Implementation Research at IVR

Initiative for Vaccine Research

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- Why is it critical for IVR to contribute to implementation research?
- What is IVR’s added value in this area?
- What is our current emphasis in implementation research?
- What is our current experience and what have we learnt?
- Where are our efforts leading us?
Implementation Research for Immunization: a definition of scope

Optimise the public health benefit of vaccines and immunization through:

- Research that facilitates the continuing evolution of immunization programmes
- Research to establish the technical evidence base for programmatic decision-making
- Research into the institutional and policy context of immunization

Why is it critical for WHO to be engaged in implementation research?

- To assure the relevance and optimal public health use of vaccine interventions
  - Examples: critical review of immunization schedules; HIV vaccine use & delivery scenarios
- To provide validated data for vaccine planning
  - Examples: global disease burden estimates, global costing efforts
- To provide tools for decision making and assure comparability of methods
  - Examples: measles strategic planning tool; harmonization of cost-effectiveness analysis
Evidence-Based Decision Making Concept

1. Burden of Disease
   What is the situation with mortality and morbidity of VPDs in countries?

2. Cost Effectiveness Analysis
   What are the strategies that maximize outcomes for every dollar spent?

3. Supply and Procurement
   Supply? Procurement?

4. Planning and Budgeting
   Who is going to pay? Options and strategies for financing? Financial sustainability?

Country Context

Examples of current research efforts

- Measles strategic planning tool
- Future access and public health use of HIV vaccines
- Immunization schedules
- Harmonization of methods for cost effectiveness analysis
Measles strategic planning tool

- Developed in response to country demand for tool to facilitate evidence-based decision making in how best to reach measles mortality reduction goal
- Allows quantitative evaluation of strategies
- Part of AIM e-learning series: Partnership with PATH, UNICEF, CDC
- Self-paced electronic tutorials and case studies
Measles strategic planning tool

Developed in response to country demand for tool to facilitate evidence-based decision making in how best to reach measles mortality reduction goal

Part of AIM e-learning series: Partnership with PATH

Ghana: 2006 Immunity profile

Measles mortality trends under different programme options

- Option 1: Improve routine coverage + Introduce 2nd dose at age 2 in 2008
- Option 2: Improve routine coverage + Introduce 2nd dose at age 2 in 2008 + One-time SIA in 2007
- Option 3: Improve routine coverage + One-time SIA in 2007 + Recurrent SIA every 4 years, starting in 2011, ending by 2020
- Option 4: Improve routine coverage + Change age of 1st dose to 1.25 in 2008 + Introduce 2nd dose at age 2 in 2008 + One-time SIA in 2007
- Baseline
Future access and public health use of HIV vaccines: 
Rationale and overall goal

- **Problem:**
  - Delayed and ineffective access to future HIV vaccines at country level due to potential supply and delivery constraints

- **Solution strategy:**
  - Modelling data on vaccination policy considerations to assist countries for future HIV vaccination strategies and effective delivery systems;
  - Information to delineate the long-term financial requirements for sustainable HIV vaccination programmes

Future access and public health use of HIV vaccines: 
Activities in progress

- **Policy-maker survey** on vaccine delivery strategies.
- **Cost studies** for future HIV vaccination programs.
- **Simulation HIV VaccSim modeling exercises** analyzing the cost-effectiveness of potential HIV vaccination strategies.
- **Assistance for in-country capacity development** utilizing simulation model-based public health policy evaluations.
- **Harmonize and standardize** HIV VaccSim with other existing HIV vaccine mathematical models

(AIDS. 2005 Sep 2;19(13):w1-w6)
Cost effectiveness and delivery study for future HIV vaccines

WHO-UNAIDS collaborative group on cost-effectiveness, delivery and future access to HIV vaccines

Research teams from five countries, Brazil, China, Kenya, Peru and Thailand, have initiated a policy-maker survey on vaccine delivery, cost studies for future HIV vaccination programmes, and associated simulation modeling exercises analysing the relative cost-effectiveness of potential HIV vaccination strategies. The survey assesses challenges and opportunities for future country-level HIV vaccination strategies, providing data on the vaccine characteristics (e.g., vaccine efficacies for susceptibility, infectiousness and disease progression) and vaccination programme strategies to be considered in the cost-effectiveness modeling analyses. The study will provide decision-makers with modeling data on vaccination policy considerations that will assist in developing country-level capacities for future HIV vaccine policy adoption and effective delivery systems, and will help delineate the long-term financial requirements for sustainable HIV vaccination programmes. The WHO-UNAIDS HIV Vaccine Initiative and the collaborating researchers welcome comments or questions from policy makers, health professionals and other stakeholders in the public and private sectors about this effort to help advance policy and capacity related to future potential HIV vaccines.

AIDS 2005, 19:w1–w6

Keywords: access, AIDS, capacity, cost effectiveness, delivery, HIV, immunization strategies, policy, vaccine

Future access and public health use of HIV vaccines: Findings and implications

- Vaccination strategies can be a critical determinant of HIV vaccine impact.
- Impact of HIV vaccines can show synergistic effects when assessed in combination with other prevention technologies.
- Computer simulation methods can contribute importantly to the development of good HIV vaccination policies, if applied to specific country circumstances.
- Project is an important model that could be applied to other future complex vaccines (e.g., malaria)
Research into the optimal use of vaccines: Immunization schedules

- "Standard" EPI schedule: what does it mean and is it appropriate for the delivery of conjugate vaccines?
- What are experiences with existing schedules for conjugated vaccines?
- What do we know about direct/indirect effects, can it be generalized integrated in immunization strategies? What information is missing?
- What are key implementation issues, feasibility, cost?
- Are there consequences for future vaccine development, evaluation and licensing?

- Develop a comprehensive research package for IVR in close interaction with partners to build the evidence for optimal immunization schedules

Harmonization of costing and cost-effectiveness analysis in the field of immunization

- Use of inconsistent methods for CE in immunization can make results across different vaccines and even for the same non-comparable
- CE results are sensitive to methodological differences in:
  - What costs are included
  - How costs are calculated
  - Choice of modeling approaches
  - etc
- Call for immunization-specific guidelines for cost effectiveness analysis
CEA Harmonization Guidelines
Aim and Status

- provide clear, concise and practical guidance of a high standard for "doers" of economic evaluations;
- meet the needs of decision-makers for relevant, reliable and consistent economic evaluations;
- Special focus on low- and middle countries;
- Allow users address applicability, comparability, and generalizability of published results to their settings.

What have we learnt?

- Strong demand from countries for solutions that require implementation research
- Demand for harmonization of approaches to which IMR can respond effectively
- Partnering can be very effective, if built on the respective strength of groups involved
- Close Link to vaccine implementation teams increases research relevance
- Effective use of country contacts has proven very beneficial

- Taking a facilitators/convenors role can be more efficient than implementing large projects.
- Dispersion of efforts to be avoided and coordination with partners needs to be improved
- Mutual strengths of partners needs to be better exploited
- There is currently no established funding streams
**Where do our efforts lead us?**

- Establish research on immunization schedules as a coherent research effort
- Operationalize HIV project at country level, and use experiences and established networks for other complex vaccines
- Develop operational research agenda for vaccine delivery strategies beyond infant age (HIV, HPV,…)
- Establish a standing advisory committee on Quantitative Immunization and Vaccines Related Research
- Build stronger partnership with external research groups/donors, and assume convening function in line with WHO mandate

> Be selective and strategic when committing to research!

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Thank you!
Conduct Simulations on Potential Impact of Future Vaccines

Expectations on HIV Vaccine efficacy in study countries

VE susceptibility  VE infectiousness  VE progression
HIV Vaccine KI Survey conclusions Peru

- The most important barriers to future vaccine delivery are:
  - access to information /counseling; managerial, training and planning issues; and logistical issues;
- Prevalence, incidence and risk behavior are perceived as key criteria to prioritize target populations;
  - MSM, male CSW, women in reproductive age, urban population and female CSW
- MOH, through regular EPI vaccination in public hospitals and clinics, should be the main institution to implement future HIV Vaccine delivery strategies

Optimal schedules need to account for delays from the printed schedule:

Summary distributions of the age at DTP1-3, MCV1 & BCG

\[
\text{median (75th percentile) delay from the target age} \]

- Median delay from target age (birth) = 1.2m (25% > 2.8m)
- Delay = 1.2m (2.9m)
- Delay = 1.5m (4m)
- Delay = 2.2m (5.4m)
- Delay = 1.3m (4m)
Global Disease Burden Estimates: The experience of Hib/Pneumococcal Disease (2)

- WHO, PneumoADIP, and Hib Initiative collaboration

- 66 persons, 2.5 years, ~$500,000 US$ cost
  - Weekly teleconferences
  - 12 in-person meetings

- 14,000 scientific articles reviewed

- 2 expert committee meetings:
  - June 2005
  - October 2006

- Estimates to be finalized in May 2007

Future access and public health use of HIV vaccines: Key objectives

- Assess the capacities for delivering future HIV vaccines in countries with varying epidemics (Peru, Brazil, Kenya, Thailand and China)

- Identify potential target groups for vaccination and assess various delivery strategies for these targets

- Conduct CEA of vaccination programs with different country settings, target groups, costs and vaccine efficacies

- Synthesize multidisciplinary data into a simulation modeling tool

Enable policy makers at country level to assess the potential epidemiologic impacts and cost effectiveness of HIV vaccines and vaccination strategies.
### Inconsistent CEA methods in immunization

#### Examples

- **Review of CE Pneumo conjugate vaccines in high-income countries** ranged from (Beutels et al 2007)
  - Cost-savings to over €10,000/QALY gained (societal perspective)
  - €20,000 to €142,000/QALY gained (payer perspective)

- **Review of CE Rotavirus vaccines in high and low income countries** (Walker et al 2007)
  - Rotavirus Vaccine cost ranged from US$ 0.45 – 30
  - Additional administration costs ranged from US$ 0.18 to 12.
  - Cost per dose ranged from US$ 3.6 - 51

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### Estimating Disease Burden

#### Core Normative Function of WHO

- Accountability to member states
- Ability to undertake wide consultation drawing on competing sources of expertise
- Data from network of country and regional offices
- Partnership with other relevant UN bodies (UNSD, UNICEF, UN Pop Division, World Bank, etc)
- WHO "4 step + 1" process (see next slide)

#### Requires disease and programmatic expertise

- Draws on strengths of IVR/IVB staff
### Global Disease Burden Estimates:

- WHO disease burden estimates must be "beyond reproach": 4 step (+ 1) process
  1. Database of evidence
    - Systematically collected
    - Publicly available
  2. Methods for estimation
    - Transparent methods
    - Manuscript prepared for peer-review
    - Communication of uncertainty of estimates
  3. Independent expert group
  4. Clearance through WHO-EIP
    - Compatibility with other disease burden estimates
      - +1 Country consultation prior to release of country-level estimates

### Where do we see IVR's comparative advantage?

- WHO core functions: norms and standards and monitoring disease trends.
- Builds on the role of neutral broker and independent adviser and shaping the research agenda in a relevant and credible way.
- Integration and harmonization across the broader public health agenda.
- Identify key research questions in close link with control and normative activities in immunization, and assure testing for technical feasibility.
- Link to research and product development early on in relation to product presentation and possible immunization strategies.
Tools for decision making

- As countries are choosing between different interventions, they need to visualize the impact of different choices at 1, 5, 10, 20 years into the future.

- The challenges:
  - Disease-specific or multiple disease at once?
  - Concentrating on vaccines, vs. linking vaccines to other interventions

- Solutions:
  - Standardization/Harmonization of tools
  - Clear links showing how tools relate to each other