VACCINE DELIVERY RESEARCH DIGEST

UNIVERSITY OF WASHINGTON GLOBAL HEALTH START PROGRAM REPORT TO THE BILL AND MELINDA GATES FOUNDATION

MARCH 15, 2015

PRODUCED BY: LONG JE, DUERR AC

TABLE OF CONTENTS

1.	 The development of global vaccine stockpiles. A review of vaccine stockpiles currently in use and how they can be optimized in the future. 	3
2.	 Strengthening routine immunization systems to improve global vaccination coverage. A brief history of global vaccine coverage, and assessment of challenges that need to be addressed to improve future coverage. 	4
3.	 Vaccinations against respiratory tract infections at Hajj. A systematic review of available data on uptake and effectiveness of vaccination to protect against RTI during Hajj. 	5
4.	Maternal and neonatal tetanus elimination: from protecting women and newborns to protecting all.	6
5.	 An assessment of the successes, challenges and remaining needs to reach MNT elimination. Vaccination coverage in India: A small area estimation approach. A small area estimation used to predict vaccine coverage rates in areas not recently surveyed. 	7
6.	 Next generation vaccines: single-dose encapsulated vaccines for improved global immunisation coverage and efficacy. An overview of the basis and benefits of single-dose encapsulated vaccines and the barriers to development. 	8
7.	 Serogroup A meningococcal conjugate (PsA-TT) vaccine coverage and measles vaccine coverage in Burkina Faso-Implications for introduction of PsA-TT into the Expanded Programme on Immunization. A study to examine the success of a PsA-TT vaccine campaign. 	9
8.	 Low rate of influenza and pneumococcal vaccine coverage in rheumatoid arthritis: Data from the international COMORA cohort. A study examining influenza and pneumococcal vaccine coverage among people with rheumatoid arthritis. 	10
9.	 Cross-border collaboration between China and Myanmar for emergency response to imported vaccine derived poliovirus case. A case report describing a collaborative public health response to polio between China and Myanmar in 2012. 	11
10.	 Comparison of impact and cost-effectiveness of rotavirus supplementary and routine immunization in a complex humanitarian emergency, Somali case study. A cost-effectiveness analysis of adding rotavirus to routine vaccination programs. 	12

Appendix: PubMed Search Terms

13



1. THE DEVELOPMENT OF GLOBAL VACCINE STOCKPILES.

Yen C, Hyde TB, Costa AJ, Fernandez K, Tam JS, Hugonnet S,et al. Lancet Infect Dis. 2015 Mar;15(3):340-347. Epub 2015 Feb 6. PMID: 25661473

ABSTRACT

Global vaccine stockpiles, in which vaccines are reserved for use when needed for emergencies or supply shortages, have effectively provided countries with the capacity for rapid response to emergency situations, such as outbreaks of yellow fever and meningococcal meningitis. The high cost and insufficient supply of many vaccines, including oral cholera vaccine and pandemic influenza vaccine, have prompted discussion on expansion of the use of vaccine stockpiles to address a wider range of emerging and re-emerging diseases. However, the decision to establish and maintain a vaccine stockpile is complex and must take account of disease and vaccine characteristics, stockpile management, funding, and ethical concerns, such as equity. Past experience with global vaccine stockpiles provide valuable information about the processes for their establishment and maintenance. In this Review we explored existing literature and stockpile data to discuss the lessons learned and to inform the development of future vaccine stockpiles.

WEB: http://dx.doi.org/10.1016/S1473-3099(14)70999-5

IMPACT FACTOR: 19.45

CITED HALF-LIFE: 4.80

UW EDITORIAL COMMENT: Table 1 provides a summary of the currently available vaccine stockpiles by vaccine type, including the number of doses available and managing party. The structure of International Coordinating Groups (ICGs), which manage meningococcal, yellow fever, and oral cholera vaccines, can be seen in Figure 1. Each stockpile also includes a revolving fund mechanism to maintain sustainability and effectiveness if a funding shortage should occur. Panel 1 enumerates the key factors to consider when determining if a stockpile should be established for a particular vaccine, including factors of the disease, the vaccine, and the management of the stockpile.



2. STRENGTHENING ROUTINE IMMUNIZATION SYSTEMS TO IMPROVE GLOBAL VACCINATION COVERAGE.

Sodha SV, Dietz V.

Br Med Bull. 2015 Mar;113(1):5-14. Epub 2015 Feb 3. PMID: 25649959

ABSTRACT

BACKGROUND: Global coverage with the third dose of diphtheria-tetanus-pertussis vaccine among children under 1 year of age stagnated at ~ 83-84% during 2008-13.

SOURCE OF DATA: Annual World Health Organization and UNICEF-derived national vaccination coverage estimates.

AREAS OF AGREEMENT: Incomplete vaccination is associated with poor socioeconomic status, lower education, non-use of maternal-child health services, living in conflict-affected areas, missed immunization opportunities and cancelled vaccination sessions.

AREAS OF CONTROVERSY: Vaccination platforms must expand to include older ages including the second year of life. Immunization programmes, including eradication and elimination initiatives such as those for polio and measles, must integrate within the broader health system.

CONCLUSION: The Global Vaccine Action Plan (GVAP) 2011-20 is a framework for strengthening immunization systems, emphasizing country ownership, shared responsibility, equity, integration, sustainability and innovation.

AREAS TIMELY FOR DEVELOPING RESEARCH: Immunization programmes should identify, monitor and evaluate gaps and interventions within the GVAP framework.

WEB: http://dx.doi.org/10.1093/bmb/ldv001

IMPACT FACTOR: 3.95

CITED HALF-LIFE: 10.00

UW EDITORIAL COMMENT: This article provides a review of the history of global vaccine and the challenges that are currently impeding improvements to vaccination coverage. Completion of the third DTP vaccine is often used as a marker for successful vaccination campaigns, and Figure 1 provides an overview of DTP3 coverage globally and by WHO region from 1980-2013. Coverage increased drastically between 1980 -1990, but has stagnated since this time. Figure 2 provides further information about the annual rates of change for DTP3 as well as polio (3rd dose) and measles vaccines, all showing similar trends. A number of factors improved coverage, including improved national planning and increased budgeting for immunizations, GAVI, periodic intensification of routine immunization (PIRI), and the Reaching Every District (RED) initiative. Current challenges include a 27-fold increase in the price of a full vaccination course since 1976, increase in the number of recommended vaccines leading to issues with supply chain and storage, caregiver concern about multiple injections, and subnational inequality of resources.



3. VACCINATIONS AGAINST RESPIRATORY TRACT INFECTIONS AT HAJJ.

Alqahtani AS, Rashid H, Heywood AE. Clin Microbiol Infect. 2015 Feb;21(2):115-127. Epub 2014 Dec 4. PMID: 25682277

ABSTRACT

The transmission of respiratory tract infections (RTIs) is very high among the Hajj congregation in Mecca, Saudi Arabia. Despite recommendations for vaccinations, pilgrims remain at increased risk of RTIs. In this paper we systematically reviewed available studies assessing the uptake and effectiveness of vaccinations against RTIs among Hajj pilgrims and enumerated important demographic factors, if described, associated with vaccine uptake. Of the 42 included studies, 29 reported on the uptake and effectiveness of influenza vaccine among pilgrims, eight studies reported the uptake of other vaccines, notably pneumococcal, diphtheria and bacillus Calmette-Guérin vaccines, and the remaining five studies described both influenza and non-influenza vaccines. The uptake of seasonal influenza vaccine ranged from 0.7% to 100% across the study populations, with coverage highest in the elderly and those with pre-existing co-morbidities. The effectiveness of influenza vaccine was variable across studies but was significantly effective against laboratory-confirmed influenza (risk ratio 0.56; 95% CI 0.41-0.75; p < 0.001) in pooled metadata from six studies. Uptake of diphtheria and pneumococcal vaccines was low, and the only study reporting pertussis among Hajj pilgrims found the presence of pre-Hajj immunity to be significantly protective against disease. Despite favourable evidence of effectiveness, our review shows variable uptake of vaccines across a number of studies with few data available on the uptake of non-influenza vaccines. Mixed-method studies are needed to gauge knowledge, attitudes and practices of Hajj pilgrims regarding vaccination, and randomized controlled trials are required to confirm the efficacy of vaccines and improve uptake in this vulnerable travelling population.

WEB: http://dx.doi.org/10.1016/j.cmi.2014.11.026

IMPACT FACTOR: 4.58

CITED HALF-LIFE: 4.00

UW EDITORIAL COMMENT: Figure 2 provides a forest plot of the 6 studies (of 42 included in the systematic review) that reported laboratory confirmed influenza status. This meta-analysis found a statistically significant protective effect of influenza vaccine (fixed effect RR= 0.56, 95% CI 0.41 – 0.75, p<0.0001). The review found mixed results regarding vaccination uptake, although there was some evidence that influenza vaccination was lower in Saudi Arabian pilgrims compared to international pilgrims. The authors hypothesize this could be due in part to misperceptions about vaccination. This systematic review was limited by heterogeneity in both quality and content of data included, with varying definitions of RTI and methods of measuring vaccine exposure. Additionally, the inclusion of only English language publications may have limited the results.



4. MATERNAL AND NEONATAL TETANUS ELIMINATION: FROM PROTECTING WOMEN AND NEWBORNS TO PROTECTING ALL.

Khan R, Vandelaer J, Yakubu A, Raza AA, Zulu F. Int J Womens Health. 2015 Feb 3;7:171-80. eCollection 2015. PMID: 25678822

ABSTRACT

A total of 35 of the 59 countries that had not eliminated maternal and neonatal tetanus (MNT) as a public health problem in 1999 have since achieved the MNT-elimination goal. Neonatal tetanus deaths have decreased globally from 200,000 in 2000 to 49,000 in 2013. This is the result of increased immunization coverage with tetanus toxoid-containing vaccines among pregnant women, improved access to skilled birth attendance during delivery, and targeted campaigns with these vaccines for women of reproductive age in high-risk areas. In the process, inequities have been reduced, private-public partnerships fostered, and innovations triggered. However, lack of funding, poor accessibility to some areas, suboptimal surveillance, and a perceived low priority for the disease are among the main obstacles. To ensure MNT elimination is sustained, countries must build and maintain strong routine programs that reach people with vaccination and with clean deliveries. This should also be an opportunity to shift programs into preventing tetanus among all people. Regular assessments, and where needed appropriate action, are key to prevent increases in MNT incidence over time, especially in areas that are at higher risk. The main objective of the paper is to provide a detailed update on the progress toward MNT elimination between 1999 and 2014. It elaborates on the challenges and opportunities, and discusses how MNT elimination can be sustained and to shift the program to protect wider populations against tetanus.

WEB: http://dx.doi.org/10.2147/IJWH.S50539

IMPACT FACTOR: 0.00

CITED HALF-LIFE: 0.00

UW EDITORIAL COMMENT: Figure 1 provides a map of which countries have not yet eliminated maternal and neonatal tetanus (MNT). Due to availability of surveillance data and the high case fatality rate, neonatal tetanus death is often used as a proxy for measuring MNT. Figure 2 shows the time trend in reduction of neonatal tetanus death, as well as the coverage levels of TT2+. Figure 4 highlights the progress that has been made since 1999 in reaching women of reproductive age with supplementary immunization activity. However as this figure shows, there is still a large number of women at risk for MNT that are not currently being targeted (approximately 88.3 million women across 24 countries in 2013). The authors estimate that it will cost approximately \$170 million to target these women, of which \$91 million was still unfunded as of June 2014.



5. VACCINATION COVERAGE IN INDIA: A SMALL AREA ESTIMATION APPROACH.

Pramanik S, Muthusamy N, Gera R, Laxminarayan R. Vaccine. 2015 Feb 11. pii: S0264-410X(15)00150-4. [Epub ahead of print] PMID: 25681661

ABSTRACT

Information on population health indicators in India come from a number of surveys that vary in periodicity, scope and detail. In the case of immunization, the most recent coverage indicators are derived from the first round of Annual Health Survey (AHS-1, 2010-11), but these were conducted only in 9 of 35 states and union territories. The most recent national surveys of immunization coverage were conducted in 2009 (Coverage Evaluation Survey) by UNICEF. Therefore, reliable immunization coverage data for the entire country since 2009 is lacking. We used an established approach of small area estimation to predict coverage rates of several vaccinations for the remaining 26 states (not covered by AHS-1) in 2011. In our method, we considered a linear mixed model that combines data from five cross sectional surveys representing five different time points. Our model encompasses sampling error of the survey estimates, area specific random effects, autocorrelated area by time random effects and hence, borrows strength across areas and time points both. Model-based estimates for 2011 are almost identical to the AHS-1 estimates for the nine states, suggesting that our model provides reliable prediction of vaccination coverage as AHS-1 estimates are highly precise because of their large sample size. Results indicate that coverage inequality between rural and urban areas has been reduced significantly for most states in India. The National Rural Health Mission has had both supply side and demand side effects on the immunization programme in rural India. In combination, these effects may have contributed to the reduction of vaccination coverage gaps between urban and rural areas.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.01.083

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Figure 2 shows vaccination coverage in rural areas by state, comparing the most recent national survey conducted in 2009 to the predicted vaccination coverage estimates for 2011. The national rural coverage rate is highlighted, showing how varied rates by state are compared to the national average. Figure 4 focuses on the inequality in coverage between rural and urban areas. The graph shows that, according to the predicted values from this model, there has been a large reduction in inequality since the last national survey, which the authors hypothesized is due in part to the National Rural Health Mission. One limitation of this analysis is that many of the surveys relied on maternal recall to assess immunization status, and the proportion of data that used this measure varied by year and geography. This could create differential ascertainment of the outcome. Additionally, many predictors of vaccination rates, particularly related to supply, could not feasibly be assessed.



6. NEXT GENERATION VACCINES: SINGLE-DOSE ENCAPSULATED VACCINES FOR IMPROVED GLOBAL IMMUNISATION COVERAGE AND EFFICACY.

Walters AA, Krastev C, Hill AV, Milicic A.

J Pharm Pharmacol. 2015 Feb 2. [Epub ahead of print] PMID: 25644530

ABSTRACT

OBJECTIVES: Vaccination is considered the most successful health intervention; yet incomplete immunisation coverage continues to risk outbreaks of vaccine preventable diseases worldwide. Vaccination coverage improvement through a single-dose prime-boost technology would revolutionise modern vaccinology, impacting on disease prevalence, significantly benefiting health care and lowering economic burden of disease.

KEY FINDINGS: Over the past 30 years, there have been efforts to develop a single-dose delayed release vaccine technology that could replace the repeated prime-boost immunisations required for many current vaccines. Biocompatible polymers have been employed to encapsulate model vaccines for delayed delivery in vivo, using either continuous or pulsed release. Biomaterial considerations, safety aspects, particle characteristics and immunological aspects of this approach are discussed in detail.

SUMMARY: Despite many studies showing the feasibility of vaccine encapsulation for single-dose primeboost administration, none have been translated into convincing utility in animal models or human trials. Further development of the encapsulation technology, through optimising the particle composition, formulation, antigen loading efficacy and stability, could lead to the application of this important approach in vaccine deployment. If successful, this would provide a solution to better global vaccination coverage through a reduction in the number of immunisations needed to achieve protection against infectious diseases. This review provides an overview of single-dose vaccination in the context of today's vaccine needs and is derived from a body of literature that has not been reviewed for over a decade.

WEB: <u>http://dx.doi.org/10.1111/jphp.12367</u>

IMPACT FACTOR: 2.16

CITED HALF-LIFE: 0.00

UW EDITORIAL COMMENT: The focus of this article is on a single vaccination that mimics multiple doses by providing a soluble form similar to currently existing vaccines, as well as an encapsulated form that would be utilized through pulse release of antigen, after a period of time, acting as a booster. This would eliminate the need for multiple vaccinations, however there are still many barriers that have hindered the development of this vaccine type beyond *in vitro* testing. Table 3 provides a list of reference papers that have attempted single dose encapsulation, and what they found. Factors that influence development include the time delay needed for the encapsulated vaccine delivery, the composition and size of the microcapsule, and the thermostability of the formulation at body temperature over time.



7. SEROGROUP A MENINGOCOCCAL CONJUGATE (PSA-TT) VACCINE COVERAGE AND MEASLES VACCINE COVERAGE IN BURKINA FASO-IMPLICATIONS FOR INTRODUCTION OF PSA-TT INTO THE EXPANDED PROGRAMME ON IMMUNIZATION.

Meyer SA, Kambou JL, Cohn A, Goodson JL, Flannery B, Medah I, et al. Vaccine. 2015 Mar 17;33(12):1492-8. Epub 2015 Jan 28. PMID: 25636915

ABSTRACT

BACKGROUND: A new serogroup A meningococcal conjugate vaccine (PsA-TT, MenAfriVac[™]) has been developed to combat devastating serogroup A Neisseria meningitis (MenA) epidemics in Africa. A mass immunization campaign targeting 1-29 year olds was conducted in Burkina Faso in December 2010. Protection of subsequent infant cohorts will be necessary through either introduction of PsA-TT into the routine Expanded Programme on Immunization (EPI) or periodic repeat mass vaccination campaigns.

OBJECTIVES: To inform future immunization policy for PsA-TT vaccination of infants through a comparison of PsA-TT campaign vaccination coverage and routine measles-containing vaccine (MCV) coverage in Burkina Faso.

METHODS: A national survey was conducted in Burkina Faso during December 17-27, 2011 using stratified cluster sampling to assess PsA-TT vaccine coverage achieved by the 2010 nationwide immunization campaign among 2-30 year olds and routine MCV coverage among 12-23 month olds. ...

RESULTS: National overall PsA-TT campaign coverage was 95.9% (95% CI: 95.0-96.7) with coverage greater than 90% all 13 regions of Burkina Faso. National overall routine MCV coverage was 92.5% (95% CI: 90.5-94.1), but ranged from 75.3% to 95.3% by region. The primary predictor for PsA-TT vaccination among all age groups was a head of household informed of the campaign. PsA-TT vaccination was more likely in residents of rural settings, whereas MCV vaccination was more likely in residents of urban settings.

CONCLUSIONS: Overall national vaccination rates in Burkina Faso were similar for PsA-TT and MCV vaccine. The regions with MCV coverage below targets may be at risk for sub-optimal vaccination coverage if PsA-TT is introduced in EPI. These results highlight the need for assessments of routine vaccination coverage to guide PsA-TT immunization policy in meningitis belt countries.

WEB: <u>http://dx.doi.org/10.1016/j.vaccine.2015.01.043</u>

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: Table 4 summarizes the predictors associated with PsA-TT and MCV vaccination. The survey found high rates of recall-only reporting of MCV vaccination (38.9% by recall only vs. 53.6% confirmed by vaccination card or book), which limits the interpretation of routine MCV vaccination found by this analysis, as it is likely that some of the MCV reported may be from supplementary immunization activities.



8. LOW RATE OF INFLUENZA AND PNEUMOCOCCAL VACCINE COVERAGE IN RHEUMATOID ARTHRITIS: DATA FROM THE INTERNATIONAL COMORA COHORT.

Hmamouchi I, Winthrop K, Launay O, Dougados M. Vaccine. 2015 Mar 17;33(12):1446-52. doi:. Epub 2015 Feb 7. PMID: 25659279

ABSTRACT

BACKGROUND: Rheumatoid Arthritis (RA) patients are at increased risk of suffering from respiratory infections than the general public. Vaccinations against Streptococcus pneumococcus and influenza are recommended, but not often used in RA. Our objectives were: (1) to describe pneumococcal and influenza vaccine coverage in RA patients across various countries and (2) to identify factors associated with their usage.

METHODS: Using data from the COMORA cohort, 3920 RA patients were enrolled across 17 countries. We collected patient demographic and disease characteristics, and reported vaccine use over a six month time period. We used logistic regression to evaluate factors related to pneumococcal and influenza vaccine coverage.

RESULTS: Overall vaccination coverage within the recommendations was low with huge disparities between countries: 17.2% (95%CI: 16.0-18.4) for pneumococcal vaccination (from 0% in Morocco to 56.5% in France) and 25.3% (95%CI: 23.8-26.5) for influenza vaccination (less than 1% in Morocco and Egypt to 66.2% in Japan). In countries where immunization was more frequent, we found that predictive factors of vaccination were older age, lower disease activity, higher educational level, use of biotherapy, absence of corticosteroid therapy, and presence of comorbidities.

CONCLUSIONS: Despite international recommendations for influenza and pneumococcal vaccination, we observed a low prevalence of these vaccinations among RA patients, with huge disparity between countries. Efforts are needed to better inform patients and physicians regarding the need for vaccinations.

WEB: http://dx.doi.org/10.1016/j.vaccine.2015.01.065

IMPACT FACTOR: 3.49

CITED HALF-LIFE: 4.90

UW EDITORIAL COMMENT: This study utilized data from an existing cohort to determine vaccination rates in those with rheumatoid arthritis. Table 1 and Table 2 provide the rates of pneumococcal vaccine and influenza vaccine, respectively, by country. The authors note that differences in countries are due in part to different national approaches to vaccination of people over the age of 65 and the immunocompromised. Additionally, pneumococcal vaccine is not available in some countries in Asia and South America. Finally, high prices and low supply may be responsible for low rates in Morocco and Egypt. One limitation of this assessment is that it relied on self-reported data and therefore did not verify vaccination records.



9. CROSS-BORDER COLLABORATION BETWEEN CHINA AND MYANMAR FOR EMERGENCY RESPONSE TO IMPORTED VACCINE DERIVED POLIOVIRUS CASE.

Wang HB, Zhang LF, Yu WZ, Wen N, Yan DM, Tang JJ, et al. BMC Infect Dis. 2015 Jan 17;15(1):18. [Epub ahead of print] PMID: 25595618

ABSTRACT

BACKGROUND: This report describes emergency response following an imported vaccine derived poliovirus (VDPV) case from Myanmar to Yunnan Province, China and the cross-border collaboration between China and Myanmar. Immediately after confirmation of the VDPV case, China disseminated related information to Myanmar with the assistance of the World Health Organization.

METHODS: A series of epidemiological investigations were conducted, both in China and Myanmar, including retrospective searches of acute flaccid paralysis (AFP) cases, oral poliovirus vaccine (OPV) coverage assessment, and investigation of contacts and healthy children.

RESULTS: All children <2 years of age had not been vaccinated in the village where the VDPV case had lived in the past 2 years. Moreover, most areas were not covered for routine immunization in this township due to vaccine shortages and lack of operational funds for the past 2 years.

CONCLUSIONS: Cross-border collaboration may have prevented a potential outbreak of VDPV in Myanmar. It is necessary to reinforce cross-border collaboration with neighboring countries in order to maximize the leverage of limited resources.

WEB: http://dx.doi.org/10.1186/s12879-015-0745-y

IMPACT FACTOR: 2.56

CITED HALF-LIFE: 3.40

UW EDITORIAL COMMENT: This paper describes a case study in which one initial case led to a collaborative effort between China and Myanmar to determine the oral poliovirus vaccination coverage and acute flaccid paralysis cases in the region from which the case arose, and implementation of SIAs to address coverage gaps. From this investigation, it was found that both AFP surveillance and oral poliovirus vaccine coverage were low in some areas of the region, with almost no vaccination coverage in the 2 years prior in one township. The authors note that collaboration between the two countries was crucial to allow for prompt identification and mitigation of the problem. They propose the following mechanisms to maintain and improve collaboration in the future: identify key contacts within each country, regularly share coverage and surveillance data, prompt notification of any future polio cases, cross-border meetings, synchronized SIA efforts, and shared personnel and resources.



10. COMPARISON OF IMPACT AND COST-EFFECTIVENESS OF ROTAVIRUS SUPPLEMENTARY AND ROUTINE IMMUNIZATION IN A COMPLEX HUMANITARIAN EMERGENCY, SOMALI CASE STUDY.

Gargano LM, Tate JE, Parashar UD, Omer SB, Cookson ST. Confl Health. 2015 Feb 9;9:5. eCollection 2015 PMID: 25691915

ABSTRACT

BACKGROUND: A humanitarian emergency involves a complete breakdown of authority that often disrupts routine health care delivery, including immunization. Diarrheal diseases are a principal cause of morbidity and mortality among children during humanitarian emergencies. The objective of this study was to assess if vaccination against rotavirus, the most common cause of severe diarrhea among children, either as an addition to routine immunization program (RI) or supplemental immunization activity (SIA) would be cost-effective during a humanitarian emergency to decrease diarrhea morbidity and mortality, using Somalia as a case study.

METHODS: An impact and cost-effectiveness analysis was performed comparing no vaccine; two-dose rotavirus SIA and two-dose of RI for the 424,592 births in the 2012 Somali cohort. The main summary measure was the incremental cost per disability-adjusted life-year (DALY) averted. Univariate sensitivity analysis examined the extent to which the uncertainty in the variables affected estimates.

RESULTS: If introduced in Somalia, a full-series rotavirus RI and SIA would save 908 and 359 lives, respectively, and save US\$63,793 and US\$25,246 in direct medical costs, respectively. The cost of a RI strategy would be US\$309,458. Because of the high operational costs, a SIA strategy would cost US\$715,713. US\$5.30 per DALY would be averted for RI and US\$37.62 per DALY averted for SIA. Variables that most substantially influenced the cost-effectiveness for both RI and SIA were vaccine program costs, mortality rate, and vaccine effectiveness against death.

CONCLUSIONS: Based on our model, rotavirus vaccination appears to be a cost-effective intervention as either RI or SIA, as defined by the World Health Organization as one to three times the per capita Gross Domestic Product (Somalia \$112 in 2011). RI would have greater health impact and is more cost effective than SIA, assuming feasibility of reaching the target population. However, given the lack of infrastructure, whether RI is realistic in this setting remains unanswered, and alternative approaches like SIA should be further examined.

WEB: http://dx.doi.org/10.1186/s13031-015-0032-y

IMPACT FACTOR: 0.00

CITED HALF-LIFE: 0.00

UW EDITORIAL COMMENT: In Table 2 the authors provide a breakdown of the success and cost of routine immunization compared to SIAs, then summarize the cost-effectiveness of each approach in Table 3. Figure 1 provides the results of the sensitivity analysis comparing the two approaches.



APPENDIX: PUBMED 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])) NOT ("in vitro"[tiab] OR "immune response"[tiab] OR gene[tiab] OR chemistry[tiab] OR genotox*[tiab] OR sequencing[tiab] OR nanoparticle*[tiab] OR belief[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 mice[tiab] OR mouse[tiab] OR murine[tiab] OR porcine[tiab] OR ovine[tiab] OR fish[tiab])) AND (English[LA]) AND ("2015/1/15"[PDAT] : "2015/02/14"[PDAT]))

*On March 3, 2015, this search of English language articles published between January 15, 2015 and February 14, 2015 and indexed by the US National Library of Medicine resulted in 152 unique manuscripts.

