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VACCINE DELIVERY RESEARCH DIGEST

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

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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LIST OF ARTICLES

1. **Changes in the incidence of pneumonia, bacterial meningitis, and infant mortality 5 years following introduction of the 13-valent pneumococcal conjugate vaccine in a "3+0" schedule.** {Abstract & START Commentary} {Full article}
    - The results of introduction of the 13-valent pneumococcal vaccine in a "3+0 schedule" in Nicaragua included fewer pneumonia hospitalizations for infants and one-year olds, decreased post-neonatal infant mortality, decreased pneumonia related mortality, and lowered bacterial meningitis rates.

2. **Data and product needs for influenza immunization programs in low- and middle-income countries: Rationale and main conclusions of the WHO preferred product characteristics for next-generation influenza vaccines.** {Abstract & START Commentary} {Full article}
    - The current influenza vaccines are not ideal for use in low and middle-income countries and this article outlines data needed to ensure the value add of influenza vaccines in these settings.

3. **A forecast of typhoid conjugate vaccine introduction and demand in typhoid endemic low- and middle-income countries to support vaccine introduction policy and decisions.** {Abstract & START Commentary} {Full article}
    - To better inform necessary capacity for typhoid conjugate vaccine production following WHO prequalification, the authors forecasted vaccine demand in the first 5 years based on rapid or slow vaccine introduction in 18 and 5 countries respectively.

4. **Global dynamics of a mathematical model for the possible re-emergence of polio.** {Abstract & START Commentary} {Full article}
    - A compartmental model in Europe is used to demonstrate the possibility of the re-emergence of polio with the influx of unvaccinated individuals into a region with low vaccine coverage.

5. **Global yellow fever vaccination coverage from 1970 to 2016: an adjusted retrospective analysis.** {Abstract & START Commentary} {Full article}
    - The authors quantify yellow fever vaccine coverage using three different vaccine population coverage values, demographic data, and tracked vaccine coverage from 1970 to 2016. Despite improvements from 1970, a major gap in vaccine coverage remains between current levels and the 80% WHO recommended threshold.

6. **The importance of vaccine supply chains to everyone in the vaccine world.** {Abstract & START Commentary} {Full article}
    - Authors identify how different members of the vaccine community are influenced by vaccine supply chains and emphasize the importance of supply chain considerations during the vaccine development process.

7. **Impact of the introduction of pneumococcal conjugate vaccination on pneumonia in The Gambia: population-based surveillance and case-control studies.** {Abstract & START Commentary} {Full article}
    - A population-based surveillance and case-control study in The Gambia evaluated PCV7 and PCV13 (introduced in 2009 and 2011 respectively) on pneumonia incidence. PCV reduced hospitalizations for pneumonia and incident severe childhood pneumonia and

there was a dose-response relationship with PCV doses and vaccine effectiveness among the case-control participants.

8. **Capturing Budget Impact Considerations Within Economic Evaluations: A Systematic Review of Economic Evaluations of Rotavirus Vaccine in Low- and Middle-Income Countries and a Proposed Assessment Framework.** {Abstract & START Commentary} {Full article}
    - This review summarizes necessary components to complete a budget impact analysis and the feasibility of adaptation of cost-effectiveness analyses. Rotavirus economic evaluations were included as examples and more cost effectiveness analysis were completed, however most did not include necessary budget impact information.

9. **Live-attenuated tetravalent dengue vaccines: The needs and challenges of post-licensure evaluation of vaccine safety and effectiveness.** {Abstract & START Commentary} {Full article}
    - Authors discuss research questions for future dengue vaccine trials and concerns regarding variability in vaccine efficacy and evaluation of vaccine in low and middle-income countries lacking suitable monitoring systems.

10. **The health-economic studies of HPV vaccination in Southeast Asian countries: a systematic review.** {Abstract & START Commentary} {Full article}
    - This review summarizes the health economics of HPV in Southeast Asia, which is pertinent due to the high number of cervical cancer cases in the region.

DETAILS OF ARTICLES

1. Changes in the incidence of pneumonia, bacterial meningitis, and infant mortality 5 years following introduction of the 13-valent pneumococcal conjugate vaccine in a "3+0" schedule
   Becker-Dreps S, Blette B, Briceno R, Aleman J, Hudgens MG, Moreno G, et al.
   PLoS One. 2017 12(8):e0183348. 2017/08/17
   PubMed ID: 28813518

ABSTRACT
BACKGROUND: Streptococcus pneumoniae causes about 826,000 deaths of children in the world each year and many health facility visits. To reduce the burden of pneumococcal disease, many nations have added pneumococcal conjugate vaccines to their national immunization schedules. Nicaragua was the first country eligible for GAVI Alliance funding to introduce the 13-valent pneumococcal conjugate vaccine (PCV13) in 2010, provided to infants at 2, 4, and 6 months of age. The goal of this study was to evaluate the population impact of the first five years of the program.
METHODS: Numbers of visits for pneumonia, pneumonia-related deaths, and bacterial meningitis in both children and adults, and infant deaths between 2008 and 2015 were collected from all 107 public health facilities in Leon Department. Vital statistics data provided additional counts of pneumonia-related deaths that occurred outside health facilities. Adjusted incidence rates and incidence rate ratios (IRRa) in the vaccine (2011-2015) and pre-vaccine periods (2008-2010) were estimated retrospectively using official population estimates as exposure time.
RESULTS: The IRRa for pneumonia hospitalizations was 0.70 (95% confidence interval [CI]: 0.66, 0.75) for infants, and 0.92 (95% CI: 0.85, 0.99) for one year-olds. The IRRa for post-neonatal infant mortality was 0.56 (95% CI: 0.41, 0.77). In the population as a whole, ambulatory visits and hospitalizations for pneumonia, as well as pneumonia-related mortality and rates of bacterial meningitis were lower in the vaccine period.
CONCLUSIONS: During the first five years of program implementation, reductions were observed in health facility visits for pneumonia in immunized age groups and infant mortality, which would be hard to achieve with any other single public health intervention. Future study is warranted to understand whether the lack of a booster dose (e.g., at 12 months) may be responsible for the small reductions in pneumonia hospitalizations observed in one year-olds as compared to infants.

WEB: 10.1371/journal.pone.0183348
IMPACT FACTOR: 3.54
CITED HALF-LIFE: 2.70

START COMMENTARY: The observational study compared pre- and post-vaccine periods for outcomes of pneumonia/pneumonia-related hospitalizations and mortality stratified age groups among children (infants and one-year olds) and adults. The incorporation of PCV13 coverage was not a part of the statistical analysis, however authors noted coverage rates as 63% for infants receiving all three doses and 87% for one-year olds (catch-up dose during first year) in 2011 and 97% for infants in 2012. Figure 1 and Table 1 graphically and quantitatively depict pneumonia health facility (hospitalizations, primary care centers, and health posts) visits for infants and one year olds, who had 30% and 8% reductions in all-cause pneumonia hospitalizations from the pre- to post-vaccine time periods respectively. The small reduction observed among one-year olds is potentially due to the lack of a booster dose available to this age group. Adults and older adults had 50% and 42% reduction in pneumonia-related mortality. A criticism of the analysis is the lack of causality that can be drawn, due to no laboratory confirmation of *S. pneumoniae* pathogen and the observational study design preventing determination of the direct effect of PCV13 on disease or death.

2. Data and product needs for influenza immunization programs in low- and middle-income countries: Rationale and main conclusions of the WHO preferred product characteristics for next-generation influenza vaccines
   Neuzil KM, Bresee JS, De La Hoz F, Johansen K, Karron RA, Krishnan A, et al.
   Vaccine. 2017 Sep 08. 2017/09/13
   PubMed ID: 28893473

ABSTRACT
In 2017, WHO convened a working group of global experts to develop the Preferred Product Characteristics (PPC) for Next-Generation Influenza Vaccines. PPCs are intended to encourage innovation in vaccine development. They describe WHO preferences for parameters of vaccines, in particular their indications, target groups, implementation strategies, and clinical data needed for assessment of safety and efficacy. PPCs are shaped by the global unmet public health need in a priority disease area for which WHO encourages vaccine development. These preferences reflect WHO's mandate to promote the development of vaccines with high public health impact and suitability in Low- and Middle-Income Countries (LMIC). The target audience is all entities intending to develop or to achieve widespread adoption of a specific influenza vaccine product in these settings. The working group determined that existing influenza vaccines are not well suited for LMIC use. While many developed country manufactures and research funders prioritize influenza vaccine products for use in adults and the elderly, most LMICs do not have sufficiently strong health systems to deliver vaccines to these groups. Policy makers from LMICs are expected to place higher value on vaccines indicated for prevention of severe illness, however the clinical development of influenza vaccines focuses on demonstrating prevention of any influenza illness. Many influenza vaccine products do not meet WHO standards for programmatic suitability of vaccines, which introduces challenges when vaccines are used in low-resource settings. And finally, current vaccines do not integrate well with routine immunization programs in LMICs, given age of vaccine licensure, arbitrary expiration dates timed for temperate country markets, and the need for year-round immunization in countries with prolonged influenza seasonality. While all interested parties should refer to the full PPC document for details, in this article we highlight data needs for new influenza vaccines to better demonstrate the value proposition in LMICs.

WEB: 10.1016/j.vaccine.2017.08.088
IMPACT FACTOR: 2.66
CITED HALF-LIFE: 5.50

START COMMENTARY: The PPC Advisory group identified young children (less than five years of age) as the high-risk group to target for improved influenza vaccine efficacy due to existing systems for vaccine delivery in LMIC settings. Five and ten-year strategic goals set forth by the PPC aim to improve seasonal influenza vaccine protection for high risk groups by 2022 and to have a vaccine in clinical development to increase vaccine protection to at least 5 years by 2027. The advisory group concluded that adult immunization delivery systems need to be strengthened in LMICs, more robust data demonstrating vaccine efficacy against severe illness in LMICs, innovations in vaccine delivery (e.g., thermostability and needle-free administration), and further evaluation of current influenza vaccine technologies is needed.

3. A forecast of typhoid conjugate vaccine introduction and demand in typhoid endemic low- and middle-income countries to support vaccine introduction policy and decisions
   Mogasale V, Ramani E, Park IY, Lee JS
   Hum Vaccin Immunother. 2017 Sep 02. 13(9):2017-2024. 2017/06/13
   PubMed ID: 28604164

ABSTRACT
A Typhoid Conjugate Vaccine (TCV) is expected to acquire WHO prequalification soon, which will pave the way for its use in many low- and middle-income countries where typhoid fever is endemic. Thus it is critical to forecast future vaccine demand to ensure supply meets demand, and to facilitate vaccine policy and introduction planning. We forecasted introduction dates for countries based on specific criteria and estimated vaccine demand by year for defined vaccination strategies in 2 scenarios: rapid vaccine introduction and slow vaccine introduction. In the rapid introduction scenario, we forecasted 17 countries and India introducing TCV in the first 5 y of the vaccine's availability while in the slow introduction scenario we forecasted 4 countries and India introducing TCV in the same time period. If the vaccine is targeting infants in high-risk populations as a routine single dose, the vaccine demand peaks around 40 million doses per year under the rapid introduction scenario. Similarly, if the vaccine is targeting infants in the general population as a routine single dose, the vaccine demand increases to 160 million doses per year under the rapid introduction scenario. The demand forecast projected here is an upper bound estimate of vaccine demand, where actual demand depends on various factors such as country priorities, actual vaccine introduction, vaccination strategies, Gavi financing, costs, and overall product profile. Considering the potential role of TCV in typhoid control globally; manufacturers, policymakers, donors and financing bodies should work together to ensure vaccine access through sufficient production capacity, early WHO prequalification of the vaccine, continued Gavi financing and supportive policy.

WEB: 10.1080/21645515.2017.1333681
IMPACT FACTOR: 1.44
CITED HALF-LIFE: 1.80

START COMMENTARY: The vaccine demand forecast approach is applied to anticipate future demand of TCV in 92 countries and 35 Indian states from the Mogasale et. al. 2014 typhoid fever global burden of disease study. Vaccine introduction forecast methodology (Figure 3) was based on a composite score of disease burden, previous vaccine adoption history, immunization system capacity, and previous typhoid surveillance and vaccination experience. Adjustment to scores was made after consultation with typhoid fever experts. Vaccination strategies proposed two doses, (9 month and 15-18-month administration), one dose (9 months), and both had an optional single catch up dose. The vaccine demand forecast considered country-specific vaccine coverage rates for measles, as it is given at the same age as TCV, and wastage for routine and campaign-based vaccination strategies. The rapid introduction scenario had earliest roll out by 2020 in Bangladesh, Nepal, Cuba and the state of Delhi in India. These jurisdictions had in-country manufacturing, previous experience with typhoid vaccine, and/or an already-licensed vaccine in country, which makes them best suited for earlier vaccine introduction. Figure 1 depicts the number of countries for the slow and rapid introduction, ranging from 7 to 17 countries adopting TCV within the first 5 years. The main caveat to the results were the numerous assumptions (e.g., TCV introduction would be similar to hepatitis B introduction) and wide range of vaccines needed. Factors that may increase demand (WHO recommendation, advocacy groups for TCV) or decrease demand (improved water and sanitation due to economic progress, competitor vaccine introduction, political priorities) are among the unknown, influencing factors to TCV introduction.

4. Global dynamics of a mathematical model for the possible re-emergence of polio
   Denes A, Szekely L
   Math Biosci. 2017 Aug 30. 293(64-74). 2017/09/02
   PubMed ID: 28859911

ABSTRACT
Motivated by studies warning about a possible re-emergence of poliomyelitis in Europe, we analyse a compartmental model for the transmission of polio describing the possible effect of unvaccinated people arriving to a region with low vaccination coverage. We calculate the basic reproduction number, and determine the global dynamics of the system: we show that, depending on the parameters, one of the two equilibria is globally asymptotically stable. The main tools applied are Lyapunov functions and persistence theory. We illustrate the analytic results by numerical examples, which also suggest that in order to avoid the risk of polio re-emergence, vaccinating the immigrant population might result insufficient, and also the vaccination coverage of countries with low rates should be increased.

WEB: 10.1016/j.mbs.2017.08.010
IMPACT FACTOR: 1.64
CITED HALF-LIFE: 0.00

START COMMENTARY: Figure 1 outlines the polio transmission diagram for a European population interacting with a refugee population. The European population consists of five compartments: susceptible, infected, vaccinated individuals who remain susceptible to carrying the virus, vaccinated individuals who are carriers of the virus, and recovered individual (through gained immunity or vaccination). The refugee population makes up three compartments in the model, including: susceptible, infected and recovered individuals. Birth rates and immigration rates capture the inflow of individuals in to the susceptible categories, while death rates can flow out of all compartments. The author's utilize differential equations for the transmission system, incorporating partial and full vaccine coverage.

Figures 2, 3, and 4 graphically demonstrate the impact of variations on the immigrant oral polio vaccine (OPV) coverage, IPV coverage (full and partial), and the basic reproductive number. Figure 2 depicts the basic reproductive number greater than 1 and immigrant vaccination coverage of 85% with increasing persistent populations of infected Europeans, vaccinated carriers of the disease and infected refugees. Figure 3 demonstrates higher immigrant OPV coverage was not sufficient to overcome endemicity in a country with low vaccination coverage. Disease extinction is achieved with a higher European vaccination coverage and higher immigrant OPV coverage (95%) resulting in a lower basic reproductive number (Figure 4).

5. Global yellow fever vaccination coverage from 1970 to 2016: an adjusted retrospective analysis
Shearer FM, Moyes CL, Pigott DM, Brady OJ, Marinho F, Deshpande A, et al.
Lancet Infect Dis. 2017 Aug 16. 2017/08/22
PubMed ID: 28822780

ABSTRACT
BACKGROUND: Substantial outbreaks of yellow fever in Angola and Brazil in the past 2 years, combined with global shortages in vaccine stockpiles, highlight a pressing need to assess present control strategies. The aims of this study were to estimate global yellow fever vaccination coverage from 1970 through to 2016 at high spatial resolution and to calculate the number of individuals still requiring vaccination to reach population coverage thresholds for outbreak prevention.
METHODS: For this adjusted retrospective analysis, we compiled data from a range of sources (eg, WHO reports and health-service-provider registeries) reporting on yellow fever vaccination activities between May 1, 1939, and Oct 29, 2016. To account for uncertainty in how vaccine campaigns were targeted, we calculated three population coverage values to encompass alternative scenarios. We combined these data with demographic information and tracked vaccination coverage through time to estimate the proportion of the population who had ever received a yellow fever vaccine for each second level administrative division across countries at risk of yellow fever virus transmission from 1970 to 2016.
FINDINGS: Overall, substantial increases in vaccine coverage have occurred since 1970, but notable gaps still exist in contemporary coverage within yellow fever risk zones. We estimate that between 393.7 million and 472.9 million people still require vaccination in areas at risk of yellow fever virus transmission to achieve the 80% population coverage threshold recommended by WHO; this represents between 43% and 52% of the population within yellow fever risk zones, compared with between 66% and 76% of the population who would have required vaccination in 1970.
INTERPRETATION: Our results highlight important gaps in yellow fever vaccination coverage, can contribute to improved quantification of outbreak risk, and help to guide planning of future vaccination efforts and emergency stockpiling.

WEB: 10.1016/S1473-3099(17)30419-X
IMPACT FACTOR: 5.82
CITED HALF-LIFE: 4.70

START COMMENTARY: The methodology for consideration of vaccination strategies ranged from conservative (untargeted, biased campaigns – no account for vaccine history and inadvertent targeting of previously vaccinated individuals) to optimistic (targeted campaigns – account for vaccine history and intended for unvaccinated individuals), thus providing a range of possible scenarios. Vaccine coverage was based on an untargeted, unbiased vaccination campaign scenario and 1970-2016 estimates for South America and Africa are presented in Figure 1. Patterns of high and low vaccine rates oscillated over the ten-year increments in Brazil and west and Central Africa. Overall Latin America had higher coverage than Africa. Discrepancies in vaccine coverage compared across targeted and untargeted, biased estimates varied widely in Latin America, which could potentially be due to differences in data availability as compared to other countries (Figure 2). Most countries (all countries in South America and Africa except Bolivia, Peru, and Senegal) were below the recommended 80% coverage in all vaccination scenarios. Utilization of the same approach for yellow fever vaccine coverage across two large and diverse continents provided additional insight for potential focus geographies, however further analyses specific more homogenous setting can help minimize discrepancies in vaccine coverage.

6. The importance of vaccine supply chains to everyone in the vaccine world
   Lee BY, Haidari LA
   Vaccine. 2017 Aug 16. 35(35 Pt A):4475-4479. 2017/06/21
   PubMed ID: 28629921

ABSTRACT
While the focus of many in the vaccine world has been on developing new vaccines and measuring their effects on humans, failure to understand and properly address vaccine supply chain issues can greatly educe the impact of any vaccine. Therefore, everyone involved in vaccine decision-making may want to take into account supply chains when making key decisions. In fact, considering supply chain issues long before a vaccine reaches the market can help design vaccines and vaccine programs that better match the system. We detail how vaccine supply chains may affect the work and decision making of ten examples of different members of the vaccine community: preclinical vaccinologists, vaccine clinical trialists, vaccine package designers, health care workers, epidemiologists and disease surveillance experts, policy makers, storage equipment manufacturers, other technology developers, information system specialists, and funders. We offer ten recommendations to help decision makers better understand and address supply chains.

WEB: 10.1016/j.vaccine.2017.05.096
IMPACT FACTOR: 2.66
CITED HALF-LIFE: 5.50

START COMMENTARY: Due to diversity of stakeholders that participate in vaccine development, delivery, and planning, greater communication to ensure continuity of vaccine supply chains is needed across industries. Nine types of vaccine stakeholders highlight the following opportunities for vaccine supply chain improvement:

1. Raise awareness of supply chain issues
2. Educate and train various decision makers on supply chain principles and practices
3. Incorporate supply chain experts and considerations into all vaccine decision making
4. Improve communication between vaccine decision makers and vaccine supply chain experts
5. Develop computational simulation models of global and country-level supply chains to serve as virtual laboratories to help evaluate supply chains and test different policies, interventions, and technologies
6. Establish as a condition of major vaccine-related decisions (e.g. funding, new policy change, new vaccine introduction, etc.) the mapping and modeling of the relevant supply chain and the impact and value of the new policy, intervention, technology, or funds
7. Utilize supply chain models and other analyses to generate target product profiles (TPPs) to guide the design and development of new technology
8. Develop a database of vaccine decisions and how supply chain considerations and changes affected these decisions
9. Develop and disseminate a playbook on how a country's supply chain can be approached and improved when making vaccine decisions
10. Begin implementing these changes systematically in countries, documenting and disseminating their effects, impact, and value (Table 1)

7. Impact of the introduction of pneumococcal conjugate vaccination on pneumonia in The Gambia: population-based surveillance and case-control studies
   Mackenzie GA, Hill PC, Sahito SM, Jeffries DJ, Hossain I, Bottomley C, et al.
   Lancet Infect Dis. 2017 Sep. 17(9):965-973. 2017/06/12
   PubMed ID: 28601421

ABSTRACT

BACKGROUND: Pneumococcal conjugate vaccines (PCVs) are used in many low-income countries but their impact on the incidence of pneumonia is unclear. The Gambia introduced PCV7 in August, 2009, and PCV13 in May, 2011. We aimed to measure the impact of the introduction of these vaccines on pneumonia incidence.

METHODS: We did population-based surveillance and case-control studies. The primary endpoint was WHO-defined radiological pneumonia with pulmonary consolidation. Population-based surveillance was for suspected pneumonia in children aged 2-59 months (minimum age 3 months in the case-control study) between May 12, 2008, and Dec 31, 2015. Surveillance for the impact study was limited to the Basse Health and Demographic Surveillance System (BHDSS), whereas surveillance for the case-control study included both the BHDSS and Fuladu West Health and Demographic Surveillance System. Nurses screened all outpatients and inpatients at all health facilities in the surveillance area using standardised criteria for referral to clinicians in Basse and Bansang. These clinicians recorded clinical findings and applied standardised criteria to identify patients with suspected pneumonia. We compared the incidence of pneumonia during the baseline period (May 12, 2008, to May 11, 2010) and the PCV13 period (Jan 1, 2014, to Dec 31, 2015). We also investigated the effectiveness of PCV13 using case-control methods between Sept 12, 2011, and Sept 31, 2014. Controls were aged 90 days or older, and were eligible to have received at least one dose of PCV13; cases had the same eligibility criteria with the addition of having WHO-defined radiological pneumonia.

FINDINGS: We investigated 18 833 children with clinical pneumonia and identified 2156 cases of radiological pneumonia. Among children aged 2-11 months, the incidence of radiological pneumonia fell from 21.0 cases per 1000 person-years in the baseline period to 16.2 cases per 1000 person-years (23% decline, 95% CI 7-36) in 2014-15. In the 12-23 month age group, radiological pneumonia decreased from 15.3 to 10.9 cases per 1000 person-years (29% decline, 12-42). In children aged 2-4 years, incidence fell from 5.2 to 4.1 cases per 1000 person-years (22% decline, 1-39). Incidence of all clinical pneumonia increased by 4% (-1 to 8), but hospitalised cases declined by 8% (3-13). Pneumococcal pneumonia declined from 2.9 to 1.2 cases per 1000 person-years (58% decline, 22-77) in children aged 2-11 months and from 2.6 to 0.7 cases per 1000 person-years (75% decline, 47-88) in children aged 12-23 months. Hypoxic pneumonia fell from 13.1 to 5.7 cases per 1000 person-years (57% decline, 42-67) in children aged 2-11 months and from 6.8 to 1.9 cases per 1000 person-years (72% decline, 58-82) in children aged 12-23 months. In the case-control study, the best estimate of the effectiveness of three doses of PCV13 against radiological pneumonia was an adjusted odds ratio of 0.57 (0.30-1.08) in children aged 3-11 months and vaccine effectiveness increased with greater numbers of doses (p=0.026). The analysis in children aged 12 months and older was underpowered because there were few unvaccinated cases and controls.

INTERPRETATION: The introduction of PCV in The Gambia was associated with a moderate impact on the incidence of radiological pneumonia, a small reduction in cases of hospitalised pneumonia, and substantial reductions of pneumococcal and hypoxic pneumonia in young children. Low-income countries that introduce PCV13 with reasonable coverage can expect modest reductions in hospitalised cases of pneumonia and a marked impact on the incidence of severe childhood pneumonia.

FUNDING: GAVI's Pneumococcal vaccines Accelerated Development and Introduction Plan, Bill & Melinda Gates Foundation, and UK Medical Research Council.

WEB: 10.1016/S1473-3099(17)30321-3
IMPACT FACTOR: 5.82
CITED HALF-LIFE: 4.70

START COMMENTARY: PCV13 coverage improved throughout 2014, reaching 95% coverage by the end of the year among the population surveillance study. There was an overall decreasing trend in pneumonia incidence across radiological pneumonia with consolidation, clinical pneumonia, pneumococcal pneumonia, and hypoxic pneumonia from 2008 to 2015. In 2011 and 2013, for clinical pneumonia and radiological pneumonia (respectively) there were increasing trends for those years that may have been influenced by the non-specific clinical signs observed during these years.

For the case-control analysis, a dose response association was observed with increasing number of PCV13 doses associated with increased effectiveness (Table 3). The 2-11 month age group may serve as a future target population for decreasing hospital utilization in similar geographical contexts as demonstrated by the 9.3 incident cases per 1000 person-year absolute reduction in hospitalized clinical pneumonia from baseline (2008-2010) to endpoint (2014-2015) periods.

8. Capturing Budget Impact Considerations Within Economic Evaluations: A Systematic Review of Economic Evaluations of Rotavirus Vaccine in Low- and Middle-Income Countries and a Proposed Assessment Framework
   Carvalho N, Jit M, Cox S, Yoong J, Hutubessy RCW
   Pharmacoeconomics. 2017 Sep 13. 2017/09/15
   PubMed ID: 28905279

ABSTRACT
BACKGROUND: In low- and middle-income countries, budget impact is an important criterion for funding new interventions, particularly for large public health investments such as new vaccines. However, budget impact analyses remain less frequently conducted and less well researched than cost-effectiveness analyses.
OBJECTIVE: The objective of this study was to fill the gap in research on budget impact analyses by assessing (1) the quality of stand-alone budget impact analyses, and (2) the feasibility of extending cost-effectiveness analyses to capture budget impact.
METHODS: We developed a budget impact analysis checklist and scoring system for budget impact analyses, which we then adapted for cost-effectiveness analyses, based on current International Society for Pharmacoeconomics and Outcomes Research Task Force recommendations. We applied both budget impact analysis and cost-effectiveness analysis checklists and scoring systems to examine the extent to which existing economic evaluations provide sufficient evidence about budget impact to enable decision making. We used rotavirus vaccination as an illustrative case in which low- and middle-income countries uptake has been limited despite demonstrated cost effectiveness. A systematic literature review was conducted to identify economic evaluations of rotavirus vaccine in low- and middle-income countries published between January 2000 and February 2017. We critically appraised the quality of budget impact analyses, and assessed the extension of cost-effectiveness analyses to provide useful budget impact information.
RESULTS: Six budget impact analyses and 60 cost-effectiveness analyses were identified. Budget impact analyses adhered to most International Society for Pharmacoeconomics and Outcomes Research recommendations, with key exceptions being provision of undiscounted financial streams for each budget period and model validation. Most cost-effectiveness analyses could not be extended to provide useful budget impact information; cost-effectiveness analyses also rarely presented undiscounted annual costs, or estimated financial streams during the first years of programme scale-up.
CONCLUSIONS: Cost-effectiveness analyses vastly outnumber budget impact analyses of rotavirus vaccination, despite both being critical for policy decision making. Straightforward changes to the presentation of cost-effectiveness analyses results could facilitate their adaptation into budget impact analyses.

WEB: 10.1007/s40273-017-0569-2
IMPACT FACTOR: 3.57
CITED HALF-LIFE: 8.20

START COMMENTARY: Authors developed and applied a budget impact analysis (BIA) checklist and a modified checklist for cost effectiveness analysis (CEA; Table 2) to assess budget impact and cost effectiveness analyses of rotavirus vaccination identified in a literature search. “Time dependencies and discounting” categories scored poorly on the checklists for both BIAs and CEAs. The checklist provides a systematic tool to assess BIAs and CEAs for decision makers in low-and middle-income countries.

9. Live-attenuated tetravalent dengue vaccines: The needs and challenges of post-licensure evaluation of vaccine safety and effectiveness
Wichmann O, Vannice K, Asturias EJ, De Albuquerque Luna EJ, Longini I, Lopez AL, et al.
Vaccine. 2017 Sep 08. 2017/09/13
PubMed ID: 28893477

ABSTRACT
Since December 2015, the first dengue vaccine has been licensed in several Asian and Latin American countries for protection against disease from all four dengue virus serotypes. While the vaccine demonstrated an overall good safety and efficacy profile in clinical trials, some key research questions remain which make risk-benefit-assessment for some populations difficult. As for any new vaccine, several questions, such as very rare adverse events following immunization, duration of vaccine-induced protection and effectiveness when used in public health programs, will be addressed by post-licensure studies and by data from national surveillance systems after the vaccine has been introduced. However, the complexity of dengue epidemiology, pathogenesis and population immunity, as well as some characteristics of the currently licensed vaccine, and potentially also future, live-attenuated dengue vaccines, poses a challenge for evaluation through existing monitoring systems, especially in low and middle-income countries. Most notable are the different efficacies of the currently licensed vaccine by dengue serostatus at time of first vaccination and by dengue virus serotype, as well as the increased risk of dengue hospitalization among young vaccinated children observed three years after the start of vaccination in one of the trials. Currently, it is unknown if the last phenomenon is restricted to younger ages or could affect also seronegative individuals aged 9 years and older, who are included in the group for whom the vaccine has been licensed. In this paper, we summarize scientific and methodological considerations for public health surveillance and targeted post-licensure studies to address some key research questions related to live-attenuated dengue vaccines. Countries intending to introduce a dengue vaccine should assess their capacities to monitor and evaluate the vaccine's effectiveness and safety and, where appropriate and possible, enhance their surveillance systems accordingly. Targeted studies are needed, especially to better understand the effects of vaccinating seronegative individuals.

WEB: 10.1016/j.vaccine.2017.08.066
IMPACT FACTOR: 2.66
CITED HALF-LIFE: 5.50

START COMMENTARY: Phase 3 study of Dengvaxia ® demonstrated protective effects against hospitalization for dengue among ages nine and older (three years after first dose), but excess hospitalizations were observed in the two – five year age group (RR = 0.50 vs. 7.45). These findings motivated vaccination start for individuals 9 years and older.

The risk management plan (RMP) outlined by the manufacturer outlines the following three areas important for country policy making for the tetravalent dengue vaccine:

(1) Safety-related questions
(2) Effectiveness and impact-related questions
(3) Methodological questions (Box 1)

Challenging issues identified by authors include limitations to accurate case identification, longitudinal assessment of severe dengue following vaccination, limitations of database linkages, lack of retrospective diagnostics for dengue-vaccinated individuals, prospective studies of dengue naïve individuals, and multiple, geographically diverse studies of vaccine effectiveness.

10. The health-economic studies of HPV vaccination in Southeast Asian countries: a systematic review
    Setiawan D, Oktora MP, Hutubessy R, Riewpaiboon A, Postma MJ
    Expert Rev Vaccines. 2017 Sep. 16(9):933-943. 2017/07/22
    PubMed ID: 28730914

ABSTRACT
INTRODUCTION: The cervical cancer-related burden is an important problem in Southeast Asian (SEA) countries. However, only 3 out of 11 countries implement the comprehensive prevention program. Areas covered: This is a retrospective review from all relevant studies until 2015 from two main databases, MEDLINE/Pubmed and Embase in order to provide an evidence on the health economics of HPV vaccination in the region. Expert commentary: The implementation of HPV vaccination will generate substantial health and economic benefit in SEA countries since the number of cervical cancer cases in this region are generally high. Therefore, a clear recommendation on how HPV vaccination should be implemented in a country, for example on how many doses will be used, how much cost is required or is it a school based- or clinical based-delivery, is critically required.

WEB: 10.1080/14760584.2017.1357472
IMPACT FACTOR: 2.67
CITED HALF-LIFE: 4.20

START COMMENTARY: The review included five SEA countries across a range of income levels, with the Philippines and Vietnam classified as lower-middle income countries, Thailand and Malaysia as upper-middle income countries, and Singapore as a high-income country. Six of the ten included studies considered combination vaccination and screening strategies, with two studies concluding an increase in screening coverage as cost-effective and four studies concluding combined screening (pap-smear/visual inspection with acetylic acid) as cost-effective (Table 3). Different combination strategies were suggested, including vaccination and screening five times in a lifetime in Thailand and vaccination and targeted screening of older women in Vietnam.

There were three studies that evaluated both bivalent and quadrivalent HPV vaccines, but the cost-effectiveness analysis of two of these studies had opposing results. These contrasting findings were observed in other geographies (e.g., Ireland, Canada, UK, Colombia) and is likely influenced by variations in burden of cervical cancer, genital warts, genital cancer, and oropharyngeal cancer that would be prevented by the vaccine. The incremental cost-effectiveness ratio (ICER) was compared to the Commission on Macroeconomic in Health's cost-effectiveness threshold in two studies in Thailand and Vietnam. The cost-effectiveness threshold required lower HPV vaccine prices to achieve cost-effectiveness; however, a more realistic approach to evaluating HPV vaccine for universal coverage to inform decision makers, would utilize HPV vaccine prices based on country GDPs. Additionally, the application of the Commission on Macroeconomic in Health's threshold is not universal to low and middle-income countries, and the authors recommend a country specific threshold for future analysis.

The primary limitation of the results of this review is the lack of representation for all countries of the SEA region. Additionally, the variations in methodologies, age targets, vaccine prices, and vaccine schedules impedes the collapsibility of the findings across various countries. The potential economic and health benefits of HPV vaccine for this region was clearly outlined, however opportunities for improvements in screening coverage and health promotion remain.

APPENDIX

(((((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]) ("2017/7/15"[PDAT] : "2017/8/14"[PDAT]))

* September 25, 2017, this search of English language articles published between August 15, 2017 and September 14, 2017 and indexed by the US National Library of Medicine resulted in 223 unique manuscripts.