Report from the Polio Working Group Meeting

Yagob Al-Mazrou
Chair, SAGE Working Group
April 12, 2016

Overview

- Background
- WG Discussion and Recommendations
  - Risk of continued VDPV2 circulation
    - cVDPV2 epidemiology
    - Risk mitigation strategy
  - Country readiness criteria for tOPV-bOPV switch
  - Future immunization policy against poliovirus
- Proposed Recommendations for SAGE

Background: SAGE Recommendations in October 2015

2015, 90, 681-700 No. 50

World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

11 DECEMBER 2015, 90th YEAR / 11 DÉCEMBRE 2015, 90e ANNÉE
No. 50, 2015, 90, 681–700
http://www.who.int/wer

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Meeting of the Strategic Advisory Group of Experts on immunization, October 2015 – conclusions and recommendations

The Strategic Advisory Group of Experts on immunization (SAGE)[1] met on 20–22 October 2015. This report summarizes the discussions, conclusions and recommendations.[2] For the malaria session, SAGE was joined by the Malaria Policy Advisory Committee (MPAC) and the conclusions and recommendations concerning malaria vaccine are those of both committees.

Report from the WHO Department of Immunization, Vaccines and Biologicals

The core message of the report, "closing the immunization gap", is reflected in most of the following activities.

The report addressed vaccine research coordinated by WHO, highlighting unprecedented contributions in the development of Ebola vaccines, emphasizing collaborative efforts, adaptation of traditional research and development models, compressed timeframes and innovative partnerships. The report flagged the Global Vaccine & Immunization Research Forum,[3] which will be held in March 2016.

The report highlighted global progress made on increasing vaccination coverage including reaching 90% coverage with the first dose of diphtheria-tetanus-pertussis (DTP) containing vaccine globally.

Réunion du Groupe stratégique consultatif d'experts sur la vaccination, octobre 2015 – conclusions et recommandations

Le Groupe stratégique consultatif d'experts sur la vaccination (SAGE)[1] s'est réuni du 20 au 22 octobre 2015. Le présent rapport résume les discussions, conclusions et recommandations auxquelles il est parvenu.[2] Le Comité de pilotage de la politique de lutte antipaludique (MPAC) s'est joint au SAGE pour la session consacrée au paludisme: les conclusions et recommandations relatives au vaccin antipaludique émanent donc de ces deux Comités.

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

Ce rapport est essentiellement axé sur la nécessité de combler les lacunes de la couverture vaccinale, message qui est reflété dans la plupart des activités mentionnées ci-dessous.

Le rapport évoque les travaux de recherche vaccinale coordonnés par l'OMS, soulignant les contributions sans précédent apportées au développement des vaccins contre Ebola, dans un contexte de collaboration, d'adaptation des modèles traditionnels de recherche et développement, de compression des délais et d'établissement de partenariats novateurs. Il indique en outre que le Forum mondial de recherche sur les vaccins et la vaccination[3] se tiendra en mars 2016.

Le rapport souligne les progrès réalisés dans le monde entier en matière de couverture vaccinale, notant en particulier que la couverture par la première dose du vaccin antidiphtérique-antitétanique-anticoquelucheux (DTC)

[1] See http://www.who.int/immunization/policy/sage/en/; accessed October 2015.

[2] The complete set of presentations and background materials used for the SAGE meeting of 20–22 October 2015 together with the list of SAGE members and the summarized declarations of interests provided by SAGE members are available at http://www.who.int/immunization/sage/meetings/2015/october/en/index.html; accessed October 2015.

[3] See http://www.who.int/immunization/research/forums_and_initiatives/gvirf/en/.

[1] Voir http://www.who.int/immunization/policy/sage/fr/: consulté en octobre 2015.

[2] La série complète des communications et des documents de travail utilisés pour la réunion du SAGE du 20 au 22 octobre 2015, ainsi que la liste des membres du SAGE et les résumés de leurs déclarations d'intérêts sont disponibles à l'adresse: http://www.who.int/immunization/sage/meetings/2015/october/en/index.html: consulté en octobre 2015.

[3] Voir http://www.who.int/immunization/research/forums_and_initiatives/gvirf/en/.

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WORLD HEALTH ORGANIZATION Geneva
ORGANISATION MONDIALE DE LA SANTÉ Genève

Annual subscription / Abonnement annuel Sw. fr. / Fr. s. 346.–

12.2015
ISSN 0049-8114
Printed in Switzerland

- SAGE reaffirmed that withdrawal of OPV2 should proceed in April 2016 even in the event of further change in IPV supply

- SAGE concluded the public health risks associated with the continued use of the type 2 component contained in tOPV outweigh the risk of new VDPV2 emergence after use of OPV2 is stopped.

- SAGE requested Polio WG to provide urgent guidance on optimal management of IPV supply and mitigation of other risks in case the IPV supply is further reduced

Polio WG Discussions

- Following up on the SAGE recommendations, the WG met on 19-20 January 2016, had a conference call (3 March 2016) and exchanged e-mails to:
  - appraise the current epidemiology of cVDPV2
  - examine the status of preparation for OPV type 2 withdrawal (esp. IPV supply situations)

- It also started discussions on the roadmap for SAGE discussions and recommendations on future polio immunization policy

WG discussion and Recommendations:
cVDPV2 Epidemiology

Risk of cVDPV2

- The WG acknowledged the progress made in eliminating persistent cVDPV2 in Pakistan and Nigeria (i.e. no case since May 2015)

- The WG judged that the response to the VDPV type 2 outbreak in Myanmar is adequate. However, the WG was concerned about the situations in Guinea and DRC. The WG recommends that:
  - The program intensify programme surveillance in Guinea and its neighbouring and recently Ebola-affected countries of Sierra Leone and Liberia.
  - The outbreak response in Guinea and DRC should continue, if needed, with mOPV2 after the switch

- To ensure all type 2 polioviruses are notified under the International Health Regulations (IHR), the WG agreed that WHO should amend and broaden the WHO surveillance case definition to include type 2 Sabin in addition to (all types of) wild and vaccine-derived poliovirus after 1 August 2016.

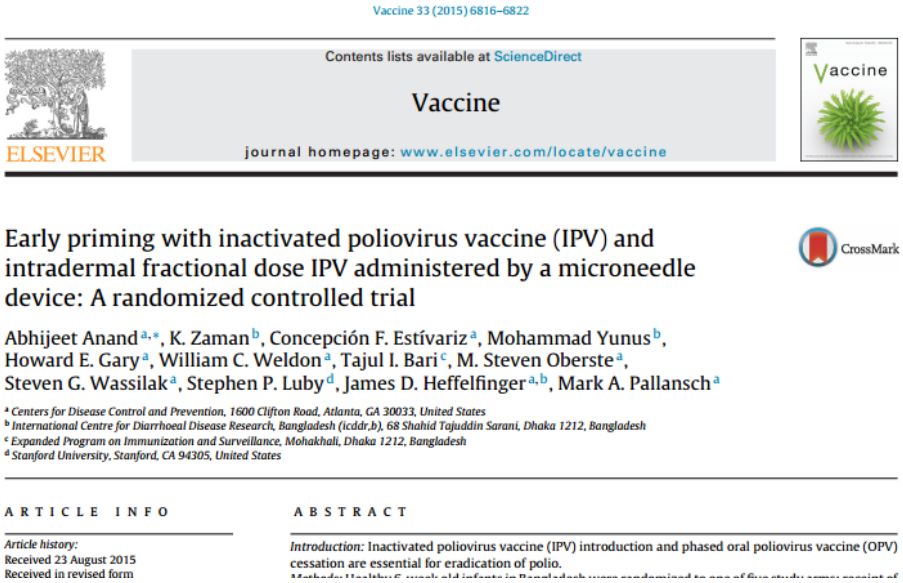
WG discussion and Recommendations:

Country Readiness Criteria

Country Readiness Criteria: WG Assessment

- The WG acknowledged the strong and sustained progress toward addressing the readiness criteria for the tOPV-bOPV switch, including the completion of phase I for WPV2/VPDV2 in most countries, under the Global Action Plan for Containment (GAP III)
- The WG expressed concern that the IPV supply shortage will likely persist into 2017/18, and endorsed the program's proposal to prioritize IPV supply to Tier 1 and 2 countries
- The WG encourages countries to consider the use of two fractional intradermal (ID) dose of IPV in the routine immunizations to address IPV shortage

Two fractional doses versus one full dose



Vaccine 33 (2015) 6816–6822

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Early priming with inactivated poliovirus vaccine (IPV) and intradermal fractional dose IPV administered by a microneedle device: A randomized controlled trial

Abhijeet Anand[a,*], K. Zaman[b], Concepción F. Estívariz[a], Mohammad Yunus[b], Howard E. Gary[a], William C. Weldon[a], Tajul I. Bari[c], M. Steven Oberste[a], Steven G. Wassilak[a], Stephen P. Luby[d], James D. Heffelfinger[a,b], Mark A. Pallansch[a]

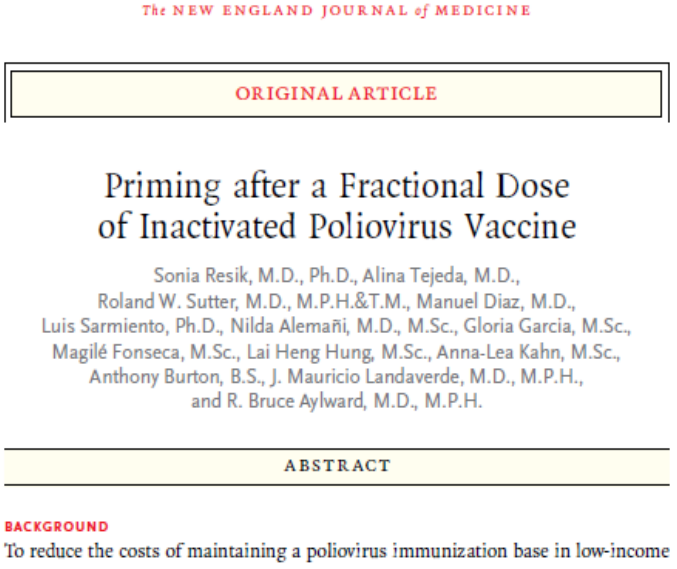
[a] Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, GA 30033, United States
[b] International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), 68 Shahid Tajuddin Sarani, Dhaka 1212, Bangladesh
[c] Expanded Program on Immunization and Surveillance, Mohakhali, Dhaka 1212, Bangladesh
[d] Stanford University, Stanford, CA 94305, United States

ARTICLE INFO

Article history:
Received 23 August 2015
Received in revised form

ABSTRACT

Introduction: Inactivated poliovirus vaccine (IPV) introduction and phased oral poliovirus vaccine (OPV) cessation are essential for eradication of polio.



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Priming after a Fractional Dose of Inactivated Poliovirus Vaccine

Sonia Resik, M.D., Ph.D., Alina Tejeda, M.D., Roland W. Sutter, M.D., M.P.H.&T.M., Manuel Diaz, M.D., Luis Sarmiento, Ph.D., Nilda Alemañi, M.D., M.Sc., Gloria Garcia, M.Sc., Magilé Fonseca, M.Sc., Lai Heng Hung, M.Sc., Anna-Lea Kahn, M.Sc., Anthony Burton, B.S., J. Mauricio Landaverde, M.D., M.P.H., and R. Bruce Aylward, M.D., M.P.H.

ABSTRACT

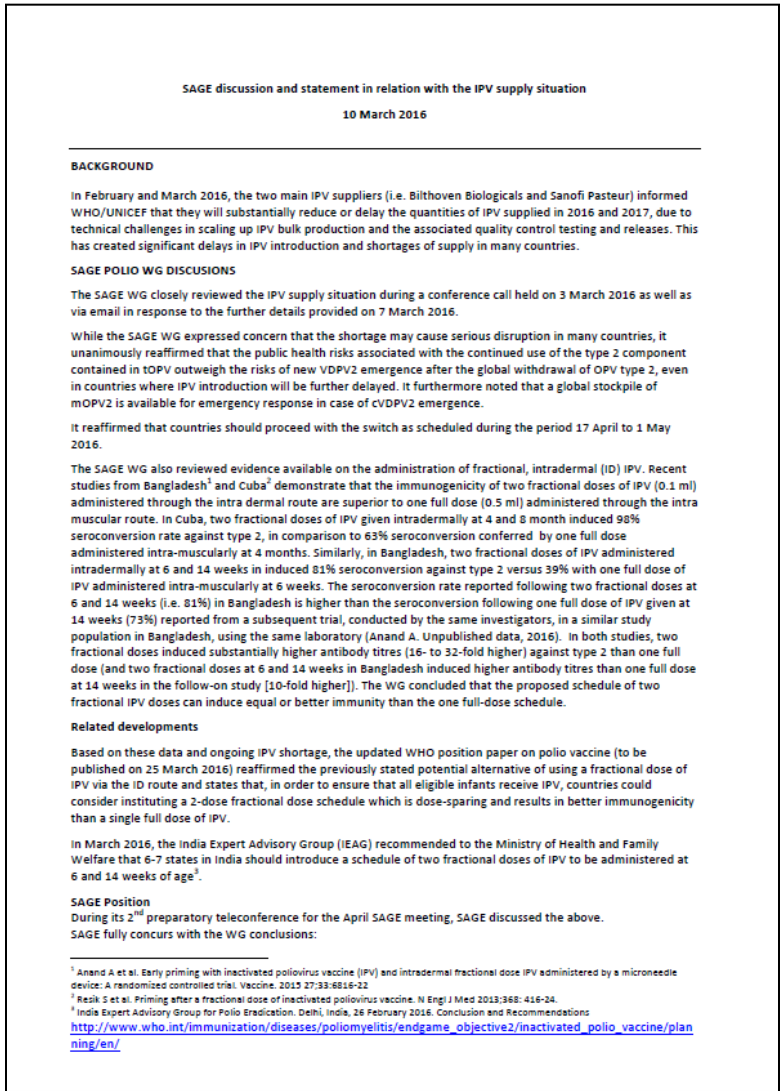
BACKGROUND

To reduce the costs of maintaining a poliovirus immunization base in low-income

Author	Year published	Country	Schedule	One full-dose IPV	*Two fractional doses given intradermally*
Resik S	2013 Shown above	Cuba	IPV	63% (4 mos)	**98%** (4+8 mos)
Anand A	2015 Shown above	Bangladesh	IPV	39% (6 wks)	**81%** (6+14 wks)
Anand A	2016 In publication	Bangladesh	IPV	73% (14 wks)	--

→ ***Two fractional doses are more immunogenic than one full dose***

SAGE Recommendations in relation to IPV Shortage



SAGE discussion and statement in relation with the IPV supply situation

10 March 2016

BACKGROUND

In February and March 2016, the two main IPV suppliers (i.e. Bilthoven Biologicals and Sanofi Pasteur) informed WHO/UNICEF that they will substantially reduce or delay the quantities of IPV supplied in 2016 and 2017, due to technical challenges in scaling up IPV bulk production and the associated quality control testing and releases. This has created significant delays in IPV introduction and shortages of supply in many countries.

SAGE POLIO WG DISCUSIONS

The SAGE WG closely reviewed the IPV supply situation during a conference call held on 3 March 2016 as well as via email in response to the further details provided on 7 March 2016.

While the SAGE WG expressed concern that the shortage may cause serious disruption in many countries, it unanimously reaffirmed that the public health risks associated with the continued use of the type 2 component contained in tOPV outweigh the risks of new VDPV2 emergence after the global withdrawal of OPV type 2, even in countries where IPV introduction will be further delayed. It furthermore noted that a global stockpile of mOPV2 is available for emergency response in case of cVDPV2 emergence.

It reaffirmed that countries should proceed with the switch as scheduled during the period 17 April to 1 May 2016.

The SAGE WG also reviewed evidence available on the administration of fractional, intradermal (ID) IPV. Recent studies from Bangladesh[1] and Cuba[2] demonstrate that the immunogenicity of two fractional doses of IPV (0.1 ml) administered through the intra dermal route are superior to one full dose (0.5 ml) administered through the intra muscular route. In Cuba, two fractional doses of IPV given intradermally at 4 and 8 month induced 98% seroconversion rate against type 2, in comparison to 63% seroconversion conferred by one full dose administered intra-muscularly at 4 months. Similarly, in Bangladesh, two fractional doses of IPV administered intradermally at 6 and 14 weeks in induced 81% seroconversion against type 2 versus 39% with one full dose of IPV administered intra-muscularly at 6 weeks. The seroconversion rate reported following two fractional doses at 6 and 14 weeks (i.e. 81%) in Bangladesh is higher than the seroconversion following one full dose of IPV given at 14 weeks (73%) reported from a subsequent trial, conducted by the same investigators, in a similar study population in Bangladesh, using the same laboratory (Anand A. Unpublished data, 2016). In both studies, two fractional doses induced substantially higher antibody titres (16- to 32-fold higher) against type 2 than one full dose (and two fractional doses at 6 and 14 weeks in Bangladesh induced higher antibody titres than one full dose at 14 weeks in the follow-on study [10-fold higher]). The WG concluded that the proposed schedule of two fractional IPV doses can induce equal or better immunity than the one full-dose schedule.

Related developments

Based on these data and ongoing IPV shortage, the updated WHO position paper on polio vaccine (to be published on 25 March 2016) reaffirmed the previously stated potential alternative of using a fractional dose of IPV via the ID route and states that, in order to ensure that all eligible infants receive IPV, countries could consider instituting a 2-dose fractional dose schedule which is dose-sparing and results in better immunogenicity than a single full dose of IPV.

In March 2016, the India Expert Advisory Group (IEAG) recommended to the Ministry of Health and Family Welfare that 6-7 states in India should introduce a schedule of two fractional doses of IPV to be administered at 6 and 14 weeks of age[3].

SAGE Position

During its 2nd preparatory teleconference for the April SAGE meeting, SAGE discussed the above.
SAGE fully concurs with the WG conclusions:

[1] Anand A et al. Early priming with inactivated poliovirus vaccine (IPV) and intradermal fractional dose IPV administered by a microneedle device: A randomized controlled trial. Vaccine. 2015 27;33:6816-22
[2] Resik S et al. Priming after a fractional dose of inactivated poliovirus vaccine. N Engl J Med 2013;368: 416-24.
[3] India Expert Advisory Group for Polio Eradication. Delhi, India, 26 February 2016. Conclusion and Recommendations
http://www.who.int/immunization/diseases/poliomyelitis/endgame_objective2/inactivated_polio_vaccine/planning/en/

- Given the urgency of the situation, SAGE issued a statement in March 2016:
  - SAGE re-affirmed its October 2015 conclusion that the Switch should proceed in April 2016, even with the recent decline in IPV supply
  - SAGE recommended that countries consider adopting a two fractional doses IPV schedule

- These recommendations are in line with its previous SAGE recommendations (April 2012) on the use of fractional ID IPV and recommendations by WG.

Country Readiness Criteria: WG Assessment (continued)

- Based on the mathematical models considered, the program should expect at least 1-2 cVDPV type 2 outbreaks within the first 12 months following the switch, with Pakistan representing a high-risk area.
- It is important to fully sequence any newly detected type 2 VDPV strain rapidly, to identify whether or not an outbreak response is required because iVDPV will require a different set of response activities
- The WG endorsed the revised protocol, including the following key principles:
  - The use of IPV in the case of "confirmed" outbreaks in Zone 1-2 countries with 4 or more SIAs
  - Target age group (0-5 years unless epidemiology suggests older persons involved)
  - Minimum target population (2 million)
  - GPEI Eradication & Outbreak Management Group (EOMG) be the expert committee advising DG

WG discussion and Recommendations:

Future Immunization Policy

Context

- tOPV to bOPV switch with at least one-dose of IPV in 2016
- All OPV withdrawal expected by 2020
- The decision for future immunization policy is needed by 2017 to allow sufficient vaccine quantities and funding

Planning Assumptions

- Timeline
  - Certification of eradication by 2019
  - bOPV withdrawal in 2020
- Need to continue vaccination against polio
- Time Horizon: 2020 – 2030
- Vaccines available: IPV, S-IPV, Hexavalent
- Target price: $ 0.50 per dose for stand alone

Key Considerations and Output

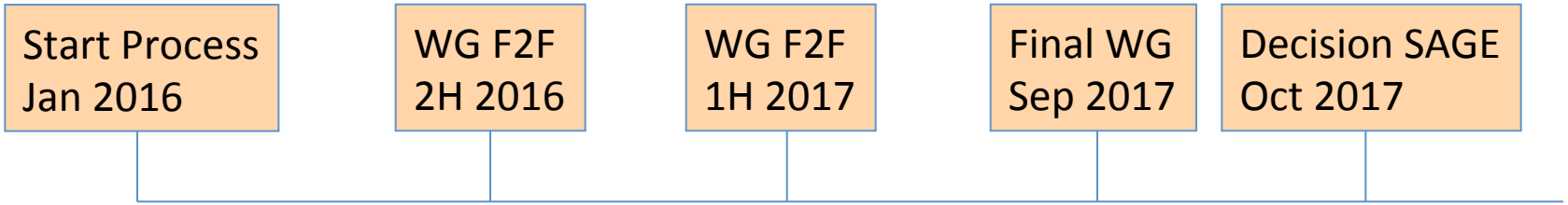
Key considerations

- Vaccine availability (i.e. Full dose IPV, hexavalent, new products such as sIPV, VLP, patches)
- Vaccine price (e.g. full-dose, fractional dose, combination)
- Funding availability (i.e. willingness of donor to support IPV in RI)

Output

- Explicit decision to continue polio vaccination
- IPV schedule (# of doses, timing, formulation) after OPV withdrawal
- Criteria for countries to stop polio vaccination (e.g. surveillance capacity, absence of iVDPV)

Timeline for review and decision-making



After 2017, recommendation should be translated into actual demand/supply of doses/year per product: 1) standalone IPV; or 2) hexavalent combination IPV vaccine.

WG Recommendations: Summary (1/3)

The WG recommends that SAGE:

- **Recommends:** IPV suppliers should make their best effort to fulfil commitment to supply IPV, and inform Polio WG of any further change in IPV supply situation
- **Reaffirms**: its March 2016 recommendations that all countries must stop using tOPV in April 2016, even with insufficient IPV supply or delay in introducing bOPV in some countries
- **Reaffirms** : its March 2016 recommendations that, in the face of IPV supply constraints, countries should consider adopting a two fractional dose schedule into their routine immunization schedule
- **Recommends:** GPEI should ensure high quality SIAs in Guinea and DRC, if necessary, with mOPV2 after April 2016 and intensify programme surveillance in these countries as well as recently Ebola-affected countries (e.g. Sierra Leone and Liberia)

WG Recommendations: Summary (2/3)

The WG recommends that SAGE:

- **Urges:** all countries to ensure completion of phase I of GAP III for all type 2 poliovirus, including Sabin2 and strengthen national intersectoral collaboration to comply with phase II of GAPIII endorsed by 2015 WHA
- **Recommends:** GPEI should respond to any type 2 VDPV emergence after April 2016 as an emergency, as per updated type 2 response protocol
- **Recommends**: WHO should amend and broaden the WHO surveillance case definition to include type 2 Sabin in addition to all types of wild and vaccine-derived poliovirus.

WG Recommendations: Summary (3/3)

The WG recommends that SAGE:

- **Endorses:** the proposed approach to consider future immunization policy against poliovirus after OPV withdrawal
- **Requests:** the Polio WG should propose a high-level policy direction during 2016 and to finalize its recommendations for SAGE consideration in 2017.

Thank you very much!