Poliovirus Surveillance among patients with Primary Immunodeficiency Disorders (PIDs)

Introduction of new guidelines

For the SAGE Meeting, April 3, 2019

iVDPVs: Background

- Healthy persons, when infected with poliovirus, excrete the virus for a period of about one month (in stool, and for a shorter period through pharyngeal spread) and then clear the infection

- Persons with primary immunodeficiencies (PIDs) affecting B-cells or combined primary immunodeficiencies, in rare circumstances, may excrete polioviruses for a longer period of time (prevalence of longer term excretion ~ 1% among PIDs [REF])
  - Prolonged excretion: 6 months – 5 years
  - Chronic excretion: >5 years

- In some instances, Sabin (vaccine) poliovirus develops into VDPV, in this case referred to as iVDPV

REF: Aghamohammadi A, Abolhassani H, Kutukculer N, Wassilak SG, Pallansch MA, Kluglein S, et al. Patients with Primary Immunodeficiencies Are a Reservoir of Poliovirus and a Risk to Polio Eradication. Front Immunol 2017; 8. DOI: 10.3389/fimmu.2017.00685

iVDPVs: Risk to poliovirus eradication

- iVDPV excretion is not compatible with global poliovirus eradication

- *Two major risks from iVDPV:*
  - *Risk of progression to paralysis and death (individual patient)*
  - *Risk of community spread and seeding of outbreaks (neurovirulence and transmissibility of iVDPVs considered equal to other VDPVs, however, only few instances have been described so far: USA, Spain)*

- **GPEI TASKS**:
  - *Detect iVDPV excretors – **iVDPV Surveillance Task Team***
    - *Strengthening surveillance to detect PID patients without paralysis - GUIDELINES*
  - *Stop poliovirus excretion – **Polio Antivirus Initiative***
    - Therapy to identified poliovirus excretors
      - combination antiviral therapy
      - poliovirus monoclonal antibodies

SAGE Recommendation from October 2016

(http://apps.who.int/iris/bitstream/10665/251810/1/WER9148.pdf?ua=1)

- *SAGE agreed with Polio Working Group's assessment that immunodeficiency-related vaccine-derived polioviruses (iVDPV) could constitute a risk in seeding communities and triggering outbreaks, and endorsed the proposed approach to expand AFP surveillance to detect more iVDPVs.*

2016, 91, 561-584 No. 48

World Health Organization
Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

2 DECEMBER 2016, 91th YEAR / 2 DÉCEMBRE 2016, 91e ANNÉE
No. 48, 2016, 91, 561–584
http://www.who.int/wer

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Meeting of the Strategic Advisory Group of Experts on immunization, October 2016 – conclusions and recommendations

The Strategic Advisory Group of Experts (SAGE) on immunization[1] met on 18–20 October 2016. This report summarizes the discussions, conclusions and recommendations.[2]

Report from the WHO Department of Immunization, Vaccines and Biologicals

The report addressed 4 main themes: the progress and failures observed; the current and recurrent challenges; the actions taken to accelerate progress; and the role of WHO.

The contribution of vaccination to the global reduction of mortality in children aged <5 years, and the broader impact of immunization in economic and productivity gains as well as community benefits were noted. SAGE emphasized the need for stronger communication on these health and non-health benefits of immunization.

The report noted that an additional 5.9 million children need to be vaccinated to achieve the goal of 90% 3rd dose diphtheria-tetanus-pertussis vaccine (DTP3) coverage by 2020. It called for accelerating the use of pneumococcal conjugate vaccine (PCV) and rotavirus vaccine as both have led to substantial reductions in childhood mortality.

The report cautioned that as immunization programmes are becoming more

Réunion du Groupe stratégique consultatif d'experts sur la vaccination, octobre 2016 – conclusions et recommandations

Le Groupe stratégique consultatif d'experts (SAGE) sur la vaccination[1] s'est réuni du 18 au 20 octobre 2016. Le présent rapport résume les discussions, conclusions et recommandations auxquelles il est parvenu.[2]

Rapport du Département Vaccination, vaccins et produits biologiques de l'OMS

Le rapport présenté était axé sur 4 thèmes principaux: les progrès et les échecs observés; les difficultés existantes et récurrentes; les mesures prises pour accélérer les progrès et le rôle de l'OMS.

Le rapport a évoqué la contribution de la vaccination à la réduction mondiale de la mortalité des enfants de <5 ans, ainsi que ses retombées positives plus générales sur l'économie, la productivité et le bien-être des communautés. Le SAGE a souligné la nécessité d'intensifier les efforts de communication pour mieux faire connaître les avantages de la vaccination, tant dans le domaine de la santé que dans d'autres domaines.

Le rapport a indiqué que 5,9 millions d'enfants supplémentaires devront être vaccinés pour atteindre l'objectif d'une couverture de 90% par la 3e dose de vaccin antidiphtérique-antitétanique-anticoquelucheux (DTC3) d'ici 2020. Il a appelé à une utilisation accélérée du vaccin antipneumococcique conjugué (VPC) et du vaccin antirotavirus, qui ont tous deux contribué à la baisse substantielle de la mortalité de l'enfant.

Le rapport a fait valoir que face à la complexité croissante des programmes de vaccination,

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[1] See http://www.who.int/immunization/sage/en/index.html; accessed October 2016.

[2] Presentations and background materials used for the SAGE meeting together with the list of SAGE members and summarized declarations of interests are available at http://www.who.int/immunization/sage/meetings/2016/october/en/index.html; accessed October 2016.

[1] Voir http://www.who.int/immunization/sage/fr/index.html; consulté en octobre 2016.

[2] Les communications et les documents de travail utilisés pour la réunion du SAGE, ainsi que la liste des membres du SAGE et une synthèse de leurs déclarations d'intérêts sont disponibles à l'adresse: http://www.who.int/immunization/sage/meetings/2016/october/en/index.html; consulté en octobre 2016.

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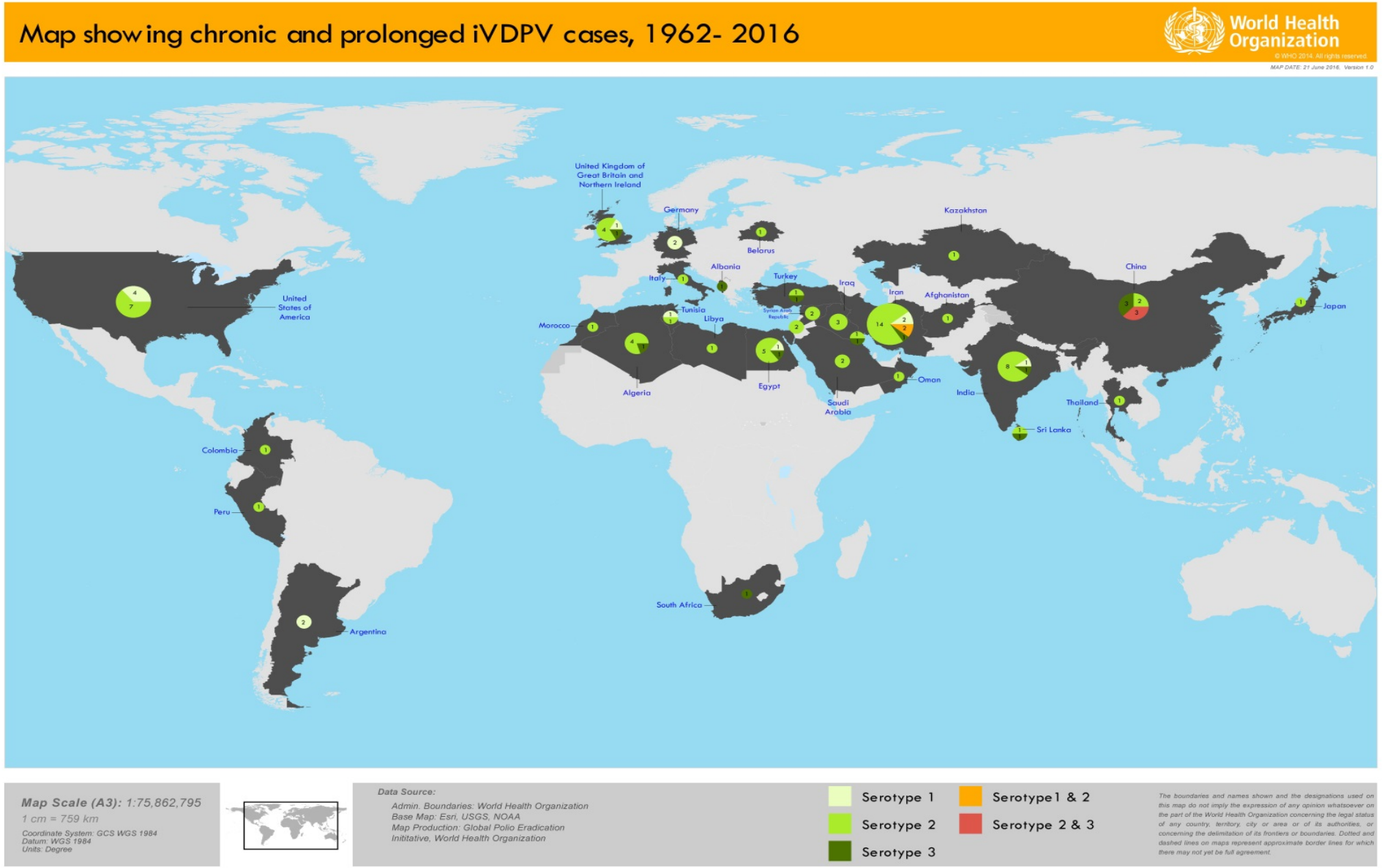
iVDPVs: Current understanding of global burden: Analysis of WHO Registry Capturing iVDPV cases since 1962

REF: Macklin G, Liao Y, Takane M, Dooling K, Gilmour S, Mach O, et al. Prolonged Excretion of Poliovirus among Individuals with Primary Immunodeficiency Disorder: An Analysis of the World Health Organization Registry. Front Immunol 2017; 8:1103. DOI: 10.3389/fimmu.2017.01103

Demographic data, n = 141

Attribute	Percentage
Gender (n=135)	
Male	58.2% (82/135)
Age distribution (n=137)	
<1 yr	58.3% (80/137)
1-4 yrs	27.7% (38/137)
5-9 yrs	5.8% (8/137)
10-19 yrs	5.1% (7/137)
20-29 yrs	1.5% (2/137)
30+ yrs	1.5% (2/137)
Residence (n=141)	
Low income	0.7% (1/141)
Lower-middle income	30.4% (43/141)
Upper-middle income	47.5% (67/141)
High income	21.3% (30/141)

iVDPV Cases: Geographic Distribution



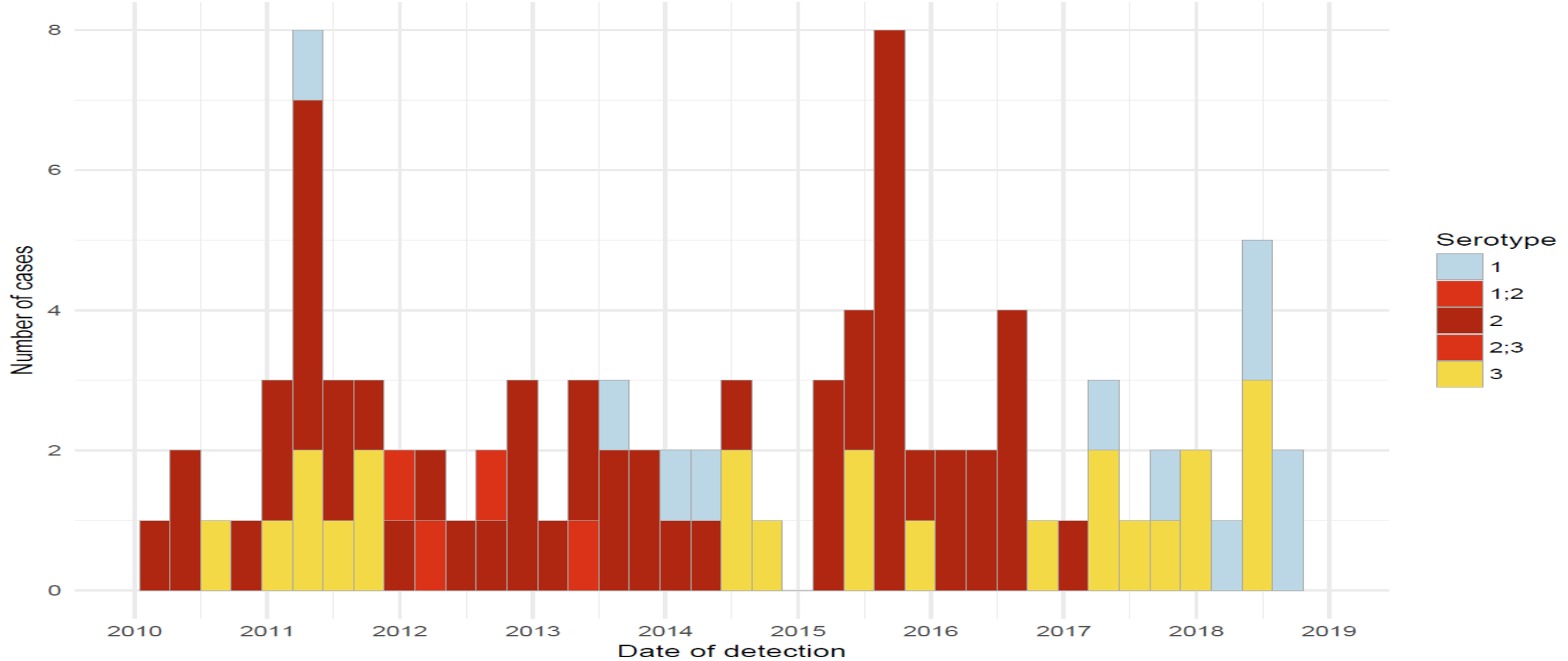
Underlying immunodeficiency disorder, and outcome

Attribute	Percentage
Diagnosis (n=120)	
XLA	10.8% (13/120)
Other antibody disorders	20.0% (24/120)
SCID	31.7% (38/120)
CVID	18.3% (22/120)
MHC class II deficiency	5.8% (7/120)
Other	13.3% (16/120)
Paralysis (n=138)	
Yes	63.8% (90/138)
Outcome (n=141)	
Alive	44.7% (63/141)
Dead	44.7% (63/141)
Lost to follow up	10.6% (15/141)

Virologic and excretion length information

Attribute	Percentage
Serotype (n=141)	
Type 1	17.0% (24/141)
Type 2	58.2% (82/141)
Type 3	20.6% (29/141)
Combination 1+2	2.1% (3/141)
Combination 2+3	2.1% (3/141)
All type 2 associated	**62.4% (88/141)**
Length of excretion (n=63) [Alive and not lost to follow up]	
Stopped excreting	74.6% (47/63)
Less than 6 months	1.6% (1/63)
Prolonged (≥6 months - ≤5 years)	22.2% (14/63)
Chronic (>5 years)	1.6% (1/63)

iVDPV Serotypes per and post OPV switch



iVDPV Detection in 2018

	N=11
Country	Egypt 6x; China 2x; Iran, Colombia, South Africa
Serotype	iVDPV1 6x; iVDPV2 0x; iVDPV3 5x
Divergence	0.6-2.6 %
Length of excretion	>=6 months (10x); <6 months (1x)
Median age	2 years
PID	SCID (5x); other antibody disorder (2x); unknown (4x)

Guidelines

- Purpose:

Provide clear, concrete instructions to introduce and conduct surveillance for poliovirus among patients diagnosed with primary immune deficiency

- Audience:
  - Polio program country and regional teams, mid-level managers
  - Polio surveillance staff
  - **Staff at specialized immunology and pediatric centers** – (one page guide will be developed for physicians)

Basis for the Guidelines Development

- Experience from iVDPV pilot studies in multiple countries
- Collaboration with the Jeffrey Modell Foundation and results from their studies
- Consultation with SAGE WG on polio

Poliovirus Excretion Among Persons With Primary Immune Deficiency Disorders: Summary of a Seven-Country Study Series

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Background. Persons with primary immune deficiency disorders (PID), especially those disorders affecting the B-cell system, are at substantially increased risk of paralytic poliomyelitis and can excrete poliovirus chronically. However, the risk of prolonged or chronic excretion is not well characterized in developing countries. We present a summary of a country study series on poliovirus excretion among PID cases.

Methods. Cases with PID from participating institutions were enrolled during the first year and after obtaining informed consent were tested for polioviruses in stool samples. Those cases excreting poliovirus were followed on a monthly basis during the second year until 2 negative stool samples were obtained.

Results. A total of 562 cases were enrolled in Bangladesh, China, Iran, Philippines, Russia, Sri Lanka, and Tunisia during 2008–2013. Of these, 17 (3%) shed poliovirus, including 2 cases with immunodeficient vaccine-derived poliovirus. Poliovirus was detected in a single sample from 5/17 (29%) cases. One case excreted for more than 6 months. None of the cases developed paralysis during the study period.

Conclusions. Chronic polioviruses excretion remains a rare event even among individuals with PID. Nevertheless, because these individuals were not paralyzed they would have been missed by current surveillance; therefore, surveillance for polioviruses among PID should be established.

Implementing surveillance: Objective

- To detect excretors of Poliovirus among patients with PID
- To outline effective case management protocols for excretors
- To propose a public health response that reduces both the individual's risk of developing poliomyelitis and the community's risk of poliovirus transmission

Case definition and Classification

PID patients at risk for excreting poliovirus

An individual of any age who has a primary humoral (B-cell) or humoral (B-cell)/cellular (T-cell) combined immunodeficiency disorder **confirmed by** levels of **immunoglobulin below standards** for age **and** by **diagnosis from a specialized physician**

- **Stool samples collected using AFP guidelines from persons satisfying case definition**

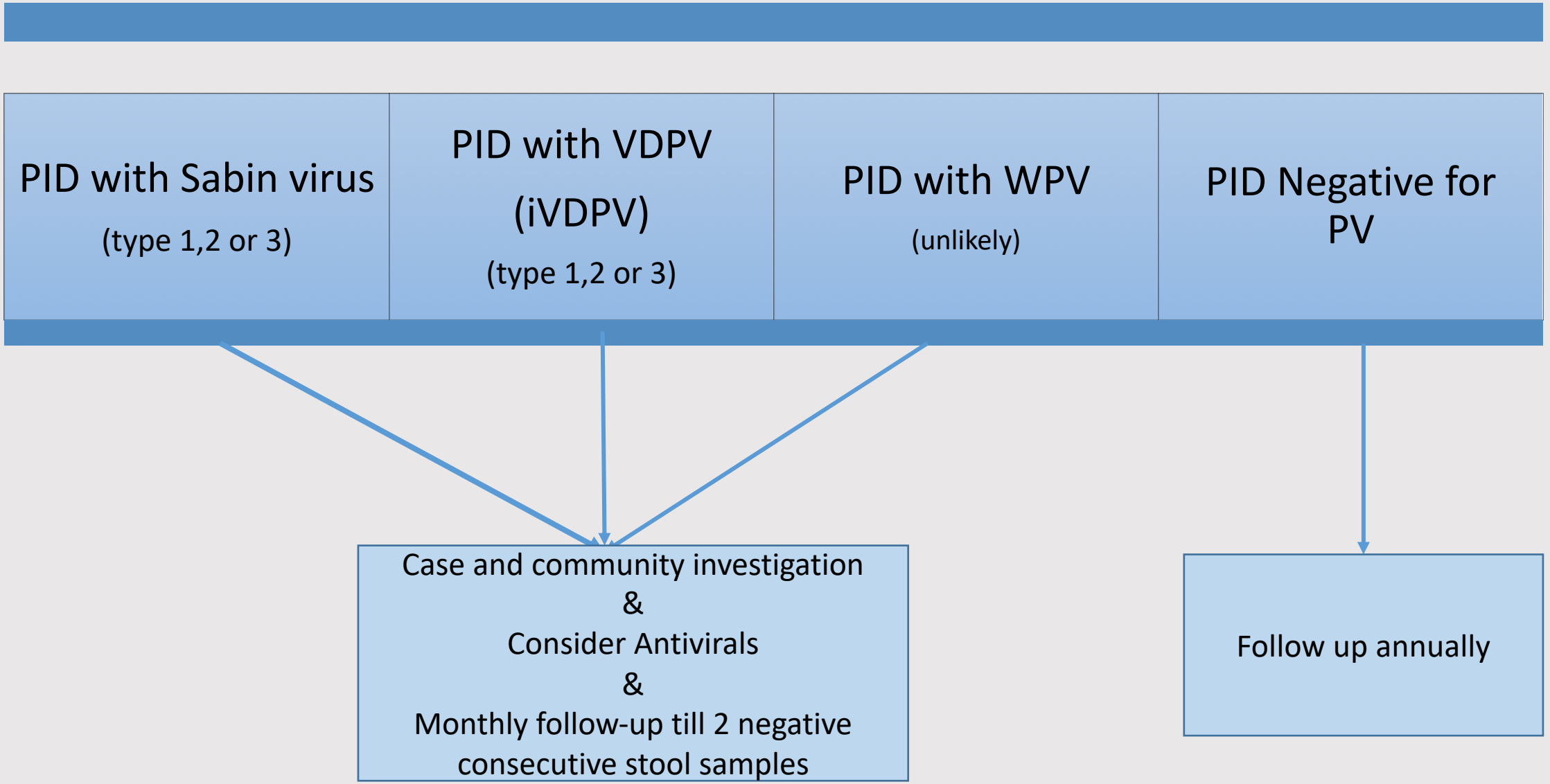
Examples:

- Antibody disorder, including X-linked agammaglobulinemia
- Severe combined immunodeficiency disorder and other combined deficiencies.
- Common variable immunodeficiency disorder (CVID)
- Others, including major histocompatibility complex deficiencies

Does not include:

- Secondary immunodeficiency (infection including HIV or therapy)
- Isolated deficiencies of IgA or IgE
- Malnutrition

Case classification and follow up



Case management

- Advise no OPV for PID patients and immediate family
- Case and community investigation
- Consider antivirals

N.B. Management of PID is not part of the guidelines; polio program is not in a position to guide or support PID management

Current Status and plan

- Countries continue with iVDPV surveillance which started as pilot studies: Egypt, Sri Lanka, Tunisia, Iran
- New countries have initial funding for pilots: Pakistan, India, China
- Most countries with AFP surveillance do detect iVDPVs in paralyzed children as part of AFP or other surveillance on their own
- Priority countries are being identified in each WHO region to roll-out **systematic** surveillance utilizing these guidelines focusing on PID children without paralysis

Summary

- Guidelines are simple to implement however challenging to communicate with unfamiliar partners in unfamiliar places

- New partnerships (with tertiary health care institutions) in non-polio-traditional countries will need to be established

- Endorsement from SAGE would play an important role