

## Evidence-Based Options to Improve Routine Immunization

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### RELEVANCE

Routine immunization is a cornerstone of public health, believed to save an estimated 2-3 million lives annually. Therefore, individual nations and international organizations lay considerable emphasis on robust vaccination programs. India is one of the few countries where universal routine childhood immunization is provided free of charge. Despite this impressive arrangement, immunization coverage through the National program remains unsatisfactorily low. This not only hampers disease control, but consequently diminishes public support for vaccination, and tarnishes the prestige of the program, setting up a vicious cycle. Similarly the occurrence of expected and unexpected adverse events can shake public and professional confidence.

Therefore, it is worthwhile to examine evidence-based interventions to enhance vaccination coverage or improve acceptability or increase effectiveness of the routine immunization program. The question (stated in the PICO format) addressed here is: "In order to improve routine immunization (*P-problem*), which interventions (that are feasible, cost-effective and can be integrated into the existing program) (*I-intervention*), can increase vaccination coverage/vaccination demand or improve acceptability or enhance cost-effectiveness or reduce side effects (*O-outcomes*), as compared to the current situation (*C-comparison*)."

### CURRENT BEST EVIDENCE AND CRITICAL APPRAISAL

An exhaustive literature search in the Cochrane

Library and PubMed using the search strategy shown in **Table I** was conducted and updated on 28 September, 2009. Owing to the magnitude and public health importance of the question, systematic reviews were preferentially sought. A summary of current best evidence and critical appraisal is presented.

### Improving Vaccination Coverage

A 2008 systematic review(1) of methods to improve immunization coverage screened over 11000 papers across three decades. The authors narrowed the list to 60, assessed methodological quality and rejected 35. The remaining studies included comparative trials, pre and post intervention comparisons and observational studies. After reviewing the data, 11 studies with interventions facilitating access to immunization were identified. The individual studies and the review itself had several methodological limitations (combining different study-designs, post-hoc selection of outcome,

**TABLE I** SEARCH STRATEGY FOR SYSTEMATIC REVIEWS AND OUTPUT

Search term	Output	Relevant
Immunization	22	3
Vaccination	31	3
Vaccine	95	4
Cold chain	3	2
Injection	82	3
Routine immunization	96	4
Immunization coverage	68	5
Vaccination coverage	59	3
Cold chain	25	2
Injection pain	10	3
Vaccination pain	16	3

absence of comparison, etc). However, all were conducted in developing countries and appraisal of quality was fairly rigorous.

One trial each from Ghana(2) and Mexico(3) reported significant increase in vaccination coverage when non-professional health-workers visited homes to mobilize the community for vaccination. A smaller Cambodian study(4) reported marginal increase in coverage when contractors were hired to improve vaccination coverage and equity. Four pre and post intervention studies demonstrated the benefit of out-reach immunization in schools(5), flexible immunization timings and venues(6), community mobilization through home visits(7,8), mass media campaign to communicate information(9) and reorganization of health-care facilities(10). Naturally, the findings are less robust than randomized controlled trials (RCTs).

Another narrative review examined almost 4000 publications on interventions to improve immunization coverage in developed countries(11). Despite being outdated by a decade, the strengths of the review are that the authors segregated studies based on design, undertook methodological appraisal, employed criteria for eligibility and included hard outcomes such as coverage and/or doses administered. They regarded the evidence to be strong if it originated from studies with suitable design, proper execution, sufficient effect size, showed consistent effects across studies and did not rely on 'expert opinion'. While the approaches (physician/provider education, community participation, clinic-based client education, reminder/recall systems, free vaccination, incentives, reducing out-of-pocket expenses for vaccination) are generally applicable in developing country settings, the specific intervention used in most of the studies is either not applicable, or did not show a statistically significant benefit that can justify the extra cost. Making vaccination mandatory for school/child-care/college entry improved coverage and also reduced disease morbidity to some extent.

### ***Improving Vaccination Rates***

A Cochrane review updated till 2008(12) examined five databases for randomized controlled trials,

controlled pre and post intervention studies, and interrupted time series studies on effectiveness of reminder/recall systems for improving vaccination rates. Meta-analysis of 15 studies in over 15000 participants showed that client reminders were effective for improving childhood vaccination rates (odds ratio 1.47, 95% CI 1.28-1.68). This result was consistent across various groups of vaccine recipients (children/adults/those receiving only influenza vaccine) and irrespective of the reminder method used (postal, letter, or telephonic). Combined physician plus client reminder also improved vaccination rates.

The usual methodological refinements of Cochrane reviews were present. However, one of the studies included in the meta-analysis was not a RCT and the authors did not perform sensitivity-analysis with methodologically superior trials. A re-analysis of four trials with adequate allocation concealment showed a similar result to the overall pooled estimate, suggesting robustness.

### ***Improving the Cold-chain***

Maintenance of the cold-chain is critical for the success of immunization programs. Although two systematic reviews addressed unexpected breaches in temperature control, neither addressed interventions to ensure cold chain efficiency. One review reported that despite the presence of trained vaccination officers at many points, optimal temperature control and recording thereof were lacking(13). Another reported that a significant proportion of vaccines underwent freezing at various links in the cold-chain(14). Although the data are not derived from India, both raise concerns because similar unanticipated cold-chain breaks could be occurring in our country, which could jeopardize the entire program, and, therefore call for stringent monitoring of the cold-chain, despite reassuring reports of cold-chain adequacy.

### ***Increasing Vaccine Acceptability***

#### ***Reducing pain during vaccination***

Topical anesthetics, in particular pre-injection EMLA cream, reduce injection-related pain(15). As EMLA is safe in infants, and does not adversely

### EURECA CONCLUSION IN THE INDIAN CONTEXT

- Routine immunization can be improved through judicious application of interventions to increase community participation, involve non-professional health workers, create vaccine demand, use a vaccination reminder/recall system and reduce undesirable side effects.
- These efficacious evidence-based interventions need to be tested in the Indian setting before adoption on a national scale.

affect vaccine immunogenicity; it is frequently used in developed countries. However, EMLA is expensive and requires time to act; hence is unsuitable for busy immunization sessions. Refinements in local anaesthetic application include less expensive, fast-acting sprays and other technically demanding procedures; all are unsuitable for routine immunization in India.

Non-pharmacological interventions include sweetened solutions such as sucrose water although it does not work well beyond 4-6 months of age. A combination of direct parental contact and sucrose seems to have an additive beneficial effect. However, sucrose water must be used cautiously owing to problems due to spoilage, storage and contamination. Breastfeeding and even non-nutritive sucking reduce pain in very young infants(15).

A meta-analysis(16) of pain management by distraction using various techniques (music, movies, non-procedural chatting, interactive toys, etc), showed a modest impact in decreasing distress behavior. Experts advise that age and cognitive maturity of children are important considerations to optimize results. Parental behaviour (maternal more than paternal) before and during the procedure affects infant behaviour significantly. Overly sympathetic, critical, apologetic or reassuring parents increase child distress. In contrast, humor and conversation (unrelated to the injection) were beneficial. Parents trained in reassurance ended up distressing themselves and their children more than parents trained to distract children by storytelling, reading aloud, deep breathing, and blowing.

Other potentially useful intervention such as using long thin needles, applying pressure at the injection site, giving multiple injections

simultaneously rather than sequentially are not backed by robust evidence.

#### *Reducing adverse effects associated with vaccination*

A 2007 literature review(17) on prophylactic acetaminophen and ibuprofen for preventing adverse reactions following immunization identified five randomized trials. Three reported that acetaminophen (10-15 mg/kg/dose) or ibuprofen (20 mg/kg/day) before/during and after immunization reduced fever, pain, fussiness, and local redness associated with DPT vaccination.

#### *Increasing Vaccine Demand*

A systematic review of 69 papers on the impact of mass media on health services utilization showed a positive impact by encouraging effective services and discouraging those of unproved effectiveness(18).

#### EXTENDIBILITY

Review of literature has identified several interventions that can improve routine immunization. These are of varying complexity, cost-intensity, technical feasibility, logistic difficulty and effectiveness. Assessment of extendibility includes much more than feasibility in the Indian setting. It includes value-based judgements (at the national, state and local levels) based on current vaccination coverage, recognition of predisposing factors for poor coverage, administrative structure, allocation of responsibility, utilization of resources (manpower, material and finances), competing demands, and perception of the community, lay press, and non-professional workers. For these reasons, highly efficacious interventions that are also apparently

cost-effective, feasible and easy-to-integrate in the National routine immunization program, need not necessarily result in the same effectiveness. It must also be noted that many efficacious interventions may have outlived their usefulness owing to changes in information technology, economic progress and general development. Nevertheless, increasing community participation, involving non-professional health workers, creating vaccine demand through the mass media, introducing a reminder/recall system and increasing vaccine acceptability through pharmacological and non-pharmacological interventions to reduce undesirable side effects, are likely to be useful.

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