National Decision-Making for Immunization Programs
2014 ADVAC

Scenario A

Professor Watson is a respected researcher at the national medical university and has just been appointed to the national immunization technical advisory group (NITAG). On his Disclosure of Interests, he reported that he is the Principle Investigator on an HPV vaccine trial, using one of the two HPV vaccines licensed for use in the country. At its next meeting, the NITAG is to discuss the recommendations on the use of HPV vaccine. The committee will consider stating a preference for one of the two currently licensed products. Professor Watson is upset because the committee Chair has asked him to recuse himself from the meeting during the session relating to the use of HPV vaccines. He states that he is receiving no personal benefit from the trial and should be allowed to participate as he knows HPV vaccines better than any other members on the group. You are Executive Secretary of the NITAG. What would you do?

Scenario B

Whole cell pertussis vaccine has long been used in your country, but you are considering the use of a new acellular vaccine that has recently been licensed. As Secretariat to the NITAG, you need to prepare evidence for review by the committee. What type of information would you look for?

Scenario C

Technovac, a vaccine manufacturing company, sends an email to the NITAG Chair, stating that they have important yet unpublished new data that may lead to a modification of the recommendations on use of Picote vaccine. They request that the committee reconsider its recommendations for use of the vaccine at its next meeting, and they will come and present their new data to the committee. You are Executive Secretary of the NITAG and are working on the agenda for the upcoming meeting. How should you respond to this request?

Scenario D

The association of paediatricians from Bruntland refuses to follow the recommendations of the national technical advisory group organized under the aegis of the Ministry of Health. The association has written a letter to you, as Executive Secretary of the NITAG, stating that the committee is not credible and does not properly review evidence. How would you approach developing a response to this letter?

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The role of economic information in decision-making by the Advisory Committee on Immunization Practices

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ABSTRACT

With cost of vaccines steadily increasing, recommendations of the Advisory Committee on Immunization Practices (ACIP) have growing economic implications for the public. We used semi-structured telephone interviews to assess the knowledge, attitudes, and practices of the 15 voting members of the 2006–2007 ACIP regarding the use of economic information by the committee in their deliberations about new vaccine recommendations. These interviews demonstrated the importance of economic information in ACIP deliberations, but also revealed that many members felt economic information should not be outweighed by the more important issues of vaccine efficacy, disease burden, and safety. In addition, though members had variable levels of expertise in analyzing economic data, there was a general concern that assumptions inherent in the development of cost-effectiveness models made interpretation of the data resulting from these models difficult. To counteract this concern, several ACIP members suggested standardizing the process of how economic data are presented to the committee so that a more uniform consideration of consequential information might be undertaken by the ACIP in their deliberations.

1. Introduction

Over the last several years the United States child and adolescent immunization schedule has become increasingly complex and costly [1]. In 2001, vaccines protecting against 12 antigens were recommended for routine use in children <18 years of age [2] at a per-child cost in the public sector of ~$400 (using federal contract prices expressed in 2001 dollars) [1]. Compare this to the 2008 schedule, with vaccines against 14 antigens recommended by the age of 6, and an additional 2–3 recommended vaccine series for young adults [3] (differences due to gender-specific recommendations for human papillomavirus vaccine). Consistent with this increased number of vaccines, the public-sector cost of immunizing today's children has risen dramatically to $950 for males and $1250 for females [4]. Though immunizing children is generally considered a cost-effective health intervention [5], the increased total cost of vaccines has placed a substantial financial burden on individuals, private insurers, and public vaccine financing programs [6–8].

National policies regarding vaccine administration and utilization are determined by the Advisory Committee on Immunization Practices (ACIP) which serves to advise the U.S. Department of Health and Human Services and the Centers for Disease Control and Prevention (CDC) on the control of vaccine-preventable diseases in the civilian population [9]. The ACIP is a federal advisory committee comprised of 15 voting members with expertise in the fields of infectious diseases, immunization practices and public health, vaccine research, or community aspects of immunization programs [9]. The ACIP also includes 8 non-voting ex-officio members from different government agencies with an interest in vaccine-preventable diseases (e.g., Department of Veterans Affairs), and several non-voting liaison representatives from 25 medical organizations (e.g., American Academy of Pediatrics). These non-voting members provide additional opinions and information during the deliberation process.

One of the main tasks of the ACIP is to develop recommendations on population groups and/or circumstances where vaccines should be given. Vaccines that are recommended by the ACIP for routine use in children under the age of 18 years typically become incorporated into the vaccines for children (VFC) program through a separate ACIP voting process. VFC is a federal entitlement program that serves as a vital financing mechanism to provide government-purchased vaccine for more than 70 million eligible children and

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adolescents through 18 years of age. It is estimated that as much as 55% of all childhood vaccine doses are purchased through this program [6,7,10].

Because the actions of the ACIP are integrally tied to public vaccine financing programs, and because many health plan coverage patterns are aligned with ACIP recommendations [11], actions of the ACIP can have far-reaching economic influences in both the public and private sectors. Unlike many other westernized countries, the ACIP charter is unique in that it explicitly allows for cost-effectiveness information (though not vaccine price) to be considered when the committee deliberates about new vaccine recommendations [12,13]. However, the extent to which ACIP members understand and/or incorporate economic information into their discussions and decisions about new vaccine recommendations is unknown.

The goal of this study was to describe the knowledge, attitudes, and current and preferred practices of the 15 voting members of the 2006 ACIP regarding the use of economic information in their deliberations about new vaccine recommendations. Specifically, we sought to understand how ACIP members incorporate available economic data in their decision-making as individuals and as a committee, and preferences for presentation of economic data. We intended that study findings would illuminate possible opportunities to enhance the ACIP decision-making process about new vaccine recommendations.

2. Methods

The project team developed a semi-structured interview guide that was administered to each of the 15 voting members of the ACIP between September 2006 and January 2007. During this time, the ACIP committee was comprised of 13 physicians, 1 pediatric nurse practitioner with expertise in infectious diseases and 1 lay consumer representative. Physicians were generalists (7 pediatricians and 6 internal medicine physicians), some of who had subspecialty training in infectious diseases ($n = 6$) or currently worked in the public health arena ($n = 4$). All members participated. Interviews were administered by telephone after verbal informed consent was obtained. Audiotapes of these interviews were transcribed verbatim to ensure accuracy. The Institutional Review Board at the University of Michigan approved all study activities.

Each interview was comprised of case scenarios and open-ended questions. Scenarios were developed initially based on study team consensus, and further refined to incorporate feedback of pilot testing among vaccination experts who were not current members of the ACIP. The case scenarios described a hypothetical vaccine, "ChildVax", that the ACIP was asked to consider recommending. ChildVax was described as having a favorable safety profile and efficacy, but also as the "most expensive broadly recommended childhood vaccine series to date" (in comparison to the HPV vaccine which was the most expensive recommended vaccine at the time of the study at a list price of $120/dose) [4]. Information about disease severity and disease burden potentially prevented by ChildVax was not provided. Respondents were then presented in a stepwise manner with increasingly detailed economic information about the vaccine (price and cost-effectiveness) and asked to describe how this information affected their individual-level deliberations. This stepwise progression of information allowed differentiation between issues of efficacy and safety of a vaccine versus issues of price and cost-effectiveness. Open-ended questions queried respondents about how they used economic information in their deliberations about new vaccine recommendations, how the ACIP as a group should use this information, and preferences for how this information should be presented. Although both the case scenarios and interview questions were identical for each study subject, because responses were open-ended, some of the issues summarized in this report were addressed by only a subset of participants.

Three authors (AC, AFD, MMD) independently reviewed the interview transcripts and generated a set of central emerging themes, as well as the perspectives of respondents that supported those themes. Themes were stimulated, in part, by the topic areas the authors presented to respondents in the interviews, but also included several issues that respondents raised on their own initiative beyond the anticipated topics. Coding discrepancies were resolved on a case by case basis and the final analysis was based on themes coded with consensus among the three reviewers. Major themes in response to the case scenarios are presented; for each theme, we characterize the ways in which members of the ACIP responded similarly or differently. Themes of responses to open-ended questions that queried participants about their views outside of case scenarios are also described.

3. Results

3.1. Responses to case scenarios

3.1.1. Influence of price and cost-effectiveness data on individual perspectives

When queried about how the price of the ChildVax vaccine series (without cost-effectiveness information) would affect their deliberations about the vaccine, members uniformly indicated that vaccine price alone would not be influential. Instead, all members indicated that additional information would need to be considered in conjunction with price, including disease burden and disease severity.

In contrast, all members indicated that cost-effectiveness data would influence their thinking about ChildVax. Cost-effectiveness data were felt to provide a sense of the "relative value" of the vaccine (i.e. the combination of reductions in morbidity/mortality and health care utilization compared to cost of vaccine) compared to other vaccines, and two members noted that this type of data provided a context for comparison with other data that the committee typically considers when deliberating about new vaccine recommendations (e.g., disease burden). As a caveat, two members indicated that the extent to which cost-effectiveness data would influence their thinking depended on the burden of the disease in question. Additionally, another member had concerns that, in general, cost-effectiveness data do not fully capture the more broadly defined "value" of a vaccine.

Most members ($n = 8$) did not have a specific target cost-effectiveness threshold value for new vaccines. One member noted that $50,000 per quality adjusted life year (QALY) is often cited as a threshold value below which the cost-effectiveness of the vaccine would be more acceptable, and another noted a range of $50,000–150,000 as an acceptable threshold. Other members ($n = 2$) indicated that disease burden and severity would need to be considered when deciding on an acceptable threshold value for vaccine cost-effectiveness.

Members were then asked about their willingness to recommend ChildVax without any economic data (price or cost-effectiveness data). While a few members ($n = 3$) indicated that this lack of information would not affect their willingness to recommend the vaccine, many ($n = 7$) indicated that it would, with some ($n = 3$) noting that they have come to expect cost-effectiveness data to be available for all newly licensed vaccines. In fact, one member indicated that the only way the ACIP should not be presented with cost-effectiveness data was if the vaccine under consideration was so inexpensive that the question of cost-effectiveness was no longer relevant.

3.2. Use of economic information by the ACIP more broadly

3.2.1. How should economic information ideally be used by the ACIP?

The majority of ACIP members ($n = 10$) indicated that economic information should be an important, but not dominant, factor considered during the committee's deliberations about new vaccine recommendations. These members agreed that disease burden, vaccine safety and vaccine efficacy should be given greater weight than economic information. Individual views about the degree to which economic data should be used by the ACIP varied widely among the other members. For example, one member felt the ACIP should make recommendations irrespective of the economic impact of those recommendations, while two others recognized a need to be cognizant of cost but that this information would not necessarily influence their recommendation. Two others were ambivalent, being torn between making strictly "science-based recommendations" and including economic information as a factor in their decision.

3.2.2. How does ACIP currently use economic information in deliberations about vaccine recommendations?

There was not a uniform perception of the manner in which ACIP currently uses economic information in their deliberations. A general theme that emerged from this line of discussion was that the importance the ACIP currently gives to economic information may vary depending on the disease/vaccine in question. In general, as disease severity increased, issues of cost and cost-effectiveness were thought to become less influential. For example, the quadrivalent meningococcal conjugate vaccine (MCV4) was cited by several members ($n = 4$) as a "special case" where the less favorable cost-effectiveness ratio for the vaccine was acceptable due to the severe nature of the disease. All members indicated that their perspectives on the influence of cost and cost-effectiveness data did not differ based on whether the vaccine under consideration was for children/adolescents or adults.

3.2.3. How familiar are members of the ACIP with the use of economic data?

Only four members indicated that they had prior experience with economic analyses before becoming an ACIP member. There were mixed opinions about whether providing training for members in economic analyses would be beneficial. On one hand, several ($n = 5$) members suggested that training would not be a valuable use of the committee's time and that a better strategy would be to take their cues from the opinions of "experts" who were better able to assess whether an economic analysis had been well done. However, others ($n = 4$) felt that some level of training would be useful, and suggested a variety of venues to achieve this, including written information, didactic educational sessions, or even a list of "minimal acceptable factors" for a well-done cost-effectiveness study.

3.2.4. What type of economic information does the ACIP want?

When queried about their preferred format for cost-effectiveness data, several members ($n = 6$) were satisfied with presentation of QALYs alone. However, six members expressed a preference for a variety of measures to be presented (e.g., dollars per QALY, dollars per illness episode prevented) so that a full picture of the economic impact of new vaccine recommendations could be provided. Specific problems associated with QALYs were cited by the members and included difficulty in explaining QALYs to policy makers and the "arbitrary nature" of some of the data used to derive the QALYs.

The source and validity of data used in presentations of economic information to the ACIP was an explicit concern for the majority ($n = 10$) of members of the group. There was discomfort with the wide range of the confidence intervals sometimes produced by economic analyses. Some ($n = 4$) felt this uncertainty hindered the ability of the group to identify the appropriate course of action about a given vaccine. Furthermore, several ($n = 5$) members expressed frustration with the variety and apparent "randomness" of some of the assumptions upon which economic models are based, and the difficulty in understanding which of these assumptions were valid. There was also concern about the perception that models could be manipulated to bias the economic picture toward a more favorable cost-effectiveness profile—this was a particular concern for models generated or sponsored by vaccine manufacturers.

3.2.5. Additional suggestions from the committee

A major theme in the interviews was concern by members of ACIP about the validity and "believability" of data derived from cost-effectiveness models. Several suggestions were offered about processes that might counter this problem. One was to perform more than one analysis for any given vaccine so that different groups, which would likely undertake the analysis with different assumptions and/or approaches, could provide a more robust view of the economics of the vaccine in question. Another was to have an independent group, unrelated to the CDC or industry, review cost-effectiveness models outside of ACIP deliberations in order to provide another opinion about the quality of the analyses performed and potential implications for vaccine policy. This idea is similar to that used for the National Health Service in the United Kingdom, which some commentators (not associated with the ACIP) have suggested should also be adopted for the US health care system more broadly [14].

Many members ($n = 7$) explicitly expressed support for standardizing the process of performing and presenting economic information to ACIP. Making the presentation format for cost-effectiveness ratios consistent across studies was suggested by two members as a mechanism to minimize confusion, and to allow easier comparison between multiple cost-effectiveness studies for the same vaccine, or between one vaccine and another. One member suggested generating a "set of standards" that should be presented for each vaccine, enabling members to compare the vaccine in question to a "norm," and thus discern the relative value of that vaccine to other vaccines or other preventive interventions. Members unanimously indicated that they wanted analyses to be presented clearly and simply, with terms and assumptions specified, and conclusions summarized. However, this need for simplification was tempered by recognition that analyses presented too concisely could lack sufficient information to adequately understand the assumptions driving the model.

3.2.6. Vaccine recommendations versus vaccine financing

Although we did not ask specific questions about vaccine financing, more than half of the members ($n = 8$) found it difficult not to consider the cost of vaccines and the impact on public spending when making recommendations. For example, one member noted that because ACIP recommendations were tied to inclusion of vaccines in the VFC program, it was difficult for this member to see how the ACIP could divorce itself completely from vaccine financing issues when considering new vaccine recommendations.

4. Discussion

This study illustrates that members of the Advisory Committee on Immunization Practices are variably comfortable in their

understanding of the methodologic details of cost-effectiveness analysis, yet are acutely aware of the need to incorporate some form of economic information into their vaccine deliberations. Responses to case scenarios demonstrated that cost-effectiveness, but not price, was an influential factor in the deliberation process. All members agreed that economic information needed to be considered in the context of disease burden and severity and vaccine safety.

There was a strong sense that the ACIP would benefit from standardizing the presentation and consideration of economic information. Standardization of information could address several important issues raised by the committee members in our study. First, if the base-case assumptions in economic model inputs were transparent, ACIP members could better understand the potential impacts of a vaccine on medical, public health, and economic outcomes. Standardization of information could also reduce the potential for bias in cost-effectiveness analyses, especially since these types of analyses rely heavily on data from the vaccine's manufacturer. In addition, standardization might allow the ACIP members to examine economic analyses earlier in the decision pipeline, thus enabling them to be better informed about conclusions from, and limitations to, the economic data at hand. Finally, standardization could facilitate comparison of information from one vaccine relative to another or between vaccines and other preventive interventions.

New guidelines have recently been developed by the CDC to standardize the way economic information is presented to the ACIP [15]. These guidelines include anonymous peer review before presentation of a report that details the economic study under consideration, and provide criteria for how economic information should be presented during ACIP meetings. These guidelines officially go into effect at the June 2008 ACIP meeting and are described in detail on the CDC/ACIP website (http://www.cdc.gov/vaccines/recs/acip/economic-studies.htm) [15]. This new process of standardization may counteract some of the discomfort described by the participants in our study related to the "uncertainty of assumptions" used in economic evaluations. However, our results also suggest that a "guided interpretation" of the results of these standardized analyses may also be of use given that several of the study participants voiced unfamiliarity with interpretation of economic data.

The maximum tenure as a voting member on the ACIP is 4 years, thus a limitation of our study is that the issues and views captured by our analysis could change over time as new members become appointed. However, several key opinions about the relative importance of and need for economic information was expressed by all members of the committee, appointed at different times. These opinions are therefore more likely to represent issues that are inherent to the ACIP deliberation process, rather than member-specific issues.

In summary, our study identified several key issues brought forth by the members of the ACIP regarding the incorporation of economic information in the deliberation process for new vaccines. There was a general belief that economic information is a meaningful factor to be considered, but that this information should be regarded in the context of disease- and vaccine-specific characteristics. Furthermore, because it is difficult to determine the validity of assumptions underlying economic models, cost-effectiveness data are interpreted cautiously. Standardization in the way that economic information is gathered, presented and considered was suggested as a mechanism to improve the ACIP deliberation process. The newly developed standardization process, which was approved by the ACIP in June 2007 and will be implemented beginning with the June 2008 ACIP meeting, may provide an opportunity to evaluate how this process impacts ACIP deliberations [15].

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Modifying the GRADE framework could benefit public health

The commitment in recent years to ensuring that rigorous evidence is available to guide medical practice and health policy making is commendable. To guide the assessment of evidence, various approaches have emerged in recent years. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework has enjoyed particular popularity, providing a systematic and intelligible approach to ranking available research outcomes.[1]

The merits and limitations of the GRADE framework for systematically evaluating the quality of evidence for guiding clinical practice guidelines have recently been eloquently debated.[2 3] We will not dwell on the methodological allegations that GRADE suffers from external and internal inconsistency, potential for bias and lack of validation, nor the possibility that these apparent flaws are a result of maladroit operators rather than framework deficiencies. Our concern is that the GRADE framework may have some unforeseen detrimental public health impacts unless modified.

The large-scale vigorous adoption of the framework across the global public health sector clearly demonstrates a laudable desire to unlock the previously impenetrable black box of policy formulation that resided in the hands of a limited number of "experts" and bureaucrats. In this regard, having the piercing spotlight of a framework, in which the evidence underpinning decisions is openly presented and transparently evaluated for robustness, should be broadly welcomed.

Our concern relates to the adequacy of the traditional hierarchy of research design used to categorise the "strength of evidence" when applied to preventive public health programmes.[4] Although the hierarchy is well suited to the relatively narrow domain of therapeutic effectiveness, it performs less satisfactorily when broader evidence streams at population level need to be synthesised to inform decisions on public health programme strategies. This is particularly pertinent to environmental modification strategies and immunisation programmes, where the archetypal double-blinded randomised control trial (RCT) may not be technically or ethically feasible nor provide the true measure of population impact or public health benefit. In certain situations, the evidence from observational study designs or, heaven forbid, ecological analyses or opportunistic outbreak investigations, may provide a more adequate measure of a public health strategy's impact.

Immunisation is a particular case in point. High immunisation coverage against a specific pathogen often provides indirect benefits beyond those that can be ascertained through traditional RCTs, particularly population herd immunity and a reduced effective reproduction number of the targeted pathogen. The indirect effects on the cocirculation of other pathogens can also typically be ascertained with any certainty only through the use of observational epidemiological methods. However, such evidence is rated of inferior quality through frameworks such as GRADE.

Often, ethics committees make their own assessment of the evidence and appropriately rule as unethical the RCTs required to achieve high ratings on GRADE. This is illustrated in a recent World Health Organization measles position paper, where ethically responsible reliance on a 1968 quasi-RCT, which followed 21 653 children in the UK aged 10–24 months for 2 years and 9 months after vaccination and found a 94% protective effect of live, monovalent vaccine against measles, resulted in a "moderate level of scientific evidence" using GRADE.[5]

Unfortunately, uninformed comparisons of GRADE scores of health interventions by governments deciding on where to spend their limited health budgets may result in measles vaccination being deprioritised because it did not achieve a "high evidence score". Similarly, antivaccination lobby groups may abuse such ratings to instil doubt and concern in the community, with tragic resurgences of preventable diseases.

The GRADE system addresses one evidence domain, the classical scientific evidence. To ensure its value in informing public health prevention programmes, additional epidemiological domains should be evaluated, and a set of ratings should be provided to ensure the use of comprehensive public health evidence in informing policy making. We propose that these domains could include adaptations of those originally proposed by Bradford–Hill for assessing causality,[6] in particular, the *consistency of evidence* over time in a variety of geographical locations and as gathered by different researchers, the *specificity* of the intervention in relation to its observed effects, the *coherence* of different sources of available evidence and the *gradient* of effects with scale of population level impact compatible with degree of coverage.

GRADE and similar frameworks provide an explicit description of the quality of data supporting policy decisions. It is essential that such frameworks, which are well suited for advising clinical therapeutic decisions, are not carelessly applied to complex policy making in preventive programmes, where non-RCT evidence may be the only or most appropriate and valid data available. We propose that, when ranking the available evidence for these programmes, a GRADE-plus framework is applied that equally weights the quality of appropriate experimental and observational data.

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EXPERT REVIEWS

Establishing global policy recommendations: the role of the Strategic Advisory Group of Experts on immunization

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The vaccine landscape has changed considerably over the last decade with many new vaccines and technological developments, unprecedented progress in reaching out to children and the development of new financing mechanisms. At the same time, there are more demands and additional expectations of national policy makers, donors and other interested parties for increased protection through immunization. The Global Immunization Vision and Strategy (GIVS), which broadens the previous scope of immunization efforts, sets a number of goals to be met by countries. The WHO has recently reviewed and adjusted both its policy making structure and processes for vaccines and immunization to include an enlarged consultation process to generate evidence-based recommendations, thereby ensuring the transparency of the decision making process and improving communications. This article describes the process of development of immunization policy recommendations at the global level and some of their impacts. It focuses on the roles and modes of operating of the Strategic Advisory Group of Experts on immunization, which is the overarching advisory group involved with the issuance of policy recommendations, monitoring and facilitating the achievement of the GIVS goals. The article also describes the process leading to the publication of WHO vaccine position papers, which provide WHO recommendations on vaccine use. WHO vaccine-related recommendations have become a necessary step in the pathway to the introduction and use of vaccines, especially in developing countries and, consequently, have a clear and significant impact.

Keywords: global • goals • immunization • policy recommendations • Strategic Advisory Group of Experts • vaccine position paper • WHO

WHO mandate & goals

WHO's role & mandate

The WHO's Constitution, signed by 193 Member States, recognizes WHO as a UN specialized agency [1] whose objective is the attainment by all peoples of the highest possible level of health [2]. The Constitution mandates WHO to set standards and formulate global health policy recommendations. Article 2 of the Constitution states that the organization shall act as the directing and coordinating authority on international health work and shall establish and maintain effective collaboration with the UN, specialized agencies, governmental health administrations, professional groups and such other organizations as may be deemed appropriate. It specifically stresses the need to:

- Promote cooperation among scientific and professional groups that contribute to the advancement of health;
- Provide information, counsel and assistance in the field of health;
- Assist in developing an informed public opinion among all peoples on matters of health;
- Develop, establish and promote international standards with respect to food, biological, pharmaceutical and similar products.

In May 1974, the World Health Assembly [3] requested that WHO provide technical advice on the use of vaccines and assist countries in developing suitable programs. This led to the Expanded Program on Immunization (EPI), whose aim was to use available immunization

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tools to produce the maximum impact on avoidable mortality. The initial phase of this program focused on extending immunization to cover a maximum number of infants and pregnant women with the vaccines available at that time. This resulted in a rapid improvement in global immunization coverage [4]. In the 1990s, global immunization coverage in excess of 70% was maintained with basic EPI vaccines (diphtheria, tetanus, polio, pertussis, measles, BCG, yet this success masked large disparities between and within countries with millions of children left exposed to potentially fatal childhood diseases [4].

This led to a new vision, driven by the considerable changes in the field of immunization, including an increasing demand for vaccines, rapid progress in availability of new vaccines and technological developments, continuing health-sector development, increasing awareness of the vulnerability to pandemics and other health emergencies and more potential opportunities for partnerships [5].

In 2005, the 58th World Health Assembly, recognizing the value of immunization and the role that vaccines and immunization can play in reducing mortality in individuals under 5 years of age and the attainment of the Millennium Development Goals, welcomed the Global Immunization Vision and Strategy (GIVS) 2006–2015, which was developed by WHO and UNICEF as a framework for strengthening national immunization programs [6,7]. The goal of GIVS is to protect as many people as possible against a larger number of diseases by expanding the reach of immunization to every eligible person and ensuring that immunization is high on every health agenda. GIVS aims to increase, or at least sustain, very high levels of vaccine coverage for all age groups, to introduce new vaccines and to link immunization with the delivery of other health interventions. GIVS acknowledges that immunization can benefit from, and contribute to, the development of the health sector and help overcome system-wide barriers. The vision was inspired by seven guiding principles, which include exclusive reliance on assured quality and safe products and services, as well as policies and strategies based on evidence and best practices. These principles are reflected in the vision's global goals (see **Box 1**).

Goals & nature of WHO recommendations

WHO recommendations for vaccine use are of both a scientific and strategic nature and are intended primarily for Member States, specifically for the government agencies responsible for decision making, implementation of immunization programs, surveillance of vaccine-preventable diseases, vaccine safety and licensing, and National Immunization Technical Advisory Groups (NITAGs). Recommendations are also useful for international professional associations, nonprofit organizations, bilateral and multilateral donor agencies, and international organizations such as UNICEF and the Global Alliance for Vaccines and Immunization (GAVI) Alliance to help adjust country programs and assistance, including vaccine procurement. The recommendations are also of interest to the pharmaceutical industry. A robust and clear policy process would mean that the global priorities for vaccine development are recognized and the investments by donors aligned with these priorities, and that industry innovation and production focuses on needed vaccines presented in a relevant formulation. Any gaps in the process may result in costly mistakes and delays in implementing a public health intervention that could have major benefits.

Global recommendations are particularly needed in the context of global efforts for disease control such as pandemic influenza, or disease eradication as in the case of the global polio eradication initiative. During the A (H1N1) 2009 pandemic, a small number of industrialized countries had access to most of the global vaccine output over the next 12 months as advanced-purchase agreements limited availability for the rest of the world (especially developing countries). The decision by some national regulatory authorities only to license nonadjuvanted higher antigen content pandemic vaccine rather than antigen-sparing products further limited the global production capabilities [8].

Polio eradication requires that countries achieve a high level of population immunity through routine and supplementary immunization activities. Low immunization rates and resulting outbreaks at country level pose a serious threat to nonimmune children and adults throughout the world. This threat has increased tremendously with the rapid and continuing development of international travel and mass population movements. In 2009, 19 countries previously considered polio-free reported cases and outbreaks caused by imported viruses emerging from Nigeria [9].

Procedure for the formulation of global recommendations: the immunization policy advisory framework

Formulating recommendations involves a systematic effort to gather scientific evidence, which is then considered carefully by the best experts. WHO uses its convening power to receive recommendations from independent external advisory committees comprising experts from various geographical and institutional backgrounds. The experts act in their own capacity, not on behalf of the countries or organizations they come from. They are not paid for this work and receive no personal benefit. The committees' deliberations are issued in the form of advice to the WHO Director-General or her representatives. WHO then uses this advice to promulgate WHO immunization policy recommendations.

Since 2005, WHO has aimed to strengthen its normative and policy-setting functions for immunization and increase the acceptance of WHO policy recommendations on vaccines and immunization. It therefore made adjustments to its immunization-related advisory committees and their processes. This entailed amending the number and terms of reference of the committees, optimizing their coordination, and improving the mode of operating of the committees with particular emphasis on evidence-based decision making and transparency to enhance credibility and impact.

The main group involved with the development of global policy recommendations and strategic advice related to vaccines and immunization to WHO is the Strategic Advisory Group of Experts (SAGE). SAGE also provides support for regional and national programs through its development of immunization norms and good practices. Established in 1999 through

Box 1. Global goals from the Global Immunization Vision and Strategy 2006–2015.

By 2010

- Countries will reach at least 90% national vaccination coverage and at least 80% vaccination coverage in every district or equivalent administrative unit
- Globally, mortality due to measles will have been reduced by 90% compared with the 2000 level

By 2015 or earlier

- The vaccination coverage goal reached in 2010 will have been sustained
- Global childhood mortality due to vaccine-preventable diseases will have been reduced by at least two-thirds compared with 2000 levels
- Every person eligible for immunization included in national programs will have been offered vaccination with vaccines of assured quality according to established national schedules
- Immunization with newly introduced vaccines will have been offered to the entire eligible population within 5 years of these new vaccines in national immunization programs
- All countries will have developed the capacity at all levels to conduct case-based surveillance of vaccine-preventable diseases, supported by laboratory confirmation where necessary, in order to measure vaccine coverage accurately and use these data appropriately
- All national immunization plans will have been formulated as an integral component of sector-wide plans for human resources, financing and logistics
- All national immunization plans will have been formulated, costed and implemented so as to ensure that human resources, funding and supplies are adequate

the merging of two previous committees, notably the Scientific Advisory Group of Experts (which served the Program for Vaccine Development) and the Global Advisory Group (which served the EPI program), SAGE was restructured in 2005. Its activities and modes of operating were then adjusted to suit the requirements of WHO's GIVS [6]. The mandate of SAGE now extends to all vaccine-preventable diseases throughout all age groups [10]. SAGE provides recommendations on issues ranging from research and development to vaccine administration and linkage with other health interventions.

Specifically, SAGE advises on:

- Major issues and challenges to be addressed with respect to achieving the goals of GIVS;
- The adequacy of progress towards the achievement of the goals of the GIVS;
- Immunization program response to current public health priorities;
- Policies, goals and targets including those related to vaccine research and development;
- Adequacy of WHO's strategic plan and priority activities to achieve the GIVS goals considering the comparative advantages and respective roles of partner organizations;
- Cross-departmental activities and initiatives related to vaccine and immunization technologies, strategies and linkages with other health interventions;
- Engagement of WHO in partnerships that will enhance achievement of global immunization goals.

WHO immunization-related policy recommendations, including those in the WHO position papers on vaccines, follow the advisory processes established through/for SAGE. These position papers are summaries of information about licensed vaccines of public health interest, which are based on an extensive review and ranking of evidence by experts, and include inputs from interested stakeholders including industry. They are designed to be used by immunization and public health staff to make decisions about the public health value and use of specific vaccines. Figure 1 summarizes the pathways for the issuance of WHO recommendations. Over the past 5 years, SAGE has provided recommendations to WHO on the use of tetanus, *Haemophilus influenza* type b, rotavirus, mumps, Japanese encephalitis, pneumococcal conjugate and polysaccharide, BCG, rabies, human papillomavirus, typhoid, hepatitis B, measles, poliomyelitis, cholera and pertussis vaccines. These were used to develop new, or update previous, WHO position papers [11–27]. Guidance was also provided on the use of H5N1 [28] and H1N1 pandemic influenza vaccines [8].

A number of technical advisory committees complement and support the work of SAGE. They cover a wide range of issues including technical analysis and guidance, development of norms and standards, vaccine safety, global research and vaccine design. The main groups are the Global Advisory Committee on Vaccine Safety (GACVS), the Expert Committee on Biological Standardization (ECBS), the Immunization Practice Advisory committee (IPAC), and the Quantitative Immunization and Vaccine Research Advisory Committee.

The ECBS was established in 1947 to set norms and standards for the manufacturing, licensing and control of biological products in order to guarantee the quality of vaccines and other biological products. ECBS is commissioned by the WHO to establish detailed recommendations and guidelines for the manufacturing, licensing and control of blood products, cell regulators, vaccines and related *in vitro* diagnostic tests. The committee also develops and disseminates reference preparations (i.e., international standard materials that are used as reference materials by manufacturers and regulatory authorities to calibrate regional, national or in-house working

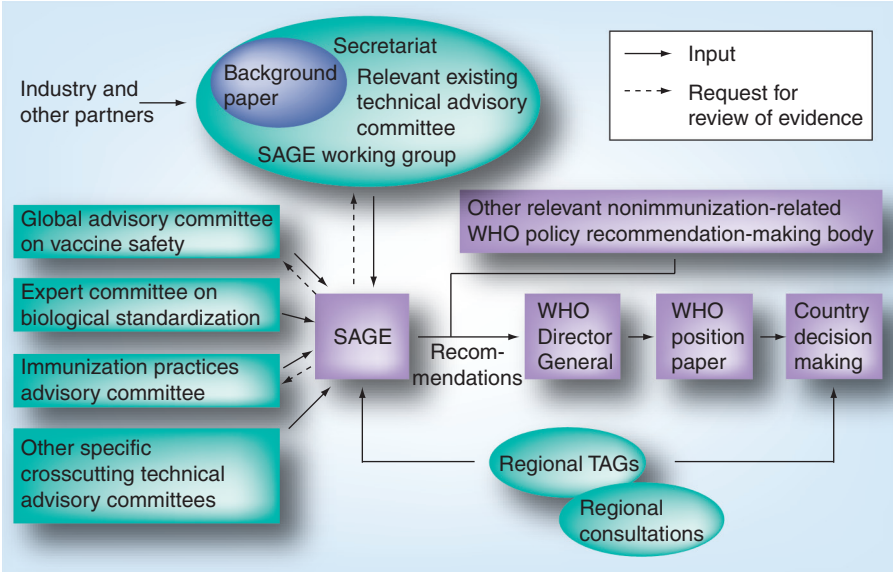

Figure 1. Pathways for WHO recommendations on vaccine use.
SAGE: Strategic Advisory Group of Experts; TAG: Technical Advisory Group.

standards and which often form the basis for licensing and batch release [29]). Historically, standards were established after a new vaccine had been licensed, but ECBS is now more proactive and steps in at the beginning of the production cycle. ECBS recommendations are published in the WHO Technical Report Series (more information on the committee is available at [101]).

The GACVS was established in 1999 to respond promptly to vaccine safety issues of potential global importance. The committee does not directly determine immunization policies, but it does express its scientific opinion on vaccine safety, which could result in policy changes [30]. The committee evaluates vaccine safety by thoroughly reviewing the latest developments in basic science, epidemiology and clinical practice. The committee works in close cooperation with relevant stakeholders, including experts from national authorities, academic institutions and the pharmaceutical sector. The committee is at liberty to request, monitor and evaluate specific studies that seek to explore a possible link between vaccines or their components and adverse effects. The impartiality of the committee is essential. While GACVS focuses on risk assessment, SAGE deals with risk management. GACVS has, on occasion, found that the alleged harmfulness of certain vaccines to be unsubstantiated, yet has also promptly recognized, when the evidence was clear, the link between a given vaccine and particular adverse effects [31]. In addition to the reports published in the *Weekly Epidemiological Record*, emphasis is placed on making information available promptly via the website where all the committee's findings can be consulted [102].

The IPAC was established in June 2010 and represents an expansion of the mandate for the earlier Technologies and Logistics Advisory Committee [32,103]. IPAC's mandate is to advise WHO on the formulation of immunization strategies and operational standards, the tools and technologies necessary to reach and sustain high levels of immunization coverage as required in GIVS, and to promote immunization services of high quality. IPAC's main focus is on practices at an operational and procedural level. The recommendations of IPAC will need to be endorsed by SAGE.

The Quantitative Immunization and Vaccine Research Advisory Committee advises WHO on the estimations of the burden of vaccine-preventable diseases, modeling of vaccine interventions, economic evaluations of vaccines, immunizations, related technologies and interventions, and analytical components of operational and implementation research [104].

Technical advisory groups on immunization have also been established in each of the six WHO regions (Africa, the Americas, the Eastern Mediterranean, Europe, Southeast Asia and the Western Pacific). While names differ between the Regions (Task Force on Immunization, Technical Consultative Group, and European Technical Advisory Group of Experts, Technical Advisory Group), the functions of these groups are essentially similar. They provide WHO Regional Directors and countries in the respective regions with recommendations on regional immunization priorities and strategies in light of particular regional epidemiological and social issues. Recommendations from these groups are also brought to the attention of Regional Committees, the regional equivalents to the global World Health Assembly. These groups make regional recommendations or recommendations at a national or local level that countries should follow.

Countries have autonomy for decision making regarding their national policies and strategies in the light of existing problems and allowing for optimal solutions to be specifically adapted. Countries are responsible for implementing their own national programs and monitoring the resulting impact. Key to improving routine immunization programs and introducing new vaccines and immunization technologies is for countries to ensure that they have the necessary evidence and clear processes to enable informed decision making. Similarly, such evidence and processes are needed to justify the continuation of, or any necessary adjustments to, existing immunization programs and policies. At the global level, the goal is therefore not to prescribe rigid recommendations or immunization schedules that all programs must follow, but rather to offer a framework that countries can adapt to existing schedules and local epidemiological, economical and other circumstances in the context of other health priorities [29].

The majority of industrialized and an increasing number of developing countries have established national technical advisory bodies to guide their immunization policies; other countries are working towards or contemplating the establishment of such bodies. These advisory bodies are often referred to as NITAGs. NITAGs are committees involving national experts supplying guidance to policy makers and program managers to enable them to make evidence-based immunization-related policy and program decisions. One of WHO's priorities is the supporting of the

establishment/strengthening of NITAGs that can convert global or regional policy recommendations into national policy. This is part of the process to ensure evidence-based decision making at country level, which is particularly needed in view of the complexity of the immunization programs and the cost of new vaccines [33].

Strategic Advisory Group of Experts

Composition & membership selection process

SAGE has 15 members, who are renowned immunization, vaccine and public health experts from around the world. Members serve in their personal capacity and represent a broad range of disciplines encompassing many aspects of immunization and vaccines, for example, epidemiology, public health, vaccinology, pediatrics, internal medicine, infectious diseases, immunology, drug regulation, program management, immunization delivery, healthcare administration, health economics and vaccine safety [105].

The membership of SAGE also reflects a spectrum of professional affiliation (e.g., academia, clinical practice, research institutes and governmental agencies including national immunization programs, public health departments and regulatory authorities), the three strategic areas of WHO's work relating to immunization (accelerating innovation, ensuring quality and safety, and maximizing access and links with other health interventions), and geographical and diversity balance.

SAGE undergoes a regular rotation of membership. Members are appointed to serve an initial term of 3 years, which can only be renewed once. Periodic public calls for nominations are issued. After determination of eligibility, nominations are submitted to an independent selection panel including representatives of key partner organizations. From the pool of nominees, the panel identifies the most suitable members on the basis of their qualifications, ability to contribute to the accomplishment of SAGE's objectives and consideration of the expertise already available in the group. Those members are then proposed for appointment by the WHO Director-General. Preference is given to experts with a wider scope of expertise.

SAGE uses a rigorous process to manage potential conflicts of interest and regularly looks for ways to improve its procedures. Prior to being appointed as SAGE members and prior to renewal of a term, nominees and current SAGE members are required to complete a declaration of interest using a standard form. Individuals with a potential conflict of interest that could affect the impartiality and independence of their advice will not be retained for membership. Members of SAGE update their declarations of interest regularly (i.e., ahead of each 6-monthly meeting). The WHO Secretariat consults with the SAGE Chairperson to discuss any interests that are disclosed and a decision is taken on appropriate measures. If members have interests that are relevant to a meeting, the interests are disclosed to the group, and members may be excluded from discussions or decision making on those topics. Potential conflicts of interests, however, are rare as early screening of personal and professional interests prevent conflicts from arising. A register of members' interests is maintained by WHO and summaries of members' interests relevant to the meeting's topics are published on the website. Although serving on SAGE represents a significant time commitment, SAGE members are not remunerated for their participation on SAGE. Only meeting-related travel expenses are covered by WHO in accordance with the organization's rules.

Functioning of SAGE & conduct of meetings

SAGE normally meets twice annually in April and November. The frequency of meetings may, however, be adjusted as necessary. For example, an extraordinary meeting occurred in July 2009 to deal with urgently needed advice on vaccination against the influenza A (H1N1) 2009 pandemic [8]. Regular meetings run normally over 2–3 days.

SAGE deliberations are undertaken in an open forum with a view to ensure transparency of the decision-making process. Decisions and recommendations are, as a rule, taken by consensus. UNICEF, the Secretariat of the GAVI Alliance, and WHO Headquarters and Regional Offices, Chairs of WHO regional technical advisory groups and of other important WHO headquarters' technical advisory groups participate as observers in SAGE meetings.

The WHO invites other observers to SAGE meetings, including representatives from international professional organizations (such as the International Pediatric Society, the World Medical Association and the International Council of Nurses), other nongovernmental organizations (such as Médecins Sans Frontières and OXFAM International), technical agencies (such as the US CDC, the UK Health Protection Agency and the European CDC), donor organizations, country representatives, vaccine manufacturers' associations, immunization technologies and other industry experts.

Additional and specific contributions may be elicited, as appropriate, to contribute expert information on agenda items for which the appropriate expertise is not held by SAGE.

The participation of the many organizations mentioned above and involved in immunization is important. There is full transparency to all of the available evidence and scope of discussion. This helps build credibility and facilitates the 'buy in' by organizations and countries. Representatives from the various institutions may also bring valuable contributions to the discussion including submitting the views from their respective organizations. The Chair invites participants to make comments to ensure that there is no undue influence nor imbalance in contributions during the meeting. The decisions on any recommendations rest with SAGE members. At the end of each session, the Chair summarizes the key points made by SAGE members, proposes conclusions, and calls for any objection or suggestions for modifications from members to the proposed summaries/conclusions. The conclusions and recommendations are adapted until there is consensus among members.

The SAGE Chair briefs the WHO Director-General after the meeting and within 2 months of the meetings, the conclusions and recommendations are published in WHO's *Weekly Epidemiological Record*. Initially published in English and French, reports are also translated in the additional four official WHO languages, that is Arabic, Chinese, Russian and Spanish and are posted on the WHO website. WHO recommendations are also

actively disseminated to the intended target audiences and particularly to country-level officials. The SAGE recommendations are shared promptly with national immunization managers and regional technical advisory groups.

Development of recommendations & the basis for decision making

In advance of its deliberations, SAGE is provided with reviews of the evidence and background documentation. Some topics do require a preceding review of the evidence by some of the technical advisory committees, such as a review of vaccine safety issues by the GACVS. A comprehensive background paper may be prepared as was the case for discussions on the use of new vaccines against the human papillomavirus [106]. When questions for SAGE are particularly focused, such as the updating of a recommendation on the specific route of administration for rabies vaccine or for deciding on the need for a second routine dose of measles vaccine, then SAGE is presented with the specific relevant evidence. SAGE is provided with both published and as yet unpublished evidence.

There are three models for the preparation of background information and evidence review by SAGE, specifically through work done by the WHO Secretariat, the work of an existing relevant technical advisory committee, or through a SAGE working group. The latter has become a more common route for consideration of more complex issues. As of June 2010, there were seven SAGE working groups: H5N1 influenza, pertussis, meningococcal, rubella, hepatitis A, measles and seasonal influenza vaccines.

Working groups are established on a time-limited basis. They review and provide evidence-based information and options for recommendations together with implications of the various options that will then be discussed openly by SAGE [107]. The need and charge for a working group are discussed and agreed upon during SAGE meetings or at the preparatory teleconferences. Each working group operates under specific terms of reference developed jointly by SAGE and the Secretariat. Each group is composed of two or more SAGE members (one of whom functions as the working group Chair), and additional appropriate experts. Representatives of partners' organizations and members of regional technical consultative groups may be included. SAGE members and experts who have topic-specific conflicts of interest cannot serve on the working groups. Public calls are made for the identification of experts to serve on the working groups. WHO staff serve as Secretariat for the working groups.

The SAGE working groups do not submit consensus advice or recommendations directly to WHO but are accountable to SAGE. Working group Chairs, other working group members, and working groups *per se* are not empowered to speak on behalf of SAGE. Rather, they are utilized by SAGE to gather and organize information upon which SAGE can deliberate and act. Thus, while working groups should examine an area in detail and define the issues, including the development of options for recommendations, the actual processes culminating in development of recommendations must occur in the open public forum of SAGE meetings.

In making its recommendations, SAGE takes into consideration issues such as disease epidemiology (disease burden including age specific mortality, morbidity and societal impact; projections for future disease burden; specific risk groups; epidemic potential; disease occurrence over time; serogroup or serotype distribution for serogroup or serotype-specific vaccines; and changes in epidemiology over time), clinical characteristics (clinical management of disease; disease severity; primary/secondary/tertiary care implications; long-term complications of disease; and medical requirements), vaccine and immunization characteristics (efficacy; effectiveness and population impact of vaccine; indirect effects; vaccine safety; cold chain and logistics concerns; vaccine availability and supply; vaccine markets and demands; vaccine schedules; schedule acceptability; and ability to deliver), economic considerations (disease; vaccine and vaccine delivery costs; perspective for vaccine price reduction; vaccine cost and cost–effectiveness of immunization programs; and affordability of immunization), health system opportunities and the existence of, and interaction with, other existing intervention and control strategies.

A careful and critical appraisal of the scientific evidence is a necessary step in recommendation and guidance development. A strong evidence base, when available, is critical to ensure the most appropriate recommendations. While the evidence reviewed is the result of scientific endeavors, evaluating the quality of the evidence and making recommendations are activities that require expert interpretation and judgement. In addition to the results of data themselves, consideration should be given to the methodology and study design used to conduct such studies. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach is one of many frameworks developed over the years to assess the quality of evidence [34]. In April 2007, SAGE adopted the use of the GRADE methodology to score the quality of evidence in support of key recommendations included in the WHO vaccine position papers.

When information is lacking, SAGE may make provisional recommendations and request the WHO and international community at large to initiate specific research projects. In the absence of specific evidence, in urgent situations, SAGE may also have to make recommendations relying mostly on expert judgement.

In an attempt to minimize delays between vaccine availability and issuance of recommendations on vaccine use, it is important that SAGE anticipates the availability of new vaccines and identifies any gaps in knowledge that may prevent timely recommendations being made.

SAGE's work needs to be coordinated with other possible preventative interventions and policies to control diseases, for example, immunization against human papillomavirus as part of cervical cancer prevention and future immunization against malaria as part of malaria control programs. Careful consideration was given in 2009 to integration of Intermittent Preventative Treatment of malaria in infants when given at the routine EPI-scheduled immunizations [35].

After each meeting, presentations delivered at the SAGE meeting are made available on the SAGE website together with relevant background documents.

Scope of SAGE's work & agenda setting

Agenda items include topics presented for information purposes, for discussion or for decision. Each meeting's agenda is composed of both recurrent items that are mostly for information and a series of six to ten specific items for decision. For the latter, a SAGE output and recommendation is normally expected but such items can also be for information, such as vaccine horizon scanning to help the committee keep abreast of new developments.

Recurrent agenda items include reports from: WHO headquarters, key advisory committees, the GAVI Alliance and from the WHO regions. The WHO report highlights progress in the implementation of previous recommendations. The Secretariat keeps a tracking sheet of all SAGE's recommendations that apply to the Secretariat [108]. This tracking sheet is regularly updated and highlights the key actions taken in response to the recommendations and their progress. At each meeting, three of the six WHO regional offices deliver reports on their situation, their challenges and their progress; in this way, each region is reviewed annually. SAGE is also informed of policies and recommendations set by the WHO Regional technical advisory groups. These reports are essential to keep SAGE abreast of key local issues, priorities, progress and challenges in the implementation of its recommendations.

Specific topics reviewed by SAGE over each previous year fall under two broad categories: recommendations on vaccine use, and strategic issues that can relate to new or existing vaccines, vaccine delivery/operational issues, financial sustainability and surveillance.

SAGE works with WHO to develop its priorities of work and agendas for forthcoming meetings. The views of countries, regions and partners are solicited. Requests for advice from countries are generally channelled through the regional technical advisory groups and regional offices. A 2–3-year 'horizon list' of items for SAGE discussion is maintained by the Secretariat.

In view of the limited number of topics that can be discussed at any given meeting, the final list of agenda items requires both consideration of the importance and urgency of the expected output from SAGE and the level of readiness that would lead to a fruitful session. If critical pieces of evidence are lacking or the necessary compilation and review of evidence cannot be achieved in good time, ahead of the meeting, the related session will be postponed. Preparation for a session may require anywhere from 2 months to several years.

The final list of agenda items is normally settled 2 months ahead of each regular biennial SAGE meeting during the first of two preparatory teleconferences. These teleconferences take place 2 months and 1 month prior to dates set for the meetings.

A list of topics discussed by SAGE is available on the web through the agenda search tool [109].

Vaccine position papers

Since 1998, WHO regularly produces and updates evidence-based vaccine position papers that summarize information on available licensed vaccines against infectious diseases of public health interest. These papers are concerned primarily with vaccines used in large-scale immunization programs. The format of these papers has been adjusted over time and they now contain four sections: an introduction, a section providing information on the respective disease (disease epidemiology, the pathogen, the disease), a section providing information on the available vaccines (composition, safety, immune response, efficacy and effectiveness, cost–effectiveness and any other relevant issue), and the WHO position on the optimal vaccine use.

The position papers are produced for use mainly by national public health officials and immunization program managers. However, they may also be of interest to international funding agencies, the vaccine manufacturing industry, the medical community and the scientific media.

The papers are drafted or updated based on an extensive literature review and are the result of a wide-ranging consultative process by various experts and interest groups both inside and outside the WHO. Initial drafts are sent for review by regional advisers, interested parties, world experts in the specific area covered by the vaccine, industry and SAGE members. Since April 2006, the drive for new or updated position papers has followed the discussions and recommendations of SAGE [29].

Grading tables that assess the quality of the evidence are also developed and are posted on the website. These tables are referenced in the position papers and follow the GRADE approach [34].

The position papers are prepared in English, published in English and French in the *Weekly Epidemiological Record* of the WHO and are made available on the web (together with a list of key relevant references that have been used for the development or updating of the position papers). The position papers, like SAGE meeting reports, are subsequently translated into the other four WHO headquarters' official languages. One page summaries and PowerPoint presentations summarizing the main content and recommendations from the vaccine position papers are also prepared and are posted on the website.

Contribution to achieving the global goals & impact of recommendations

Relevance of SAGE discussions to the achievement of global goals

The following are examples of agenda items discussed by SAGE that are of great importance in achieving the GIVS goals.

It has been estimated that 24 million children annually are not immunized or their immunizations are delayed and innovative ways are needed to reach them. Following a request from SAGE in November 2007, the results of detailed analyses of such children were discussed at the October 2009 meeting [34]. The analyses by The Swiss Tropical Institute considered children who had received no vaccinations and those who had received one dose or more of any of the following vaccines (BCG, diphtheria–tetanus–pertussis, oral polio vaccine, and measles-containing vaccines) but were not fully immunized. The CDC performed a systematic review of peer-reviewed literature. IMMUNIZATIONbasics reviewed the gray literature (studies,

reviews or reports written after 1980 that had not been published or were published in publications that are not peer reviewed) from studies in low-income and middle-income countries.

SAGE concluded that factors such as the distance from vaccination sites, the motivation of healthcare staff, lack of resources and false contraindications were key determinants for children remaining unvaccinated or undervaccinated. Demand-side factors, including family characteristics, parental attitudes and knowledge, the caregiver's educational level and religious beliefs, also affected whether a child was immunized. The importance of understanding local determinants was emphasized. Operational research at the local level is important for understanding and addressing these gaps.

There have been several discussions on mortality reduction from measles with adjustment of immunization strategies based on the analysis of country experiences combined with mathematical modeling [36,37]. SAGE has provided criteria that can be used by countries and regions to make rational decisions on: first, when to start a second dose of measles-containing vaccine delivered through routine services (routine MCV2); second, the optimal age of administration of routine MCV2; and third, when regular vaccination campaigns can be suspended in place of routine MCV2. SAGE has approved a comprehensive program of work to assess the feasibility of measles eradication and has also highlighted the need for resources both from WHO and from donors prior to setting a measles eradication goal [34].

SAGE also issued recommendations on the use of new vaccines such as those against rotavirus infection and pneumococcal disease (discussed previously). Successful implementation of these vaccines has a major potential to contribute to the mortality reduction goals [37,38].

In setting the future agenda, developing integrated strategies will be of increasing importance: examples are comprehensive approaches to disease control, be it for meningitis, pneumonia, diarrheal diseases, cancer or epidemic/pandemic prevention. In 2009, SAGE endorsed the co-administration of intermittent preventive treatment in infants for malaria at the same time as routine immunization visits, concluding that using immunization contacts to assist another child health program was a positive contribution to the well-being of children that would help develop and strengthen sustainable health services [34].

SAGE has been involved in repeated discussions on the direct or indirect impact of the financing of immunization. One financing instrument for new vaccines is the Advanced Market Commitment (AMC). This involves a financial commitment being made by donors to subsidize vaccine demand by GAVI-eligible countries at a set purchase price as long as the vaccine in question meets a specific Target Product Profile (TPP). The goal of an AMC is to motivate suppliers and accelerate vaccine introduction [39]. The TPP sets the minimal technical requirements for efficacy and safety that a candidate product must meet. SAGE endorsement of the TPP for pneumococcal conjugate vaccines was an essential step in the AMC process for that particular product. SAGE has also been concerned about the financing of vaccines for low–middle-income countries that are not eligible for GAVI support [40].

Impact of WHO recommendations

Since the impact of WHO recommendations depend on so many external factors, determining those that are based on SAGE's input and evaluating precisely their specific contribution to achieving the GIVS goals is not easy.

In industrialized countries, the introduction of *Haemophilus influenza* type b (Hib) vaccine more than 15 years ago has almost eliminated Hib-related disease. Despite a position paper in 1998 recommending its use [41], by the end of 2005 only 65 of the world's 156 nonindustrialized countries (42%) had introduced this vaccine [42]. However, by the end of 2009, 154 states (80%) had introduced Hib vaccination. Multiple factors contributed to the accelerated introduction of new vaccines in the last 4 years [43]. This included the reinforcement of SAGE's recommendation on the use of the Hib vaccine in light of recent data, which led to the publication by WHO of a revised position statement recommending the global use of Hib vaccine even in the absence of local surveillance data [12]. In low-income countries, the uptake of these new vaccines has been greatly facilitated by the recent assistance from the GAVI Alliance and the GAVI Fund and the advance of the GAVI Alliance-supported Hib Initiative [43]. By the end of 2009, only 32 (16%) and 22 (11.5%) of 193 WHO Member States had introduced pneumococcal conjugate and rotavirus vaccines, respectively, in their routine immunization programs. SAGE has recommended the worldwide use of the pneumococcal conjugate vaccine [38] and recommended the use of two recently licensed rotavirus vaccines [37]. These recommendations helped to secure a commitment to support the introduction of these vaccines by the GAVI Alliance, which will enable them to be used in some of the world's poorest countries. The impact of the SAGE recommendations will hopefully contribute to the wider utilization of these vaccines.

In 2008, an independent Stakeholder's Panel was asked by the WHO to investigate the impact of policy recommendations and norms and standards on immunization set by the WHO. The panel's mandate also included the effects of recommendations formulated by WHO key advisory committees, especially those of SAGE. The panel's review was informed by a country survey aimed at understanding the impact of WHO guidance on vaccines and immunization on key national level decision makers and eliciting suggestions for improvement in content, communication and access [110]. The panel concluded that "WHO vaccine advisory committees play an increasingly central role in determining global and national vaccine policy. In particular, SAGE recommendations have become a necessary step in the pathway to the introduction and use of vaccines, especially in developing countries and, as a consequence, have clear and significant impact." The panel further commented that, "because policy recommendations are only part of an integrated process leading to successful immunization, it is not possible to enumerate specific children who have been successfully immunized because of the resulting improved vaccine advisory committees procedures and policies. The GAVI Alliance now predicates its actions on SAGE recommendations and WHO vaccine position papers. Countries, particularly developing countries, reported that WHO recommendations are central to their

policy-making process. Evidence of SAGE recommendations driving new vaccine introduction and immunization practice includes the rapidly expanding use of Hib and pneumococcal vaccines. Committee meetings are highly visible and well attended, and reviews by these committees are viewed as critical to the policy pathway for adoption of new vaccines. WHO should be proud of its accomplishments to date to increase the qualifications and credibility of members, transparency of process, effective use of evidence, and quality of resulting reports and recommendations" [111]. The stakeholder's panel recommended that the WHO take immediate steps to consolidate and build on the successes of its vaccine advisory committees reformation. The panel concluded that the WHO needs to better engage the country offices in the dissemination of information at a country level. As a result, the WHO is ensuring the translation of policy recommendations in all WHO headquarters' official languages and is taking a more proactive approach to the dissemination of related information through country offices. Summaries of position papers are posted on the website together with PowerPoint presentations highlighting the key points of each position paper. In addition, the WHO recommendations contained in the position papers are being published in the journal *Vaccine*.

The credibility of SAGE processes including its culture of evaluation and communication of decisions are likely to be drivers of considerable influence. Not only do SAGE recommendations have an impact on agencies investing in immunization, but they also have impact on accelerating the late-stage development of vaccines such as a malaria vaccine [35].

SAGE recommendations are expected to lead to higher level policy whose purpose is to accelerate the achievement of current and future global goals. Topics discussed at the WHO Executive Board meeting in January 2010 included measles eradication; a draft resolution on the prevention and treatment of pneumonia; and the prevention and control of viral hepatitis. These topics were then presented to the World Health Assembly in May 2010 at which Bangladesh requested that cholera prevention and control in Asia and Africa be included on the Executive Board's May 2010 agenda. All of these discussions have built on previous policy recommendations made by SAGE.

Expert commentary & five-year view

The last 5 years have seen a progressive improvement in the functioning of SAGE so that the committee works to the highest standards of quality and transparency with respect to the review of scientific evidence and has become increasingly relevant to countries and partners. SAGE's relevance extends to all WHO Member States. One of the strengths of SAGE is its willingness and readiness to change. Within the next 5 years, the GIVS will come to an end. A process to review its impact and develop a new vision and new goals for the next 10 years is now starting. As the capacity for decision making at country level is strengthened in particular with the development of national technical advisory committees on immunization, there will be an increased requirement for effective dialog with and between countries and regions.

Key issues

- A series of global goals embracing the guiding principles of the 2005 Global Immunization Vision and Strategy have been set for the period to 2015. The achievement of these goals will be critical to the attainment of the Millennium Development Goals and in particular those that relate to mortality reduction in children less than 5 years of age.
- The Strategic Advisory Group of Experts (SAGE) on immunization is the overarching WHO advisory committee providing advice on issues ranging from vaccine research and development to immunization delivery. Its remit extends to all vaccine-preventable diseases and focuses on the issuance of policy and strategy recommendations on the use of specific vaccines, which then form the basis for WHO vaccine position papers. SAGE therefore plays an essential role with respect to policy development, program implementation and progress monitoring.
- SAGE's membership and processes are aimed at ensuring a balanced view that takes account of benefits and risks, cost and opportunities.
- SAGE considers its recommendations in the context of the wider health system and public health needs and it tries to keep advice on vaccines in the perspective of other health interventions.
- SAGE is composed of independent experts rather than by representatives of organizations. Processes are in place to prevent and manage conflicts of interest with detailed screening of declarations of interest prior to nomination for membership and prior to each meeting. Any relevant interests and subsequent action in terms of members' participation in meetings or at specific discussions are disclosed publicly.
- SAGE deliberations occur in a transparent manner during plenary meetings that are open to members of the vaccine community. The transparency of the process extends to the public posting of information and evidence that served as the basis for SAGE's decision making.
- SAGE's recommendations are evidence based. In making its recommendations, in addition to vaccine effectiveness and safety issues, SAGE considers issues such as epidemiology, clinical characteristics, programmatic issues, vaccine availability, economic considerations, health system opportunities and the existence of, and interaction with, other established intervention and control strategies.
- The interaction between SAGE and the regional and country levels is bidirectional. Global recommendations are important to drive progress and offer a framework that countries can adapt to local epidemiological, economical and other circumstances in the context of their other health priorities. In turn, hearing from countries and regions on priorities, need for direction and feedback on their ability to implement recommendations and any challenges encountered is essential to give context and relevance to SAGE's work.
- WHO recommendations, which derive from SAGE recommendations, are used by countries and other key immunization partners, such as the GAVI Alliance and industry, look at SAGE recommendations to guide their investment decisions.

Disclaimer

Philippe Duclos and Jean-Marie Okwo-Bele are World Health Organization staff members. The opinions expressed in this article are those of the authors and do not necessarily represent the decisions, official policy or opinions of the World Health Organization.

Financial & competing interests disclosure

Since 2005, Philippe Duclos has served as Executive Secretary of the Strategic Advisory Group of Experts and and David Salisbury has been a member of SAGE from 2003 through 2010 and Chaired the group from 2005 through August 2010. Jean-Marie Okwo-Bele is the Director of the Department of Immunization, Vaccines and Biologicals. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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National Immunization Technical Advisory Groups (NITAGs): Guidance for their establishment and strengthening☆

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ABSTRACT

The majority of industrialized and some developing countries have formally established national technical advisory bodies to guide immunization policies; other countries are working towards or contemplating the establishment of such bodies. These advisory bodies are often referred to as National Immunization Technical Advisory Groups (NITAGs). A NITAG is a technical resource supplying guidance to national policy makers and programme managers to enable them to make evidence-based immunization related policy and program decisions. The focus of this paper is to: (1) review the value and functions of a NITAG; (2) provide directions and identify issues for countries to consider when establishing or improving the functioning of a NITAG; and (3) outline potential WHO and partners' roles and activities in support of the establishment and strengthening of NITAGs.

1. Background

While for many years, at both the global and the country levels, the focus of immunization programmes has been on infants and a limited number of traditional vaccines, the vaccine world has evolved with new demands and expectations of global and national policy makers, donors, other interested parties, and the public. The development and availability of several new vaccines targeting a variety of age groups, the emergence of new technologies, the increased public focus on vaccine safety issues, the enhanced procedures for regulation and approval of vaccines, the need to expand the immunization schedule with consideration of all age groups and specific at-risk populations are all demanding increased attention [1].

Key to improving routine immunization programmes and sustainably introducing new vaccines and immunization technologies is for countries to ensure that they have the necessary evidence and clear processes to enable informed decision making in the establishment of immunization programme priorities and the introduction of new programme strategies, vaccines and technologies. Similarly, such evidence and processes are needed to justify the continuation of, or any necessary adjustments to, existing immunization programmes and policies.

Whereas developing countries have long struggled with vaccine funding problems and limited ability to optimize coverage with standard immunization programs, even industrialized nations today face problems involving the financing and delivery of expanded vaccine programs. While there is increased funding flowing through new financing mechanisms to support the introduction of new vaccines by developing countries [2–4], from a public health perspective, the overall limited financial resources require that distribution of funds must be undertaken in as fair and as effective a manner as possible in order to achieve the best possible outcomes. Therefore decisions on introducing new vaccines into national immunization programs should be unbiased, comprehensive and systematic and based on deliberate, rational, comprehensible and evidence-based criteria [5]. Certainly all governments have to consider opportunity costs in their investments.

At present, the majority of industrialized and some developing countries have formally constituted national technical advisory bodies to guide immunization policies. Other countries are only starting to work towards or are just contemplating the establishment of such bodies. Still others have not even embarked on thinking about such a body. These advisory bodies are often referred to as National Immunization Technical Advisory Groups (NITAGs) and will be referred to as such in the remainder of this document. They can also be referred to using different names such as National Advisory Committee on Immunization or National Committee on Immunization Practice to name a few of the most commonly used titles. Many countries still lack credible decision-making processes

Abbreviations: ICC, Coordinating Committees; NITAG, National Immunization Technical Advisory Group; SIVAC, Supporting Independent Immunization and Vaccine Advisory Committees; UNICEF, United Nations Children's Fund; WHO, World Health Organization.

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that can facilitate the review and assessment of immunization interventions and strategies [6].

The focus of this document is to: (1) review the value, roles and functions of a NITAG; (2) provide directions and identify issues for countries to consider when establishing or improving the functioning of a NITAG; and (3) outline potential WHO and partners' roles and activities in support of the establishment and strengthening of NITAGs.

2. Value, roles and functions of a National Immunization Technical Advisory Group

A NITAG is both a technical resource and a deliberative body to empower the national authorities and policy makers to make evidence-based decisions. Such a resource is particularly important in view of the complex and vast bodies of evidence and the global interdependence and integration of health systems.

A well balanced and institutionalized group can aid a national programme to resist pressure from any interest or lobby group with narrow scopes or interests, including, but not only, that of industry and anti-immunization groups. This protective function is important, because without it, pressure from special interest groups could result in programme changes that are not well justified in the local context and may even cause harm.

A major advantage of a NITAG is the credibility of the process by which major policy decisions are made, which in turn adds credibility to the national immunization programme and to the government at large [7,8]. This credibility is of course linked to the rigor, transparency, and informed/evidence-based processes by which the NITAG arrives at its decisions. Highly credible decisions can positively impact perceptions within the government, within the country or even beyond the country, thereby lending additional weight to proposed adjustments to the immunization programme and enhancing the ability to secure government or donor funding, support from professional organizations, and acceptance from the public.

In addition, a standing NITAG will facilitate a more comprehensive and cohesive country immunization program perspective that cannot easily be achieved by a series of disease or vaccine specific task forces or *ad hoc* committees composed of specific disease experts and advocates. These latter groups often provide recommendations in isolation without consideration of the complete immunization program picture within the full context of other intervention strategies. Ideally, disease-specific technical working groups should be supported by and report to a NITAG.

A NITAG or even a group which may have a broader mandate, such as an infectious disease control committee, will help consolidate programmes and have a more comprehensive and integrated approach in terms of interventions and target populations (*e.g.* they ideally would, consider the health of the entire population *versus* that of infants only). In theory, advisory groups could have a broader health mandate that extends beyond vaccines and immunization. However, an immunization focus is recommended to ensure that the required expertise is included on the committee and due attention given to vaccines, which could not be given by a more generic or all-purpose advisory committee serving the Ministry of Heath.

NITAGs mandates usually include to recommend national immunization policies and strategies that take into account the local epidemiologic and social contexts; and possibly to advise on implementation of national immunization programmes and to monitor programme impact.

With the above in mind, the overall objective of establishing a functioning technical advisory body at the country level is to provide guidance to policy makers and programme managers for making evidence-based immunization related policy decisions, including choices of new vaccines and technologies and needed adjustments to existing programmes and schedules. The proposed broad general terms of reference for such a group are as follows:

- Conduct policy analyses and determine optimal national immunization policies.
- Guide the national government and the national immunization programme on the formulation of strategies for the control of vaccine preventable diseases through immunization.
- Advise the national authorities on the monitoring of the immunization programme so that impact can be measured and quantified.
- Advise the government on the collection of important disease and vaccine uptake data and information.
- Identify the need for further data for policy making.
- Guide, where appropriate, organizations, institutions or government agencies in the formulation of policies, plans and strategies for research and development of new vaccines and vaccine delivery technologies for the future.

Each country will have to adjust its NITAG's terms of reference based on its own needs and resources. Therefore, the terms of reference proposed above are general and not necessarily exhaustive or inclusive.

Although the role of NITAGs is essentially consultative and the ultimate decisions about programs remains in the hand of government officials, this process requires the acceptance of the government to yield some level of control over the decision-making process. One of the indirect benefits of a NITAG is to help keep the national authorities and those working for the national immunization programme updated on the latest scientific developments in the area of vaccines and vaccine-preventable disease epidemiology and control. Such a group also helps to foster inter-departmental linkages and promote partnership among government, civil society, industry and donors to promote immunization in a sustainable, scientifically sound and credible manner.

There are cautions to be considered in the formation of a NITAG. A NITAG should have only a technical advisory role for in the development of vaccine recommendations and should not serve as an implementing, coordinating or regulatory body. Therefore, an NITAG should be distinguished from the Inter-agency Coordinating Committees (ICC) that are already established in countries eligible for funding by the GAVI Alliance [9]. The main purpose of these ICCs is to coordinate and support funding, planning, implementation, and advocacy. The ICCs' work is primarily operational, not technical in nature, and these groups are not intended to replace NITAGs or to substitute partners' inputs for the deliberative opinions of proper national decision making bodies. In some settings, however, due to a lack of NITAGs, ICCs have been asked for advice on certain immunization policy related issues. In some places ICCs have even gone as far as establishing their own technical advisory groups, recognizing the importance of such advice in vaccine decision making. NITAGs should also clearly be distinguished from National Regulatory Authorities, which have licensing, testing, inspecting, quality control and post marking surveillance functions. Finally, NITAGs should be distinguished from disease-specific technical advisory working groups, such as those on polio, measles, and hepatitis, which are formulated to focus on one disease for a specified time period and deliverable(s) and whose recommendations and work would be better harnessed under the umbrella of a NITAG as noted above.

If a NITAG is to succeed, there are modest but required costs for its establishment and functioning both in terms of managerial support and financial investments that are required if it is to succeed. NITAGs will also potentially add some delays in the immunization and program decision making process given that without a NITAG a decision could be made instantaneously—though such a decision is

unlikely to be evidence based, robust, thoughtful and useful. Attention does need to be paid to avoiding undue delays that might be caused by inertia on the part of a NITAG or its secretariat.

As an alternative to a NITAG, some very small countries and countries with limited technical resources may prefer collaboratively to explore a sub-regional or inter-country mechanism to provide independent and expert advice rather than rely on an individual country approach. This, however, requires a genuine willingness to accept extra-national recommendations as well as the necessity for this inter-country group to understand and appreciate the specific situations and needs of individual countries.

In some countries such as the United States of America, Canada and India, professional organizations such as the National Academy of Pediatrics or other similar groups may have established a national advisory process to issue recommendations on vaccine use that are intended for their members [10,11]. In such situations it is important to ensure close liaison between these groups and the NITAG so that one will not end up with conflicting recommendations that would be counterproductive and undermine the credibility of either group. As an example, such a situation with issuance of different recommendations by the US Advisory Committee on Immunization Practices and the Committee on Infectious Diseases of the American Academy of Pediatrics (the so-called Red Book Committee) existed in the past in the United States. Over the years, however, these two committees have worked increasingly closely and now publish harmonized immunization recommendations [7,12].

3. Guidance for the membership and mode of operation of a NITAG

The following discussion identifies elements that need to be well defined in the membership and mode of operations of a NITAG. The proposed structure for NITAGs outlined below may in part be seen as an example towards which to aim, but it is well accepted that establishing a fully functional NITAG may take a number of years. Furthermore, the guidance provided below is general guidance and the optimal process for reaching the best evidence-based decisions may vary from country to country. Each NITAG's composition and *modus operandi* must be adjusted to take into account the local situation, resources and the social and legal environment.

The following set of recommendations was initially developed by WHO with input from and review by a group of external experts and building on the experience from existing NITAGs (such as but not limited to those in Canada, the United Kingdom and the United States) that enjoy credibility and recognition at country level and across borders. Admittedly these recommendations are based on limited robust scientific evidence. Indeed there is variability in the mode of operating of what seem to be successful committees [6,12–16]. Furthermore, little has been published when it comes to the process of establishing immunization policy recommendations [17], making it more difficult to assess the key important elements of successful committees. More has been published on the elements to take into consideration than on the optimal structure of a committee. The initial guidance referred to above has been further adjusted in this document to take into account the observations, challenges and successes of recent efforts at establishing and strengthening NITAGs reported during regional meetings of immunization managers and regional technical advisory groups on immunization. These meetings have included participation of NITAG Chairs and members.

3.1. Establishment of the committee

The committee should be formally established through a ministerial decree or any other appropriate administrative mechanism, including legislative action if necessary. Such a formal establishment process may also help with securing the necessary funding for the operation of the committee operation and secretariat support.

To ensure that the government gives proper attention to committee recommendations, it is important that the committee reports to a high level official of the Ministry of Health who is not a member of the group. A formal relationship should be established between the committee and the Ministry of Health, delineating roles and responsibilities. This would include clarifying reporting requirements, financial arrangements and secretariat support. This may include appointing an Executive Secretary who may or may not be a staff member from the Ministry of Health. It is recommended that the immunization program provides secretariat service to the NITAG, and that the immunization program manager be closely in touch with this process. Terms of reference must be clearly stated.

It is recommended that the Ministry of Health budgets this activity in its annual and multi-year plans. This should be reviewed on a regular basis to determine if budgets remain adequate for the demands placed on committees.

3.2. Membership and composition of NITAGs

3.2.1. Size

There are no fixed rules about the size of a NITAG but this can and should be influenced by local considerations such as the need for geographic representation, the size of the country, the availability of resources and so on. Experience has shown that successful committees function with about 10–15 core members who serve in their personal capacity and represent a broad range of disciplines encompassing many aspects of immunization and vaccines [6,12–16]. This allows for some useful redundancy of expertise that ensures more fruitful and balanced debate. As well, some redundancy is helpful as not all members will likely be able to attend all meetings. For committees with a small number of members the effect of absentees would be particularly noticeable. Too large a committee is more costly and more difficult to manage. Beyond a limited number of members, as long as the necessary expertise is already captured on the committee, there is little to be gained by enrolling additional members. Groups with an odd number of members may be more effective for resolving disagreements and reaching more speedy decisions [18–21].

3.2.2. Composition

The composition of the group should include two categories of members: core and non-core members. All core members should be independent and credible experts who serve in their own capacity and who do not represent the interests of a particular group or stakeholder. Members should refrain from promoting the policies and views and products of the organization for which they work.

Independence from government is defined by the absence of a direct or indirect supervisory relationships within the immunization program, or ideally, within the larger Ministry of Health. Members should feel free and encouraged to express their views even if at odds with those of the immunization programme managers or Ministry of Health policies. Core members only should participate in advising and deciding on the final set of recommendations.

Non-core members can be further subdivided into two groups, namely *ex officio* [22] and liaison members [23]. *Ex officio* members hold key positions with important government entities they represent (*e.g.* National Regulatory Authorities or drug/vaccine licensing bodies and from the National Control Laboratory performing the controls of vaccines, and administrative groups with responsibility for immunization programmes, planning, education, finance, and other activities) and their presence is solicited because of the position held. Liaison members generally represent various impor-

tant professional societies or associations, other national advisory committees, and key technical partners (*e.g.* WHO and UNICEF) [12–14,17]. The determination of who should serve as a representative of the organization should be left to the organization itself, who will identify the most appropriate individual from its membership. A rotation process can also be decided by the organization although it is better to have some stability rather than have a too frequent change of liaison representatives. The role of non-core members is to contribute to the discussion and to help provide background information or needed evidence. They should not be directly involved in deciding on the final set of recommendations. An individual can serve in only one capacity. The participation of liaison members can also facilitate the quick dissemination of the recommendations back to the membership of the professional organization when settled. This helps to ensure support for and quick and smooth implementation of the new recommendations.

It is recommended that the committee be multidisciplinary and represent a broad range of skills and expertise through the selection of technically sound and experienced individuals as members. At a minimum and when feasible (*i.e.* depending on the size and capacity of country), it is recommended for countries to consider including experts as core members from the following disciplines/areas: clinical medicine (paediatrics and adolescent medicine, adult medicine, geriatrics), epidemiologists, infectious diseases specialists, microbiologists, public health, immunology, vaccinology, immunization programme, and health systems and delivery. Consideration should also be given to appointing members with expertise in clinical research (clinical trials design) and health economics. Such expertise, however, may be limited in some settings and individual countries could consider providing ability to interpret cost-effectiveness studies *via* the secretariat and/or expertise beyond that of the core group. The collective expertise should obviously be adjusted to the specific terms of reference for the group.

Other considerations in terms of membership include: gender distribution, geographic diversity, representation of special population groups, and the need or not to ensure representation of the public. This latter member might be a consumer representative who could bring the consumer's perspective or social and community aspects of immunization programmes. If public representation is desired, decisions need to be made on how this could be done (*i.e.* through a seat on the core membership or rather through *ex officio* or liaison members) and how to identify a suitable representative.

Given the substantial financial implications that recommendations may have for the public and private sectors, as well as for vaccine manufacturers, members should be free of conflicts of interest and enjoy satisfactory credibility. Members with declared interests compatible with serving on the committee will be asked to recuse themselves from participating in the discussion and decision making of the issues relating to that interest. A member who is in any doubt as to whether they have a conflict of interest that should be declared, or whether they should take part in the proceedings, should ask the Secretariat and Chairperson for guidance. Appearance of conflicts of interests should be avoided through both pre- and post-appointment considerations and regular open disclosure of competing interests (see below).

It is important to differentiate members involved in the decision-making process from observers or invited experts. Observers or invited experts may contribute to the discussion and can help to provide background material or needed evidence, but they should not be involved in the final decision making, regardless of whether they represent particular interests.

The Chair and members of the Committee will play a critical role in ensuring the Committee's continued standing as an internationally recognized leading body in the field of immunization and that it continues to observe the highest standards of impartiality, integrity and objectivity in its deliberations and that its recommendations are driven by available scientific evidence. Thus the Chair and members of the Committee should be chosen carefully and thoughtfully.

3.2.3. Nomination process

Members, including the Chair, should be nominated and appointed formally by senior level government officials through a well-defined process. Public calls for nominations and the establishment of an independent selection process may be envisioned for the purposes of transparency and credibility. Moreover, the Chair should be identified as a senior, widely respected and independent core member.

Prior to being appointed it is important that members be asked to complete a declaration of interests with enough detail and specificity to identify what would constitute a potential conflict of interest. A conflict of interest involves a conflict between the public duty and private interests of a public official, in which the public official's private capacity interests could improperly influence the performance of their official duties and responsibilities [24]. Conflicts of interest can be of a personal (*e.g.* owning shares in a vaccine manufacturing company, direct employment of the candidate or an immediate family member by a vaccine manufacturer, serving on a vaccine company board, or acceptance of honoraria or travel reimbursement by a vaccine manufacturer or its parent company) *versus* non-personal nature (*e.g.* research grant to an institution) and can be specifically or not related to the object of discussions and decisions to be taken by the group.

It should then be determined by the Secretariat and the chairperson if the declared interests, which indicate actual or potential conflicts, would completely preclude the expert from serving on the committee or if they should just be reported and the member be excluded from decision making or even discussing specific issues at a given meeting. (*e.g.* members with a personal specific interest will be asked to leave the room for the discussion and decision making; members with a personal non-specific interest could participate in discussions but not take part in the decision making; members with non-personal specific interests could answer direct questions from the chairperson but not take part in the decision making; members with non-personal non-specific interests could participate in the discussion and the decision making). Other categorization of conflicts of interest include major or minor conflicts, and actual, apparent or potential conflicts of interest [25–28].

The declaration of interest should be kept up to date. The most convenient approach may be to ask members to update their declaration of interest as need be before each meeting. Reported interests may be disclosed during the meeting and possibly posted in a summarized manner on the Internet and/or made available at public request. Screening for conflicts of interest should be rigorous and balance the possibility of bias caused by a conflict with the need for vaccine and immunization expertise. Some data important to the committee can be obtained only through working relationships with vaccine manufacturers. Additionally, many of the top national experts in the field of immunization and vaccines will have some relationship with various interest groups, including industry, professional associations, and governments. Consequently, the goal is not to include only persons with absolutely no relevant interests but to manage potential conflicts of interest in a transparent and ethical fashion.

An increasing number of allegations of collusion between national government and industry, particularly in the context of the introduction of expensive new vaccines, have recently been reported in the media. It is therefore essential that due attention be paid to the declaration of interests and their disclosure.

Members may also be required to sign a confidentiality agreement if, in the process of the meeting or work of the group, they

are provided in trust with confidential information. Confidentiality agreements should also be signed by special invitees.

The format for the declarations of interests and confidentiality agreements should be adjusted to fit the specific requirements and practice of the country. Clearly the assessment of what would constitute a conflict of interest is context dependent. For example, a consultation fee of US$ 1000 will have a variable weight and impact depending on the country's average wages.

Examples of such documents and summaries of reported interests can be found at http://www.who.int/immunization/sage/national_advisory_committees/en/index2.html.

3.2.4. Rotation of membership for core members

A process of rotation for core members with limited duration of terms of service is essential for the credibility of the group and standard operating procedures which specify the nomination, rotation and termination processes should be developed [12]. Subject to the above, members would normally be appointed for a term of a fixed number of years, which possibly could be renewed (though the number of renewals allowed should be specified and limited). Care should be taken to ensure there is continuity in the committee so that not all members' terms would expire at the same time. Terms of three to four years with or without provisions for renewal of a term are common practices. Renewal of appointments at the end of the first period of office if provisions for such renewals have been made should be subject to satisfactory appraisal. There should be no expectation of automatic reappointment and this should be made clear to all members when they are appointed.

Possible reasons for termination of membership should be made clear and include the following: a failure to attend a specified number of consecutive meetings; a change in affiliation resulting in a conflict of interests; and a lack of professionalism involving, for example, a breach of confidentiality.

3.3. Modes of functioning of the NITAG/process of meetings

3.3.1. Conduct of meetings: process and basis for decision making

It is highly recommended that the immunization program and/or Ministry of Health provide new committee members with briefing sessions and/or information packages and orient the members to the terms of reference and group operating procedures. When a new NITAG is created it may be helpful at least for the first meeting or, in advance of the first meeting or during a pre-meeting session, to allow time and venues for members to become acquainted and discuss processes so that they feel at ease during the committee's discussions and deliberations. In this regards, provision of information on context, clarification of roles and responsibilities and mutual expectations may be important.

Standard operating procedures are required that specify the preparation and circulation of agendas, background documents and information, as well as the conduct of meetings and the process for recording and communicating of the committee's conclusions and recommendations.

The following elements should be decided upon and made clear in the standard operating procedures of the group:

- *Open versus closed meetings*. Combinations of this may occur. For example, formal NITAG deliberations may be open while working group sessions are closed (see thereafter). Open meetings increase transparency and may improve public acceptance but at the same time may make the process less efficient and may inhibit NITAG members from speaking as openly as they otherwise would.
- *Participation of industry and participation of observers*. Manufacturers should usually not be allowed in meetings but occasionally invited in highly structured participation settings to inform the committee about their products. If and when manufacturers are invited to observe meetings, the setting and handling must prevent undue influence by these manufacturers.
- *Process to review and share evidence with the group*. In preparation for the meeting specific questions put to the committee should be clearly articulated. The agenda should be circulated at least a week before the meeting with necessary relevant background documents to allow for committee members to prepare themselves for the discussions ahead.
- *Process for decision making, i.e. decision by vote or consensus*. Each of the different approaches has its own advantages and inconveniences and one approach cannot be prescribed over the other.
- *Establishment of working groups and their mode of operation*. Committee's working groups may be a helpful resource for gathering, analyzing and preparing information for presentation and for decision making by the full NITAG. It is advisable that such working groups comprise a minimal number of core members with additional subject-matter experts. These may include relevant *ex officio* or liaison members and invited national or international experts. Vaccine manufacturer's representatives should not serve on the working groups although they could be asked to provide specific information to the working groups. Alternatively other mechanisms to bring information and facilitate the decision-making process could be used, such as through reliance on the secretariat, or through preparation by paid consultants. In the latter instance, the consultant should not have any conflicts of interest that might cause concern about the validity and independence of the prepared document.
- *Basis for decision making*. Various similar approaches have been published [12,29–33].

  Elements of information that should be considered when making recommendations include the following:

  Disease epidemiology [34] (disease burden including age specific burden for mortality, morbidity, and societal impact; age distribution of disease; projections for future disease burden; specific risk groups; epidemic potential; disease occurrence over time; serogroup or serotype distribution for serogroup or serotype specific vaccines; and changes in epidemiology over time).

  Clinical characteristics (clinical management of disease, disease severity, primary/secondary/tertiary care implications, and long term complications of disease and health requirements).

  Economic considerations (projections for future disease burden to the health care system, cost of disease including the impact of epidemics on social and political structures, cost and cost effectiveness [35,36], and affordability of immunization).

  Vaccine and immunization characteristics (efficacy, effectiveness and population impact of vaccine; indirect effects; vaccine safety; cold chain and logistics concerns; vaccine availability; vaccine schedules; acceptability of vaccine and vaccine schedules to the public and health professionals).

  Political and public health considerations (actions in other countries; regional and global recommendations if available; potential of disease for international spread and pandemic potential).

When national data are not available, information generated from countries with similar characteristics can be used. Where sufficient data is not available, the committee should solicit additional data/work to secure the relevant data. In the absence of data or when data is inadequate, expert options can be used to make recommendations. When data permit, specific rules of evidence can be used to judge the quality of data and make decisions regarding the strength of recommendations [37–44]. A theoretical framework/explicit process for decision making could be developed and

go as far as using grading of evidence but very few committees currently have such a structured approach [31,45].

- *Process for deciding on agenda items and input requested from the committee*. Although most of the questions put before the committee should come from the Ministry of Health, it is appropriate that the members of the committee themselves be asked to contribute to the development of the agenda and based on their expertise identify important issues to be discussed. Industry and professional societies could also put forth suggestions.

It is essential that sufficient administrative (*e.g.* secretarial) support be provided to prepare for meetings. Given that members have to invest the necessary time in getting ready for the meeting and reviewing information ahead of meetings, the secretariat should ensure that all background information is well prepared. This is especially important as generally members are not or are only minimally financially compensated for serving on an advisory group. Travel expenses should be compensated.

3.3.2. Meeting frequency

Although there should be flexibility in calling a meeting at any point to discuss important decisions or urgent matters in rare occasions that may require the organization of additional meetings, there should be regular or fixed meetings scheduled in advance. It is recommended that the NITAGs meet regularly and at least twice a year, with a meeting on a yearly basis being a very strict minimum. Several groups such as those in Canada, the Unites States or the United Kingdom operate successfully with three or four meetings a year. A higher number of meetings may be more difficult to manage both for committee members and for the secretariat but allow for more issues to be discussed in a satisfactory manner and also allows for reducing the time lag for issuance of the needed recommendations.

3.3.3. Communication/reports

Summary minutes of each meeting with the focus on the main conclusions and recommendations must be available and endorsed by the group within a reasonable time period after the meeting (within no more than two months after a meeting). A clear process must be in place for the recommendations to be communicated to the decision makers.

It must be decided if the minutes are public or private and if public how they will be published, *i.e.* through government bulletins, journals, website, or other mechanisms. Generally speaking public dissemination of the minutes, if/when appropriate, is encouraged as it lends more credibility and transparency of the decision-making process. Although one may fear that this could potentially expose the government to criticism if recommendations from the NITAG were not implemented, this would not necessarily occur as long as reasons for not implementing the NITAG recommendations are well justified and transparent (*e.g.* inability to secure sufficient funds and higher opportunity costs). Some committees periodically publish books or compendiums that include all committee recommendations on vaccine use. In other circumstances, recommendations and information about the committees and their work is posted on a website (*e.g.* http://www.advisorybodies.doh.gov.uk/jcvi/; http://www.phac-aspc.gc.ca/naci-ccni/; http://www.cdc.gov/vaccines/recs/acip/). Consideration should also be given to a communication strategy/plan.

3.4. Evaluation

It is extremely difficult to come up with a specific outcome indicator that objectively assesses the performance of a NITAG as a recommendation taken in a particular country may be the proper decision at that time but may not be the right one in another setting or another time. Nevertheless, consideration should be given to developing process and output and intermediate outcome measures to demonstrate the contributions of NITAG to the overall improvement of the immunization decision-making process.

Indicators for a "well-functioning" NITAG have been proposed that can help countries assess where they stand and allow for monitoring of progress at regional or global levels, particularly when combined as a composite indicator. Focusing on the needed formal, independent, and technical nature of NITAGs, the following indicators have been proposed: formal legislative or administrative basis (*e.g.* a Ministerial decree) establishing the committee in a sustainable manner; availability of formal written Terms of Reference; core members required to systematically declare any interest; technical competence (core membership with a least 5 main expertise areas represented among members (paediatrics, public health, infectious disease, epidemiology, immunology), committee meets at least once a year on a regular basis, agenda (and background documents) distributed to members at least 1 week ahead of meetings. These proposed process indicators have the advantage of simplicity and are applicable in all regions and all cultures making it easy for the immunization managers to determine if the NITAG complies with each of these criteria [46]. They, however, represent a minimum that can be particularly useful to monitor progress at the global level.

It is important that the NITAG be consulted for all key policy decisions and that all NITAG recommendations be given due consideration by the Ministry of Health. Intermediate outcomes measure could therefore include the number or proportion of recommendations given due consideration or implemented, as well as the proportion of key decision taken by the Ministry of Health that have been made through soliciting the advice of the NITAG.

Recommendations should be regularly revisited and revised if need be based on the availability of new evidence and particularly with the benefit of accrued surveillance data and this could also be taken into account in the evaluation of NITAGs.

4. WHO's and partners' roles and support for the establishment, strengthening and functioning of NITAGs

WHO has placed a high priority on the development of national decision making process and capabilities. The directions for countries to consider when establishing or improving the functioning of a NITAG take time and are not always easy to follow as many countries do not always have the culture of elements such as the independence of expertise, a clearly defined approach in the case of conflict of interest and a well established evidence based process for decision making. In most of the countries where the NITAGs are functioning quite well, these elements have been introduced progressively and sometimes it took several decades to reach such levels of excellence. Therefore, to assist in the rapid establishment or strengthening of functional, sustainable independent NITAGs, and to benefit from the experience of the most advanced committees, the WHO is working through its regional and country offices and with partners to support countries with the following activities:

- Providing more specific regional guidance documents and facilitation of access to framework documents such as standard declarations of interest.
- Fostering linkages among and between committees.
- Providing technical guidance for the establishment/strengthening of the NITAG.

- Providing technical guidance to the NITAGs in the formulation of immunization policies and strategies for vaccine preventable disease control.
- Providing global and regional policy recommendations and giving access to references and other background material that constitute the evidence for such recommendations [47].
- Providing regular updates and latest developments on the vaccine pipeline, guidance about recommended immunization schedules, vaccine delivery technology, vaccine preventable disease surveillance, safety and quality data/information, *etc*. WHO will send, on a regular basis, information on the latest developments in vaccines and immunization to the chairman of the NITAG who, in turn, will circulate it to the other members.
- Providing assistance or guidance in identifying potential sources of financial support to help with the establishment of a NITAG.
- Developing training materials.
- Facilitating exchange between NITAGs and participation of NITAGs chairperson at regional immunization meetings.

Among key WHO partners taking part in the direct support to countries are the US Centers for Disease Control and Prevention, the ProVac Initiative, launched in 2006 to provide technical cooperation and strengthen national capacity to make evidence-based, informed decisions in the context of the introduction of new and underutilized vaccines [32], and the more recent SIVAC (Supporting Independent Immunization and Vaccine Advisory Committees) Initiative [48]. The objective of this latter Initiative is to assist in the establishment or strengthening of functional, sustainable independent NITAGs in GAVI-eligible and middle income countries in making recommendations for program improvements and vaccine introductions through technical assistance, training, development of tools and information sharing. More information and link to these resources can be found at: http://www.who.int/immunization/sage/national_advisory_committees/en/index.html.

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Conflict of interest

Philippe Duclos has no financial interests relevant to this paper.

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LETTERS

GRADE for the advancement of public health

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The recent debate in this journal about the applicability of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to public health interventions is both important and timely.[1 2] To say it upfront, we are enthusiastic about the transparent, systematic, comprehensive and nevertheless straightforward way in which GRADE guides its users in judging the quality of evidence and in classifying the strength of a recommendation. We do, however, continue to struggle to apply GRADE to a range of public health questions.

Sir Austin Bradford Hill[3] has been called on by those proposing a GRADE-plus framework[2] and by advocates of the status quo.[1] We believe that assessing GRADE's compatibility with Hill's viewpoints is less about ticking the box—the presence or absence of a viewpoint—but rather about how individual viewpoints are considered in upgrading or downgrading. These more subtle reflections will make a critical difference when we take stock of and assess our confidence in the full spectrum of public health evidence, which more often than not is derived from non-randomised studies. Let us illustrate our point in relation to consistency.

Hill placed 'a great deal of weight upon similar results reached in quite different ways',[3] an issue pertinent to complex interventions that are highly dependent on context.[4] In GRADE, an important inconsistency in the size of an effect results in downgrading the level of evidence by 1. Yet wouldn't Hill's original thinking suggest that if a public health intervention delivers similar impacts in different settings and countries, under different circumstances and at different times, and as measured by different researchers using a variety of study designs, the level of evidence should be upgraded? Wouldn't this imply the need for a criterion that examines such *consistency between populations and settings* explicitly?

Currently, GRADE is not being widely implemented in systematic reviews of complex interventions; indeed we were unable to locate any published examples. Is it that the public health community is resistant to change and unwilling to reap the benefits of GRADE? Or are there indeed substantial problems in the applicability of the framework to questions outside clinical practice, turning GRADE into a straightjacket? There is a simple way to find out and to proceed in an evidence-based way: testing GRADE across a range of public health interventions should inform whether the approach works in its current form or whether modifications are justified.

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Association between child malnutrition and maternal common mental disorders: the potential role of disability

In 1996 one of the authors (CTM) was the leading author of a clinically based case–control study conducted in Brazil, which investigated the association between child stunting and maternal common mental disorders (MCMD).[1] A positive association (OR 2.8; 95% CI 1.2 to 6.9) was found in that case. Similar methods and results have been reported in another study conducted in Pakistan (OR 3.9; 95% CI 1.95 to7.86).[2]

Harpham *et al*[3] were the first to test this association through population surveys in a multicentre study. They found significant positive associations between child stunting and MCMD in two out of four countries, namely India (OR 1.4; 95% CI 1.2 to 1.6) and Vietnam (OR 1.4; 95% CI 1.1 to 1.8). In Peru and Ethiopia, there was no significant association. There was congruence in the results of clinical and population-based studies.

We conducted a population survey with the same objective in Brazil. From a low income region of 884 668 inhabitants, a probabilistic sample of 944 mothers of children aged 0–60 months was selected for investigation of the prevalence of child stunting. A multistage sampling design was adopted, and it consisted of three steps: municipalities were randomly selected; sectors within each municipality were established; one household was defined within each sector from which consecutive households where children aged 0–5 years resided were selected. Child stunting, an indicator of chronic protein energy malnutrition, was defined by a cutoff of 2 Z-scores of height for age. A subsample of all the mothers of children aged 6–24 months was utilised for our study. As in the study of Harpham *et al*,[3] for an evaluation of the prevalence of MCMD our sample was assessed by the SRQ-20 (cutoff of 7/8), which was interviewer administered along with a questionnaire that included the collection of data on mother/child health, socioeconomic and demographic conditions. The project was approved by the ethics committee of the Federal University of Alagoas, process no 000465/2007–96.

The proportion of MCMD was 44.3%. There was no statistical association between child stunting and MCMD (OR 0.9; 95% CI 0.42 to 1.9). The number of subjects presenting with child stunting among those with and without MCMD was 13 (10.5%) and 18 (11.5%), respectively. In the logistic regression analysis, in which the independent variables (MCMD, age and education of the mother, number of children, employment status, social class, breastfeeding and birth weight) were included in accordance with the dependent variable stunting, the significant variables in the final model remained the same as those detected in the univariate analysis: low birth weight (OR 3.6; 95% CI 1.08 to 12.4) and breastfeeding (OR 6.7; 95% CI 1.76 to 25.5). There was no statistical association between child stunting and MCMD (OR 0.9; 95% CI 0.42 to 1.9). In the logistic regression, the variables associated with child stunting were low birth weight (OR 3.6; 95% CI 1.08 to 12.4) and no breastfeeding (OR 6.7; 95% CI 1.76 to 25.5).

When the studies with clinical samples[1 2] used to evaluate the association between child stunting and MCMD are compared with studies using population samples for the same purpose[3] (and the current study), the former present a stronger association (OR of approximately 3), whereas in the latter the highest significant OR is 1.4. One hypothesis to explain this difference is that in clinical samples, MCMD cases present more disabilities than those from the community. These disabilities would impair mothers in their role as caretakers. Therefore, the association would not be between child stunting and MCMD, but between child stunting and disability linked to MCMD.

For future studies, the administration of an instrument such as the Sheehan disability scale[4] for evaluation of the level of impairment in the SRQ-positive cases is suggested. If our hypothesis is correct, the association with child stunting would be stronger in SRQ-positive mothers with higher scores on the Sheehan disability scale. The implications

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Indicators to assess National Immunization Technical Advisory Groups (NITAGs)☆

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ABSTRACT

A National Immunization Technical Advisory Group (NITAG) is an expert advisory committee that provides evidence-based recommendations to the Ministry of Health (MoH) to guide immunization programs and policies. The World Health Organization (WHO), the Initiative for Supporting National Independent Immunization and Vaccine Advisory Committees (SIVAC) at Agence de Médecine Préventive (AMP) and the US Centers for Disease Control and Prevention (US CDC) engaged NITAG stakeholders and technical partners in the development of indicators to assess the effectiveness of NITAGs. A list of 17 process, output and outcome indicators was developed and tested in 14 countries to determine whether they were understandable, feasible to collect, and useful for the countries. Based on the findings, a revised version of the indicators is proposed for self-assessment in the countries, as well as for global monitoring of the NITAGs.

1. Background

As an independent expert advisory committee, a National Immunization Technical Advisory Group (NITAG) provides evidence-based recommendations to the ministry of health (MoH), policy makers and program managers to guide policies and formulate strategies. NITAGs aim to support and empower the government and national authorities evidence-based decision making. As such, they serve to promote the adoption of policies based on national priorities, help resist pressure from interest groups, reinforce the credibility of national vaccine and immunization strategies, and enhance the ability to secure government or donor funding.

An important question, however, is how would we know if NITAGs are meeting their intended purpose? Most stakeholders, including policymakers, managers, providers and consumers of vaccines and immunization services, are indeed interested to know if and how establishing an independent body of experts would

Abbreviations: AMP, Agence de Médecine Préventive; EPI, Expanded Program on Immunization; JRF, Joint Reporting Form; NIP, National Immunization Program; MoH, Ministry of Health; NITAG, National Immunization Technical Advisory Group; SIVAC, Supporting Independent Vaccine Advisory Committees; SOPs, Standard Operating Procedures; ToRs, Terms of Reference; US CDC, United States Centers for Disease Control and Prevention; WHO, World Health Organization.

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make any difference in improving immunization services and the health of the population.

This paper is intended to reflect on this complex issue and suggest a self-assessment tool. This tool is not designed to provide all the evaluative answers as priorities, interests and capacities vary from one country to another. It does, however, suggest a list of indicators for various stakeholders to consider as they assess the contributions of NITAGs in their respective settings.

The proposed tool was developed with an understanding and recognition of the diversity of various perspectives and the different level of development of NITAGs (long-time ago established ones versus more recently ones). The users of this tool, at any level, will decide which of the proposed indicators best fits their needs and priorities. For example, global experts and leaders may be focusing on the industry's role in the overall decision making process, whereas, national authorities and their constituents may want to know if introduction of new vaccines are cost-effective in the long run. Moreover, managers and providers may be interested in the efficacy of a particular vaccine in a certain population, whereas consumers and the general population may be concerned about the risks or adverse events of vaccines.

Accordingly, the World Health Organization (WHO), the Agence de Médecine Préventive (AMP) through the Initiative for Supporting National Independent Immunization and Vaccine Advisory Committees (SIVAC [1]), in collaboration with the US Centers for Disease Control and Prevention (CDC) and NITAG members from 14 countries, developed a set of output and outcome indicators based on the stakeholders' perspectives methodology [2]. As mentioned, the primary objective of the tool is to provide the countries with an opportunity to evaluate their NITAGs by incoporating various perspectives and interests. It can also serve as a tool for WHO, SIVAC, technical partners and the immunization community to identify gaps and opportunities related to NITAG strengthening [3].

This article describes the process of developing NITAG indicators, presents the pilot testing results, and concludes with the final list of 17 indicators proposed for self-assessment in the countries.

2. Methods

2.1. Development of the NITAG indicators

In 2009, the WHO, AMP/SIVAC and the CDC developed 6 process indicators that were included in the WHO/UNICEF Joint Reporting Form (JRF) [4,5]. As a monitoring system adopted by the WHO and UNICEF in 1998, the JRF collects self reported national-level data on selected vaccine-preventable diseases cases, immunization coverage, recommended immunization schedules, vaccine supply and other information on the structure, and policies and performance of national immunization systems.

NITAG process indicators included in the JRF included existence of: formal written terms of reference; legislative or administrative basis establishing the committee; core membership with at least 5 main expertise areas represented among members; committee meeting at least once a year; agenda and background materials distributed ahead of meetings; and declaration of interests by committee members. In developing the process indicators, WHO, AMP and partners aimed to create a mechanism to assess the basic functionality of NITAGs. While these process indicators are advantageous because of their simplicity and applicability for all regions and allow for monitoring of progress at regional and global level, they do not capture information to assess the effectiveness and impact of NITAGs.

In 2010, WHO and AMP together with other partners and several countries decided to apply a different methodology, the stakeholders' perspectives methodology, to develop a set of output and outcome indicators [2]. This approach recognizes that there are a number of individuals and organizations with possibly different expectations for how a NITAG should perform and what it should deliver. Accordingly, we need to look at NITAG effectiveness through multiple lenses, and talk about it in terms that are relevant to the various interested parties.

As an example of how this methodology is applied, if one considers what the value of vaccinating a child is, the answer will depend on who we ask–a parent, in addition to having a peace of mind that her child doesn't get sick and suffer, may also express relief for not having to take time off from work to attend to a sick child; a provider may feel good about offering a safe product to the family, establishing long term relations and providing additional services in the future; a manager or scientist may be focused on protecting the vulnerable populations and preventing outbreaks through building herd immunity; a vaccine producer may be concerned about its reputation and a return on its investment; and a national authority may be driven by savings through prevention of hospital visits, etc. In other words, every individual and organization has a particular interest in the aftermath of a vaccinated child.

The stakeholders' perspectives approach focuses on 5 categories of stakeholders: authorities, managers, implementers, recipients and beneficiaries. Their interests and perspectives typically reflect a value chain of inputs, activities and outputs/outcomes. Inputs are the funding, staffing, directives and constraints that are provided to a NITAG. Activities or the various work efforts undertaken by a NITAG may include: holding meetings, collecting data related to local and regional needs and responding to questions from decision-makers. Activities produce outputs, which in turn, contribute to outcomes. In terms of a NITAG, the main output is considered to be the "evidence-based recommendations" given directly to the recipients, i.e. ministry of health and other decision-makers. After receiving the evidence-based recommendations, the ministry of health may accept and implement them, which in turn, should contribute to the intended improvements in population health.

For example, if a NITAG was to recommend the introduction of a new vaccine, a policymaker or authority may decide not to introduce it because of concerns about the funding implications (i.e. input) of this decision, whereas a parent may worry about the vaccine safety (i.e. intermediate outcome). So, how do we decide on the effectiveness of a NITAG when each stakeholder may have a different interest? The stakeholders' perspectives methodology adeptly allows for these varying interests to be incorporated and analyzed so that the agreed-upon indicators can be meaningful and useful to all involved parties.

After brainstorming with a number of current and former NITAG members, a total of 31 indicators were considered. From the 31 indicators originally considered, 17 were selected based on the following inclusion criteria: understandability, ease of collection and perceived usefulness. The inclusion criteria are described in the article. The excluded indicators are listed in Appendix 1.

The 17 selected indicators are classified in 3 categories and include 10 *process or activity indicators* to monitor the functionality of a NITAG, based on global recommendations and best practices; 3 *output indicators* to assess the quality and relevance of evidence-based recommendations; and 4 *outcome indicators* to evaluate the impact of technical recommendations on government policies and strategies.

2.2. Piloting of the NITAG indicators

In 2011, a protocol and questionnaire were developed for piloting the 17 indicators in the countries. The indicators were tested in 14 countries (Table 1), which were selected to ensure representation of a broad range of socio-economic development, as well as

Table 1
Pilot testing of National Immunization Technical Advisory Groups (NITAG) indicators in selected countries, by World Health Organization (WHO) Region.

Region according to the WHO classification	Country
Africa	South-Africa
Eastern Mediterranean	Iran, Oman, Sudan
Europe	Belarus, France, United Kingdom
Americas	Mexico
South-East Asia	Indonesia, Sri Lanka, Thailand
Western Pacific	Australia, Mongolia, South Korea

countries with long- and newly established NITAGs [6–15]. The aim of the piloting was to help refine the set of indicators and their definitions. Specifically its purpose was to determine whether or not the proposed indicators were understandable (i.e. clear and relevant), feasible to collect (i.e. human resource and funding cost), and useful (i.e. applied to action) primarily for the NITAG members, immunization managers, internal groups, such as scientific societies or associations and external partners, such as WHO and SIVAC.

The pilot testing was coordinated by regional focal points. The focal points were in charge of contacting the interviewees identified in each country to participate in the pilot, coordinating the work, and translating the questionnaire from English to French, Russian, and Spanish. The interviewees were selected from among the most knowledgeable persons serving the selected country's NITAG, including NITAG Chairs, members Immunization managers and MoH staff. The protocol and questionnaire were distributed to each interviewee. Focal points explained the methodology to the interviewees via teleconferencing, and assisted with the data collection. During the pilot testing, the interviewees were encouraged to provide additional relevant information and input on the ease of data collection.

3. Results: a proposed list of NITAG indicators for the countries

The pilot results indicated that the indicators were clear and deemed relevant by the interviewees and required minor wording revisions.

An example of a revision included the question "How many recommendations issued by the NITAG took into account the availability of the vaccine?" In several countries, NITAGs take vaccine availability into account in their decision-making processes, but in others, vaccine availability is only discussed after the recommendation is issued by the NITAG. Therefore, to avoid misunderstandings, the definition and instructions for this question were revised.

The pilot also highlighted important issues in the feasibility of collecting the data, such as years of collection. In particular, the number of years was shortened to only 1 year (instead of 3), in order to avoid recall bias.

Finally, the pilot highlighted the usefulness of the indicators for the countries and their interests in monitoring their activities. Countries expressed a need to show the impact of their work in shaping immunization policies. As a consequence of the pilot, several countries (including long time ago established NITAG) decided to review their NITAGs' terms of reference and standard operating procedures. This was the best indicator of the usefulness of these indicators.

In light of the findings, a revised version of the list of 17 indicators is proposed for self-assessment in the countries (Table 2).

Table 2
Proposed list of National Immunization Technical Advisory Groups (NITAG) indicators for self assessment in the countries.

Process indicators	
Legislative/administrative basis*	Is there a legislative or administrative basis for the NITAG?
Advisory role only	Is the NITAG role technical advisory only?
Terms of reference*	Are there formal terms of reference for the NITAG?
Membership*	Is there a clearly defined selection process to become a core member and the Chairperson of the NITAG? Are the main areas of expertise recommended by WHO represented by core members? Are there non-core members? Are there rules for the rotation process for core members?
NITAG functioning SOPs	Are there clearly defined NITAG functioning SOPs?
Independent chairperson	Is the NITAG Chairperson independent from the MoH and the immunization program?
Number of meetings*	How many meetings were held in each of the past 3 years?
Agenda and background documents distribution*	Were the agenda and background documents distributed and received at least 1 week in advance for each of the past 3 NITAG meetings?
Declaration of interests*	Is there a conflict of interest policy in place? Were all core members asked to declare their interests at the beginning of each of the past 3 years? Were all core members asked to declare their interests at the beginning of the past 3 NITAG meetings?
Official requests for recommendations received and addressed	How many official requests for recommendations has the NITAG received from the MoH and/or the immunization program? How many of them has the NITAG addressed?
Output indicators	
Evidence-based methodology for recommendations	How many recommendations were issued by the NITAG? How many of these recommendations made reference to peer-reviewed published material?
Country-specific criteria for recommendation	How many recommendations issued by the NITAG were supported by local evidence or contextual information?
Vaccine availability and delivery capacity criteria for recommendations	How many recommendations issued by the NITAG took into account the vaccine availability and delivery capacity at national level?
Outcome indicators	
MoH decisions made in consultation with the NITAG	How many MoH immunization-related decisions were made in consultation with the NITAG?
Recommendations accepted by the MoH	How many recommendations issued by the NITAG were accepted by the MoH? How many recommendations issued by the NITAG were not accepted by the MoH?
Recommendations which were not adopted by scientific or professional organizations	How many recommendations issued by the NITAG were not adopted by scientific and professional organizations?
Recommendations implemented in the country	How many recommendations were implemented in the country? How many recommendations were not implemented in the country?

* These 6 indicators are also included in the JRF.

4. Discussion

The primary objective of this exercise was to develop a set of indicators for countries to consider in assessing their NITAGs' performance. Countries may review the indicators annually to evaluate their progress toward achieving and institutionalizing more standardized and evidence-based processes for immunization policymaking. The findings suggest that the proposed list of NITAG indicators will be well-received and serve as a useful self-assessment tool for countries.

There are 3 main limitations to this study. The first limitation of this methodology is that the indicators reflect only the work of the NITAGs, while the decision making process in the countries is often more complex and involves many actors. Although the outcome indicators are an attempt to analyze the NITAGs' impact, it will be difficult to assess the reasons for which a recommendation is accepted and implemented, or not, by the ministry of health. Thus, the outcome indicators can be complemented by semi-structured interviews with ministry of health staff to capture the context and the reasons behind the decisions.

The second limitation is the duration of this study as it only reflected data from the previous year. The pilot showed that it was difficult to get information older than 1 year as there was a high turnover in the NITAGs' executive secretaries (function usually provided by the MoH). To address this limitation, the countries are recommended to do this self-assessment on an annual basis, at the same time period every year, in order to be able to monitor the evolution and progress of the NITAG.

The third limitation is linked to the methodology of self-assessment, which can be subjective. To address this limitation, one possible solution would have been to recommend an external review rather than a self-assessment exercise. However, it was not feasible due to lack of resources in most countries and the growing number of countries establishing a NITAG.

As the aim of the pilot testing was to evaluate the indicators in order to refine them and come up with a useful tool for the countries, this article does not include the results of each question per country. However, some summary results can be interesting for the reader to know as they illustrate the need for the countries to evaluate their NITAGs. For example it can be interesting to note that only 2 of the process indicators as expressed in the JFR (in 2010) were met by all countries. Those 2 indicators were the presence of terms of reference and the representativeness of a diverse range of expertise in the membership of the NITAG. Another result of interest is that in 77% of the cases, NITAG recommendations were accepted by the MoH and in 71% of the cases NITAG recommendations were implemented by the countries (in 2010). These results have to be taken with caution and it should not be assume that they can be extrapolated to represent the experience of all countries as they come from a pilot test with indicators that were not yet completely finalized and validated, and that were tested on a sample of countries only which doesn't represent the global reality of NITAGs. It will be more interesting to know the detailed country results when the tool will be available and used by all countries. Countries will be supported and encouraged to publish their results as they become available, and upon a couple years of use and feed-back the set of indicators will be further refined.

5. Conclusion

The WHO, AMP/SIVAC and US-CDC propose the use of 17 indicators as a tool for self-assessment of NITAGs. These indicators can also be used to monitor NITAG developments globally and to guide support to countries in identifying and promoting promising practices to improve NITAGs' effectiveness. This proposed list of indicators can be considered by all stakeholders, and will be most useful to countries which decide to assess their NITAGs and need a specific tool to assist them in this process.

The proposed list of indicators will be made available to the countries with a guide defining each indicator, examples and details on how to collect and analyze them. This package named "instructions for assessment of NITAGs" will be accessible for free on the NITAG Resource Center (www.nitag-resource.org), a collaborative platform aiming at increasing the collaboration between NITAGs and themselves and with the technical partners.

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Appendix A. Appendix 1

Potential National Immunization Technical Advisory Groups (NITAG) indicators excluded from the final list of indicators.

Process indicators	
Quorum of core members in meetings	How many meetings were held with a quorum of core members?
Minutes published	How many meetings have validated minutes published?
Outcomes evaluation	Is there formalized process to evaluate outcomes of NITAG and to feed them back into the NITAG processes and workplans?
Annual work plan	Is there an annual work plan in place?
Annual budget	Is there an annual budget to cover cost of running the NITAG?
Confidentiality agreement	How many members have confidentiality agreement on file?
Internet access	How many members and secretariat staff have access to internet and emails?
Executive secretariat staff	How many staff work for the NITAG executive secretariat?

Output indicators	
Understandability of recommendations and proper dissemination	How many recommendations were written in understandable terms and disseminated by proper channels?
Outcome indicators	
Incorporation of recommendations into continuing medical education programs	How many recommendations were incorporate into continuing medical education program?
Number of people targeted within a timeframe	How many people targeted by the recommendation can be accommodated within specified time frame?
Waiting time before reception of the vaccine	What is the waiting time before receiving the vaccine?
Incidence/prevalence decrease	What is the percentage of reduction of incidence/prevalence?
Cost per health outcomes	What are the cost per newly fully vaccinated person and cost per disease averted?

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UNIVERSAL IMMUNIZATION PROGRAMME IN INDIA: THE DETERMINANTS OF CHILDHOOD IMMUNIZATION

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Abstract: The study analyses the effects of some selected demographic and socioeconomic predictor variables on *likelihood of immunization* of a child for six vaccine-preventable diseases covered under UIP. It focuses on immunization coverage a) in all India, b) in rural and urban areas, c) for DPT, Polio, and partial immunization, d) for three groups of states, namely, *Empowered Action Group*, *North-Eastern* and *other* states, and e) for three states, namely, Bihar, Tamilnadu, and West Bengal. The study applies *logistic regression* model to *National Family Health Survey*-2 (1998-99) data. Excepting a few cases, the results are robust.

[Keywords: Immunization, UIP, NFHS-2, Logit, Unadjusted and Adjusted Likelihood]

JEL Classification: C25, I18, J13

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1. INTRODUCTION:

Social, cultural and economic factors continue to inhibit women from gaining adequate access even to the existing public health facilities. This handicap does not merely affect women as individuals; it also has an adverse impact: on the health, general well-being and development of the entire family, particularly children. This area is of grave concern in the public health domain. In the vulnerable sub-category of women and girl child, this has a multiplier effect for the future generations.

Available data for Indian states shows a close correlation between maternal mortality and infant mortality rate (Padhi, 2001). There is global evidence showing that wherever infant mortality is high, fertility is also high (Kulkarni, 1992; Ghosh, 1991; Sai, 1988). 'Any attempt to reduce fertility without reducing mortality would be like putting the cart before the horse' (Kulkarni, 1992). Thus to reduce fertility, child survival rate should be raised first. And this can be best done by universal immunization to all eligible mothers and children. This would in turn raise the overall health standard of the mass; reduce morbidity and mortality and lower fertility.

In India, under Universal Immunization Programme (UIP) vaccines for six vaccine-preventable diseases (tuberculosis, diphtheria, pertussis (whooping cough), tetanus, poliomyelitis, and measles) are available for free of cost to all. UIP was launched in 1985 with much dynamism to attain the target to immunize all eligible children by 1990. Lot of energy and money has been spent on the UIP but it does not reap the much hyped outcome. Unmistakably, various survey results show the glaring gap between the target and achievement even after several years. Given the tight budgetary allocations, one should take care of effectiveness of the Programme. Here lies the necessity of the present study. The study tries to find out the causes of poor immunization coverage rate in India.

There are some bottlenecks from both supply- and demand-side. In a developing country like India, any programme like UIP could be affected by supply-side financial constraints when the overall Central and State budgetary allocations on health care are meagre and availability of supply-side data at disaggregated level is rare. Thus supply-side analysis is beyond the scope of the present study. The study hence concentrates purely in the demand-side assuming the *ceteris paribus* supply-side constraints.

The second section reviews literature relating to universal immunization programme. The data source and methodology are given in the third section. The study uses *National Family Health Survey* (NFHS)-2 (1998-99) data, richness of which is well-acknowledged. Bivariate and multivariate *logit* regression analyses are done. Fourth section summarizes the results of determinants of full immunization in India. Some vaccine-specific and state-specific extensions are presented in section five. Section six concludes the study with some policy implications.

2. UNIVERSAL IMMUNIZATION PROGRAMME AND LITERATURE REVIEW:

2.1: STATE INTERVENTION AND UIP

Kethineni (1991) discusses the political economy of state intervention in health care. He mentioned that in case of vaccination, as the private marginal benefits are less than the social marginal benefits, it would be advantageous for state intervention by bearing the cost. State intervention is considered necessary to reduce inequalities in the access to health care and income distribution in the long run. Disease and poverty form a vicious circle. "Men and women were sick because they were poor; they became poorer because they were sick and sicker because they were poor"[1].

[1] Winslow, 1951, pp-9.

The report of the sub-committee on national health prepared for the consideration of National Planning Committee of the Indian National Congress also had advocated state intervention to preserve and maintain health of the people by organizing and controlling health care to achieve proper integration of curative and preventive services[2]. But Kethineni (1991) argued that in India state intervention in the health care sector overemphasized on curative services largely for the urban elites leaving the majority of the rural population at bay. As a consequence the benefits of health care system accrued mainly to the upper and middle classes while the poor remained beyond the purview of modern health care system.

The Govt. of India (GoI) took steps to strengthen maternal and child health services as early as in the *First* and *Second Five-Year Plans* (1951-56 and 1956-61). As part of the *Minimum Needs Programme* initiated during the *Fifth Five-Year Plan* (1974-78), maternal health, child health, and nutrition services were integrated with family planning services. The primary aim at that time was to provide at least a minimum level of public health services to pregnant women, lactating mothers, and preschool children[3]. As part of *National Health Policy*, the *National Immunization Programme* is being implemented on a priority basis. In the wake of diphtheria, pertussis, tetanus, and poliomyelitis and childhood tuberculosis, the *Expanded Programme on Immunization* (EPI) was initiated in India in 1978 (WHO launched it globally in 1974) with the objective to reduce morbidity, mortality and disabilities by making free vaccination services easily available to all eligible children and pregnant women by 1990[4]. Achievement of self-sufficiency in the production of vaccines was also a part of the programme.

[2] National Planning Committee, 1948, pp-224-5.
[3] Kanitkar, 1979.
[4] Sokhey, 1988.

Universal childhood immunization has been accepted by world public health leaders as both an affordable and cost effective strategy not only for child survival but also for promoting primary health care[5]. In India, the UIP was launched in 1985-86 to extend immunization coverage among the eligible children and to improve the quality of services. The UIP is a carefully planned strategy for systematic district-wise expansion of the immunization programme to cover all the districts by 1989-90[6]. The objective of UIP was to cover at least 85% of all infants against the six vaccine-preventable diseases by 1990 and to achieve self-sufficiency in vaccine production and the manufacture of cold-chain equipment[7]. The target in UIP districts is to achieve universal coverage within one year (1986) and maintain the same in the subsequent years. This scheme has been introduced in every district of the country, and the target now is to achieve 100% immunization coverage although technically 85% coverage levels would ensure *herd immunity*. More than 90 million pregnant women and 83 million infants are to be immunized over a five year period under the UIP[8]. The programme was given the status of a *National Technology Mission* in 1986 (GoI, 1988) to provide a feeling of urgency and commitment to achieve the goals within the specified period. UIP became a part of the *Child Survival and State Motherhood* (CSSM) Programme in 1992 and *Reproductive and Child Health* (RCH) Programme in 1997[9]. The GoI constituted a *National Technical Committee on Child Health* on 11th June, 2000 and launched *Immunization Strengthening Project* on recommendation of the Committee[10]. The *Department of Family Welfare* established a *National Technical Advisory Group on Immunization*

[5] The Task Force for Child Survival, *Protecting the World's Children*, Bellagio II, Colombia, Oct, 1985.
[6] GoI, MoHFW, 1985; Sokhey, 1985
[7] GoI, MoHFW, 1991
[8] Sokhey, 1988.
[9] Annual Report, 2002-03, MoHFW, pp-176.
[10] Annual Report, 2002-03, MoHFW, pp-173.

on 28th August, 2001 to assist GoI in developing a nationwide policy framework for vaccines and immunization[11].

According to *United Nations Children's Fund*[12] (UNICEF) vaccine-preventable diseases (VPDs) cause an estimated 2 million deaths or more every year, of which approximately 1.5 million deaths occur among children below five year age (EXHIBIT-A). These 1.5 million deaths represent approximately 15 percent of under-five deaths. Reducing child mortality by two thirds between 1990 and 2015 is the fourth of eight *Millennium Development Goals* endorsed by world leaders in the *Millennium Declaration* in 2000.

2.2: *A CRITICAL REVIEW OF UIP EXPERIENCE IN INDIA*

Various survey results bear the testimony to the glaring gap between the goals aspired for and the targets reached. To quote, "…achievement of the target of protecting 100% of pregnant women with TT and 85% of infants with vaccines …remains a distant dream"[13]. This *National Review* mentioned some *supply side bottlenecks* that may hinder the UIP to achieve its goals. But Padmanabha (1992) argues that '…the Programme suffers not so much from lack of funds as from functional isolation'. Public health should not be treated as the sole responsibility of the health sector. Policies and programmes in other sectors such as environment, education, welfare, industry, labour, information, etc, have also be informed and influenced by public health considerations (Gopalan, 1994).

No matter how noble the idea of UIP, a 'non-controversial' programme of GoI, it faces severe criticism from many scholars. As Banerjee (1986, 1993) pointed out that it is a part of 'ill conceived and unimaginative global venture' and '… revealed many serious flaws in the programme itself. The most outstanding among them was that a massive,

[11] Annual Report, 2002-03, MoHFW, pp-174.
[12] UNICEF, 2005, pp-vii.
[13] Gupta, J.P. and Murali, Indira, 1989, National Review of Immunization Programme in India, pp-160.

expensive and a very complicated programme had been recommended for launching without even finding out what the problem was, leave alone the other important epidemiological considerations, such as incidence rates under different ecological conditions and time trends of the chosen diseases'. Banerjee (1993) mentioned that the programme is an 'onslaught' of the totalitarian approach of the developed *North* to 'sell' their 'social' products in the vast 'market' of developing *South* deviating from the *Alma Ata Declaration* (WHO, 1978). Banerjee (1992) mentions that 'the *Union Department of Family Welfare* did not have most basic epidemiological data concerning the extent of the problems, leave aside their significance in relation to other health problems of the country'. It hits the UIP as 'a nation-wide evaluation of UIP in 1990[14] revealed shocking acts of omission and commission by the bureaucrats'. Banerjee (1990) dubs UIP as 'an unholy alliance of national and international power brokers (who) could impose their will on hundreds of millions of human beings living in the poor countries of the world and make them forget all that happened at *Alma Ata* (*USSR*) in 1978'. Madhavi (2003) also noted strong indications of immunization policy in India, instead of being determined by disease burden and demand, is increasingly driven by supply push, generated by industry and mediated by international organizations.

The programme monitors its performance not by measuring the impact on morbidity and mortality rates but by assessing percentage coverage of the target population. But this criterion of assessing performance cannot be acceptable because the objective is to reduce morbidity and mortality due to the six vaccine-preventable diseases and not to merely increase coverage of vaccination, since the latter is important only as far as it helps in achieving the former objective[15].

[14] Gupta and Murali, 1989.
[15] Sathyamala, Immunization, The Technology Missions, Seminar 354—Feb, 1989, pp-28.

There are no studies to show the general pattern of morbidity among under-five children in India. According to the *Survey of Causes of Death in Infants* (*Rural*) conducted by the *Registrar General* and quoted in the booklet on the *National Mission on Immunization* (GoI, 1988), prematurity, respiratory infection of the new-born, followed by diarrhea, none of which is a vaccine-preventable disease, account for approximately 65% of deaths among 'causes peculiar to infancy'. The selection of the six vaccine-preventable diseases which account for barely 10-12% of the total deaths in under-five children as the most important set of diseases tackled at the national level cannot be justified epidemiologically.

Another route of attack on UIP is the basis on which immunization was chosen as the most effective way to tackle the diseases. For instance, measles in a healthy child is a negligible disease but mortality due to measles is 400 times greater in an undernourished population and the spread and severity of the epidemic is directly linked to overcrowding. Similarly, if an adequate amount of safe drinking water is made available, poliomyelitis will cease to be a problem[16]. Thus provision of basic survival needs could have been an alternative to universal immunization.

Ghosh (1991) also argues that the goals of '*Health for All*' can be 'achieved partly by immunization and partly by better nutrition. Preventive health care, therefore, requires immunization as well as good sanitation, proper nutrition, and availability of safe drinking water as the *minimum* of social needs that must be met before we embark on an ambitious plan of government outlay for *development*'. He also asks for 'convergence of services' instead of several projects with similar goals to make effective and efficient use of the funds.

2.3: *PULSE POLIO IMMUNIZATION*

[16] *Ibid*, pp-27

Pulse Polio Immunization Programme began in December, 1995 as part of a major national effort to eradicate polio. In the context of Polio eradication, George, *et al* (2004) argued for reassessing eradication strategy in view of the prevailing epidemiological situation in the country. Almost all of the 91 polio cases reported in India as on November 20, 2004, are from Bihar and UP[17]. It is also important to concede that, compared to 1995 (year of launch of *Pulse Polio Immunization*), drinking water and sanitation in the country has improved. In India, the risk of getting vaccine-associated polio is much higher than contracting the wild poliovirus infection[18]. Thus George, *et al* (2004) argued that Pulse Polio Immunization in India, as a whole, should be replaced by a regional approach in conducting sub-national immunization days (SNIDs) (as the risk is 6.26 times higher).

Proponents of *Polio Eradication* in India are in favour of 'multiple doses' protection. But there is no clear cut number of this 'multiple doses'. As a consequence, a substantial proportion of Indian children have received up to 25 doses (Sathyamala *et al*, 2005). George, *et al* (2004) termed this 'flooding' of the 'intestines of our child population with live, attenuated polio vaccine'. In Rajasthan, between January 1 and July 31, 1999, 24 children, some of whom had been administered a high number of OPV doses had died owing to polio (Paul, 2004). Numerous doses of OPV have changed the epidemiological behavior of wild poliovirus in the Indian environment. Confusion is going on among the programme managers about the introduction of more expensive and injectable inactivated polio virus (IPV) to counter vaccine-associated paralytic poliomyelitis.

2.4: *FACTORS AFFECTING IMMUNIZATION*

George *et al* (1993) highlights the health indicators of Indian states that follow two broad patterns of growth. One classified by Maharashtra

[17] http://www.childinfo.org
[18] http://www.childinfo.org

and Punjab which have attained relatively high health indicators against the backdrop of a high per capita income (PCI) and high CMIE index of economic development. The other is characterized by Kerala with a very good development of health indicators against the background of a low PCI, low level of industrialization, but relatively good infrastructural indicators. 'The first pattern could be attributed to the *trickle down effect* of capitalist modernization of an industrial-cum-agrarian variety in Maharashtra and of a predominantly agrarian variety in Punjab (Duggal, 1992); the second pattern is rooted in certain social, political, geographic and demographic particularities of Kerala (Tharakan, 1984; Nag, 1989)'.

Decentralization is also a highly popular component in policy reform. Within the health sector, decentralization of finances and responsibilities is one of the essential topics that has emerged in the agenda of national governments and international organizations. Devolving some of the centralized responsibilities to local levels is likely to improve both *technical efficiency* and *allocative efficiency* (Peabody, 1999). Robalino *et al* (2001) shows that higher fiscal decentralization is consistently associated with lower mortality rate and the benefits of fiscal decentralization is predominantly important for poor countries. Khaleghian (2003) finds that decentralization has a positive impact on immunization in low-income countries but the reverse happens for middle-income countries.

'Efforts to augment demand generation and community participation for immunization must focus on the consumers of the programme with due regard to their problems, needs, biases and aspirations. Highest level of political commitment to the programme can have a maximal translation into action by appropriate health education and dissemination of information in a language people can understand and with a cultural bias familiar to them'[19]. Mass communication for UIP

[19] GoI (1985), pp-40.

has no doubt helped to create claim for immunization services. In some states, notably in Punjab, the *Song and Drama* division of the *Ministry of Information and Broadcasting* has trained folk artists to spread messages on immunization and child health[20].

Education is an important determinant of immunization coverage. It also affects mortality and fertility inversely (Ghosh, 1991). 'The evidence from Kerala and Punjab shows that the effect of education on the proximate variables of both fertility and mortality can explain more than anything else the relatively higher decline of vital rates in these states' (Nag, 1989). Ghosh (1991) also argues for enhancing female education. 'There is a vast amount of demographic literature indicating that female literacy exerts greater influence on fertility and child mortality than male literacy' (Bhat *et al*, 1992). Role of education/ literacy/ female literacy is also agreed by many other researchers (Gupta *et al*, 1992; Dreze, 1993; George *et al*, 1993; Rajan *et al*, 1993; Rajan *et al*, 1993a; Pebley *et al*, 1996; Gage *et al*, 1997; Desai *et al*, 1998; Gauri *et al*, 2002) in making people more health conscious. Padmanabha (1992) also agrees to the importance of literacy and argues that 'because of low literacy levels in a large part of the country, communication with masses, particularly at the community level is only effective through political and local leadership'.

Infrastructural indicators such as electrification, all weather roads are also important factors (George *et al*, 1993).

3. DATA SOURCE AND METHODOLOGY:

All data is sourced from *National Family Health Survey* (NFHS)-*2*, undertaken in 1998-99. NFHS-2 covers a representative sample of more than 90,000 ever-married women of age 15-49 years from 26 states of India that comprise more than 99% of India's population. The survey provides state-level estimates of demographic and health parameters as

[20] Kulkarni (1992), pp-1335.

well as data on various socioeconomic factors that are critical for bringing about desired changes in India's demographic and health situation. Though it has some limitations, it is regarded as 'storehouse of demographic and health data in India'[21].

NFHS-2 data on immunization is based on vaccination card for each child born since January 1995 (or since January 1996 in states in which the survey began in 1999) or on mother's report in case of non availability of the card. EXHIBIT-B shows the percentages of rural and urban children age 12-23 months who received specific vaccinations at any time before the interview and before 12 months of age. The 12-23 month age group was taken for analysis because both international and GoI guidelines specify that children should be fully immunized by the time they complete their first year of life.

In NFHS-2, children who received BCG, measles, and three doses each of DPT and Polio (excluding Polio 0) are considered to be fully vaccinated. Based on information obtained from 'either source', 42% of children are fully vaccinated and 14% have not received any vaccinations. Coverage for BCG, DPT, and Polio (except Polio 0) vaccinations is much higher than the percentage fully vaccinated. According to the immunization schedule, all primary vaccinations, including measles, should be completed by the time a child is 12 months old. EXHIBIT-B shows that only 35% of all children were fully vaccinated by age 12 months. The analysis of vaccine specific data indicates much higher coverage of all vaccines in urban areas (61%) than rural areas (37%) for children age 12-23 months. The proportion fully vaccinated during the first year of life is also much higher in urban areas (52%) than rural areas (29%). Dropout rates for both DPT and Polio are lower in urban areas than in rural areas. Immunization coverage in India has improved since the time of NFHS-1 (1992-93) when the proportion of

[21] Rajan *et al* (2004).

children fully vaccinated was 36% (six percentage points increase in six years!) and the proportion who received none was 30%. But these marginal improvements indicate that achievement is lagging far behind than the goal of universal immunization programme in India.

An immunization coverage model is used in this study to estimate the effects of the selected background variables on immunization coverage. The measure of a child's immunization is a binary variable that indicates whether a child has had all six vaccinations or not. The analyses use *bivariate* (*unadjusted*) and *multivariate* (*adjusted*) *binary logit regression* analysis. The logit model is based on *cumulative logistic probability function* and it closely resembles the t distribution with 7 degrees of freedom. Logistic regression results are presented in *multiple classification analysis* (MCA) form. Unlike OLS regression, logistic regression does not assume *linearity* of relationship between the dependent and independent variables, does not require *normally* distributed variables, does not assume *homoscedasticity*, and in general has less stringent requirements.

The *multivariate binary* logit model is specified as:

$$P = F(z) = \frac{1}{1+e^{-z}} \qquad \ldots\ldots\ldots\ldots (1)$$

where $z = \alpha + \beta_1 X_1 + \beta_2 X_2 + \ldots\ldots + \beta_k X_k$. Here e represents the base of natural logarithms, which is approximately equal to 2.718 and P is the estimated probability of vaccination given X_i's. It is noteworthy that z is not the response variable but a linear function of a set of predictor variables.

$$(1) \Rightarrow \frac{P}{1-P} = e^{z} = \Omega = Odds$$

$$\text{and, } \log itP = \log\frac{P}{1-P} = z = \log\Omega = LogOdds \qquad \ldots\ldots\ldots\ldots (2)$$

$$\text{Hence, } \log\Omega = \alpha + \beta_1 X_1 + \beta_2 X_2 + \ldots\ldots + \beta_k X_k \qquad \ldots\ldots\ldots\ldots (3)$$

Thus $\log\Omega$ is calculated first, then $\Omega = e^{\log\Omega}$ and then $P = \frac{\Omega}{1+\Omega}$. P is presented in percentage form (multiplying P by 100).

Unadjusted values are calculated from logit regressions incorporating only one predictor variable. Adjusted values are calculated from logit regressions incorporating all predictor variables simultaneously. When calculating the adjusted values for a particular predictor variable, all other predictor variables are controlled by setting them to their mean values in the underlying regression[22].

Here each individual observation has a probability, and the overall likelihood is the product of these individual probabilities. Hence, *a very small likelihood does not necessarily mean a poor fit.* The *binary dependent-variable model is not likely to yield a* R^2 *close to* 1[23]. If one assumes that the true probabilities of an event occurring were uniformly distributed across a given interval, it would be possible to show an upper bound for R^2 of 1/3. Thus it is not surprising that in estimating a linear probability model one is likely to obtain a low R^2.

4. DETERMINANTS OF FULL IMMUNIZATION IN INDIA:

Children are the units of the analysis. A child data file is created by merging selected household and mother's characteristics from household and women's data files respectively. Thus, the child data file contains selected characteristics of children aged 12-23 months, selected characteristics of their mothers and selected characteristics of the households in which the mother and child reside. The analysis of immunization coverage focuses on the 10,076 children of 12-23 months of age during the Survey.

The analysis of immunization coverage uses a number of demographic and socioeconomic variables. The dependent variable is full immunization that says whether a particular child is fully immunized or

[22] For detail, see Retherford and Choe (1993).
[23] See Morrison (1972); Pindyck and Rubinfeld (1998), pp-317.

not. The selected predictor variables are sex of the child (male, female), birth order of the child (1, 2, 3, 4 and above), residence (rural, urban), mother's education (illiterate, < middle school complete, middle school complete, high school complete and above), mother's age (15-19, 20-24, 25-29, 30-49), antenatal care (yes, no), religion (Hindu, Muslim, Christian and other minorities), caste/ tribe (general, scheduled caste, scheduled tribe, other backward class[24]), standard of living index (low, medium, high), media exposure (yes, no), mother's awareness (yes, no), sex of household head (male, female), mother's empowerment index (low, medium, high), zone of states (Central, North, East, Northeast, West, South) and electricity (yes, no).

An attempt has been made to construct an indicator (*Mother's Empowerment Index* or *mindex*) to see how mother's decision-making power in the household affects the likelihood of immunization. Such an index could vary widely with changes in its components or their weights. The following six recoded variables are chosen for its construction: who decides on obtaining health care, permission needed to go to market, permission needed to visit relatives or friends, allowed to have money set aside, contribution to total family earnings and who decides how the money will be spent. Some other variables (*e.g.*, form of payment, current type of employment, *etc.*) could also have been included but these were dropped, so that the sample size is not reduced abysmally. The *method of unweighted aggregation* is followed by which the scores of the above-mentioned six recoded variables are simply added to get the scores of *mindex*. The *mindex* is then categorized as: low (0) if score ≤ 2, medium (1) if score = 3, and high (2) if score ≥ 4. Percentage distribution of *mindex* by states is shown in EXHIBIT-C. From EXHIBIT-C, it is evident that excluding Bihar, the other *Empowerment Action Group* (EAG) of states are among the bottom eight states, but the three *Northeastern* (NE)

[24] SC, ST and OBCs are those castes and tribes identified by GoI as socially and economically backward and in need of protection from social injustice and exploitation.

states (Arunachal Pradesh, Mizoram and Meghalaya) are among the top six states in terms of *mindex*.

For the variable zone of states, *Central* includes Madhya Pradesh and Uttar Pradesh; *North* includes Delhi, Haryana, Himachal Pradesh, Jammu and Kashmir, Punjab and Rajasthan; *East* includes Bihar, Orissa and West Bengal; *Northeast* includes Arunachal Pradesh, Assam, Manipur, Meghalaya, Mizoram, Nagaland and Sikkim; *West* includes Goa, Gujarat and Maharashtra; *South* includes Andhra Pradesh, Karnataka, Kerala and Tamilnadu. Media exposure includes whether a children's mother reads newspaper once a week or watches TV every week or listens to radio every day or every week. Mother's awareness includes whether discussed immunization with family planning workers or whether discussed immunization during health facility visits.

The hypothesized direction of relationship between dependent variable and each of the predictor variables are presented in EXHIBIT-D.

Before going to the regression results, it is important to look at the possible collinearities among the predictor variables to avoid the problems of *multicollinearity*. In most real life observational research (as opposed to experimental research, where treatments can be randomized), a certain amount of multicollinearity is inevitable, because most of the predictor variables (such as mother's age and birth order of children) are correlated to some extent. As a rule of thumb, when two predictor variables are correlated but both are relevant to explanation from a theoretical point of view, one should not eliminate one of the variables to reduce multicollinearity, unless the correlations are higher in absolute magnitude than about 0.8[25]. But the *Pearson Correlation Matrix* (not shown) shows the maximum correlation coefficient is 0.6 which is much less than the threshold magnitude. Also given the huge observations in

[25] Retherford and Choe (1993), pp-39-40. Hill and Adkins (2001) suggest this threshold to be 0.9 (pp-264).

the data, the present analysis enjoys the luxury of keeping all the predictor variables.

- *EFFECT ON FULL IMMUNIZATION COVERAGE IN INDIA*

There is slight gender discrimination of being vaccinated in India (see EXHIBIT-E). Chance of being fully vaccinated is 41 percent for girls and 43 percent for boys. The adjusted results indicate more poor position. Here the percentages are 39 and 43 respectively. This gender discrimination is statistically significant also. Some researchers also noted such behavior of families to neglect and discriminate female children (Das Gupta, 1987; Rajeshwari, 1996; Islam *et al*, 1996). However, Hill *et al* (1995) noted that although there are substantial mixed variations in immunization coverage by sex, the median difference across all countries is very close to zero.

There is a consistently inverse relationship between immunization coverage and birth order of a child. Majority of first-order births occur to younger women who are more likely than older women to utilize maternal and child health care services. The different likelihoods of immunization for different birth orders are also strongly significant.

One can think of two countervailing effects of increasing birth-order on likelihood of vaccination. The positive one could be some kind of *learning effect* about immunization which almost does not vary with higher birth-order. The negative one could be some kind of *negligence effect* to the higher order births and this effect perhaps increasingly increases with higher birth-order. Thus for higher order births, it seems that the *negligence effect* more than offset the *learning effect*.

Another variable namely, sex-wise birth-order is constructed to see whether likelihood of vaccination decreases with increase in birth-order for girls only or not. Likelihood (unadjusted) of vaccination decreases with increase in birth-order irrespective of sex of a child, and

surprisingly, the rate of decrease is lower for girl children except third birth-order (see EXHIBIT-E†).

Urban children are much more likely to be fully vaccinated than rural ones. The chance of being fully immunized is 37 percent for rural children whereas it is 60 percent for urban children. But the adjusted effects are almost same (41 and 42 respectively) and the rural/ urban difference is not significant. It suggests that the unadjusted effect of rural/ urban residence is actually due to the other predictor variables correlated with residence. High immunization coverage in urban areas is however supported by many researchers (Pebley *et al*, 1996; Padhi, 2001).

There is a strong positive relationship between mother's education and children's immunization coverage. The chance is almost three times higher for the children of mothers with high school or above education than the children of illiterate mothers. The adjusted effects are lower than unadjusted ones but still strongly significant and the effect levels off at higher level of education. Such positive effect of maternal education is also hypothesized by Padhi (2001), Dasai *et al* (1998), Islam *et al* (1996), Gage *et al* (1997), Pebley *et al* (1996) and Mosley *et al* (1984) though Gauri *et al* (2002) finds a spurious effect.

The variable father's education is also tried to see how likelihood of vaccination affected by it as around 60% of Indian mothers are illiterate. Effect of father's education (unadjusted) is significantly positive but its extent is less than that of mother's education (see EXHIBIT-E†).

Chance of immunization of children increases with their mother's age only up to the age group of 25-29 and then decreases. A positive relationship is also noted by Steele *et al* (1996). In the context of rural Bangladesh, Islam *et al* (1996) shows that likelihood of vaccination decreases for the mothers' older than 28 years.

Antenatal care during pregnancy has a strong positive direct effect on vaccination. The chances of immunization are a mere 18 percent for the children of mothers with no antenatal care during pregnancy and 57 percent for the children of mothers with some antenatal care. The adjusted chances are 30 percent and 48 percent respectively. Such a positive relationship is also noted by Islam *et al* (1996).

Chance of immunization varies with religion also. The likelihood of being fully immunized is 42 percent for children from Hindu household, 33 percent for children from Muslim household and 64 percent for children from Christian and other minority community household. The adjusted chances are 42, 32 and 56 percent respectively.

Caste/ tribe also affect full immunization. The chance of being fully vaccinated is 47 percent for children from general category household, 40 percent for children from SC household, 26 percent for children from ST household and 43 percent for children from OBC household. The result is also consistent with the relative order of socioeconomic status of different categories of caste/ tribe. But the adjusted chance does not mark the relative order of socioeconomic status of SCs and they are 42 percent, 44 percent, 31 percent (only significant) and 41 percent respectively. This implies that the adjusted effect ignores some important effects of other variables correlated with caste/ tribe and the unadjusted differences by caste/ tribe stem mainly from the relatively lower socioeconomic status of families belong to backward classes.

Chance of immunization increases with standard of living index of children's household. The unadjusted chances are 30 percent for children from low SLI household, 43 percent for children from medium SLI household and 65 percent for children from high SLI household. When all other predictor variables are controlled, these percentages become 39, 40 and 46 (only significant) respectively. It indicates that the effect of SLI on full immunization largely disappears, suggesting that the

unadjusted likelihoods actually reflect the effects of other variables (*e.g.*, education) that are correlated with SLI. The result is consistent with expectation as under UIP, vaccines are available free of cost. Mosley *et al* (1984) also argues for household income as a proximate determinant of immunization coverage. Islam *et al* (1996) also noted such positive relationship with household income.

Unadjusted chances of being fully vaccinated are 25 percent for children whose mothers are not exposed to mass media and 56 percent for children whose mothers have some media exposure. The adjusted likelihood is 38 percent and 43 percent respectively. This indicates that media exposure has significantly positive effect on immunization. But Gauri *et al* (2002) does not find any significant effect of media.

Mother's awareness about immunization also has significantly strong positive effect on vaccination. The unadjusted chances are 33 percent for children of unaware mothers and 58 percent for children of mothers with some awareness. Adjusted chances are 36 percent and 51 percent respectively.

Unadjusted chance of being fully immunized is 48 percent for children from households with female headship and 42 percent for children from households with male headship. But the adjusted chances are 40 percent and 41 percent (not significant) respectively. It implies that sex of household headship affects immunization mainly through other predictor variables correlated with sex of household headship. However, in the context of rural Orissa, Panda (1997) shows that children from male headship households are more likely to be immunized than those from female headship households. Moreover, he shows that the gender inequality (boys are more likely than girls) in preventive health care persists regardless of the gender of the household headship.

Both unadjusted and adjusted effects of mother's empowerment index are almost positively related to immunization coverage. The chances of being immunized are 39 percent for children of mothers with

low empowerment index, 51 percent for children of mothers with medium empowerment index and 58 percent (all significant) for children of mothers with high empowerment index for unadjusted and 41, 40 and 43 (none significant) percent respectively for adjusted. It indicates that the effect of MEI on full immunization largely disappears, suggesting that the unadjusted likelihoods actually reflect the effects of other variables (*e.g.*, mother's employment type) that are correlated with MEI.

The variable mother's employment type is also tried to see how likelihood of vaccination affected by it as most Indian mothers does not contribute to total family earnings. Likelihood (unadjusted) decreases for children whose mother is non-wage employee but increases (not significant) for children whose mother is wage employee compared to non-working mothers (see EXHIBIT-E†).

There is strong effect of zone of states on immunization. The immunization rate varies widely across different zones as well as within the same zone. Low likelihood in Northeast is mainly due to high weight given to Assam (with 233 observations out of a total of 332 observations for Northeast or 70% of the total observations) that has only 17% coverage rate of full vaccination.

Electricity also has significant effect on full immunization in India. It shows that electricity has significantly strong positive effect on immunization possibly through electronic mass media. Islam *et al* (1996) also noted such a positive relationship.

- *EFFECT ON FULL IMMUNIZATION COVERAGE IN RURAL INDIA*

Separate regressions for rural and urban areas are tried to see clearly how the effects vary due to change in place of residence in lieu of a residence dummy. These regression results are compared with the all-India 'reference' regressions. Unadjusted and adjusted effects on full immunization coverage in rural India (sample size 7795) are presented in EXHIBIT-E.

The relationship between child's birth order and likelihood of immunization becomes strictly negative here. This result indicates strong negative effect on immunization. Mother's education has a strictly positive impact on immunization. The relationship between mother's age and immunization coverage also remains same except for the last age group in adjusted case supporting that vaccination chance increases with mother's age only up to 25-29 year age group. Caste/ tribe have similar effects as before except the fact that SC children are more likely to be vaccinated. Effects of other variables remain same as the baseline regression.

- *EFFECT ON FULL IMMUNIZATION COVERAGE IN URBAN INDIA*

Unadjusted and adjusted effects on full immunization coverage in urban India (sample size 2281) are also presented in EXHIBIT-E. Gender discrimination of being fully immunized is slightly favourable to girls in urban India in contrast to the earlier results.

The positive relationship between mother's education and immunization coverage holds well in case of unadjusted case but it becomes inverted-U shaped after controls. The relationship between mother's age and immunization coverage remains inverted-U shaped as before for unadjusted case but it becomes strictly increasing after controls. Effect of caste/ tribe is consistent with the relative order of socioeconomic status of different categories of caste/ tribe except OBCs (not significant). Though the relationship between SLI of children's household and chance of immunization remains upward sloping in unadjusted case, it becomes U-shaped (not significant) after controls. Children from female-headed households are more likely to be fully immunized even after the controls. Though the relationship between mother's empowerment index and chance of immunization remains upward sloping in unadjusted case, it becomes U-shaped (not significant) after controls. Effect of zone of states remains same as before except Northeast and South zones. Electricity also affects immunization in the

same way but in higher extent. Effects of other variables remain same as the reference regression.

- *ADJUSTED EFFECT OF DEMOGRAPHIC FACTORS ON FULL IMMUNIZATION IN INDIA*

Here a separate regression is tried incorporating only the demographic factors to see their independent effect. The adjusted effects of demographic factors on full immunization coverage in India are shown in EXHIBIT-F.

Urban children are significantly more likely to be vaccinated even if rural/ urban differential vanished after controls in all-India regression. It implies that the unadjusted likelihoods for residence in all-India regression capture mainly the effects of the selected socioeconomic variables. Hence it can be assumed that the rural-urban disparity is not due to the demographic factors but the socioeconomic factors. Likelihood of immunization decreases for backward caste children according to their relative social status except SCs. Children from female-headed households are more likely to be vaccinated (not significant). Other variables have similar effects as in the all-India case.

- *ADJUSTED EFFECT OF SOCIOECONOMIC FACTORS ON FULL IMMUNIZATION IN INDIA*

Here another regression is tried incorporating only the socioeconomic factors to see their independent effect. The adjusted effects of socioeconomic factors on full immunization coverage in India are shown in EXHIBIT-G.

The relationship between mother's education and immunization becomes strictly positive here. Effect of SLI of children's family is U-shaped as in case of urban India. Mother's empowerment index affects immunization strictly positively. It implies that the unadjusted likelihoods for MEI in all-India regression capture mainly the effects of the selected demographic variables. Other variables have analogous effects as in the reference regression.

5. VACCINE-SPECIFIC AND STATE-SPECIFIC PATTERN: VARIANTS AND EXTENSIONS

- *ADJUSTED EFFECT ON DPT IMMUNIZATION COVERAGE IN INDIA*

As coverage rate is generally lower for DPT vaccine than Polio, the study attempts to explore the effects on DPT and Polio immunization separately. Here a child is immunized against DPT means that the child completed all three doses of DPT. The adjusted effects on DPT immunization coverage in India are presented in EXHIBIT-H.

The effect of mother's education becomes strictly positive here. Immunization chance increases with mother's age only up to 25-29 years age group of mothers and then decreases for children of more aged mothers. The relationship between mother's empowerment index and immunization becomes inverted-U shaped (though not significant). Other variables have similar effects as in the reference regression.

- *ADJUSTED EFFECT ON POLIO IMMUNIZATION COVERAGE IN INDIA*

Here a child is immunized against Polio means that the child completed all three doses of Polio (excluding Polio 0). The adjusted effects on Polio immunization coverage in India are presented in EXHIBIT-H.

Effect of mother's education is strictly positive. Immunization chance increases with mother's age only up to 25-29 years age group of mothers and then decreases for children of more aged mothers. Excluding SC and OBC, likelihood of immunization decreases for ST children. Other variables have analogous effects as in the reference regression.

- *ADJUSTED EFFECT ON PARTIAL IMMUNIZATION COVERAGE IN INDIA*

Partially immunization means that whether a child received any of the above-mentioned six vaccines or not. The adjusted effects on partial immunization coverage in India are shown also in EXHIBIT-H.

Likelihood increases for second birth order and then decreases (not significant) for higher birth order children. Effect of mother's education is strictly positive. Immunization chance increases with mother's age only up to 20-24 years age group of mothers and then decreases (not significant) for children of more aged mothers. Excluding OBCs,

likelihood of partial immunization decreases for ST children. The relationship between mother's empowerment index and immunization becomes inverted-U shaped. Other variables have similar effects as in the baseline regression.

- *ADJUSTED EFFECT ON FULL IMMUNIZATION IN THREE STATES OF INDIA*

Three states of India, namely Bihar, Tamilnadu and West Bengal are selected for state-level analysis. These states are selected because Bihar (11%) and Tamilnadu (89%) are two extreme cases and West Bengal (44%) is one with just above the national average (42%) in terms of coverage of full vaccination.

- *ADJUSTED EFFECT ON FULL IMMUNIZATION IN BIHAR*

The adjusted effects on full immunization coverage in Bihar are presented in EXHIBIT-I for 879 children. Higher birth order children are less likely to be vaccinated excluding second order (not significant) births. Residence has a significantly positive effect favouring urban children. Relationship between mother's education and immunization becomes inverted-U shaped. Immunization chance does not affected significantly by mother's age or antenatal care or caste/ tribe or media exposure or mother's awareness or mother's empowerment index or electricity. Chance of immunization significantly decreases for children from male-headed households compared to those from female-headed households.

- *ADJUSTED EFFECT ON FULL IMMUNIZATION IN TAMILNADU*

The likelihood of immunization is not significantly much affected by almost all the predictor variables. Chance of vaccination is almost certain for the children of Tamilnadu. Herd immunity is already achieved by Tamilnadu and in near future hopefully it will achieve *universal immunization*. The Programme managers of UIP could cite Tamilnadu as a model as far as the performance of vaccination is concerned.

The adjusted effects on full immunization coverage in Tamilnadu are presented in EXHIBIT-I for 430 children. Gender discrimination on

immunization is not significant. Residence has significantly positive impact favouring urban children. Immunization chance does not affected significantly by birth order or mother's education or religion or caste/ tribe or SLI or media exposure or mother's awareness or sex of household head or mother's empowerment index.

- *ADJUSTED EFFECT ON FULL IMMUNIZATION IN WEST BENGAL*

The adjusted effects on full immunization coverage in West Bengal are presented in EXHIBIT-I for 398 children. Gender discrimination on immunization is also not significant here. Higher birth order children are less likely to be vaccinated except the last category. Immunization chance does not affected significantly by residence or antenatal care or SLI or sex of household head. Chance of immunization skyrocketed significantly for children of at least middle school educated mothers. Likelihood increases with mother's age up to 25-29 year age group and then decreases. OBC children are least likely to be vaccinated.

- *ADJUSTED EFFECTS ON FULL IMMUNIZATION IN THREE STATE-WISE AREAS*

A backward group of states with weak socio-demographic indicators is formed as *Empowered Action Group* (EAG) consists of Bihar (including Jharkhand), MP (including Chattisgarh), Orissa, Rajasthan, and UP (including Uttaranchal). The group was formed in 2001 under the *Ministry of Health and Family Welfare* (MoHFW) to design and implement area specific programmes to strengthen the primary health care infrastructure. The group of *North-Eastern* states consists of seven states namely, Arunachal Pradesh, Assam, Manipur, Meghalaya, Mizoram, Nagaland, and Sikkim (excluding Tripura). The remaining thirteen states (AP, Goa, Gujarat, Haryana, HP, J&K, Karnataka, Kerala, Maharashtra, Punjab, TN, WB, and Delhi) are clubbed as *other* states. Immunization coverage rates are 20.1%, 20.2% and 65.7% and the sample sizes are 4244, 332 and 4359 for EAG, NE, and other group of states respectively.

Effects on full immunization for EAG, North-Eastern and other states are given in EXHIBIT-I and these are compared with the national

level effects. Male children are more likely to be vaccinated in each case. Children of higher birth-order are less likely to be vaccinated except the North-eastern children of fourth or higher birth-order (not significant). Urban children are more likely to be immunized (not significant) in each case. Children of more educated mothers are more likely to be immunized except the children of mothers with at least high school education in EAG states. The likelihood of immunization increases with mother's age up to 25-29 year age group everywhere except North-Eastern states (not significant). Children of mothers with some antenatal care are more likely to be vaccinated. Muslim children are least likely to be immunized and Christian and other minority community children are most likely to be vaccinated in each case. ST children are least likely to be vaccinated in each case except North-Eastern states (not significant). The effect of household SLI is almost positive everywhere but the North-Eastern states (not significant). Effects of media and mother's awareness are both positive. Likelihood decreases for children from male household headship in only EAG and North-eastern states (none significant). Likelihood increases with mother's empowerment index in North-eastern states and other states but the relationship becomes U-shaped for EAG states and India as a whole. Electricity has a positive effect in each case.

6. CONCLUSION AND POLICY IMPLICATIONS:

Six vaccine-preventable diseases are covered under UIP, and vaccination is given free of cost to every child in India. Though vaccines are available for free, the goals of UIP are far from being achieved after almost one and a half decades since its inception. The present study made an attempt to investigate the demographic and socio-economic determinants of immunization in India. It is possible to give a *big push* to the immunization uptake, only when one understands the demand-side factors well, to achieve the chartered goals of UIP.

- *FINDINGS OF THE STUDY*:

The study analyses the effects of some selected demographic and socioeconomic predictor variables on the chance of immunization of a child. It focuses on immunization coverage for children (a) in all India, (b) in rural and urban areas in India, (c) for DPT, Polio and partial immunization for all India, (d) for three groups of states, namely, *Empowered Action Group*, *North-eastern* and *other* states, and (e) for three states namely, Bihar, Tamilnadu (two extremes in immunization coverage performance) and West Bengal (national average). The study applies *binary bivariate* and *multivariate logit* model to *National Family Health Survey-2* (1998-99) data. Excepting a few cases, the results are very much consistent across the different models.

ROBUST RESULTS:

- Boys are more likely to be immunized than girl children.
- Children of higher-order births are less likely to be vaccinated. This is true irrespective of the sex of a child, but the rate of decrease is higher for girl children, except third birth-order. It seems that the *negligence effect* more than offset the *learning effect*. The result perhaps shows the apathy on part of the parents to immunize their children of higher-order births.
- The likelihood of immunization is higher for children from urban areas.
- Likelihood of vaccination increases with mother's education level, mother's age up to 29 years, mother's exposure to mass media and mother's awareness about immunization.
- Some antenatal care during pregnancy raises immunization chances significantly. This increases possibility to meet health personnel who help mothers to raise awareness by disseminating information regarding immunization.

- Among the religious groups, Muslim children are least likely to be immunized whereas children from Christian and other religious minority communities are most likely to be immunized.
- Immunization chance increases with the standard of living index of children's household.
- Children from the West zone are most likely to be immunized, followed by South, North, East, Central and Northeast respectively.
- Children from households with electricity are more likely to be immunized.

TENTATIVE[26] *RESULTS*:

- Compared to general caste children, OBCs are less likely to be immunized, followed by the SCs and STs. Likelihood is least for ST children in India as a whole, eight EAG and thirteen *other* states, and for OBC children in seven North-eastern states.
- Possibility of immunization is higher for children in female-headed households.
- Likelihood of immunization increases with mother's empowerment index. In North-eastern and other states, the relationship between mother's empowerment index and likelihood of immunization is upward sloping but it becomes U-shaped for EAG states and India as a whole.

- *BROAD POLICY AREAS*:

The need of the hour is an equitable, participatory and intersectoral approach to health and health care (Bose, 2001). Provision of vaccination should not be treated as the sole responsibility of the health sector. Policies and programmes in other sectors such as education, welfare, industry, labour, information, environment, etc. have also to be informed and influenced by public health considerations

[26]: These results are not consistent across different models.

(Gopalan, 1994). To reach the goal of UIP in India, the policy managers should also try to:

- Enhance (female) education through *Education for All* and incorporate primary health information in the curricula.
- Generate enough employment opportunity supported by the Government (*e.g.*, some kind of *Employment Guarantee Programme*).
- Increase infrastructure to provide antenatal care universally.
- Spread more and more basic information regarding vaccination through electronic mass media.
- Enhance coverage in EAG and North-eastern states by organizing more sub-national immunization days (SNIDs).
- Spread news to break religious misbeliefs against vaccination.
- Raise number of health personnel to improve mother's awareness.
- Provide urban facilities in rural areas if possible with the help of corporate social responsibility.
- Provide electricity to every village if possible through non-conventional energy resources.
- Promote small family norm and discourage early marriage.

Some supply-side facility enhancement can also improve demand for vaccination. For example, physician and clinic hours might be increased to reduce waiting time of the parents to immunize their children or introduction of mobile units in thinly populated rural areas to minimize travel time of parents to curtail their economic disincentives.

Higher budgetary allocation for preventive care might improve immunization coverage but only in the short run. But as immunization is a long term process, one should give thrust to improve its demand given the meagre Central as well as State budgetary allocation on health sector as a whole for decades and evaporating *aids* and *soft loans* from international organizations.

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APPENDIX:

EXHIBIT-A: CHILD DEATHS CAUSED BY SELECTED VIPS, 2002

Cause of Death	Children under five	Children five and older
Diphtheria	4,000	1,000
Measles	540,000	71,000
Neonatal Tetanus	180,000	—
Pertussis	294,000	—
Tetanus (excluding neonatal tetanus)	18,000	15,000

Source: UNICEF, 2005, pp-vii.

EXHIBIT-B: CHILDHOOD IMMUNIZATION BY SOURCE OF INFORMATION

Percentage of children age 12-23 months who received specific vaccinations at any time before the interview and before 12 months of age by source of information on vaccination history and residence, India, 1998-99

Source information	Percentage vaccinated											Number of children
	BCG	Polio 0	DPT 1	DPT 2	DPT 3	Polio 1	Polio 2	Polio 3	Measles	All[1]	None	
A	**URBAN**											
Vaccination Card	96.6	33.0	98.9	96.4	91.1	98.5	96.0	90.8	81.0	77.5	0.1	1048
Mother's report	78.4	14.9	75.3	69.5	58.3	86.9	83.7	67.5	59.2	46.0	11.7	1233
Either source	86.8	23.3	86.1	81.9	73.4	92.2	89.4	78.2	69.2	**60.5**	6.4	2282
B	85.1	23.3	83.6	79.1	70.6	89.4	86.1	74.9	59.7	**51.9**	8.6	2282
A	**RURAL**											
Vaccination Card	94.5	19.8	98.4	91.4	83.0	97.9	91.1	83.0	69.7	65.4	0.1	2344
Mother's report	55.3	5.9	53.7	46.6	35.5	73.8	68.0	47.7	34.8	24.3	23.9	5450
Either source	67.1	10.1	67.1	60.1	49.8	81.1	75.0	58.3	45.3	**36.6**	16.7	7795
B	64.3	10.1	64.4	57.0	46.6	77.5	71.1	54.4	36.2	**29.3**	20.2	7795
A	**TOTAL**											
Vaccination Card	95.2	23.9	98.6	92.9	85.5	98.1	92.6	85.4	73.2	69.1	0.1	3393
Mother's report	59.6	7.6	57.6	50.8	39.7	76.2	70.9	51.3	39.3	28.3	21.6	6684
Either source	**71.6**	**13.1**	71.1	65.0	**55.1**	83.6	78.2	**62.8**	**50.7**	**42.0**	**14.4**	10076
B	69.1	13.1	68.8	62.1	52.1	80.3	74.6	59.2	41.7	**34.5**	17.5	10076

Note: Table includes only surviving children from among the two most recent births in the three years preceding the survey. [1]: BCG, measles, and three doses each of DPT and Polio vaccines (excluding Polio-0).**A: Vaccinated any time before the interview, B: Vaccinated by 12 months of age** (for children whose information was based on the mother's report, the proportion of vaccinations given by 12 months of age is assumed to be the same age for children with a written record of vaccination).

Source: NFHS-2, India, table-6.9, pp-204

EXHIBIT-C: PERCENTAGE DISTRIBUTION OF MOTHER'S EMPOWERMENT INDEX BY STATES

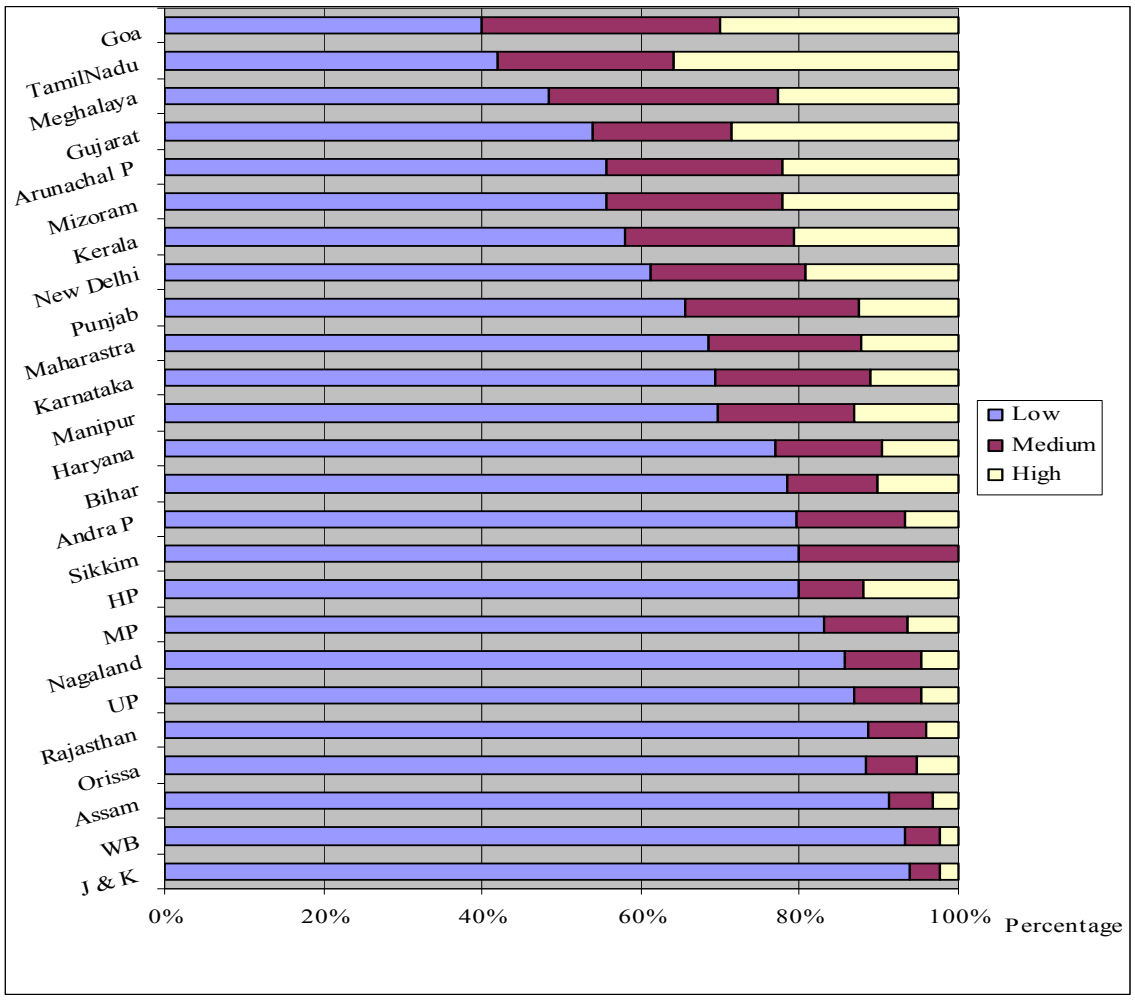

EXHIBIT-D: HYPOTHETICAL RELATIONSHIP OF VARIABLES WITH FULL IMMUNIZATION

Variable	Variable Name	Hypothesized Sign
Sex of child	sexchi	+
Birth order	border	+
Residence	res	+
Mother's education	medu	+
Mother's age	mage	+
Antenatal care	antcare	+
Religion	religion	+/-
Caste/ Tribe	cast	+/-
Std. of Living Index	stdliv	+
Media Exposure	media	+
Mother's awareness	maware	+
Sex of HH-Head	sexhead	-
Mother's Empowerment Index	mindex	+
Zone	zone	+/-
Electricity	elect	+

EXHIBIT-E: SUMMARY OF EFFECTS (P IN %) ON FULL IMMUNIZATION COVERAGE

Background Variables		India		Rural		Urban	
		Unadjusted	**Adjusted**	**Unadjusted**	**Adjusted**	**Unadjusted**	**Adjusted**
Sex of child	Female[#]	**41***	**39**	**35***	**31**	**61***	**64**
	Male	**43****	**43****	**38***	**34***	**60**	**63**
Birth order	1[#]	**54***	**49**	**48*****	**42**	**69***	**71**
	2	**49***	**43***	**44***	**36***	**65****	**64****
	3	**39***	**35***	**34***	**29***	**58***	**59***
	4+	**24***	**35***	**22***	**24***	**38***	**49***
Residence	Rural[#]	**37***	**41**	—	—	—	—
	Urban	**60***	**42**	—	—	—	—
Mother's Education	Illiterate[#]	**28***	**36**	**26***	**29**	**39***	**51**
	Lit, <mid	**52***	**45***	**48***	**36***	**65***	**67***
	Mid sch.	**63***	**52***	**59***	**43***	**71***	**71***
	High sc+	**73***	**52***	**69***	**44***	**76***	**69***
Mother's age	15-19[#]	**37***	**28**	**35***	**22**	**47**	**45**
	20-24	**45***	**38***	**40***	**30***	**61***	**58***
	25-29	**46****	**47***	**40***	**39***	**64***	**66***
	30-49	**33***	**47***	**25***	**36***	**60***	**74***
Antenatal care	No[#]	**18***	**30**	**17***	**23**	**28***	**52**
	Yes	**57***	**48***	**53***	**41***	**66***	**65***
Religion	Hindu[#]	**42***	**42**	**37***	**33**	**63***	**65**
	Muslim	**33***	**32***	**25***	**25***	**49***	**55***
	Christ &	**64***	**56***	**59***	**49***	**77***	**69**
Caste/ Tribe	General[#]	**47***	**42**	**40***	**34**	**63***	**64**
	SC	**40***	**44**	**37*****	**37*****	**53***	**62**
	ST	**26***	**31***	**24***	**23***	**46***	**51*****
	OBC	**43***	**41**	**38**	**32**	**63**	**65**
Standard of Living Index	Low[#]	**30***	**39**	**29***	**31**	**43***	**65**
	Medium	**43***	**40**	**39***	**33**	**57***	**60**
	High	**65***	**46***	**58***	**37****	**72***	**66**
Media Exposure	No[#]	**25***	**38**	**24***	**30**	**38***	**61**
	Yes	**56***	**43***	**52***	**35***	**65***	**64**
Mother's Awareness	No[#]	**33***	**36**	**28***	**28**	**52**	**56**
	Yes	**58***	**51***	**53***	**42***	**72***	**71***
Sex of HH-Head	Female[#]	**48**	**40**	**40***	**32**	**65***	**64**
	Male	**42***	**41**	**36*****	**33**	**60**	**63**
Mother's Empowerment Index	Low[#]	**39***	**41**	**34***	**32**	**56***	**63**
	Medium	**51***	**40**	**44***	**32**	**68***	**62**
	High	**58***	**43**	**50***	**34**	**72***	**65**
Zone	Central[#]	**22***	**28**	**19***	**23**	**36***	**42**
	North	**43***	**39***	**36***	**31***	**58***	**58***
	East	**27***	**31*****	**25***	**25**	**44****	**46**
	Northeast	**20**	**21****	**17**	**15***	**46**	**45**
	West	**71***	**66***	**68***	**61***	**75***	**76***
	South	**70***	**60***	**66***	**52***	**79***	**77***
Electricity	No[#]	**24***	**37**	**24***	**30**	**32***	**46**
	Yes	**57***	**44***	**52***	**36***	**63***	**65***

[#]: Reference category; Significance level: ***10%, **5%, *1%.

EXHIBIT-E[†]: UNADJUSTED EFFECTS ON FULL IMMUNIZATION COVERAGE IN INDIA

Background Variables		P (in%)
Sex-wise Birth-order	Female, Birth-1[#]	**53****
	Female, Birth-2	**49****
	Female, Birth-3	**36***
	Female, Birth-4	**23***
	Male, Birth-1	**55**
	Male, Birth-2	**49*****
	Male, Birth-3	**42***
	Male, Birth-4	**25***
Father's Education	Illiterate[#]	**27***
	Lit, < mid. sch.	**40***
	Middle sch. comp.	**47***
	High sch. & +	**56***
Mother's Employment	Not working[#]	**43***
	Work, non-wage	**36***
	Work, wage	**44**

EXHIBIT-F: ADJUSTED EFFECTS OF DEMOGRAPHIC FACTORS IN INDIA

Background Variables		β	$SE.$	$\log\Omega$	Ω	P (in %)
Sex of child	Female[#]			-0.494	0.610	**38**
	Male	0.122**	0.048	-0.372	0.689	**41****
Birth order	1[#]			0.116	1.123	**53**
	2	-0.338*	0.066	-0.222	0.801	**44***
	3	-0.771*	0.079	-0.655	0.519	**34***
	4+	-1.219*	0.087	-1.103	0.332	**25***
Residence	Rural[#]			-0.511	0.600	**38**
	Urban	0.349*	0.059	-0.162	0.851	**46***
Mother's age	15-19[#]			-1.185	0.306	**23**
	20-24	0.604*	0.082	-0.581	0.559	**36***
	25-29	1.063*	0.094	-0.122	0.885	**47***
	30-49	1.073*	0.111	-0.112	0.894	**47***
Antenatal care	No[#]			-1.103	0.332	**25**
	Yes	1.077*	0.057	-0.026	0.975	**49***
Religion	Hindu[#]			-0.388	0.679	**40**
	Muslim	-0.512*	0.074	-0.900	0.407	**29***
	Christ and minorities	0.702*	0.116	0.314	1.370	**58***
Caste/ Tribe	General[#]			-0.271	0.763	**43**
	SC	-0.140**	0.070	-0.411	0.663	**40****
	ST	-0.746*	0.098	-1.017	0.362	**27***
	OBC	-0.192*	0.061	-0.463	0.629	**39***
Sex of HH-Head	Female[#]			-0.406	0.667	**40**
	Male	-0.028	0.097	-0.434	0.648	**39**
Zone	Central[#]			-1.082	0.339	**25**
	North	0.617*	0.081	-0.465	0.628	**39***
	East	0.116	0.072	-0.966	0.381	**28**
	Northeast	-0.353**	0.160	-1.435	0.238	**19****
	West	1.771*	0.082	0.689	1.991	**67***
	South	1.540*	0.075	0.458	1.581	**61***
Constant		-1.869*	0.137	-1.869	0.154	13
N	**10017**			**Cox & Snell** R^2		**0.270**
Model χ^2	**3127.49***			**Nagelkerke** R^2		**0.363**

[#:] Reference category; Significance level: **5%, *1%.

EXHIBIT-G: ADJUSTED EFFECTS OF SOCIOECONOMIC FACTORS IN INDIA

Background Variables		β	*S.E.*	$\log\Omega$	Ω	P **(in %)**
Mother's Education	Illiterate[#]			-0.786	0.456	**31**
	Lit, < mid. sch. com.	0.677*	0.063	-0.109	0.897	**47***
	Middle sch. comp.	0.994*	0.083	0.208	1.232	**55***
	High sch. comp. & +	1.240*	0.082	0.454	1.575	**61***
Standard of Living Index	Low[#]			-0.265	0.767	**43**
	Medium	-0.205*	0.058	-0.470	0.625	**38***
	High	-0.177**	0.087	-0.442	0.643	**39****
Media Exposure	No[#]			-0.678	0.508	**34**
	Yes	0.524*	0.056	-0.154	0.857	**46***
Mother's Awareness	No[#]			-0.699	0.497	**33**
	Yes	0.864*	0.048	0.165	1.179	**54***
Mother's Empowerment Index	Low[#]			-0.465	0.628	**39**
	Medium	0.265*	0.070	-0.200	0.819	**45***
	High	0.407*	0.077	-0.058	0.944	**49***
Electricity	No[#]			-0.893	0.409	**29**
	Yes	0.907*	0.055	0.014	1.014	**50***
Constant		-1.833*	0.051	-1.833	0.160	14
N	**9951**			**Cox & Snell** R^2		**0.206**
Model χ^2	**2295.86***			**Nagelkerke** R^2		**0.277**

[#]: Reference category; Significance level: ***10%, **5%, *1%.

EXHIBIT-H: ADJUSTED EFFECTS (P IN %) ON DPT, POLIO AND PARTIAL IMMUNIZATION COVERAGE IN INDIA

Background Variables		DPT	Polio	Partial
Sex of child	Female[#]	**58**	**67**	**93**
	Male	**61****	**68**	**94***
Birth order	1[#]	**66**	**73**	**93**
	2	**62****	**70*****	**94*****
	3	**54***	**64***	**93**
	4+	**51***	**61***	**92**
Residence	Rural[#]	**59**	**67**	**93**
	Urban	**61**	**69**	**93**
Mother's Education	Illiterate[#]	**52**	**63**	**90**
	Lit, < mid. sch. com.	**62***	**70***	**93***
	Middle sch. comp.	**71***	**74***	**95***
	High sch. comp. & +	**73***	**77***	**98***
Mother's age	15-19[#]	**49**	**60**	**92**
	20-24	**57***	**67***	**94****
	25-29	**64***	**71***	**93**
	30-49	**62***	**69***	**92**
Antenatal care	No[#]	**47**	**57**	**89**
	Yes	**66***	**73***	**95***
Religion	Hindu[#]	**60**	**68**	**94**
	Muslim	**49***	**60***	**90***
	Christ and minorities	**74***	**78***	**94**
Caste/ Tribe	General[#]	**61**	**67**	**93**
	SC	**62**	**70*****	**93**
	ST	**45***	**59***	**90***
	OBC	**60**	**70****	**94***
Standard of Living Index	Low[#]	**56**	**65**	**92**
	Medium	**59*****	**68****	**93****
	High	**65***	**72***	**95***
Media Exposure	No[#]	**55**	**66**	**92**
	Yes	**62***	**69*****	**94***
Mother's Awareness	No[#]	**53**	**63**	**89**
	Yes	**70***	**76***	**97***
Sex of HH-Head	Female[#]	**57**	**68**	**93**
	Male	**59**	**68**	**93**
Mother's Empowerment Index	Low[#]	**59**	**67**	**93**
	Medium	**60**	**68**	**94**
	High	**57**	**69**	**92**
Zone	Central[#]	**45**	**58**	**89**
	North	**50****	**62****	**91**
	East	**47**	**59**	**93***
	Northeast	**42**	**46***	**84***
	West	**79***	**81***	**97***
	South	**79***	**81***	**96***
Electricity	No[#]	**57**	**64**	**92**
	Yes	**61****	**70***	**94***

[#]: Reference category; Significance level: **5%, *1%.

EXHIBIT-I: ADJUSTED EFFECTS (P IN %) ON FULL IMMUNIZATION COVERAGE

Variables		Bihar	TN	WB	India	EAG States	N-E States	Other States
Sex of child	Female[#]	**6**	**93**	**40**	**39**	**15**	**11**	**68**
	Male	**9****	**94**	**44**	**43****	**18***	**19*****	**69**
Birth order	1[#]	**10**	**95**	**52**	**49**	**21**	**18**	**76**
	2	**11**	**92**	**44**	**43***	**20**	**15**	**69***
	3	**9**	**95**	**30***	**35***	**17****	**8**	**63***
	4+	**4****	**88**	**32****	**35***	**12***	**17**	**57***
Residence	Rural[#]	**7**	**90**	**43**	**41**	**16**	**14**	**68**
	Urban	**13****	**97****	**35**	**42**	**19**	**22**	**69**
Mother's Education	Illiterate[#]	**7**	**92**	**37**	**36**	**15**	**11**	**62**
	Lit, < mid. sch. com.	**11**	**93**	**37**	**45***	**19****	**16**	**71***
	Middle sch. comp.	**13*****	**89**	**63***	**52***	**28***	**19**	**74***
	High sch. comp. & +	**12*****	**97**	**65***	**52***	**25***	**39***	**76***
Mother's age	15-19[#]	**7**	**86**	**36**	**28**	**11**	**23**	**56**
	20-24	**6**	**93*****	**45**	**38***	**14*****	**15**	**67***
	25-29	**9**	**95****	**50*****	**47***	**20***	**16**	**73***
	30-49	**10**	**93**	**25**	**47***	**21***	**11**	**71***
Antenatal care	No[#]	**7**	**85**	**34**	**30**	**14**	**9**	**56**
	Yes	**9**	**94*****	**43**	**48***	**23***	**20****	**70***
Religion	Hindu[#]	**9**	**93**	**48**	**42**	**18**	**16**	**70**
	Muslim	**3***	**97**	**29***	**32***	**11***	**10**	**59***
	Christ and minorities	**50*****	**84**	**56**	**56***	**39***	**21**	**75*****
Caste/ Tribe	General[#]	**8**	**99**	**41**	**42**	**18**	**19**	**67**
	SC	**9**	**92**	**46**	**44**	**19**	**15**	**69**
	ST	**2**	**93**	**51**	**31***	**12****	**12**	**60****
	OBC	**8**	**94**	**16***	**41**	**16**	**10**	**73***
Standard of Living Index	Low[#]	**6**	**95**	**43**	**39**	**14**	**17**	**69**
	Medium	**11****	**91**	**41**	**40**	**18***	**14**	**66**
	High	**11**	**96**	**41**	**46***	**19****	**13**	**74*****
Media Exposure	No[#]	**7**	**92**	**37**	**38**	**16**	**12**	**67**
	Yes	**9**	**94**	**46*****	**43***	**18**	**19**	**69**
Mother's Awareness	No[#]	**7**	**91**	**27**	**36**	**15**	**14**	**62**
	Yes	**10**	**94**	**52***	**51***	**22***	**20**	**74***
Sex of HH-Head	Female[#]	**15**	**97**	**43**	**40**	**19**	**19**	**65**
	Male	**7*****	**93**	**42**	**41**	**17**	**15**	**69**
Mother's Empowerment Index	Low[#]	**8**	**93**	**42**	**41**	**17**	**14**	**67**
	Medium	**5**	**96**	**26*****	**40**	**13****	**16**	**72****
	High	**7**	**92**	**55**	**43**	**15**	**28**	**73***
Electricity	No[#]	**8**	**88**	**39**	**37**	**15**	**14**	**59**
	Yes	**7**	**94****	**51****	**44***	**20***	**16**	**72***

[#]: Reference category; Significance level: ***10%, **5%, *1%.

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A systematic review of national immunization policy making processes☆

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ABSTRACT

This systematic review aimed to collect and synthesize information available on immunization policy making processes in countries across the globe. Twenty-nine published articles and five websites in either English or French provided varied information on the immunization policy making processes in 33 countries. The information retrieved varied from players involved to types of evidence used when making immunization policies. Fourteen countries reported the presence of a National Immunization Technical Advisory Group (NITAG), an advisory body that provides immunization recommendations to the national government to facilitate their policy making. In conclusion, there is relatively limited information available on immunization policy making processes at the national level.

1. Introduction

Although virtually all countries have a National Immunization Program of some kind, the processes leading to decisions on which vaccines to include are not well described. Yet it is important to understand how vaccine policies are developed given the amount of money spent on vaccines, the increased prices of newer vaccines, the fact that vaccines guard against some of the most deadly diseases, and that they are among the most effective of public health interventions. To facilitate the immunization policy making process, some countries have established national technical advisory bodies, often referred to as National Immunization Technical Advisory Groups (NITAGs). These are ideally independent, expert advisory committees that provide technical advice on vaccines and immunizations and make recommendations to guide policy makers and program managers [1]. As information on the presence, characteristics and functioning of these groups appeared limited, we conducted a systematic review of all information available on immunization policy making processes at the national level, including the presence and characteristics of NITAGs.

2. Methods

2.1. Eligibility criteria

Publications, reports and government websites were eligible for inclusion in this review if they contained a description of the process of immunization policy making at a national level. Countries were defined as member states of the World Health Organization (WHO) for the purpose of this article [2]. Because the primary author (MB) has working knowledge of English and French, publications, reports and websites in these languages were eligible for inclusion. Additional eligibility criteria included:

1. Description of immunization policy making processes including players and/or factors involved.
2. The processes described must be that of the national level of a specified country.

2.2. Search strategy

The search strategy was developed in the database Medline using the OVID platform and adapted to another database, Global Health. The search strategies combined a search for immunization or vaccination as well as a search for policy making or decision making in Medline (1950–April Week 2, 2008) and Global Health (formerly CAB Health) (1973–April 19, 2008) (Fig. 1). The search strategies were not restricted by language or date.

The secondary references of eligible studies were screened to determine if any of the references could potentially be included in the review.

Abbreviations: NITAG, National Immunization Technical Advisory Groups; UK, United Kingdom; USA, United States of America; WHO, World Health Organization.

☆ One of the authors is a staff member of the World Health Organization. The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions, policy or views of the World Health Organization.

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OVID Medline

#1 ((((immuni* or vaccin* or innoculat*) in ti,ab) or ((explode "Immunization-" / all SUBHEADINGS in MIME,MJME,PT) or (explode "Vaccines-" / all SUBHEADINGS in MIME,MJME,PT) or (explode "Immunization-Programs" / all SUBHEADINGS in MIME,MJME,PT)))

#2 ((((mak* or responsib* or authori*) near3 (policy or policies or decision*)) in ti,ab) or ((explode "Decision-Making" / all SUBHEADINGS in MIME,MJME,PT) or ("Policy-Making" / WITHOUT SUBHEADINGS in MIME,MJME,PT))))

#1 and #2

Global Health

1) TI mak* N3 polic* or TI responsib* N3 polic* or AB mak* N3 polic* or AB responsib* N3 polic*

2) TI mak* N3 decision or TI responsib* N3 decision or AB mak* N3 decision or AB responsib* N3 decision

3) TI immuni* or AB immuni* or TI vaccin* or AB vaccin* or TI innoculat* and AB innoculat*

4) TI authori* N3 polic* or TI authori* N3 decision or AB authori* N3 decision or AB authori* N3 polic*

5) decision making or policy making

6) 1 or 2 or 4 or 5

7) 6 & 3

Fig. 1. Search strategies.

The search for grey literature was limited to the search of government websites and contact with experts. Experts who had recently worked in the topic area with the WHO headquarters were asked if they knew of any publications or reports on the topic that were not retrieved through the literature search.

The government websites of the 193 member states of the WHO were searched for information on the immunization policy development processes of the countries. When possible, government websites were accessed using a list of national government websites created by the University of Michigan [3]. When the country was not listed on this website, government websites were searched for using the Google search engine with the key words of "government" and "official" and the name of the country [4]. Once the government official website was accessed, the information on immunization policy development processes was sought by navigating through Ministry of Health or Public Health websites and other relevant pages such as that of immunizations and vaccines. The search of websites was also restricted to those in English or French.

2.3. Selection of publications

All titles and abstracts (when available) of the citations identified were screened by two reviewers independently. All records that were identified as potentially relevant were obtained in full text. If there was disagreement between the reviewers as to which citations qualified for inclusion, the citation was included and the full text was obtained. The full text articles were screened by the two reviewers independently in accordance with the inclusion criteria.

2.4. Quality assessment

Because this systematic review was descriptive in nature and did not include clinical trials or qualitative research, the quality assessment of reports did not include the traditional components used to assess the quality of intervention or qualitative studies. The author's affiliation and the sponsorship of the article was used as an indication of potential conflict of interest, as well as the date of publication as an indication of the extent that the information may be dated.

3. Results

3.1. Selection of published information

The literature search yielded 1530 potential publications for inclusion in this review. Ovid Medline yielded 1213 of the citations and Global Health another 317. Of the citations, 128 papers (94 from Medline and 34 from Global Health) were retrieved as potential candidates for inclusion based on their titles and abstracts. After review of the full papers, only 26 publications contained descriptions of immunization policy making processes at a national level. Eight of the publications were retrieved from both Medline and Global Health [5–12], while another 14 publications were retrieved from Medline only [13–26], and another four from Global Health only [27–30].

Beyond the 26 publications obtained through the literature search, 3 additional publications were included: one from reference sections of the included papers [31], one was provided through contact with an expert in the area [32], and one from the Canadian website on their NITAG. It is unknown why these publications were not obtained through the search strategy.

The websites of five of the countries provided information on national immunization policy development: Australia [33], Canada [34], New Zealand [35], the United Kingdom (UK) [36], and the United States of America (USA) [37]. Therefore, this review is based on the content of 29 publications and 5 websites.

Table 1
Characteristics of policy processes and National Immunization Technical Advisory Group (NITAG) by country with information available on immunization policy development[a].

Country	NITAG	Core members	Defined term limit for members (years)	Declare conflicts of interest	Meetings per year	Nature of meetings	Meeting minutes published on the internet	Method of final decision making	Other group that makes immunization recommendations [b]
Australia	Yes				3	Closed	Yes		
Austria	Yes	16	3		3		No		
Belgium									Yes
Brazil	Yes								
Bulgaria									Yes
Cambodia									Yes
Canada	Yes	12	4	Yes	3	Closed	Yes	Vote	
Denmark									Yes
France	Yes	16			6–8	Closed	No		
Germany	Yes	17			2				
Greece									Yes
Ireland	Yes		No		6	Closed	No	Consensus	
Italy	Yes								
New Zealand	Yes								
Luxembourg									Yes
Norway									Yes
Papua New Guinea									Yes
Portugal									Yes
Spain	Yes		No					Consensus	
Slovakia									Yes
Slovenia									Yes
Sweden									Yes
Switzerland	Yes	15	4		5	Closed	No	Vote	
Thailand									Yes
The Netherlands	Yes								
UK	Yes	16	4	Yes	3	Closed	Yes	Vote	
USA	Yes	15	4	Yes	3	Open	Yes	Vote	

[a] Blank fields indicate that information was not available—also limited information was available on Argentina, China, Finland, Iceland, Mali, and Poland but not related to the information in this table.
[b] Unknown if these groups are NITAGs as defined in this paper.

3.2. Characteristics of included publications

The 29 publications and 5 websites from which information was abstracted contained information to varying degrees on immunization policy decision making processes in 33 of the 193 WHO member states: Argentina [19], Australia [10,13,23,33], Austria [20,32], Belgium [20], Brazil [5], Bulgaria [20], Cambodia [8], Canada [10,14,31,34,38], China [27], Denmark [15,20], Finland [20], France [17,20,32], Germany [20,32], Greece [20], Iceland [20], Ireland [17,32], Italy [20,32], Luxembourg [20], Mali [9], New Zealand [6,30,35], Norway [12,20], Papua New Guinea [28], Poland [20], Portugal [10,20], Slovakia [20], Slovenia [20], Spain [17,20,32], Sweden [17,20,32], Switzerland [10,17,32], Thailand [7], The Netherlands [10,11,14,20,32], the UK [17,20,24,26,32,36], and the USA [16,18,21,22,25,26,29,37]. The most detailed information was found in publications concerning immunization policy making processes in the UK [24] and the USA [25] as well as on the websites of Australia [33], Canada [34], the UK [36], and the USA [37].

Two publications focused primarily on the process of immunization policy making within a country (the UK and the USA) and discussed a NITAG in detail [24,25]. Fourteen of the publications mentioned NITAGs in the context of discussing a specific issue such as a specific vaccine but did not offer much information on the NITAG [5,6,10,13,14,18,19,21–23,26,29–31]. The five websites provided extensive information on the NITAGs in Australia [33], Canada [34], New Zealand [35], the UK [36], and the USA [37].

3.3. Quality assessment

All authors stated affiliations which were consistent with vaccine policy stakeholders. These included members of the Ministry of Health or local universities and often both. Only two of the publications in this review were sponsored by pharmaceutical companies [6,12]. A publication from New Zealand was a collaboration between the national government, Chiron Vaccines, and the University of Auckland but provided only the fact that a NITAG exists [6]. A study from Norway was sponsored by Wyeth Lederle [12], but focused on a cost effectiveness analysis of the 7-valent pneumococcal conjugate vaccine. It is unlikely that the sponsorship of either of these papers affected the quality of the publication with respect to this review.

3.4. National policy development processes

Information was retrieved on the immunization decision making processes in 33 countries (Table 1). Belgium [20], Bulgaria [20], Cambodia [8], Denmark [15,20], Greece [20], Luxembourg [20], Norway [20], Papua New Guinea [28], Portugal [10], Slovakia [20], Slovenia [20], and Sweden [17,32] reported groups which make immunization recommendations to the government. However it was unclear from the information collected if these groups were NITAGs that are independent from the national government as defined by the WHO [1]. Cambodia has a national level immunization technical working group that identifies, implements, and monitors National Immunization Programs in Cambodia [8]. However, the members listed are government officials and representatives of international donors. In Papua New Guinea, the National Pediatric Society makes recommendations and publishes guidelines that serve as standards of care by the Health Department [28]. Denmark has a National Board of Health [15,20], Portugal has the National Vaccination Plan committee [10] and Sweden has a governmental advisory agency [15,32] that make national immunization recommendations. The National Board of Health in Denmark conducts a medical technology assessment [15] and mathematical modeling [20] when making immunization policy decisions. This board considers various types of evidence (Table 2).

Table 2
Factors considered by countries when making recommendations by presence of National Immunization Technical Advisory Groups reported[a].

Factors considered when making recommendations	Countries with NITAG	Other countries
Burden of disease	Canada [31,34] Netherlands [14,32] Spain [32] USA [37]	Argentina [19] China [27] Denmark [20] Finland [20] Iceland [20] Mali [9] Portugal [20] Poland [20] Sweden [20,32]
Economic evaluation	Canada [10,34] Netherlands [10,11,32] Switzerland [32] UK [24,36] USA [37]	Argentina [19] China [27] Denmark [20] Finland [20] Iceland [20] Luxembourg [20] Norway [12] Portugal [20] Sweden [20]
Feasibility of local vaccine production		China [27]
Feasibility of recommendation	Canada [31]	Argentina [19]
Recommendations of other countries	Brazil [5] Canada [34] Switzerland [32] UK [37]	
Public perception		Argentina [19] Denmark [20]
Vaccine safety	Canada [14] Spain [32] USA [37]	Argentina [19]
Vaccine effectiveness	Canada [14] Spain [32] USA [37]	Argentina [19]

[a] Additional factors may be considered in process. This table presents factors specifically reported.

The advisory committee in Norway also uses mathematical modeling when making immunization policy decisions [20]. In the USA, although they have the Advisory Committee on Immunization Practices (which is an independent NITAG), they also have the American Academy of Pediatrics [22,29], the American Academy of Family Physicians [20,22], the American College of Gynecologists and Obstetricians [25], and the American College of Physicians [25] all of whom make immunization recommendations. Efforts are made to harmonize recommendations between these groups [25].

The information retrieved on Thailand concerned the development of the national hepatitis B immunization policy in which many players were involved [7]: the Ministry of Public Health's Department of Communicable Disease Control, the Thai Medical Association, the pharmaceutical industry, and the media. A committee was formed with representations of government, as well as various institutes and associations. It could not be determined from the publication whether this committee and these groups are involved in making all immunization policy decisions, or were only involved for this one vaccine.

The information obtained on the remaining eight countries relates to the types of evidence used when making decisions (Table 2). Burden of disease and economic assessment are the most commonly reported types of evidence used by countries when making immunization policies.

3.5. National Immunization Technical Advisory Groups

While many countries may have established NITAGs, their presence was reported in only 14 countries (Australia [10,13,23,33], Austria [17,20,32], Brazil [5], Canada [10,31,34,38], France [17,20,32], Germany [17,20,32], Ireland [17,32], Italy [17,32], New Zealand [6,30,35], Spain [17,20,32], Switzerland [17,32], The Netherlands [10], the UK [17,20,24,26], and the USA [16,18,21,22,25,26,29,37]). There were no reports of NITAGs which had been in existence but were no longer functioning.

Generally, the NITAGs in each country provided advice and guidance to the government on the administration of vaccines to the population. For example, the terms of reference for the Australian NITAG are to provide technical advice on the administration of vaccines available in Australia, advise on and assess the evidence available on existing, new and emerging vaccines, produce the Australian Immunization Handbook, and consult with partners on matters relating to the implementation of the Australian Immunization Program [33].

It is unknown when most of the NITAGs were established, as the dates of the creation of the NITAGs were only provided for 5 of the 14 countries. The NITAG in the UK was established in 1963 [24,36], Canada [34] and the USA [25] in 1964, France in 1997 [32], and Switzerland in 2004 [32]. Although the exact year is not reported, the NITAG in New Zealand has existed since at least 1980 [30].

Of the 14 countries for which information on their NITAGs was retrieved, 12 countries provided information on their membership (all except Brazil and New Zealand) [13,16,17,24,25,32,34,36,37]. The number of members was reported for 8 of the NITAGs and varied from 12 to 17 (Austria, Canada, France, Germany, Ireland, Switzerland, the UK, the USA) [16,17,24,25,32,34,36,37]. Five of the countries reported that a defined term is given for members which lasts three to four years (Austria, Canada, Switzerland, the UK, the USA) [17,25,32,34,36,37] while the reports for Italy and Spain indicated that there is no defined term limit for committee members [32]. The chair of the committee is referred to for three of the NITAGS: Canada, France, and the USA [22,32,37]. There were between 4 and 15 ex-officio members reported by 5 of the committees [16,24,25,32–34,36,37] and between 11 and 27 liaison members reported by two committees [16,25,34,37].

All members on the NITAGs in Canada, the UK, and the USA must declare potential conflicts of interest [25,34,36,37]. In the case of a conflict of interest, the member may be excluded from the final decision making [34,36,37] or if the conflict is significant, they may have to resign [25].

The types of expertise represented on the NITAG was reported for Canada, France, Germany, Italy, New Zealand, Spain, Switzerland, the UK, and the USA [13,16,24,25,32,34–37]. These included clinical medicine, epidemiology, immunology, health economics, health planning, infectious disease, internal medicine, microbiology, nursing, pediatrics, public health, and vaccine research while some also had a community member or an insurance representative. The most commonly reported areas of expertise were infectious disease ($n=5$) followed by immunology, microbiology, pediatrics, and public health, which were all represented on four of the nine committees.

Nine of the 14 NITAGs had a defined number of meetings, of which the majority ($n=5$) met three times per year [24,25,32–34,37]. The highest number of meetings per year was reportedly held by the NITAG in France which met six to eight times per year [32], while the NITAG in Germany met only twice a year [32]. Six of the NITAGs held closed, confidential meetings (Austria, Canada, France, Ireland, Switzerland, the UK) [24,32,34], while only the NITAG in the USA had meetings open to the public [25,27]. Of the eight countries which reported taking meeting minutes, half of the countries published them on the internet (Australia, Canada, the UK, the USA) [24,25,33,34,36,37] and the other half did not publish them (Austria, France, Ireland, Switzerland) [32].

Information was given on the use of evidence in 8 of the 14 NITAGs (Table 2). Australia mentioned using evidence but did not offer further information [10,13,33]. The NITAGs in Brazil [5], Canada [34,38], and the UK [36] conduct a literature review prior to making recommendations. It was reported that the NITAG in Canada [34,38], the UK [36], and the USA [25] appraise the quality and validity of the evidence to determine if it is strong enough to justify a recommendation in their countries. Canada [34,38] and the USA [25] reported grading the evidence, while the UK's method was not specifically reported [36].

Details about the publication of NITAG recommendations are given for nine countries. While Australia [33], Austria [32], Germany [32], and the UK [24,36] produce an annual report or annual national immunization booklets including the recommendations of the NITAG that were accepted by the government, France and Ireland [32] publish their guidelines every second year in a report. Austria, Canada, New Zealand, the UK, and the USA publish their recommendations online [24,25,32,34–37].

4. Discussion

This systematic review is the first known attempt to retrieve and summarize information published about the processes of immunization policy making at a national level. Although every country with an Immunization Program presumably has gone through the process of developing their national immunization policies, the information published and available online about the process of immunization policy development was relatively limited being obtained from only 33 of 193 countries. Further, the amount of information available varied tremendously by country with the most information available on the processes in Australia, Canada, the UK, and the USA for which the information described was fairly comprehensive.

The main limitation of this review is that only publications, reports and websites in English or French were included in the review. There is likely to be additional information available on the processes of immunization policy making at a national level published in languages other than English or French, particularly on national websites, though we were unable to determine to what extent.

The assessment of the quality of information is another limitation of this study. Although the source and date of publication were documented, national policy making processes may have changed over time and it is unknown if the methods employed in the past remain the same today. As well, there are many varying perspectives of players involved in immunization policy development that may not have been reflected in the published literature due to the small number of publications and limited information provided.

Granted the above-mentioned limitations, the lack of detailed information retrieved in print and on the web points to a need for countries to enhance dissemination of information on their immunization policy making processes. This exchange of information could help countries improve their policy making processes by offering concrete examples of feasible policy making methods. Also, governments publishing their decision making processes would increase the credibility and transparency of immunization policy development.

The information retrieved about the immunization policy making processes came mostly from industrialized countries [39], however, there was information about four countries considered to be developing (Brazil, China, Papua New Guinea, and Thailand) and two countries considered to be least developed (Cambodia and

Mali). For the developing and least developed countries, the information retrieved briefly described the players involved and factors considered when making immunization policies. Overall, there was little information available about the processes of immunization policy development particularly in developing countries.

The 14 countries with NITAGs for which information was retrieved in this review are all developed with the exception of Brazil. Brazil is considered a developing country by the United Nations [39], but is known for its strong public health system. Although there are presumably many NITAGs in existence, only 14 were identified in print literature and country websites and limited information about them was published. There is little published or easily accessible website information on the NITAGs outside of those in Australia, Canada, the UK, and the USA, at least in the English and French languages. This reinforces the need for countries to publish information on their immunization policy development processes such as the presence and functioning of NITAGs.

The information collected in this review revealed many differences between countries' NITAGs. Although they have the same purpose, the methods of functioning, membership, decision making processes, and the transparency of the processes vary among groups. The reported modes of functioning of each NITAG are consistent with their purpose but vary according to the context each country.

Of note is that there were no reports of a country that had an NITAG and subsequently dissolved it. Countries wishing to form a NITAG should consider their specific needs and resources and may want to use models developed in other countries to ensure credibility, transparency, accountability, stability, and independence.

No data on process or outcome evaluation of immunization policy making were available in the literature reviewed. This is an important gap in the literature and such an assessment may need to be done in order to convince some governments of the credibility and usefulness of these groups.

This review is a concise presentation of the information retrieved from public sources on immunization policy development processes around the world. Given the effect of vaccines on population health and the vast sums of money needed and spent on vaccines, more attention on the immunization policy development processes is needed in order to document best practices which may benefit all countries. In itself, the scarcity of information raises the question of policy effectiveness and reinforces the need for increased publication to remedy the information gap on immunization policy making processes across the globe.

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Conflict of interest statement

The authors state that they have no conflict of interest.

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