D, Islam M, Im J, Ahmmed F, et al.

*Lancet Infect Dis.* 2021 Jun 19.

### ABSTRACT

**BACKGROUND:** Killed whole-cell oral cholera vaccines (OCVs) are widely used for prevention of cholera in developing countries. However, few studies have evaluated the protection conferred by internationally recommended OCVs for durations beyond 2 years of follow-up.

**METHODS:** In this study, we followed up the participants of a cluster-randomised controlled trial for 2 years after the end of the original trial. Originally, we had randomised 90 geographical clusters in Dhaka slums in Bangladesh in equal numbers (1:1:1) to a two-dose regimen of OCV alone (targeted to people aged 1 year or older), a two-dose regimen of OCV plus a water-sanitation-hygiene (WASH) intervention, or no intervention. There was no masking of group assignment. The WASH intervention conferred little additional protection to OCV and was discontinued at 2 years of follow-up. Surveillance for severe cholera was continued for 4 years. Because of the short duration and effect of the WASH intervention, we combined the two OCV intervention groups. The primary outcomes were OCV overall protection (protection of all members of the intervention clusters) and total protection (protection of individuals who got vaccinated in the intervention clusters) against severe cholera, which we assessed by multivariable survival models appropriate for cluster-randomised trials. This trial is registered on ClinicalTrials.gov, NCT01339845.

**FINDINGS:** The study was done between April 17, 2011, and Nov 1, 2015. 268...896 participants were present at the time of the first dose, with 188...206 in the intervention group and 80...690 in the control group. OCV coverage of the two groups receiving OCV was 66% (123...659 of 187...214 participants). During 4 years of follow-up, 441 first episodes of severe cholera were detected (243 episodes in the vaccinated groups and as 198 episodes in the unvaccinated group). Overall OCV protection was 36% (95% CI 19 to 49%) and total OCV protection was 46% (95% CI 32 to 58). Cumulative total vaccine protection was notably lower for people vaccinated before the age of 5 years (24%; -30 to 56) than for people vaccinated at age 5 years or older (49%; 35 to 60), although the differences in protection for the two age groups were not significant ( $p=0.3308$ ). Total vaccine protection dropped notably ( $p=0.0115$ ) after 3 years in children vaccinated at 1-4 years of age.

**INTERPRETATION:** These findings provide further evidence of long-term effectiveness of killed whole-cell OCV, and therefore further support for the use of killed whole-cell OCVs to control endemic cholera, but indicate that protection is shorter-lived in children vaccinated before the age of 5 years than in people vaccinated at the age of 5 years or older.

**FUNDING:** Bill & Melinda Gates Foundation.

**WEB:** [10.1016/S1473-3099\(20\)30781-7](https://doi.org/10.1016/S1473-3099(20)30781-7)

**IMPACT FACTOR:** 24.446

**CITED HALF-LIFE:** 4.7

## START COMMENTARY

In this follow-up to a cluster-randomized controlled trial, Ali *et al.* follow up participants after two years of the study end to determine the long-term effectiveness of killed whole-cell oral cholera vaccine (OCV). This article fills a critical gap in the literature on the long-term protection of OCVs. Ali *et al.* combined two groups of the intervention, the OCV group and the OCV and water-sanitation-hygiene (WASH) intervention group and compared this treatment group to the control (no OCV) group. The primary outcome was OCV overall protection, defined as the occurrence of first episodes of severely-dehydrating cholera during the 4 year post-vaccination period among all individuals from the beginning of the study (zero-time, defined as the date of dose one for vaccine recipients) in the two intervention groups compared to control. Another outcome was total cumulative protection against severe cholera, defined as the presence of severe dehydration and isolation of *V cholerae* 01 or 0139 during a diarrheal episode.

Across 90 clusters, there were 268,896 participants at time zero and 267,270 participants at follow up, as shown in *Figure 1*. Overall, 441 first episodes of cholera with severe dehydration were observed during the four years of follow up. Of these, 243 were in the vaccinated groups and 198 in the unvaccinated group. The cumulative 4-year overall protection was 36% (95% Confidence Interval [CI]: 19-49,  $p=0.0002$ ) after adjusting for covariates. Cumulative total vaccine protection over 4-years was 46% (95% CI 32 to 58,  $p<0.0001$ ). However, cumulative total vaccine protection was lower for those vaccinated before the age of five (24%, 95% CI 30-56) than those vaccinated aged 5 or older (49%, 95% CI 35-60), though this was not statistically significant ( $p=0.3308$ ). One key limitation is the high losses to follow up; 67% of the baseline population migrated or died during the 4-year follow up period. Another limitation was the merging of treatment groups. Although the authors justified this decision (by stating they had similar vaccine protection and the WASH intervention was stopped) and conducted analyses (compared total cumulative protection for OCV versus OCV/WASH), this may overestimate the impact of OCVs over the 4-year period. Overall, authors conclude that OCVs demonstrate sustained moderately high protection against cholera. However, given the lower protection and durability among younger populations, there is a need for more research into interventions to protect this vulnerable population.

[Return to List of Articles](#)

## 9. [Optimized supply chain model reduces health system costs in DRC.](#)

Thomas D, Motomoke E, Crawford J, Defawe O, Makaya A, Ngwato J, et al.

*Vaccine*. 2021 Jul 13;39(30):4166-4172.

### ABSTRACT

**OBJECTIVE:** In 2017, an optimized immunization supply chain (iSC) model was implemented in Equateur Province, Democratic Republic of the Congo. The optimized model aimed to address iSC challenges and featured direct deliveries to service delivery points (SDPs), longer replenishment intervals and increased cold chain capacity. This assessment examines iSC costs before and 5 months after implementing the optimized model.

**MATERIALS & METHODS:** We used a nonexperimental pre-post study design to compare iSC costs before and after implementation. We applied an activity-based costing approach with a comparison arm to assess procurement, management, storage and transportation costs for three iSC tiers: Province (n = 1); Zone (n = 4) and SDP (n = 15). We included data from 3 treatment Zones and 11 treatment SDPs; 1 control Zone and 4 control SDPs. We used sample and population data to estimate iSC costs for the entirety of Equateur Province.

**RESULTS:** In the period immediately before implementing the optimized model, estimated annual iSC costs were \$974,237. Following implementation, estimated annual iSC costs were \$642,627—a 34% (\$331,610) reduction. This change in costs was influenced by a 43% (\$180,313) reduction in SDP costs, a 67% (\$198,092) reduction in Zonal costs and an 18% (\$46,795) increase in Provincial costs. After implementing the optimized model, average iSC costs for treatment Zones was \$6,895 (SD: \$6,072); for the control Zone was \$21,738; for treatment SDPs was \$989 (SD: \$969); and for control SDPs was \$1,356 (SD: \$1,062).

**CONCLUSIONS:** We observed an absolute reduction in iSC costs in treatment Zones while control Zone post-implementation iSC costs remained the same or increased. The greatest cost reductions were for storage and transport at Zones and SDPs. Although cost implications of this model must continue to be evaluated over time, these findings are promising and will inform decisions around project expansion.

**WEB:** [10.1016/j.vaccine.2021.05.083](https://doi.org/10.1016/j.vaccine.2021.05.083)

**IMPACT FACTOR:** 3.143

**CITED HALF-LIFE:** 7.3

## START COMMENTARY

In this pre-post study, Thomas *et al.* compare costs before and after the implementation of an optimized immunization supply chain (iSC) in Equateur Province in the Democratic Republic of Congo (DRC). This article is impactful as it assesses the costs of an optimized and modernized iSC, Nouvelle Génération des Chaînes d'Approvisionnement (NGCA) which was developed by VillageReach and the DRC Ministry of Health to leverage existing resources to improve vaccine coverage in three health zones within Equateur Province. The iSC aimed to transition to routine delivery of vaccines and consumables, to increase storage capacity to support lengthened replenishment cycles, and to consolidate transportation responsibilities to higher iSC levels, which was hypothesized to lead to reduced costs. Thomas *et al.* used activity-based costing across three different periods: Period 1) September 2015-August 2016, before cold chain equipment (CCE) introduction and implementation of NGCA; Period 2) October 2016-March 2017, after the introduction of CCE and before NGCA implementation; Period 3) September 2017-January 2018 after introducing new CCE and NGCA implementation. The cost components considered in the analysis are described in detail in *Figure 3*. Costs from zones and service delivery points (SDPs) were extrapolated to the province by multiplying by population.

Key results were that the annualized total cost estimates were \$954,349 for Period I, \$974,237 for Period II, and \$642,627 for Period III. From Period II to Period III, there was an 18% (\$46,795) increase in Provincial-level costs, and a 67% decrease (\$198,092) in the overall Zonal-level statistics (*Table 1*). Sample costs from Period II to Period III (*Table 2*) showed decreases in storage, transport, management, and supply chain, but an increase in procurement costs. Two limitations of note include that the three treatment Health Zones were purposively selected based on difficult geographic accessibility, poor availability/stock, and low vaccination coverage, which may limit generalizability to other Zones. Similarly, to determine Provincial costs, Zonal and SDPs were extrapolated based on population, which may be imprecise. Lastly, detailed cost information was not considered, which may have led to underreporting of costs. Despite these limitations, this study makes an impactful contribution to the literature by showing that optimized, streamlined distribution practices can reduce costs and should be considered for further research and scale up.

[Return to List of Articles](#)

## 10. [The burden of hand, foot, and mouth disease among children under different vaccination scenarios in China: a dynamic modelling study](#)

Liu Z, Tian J, Wang Y, Li Y, Liu-Helmersson J, Mishra S, Wagner AL, et al.  
*BMC Infect Dis.* 2021 Jul 5;21(1):650.

### ABSTRACT

**BACKGROUND:** Hand, foot, and mouth disease (HFMD) is a common illness in young children. A monovalent vaccine has been developed in China protecting against enterovirus-71, bivalent vaccines preventing HFMD caused by two viruses are under development.

**OBJECTIVE:** To predict and compare the incidence of HFMD under different vaccination scenarios in China.

**METHODS:** We developed a compartmental model to capture enterovirus transmission and the natural history of HFMD in children aged 0–5, and calibrated to reported cases in the same age-group from 2015 to 2018. We compared the following vaccination scenarios: different combinations of monovalent and bivalent vaccine; a program of constant vaccination to that of pulse vaccination prior to seasonal outbreaks.

**RESULTS:** We estimate 1,982,819, 2,258,846, 1,948,522 and 2,398,566 cases from 2015 to 2018. Increased coverage of monovalent vaccine from 0 to 80% is predicted to decrease the cases by 797,262 (49.1%). Use of bivalent vaccine at an 80% coverage level would decrease the cases by 828,560. Use of a 2.0x pulse vaccination for the bivalent vaccine in addition to 80% coverage would reduce cases by over one million. The estimated  $R_0$  for HFMD in 2015–2018 was 1.08, 1.10, 1.35 and 1.17.

**CONCLUSIONS:** Our results point to the benefit of bivalent vaccine and using a pulse vaccination in specific months over routine vaccination. Other ways to control HFMD include isolation of patients in the early stage of dissemination, more frequent hand-washing and ventilation, and better treatment options for patients.

**WEB:** [10.1186/s12879-021-06157-w](https://doi.org/10.1186/s12879-021-06157-w)

**IMPACT FACTOR:** 2.688

**CITED HALF-LIFE:** 5.0

### START COMMENTARY

In this study, Liu *et al.* develop a deterministic compartmental model to predict the burden of hand, foot, and mouth disease (HFMD) under different vaccination scenarios in China. This study is



important as HFMD, caused by more than 20 types of enteroviruses, is commonly found in China, particularly among children under 5. Given a new vaccine has been developed against Enterovirus 71 (EV71) in China, there is a need to understand how different vaccination scenarios may impact future incidence of HFMD. As such, this study aims to evaluate both monovalent vaccine (against EV71), and bivalent (against EV71 and CVA16, the other common cause of HFMD). The model of enterovirus transmission reproduced observed HFMD cases among children under age 5 from 2015 to 2018. Model parameters, including transmission rate, duration of infectiousness, serotypes distribution, and vaccine efficacy were determined using a review of grey and peer-reviewed literature, and are shown in *Table 1*. Other data utilized in the model includes the national HFMD surveillance dataset, which tracks all acute infectious diseases caused by enteroviruses, demographic data including the total population of children under 5, the birth rate, and the mortality rate among children under 5. The model (shown in *Figure 1*) includes four categories: susceptible, exposed, infectious, and recovered.

The study estimated the following case numbers that were similar to the observed data (shown in *Figure 2*). *Figure 4* demonstrates the number of HFMD cases under each EV71 and bivalent vaccine coverage rates. Lui *et al.* conclude that higher vaccine coverage leads to reduced incidence, but reductions in efficiency are shown as the number needed to be vaccinated per case reduction (NNV) increased. Increasing coverage of a monovalent vaccine from 0 to 80% reduced cases by 49.1% whereas use of a bivalent vaccine at 80% coverage reduced cases by 51%. Pulse vaccination strategies prior to seasonal outbreaks would greatly impact vaccine effectiveness. The use of 2x pulse vaccination with 80% coverage would reduce cases by an estimated 1 million. Overall, Lui *et al.* conclude that bivalent vaccines are the best strategy for reducing HFMD cases. However, it is important to note that the NNV per case reduction suggests low vaccine efficiency. In conclusion, Lui *et al.* recommend bivalent vaccines with pulse vaccination before seasonal outbreaks to have the biggest impact on cases of HFMD.

[Return to List of Articles](#)

# Appendix

The literature search for the August 2021 Vaccine Delivery Research Digest was conducted on July 19, 2021. We searched English language articles indexed by the US National Library of Medicine and published between June 15, 2021 and July 14, 2021. The search resulted in 486 items.

## SEARCH TERMS

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(((((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])) 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]) ("2021/06/15"[PDAT] : "2021/07/14"[PDAT]))
```