

Immunization and Vaccine related Implementation Research (IVIR) Advisory Committee

24-26 September, Menthon Saint Bernard, France

**Professor Walter Orenstein (Chair, IVIR-AC)
Emory University, Atlanta, USA**

IVIR Advisory Committee 2018

Advises WHO on implementation research related to vaccines and immunization programs
Provides guidance on quantitative methods useful to vaccine research



Agenda

- **Theme 1 Minimize barriers for vaccine uptake**
 - Global research on Vaccine Demand and Acceptance update
 - Cervical Cancer Elimination modeling
- **Theme 2 Maximize impact of vaccines in use**
 - Measles optimal intervals between SIAs and mortality model
 - Total Systems Effectiveness (methods and tools to support country level decision making on vaccines)
 - WHO Guide on Typhoid Vaccine Cost-effectiveness
 - Multi-model comparison guidelines
- **Theme 3 Research to improve methods for monitoring of immunization programmes**
 - Data to identify areas of risk

Cervical cancer elimination model comparison

Questions

- Does IVIR-AC have any specific comments on the modeling methods of the individual models used in the cervical cancer elimination comparison study?
- What is IVIR-AC's impression of the process, methods used and interpretation of the collaborative model comparison work for defining the cervical elimination thresholds and the strategies towards global cervical cancer elimination?

Recommendations on individual models

- Individual models (Policy-1, Harvard, HPV-ADVISE and Spectrum) are well-established models and well-known for their vaccine and screening applications in multiple HIC and LMIC settings.
- Models are sufficiently distinct and compatible to explore the model uncertainty in estimating whether short and long term impacts can be achieved through feasible combined screening and vaccination strategies

Recommendations on collaborative model comparison (1)

- The Committee acknowledge that modelers responded to the questions of the feasibility of cervical cancer elimination. However, the Committee felt that it is more important to determine what the gains are at different milestones
- The arbitrary defined elimination thresholds (cases/100,000) do not show the most important public health impacts to measure, i.e., massive reduction in absolute numbers of cervical cancer cases and deaths
- The elimination thresholds should be defined in light of evidence from modeling feasibility, cost-effectiveness, financial resources required, health systems implications, and public health impact of different options
- The Committee expressed concerns about the definition of “elimination” and thought better terms would be “massive reductions in disease” or “advanced control of disease”

Recommendations on collaborative model comparison (2)

- For next steps, the economic analysis should focus on the marginal costs and marginal benefits over time, both with and without discounting.
 - In terms of marginal benefits, these should include percentage of cases and deaths averted, life years gained and DALYs averted related to cervical cancer and other cancers.
 - In terms of marginal costs, care should be given to document the most influential time dependent and scale-specific costs of setting up and maintaining screening practices, as well as the marginal costs of ramping up and maintaining vaccination coverage at high levels.
- At the same time, consideration should be given to changing costs of vaccines, screening technology and cancer treatment over time; as well as the opportunity costs to the local health systems.

Measles investment case

Questions to IVIR-AC

- IVIR-AC was requested to assess the KidRisk measles model that was used to assess the elimination goals

IVIR-AC recommendations

- IVIR-AC agrees with the conclusions of the IVIR-AC measles-rubella working group.
- It is important to measure the programmatically positive impact of measles and rubella elimination activities on the overall immunization system, including for example, strengthening the 2nd year of life platform and implementing school entry checks for not only measles and rubella, but all recommended antigens and providing those vaccines to children in need.
- IVIR-AC supports having an alternative group model the impact of the elimination program to address some of the concerns raised with the current model, to potentially use innovative modelling approaches, and to obtain greater confidence in the results.

WHO current recommendation: Optimal intervals between follow up SIA for measles

WHO Measles Position Paper 2017

- ❑ “...Programmes should conduct follow-up campaigns before the number of pre-school children susceptible to measles approaches the equivalent of one birth cohort, in order to prevent an outbreak of measles.”
- ❑ “...A more extensive assessment of accumulation of susceptible persons should be carried out at the subnational level, especially for countries close to measles elimination.

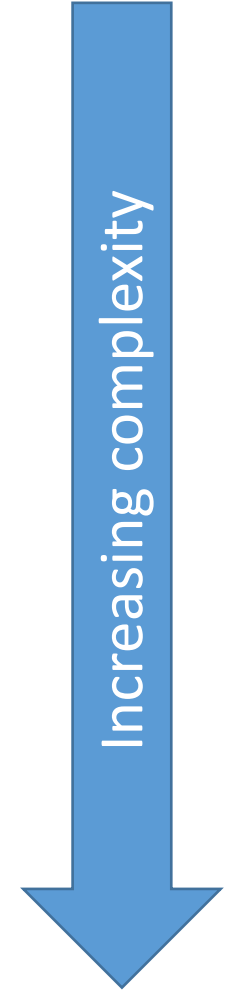
Rule of Thumb

Countries are recommended to monitor the accumulation of susceptible preschool children and conduct an SIA when the number approaches the size of one birth cohort.

Because coverage data are often unreliable, programme managers should use the **best quality data available** to determine the minimum interval between SIAs so as to prevent outbreaks.

Four alternative approaches examined

- ❑ (Jennifer) Knapp – “sophisticated” one-birth-cohort rule
- ❑ (Stéphane) Verguet – equilibrium solution to SIR equations
- ❑ (Amalie) McKee – calculation of proportion susceptible
- ❑ (Sebastian) Funk – estimation of R_n given susceptibility and contact patterns



Definition of outbreaks:

1) Incidence exceeding the median plus twice the interquartile range of incidence over the last 15 years.

– OR –

2a) Incidence exceeding one case per million population in a country if this value is > than definition #1

2b) Incidence exceeding 100 cases per million population in a particular year if this value is < than definition #1

IVIR-AC Recommendations optimal interval between follow up of measles SIAs

- **IVIR-AC was impressed with the quality of the work presented on estimating intervals for new SIAs, the potential impact of various methodologies, and the analysis of the strengths and weaknesses of the various models used.**
- **IVIR-AC emphasizes that the models should be capable of indicating when to conduct national as well sub-national SIAs.**
- **For future modelling work, IVIR-AC suggests that interruption of transmission, defined as at least 1 year of no sustained indigenous transmission, is a critical outcome to be considered regarding SIA interval and frequency**

IVIR-AC Recommendations optimal interval between follow up of measles SIAs

Issues regarding the need and performance of SIAs within routine immunization programs:

- **Considering potential concerns that SIAs may be disruptive to routine immunization systems as well as overall health systems, it is critical to document how SIAs impact these.**
 - **Protocols should be developed to assist program managers in assessing the positive and negative impacts or opportunity costs of SIAs on the overall systems, as previously recommended by IVIR-AC.**
- **It is important to investigate whether the cases are primarily due to accumulation of susceptible persons born since the last SIA or a problem with implementation and coverage of previous SIAs.**
 - **It require follow-up SIAs including older age groups.**
 - **Outbreak investigations and better surveillance are required to identify and measure causes of immunization gaps.**
- **While SIAs are needed now, the ultimate goal is a routine immunization system that is capable of inducing adequate population immunity to interrupt transmission, making SIAs unnecessary.**

Data for risk analysis

Questions to IVIR-AC:

- Review a US-CDC/WHO tool to predict the level of risk of a diphtheria outbreak by country to inform vaccination policy to prevent future epidemics, as well as predict demand for diphtheria antitoxin, assisting manufacturers with an appropriate timeline and quantity needed for production

IVIR-AC recommended:

- Recognizes the value of the Diphtheria risk survey form, designed for guiding EPI managers in high-burden countries.
- Further experience on how to keep data current and accounts of the experience of programme managers, who make use of these graded criteria-based assessments of risk to guide vaccination-related priorities, will help to further improve the survey methods and their effective use.
- Continued assessment of the correlation between predictions and outcomes and continued improvement of the tool.
- As the work proceeds, more sophisticated data analytic methods for deriving weights should also be considered to improve the usefulness of the survey data. These could be used to inform the value of weights given to different criteria, without needing to make the actual tool used by programme managers any more complicated.
- Consider using the risk model for diphtheria outbreaks as a template for other diseases.

Thank you

Ministerio de Salud y Deportes
Programa Ampliado de Inmunización

CARNET DE VACUNACIÓN

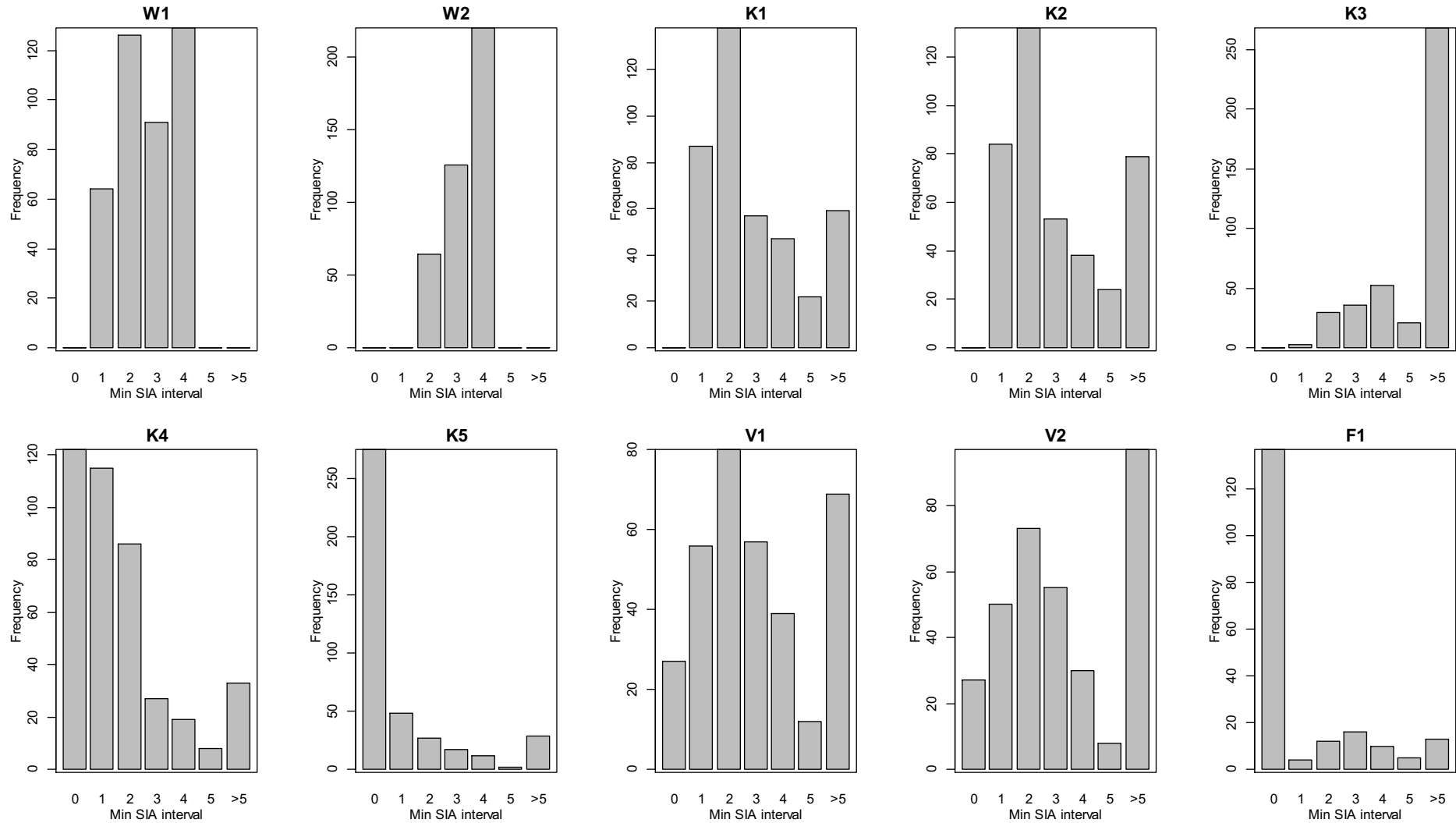
Nombre y Apellido: *Esmeralda Nelly Jimenez*
Fecha de Nacimiento: *25/05/88*
Departamento de Salud: *Salto*
Centro de Salud: *Alto*
Este es un Documento Importante

EXTRA SLIDES

Reminder: ten methods

Code	Approach	Method
W1	WHO	Categorical approach to rule-of-thumb (restrictive)
W2	WHO	Categorical approach to rule-of-thumb (permissive)
K1	Knapp	Reciprocal of MCV1 effective coverage
K2	Knapp	Reciprocal of MCV1 and MCV2 effective coverage
K3	Knapp	Reciprocal of 5 years average of susceptibility
K4	Knapp	Full susceptibility profile from 5 years and forward projection of most susceptible 1-4y cohort
K5	Knapp	Full susceptibility profile from 10 years and forward projection with susceptibility of 1-2y olds in last year
V1	Verguet	Equilibrium solution of SIR equations with MCV1
V2	Verguet	Equilibrium solution of SIR equations with MCV1 and MCV2
F1	Funk	Calculation of herd immunity threshold based on empirical contact patterns

Distribution of SIA intervals



>100

>4