Title
Impact of New Vaccine Introduction on Developing Country Immunization Programs and Health Systems: A Review of the Grey Literature

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Abstract
Given the growing intensity of new vaccine introductions (NUVIs), in 2010 the World Health Organization initiated a process to update its guidance to countries on NUVI. As a first step, WHO coordinated a multi-faceted effort to learn more about the effects of NUVI on national immunization programs and health systems. USAID’s MCHIP project agreed to review the grey literature. Through web searches and personal contacts, MCHIP identified 61 relevant documents. Although some of these sources addressed the topic only peripherally and others lacked detail, many interesting and useful findings emerged.

In most cases, NUVIs did not have major, lasting impacts on EPIs or health systems. Impact on coverage was generally minor, with some modest increases or decreases (some due to stock-outs). The main areas in which NUVI strengthened some EPIs were in public perceptions (with some notable exceptions), cold chain hardware and storage capacity, and injection safety, as well as in their potential to reduce morbidity and mortality. New vaccines were generally well accepted, except in a minority of countries where anti-vaccine movements caused problems. The main areas in which NUVI stressed some EPIs were in cold chain and logistics, some unanticipated collateral costs, and long-term financing, although in fact the high cost of new vaccines and donor requirements have also stimulated some improved financial planning. More time and attention devoted to planning and preparations – as well as a taking a longer-term view towards system improvement -- would allow EPIs to take better advantage of NUVI to strengthen weak system components.

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Introduction

Under the auspices of WHO's Impact of New Vaccine Introduction workgroup, and in response to a request by WHO's Strategic Advisory Group of Experts (SAGE), the USAID-funded Maternal and Child Health Integrated Program (MCHIP) undertook a review of the grey literature on the effects of new vaccine introduction (NUVI) on national immunization programs (Expanded Programs on Immunization - EPIs) and health systems. This review is part of a larger assessment that includes a review of published literature, an analysis of coverage data, interviews with EPI officials, and country case studies. The results are intended to inform new guidance and tools from WHO on how countries can undertake smooth NUVIS that have ongoing benefits to health services.

Materials and Methods

A small MCHIP team carried out the grey literature search and review. They focused on the experiences of lower and middle-income countries, because of the major international effort to support NUVI in those countries and because of the likelihood that their experiences would differ from those of richer countries.

MCHIP undertook numerous literature searches on the Internet, requested documents from personal contacts, and posted a call for documents on TechNet and in Global Immunization News. Besides helping identify documents, other MCHIP staff and members of the working group on new vaccines provided comments and suggestions on the draft report. The systematic search strategy focused on literature from January 2000 to October 2010, although a few relevant documents dated prior to 2000 were identified and included. The team also interviewed two persons who had been involved in planning or assessing NUVI.

A substantial effort was made to search databases using the mix of free text and MESH terms. The databases searched were Popline, PubMED, Cochrane Library, ELDIS, System for Information on Grey Literature in Europe (SIGLE), CAB Abstracts, and WHO regional office databases. The team also carried out a three-way search of the Internet, which included free text searches in Google using the same keywords; a search of conference proceedings, such as the New and Under-utilized Vaccine Retreats; a search of web pages of international organizations, bilateral agencies, nongovernmental organizations (NGOs), consultancy firms, and universities involved in the vaccine introduction, such as the Global Alliance for Vaccines and Immunization (GAVI Alliance), WHO, UNICEF, MCHIP, the Program for Appropriate Technology in Health (PATH), and the Johns Hopkins University School of Public Health.

The literature search comprised keyword terms relating to vaccines and freetext terms relating to health systems, immunization systems, health planning, and capacity. Additionally, searches were carried out using the following terms: hepatitis B, Hep B, *Haemophilus* vaccine, Hib vaccine, pneumococcal vaccine, pneumonia, PCV, rotavirus vaccine, rotavirus vaccine, meningococcal vaccine, yellow fever vaccine, Japanese encephalitis vaccine, papillomavirus vaccine, HPV vaccine, new vaccine introduction, cold chain, delivery of healthcare, “delivery of healthcare” AND immunization, “capacity building” AND immunization, and numerous other terms used interchangeably.

The review team considered as grey literature hard- or soft-copy documents that were not peer-reviewed or published commercially. From the hundreds of documents examined, the MCHIP team included 61 that contained information on the impact of NUVI on immunization programs.
and, in a few cases, the broader health system. Documents that only discussed the decision-making process to introduce new vaccines, but that did not describe the effects of the introduction afterwards, were excluded. The team had to make judgments on the reliability of sources such as websites and newspaper articles, and excluded many such sources. In general the team only accepted relevant documents, including PowerPoint presentations, that were associated with respected international organizations such as WHO, UNICEF, USAID and PATH. The review team followed the WHO health systems framework in summarizing its findings.¹

Major document types included were post-introduction evaluations (PIEs) and PIE summaries, trip reports, assessments, and meeting presentations and summaries. Most dealt with one NUVI experience, but a few covered multiple country experiences (one summarized 16 PIEs, another seven). Country experiences reviewed were mostly from low-income African countries and concerned introductions of hepB and Hib, although there were several cases from middle-income countries, from other continents, and that concerned rotavirus, pneumococcal, and human papillovirus vaccines (RV, PCV, and HPV).

The task was challenging for several reasons:
► Most documents about EPI, but not about NUVI specifically, failed to mention the effects of NUVI on the EPI or health system. PIEs and other documents describe strengths and weaknesses of EPIs but may not link these directly with the introductions.
► PIEs report on a particular point in time, which may fail to capture the changing effects of NUVI over time. For example, a report shortly after an introduction might find insufficient transportation capacity to move the new vaccine to districts around the country, but a report a year later might describe no such problem, because the problem had been addressed.
► In many cases only PIE summaries from WHO were available rather than full documents, and they sometimes contained contradictory or incomplete information.
► It was difficult to separate the effects of NUVI from the effects of donor funding that often accompanied NUVI.
► Other simultaneous government and donor initiatives and contextual factors made it difficult to link NUVI to changes in EPIs or overall health systems.
► Because introductions of PCV, RV, and HPV into developing countries began only a few years ago, there was limited information on their impact, so the review may not have fully captured some potential effects (e.g. due to RV’s age requirements or HPV’s particular target group).

Undoubtedly, the search strategy failed to capture some documentation housed on shelves and in the files of persons involved in vaccine introduction. Moreover, many additional documents available since the search phase ended at the beginning of 2011 were not included.

Despite these challenges, this review was able to capture much useful information, which, triangulated with findings from from the other studies the WHO workgroup, should provide useful lessons learned and guidance for the future.

Results

Determinants of the Impact of Vaccine Introduction on Immunization Programs

The vaccine, its formulation, presentation, and packaging. The grey literature indicated that the particular vaccine formulation, presentation, and packaging can ease or complicate the
vaccine’s immediate and longer-term impact. Generally, transitioning from DTP to DTP-HepB (liquid tetravalent) or from DTP or liquid tetravalent DTP-HepB to liquid DTP-HBV+Hib (the most common form of pentavalent) were relatively easy changes. However: (1) introducing DTP-HepB+Hib was more complicated if Hib came in lyophilized (freeze-dried) form, which required new health worker skills as well as use of syringes for reconstitution and their safe disposal; and (2) the liquid form of monovalent Hib requires substantially increased cold chain storage and distribution capacity. Both combination and monovalent vaccines have advantages and disadvantages that vary depending on the EPI and its context. A few documents indicated that adding a new monovalent vaccine was a concern to some parents and/or health staff because it implies an additional injection on the same visit, but this did not emerge consistently as a significant issue.

The introduction of RV, PCV, or HPV has the potential to stress EPIs’ budgets and the cold chain (storage capacity, volume and frequency of distribution, fuel for and maintenance of new equipment). The latter problems emerged even in lower middle-income countries with strong EPIs, although generally they were resolved within a year or two. The graphs below illustrate the impact of the relatively huge volume of several new vaccines (shown as of 2008 and at present).

**Figure 1: Vaccine Volumes Per Fully-Immunized Child (cm³), 2008 and 2012**

![Vaccine Volumes Graph](image-url)

Duration and quality of preparations for vaccine introduction. Some NUVIs were well planned and executed, but commonly mild chaos emerged as launch dates approached. Some EPIs carried out appropriate assessments as the basis for their plans, but then lacked sufficient time, staff or other resources to complete all of the planned steps. Others had sufficient planning time (a year or more), but the EPI and partners did not feel the urgency of action until the launch approached. A few countries felt compelled to implement a rolling introduction because, when the time came, they were not ready for a national one. One African country, which introduced PCV, RV, and pentavalent vaccines together in 2008/9, encountered a number of challenges, including staff shortages, late delivery and installation of refrigerators, and the need for training on a huge scale. Key recommendations of the EPI manager afterwards included multi-year planning to ensure broad and guaranteed vaccine financing at all levels and more time to address human resource, cold chain, and regulatory issues. One South American country that introduced PCV, RV, and influenza vaccines together in 2008, appears to have garnered sufficient political commitment and funding and to have carried out effective preparations so the multi-antigen introduction came off smoothly and even “strengthened local management.”

Strength of the EPI at the time of introduction. Challenging factors such as bulky, small-dose new vaccines, multiple vaccines introduced simultaneously or closely together, and political decisions to launch quickly stressed EPIs even relatively strong EPIs. In most poor countries, the availability of financial support from the GAVI Alliance and other donors, including vaccine manufacturers, mitigated the short-term financial impact of NUVI, but longer-term financial impact remains an issue of concern (see below).
Service Delivery

Vaccination schedules. Most new vaccines do not require significant changes in vaccination schedules. Exceptions are HPV, which targets adolescent or pre-adolescent girls, the birth dose of HepB, and the challenge of the strict age range for RV. The birth dose of HBV should be given in the first 24 hours of life, a period that is much more stringent than the recommended periods for OPV (within 14 days of birth) and BCG (as soon as possible after birth). WHO recommends that RV “…be administered between the ages of 6 weeks and 15 weeks, and that the maximum age for administering the last dose of either vaccine should be 32 weeks.” Some EPIs – such as those that offer DTP-containing vaccine at three, four, and five months – may need to consider modifying their schedule to improve the possibility of reaching more infants with all recommended RV doses.

Some EPIs have to deal with an additional injection being given during regular visits. In an African country, this was explored in formative research and dealt with well in health worker training and communication to caregivers. In one Eastern European country, there was some resistance among health workers to administer an additional injection (Hib monovalent vaccine).

The main impact of new vaccines on the schedule in most countries has simply been the need to modify forms, registers, and cards to accommodate the new vaccine. PIEs indicate that this has usually, but not always, been completed before the introduction.

Coverage, missed opportunities, vaccine wastage. The evidence on the impact of NUVI on coverage is mixed. Many PIEs reported that health workers and officials felt that the introduction had improved attitudes towards the EPI and had increased coverage. A synopsis of seven African PIEs reported that, “…introduction actually positively affected coverage in most countries…. It was reported that many caretakers whose children had already received DTP or had just exited the DTP series came to facilities asking for hepatitis B vaccine for their children. In countries where monovalent presentation of vaccines was introduced…, coverage was much higher with hepatitis B compared to the DTP.” A WHO group also noted that, “New vaccines have improved the overall coverage of routine EPI vaccines.”

In some cases these perceptions were based on data, in others on impressions. There are also a number of instances in the literature in which, at least temporarily, NUVI had a detrimental effect on coverage – generally because of vaccine-supply problems related to global shortages or national inability to distribute bulky new vaccine rapidly enough. Depending on how the EPI manages them, the strict lower and upper age limits for RV administration may affect coverage positively or negatively.

Shearer analyzed rises and falls in DTP3 coverage in individual countries related to 187 NUVIIs, and found them “no more likely to occur following NUVI than in non-introduction years.” Another analysis found that two years following HBV introduction, coverage levels for the new vaccine reached the level of DTP3 in about two-thirds of countries. Coverage at the time of introduction and GAVI support were strong predictors of rapid catch-up.

There are a few reports that popular fear of pneumonia and meningitis led to increased service utilization for both vaccination and other services. In general it appears that the more reliable the vaccine supply and the stronger the public interest in the disease the new vaccine addresses, the more likely NUVI will be associated with coverage increases, but clearly there are many confounding factors.
Most evidence points to less wastage of new vaccines than traditional ones, due to fewer doses per vial and/or health worker concern with wasting such expensive vaccines when they came in 10-dose vials. In a few places, the latter concern also led to more missed opportunities.

**Public perceptions of the EPI.** There are some reports that the publicity and involvement of national leaders during new vaccine launches, along with information campaigns, led to more EPI visibility within government and an improved image among the public. In a few countries, shortages of the newly introduced vaccine (particularly pentavalent vaccine) had detrimental short-term effects on coverage and community confidence in immunization services. There were also a few reports of confusion among both health workers and the public about whether children who had started their DTP series should or should not receive the new tetravalent or pentavalent vaccine.

Most countries planned and implemented communication activities to explain NUVIs to the public, typically via radio, print materials, and information from health workers. Only a few countries based communication activities on in-depth formative research with health workers, leaders and families. Some communication plans were not fully implemented because the preparatory period was too short.

One interesting pattern, found in many of the more than 25 PIEs reviewed, was good public acceptance of the new vaccine *despite* limited communication efforts and poor parental knowledge about the vaccine(s) and disease(s). Some, but fewer, countries reported both strong communication and good acceptance. Finally, there are cases of poor acceptance, regardless of any communication efforts, mainly in Eastern Europe.

The introduction of monovalent Hib lyophilized vaccine and then lyophilized tetravalent DTP-Hib in an Eastern European country led to sustained vocal opposition by the active anti-vaccination community. There was little preparation of the public on the need for Hib vaccine. No information packets with educational materials targeting parents and the medical community were developed at the central level. Education of parents was left to health workers, but this effort was clearly inadequate.

A UNICEF assessment of public attitudes towards vaccination in eight countries in Central and Eastern Europe and the Commonwealth of Independent States found:

- "...a collapse of public trust in health systems including public trust in primary health care workers and services, as well as key health messages."
- Because of such attitudes, several countries have introduced new vaccines in services with no communication activities for the public. Health workers had briefings and/or training.
- Strong anti-vaccination sentiment among younger, better educated, urban populations predisposed to resisting state interventions
- Many different communication activities taking place but with little coordination, strategy or national ownership (they were mainly donor driven)
- None of the eight countries assessed have any dedicated budget for health promotion beyond operational costs.

In summary, public acceptance of new vaccines has been strong in most countries, regardless of the extent or quality of social mobilization/communication activities. There are some reports that vaccine introductions improved the image or perceived importance of the EPI. In a small
number of countries, anti-vaccine or anti-government movements have vocally opposed new vaccines and the EPI.\textsuperscript{10, 11}

**Community involvement in immunization.** In preparation for NUVI, some EPIs engaged with community leaders and groups. Overall, however, vaccine introductions appear to have had little impact on community involvement. One exception was in one African country, where a 2004 EPI review noted strong community involvement in the programme through district assemblies and community structures/community volunteers and that DTP3/Penta3 was selected as a major indicator for monitoring the district assemblies’ performances.

**Health Workforce**

**Staff knowledge, skills, and attitudes.** Most countries prepared written introduction plans that included training of health staff. Training covered key information on handling, administering, communicating about, and recording doses of the new vaccine. Most countries also included other vaccination topics, in some cases based on a needs assessment. Some countries prepared job aids and reference materials to accompany NUVI training. As part of RV introduction in one South American country, guidelines on the vaccination schedule, vaccine storage and distribution, surveillance for adverse events, and the epidemiology of rotavirus were distributed nationwide. In one Caribbean country, a donor grant for vaccine introduction supported the revision and standardization of EPI norms and procedures, which were disseminated via nationwide training. In some countries, manuals to accompany training were prepared but not present in many health facilities six to 12 months post-introduction.

Based on information in the PIEs, it appears that the overall impact of training and other capacity-building steps associated with vaccine introduction was positive, although still insufficient in most countries to bring health worker skills to desirable levels. Commonly deficient skills noted were in management of EPI: estimating target populations; calculating coverage, dropout rates, and wastage rates; managing the cold chain; and monitoring immunization activities. In most countries, health workers observed during PIEs demonstrated good knowledge of the new vaccine. Assessments found health workers’ interpersonal communication on new vaccines to be effective in some countries and weak in others.

To prepare for vaccine introduction, most countries used a cascade training approach, with varying degrees of effectiveness. There are reports of training associated with vaccine introduction being too short, not sufficiently practical, and not reaching all peripheral facilities. There were also more positive capacity-building experiences in several countries. For the introduction of pentavalent vaccine in one African country, GAVI financial support enabled intensive training at all levels. Health staff were satisfied with the content on how to reconstitute and administer the vaccine, use and proper disposal of the auto-disable (AD) syringes, vaccine storage and management, attention to reporting and tracking of vaccine to reduce drop-out and wastage, and communication on the “five-in-one” vaccine. Training on RV in a South American country included the innovative use of a 19-minute adult education DVD that addressed all components of the program and that was reinforced by questions and answers and a skills test.\textsuperscript{12}

Health workers in some countries complained that the new vaccine had increased their workloads or confused them because of reconstitution requirements, having to give additional injections, or learning to use and properly dispose of AD syringes.\textsuperscript{5}
In summary, many countries took advantage of vaccine introductions to provide additional training and support materials to health staff. Although useful, the training related to NUVI did not sufficiently redress deficiencies in such areas as vaccine management and in collection and use of data. In a few countries, staff complained about extra work that vaccine introduction brought.

**Supervision, monitoring and evaluation.** In some countries funding from the GAVI Alliance or other donors that accompanied vaccine introduction allowed increased supervisory visits, usually for a limited time period. In some, but not all, countries, most supervision visits took place as planned. In many countries supervision teams did not leave a report of findings and recommendations at the facility, although this was supposed to happen. Many supervision systems lacked a supervision checklist and/or consistent use of a checklist.

Most supervision visits appear to have been for immunization only, although in some countries they covered broader health activities. Supervision seemed to be well functioning in one African country (“well planned and well organized… logbooks used at all HFs…feedback and recommendations documented…follow-up visits….”). Supervision in one Eastern European country was also reported to be well done.

In summary, funding that accompanied vaccine introduction enabled temporarily increased supervision in some countries, although the quality was mixed. There were many reports that supervision was not systematic (with no checklists) and that supervisors left no documentation of findings and recommendations at facilities.

**Information, Records and Forms**

Efficient and effective collection, compilation, analysis, and use of data remain challenges for many EPIs. There is no indication that vaccine introduction worsened the problem -- usually, needed changes in forms, registers, vaccination cards, and reporting formats are anticipated and made before the introduction -- but there were also no indications that the introduction process took advantage of the opportunity to improve data collection and use.

Various countries gathered and analyzed disease information as part of assessing the need for new vaccines, and NUVI appears to have stimulated some EPIs, mostly in middle-income countries, to take steps to strengthen sentinel or district surveillance systems, particularly for pneumonia and meningitis. In general, however, the poorest countries continue to have weak disease surveillance.

**Vaccine Supply, the Cold Chain, Injection Safety and Waste Management**

Depending on the new vaccine introduced, its formulation, presentation, and packaging, the introduction process may put tremendous pressure on a country’s cold chain and logistics (see Figure 1, which illustrates how the additional vaccines increase the volume of vaccine storage by a factor of two to eight times). These volume increases have significant implications for cold chain storage capacity, transport, and waste disposal.

Before introductions, many EPIs purchased and installed more cold storage capacity, refrigerators and other equipment and at least briefly addressed vaccine management in health worker training related to NUVI.
The majority of PIEs acknowledged both improvements in the cold chain as a result of NUVI preparations as well as continued important deficiencies. The improvements consisted mainly of purchase and installation of equipment, and greater storage capacity. While these contributions were valuable, support for two equally critical needs was frequently inadequate: improving health worker practices related to the supply chain and transportation of vaccine and related supplies.

Case Study 1: An African country’s EPI had to adjust to the challenges of introducing single-dose PCV7 in pre-filled glass syringes with separate unattached needles, which came in bulky packaging. There were no problems with vaccine supply or storage at the central level, but it was recognized and planned that districts required more frequent (monthly) deliveries because of limited cold storage capacity. This was difficult to do consistently in part because of substantial space required in vehicles for the large volume of PCV in addition to the many other medicines and supplies going monthly to districts. In fact, some districts required twice-monthly deliveries of the vaccine and other supplies. Immunization outreach via motorcycle also became problematic because of the bulky vaccine. The pre-filled glass syringes could be adequately incinerated at the requisite high temperatures in only one incinerator, which was located in the capital. Health workers were well oriented regarding waste management, and special safety boxes for the used syringes were provided. However, the need to move those syringes to the capital on a regular basis put additional pressure on transport (vehicles and fuel). The program has now switched to a different PCV product that is more compatible with standard vaccine handling procedures.

At a recent workshop, the team from an African country advised other countries to consider the “hidden costs” (e.g., gas and electricity) required to run new cold chain equipment installed to prepare for NUVI. Donor funding did not cover all such costs, leading to a serious depletion of resources: facilities ran out of gas to operate the additional cold chain equipment. For up to two weeks all immunization services were stopped for all antigens, so that debts could be cleared and gas cylinders could be refilled.

In general, the combination of AD syringes and training that accompanied vaccine introductions in most countries appears to have led to improvements in injection safety, although poor practices, such as recapping, were still observed during PIEs. The GAVI Alliance’s new vaccine and injection safety (INS) funding improved the availability of auto-disable (AD) syringes for injection safety in immunization. Moreover, almost all countries that received such support were able to sustain the availability of AD syringes and safety boxes, and around one-third of countries receiving INS support improved injection safety in non-immunization services.

Depending on various factors, adding a new vaccine can either increase or decrease waste disposal needs. Overall, NUVI does not appear to have had a notable impact on waste management in most countries: both incinerators and practices still needed substantial attention after new vaccines were introduced in most countries.

Case Study 2: In 2008/2009, an African country introduced three vaccines simultaneously -- PCV7, RV, and pentavalent (DTaP-IPV-Hib). This challenged every component of the EPI, including the cold chain, whose capacity for the PCV and RV alone had to increase by more than 450%. The national treasury provided limited funds in 2008, and two provinces managed to provide additional funding through replacement of redundant refrigerators. Two vaccine companies provided funding to procure 3,000 refrigerators; however, they arrived very late, and there were initial set-up problems (some did not function due to power surges). One issue was that Provincial Cold Chain Managers had other responsibilities besides EPI, including for such high priority programs as tuberculosis and HIV/AIDS. Some depots had limited capacity to increase orders due to limited cold chain capacity, resulting in facilities having to order more frequently. So overall both costs and personnel needed for cold chain operation increased substantially.
Despite its strong EPI, a European country’s introduction of MMR, pentavalent, and PCV over a four-year period presented challenges to the cold chain. Cold rooms had to be rented and cooled vans used while the number of intermediate-level cold rooms increased from five to over 90 from 2005 to 2008. Required storage volume expanded from 26.2 cm$^3$ to 550 cm$^3$ per fully immunized child at subnational levels; and vaccine distribution increased from four to eight times per year and from one to three rounds over each distribution route.

In summary, vaccine introductions have enabled many EPIs to obtain new cold rooms, refrigerators, and AD syringes. Internal distribution of high-volume new vaccines has been a major challenge, and vaccine-management practices remain deficient in many countries. Overall, vaccine introductions appear to have improved injection safety and, in some countries, waste management, but waste management commonly remains deficient.

**Financing and Sustainability**

Most new vaccines are many times more costly than traditional EPI vaccines. A preliminary WHO analysis of country data in 2009 found that the average cost per child immunized with DTP3 would increase from $11 to $30 in going from DTP to DTP-HepB to DTP-Hib-HepB. On average, WHO calculated that vaccine supply and logistics were expected to increase from 57% in 2008 to 71% in 2012 of immunization expenditures, with a much less significant increase in non-vaccine costs. Based on information in SnapShots, it would appear that the cost of new vaccines in a fully-loaded district refrigerator may be 50 times the cost of the refrigerator.

Moreover, the introduction of new vaccines implies many collateral costs. The PIE for one African country notes unexpected or under-estimated costs for: transport (fuel and per diem because of the greatly increased volume of pentavalent vaccine in small-dose vials), cold chain (airport storage), training (materials, staff time), and equipment and maintenance. In general countries that add a high-volume vaccine incur substantial new capital and recurrent costs for cold storage, transport, and vaccine carriers and cold boxes for outreach. While a donor may fund hundreds of new refrigerators for a NUVI, it is the EPI (or district health budgets) that must fund ongoing expenses for fuel, maintenance, and repair.

Donor financial support (although time-limited) has certainly eased the “sticker shock” in many countries. GAVI Alliance funding, for which some 70 countries with the lowest per capita income are eligible, has included: new vaccine support, immunization services support (ISS), health system strengthening (HSS), injection safety support, and civil society organization (CSO) support. JICA (Japanese aid), AusAID, USAID, and other donors have also provided funding to support immunization programs in some countries. (For most countries, ISS funding ended over the past few years, and injection safety funding was already phased out.)

The GAVI co-financing policy, initiated in 2008, is intended to help countries gradually assume more responsibility for the cost of new vaccines. Countries are required to co-finance (co-procure) a portion of their new vaccines from the beginning of introduction, and, in accordance with their income level, increase this proportion over time. Support for NUVI also includes a vaccine introduction grant of US$0.30 per infant in the year’s birth cohort, with a minimum award of $100,000. In addition the Advanced Market Commitment has achieved the guaranteed low price of $3.50 per dose of PCV for GAVI-eligible countries that purchase vaccine through UNICEF. As of 2009, the lowest price for non-GAVI countries of PCV7 was $25 to $26 per dose and around $16 for the full series (two or three doses) of rotavirus vaccine.
In a 2009 workshop, representatives from various African countries felt that co-financing had helped increase country ownership and commitment to immunization and enhanced evidence-based decision-making. Still, a number of those governments were struggling to meet their co-financing obligations. Many EPIs were extremely concerned about how they would cover the costs of their immunization programs once GAVI support ended, in part because future vaccine prices remain uncertain.

Health and immunization budgets in poor countries are extremely donor-dependent; in 2010, it was estimated that only 15% of vaccine financing in low-income countries came from country budgets. Government contributions to EPI mentioned at a workshop of 16 African countries were as low as 3.6%. Besides limited overall government budgets, financing of immunization in many countries faces such obstacles as inefficient national disbursement procedures and the recent creation of many new districts, which require substantial expenses and human resources. Effective advocacy for additional immunization funding within ministries of health and with ministries of finance is required if the cost of new vaccines and their delivery are to be covered on a sustainable basis in the poorest countries.

**Case Study 3:** In one African nation, the proportion of the country’s health budget allocated to the EPI has fallen substantially, and the proportion of the EPI budget for routine immunization services (vis-à-vis polio and measles campaigns) has been around 20%. New vaccines accounted for 92% of vaccine costs in 2009 (currently most of these costs are financed by GAVI). The EPI must also deal with the creation of many new districts, each needing its own human and material infrastructure for immunization. There is a severe shortage of funds for routine EPI operational costs, which contributes to “longstanding deficiencies, such as inadequate supervision, absence of monitoring and use of data for detecting and correcting problems, irregular supplies, and infrequently trained health workers.” Coverage has fallen in recent years, due to these and other factors. Although the continued effects of vaccine introduction on the EPI is unclear, the budgetary implications of vaccine introductions are very troubling. Introduction of both RV and PCV are in the current five-year EPI plan, and there is growing political pressure to introduce HPV.

The documents reviewed show that although GAVI and other donor funding has enabled many countries to introduce new vaccines and has supported improvements in financial planning and budgeting, these supports have not solved the basic problem that poor countries cannot afford the current market prices of new vaccines and their delivery. Financing of new vaccines and their collateral expenses remains a critical issue to resolve in order to prevent NUVI from reducing funding for other crucial expenditures of EPIs and ministries of health. There is growing awareness and concern of financing and sustainability issues, at both the international and country levels, but only short-term or partial solutions thus far. It would seem that solutions need to combine continued efforts to reduce vaccine prices along with more effective advocacy within countries by EPIs and their partners.

**Leadership and Governance**

As mentioned, NUVI in some countries did at least temporarily raise the EPI’s profile and image. The first families of many countries participated in new vaccine launches, but in only one case was there information on whether this opportunity led to ongoing political support for the EPI. The strong partnership for pentavalent introduction in an African country among the MOH and donors was reported to have led to sustained commitment by national authorities at all levels for immunization services.

There are some indications in the grey literature reviewed that the large costs that most new vaccines entail, as well as common requirements such as cMYPs and co-financing, have
influenced some EPIs to improve financial planning and relations with ministries of financing and planning. A grant from the Bill & Melinda Gates Foundation is enabling the Sabin Vaccine Institute’s Sustainable Immunization Financing program to encourage key stakeholders in 12 African and three Asian countries to work together to identify sustainable financing mechanisms for immunization.

Ideally, the introduction of PCV should be planned and carried out with a broad coalition of MOH units and other partners focused on addressing childhood pneumonia, and RV introduction should include similar partners to address childhood diarrhea. The documents reviewed did not describe such broad coalition-building, although this may change due to a growing international movement to encourage and facilitate such integration. An African PIE praised the integrated activities between the MOH’s EPI and disease control units in supportive supervision for child health, but it is unclear if this was related to NUVI.

Discussion and Conclusions

The basic conclusion of this review is that, over the last 10 to 15 years, NUVI s have both strengthened and stressed EPIs, although in most cases not to a major extent in either direction. Many of the commonly weak areas in EPIs have not significantly changed. After reviewing lessons learned from PIEs following PCV and RV introductions, the GAVI Alliance Board Meeting (16-17 June 2010) noted that: “Vaccine specific system strengthening is required in terms of disease and Adverse Events Following Immunization (AEFI) surveillance, Expanded Program on Immunization (EPI) training, vaccine and cold chain management.”

Reflecting on RV introduction in 14 countries between 2006 and 2009, PAHO concluded that: “Many lessons were learned from the introduction of rotavirus vaccine in the Region of the Americas: for example, the need for adequate evaluation of the cold chain and the logistics of the immunization program prior to introducing a new vaccine, the need for training at all levels, the importance of strengthening the network for ESAVI [AEFI] reporting and investigating, the importance of ensuring the sustainability of the EPI vaccine in the national budget, and the establishment of rotavirus diarrhea surveillance prior to the introduction of the vaccine and the subsequent maintenance of that surveillance as fundamental to decision-making.”

The main positive impacts of NUVI are: (1) protecting many people from illness and death; and (2) in many countries making some level of improvement in vaccination hardware, tools, systems and staff capabilities – although further improvements are needed; (3) in some countries at least “baby steps” towards improved national program and financial planning.

Despite growing attention to immunization financing issues, these are far from being resolved. NUVI s often entail a several-fold increase in vaccine costs as well as other costs to the EPI budget. The initial availability of donor funding does not obviate the need for better long-term financial planning that must include higher commitments from governments and donors. In the last decade there have been too many cases of EPIs not being concerned with solid funding commitments, even as the end of donor funding approached, assuming that the money would be found somewhere. Fortunately, there are indications that attitudes are changing. The increased costs of immunization programs (due primarily to more expensive vaccines and their collateral costs) is putting pressure on health budgets overall, requiring better processes for priority-setting and better management of resources for efficiency.

In general, particularly when the EPI is reasonably well-perceived by the public; sufficient time funding and skill devoted to planning and preparations, and the new vaccine characteristics are
appropriate for the EPIs’ capacity and capabilities, NUVI is a reasonably smooth process that in many cases contributes to at least short-term improvements in immunization service delivery and public perceptions. Unfortunately, in many of the introductions described, one or more of these conditions were not met. Even when other key conditions are favorable, an active anti-government or anti-vaccine movement can greatly complicate the introduction and its aftermath.

Clearly, NUVI does not automatically strengthen weak EPI or health system components: such improvements must be well planned and implemented. While planners must try to ensure that the introduction goes smoothly, they should also consider NUVI as an opportunity to assess and address weak system components. The objective of system strengthening tied to NUVI should not be conceived as a rapid, intense process for a few months before and after introduction, but rather as a well planned multi-year undertaking, as in the examples below.

Case Study 4: Funded by the Bill & Melinda Gates Foundation and state government resources, the Andhra Pradesh (AP) Partnership Project on Immunization (2001-2006) was implemented through a strong partnership between the Government of AP and PATH. Through the process of introducing HBV and AD syringes, the project greatly strengthened most immunization system components and bolstered routine immunization in AP’s 23 districts. In three years coverage rates increased from 58 percent to 72 percent, and drop-out rates for measles vaccination decreased from 22 percent to 8 percent. While this was not a typical NUVI, the scale was equivalent to or greater than that of most national introductions. Aspects worthy of replication by EPIs and their partners when introducing new vaccines, include: the strong, explicit focus on system strengthening; the longer-term vision that the process would take several years and not simply focus on a short preparation and introduction period; the availability of sufficient funding from several sources; development of strong monitoring and information systems and effective use of information on progress to build and sustain political support; and establishment and maintenance of a strong coalition of partners. This project was able achieve what vaccine introduction should ideally achieve everywhere, a smooth introduction of new vaccines in a manner that truly strengthens routine immunization.

Case Study 5: To support the smooth introduction of pentavalent vaccine and strengthen the EPI in a Caribbean country, the Japanese Government (JICA) provided a grant of US$10 million, administered by UNICEF, from 2001-5. While these resources did not address every weakness in the EPI, they did facilitate many advances, including:

► The revision, standardization, and extensive training on new norms and procedures
► Strengthened infrastructure, implementation, monitoring, supervision and evaluation at all levels
► Improvements in injection safety and waste management practices, as well as availability of safety boxes
► A strengthened information system at all levels
► Improved logistics planning and execution, practically eliminating stock-outs, which had been common
► Higher public demand and use of immunization services
► Improved perceptions of the EPI within and beyond of the Secretariat of Health.

Based on the findings from the grey literature, the following recommendations are offered to EPIs and their partners:

- Make unrushed, evidence-informed decisions to introduce a new vaccine, based on both operational feasibility and good evidence of need – delay the introduction if necessary.
- Accept a new vaccine only in a formulation, presentation, and packaging that makes sense for the EPI, and for which the supply seems secure.
- Take full advantage of the introduction preparations to strengthen weaker components of the EPI, both through training, supplies, equipment, and supportive supervision,
through a long-term improvement strategy. Plan improvement steps as a sustained undertaking, not as actions concentrated in a few months before and after introduction.

- In addressing cold chain needs, go beyond purchasing refrigerators and cold storage; address the additional needs for more frequent transport, per diem, and staff time, and address staff vaccine management skills and attitudes, in both the short and longer term. Plan for the added fuel costs that new equipment entails.

- Expand the focus to include the full financial implications of new vaccines, including associated costs of cold chain, training, and other critical components of the vaccination system, and advocate for more government resources to fill financing gaps.

- Gauge the level and nature of communication and mobilization regarding the vaccine introduction to the particular situation and setting. Base strategies and activities on rapid formative research when possible.

- Use the introduction period to generate support for vaccination and new or strengthened links with other health programs and governmental institutions (MOF, parliament, etc.).

- Assess any political opposition, media or other anti-vaccine groups that may latch on to NUUVI to generate public opposition, and if there is a threat of controversy, reduce the risk before introduction by engaging in dialogue with all parties.

- To the extent possible, embed planning for RV and PCV introduction into broader coalitions and strategies addressing diarrheal and respiratory disease in the country.

There are several important questions on financing that this review could not answer, but that governments and donors should strive to answer:

- What is the effect of NUUVI on both the size of and the proportional allocations in the EPI and ministry of health budgets, in the year of introduction and in subsequent years?

- Have the high costs of some new vaccines and their delivery led to reductions in funding for other vaccines, other EPI, or other health system expenses?

- To what extent has the process of NUUVI led to improvements in financial planning and/or the effectiveness of the EPI/ministry of health’s advocacy for funding with the ministry of finance or national legislature?

The new vaccines reviewed (HBV, Hib, RV, PCV, HPV and others) have a tremendous potential to reduce morbidity and mortality throughout the world. The challenge to EPIs is to achieve this goal in a well-planned manner that strengthens various weak EPI components and improves overall health system functioning.
References

Please note: this shortened version of the full paper does not cite all of the references included.