Journal INFDIS ÷

Article Doi 10.1093/infdis/jix112 :

UNIVERSITY PRESS Article Title Transitioning Lessons Learned and Assets of the Global Polio Eradication Initiative to Global and Regional Measles and Rubella Elimination

# INSTRUCTIONS

- Author groups: Please check that all names have been spelled correctly and appear in the correct order. Please also check that all initials are present. Please check that the author surnames (family name) have been correctly identified by a pink background. If this is incorrect, please identify the full surname of the relevant authors. Occasionally, the distinction between surnames and forenames can be ambiguous, and this is to ensure that the authors' full surnames and forenames are tagged correctly, for accurate indexing online. Please also check all author affiliations.
- Figures: If applicable figures have been placed as close as possible to their first citation. Please check that they are complete and 2. that the correct figure legend is present. Figures in the proof are low resolution versions that will be replaced with high resolution versions when the journal is printed.
- 3. Missing elements: Please check that the text is complete and that all figures, tables and their legends are included.
- 4. Funding: Please provide a Funding statement, detailing any funding received. Remember that any funding used while completing this work should be highlighted in a separate Funding section. Please ensure that you use the full official name of the funding body. and if your paper has received funding from any institution, such as NIH, please inform us of the grant number to go into the funding section. We use the institution names to tag NIH-funded articles so they are deposited at PMC. If we already have this information, we will have tagged it and it will appear as colored text in the funding paragraph. Please check the information is correct. [red text to be used for suppliers who are tagging the funding]
- Conflict of interest: All authors must make a formal statement indicating any potential conflict of interest that might constitute an 5. embarrassment to any of the authors if it were not to be declared and were to emerge after publication. Such conflicts might include, but are not limited to, shareholding in or receipt of a grant or consultancy fee from a company whose product features in the submitted manuscript or which manufactures a competing product. The following statement has been added to your proof: 'Conflict of Interest: none declared'. If this is incorrect please supply the necessary text to identify the conflict of interest.
- Abbreviations: some commonly used abbreviations have been automatically expanded for clarity to readers. By using the tracked 6. changes proof for reference, please check the expanded abbreviations have been made correctly and mark up any corrections (if required) here or by email, listing the line and page numbers your correction refers to.
- 7. Please review your article for patient names and confirm that there are no instances where a patient can be identified.

# MAKING CORRECTIONS TO YOUR PROOF

These instructions show you how to mark changes or add notes to your proofs using Adobe Acrobat Professional versions 7 and onwards, or Adobe Reader DC. To check what version you are using go to **Help** then **About**. The latest version of Adobe Reader is available for free from <u>get.adobe.com/reader</u>.

## **DISPLAYING THE TOOLBARS**

## Adobe Reader DC

In Adobe Reader DC, the Comment toolbar can be found by clicking 'Comment' in the menu on the right-hand side of the page (shown below).



## Acrobat Professional 7, 8, and 9

In Adobe Professional, the Comment toolbar can be found by clicking 'Comment(s)' in the top toolbar, and then clicking 'Show Comment & Markup Toolbar' (shown below).



The toolbar shown below will then be displayed along the top.



The toolbar shown below will then display along the top.  $\varnothing \ \angle \ \underline{T} \ \underline{T} \ \underline{T} \ \underline{T} \ \underline{T} \ \underline{T} \ \angle \ \partial \ \underline{\partial}^{*} \ \underline{\partial}^{*}$ 

## USING TEXT EDITS AND COMMENTS IN ACROBAT

This is the quickest, simplest and easiest method both to make corrections, and for your corrections to be transferred and checked.



## 1. Click Text Edits

 Select the text to be annotated or place your cursor at the insertion point and start typing.
 Click the **Text Edits** drop down arrow and select the

required action.

You can also right click on selected text for a range of commenting options, or add sticky notes.

## SAVING COMMENTS

In order to save your comments and notes, you need to save the file (**File, Save**) when you close the document.

## USING COMMENTING TOOLS IN ADOBE READER

All commenting tools are displayed in the toolbar. You cannot use text edits, however you can still use highlighter, sticky notes, and a variety of insert/replace text options.



#### **POP-UP NOTES**

In both Reader and Acrobat, when you insert or edit text a pop-up box will appear. In **Acrobat** it looks like this:

tone ac proteiningie, i	serve persease, resses, remov	with w
adies de l'Appareil Dig	estif -Endosconie Digestive Lille F	rance
rk, NY 10029, USA 'Depa	Replacement Text	07/07/2016 15:21:39
Gostroenterology and D	mckellak	Options 🝷
, France <sup>s</sup> CHU de Nante		
93 Nantes, France 'Dep	Gastroenterology	
ospitals Paris-Sud, Site		
ujon, Gastroentérologie,		
sité Paris Diderot Paris		
Appareil Digestif, APH		
sistance Nutritive, CHU		
rsité de Picardie Jules V		
e et Nutrition, F-3105		
UMR 1153, Equipe Epi		
té Paris Diderot – Paris	×.	

tions Inflammatoires du Tube Digestif, St Louis Hospital, Paris France:

In Reader it looks like this, and will appear in the right-hand pane: Page 1 3 ^

_	
mckellak T <sub>A</sub> Inserted Text	
21/07/2016 12:03 💦	
please insert comma here	

## DO NOT MAKE ANY EDITS DIRECTLY INTO THE TEXT, USE COMMENTING TOOLS ONLY.

# AUTHOR QUERY FORM

Journal	:	INFDIS
Article Doi	:	10.1093/infdis/jix112
Article Title	:	Transitioning Lessons Learned and Assets of the Global Polio Eradication Initiative to Global and Regional Measles and Rubella Elimination
First Author	:	Katrina Kretsinger
Corr. Author	:	Katrina Kretsinger

# AUTHOR QUERIES - TO BE ANSWERED BY THE CORRESPONDING AUTHOR

The following queries have arisen during the typesetting of your manuscript. Please click on each query number and respond by indicating the change required within the text of the article. If no change is needed please add a note saying "No change."

AQ1	Your article has been edited for grammar, clarity, consistency, and adherence to journal style and, as appro- priate, to conform with styles outlined in the American Medical Association Manual of Style (10th ed) and the Chicago Manual of Style (16th ed). Please read the article and author queries carefully to make sure your meaning has been retained. If changes are required, please enter the changes directly into the text. Note that we may be unable to make changes that conflict with journal style, obscure meaning, or create grammatical or other problems. Thank you!
AQ2	(A) The affiliations should be grouped according to department (or other subunit), primary institution, city, and state (if in the United States) or country (if elsewhere). Please ensure that each numeral is associated with a single institutional affiliation and that components of individual institutional affiliations are ordered from smallest (eg, departments) to largest (eg, universities). (B) Please ensure that the complete postal address for scholarly correspondence, as well as the highest academic degree(s) earned by the corresponding author, are specified.
AQ3	Journal style does not permit citation of footnotes in the body text. Therefore, please confirm the insertion "(whichefforts)" into the body text.
AQ4	Please confirm whether changes to the sentence "It should" retain your intended meaning. If they do not, please enter an alternative version directly into the text to ensure that your intended meaning is conveyed.
AQ5	Figure 1: Please confirm that the coverage data are unpublished. If they have been published, please delete the text "(unpublished data, WHO Joint Reporting Form, 18 July 2016)" and specify complete citation information, for inclusion into the references list.
AQ6	Figure 2: Please confirm the insertion of the sentence "Adapted with permission from the article by Patel et al [4]."
AQ7	Please specify the page number on which the quotation from 16 appears.
AQ8	Please specify the page number on which the quotation from 10 appears.
AQ9	(A) Please confirm whether changes to the sentence "The effectiveness" retain your intended meaning. If they do not, please enter an alternative version directly into the text to ensure that your intended meaning is conveyed. (B) For parallelism, please specify the population in which the effectiveness of 2 doses of MCV is 97%.
AQ10	Table 1: The period of contagiousness for polio has been converted to days, to facilitate comparison. Please confirm the change or enter revisions directly into the text.
AQ11	Several of the strategies for measles and rubella elimination have been edited for parallelism. Please con- firm whether the changes retain your intended meaning. If they do not, please enter revisions directly into the text.

AQ12	<ul><li>(A) Several of the strategies for polio eradication have been edited for parallelism. Please confirm whether the changes retain your intended meaning. If they do not, please enter revisions directly into the text.</li><li>(B) Please confirm whether the change to "offering vaccine to every eligible child" reflects your intended meaning. If it does not, please enter revisions directly into the text.</li></ul>
AQ13	Please confirm whether changes to the sentence "The process" retain your intended meaning. If they do not, please enter an alternative version directly into the text to ensure that your intended meaning is conveyed.
AQ14	Please specify citation information for the quotation beginning "without polio," as well as the page number on which the quotation appears.
AQ15	Please confirm whether changes to the sentence "The identification" retain your intended meaning. If they do not, please enter an alternative version directly into the text to ensure that your intended meaning is conveyed.
AQ16	Please confirm the deletion of the text explaining the idiom "canary in the coal mine" or, preferably, replace the idiom with a nonidiomatic phrase that reflects your intended meaning.
AQ17	Please restate the following text for clarity: "Maintaining and mainstreamingconclusion of the GPEI."
AQ18	Ref 8: Please update citation information.
AQ19	Ref 11: Please specify the URL.

SUPPLEMENT ARTICLE



# Transitioning Lessons Learned and Assets of the Global Polio Eradication Initiative to Global and Regional Measles and Rubella Elimination

1.5 AO1

Katrina Kretsinger,<sup>1</sup> Peter Strebel,<sup>1</sup> Robert Kezaala,<sup>2</sup> and James L. Goodson

1Expanded Program on Immunization, Immunizations, Vaccines, and Biologicals Department, World Health Organization, Geneva, Switzerland; 2Health Section, Program Division, United Nations Children's Fund, New York, New York; and 3Global Immunization Division, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, Georgia

The Global Polio Eradication Initiative has built an extensive infrastructure with capabilities and resources that should be tran-1.10 sitioned to measles and rubella elimination efforts. Measles continues to be a major cause of child mortality globally, and rubella continues to be the leading infectious cause of birth defects. Measles and rubella eradication is feasible and cost saving. The obvious similarities in strategies between polio elimination and measles and rubella elimination include the use of an extensive surveillance and laboratory network, outbreak preparedness and response, extensive communications and social mobilization networks, and the need for periodic supplementary immunization activities. Polio staff and resources are already connected with those of measles and rubella, and transitioning existing capabilities to measles and rubella elimination efforts allows for optimized use of resources and the best opportunity to incorporate important lessons learned from polio eradication, and polio resources are concentrated in

1.70

1.75

1.60

1 50

1.55

1.15 1.65 the countries with the highest burden of measles and rubella. Measles and rubella elimination strategies rely heavily on achieving and maintaining high vaccination coverage through the routine immunization activity infrastructure, thus creating synergies with immunization systems approaches, in what is termed a "diagonal approach."

Keywords. Measles; rubella; poliomyelitis; vaccine-preventable diseases; polio transition; polio legacy. 1.20

The world is now closer than ever before to achieving global polio eradication. Ridding the world of polio will be our greatest public health success since smallpox eradication and will 1.25 further cement the critical role of vaccines in achieving public health goals. Since the widespread use of vaccines worldwide began through the global Expanded Program on Immunization (EPI), which started in 1974 following implementation of the Smallpox Eradication Program, vaccines have been widely rec-1.30 ognized for their value as the greatest single investment that can be made for improving people's lives and public health [1, 2]. During nearly 30 years of operations, the Global Polio Eradication Initiative (GPEI) has recruited and trained millions of volunteers, social mobilizers, and health workers; accessed 1 35 households untouched by other health initiatives; mapped and brought health interventions to chronically neglected and underserved communities; and established a standardized, realtime global surveillance and response capacity [3]. As the initiative nears completion, there is an opportunity and obligation 1.40 to build a better future by applying the lessons learned from the GPEI and adapting its current infrastructure and unique

AO2 Correspondence: K. Kretsinger, Expanded Program on Immunization, Immunizations, Vaccines, and Biologicals, World Health Organization, Avenue Appia 20, CH-1211, Geneva, 1.45 Switzerland (kretsingerk@who.int).

#### The Journal of Infectious Diseases® 2017-0000-\$1-8

1.48

Published by Oxford University Press for the Infectious Diseases Society of America 2017. This work is written by (a) US Government employee(s) and is in the public domain in the US. DOI: 10.1093/infdis/jix112

functions to other global health priorities and initiatives. These priorities should include strengthening the infrastructure for delivery of routine immunization services, control of other vaccine-preventable diseases (VPDs), and measles and rubella elimination (which refers to the reduction to 0 [or a very low AO3 defined target rate of] new cases in a defined geographical area, as opposed to eradication, which refers to the complete and permanent worldwide reduction to 0 new cases of the disease through deliberate efforts).

1.80 The rationale for pivoting from polio eradication to measles and rubella elimination is compelling. Today, measles continues to be a major cause of child mortality globally [4], rubella continues to be the leading infectious cause of birth defects [5], and measles and rubella elimination goals are established 1.85 [6, 7]. Measles and rubella eradication (global elimination) is feasible and cost saving [8]. Furthermore, the strategies used by the GPEI and refined through innovations are similar to those needed for measles and rubella elimination, and currently polio resources are concentrated in the countries with the high-1.90 est measles and rubella burden. Although measles and rubella elimination strategies are similar to those used for polio eradication, the elimination strategies for measles and rubella rely more heavily on vaccine doses administered through routine immunization service delivery. Therefore, embracing measles 1.95 and rubella elimination would not create another vertical eradication program, but rather would synergistically strengthen immunization systems for all delivering all vaccines. Finally,

measles and rubella control and elimination efforts currently depend critically on substantial support from GPEI resources, and a failure to refocus these resources on measles and rubella would cause significant backsliding in already realized gains.

2.5

## **MEASLES AND RUBELLA ELIMINATION AND IMMUNIZATION SYSTEM STRENGTHENING ARE** THE MOST OBVIOUS FRONTLINE CANDIDATES FOR **TRANSITIONING OF POLIO ASSETS**

- The primary goals of polio transition planning are to protect a 2.10 polio-free world and ensure that investments made to eradicate polio will continue to contribute to future public health goals after the completion of polio eradication. Polio transition planning aims to benefit all countries and the global community,
- rather than countries in which polio resources are currently 2.15 concentrated, to achieve common goals. A priority of transition planning is to enable long-term transitions to country ownership of basic public health functions wherever possible. To be effective and sustainable, future transition opportunities for polio program resources should build from and contribute to 2.20
- existing global and regional goals, as well as national or subnational health strategies and goals.

In 2010, the World Health Assembly set 3 targets for measles control by 2015 as milestones toward the global eradication 2.25 of measles: (1) increase routine coverage with the first dose of measles-containing vaccine (MCV1) for children aged 1 year to  $\geq$ 90% nationally and  $\geq$ 80% in every district; (2) reduce the global annual measles incidence to <5 cases per 1 million population; and (3) reduce the global measles mortality by 95% from the 2000 estimate. In 2012, the World Health Assembly 2.30 approved the key document that serves as the global guide for immunizations in the world today, the Global Vaccine Action

Plan (GVAP) [6]. The GVAP set the goal to achieve measles elimination in 4 regions by 2015 and measles and rubella elimination in at least 5 of 6 World Health Organization (WHO) 2.55 regions by 2020. All 6 WHO regions have established measles elimination goals, and 3 regions have rubella elimination goals. In addition to these measles and rubella goals, Sustainable Development Goal 3.2 aims to end preventable deaths of newborns and children <5 years of age, with all countries aiming 2.60 to reduce neonatal mortality to ≤12 deaths per 1000 live births and mortality among children aged <5 years to  $\leq 25$  deaths per 1000 live births by 2030 [9]. Sustainable Development Goal 3.2 is designed to build on the United Nations Millennium Development Goal 4 (MDG4) to reduce the overall number of 2.65 deaths among children; routine MCV1 coverage was used as an indicator of progress toward MDG4 [5]. While substantial progress has been made toward these goals since 2000, the World Health Assembly 2015 global control milestones and regional measles elimination goals were not achieved, global MCV1 cov-2.70 erage has not increased substantially in recent years, and much effort will be needed to meet elimination targets.

During 2000-2015, the number of measles cases reported annually decreased worldwide from 853 479 to 254 928 (Figure 1), and annual reported measles incidence declined 2.75 75% worldwide, from 146 to 36 cases per million population [4]. Annual estimated measles deaths declined 79%, from 651 600 to 134 200 (Figure 2), and the decrease in measles mortality was among the main contributors to the decline in overall child mortality and progress toward MDG4 [10], with an estimated 2.80 20.3 million deaths averted during 2000-2015 [4]. Routine measles vaccination coverage, as measured by global coverage estimates from MCV1, increased globally during 2000-2015, from 72% to 85%, although coverage has remained at

2.85



AQ5 Figure 1. Annual reported measles cases and estimated coverage with the first dose of measles-containing vaccine (MCV1) and MCV2, 2000–2015. Coverage data were 2.52 estimated by the World Health Organization (WHO) and the United Nations Children's Fund (unpublished data, WHO Joint Reporting Form, 18 July 2016). 2.104

Cumulative measles deaths averted due to vaccination (in millions)



Figure 2. Global estimated number of measles deaths in the presence and absence of vaccination, 2000–2015. Compared with no measles vaccination, measles vaccination, measles vaccination prevented an estimated cumulative total of 20.3 million deaths during 2000–2015, represented by the shaded area between the solid trend lines. Adapted with permission from the article by Patel et al [4].

AQ4 84%–85% since 2009 (Figure 1). It should be noted that global coverage of routine MCV2 increased from 15% to 61% during 2000–2015, corresponding to an increase from 98 to 160 countries that introduced MCV2 during this period [4]. Estimated rubella-containing vaccine (RCV) coverage globally was 46% in 2015, with 147 countries having introduced RCV into their national immunization schedules [11]. While the European Region [12] and Western Pacific Region [13] have documented measles elimination in 21 and 5 countries, respectively, only 1 region, the Region of the Americas, has successfully achieved regional measles [14] and rubella [15] elimination.

Thus, while significant progress has been made toward 3.40 achieving measles control and elimination targets, as well as other global child health milestones, much work remains to be done. As noted in a recent midterm review of the Measles and Rubella Global Strategic Plan 2012-2020 (commissioned by the Measles and Rubella Initiative Management Team, conducted 3.45 by independent experts, and completed in 2016), "In principle, the 2020 goals can still be reached, but doing so would require a substantial escalation of political will and resources as well as heavy reliance on supplementary immunization activities [SIAs]" [16]. The authors of the review also note that the basic AQ7 3.50 strategies articulated in the strategic plan are sound but that full implementation of the strategies is needed and has been limited

by a lack of country ownership and global political will, as reflected in insufficient resources. As noted by the International Task Force on Disease Eradication (ITFDE), "Efforts to control and eliminate measles and rubella have accelerated incrementally since 2000, but have been greatly overshadowed in magnitude of resources and political commitment by GPEI. The impending completion of polio eradication opens a window of opportunity to devote greater attention to measles and rubella eradication" [10].

The feasibility and benefits of measles and rubella elimina-3.90 tion have been well documented. In 2015, the ITFDE reinforced the advantages of pursuing measles and rubella eradication simultaneously and the need to make resources available for this effort [10]. Measles remains a major cause of childhood mortality [4], and rubella remains the leading infectious cause 3.95 of birth defects, with >100 000 infants born with congenital rubella syndrome every year, mostly in low-income countries that have not yet introduced RCV [5]. The continuing morbidity and mortality burden of both diseases is unacceptable, owing to the availability of highly effective and inexpensive vaccines. The 3.100 Strategic Advisory Group of Experts on Immunization has recommended that routine MCV2 should be added to all national immunization schedules [17]. The effectiveness of MCV1 is 93%-95% when administered to children aged >12 months and

3.104

85%–90% when administered to infants aged 9 months, and AQ9 the effectiveness 97% for 2 doses of MCV given at least 28 days apart. Although antibody levels following vaccination may decline over time, measles and rubella vaccine–induced immunity provides long-term and likely lifelong protection. Measles is highly contagious, with a basic reproduction number ( $R_0$ ) of 12–18. Thus, 2 doses of measles vaccine are needed to reach the 89%–94% population immunity threshold required to prevent sustained measles virus transmission [18]. The effectiveness of a single dose of RCV is approximately 95% among infants 9 months of age. Since RCV is coadministered with MCV as a combined vaccine, the same strategies for vaccine delivery apply

4.5

4.10

4 30

- to both diseases. With the introduction of RCV in an increasing number of countries globally, strategies for measles elimination
  4.15 have the additional benefit of simultaneously advancing measles and rubella elimination goals. Rubella is less contagious than measles, with an R<sub>0</sub> of 6–7; therefore, the biggest challenge to measles and rubella elimination efforts is the contagiousness of measles virus. However, both diseases are preventable with 1–2
- 4.20 doses of vaccine, have clinical symptoms that are easily detected through case-based surveillance, have no known animal reservoirs, and have relatively short incubation and transmissibility windows (Table 1).
- Global measles and rubella eradication will ultimately be 4.25 cost saving, compared with other strategy scenarios of sustained control [8, 19]. High control, the policy currently pursued by global partners, costs governments and donors \$2.3

Table 1. Parameters for Eradication of Vaccine-Preventable Diseases

billion per year for the foreseeable future, while still leading to >100 000 estimated measles deaths and >100 000 CRS cases annually [4,5]. Global measles and rubella eradication would 4.55 save the current estimated treatment costs for measles virus and rubella virus infections (\$8 billion per year) and prevent disability-adjusted life-year losses (\$88 billion per year) [8].

The fundamental approach to measles and rubella elimina-AO11 tion includes the following 5 strategies: achieving and maintain-4.60 ing high vaccination coverage with 2 doses of MCV, performing effective disease surveillance, developing and maintaining outbreak preparedness and response activities, communicating with and engaging stakeholders, and implementing research AQ12 and innovations to improve the program [20]. The strategies 4.65 used for polio eradication are similar and include performing high-quality real-time surveillance and creating and maintaining state-of-the-art global laboratory networks, preparing for and responding to outbreaks, performing periodic SIAs to reach inaccessible children, offering vaccine to every eligible 4.70 child, monitoring programs and using accountability frameworks, using communication and social mobilization networks to generate demand for vaccine, and establishing and maintaining partnership coordination, advocacy, and resource mobilization activities. In addition, the framework and mechanisms 4.75 of polio certification, at the country and regional levels, is providing a model for measles and rubella elimination verification processes. Currently, in many countries, polio and measles and rubella staff are the same people or interchangeable, working

Parameter	Smallpox	Polio	Measles	Rubella
Eradication status	Eradicated	Wild polio virus type 2 eradicated, type 3 potentially eradicated, and type 1 nearly eradicated	Candidate for eradication	Candidate for eradication
Clinical presentation	Fever and rash	Acute flaccid paralysis	Fever and rash	Fever and rash
Asymptomatic infections c carriers	r No	Yes	No	No
Primary mode of transmission	Respiratory droplets	Fecal–oral route or oral–oral route	Aerosolized respiratory secretions	Aerosolized respiratory secretions
Period of contagiousness,	d 25	28–42	9	1–5
Basic reproduction numbe	r 5–7	4–13	9–18	6–7
Herd or population immun threshold, %	ity 80–85	75–92	89–94	83–85
Serotypes	1	3	1	1
Vaccine delivery	Intradermal injection	Oral drops (oral polio vaccine) or intradermal or intramuscu- lar injection (inactivated polio vaccine)	Subcutaneous injection	Subcutaneous injection
Vaccination strategy	Ring vaccination	Multiple repeated mass campaigns	Two doses of measles-containing vaccine through routine immunization, supplemented by periodic mass campaigns	One dose of rubella-containing vac- cine through routine immunization, supplemented by periodic mass campaigns
Vaccine doses needed to s transmission, no.	stop 1	≥3	1–2	1
Vaccine-derived virus transmission	No	Yes	No	No

## S4 • JID 2017:XX (XX XXXX) • Kretsinger et al

together in an interconnected fashion, often supported by existing polio assets. Work activities with considerable overlap in technical requirements and covered by the same staff include field and laboratory surveillance activities, case investigations, outbreak investigation and response, and SIA planning and implementation.

The global and regional needs for measles elimination overlap geographically with those of the 16 priority countries for polio transition, where GPEI assets are concentrated and the 5.10 highest burden of measles cases and deaths, as well as rubella and CRS cases, occur [21]. The 16 countries with 95% of polio assets and infrastructure are Afghanistan, Angola, Bangladesh, Cameroon, Chad, the Democratic Republic of the Congo (DRC), Ethiopia, India, Indonesia, Myanmar, Nepal, Nigeria, 5.15 Pakistan, Somalia, Sudan, and South Sudan. Among the estimated 20.8 million infants who did not receive MCV1 through routine immunization services in 2015, approximately 11 million (53%) were in the following 6 polio transition priority countries: India (3.2 million), Nigeria (3 million), Pakistan (2 million), Indonesia (1.5 million), Ethiopia (0.7 million), and the 5.20 DRC (0.6 million) [6].

The Region of the Americas has already demonstrated how to successfully pivot from using resources for polio eradication and outbreak response to harnessing these assets for measles 5.25 and rubella elimination. After wild poliovirus was declared eradicated in the Americas in 1994, the region maintained its investments, applying the polio lessons learned for similar strategies for the elimination of measles and rubella by achieving high population immunity and maintaining excellent surveillance [22]. The strategy for achieving high population immu-5.30 nity involved full implementation of a so-called catch-up, keep-up, follow-up strategy, in which SIAs targeting wide age ranges were followed by maintenance of high routine coverage and periodic follow-up SIAs for children aged 1-5 years [23]. 5.35 In addition, the goal of measles and rubella elimination in the Americas benefitted from high-level political support. The last cases of endemic measles and endemic rubella occurred in 2002 and 2009, respectively, and the region is now verified as AQ13 having eliminated measles and rubella [14,15]. The process of measles and rubella elimination provided opportunities for the 5.40

countries in the region to strengthen health systems and thus ultimately have the ability to reduce health inequities [24]. The same experience can and should be replicated globally.

### **MEASLES AND RUBELLA CONTROL AND** 5.45 **ELIMINATION EFFORTS CURRENTLY DEPEND HEAVILY ON POLIO ASSETS**

Many polio eradication assets and lessons learned have already been applied to measles and rubella elimination efforts. These 5.50 VPD eradication and elimination efforts have similar strategies and program implementation infrastructure needs; therefore, polio eradication activities have easily been integrated with 5.52

measles immunizations and surveillance activities [10]. Today, measles and rubella elimination efforts rely heavily on GPEI assets, including the staff, physical infrastructure, and financ-5.55 ing that are used to support the program. A 2014 survey of 467 country-level program managers in 10 countries (Afghanistan, Angola, Chad, the DRC, Ethiopia, India, Nigeria, Pakistan, Somalia, and South Sudan) found that, overall, they spent 22% of their time on routine immunization and 46% of their time 5.60 on immunization goals and activities beyond polio. They also reported spending 8% of their time on measles and rubella, highlighting the important support GPEI assets are currently providing to measles and rubella control and elimination activities [21]. The heavy dependence of EPI on GPEI resources was 5.65 highlighted in pilot case studies in the DRC and Nepal. In the DRC, staff observed that, "without polio, the whole health system would suffer." GPEI staff provided technical and operational AQ14 support for EPI, such as support for national planning, technical assistance and training of national EPI staff, and participa-5.70 tion in RI management, including supply chain management for vaccine procurement and cold chain maintenance. The consequences of losing polio assets would include the likely reversal of EPI progress in the 16 priority countries, as well as globally. Currently, GPEI assets are budgeted to taper off through 2019. 5.75 Transitioning assets and finding alternative sources of funding are critically needed to maintain the progress to date and accelerate the progress toward GVAP goals, including measles and rubella elimination.

Surveillance for VPDs, particularly measles and rubella, is 5.80 heavily dependent on GPEI resources. Overall, GPEI funds approximately \$140 million annually on all surveillance activities, for WHO personnel and operational costs, in polio-endemic and -nonendemic countries. GPEI surveillance officers, particularly in polio-nonendemic countries, play a critical role 5.85 in measles and rubella fever/rash surveillance [25]. For example, in the DRC, GPEI-funded WHO surveillance teams spent approximately one quarter of their time on surveillance of other infectious diseases [21]. Staff noted that the GPEI provides tools, training, equipment, and funding for local surveil-5.90 lance in health districts and that technical assistance to polio laboratories benefitted national laboratories with best practices shared across disease areas. In Nepal, the polio-funded WHO Immunization Preventable Disease program is the backbone of disease surveillance activities and the primary surveillance pro-5.95 gram for VPDs.

Estimates of the global costs for fully financing measles and rubella surveillance would require replacing these officers, and economic estimates for fully financed global measles and rubella surveillance place the annual cost at \$60 million [19]. 5.100Current funding dedicated to measles and rubella surveillance from global partners, including the Centers for Disease Control and Prevention, the Measles and Rubella Initiative, the Bill and Melinda Gates Foundation, and Gavi, the Vaccine Alliance, is 5.104

approximately \$35 million. Thus, a portion of the gap between current measles and rubella surveillance funding and the total cost of fully funding measles and rubella surveillance is provided through reliance on and integration with GPEI laboratory assets; this support is threatened with the scaling down of polio infrastructure.

6.5

6.50

6.52

GPEI and Measles and Rubella Initiative partner investments over decades have built up robust surveillance systems for acute flaccid paralysis, to detect polio, and for rash/fever-associated
6.10 illness, to detect measles and rubella. These 2 systems are supported by the Global Polio Laboratory Network and the Global Measles and Rubella Laboratory Network (GMRLN), which was built onto the Global Polio Laboratory Network platform; considerable overlap exists with shared staff, management, and
6.15 resources for these 2 surveillance systems, with support from the GPEI and the Measles and Rubella Initiative. GPEI assets include large networks of surveillance officers; processes for specimen collection, transport, and testing; as well as systems for data management, analysis, and use. The GMRLN surveil-

6.20 lance system provides a platform for detecting other viral VPDs, such as yellow fever, as well as emerging diseases, such as Ebola. The global Ebola emergency response relied on existing eradication infrastructure and demonstrated the critical importance of maintaining and building upon this capacity by transitioning

6.25 GPEI assets to elimination efforts involving laboratory-based surveillance, outbreak detection and response, and the ability to implement mass vaccination campaigns [26].

## 6.30 FOCUSED EFFORTS ON MEASLES AND RUBELLA ELIMINATION CAN PROVIDE SYNERGY AND BENEFITS FOR BROAD IMMUNIZATION AND SURVEILLANCE ACTIVITIES

Applying polio assets to measles and rubella elimination will benefit immunization systems because, unlike polio eradication, measles elimination requires high 2-dose coverage 6.35 through routine immunization service delivery, combined, in some settings, with periodic mass vaccination campaigns every 3-5 years. Because of the highly effective measles and rubella vaccine, repeated multiple rounds of mass vaccination targeting the same age groups will not be required, as was needed with 6.40 the use of oral polio vaccine for polio eradication. Thus, measles elimination efforts can take advantage of vertical strategies that focus on using surveillance data for action and measles outcomes to identify areas missed by vaccination and horizontal strategies that build systems and health services to sustain the 6.45 gains and achieve broader objectives. The combination of these approaches has been described as a "diagonal approach" [27].

> Measles elimination efforts incorporating a comprehensive approach for achieving high 2-dose MCV coverage improves EPI coverage broadly and strengthens the immunization system. Implementation of this strategy provides a platform for routine and mass delivery of other immunizations and

child-survival interventions. The focused approach that is needed in eradication efforts has provided methods of better using surveillance data and coverage data to identify areas of 6.55 low vaccination coverage, instilling a data-driven approach to immunization and surveillance that increases immunization coverage and equity in the entire population, including those living in hard-to-reach places. The identification of suscepti-AQ15 ble populations and the emphasis on mapping and reaching all 6.60 communities with immunizations, which is necessary for eliminating chains of transmission from all reservoirs, has proven valuable for strengthening immunization service delivery and other public health activities. The experience in the United States has demonstrated the value of measles elimination efforts 6.65 in strengthening the entire immunization system [28]. The value of focused eradication/elimination efforts should not be underestimated, and further investments in these efforts will lead to achieving high coverage and equity for all immunizations and other public health initiatives. The inextricable linkage between 6.70 achieving and maintaining measles and rubella elimination and strong immunization systems is repeatedly underlined in the final report of the Midterm Review of the Global Measles and Rubella Strategic Plan [16].

The far-reaching approach of focused eradication/elimi-6.75 nation programs extends to surveillance. Disease eradication efforts require high-quality surveillance covering entire populations. The goal-driven measles and rubella elimination activities, including detailed outbreak investigations, often provide important information about program failures that lead to 6.80 solutions for achieving high immunization coverage and equity. Because measles vaccine is highly effective and measles virus is highly contagious, measles is used as an indicator of program performance and is the canary in the coal mine for identifying AQ16 weaknesses of an immunization program. Measles can serve 6.85 as an indicator of the strength and reach of the health system [28]. When there are gaps in immunization coverage, measles is most often the first VPD one sees, indicating low immunization coverage. Analysis of measles surveillance data identifies populations and areas where immunization coverage is subopti-6.90 mal and thereby helps guide efforts to strengthen immunization service delivery.

## TRANSITIONING POLIO RESOURCES TO MEASLES AND RUBELLA ELIMINATION EFFORTS WILL HELP ENSURE THE ONGOING SUCCESS OF POLIO ERADICATION EFFORTS

The GPEI built an infrastructure for eradicating polio that can now be retooled for elimination efforts for other VPDs. GPEI assets are well positioned to support efforts to achieve the measles and rubella elimination goals that have been set by the countries of each region of the world while maintaining the essential polio functions, such as polio surveillance, that will continue to be needed after the world is certified to be free of polio. The

6.100

Midterm Review of the Global Measles and Rubella Strategic Plan noted that, at a minimum, there should be no weakening of nonpolio activities currently supported by polio assets [16].

During the first few years following the last reported polio 7.5 case, in addition to polio containment activities, there will be a need to maintain high routine immunization coverage, surveillance, and capacity for outbreak response, communications, and mass vaccination campaigns following the conclusion of the GPEI. The current measles and rubella elimination infra-7.10 structure is a natural fit to support these activities. Maintaining and mainstreaming essential polio eradication functions, such AQ17 as immunization, surveillance, communication, response, and containment, into ongoing public health programs in a poliofree world following the conclusion of the GPEI. These func-7.15 tions will still be required after polio eradication is certified globally. Countries and partner organizations must ensure that these functions continue and are mainstreamed into appropriate ongoing public health programs that have components that are aligned with these needs. Eradication of measles and rubella would require a sustained global commitment and a 7.20 clear accountability framework similar to those that exists in

## CONCLUSION

the GPEI.

7.25 As the GPEI scales down, it is imperative that we collectively use our forward vision to capitalize on the experience, momentum, and infrastructure developed over nearly 30 years to eradicate polio. A transition to measles and rubella elimination, with a mutually reinforcing synergy with systems strengthening and routine immunization, is the ideal next phase.

It will be critical to incorporate the many lessons learned from polio eradication. These include the successes, failures, innovations, and best practices that the polio program has identified over the last 3 decades that enable the assets and functions

- 7.35 to provide more-efficient, equitable, high-quality services, particularly to underserved, insecure, hard-to-reach, or high-risk communities. In many areas, the primary challenges were the poor quality of the program, the failure to reach every child, and the repeated missing of underserved populations. In particular,
- the program identified innovative strategies to work in insecure and inaccessible areas. On the management side, 5-year plans and funded budgets have been critical for programs to manage their resources effectively; chronic funding gaps meant that vulnerable countries were unable to conduct planned SIAs, which led to outbreaks and delays in eradication and insufficient pop-
- 7.45 led to outbreaks and delays in eradication and insufficient population immunity to prevent circulation of reintroduced virus. One of the most important lessons from the experience with polio is the value of prevention. Outbreaks are far more expensive than prevention activities. Thus, stopping endemic transmission once was not enough in some countries, demonstrating
- that it was essential to achieve and maintain high population7.52 immunity.

Until polio eradication is achieved, the world might not be ready to commit to another global eradication goal. However, starting the transition of assets to existing elimination efforts 7.55 will help further progress toward achieving the established regional goals for measles and rubella elimination. GPEI assets should go to support full implementation of the recommended measles and rubella elimination strategies to identify and interrupt measles and rubella virus transmission in major reservoirs, 7.60 further reduce measles mortality, improve immunization service delivery to achieve high coverage and equity, and maintain an eradication/elimination infrastructure for conducting mass vaccination campaigns and global laboratory-supported surveillance systems. Ridding the world of polio will reduce the 7.65 burden on public health programs; there will no longer be a need to dedicate resources or manpower to controlling and responding to smallpox or polio. Of course, the real impact and legacy of disease eradication is the impact that it has on improving the lives of everyone. Eradication provides true health equity for all 7.70 and forever. With polio assets, we can implement the recommended strategies for measles and rubella elimination, achieve equitable access to vaccination services, and achieve GVAP and regional elimination goals and the eventual goal of global measles and rubella eradication. 7.75

## Notes

**Disclaimer.** The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the World Health Organization, United Nations Children's Fund, or Centers for Disease Control and Prevention.

**Potential conflicts of interest.** All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

### References

- 1. Okwo-Bele JM, Cherian T. The expanded programme on immunization: a lasting legacy of smallpox eradication. Vaccine **2011**; 29 Suppl 4:D74–9.
- Ozawa S, Clark S, Portnoy A, Grewal S, Brenzel L, Walker DG. Return on investment from childhood immunization in low- and middle-income countries, 2011-20. Health Aff 2016; 35:199–207.
- Cochi SL, Hegg L, Kaur A, Pandak C, Jafari H. The global polio eradication initiative: progress, lessons learned, and polio legacy transition planning. Health Aff 2016; 35:277–83.
- Patel MK, Gacic-Dobo M, Strebel PM, et al. Progress toward regional measles elimination—worldwide, 2000-2015. MMWR Morb Mortal Wkly Rep 2016; 65:1228–33.
- Vynnycky E, Adams EJ, Cutts FT, et al. Using seroprevalence and immunisation coverage data to estimate the global burden of congenital rubella syndrome, 1996– 2010: a systematic review. PLoS One 2016;11:e0149160.
- World Health Organization. Global Vaccine Action Plan 2011–2020. http://www. who.int/immunization/global\_vaccine\_action\_plan/GVAP\_doc\_2011\_2020/en/. Accessed 16 Sept 2016.
- United Nations General Assembly. United Nations millennium declaration. New York, NY: United Nations General Assembly, 2000. http://www.un.org/millenniumgoals/. Accessed 16 September 2016.
- Thompson KM, Badizadegan ND. Modeling the transmission of measles and rubella to support global management policy analyses and eradication investment cases. Risk Anal. In press.
- 9. United Nations. Sustainable development goals. http://www.un.org/sustainabledevelopment/sustainable-development-goals/. Accessed 16 September 2016. AQ18
- 10. World Health Organization. Meeting of the International Task Force for Disease Eradication, November 2015. Wkly Epidemiol Rec 2016; 91:61–72.
   7.104

7.80

7.85

- World Health Organization. WHO/UNICEF coverage estimates 2015 revision. Immunization Vaccines and Biologicals, (IVB), World Health Organization. 194 WHO Member States. Accessed 16 July 2016.
- World Health Organization Regional Office for Europe. Fourth Meeting of the European Regional Verification Commission for Measles and Rubella Elimination (RVC). 2015. http://www.euro.who.int/\_data/assets/pdf\_file/0011/304958/4th-RVC-meeting-report.pdf. Accessed 16 September 2016.
- World Health Organization Regional Office for the Western Pacific. Hong Kong SAR (China) achieves measles-free status 2016. http://www.wpro.who.int/mediacentre/releases/2016/20160921/en/. Accessed 16 September 2016.
- Pan American Health Organization. Region of the Americas is declared free of measles. 2016. http://www.paho.org/hq/index.php?option=com\_content&view=article&id=12528%3Aregion-americas-declared-free-measles. Accessed 16 September 2016.
- Pan American Health Organization. Americas Region is declared the world's first to eliminate rubella. 2015. http://www.paho.org/hq/index.php?option=com\_content&view=article&id=10798&Itemid=1926&lang=en. Accessed 16 September 2016.
- Orenstein WA, Hinman A, Nkowane B, Olive JM, Reingold A. Measles and Rubella Global Strategic Plan 2012–2020 Midterm Review. 2016. http://www.who. int/immunization/sage/meetings/2016/october/1\_MTR\_Report\_Final\_Color\_ Sept\_20\_v2.pdf?ua=1. Accessed 16 September 2016.
- World Health Organization. Meeting of the Strategic Advisory Group of Experts on immunization, October 2016—conclusions and recommendations. Wkly Epidemiol Rec 2016; 91:961–984.
- Rota PA, Moss WJ, Takeda M, de Swart RL, Thompson KM, Goodson JL. Measles. Nat Rev Dis Primers 2016; 2:16049.

 Thompson KM, Odahowski CL. The costs and valuation of health impacts of measles and rubella risk management policies. Risk Anal 2016; 36:1357–82.

- World Health Organization. Global Measles and Rubella Strategic Plan: 2012– 2020. http://www.measlesrubellainitiative.org/wp-content/uploads/2013/06/ Measles-Rubella-Strategic-Plan.pdf. Accessed on 16 September 2016.
- 21. vandenEnt MVX, Swift RD, Sameer A, Hegg L, Eggers R, Cochi SL. Contribution of polio-funded personnel to support routine immunization strengthening in the 10 polio focus countries. J Infect Dis. **In press**.
- de Quadros CA, Andrus JK, Olive JM, Guerra de Macedo C, Henderson DA. Polio eradication from the Western Hemisphere. Annu Rev Public Health 1992; 13:239–52.
- Hersh BS, Tambini G, Nogueira AC, Carrasco P, de Quadros CA. Review of regional measles surveillance data in the Americas, 1996-99. Lancet 2000; 355:1943–8.
- Andrus JK, Cochi SL, Cooper LZ, Klein JD. Combining global elimination of measles and rubella with strengthening of health systems in developing countries. Health Aff 2016; 35:327–33.
- 25. Global Polio Eradication Initiative. Financial resource requirements. http://polioeradication.org/wp-content/uploads/2016/10/FRR2013-2019\_April2016\_EN\_ A4.pdf. Accessed 30 June 2016.
- Kouadio K, Okeibunor J, Nsubuga P, Mihigo R, Mkanda P. Polio infrastructure strengthened disease outbreak preparedness and response in the WHO African Region. Vaccine 2016; 34:5175–80.
- Orenstein WA, Seib K. Beyond vertical and horizontal programs: a diagonal approach to building national immunization programs through measles elimination. Expert Rev Vaccines 2016; 15:791–3.
- 28. Orenstein WA. The role of measles elimination in development of a national immunization program. Pediatr Infect Dis J 2006; 25:1093–101.

8.75

8.60

8.65

8.25

8.30

8.35

8.40

8.45

AQ19

8.5

8.10

8.15

8.20

8.80

8.85

8.90

8.95

8.100

8.52

S8 • JID 2017:XX (XX XXXX) • Kretsinger et al