Immunization implementation research priority setting

John Clemens, M.D.
Executive Director, icddr,b

Context: Strategic objectives of WHO's immunization implementation research agenda (2012)

- **Define a global immunization implementation research agenda and priorities;** with scope including all vaccines, health systems, and programme issues
- Map global research activities and monitor progress in the field
- Assess quality, relevance and potential policy implications from implementation research
- Build scientific consensus around useful implementation research outputs, and develop best practices and guidelines in accordance with WHO's normative role
- Build implementation research capacity in countries and regions in collaboration with partners

Immunization implementation research priority setting

Goal: To define a global immunization implementation research agenda and priorities with the potential to:

- drive immunization policy and maximize the impact of vaccines and immunization;
- help define and implement a process to facilitate efforts to generate relevant and credible evidence to support decision-making for national immunization programmes.

Recognizes the opportunities offered by the Decade of Vaccines through Strategic Objective 6 of the GVAP.

(Arora NK et al. Vaccine 2013;31S: B129-36.)

Vaccine 31S (2013) B129–B136

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Review

The need for targeted implementation research to improve coverage of basic vaccines and introduction of new vaccines

Narendra K. Arora[a,*,1], Altaf A. Lal[b,1], Joachim M. Hombach[c], Jose I. Santos[d], Zulfiqar A. Bhutta[e], Samba O. Sow[f,g], Brian Greenwood[h]

ARTICLE INFO

ABSTRACT

Role of the Ad hoc Working Group

- The prioritization exercise has been conducted with an ad hoc Working Group comprising:
  - Initially 21 independent experts; developed prioritization framework and involved in initial stages in 2012
  - 20 additional members (representing all 6 WHO Regions); per IVIR recommendation

Terms of reference

- Develop framework that enables a systematic assessment of priority on topics raised as important implementation research issues
- Review the list of suggested research topics/questions, provide additional topics/questions, decide through a transparent and systematic process which ones are relevant and necessary, and assign priority for their implementation
- Assist in the production of a concise but comprehensive report on priorities for a global implementation research agenda for consideration by the IVIR-AC

Ad hoc Working Group members

John Clemens (**Chair**)	ICDDR,B /UCLA
Shams Al Arifeen	ICDDR,B
Asad Ali	Aga Khan University
Manoj K. Das	INCLEN Trust International
Theresa Diaz	UNICEF
Nonhlanhla Dlamini	Dept. of Health, South Africa
Abdul Reza Estighamati	University of Tehran, Iran
John Grundy	Nossal Inst. for Global Health
Andrew J. Hall	LSHTM
Rana Hajjeh	US CDC
Myriam Henkens	MSF
Mark LaForce	Independent consultant
John Lloyd	Independent consultant
Lauri Markowitz	US CDC
Gabriela Montorzi	COHRED
Paba Palihawdana	EPI, Sri Lanka
David Sack	Johns Hopkins
Christian Schaetti	Swiss TPHI
Robert Steinglass	MCHIP/JSI
Yot Teerawattananon	HITAP/MOH Thailand
Pritaporn Kingkaew	HITAP/MOH Thailand

AFR:
Dicky Akanmori (WHO)
Auguste Ambendet (WHO)
Fussum Daniel (WHO)
Nehemie Mbakuliyemo (WHO)

AMR/PAHO:
Carolina Danovaro (PAHO)
Renato Valenzuela (Honduras)
Adalid Zamora (Bolivia)

EMR: Salah Al Awaidy (Oman)
Zulfiqar Bhutta (Pakistan)
Irtaza Chaudhri (WHO)

EUR: Niyazi Cakmak (WHO)
Vusala Allahverdiyeva (WHO)
Shahin Huseynov (WHO)

SEAR: Nihal Abeysinghe (WHO)
Rajendra Bohara (WHO)
Pem Namgyal (WHO)
Sudath Peiris (Sri Lanka)

WPR: David Durrheim (Australia)
Lee Jong-Koo (Korea)
Helen Oh (Singapore)
(John Vince*, PNG)

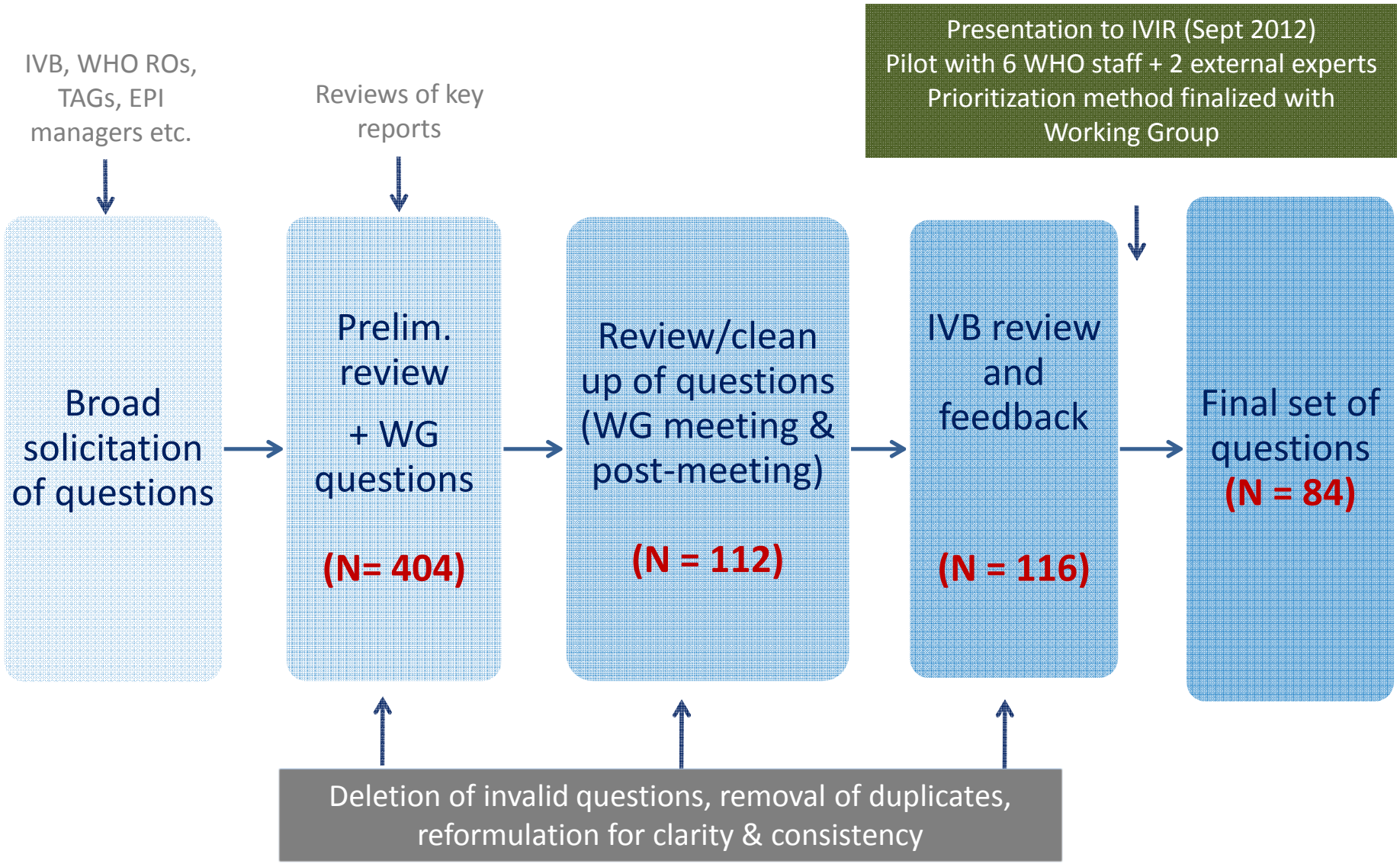
Parameters for selecting the candidate research issues

- Focus on research to improve coverage of recommended vaccines and to facilitate introduction of new, **licensed or near-to-licensing vaccines**, not focused on vaccines in early development
- Focus on research that identifies **barriers and bottlenecks** and research that tests **attractive strategies** to overcome these barriers

Guiding principles for research topics

- Focus should be on research that strives for equity in immunization progress and results
- Focus should be on research that addresses LMICs and has global scope.
- Where possible focus should be on topics addressing integration of immunization with other health services
- Focus not only on finding new ways of doing things, but also on improving the way we do things currently
- Research should envision partnerships at the intra and cross-country levels
- Research question should be addressable within a 5 year time frame

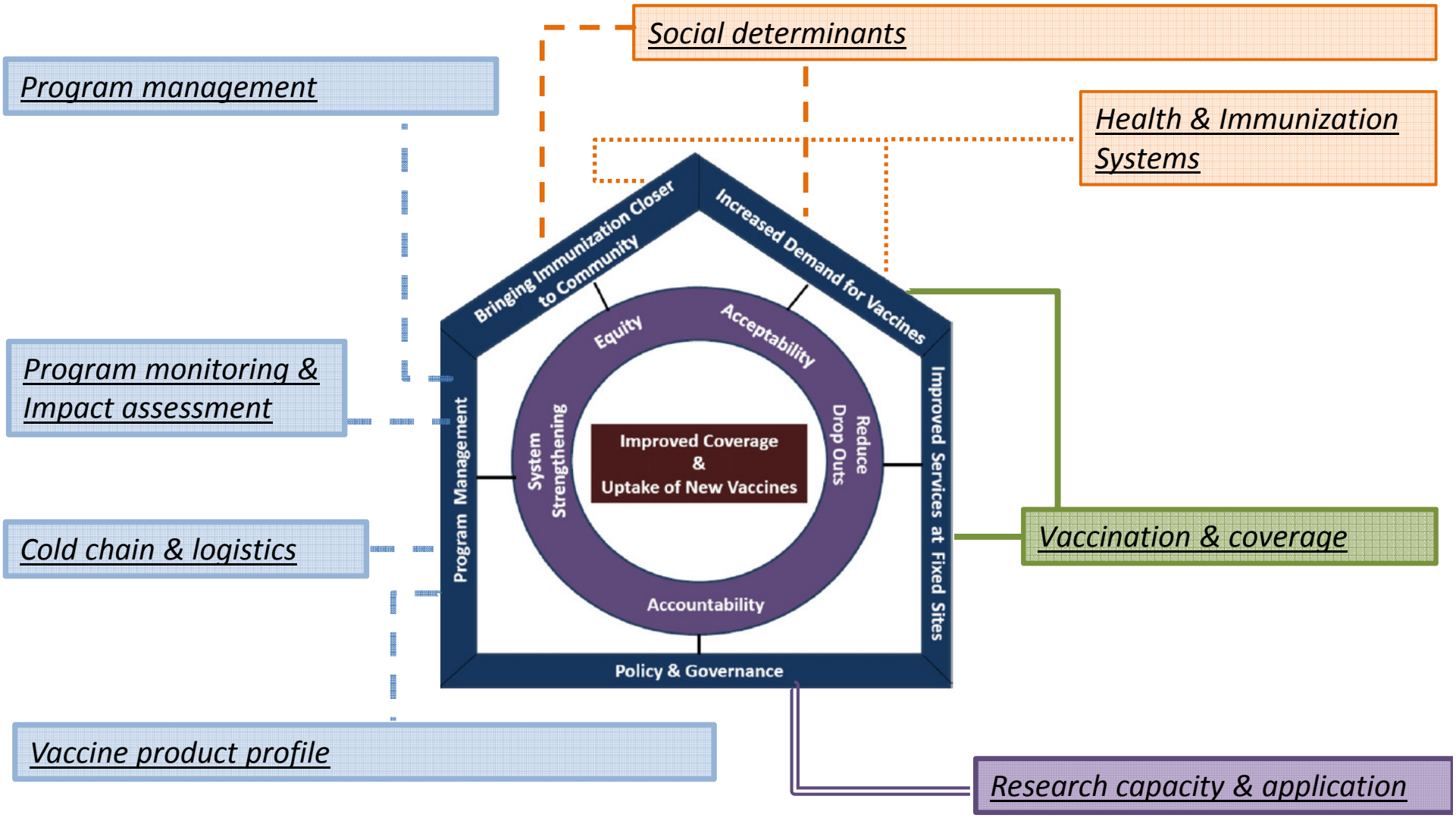
Steps in the identification of potential immunization implementation research questions for scoring



Questions grouped *post hoc* into 8 domains (5-19 per domain)

A. Health and Immunization Systems
B. Social determinants of vaccination & communication
C. Vaccine product profile
D. Immunization and coverage
E. Cold chain and logistics management
F. Program management
G. Program monitoring and impact assessment
H. Research capacity and application

Mapping of the 8 domains to the framework developed by DOV



Prioritization methods considered

- **Essential National Health Research (ENHR) methodology**
  - **developed by the Council on Health Research for Development (COHRED)**
- Child Health and Nutrition Research Initiative (CHNRI) method
- Delphi and Nominal group techniques
- 3D Combined Approach Matrix method

Prioritization criteria

- Adapted from the Essential National Health Research (ENHR) methodology*.
- Classified into four categories:
  - (1) Appropriateness [***Should we do it?***]
  - (2) Relevance [***Why should we do it?***]
  - (3) Chances of success [***Can we do it?***]
  - (4) Impact of the research outcome(s) [***What benefit will be achieved?***]
- Nine criteria in total with 3 levels each (yes, no, uncertain)
- Challenge: how to weight the responses for each research question, reflecting raters' values and preferences, to derive an additive numerical score across the 9 criteria?

** The Council on Health Research for Development COHRED, A Manual for Research Priority Setting using EHNR Strategy, COHRED document 2000.3, March 2000*

Method for weighting: PAPRIKA (Hansen P, J Multi-Crit Decis. Anal. 2009; 15: 87)

- Potentially All Pairwise Rankings of All Possible Alternatives (PAPRIKA)
- Enables incorporation of raters' value judgments about the relative importance of responses to different criteria, so that the responses can be weighted for calculation of a summary additive score
- Weights calculated based on preferences indicated when comparing different responses to **pairs** of criteria
- In this exercise, software calculated weights for each of the 27 possible responses to the 9 component criteria
- To come up with a single aggregated weight for each response, the weights for each response were averaged across all working group members who completed this exercise

Mean aggregate preference weights for ENHR criteria using Paprika

Category	Criteria	Weight for		
		Yes	Uncertain	No
Appropriateness	Significant knowledge gap?	12.07%	6.7%	0%
	Research can be concentrated ethically?	14.99%	9.1%	0%
Relevance?	Problem is significant in size/severity?	9.9%	5.1%	0%
	Research responds to population needs?	12.2%	7.3%	0%
	Research contributes to greater equity?	11.9%	6.6%	0%
Chances of Success?	Possible to conduct study within specified context and time frame?	9.2%	5.4%	0%
	Study end points can be achieved?	6.8%	4.2%	0%
Impact of Research Outcomes?	Outcomes will lead to impact on policies?	11.0%	6.2%	0%
	Research will lead to improved coverage, improved services, improved vaccine introduction, and/or improved policy/decision making?	12.3%	6.2%	0%

Rating of the Candidate Research Questions

- Each rater was asked to assign one of the following responses for each of the 9 criteria: yes, no, uncertain. Also allowed to indicate “unknown”.
- The raters were kept blinded to the weights assigned to each response by the PAPRIKA algorithm.
- Because raters differed in areas of expertise and to make it feasible to complete the ratings of all questions in a single sitting, raters were assigned to 3-4 selected domains according to their stated areas of expertise, rather than to all domains (9-19 scorers for the different domains)
- Aggregate scores for each candidate research question were averages of the scores of all raters

Completion Rates

Weighting survey :	68%
Expert profile:	82%
Ratings :	71%

Top Ranked Research Questions by Domain

Domain	Question	Score
Health and Immunization systems	What are the specific barriers to immunization among children not reached by immunization services and what are the service delivery strategies (including specific package of service) to respond effectively to those barriers?	95.1%
Social determinants	What are the profiles of high risk communities (such as gender, vulnerable populations, socio-economic factors, etc), how do these profiles influence vaccine uptake, and what are the best strategies to identify and vaccinate such groups?	91.0%
Vaccine product profile	What is the feasibility of establishing (regional) dynamic, large-linked databases for use in accessing vaccine safety concerns?	87.6%

Top Ranked Research Questions by Domain

Domain	Question	Score
Vaccine and Coverage	How should vaccination services be adapted to increase coverage of specific populations e.g. in context of HPV (different target groups); cholera vaccines (home intake of the second dose distributed when the first dose is administered under supervision); private sector availability of some oral vaccines (e.g., cholera, typhoid); or marginalised population (slums, migrants, etc.)?	93.0%
Cold chain and logistics	What would be an effective “common operating platform” for integrated logistics management of all public health activities at district level, including the certification of the trained logistics manager to lead the activity?	89.3%
Programme Management	What tools are needed for health workers to effectively assess and correct missed opportunities for children whose immunization has been delayed or whose schedules have been interrupted?	91.4%

Top Ranked Research Questions by Domain

Domain	Question	Score
Programme Monitoring and Impact Assessment	Can improvements be made to methods for estimating the size of the target populations, at the national and subnational levels?	90.4%
Research related Issues	How frequently is evidence-based information used to support NITAG (or other equivalent national) recommendations? What are the barriers and challenges to the effective functioning of NITAGS and how can they be addressed to strengthen NITAGS and vaccine policy-making at country level?	87.3%

Additional Analyses

-Rank was not sensitive to proportion of “Don’t know” (missing data) responses

-Ranks were similar regardless of whether weights were calculated for all raters versus only for raters with expertise in the domain of the research question

Limitations

- Moderate response rates and small number of raters per domain (9-19)
- Potential biases in selection of research questions for ranking
- Rankings were within domains, and did not address relative priorities among topics in different domains
- Scores did not vary greatly between ranks
- Contextual variability will likely affect rankings
- Input from stakeholders at different levels will be beneficial to validate the exercise and define application of the results

Conclusions

- The ENHR criteria proved to be adaptable to the prioritization of vaccine implementation research questions
- The PAPRIKA method enabled empiric weighting of the component criteria according to judgments by the actual raters, was simple to implement, and yielded weights that displayed face validity
- The approach appeared to discriminate between different research questions in arriving at a ranked order
- Although our process used for decision-making on research priorities is systematic, the findings **should not be used as the sole criterion for decision making** (contextual variability and other factors should be considered)