

Measles and Rubella Global Strategic Plan 2012-2020 Midterm Review

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ABBREVIATIONS AND ACRONYMS

AEFI	adverse event following immunization
AFR	African Region (of the World Health Organization)
AFRO	the World Health Organization Office for the African Region
AMR	Americas Region (of the World Health Organization)
AMRO	the World Health Organization Office for the Americas Region
ARC	American Red Cross
BMGF	Bill & Melinda Gates Foundation
CDC	Centers for Disease Control and Prevention (USA)
CIDA	Canadian International Development Agency
cMYP	comprehensive multiyear plans for immunization
C4I	communications for immunization (UNICEF)
CRS	congenital rubella syndrome
DFID	Department for International Development (United Kingdom)
DRC	Democratic Republic of the Congo
ELISA	enzyme-linked immunosorbent assay
EMR	Eastern Mediterranean Region (of the World Health Organization)
EMRO	the World Health Organization Office for the Eastern Mediterranean Region
EPI	Expanded Programme on Immunization
EUR	European Region (of the World Health Organization)
EURO	the World Health Organization Office for the European Region
FRR	Financial Resource Requirements
Gavi	Gavi, The Vaccine Alliance
Gavi-eligible Countries	Countries eligible for funding from Gavi, The Vaccine Alliance
GHSA	Global Health Security Agenda
GMRLN	Global Measles and Rubella Laboratory Network
GPEI	Global Polio Eradication Initiative
GVAP	Global Vaccine Action Plan
HSIS	Health System and Immunization Strengthening
IHR	International Health Regulations
JSI	John Snow Inc.
M	measles (vaccine)
MAPs	microarray patches
MCV	measles containing vaccine
MCV1	first dose of measles containing vaccine
MCV2	second dose of measles containing vaccine
M&RI	Measles and Rubella Initiative
MMR	Measles-mumps- rubella (vaccine)
MMR1	First dose of measles mumps rubella (vaccine)
MMR2	Second dose of measles mumps rubella (vaccine)
MMRV	Measles mumps rubella varicella (vaccine)
MR	Measles-rubella (vaccine)
MRCV	Measles rubella containing vaccine
MRCV1	First dose of measles rubella containing vaccine
MRCV2	Second dose of measles rubella containing vaccine
MTR	Midterm Review (of the <i>Global Measles and Rubella Strategic Plan 2012-2020</i>)
NVC	National Verification Committee

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PAHO	Pan American Health Organization
PRC	Polio Research Committee
ORI	Outbreak Response Immunization
PAHO	Pan American Health Organization
RCV	Rubella-containing vaccine
RITAG	Regional Immunization Technical Advisory Groups
RVC	Regional Verification Commission
SAGE	the World Health Organization's Strategic Advisory Group of Experts on Immunization
SEAR	South East Asian Region (of the World Health Organization)
SEARO	the World Health Organization's Regional Office for the South East Asian Region
SIA	supplementary immunization activity
Sphere	the Sphere project.
UNF	United Nations Foundation
UNICEF	United Nations Children's Fund
WHA	World Health Assembly
WHO	World Health Organization
WPR	Western Pacific Region (of the World Health Organization)
WPRO	the World Health Organization's Regional Office for the Western Pacific Region
VPDs	Vaccine Preventable Diseases

KEY HIGHLIGHTS

1. Eradication is the ultimate goal but it is premature to set a date for its accomplishment. Existing regional elimination goals should be vigorously pursued to enable setting a global target by 2020.
2. The basic strategic approaches articulated in the *Global Measles and Rubella Strategic Plan 2012-2020* are valid to achieve the goals but have not been fully implemented (or not appropriately adapted to local situations).
3. The report recommends a shift from primary reliance on supplementary immunization activities (SIAs) to assure two doses of measles-containing vaccine (MCV) are delivered to the target population to primary reliance on ongoing services to assure administration of two doses of MCV. Regular high quality SIAs will still be necessary while ongoing services are being strengthened.
4. The report recommends a shift from primary reliance on coverage to measure progress to incorporating disease incidence as a major indicator.
5. The report recommends that the measles/rubella vaccination program be considered an indicator for the quality of the overall immunization program and that measles/rubella incidence and measles and rubella vaccination coverage be considered as primary indicators of immunization program performance.
6. Polio transition presents both risks and opportunities: risks should be minimized and opportunities maximized.
7. A school entry immunization check could contribute significantly to strengthening overall immunization services with assurance that recommended doses of measles and rubella vaccines as well as other vaccines have been delivered and providing those vaccines at that time if the child is un or under-vaccinated.
8. Program decisions should increasingly be based on good quality data and appropriate analysis.
9. The incorporation of rubella vaccination into the immunization program needs to be accelerated - it should be accorded equivalent emphasis as measles.
10. Outbreak investigation and response are critical but the most important thing is to prevent outbreaks.

HIGH LEVEL SUMMARY

(The complete set of recommendations is in the Executive Summary and the body of the report.)

Tremendous progress has been made towards both measles and rubella elimination since 2001. Significant gains have also been made during the period 2012 – 2015 with 23/194 World Health Organization (WHO) Member States having introduced a second dose of measles containing vaccine (MCV2), 17 countries having introduced rubella containing vaccine (RCV), global coverage with MCV2 rising from 48% to 61%, and global coverage with RCV from 39% to 46%. From 2012 – 2014, 4.25 million measles deaths are estimated to have been averted relative to no measles vaccination at all. However, despite these advances, neither measles nor rubella elimination are on track to achieve the ambitious goals laid out in the *Global Measles and Rubella Strategic Plan, 2012-2020*.

The basic strategies articulated in the *Plan* are sound. However, full implementation of these has been limited by lack of country ownership and global political will, reflected in insufficient resources. 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). This report recommends focusing on improving ongoing immunization systems -- although this may delay reaching measles and rubella elimination goals -- in order to ensure that gains in measles and rubella control can be sustained. Re-orienting the measles and rubella elimination program to increase emphasis on surveillance so that programmatic and strategic decisions can be guided by data is critical. Many of the recommendations made in this report are directly aligned with the Global Health Security Agenda's (GHSAs) Action Packages, which are designed to prevent outbreaks, detect threats in real time, and rapidly respond to infectious disease threats¹.

A focus on measles surveillance can help detect populations unreached by immunization systems and, by extension, program weaknesses. Measles serves as the 'canary in the coal mine' for detecting problems with immunization programs, a characteristic whose importance has recently been highlighted in the context of global health security.

Overarching conclusions

- The *Global Measles and Rubella Strategic Plan, 2012 – 2020* set the ambitious goal of achieving measles and rubella elimination in at least five WHO regions by 2020 through the implementation of five core strategies. Significant gains toward measles elimination have been made. From 2012 – 2014, more than 4 million measles-related deaths are estimated to have been averted through measles vaccination. By end 2015, Regional Verification Commissions (RVCs) in the American, European and Western Pacific Regions had verified elimination of measles in 61 Member States and elimination of rubella in 55 Member States.
- Although all six WHO regions now have measles elimination goals by 2020 and two have rubella elimination goals by this date, recent years have seen a slowing of progress. No region except the Americas has yet achieved its 2015 milestones. All countries should continue to work toward elimination goals with a particular focus on strengthening routine immunization systems.

¹ The White House. Office of the Press Secretary. FACT SHEET: Global health Security Agenda: Getting Ahead of the Curve on Epidemic Threats. Sept 26 2014. Available at <https://www.whitehouse.gov/the-press-office/2014/09/26/fact-sheet-global-health-security-agenda-getting-ahead-curve-epidemic-th>

- The basic strategies articulated in the *Plan* are sound, however these require full implementation. The main impediments to full implementation have been inadequate country ownership and global political will, reflected in inadequate resources.
- Although all six regions have measles elimination goals with the ultimate vision of a world free of measles, it is premature to set a timeframe for eradication at this point. Instead, the annual review of progress toward the Global Vaccine Action Plan (GVAP) goals² should be used to assess progress toward measles elimination. A determination should be made, not later than 2020, whether a formal global goal for measles eradication should be set with timeframes for achievement. In the meantime, all regions should work toward achieving the regional elimination goals.
- Strengthening of immunization systems is critical to achieving regional elimination goals. Working to achieve measles and rubella elimination can help strengthen health systems in general and immunization systems in particular. The ways in which measles and rubella elimination strengthens programs should be carefully documented.
- Disease incidence, in the presence of an effective surveillance system, is the most important indicator of progress. The presence or absence of measles is one of the best indicators of overall immunization program performance.
- A costed implementation plan in response to these recommendations should be developed by the Measles and Rubella Initiative (M&RI) not later than twelve months after the release of this report.

Selected specific recommendations are highlighted here. See the Executive Summary and the body of the full report for more recommendations and more details.

Strategy 1. Monitor disease using effective surveillance and evaluate programmatic efforts to ensure progress.

- A top priority for achieving the goals of the *Measles Rubella Strategic Plan* is to enhance integrated case-based, laboratory-supported surveillance for measles and rubella. All countries must implement case-based surveillance for measles and rubella, and report case information to the WHO Regional Office on a weekly basis.
- A working group on surveillance and outbreak investigation and response should be developed at global level.
- Protocols should be updated or, when necessary, developed, to guide surveillance and outbreak investigation and response. Countries need to dedicate resources for surveillance and partners need to supplement resources as needed, including resources for staffing, laboratory support, training, and other operational costs.
- Congenital Rubella Syndrome (CRS) Surveillance, either sentinel or national level, should be implemented, especially in countries using measles rubella vaccine (MR).
- As the Global Polio Eradication Initiative (GPEI) winds down, at a minimum the current level of measles and rubella surveillance should be maintained. Wherever possible, the polio transition

² GVAP has as measles and rubella targets to achieve measles elimination in four WHO regions and rubella elimination in two WHO regions by 2015, and to achieve measles and rubella elimination in five WHO regions by 2020. World Health Organization. *Global Vaccine Action Plan 2011-2020*. Available at http://www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/ Accessed September 18 2016.

should be capitalized on to further strengthen measles and rubella surveillance, as well as surveillance for other vaccine preventable diseases (VPDs).

- Both in outbreak investigations as well as in routine surveillance, all cases should be classified to determine the proportion of cases attributable to program failure – that is, that should have been vaccinated according to the national schedule, but were not.

Strategy 2. Achieve and maintain high levels of population immunity by providing high vaccination coverage with two doses of measles- and rubella-containing vaccines.

- Measles and rubella control and elimination activities at national level should be located within the overall immunization program.
- Two doses of measles containing vaccine (MCV) or measles-rubella containing vaccine (MRCV) delivered through ongoing services is the standard for all national immunization programs. Preventive supplementary immunization activities (SIAs) should be conducted on a regular basis, if routine two dose coverage is insufficient to achieve and maintain high population immunity.
- Efforts to enhance measles and rubella prevention should take into account the importance of strengthening the overall immunization delivery system.
- A standardized method to categorize countries based on their level of disease control and likelihood of achieving and sustaining achievement of measles and rubella elimination goals should be developed. Immunization strategies and surveillance strategies should be tailored to the country categorization.
- All countries should institute a school entry check for immunization, including vaccination against measles and rubella as well as against other vaccine preventable diseases (VPDs). Vaccination should be provided to children who have not received vaccine. Every opportunity should be taken to vaccinate people not adequately vaccinated, particularly those under 15 years of age.
- In view of the changing epidemiology of measles, immunity gaps among adolescents and adults need to be addressed by removing regulatory and policy barriers and promoting effective strategies for vaccinating older children, adolescents, and adults if they are believed to be susceptible to measles and/or rubella.

Strategy 3. Develop and maintain outbreak preparedness, respond rapidly to outbreaks and manage cases.

- Emphasis should be placed on prevention of outbreaks through monitoring of risk status and increased attention to vaccination of underserved communities and in high risk settings.
- All measles outbreaks should be promptly investigated and used to develop a susceptibility profile of the population to better inform measles control and elimination strategies, including outbreak prevention and response immunization.
- Based on existing experience, training materials should be developed for use at global, regional and country levels to perform outbreak investigations as well as to understand the underlying reasons that outbreaks are occurring and disseminate results of these investigations to all levels of the system.
- There must be adequate financial, human and laboratory resources to conduct adequate outbreak investigations. Countries eligible for funding from Gavi, The Vaccine Alliance (Gavi-eligible countries) should consider using Health System and Immunization Strengthening (HSIS) funds for this.
 - Financial resources should be urgently mobilized to support outbreak investigation and control in non-Gavi eligible countries. Countries should develop national Measles Outbreak Preparedness and Response Plans. Funding requirements for the implementation of these Plans should be included in measles and rubella program Financial Resource Requirements (FRR).

- When outbreaks are detected, in addition to investigation, countries should take steps to mitigate the outbreak through vaccination. The magnitude of the response should be based on the characteristics of the outbreak, the stage of measles control, and the category to which countries belong.

Strategy 4. Communicate and engage to build public confidence and demand for immunization.

- Increased resources are needed for communication to raise the visibility of VPDs, with a focus on measles and rubella.
- Creating and promoting demand for immunization requires long term investment and should be an integral part of routine immunization strategy.
- Communication plans may target many different audiences (e.g., politicians, public health leaders and workers, healthcare providers, caregivers, etc.). Plans targeting each of these audiences should be developed and audience-specific messages developed and tested. Data on measles incidence, including complications and deaths, as well as information on the costs associated with outbreaks, should be the focus of educating various audiences about the importance of preventing the illness. Data should be supplemented by stories of actual cases to illustrate the statistical data. Collection of information on cases of CRS can also be a powerful advocacy tool.
- In advocating for improved prevention of measles and rubella, it will be important to collect stories of how a focus on those diseases not only improved their control but also helped to enhance overall immunization and health systems (see Resource Mobilization Section below).

Strategy 5. Perform the research and development needed to support cost effective operations and improve vaccination and diagnostic tools

- Programmatically-oriented operations research, in addition to technologically-oriented research, should be used to determine how to best interrupt measles transmission. Such operations research should include achieving optimal uptake of vaccination in populations, which populations should be targeted for special immunization efforts, how to optimize surveillance systems, and the economic impact of disease.
- Sustained commitment to adequately funding measles and rubella research is required. An advocacy plan to secure funding for research should be developed.
- A measles and rubella research committee focusing in a sustained fashion on advocating for, promoting, and prioritizing measles and rubella research, similar to the Polio Research Committee (PRC), is critical. The natural home for this working group is WHO.

Building on the Polio Transition

- Given the imminent reduction in polio eradication resources, which can have an adverse impact on both measles and rubella control/elimination efforts, a focus on transition of GPEI funded immunization program capacity (including surveillance capacity) is urgent and needs to be a top priority.
- All stakeholders involved in control and elimination of measles and rubella as well as those involved in immunization system strengthening should engage in polio transition planning (at all levels) to leverage the opportunity and avoid the risks of the end of the GPEI.
- Strengthening immunization systems and the control and elimination of measles and rubella should be designated as high priorities for polio transition planning and implementation.

Governance

- It is imperative that there be close collaboration and coordination between Gavi, The Vaccine Alliance (Gavi) and the M&RI, as a central element in building the overall immunization system

and in order to ensure that measles and rubella control and elimination efforts are coordinated and efficient.

- Efforts to control and eliminate measles and rubella should be integrated with the general immunization system (including surveillance) and should be used to build and enhance the overall immunization system.

Resource Mobilization

- A multi-year FRR document for measles and rubella in the context of the overall immunization system should be revised. The FRR should include demand-driven, country-driven projections on need, and reflect funding from Gavi, the M&RI, other partners and domestic financing. This document should be complemented by yearly work plans with detailed national partners' financial contributions.
- The recent welcome additional support from Gavi for measles and rubella activities provides a major step forward for achieving measles and rubella goals. However, it is not, in itself, sufficient to provide adequate assistance globally, as many countries are not Gavi-eligible or are graduating from Gavi-eligibility and key global strategies such as surveillance and research are under-resourced. Consequently, there is a need for additional funding.
- Efforts should be made to identify examples of when a focus on measles and rubella elimination has led to building of the overall immunization system (e.g., where a focus on measles and rubella led to a school entry check for those vaccines as well as other vaccines recommended for children, leading to improved coverage for all recommended vaccines).

EXECUTIVE SUMMARY

Tremendous progress has been made towards both measles and rubella elimination since 2001. Significant gains have also been made during the period 2012 – 2015 with 23/194 World Health Organization (WHO) Member States having introduced a second dose of measles containing vaccine (MCV2), 17 countries having introduced rubella containing vaccine (RCV), global coverage with MCV2 rising from 48% to 61%, and global coverage with RCV from 39% to 46%. From 2012 – 2014, 4.25 million measles deaths are estimated to have been averted relative to no measles vaccination at all. However, despite these advances, neither measles nor rubella elimination are on track to achieve the ambitious goals laid out in the *Global Measles and Rubella Strategic Plan, 2012-2020*.

The basic strategies—i.e., surveillance, achieving high levels of population immunity, outbreak prevention and control, research, and communications -- articulated in the *Plan* are sound, however these require full implementation; and, at times, adaptation to the local context. Full implementation of these strategies has been limited by lack of country and global political will and country ownership. 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). Elimination, once achieved, would be difficult to sustain without more robust routine immunization systems than currently exist in much of the world. This report recommends focusing on improving ongoing immunization systems -- although this may delay reaching measles and rubella elimination goals -- in order to ensure that gains in measles and rubella control can be sustained. Re-orienting the measles and rubella elimination program to increase emphasis on surveillance so that programmatic and strategic decisions can be guided by data on disease occurrence is critical.

The inextricable linkage between achieving and maintaining measles and rubella elimination and strong immunization systems is repeatedly underlined in the report. Measles incidence is recognized as a marker of the success of immunization systems, and of health systems overall. Because measles is one of the most contagious of the vaccine-preventable diseases (VPDs) and virtually all measles infections are clinically manifest with rash and fever, often measles is the first recognized VPD to infect population clusters of susceptible persons. Thus, a focus on measles surveillance can help detect populations unreached by immunization systems and, by extension, program weaknesses. Measles serves as the ‘canary in the coal mine’ for detecting problems with immunization programs, a characteristic whose importance has recently been highlighted in the context of global health security.

Overarching conclusions

- The *Global Measles and Rubella Strategic Plan, 2012 – 2020* set the ambitious goal of achieving measles and rubella elimination in at least five WHO regions by 2020 through the implementation of five core strategies. Significant gains toward measles elimination have been made in the past 15 years with an estimated 79% reduction in global measles mortality between 2000 and 2014 resulting in over 17 million measles-related deaths averted. From 2012 – 2014, alone, over four million measles-related deaths are estimated to have been averted through measles vaccination. During 2012-2015, the number of WHO Member States providing MCV2 nationally through routine immunization services increased from 131 (68%) to 154 (79%) and estimated global MCV2 coverage increased from 48% to 56%. By end 2015, Regional Verification Commissions (RVCs) in the American, European and Western Pacific Regions had verified elimination of measles in 61 Member States (34/35 Member States in the Americas; 21/53 Member States in Europe; and 6/27 Member States in the Western Pacific) and elimination of rubella in 55 Member States (35/35 Member States in the

- Americas; 20/53 Member States in Europe).
- Although all six WHO regions now have measles elimination goals by 2020 and two have rubella elimination goals by this date, recent years have seen a slowing of progress. No region except the Americas has yet achieved its 2015 milestones. All countries should continue to work toward elimination goals with a particular focus on strengthening routine immunization systems.
 - The basic strategies—i.e., surveillance, achieving high levels of population immunity, outbreak prevention and control, research, and communications -- articulated in the *Plan* are sound, however these require full implementation; and, at times, adaptation to the local context. The main impediments to full implementation have been inadequate country and global political will and country ownership, reflected in inadequate resources.
 - Despite the recent, welcome increase in funding for measles and rubella vaccination from Gavi, The Vaccine Alliance (Gavi), the measles and rubella program remains under-resourced both from the financial and the human resource perspectives. Critical human resource gaps exist at global and regional levels.
 - Although both the tools and the strategies to reach the 2020 goals currently exist, the further development of certain tools, e.g., microarray patches (MAPs), could enhance the likelihood of success.
 - Although all six regions have measles elimination goals and three regions have rubella elimination goals³ with the ultimate vision of a world free of measles and rubella, it is premature to set a timeframe for eradication of either disease at this point. Instead, the annual review of progress toward the Global Vaccine Action Plan (GVAP) goals⁴ should be used to assess progress toward measles elimination. A determination should be made, not later than 2020, whether formal global goals for measles and rubella eradication should be set with timeframes for achievement. In the meantime, all regions should work toward achieving the regional elimination goals.
 - Strengthening of immunization systems is critical to achieving regional elimination goals. Working to achieve measles and rubella elimination can help strengthen health systems in general and immunization systems in particular – this should be carefully documented. Measles and rubella vaccination programs should be considered ‘indicator programs’ for immunization systems, and the incidence of measles and rubella and coverage with measles and rubella vaccines should be considered among the primary indicators of immunization system performance. National and district-level coverage with the first dose of measles containing vaccine (MCV1) should be adopted as an indicator in the GVAP to align with the prioritizing of this indicator by the International Health Regulations, Global Health Security, and Gavi.
 - Measles and rubella elimination efforts should be aligned with and take advantage of changing global priorities and opportunities, for example the transition of polio assets (see below).
 - Measuring coverage with measles and rubella containing vaccines, while important, is

³ Two of these regions have a rubella elimination date by 2020 while one does not yet have a date associated with the goal.

⁴ GVAP has as measles and rubella targets to achieve measles elimination in four WHO regions and rubella elimination in two WHO regions by 2015, and to achieve measles and rubella elimination in five WHO regions by 2020. World Health Organization. *Global Vaccine Action Plan 2011-2020*. Available at http://www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/ Accessed September 18 2016.

not the best indicator of progress towards measles/rubella control/elimination. Disease incidence, in the presence of an effective surveillance system, is the most important indicator of progress. The pattern of measles incidence is one of the best indicators of overall immunization program performance.

- There is an urgent need to strengthen the collection and use of surveillance data to better guide program strategy and implementation.
- A costed implementation plan in response to these recommendations should be developed by the Measles and Rubella Initiative (M&RI) not later than twelve months after the release of this report.

Specific recommendations

This report makes specific recommendations targeting each of the *Plan's* five strategies, as well as the core areas of Building on the Polio Transition, Governance, and Resource Mobilization. Although many of these recommendations are not new, to date many of them have been incompletely implemented or not adequately adapted to the local setting. The report's major recommendations are below.

Strategy 1. Monitor disease using effective surveillance and evaluate programmatic efforts to ensure progress.

- A top priority for achieving the goals of the *Measles Rubella Strategic Plan* is to enhance integrated case-based, laboratory-supported surveillance for measles and rubella. All countries must implement case-based surveillance for measles and rubella, and report case information to the WHO Regional Office on a weekly basis.
- A working group on surveillance and outbreak investigation and response should be developed at global level; this group should also provide guidance on linking surveillance findings with programmatic changes.
- Protocols should be updated or, when necessary, developed, to guide:
 - how to conduct outbreak investigations including: critical data to be collected; criteria for laboratory confirmation, guidelines for analysis, interpretation of analysis results, and presentation of the data (see Strategy 3 below);
 - setting up and strengthening surveillance systems to detect and investigate cases of rash illness and fever which could be measles or rubella, analyze the data, and interpret and disseminate the results of analysis for action and policy. For example, analysis should identify who is transmitting disease to whom, the role of failure to vaccinate versus vaccine failure, and in what settings exposure is occurring; and
 - selecting a representative subset of cases to be studied in depth in settings of very high transmission where it may not be feasible to examine all cases in such detail.
- Sera collected to investigate cases of rash illness with fever to diagnose measles should be tested for rubella if found to be negative for measles, or tested for both measles and rubella at the same time. The results of laboratory testing should routinely be fed back to the original health care provider and the caregiver.
- Training materials should be developed based on existing experience for use at global, regional and country levels to design and improve systems to collect surveillance data, as well as to understand the underlying reasons that cases are occurring and disseminate results to all levels of the system.
- It is critical that there be country and local level ownership and use of surveillance and outbreak data for program improvement and advocacy.
- Countries need to dedicate resources for surveillance and partners need to supplement resources as needed, including resources for staffing, laboratory support, training, and other operational costs. Countries eligible for funding from Gavi (Gavi-eligible countries) should take advantage of Health

System and Immunization Strengthening (HSIS) funding to build the surveillance infrastructure which serves to optimize immunization program performance. Where appropriate, measles and rubella surveillance systems should look for opportunities to also support surveillance for other diseases, for example dengue or yellow fever

- Countries should take advantage of opportunities from the International Health Regulations (IHR) review and national implementation of WHO evaluation of core capacities and lab surveillance strengthening to strengthen surveillance for measles and rubella.
- Congenital Rubella Syndrome (CRS) surveillance, either sentinel or national level, should be implemented, especially in countries using measles rubella vaccine (MR).
- As the Global Polio Eradication Initiative (GPEI) winds down, at a minimum the current level of measles and rubella surveillance should be maintained. Wherever possible, the polio transition should be capitalized on to further strengthen measles and rubella surveillance, as well as surveillance for other vaccine preventable diseases (VPDs).
- The current measures to evaluate the quality of surveillance systems should be reviewed. Specifically, efforts should be made to determine if the indicator “occurrence of 2 cases of rash illness with fever per 100,000 children per year shown not to be measles or rubella” is adequate to say that measles would be detected if present in a given country.
- Both in outbreak investigations as well as in routine surveillance, all cases should be classified to determine the proportion of cases attributable to program failure – that is, that should have been vaccinated according to the national schedule, but were not. Remedial actions need to be tailored depending on the distribution of cases in this classification. For example, remedial action for cases attributable to program failure would be to improve coverage in groups with these same characteristics. Detailed case investigation becomes ever more important as case counts are driven down. Persons of unknown vaccine status should be considered unvaccinated and thus attributable to program failure.

Strategy 2. Achieve and maintain high levels of population immunity by providing high vaccination coverage with two doses of measles- and rubella-containing vaccines.

- Measles and rubella control and elimination activities at national level should be located within the overall immunization program.
- The incidence of measles and rubella and coverage with measles and rubella vaccines should be considered among the primary indicators of immunization system performance.
- Two doses of measles containing vaccine (MCV) or measles-rubella containing vaccine (MRCV) delivered through ongoing services is the standard for all national immunization programs. Preventive SIAs should be conducted on a regular basis, if routine two dose coverage is insufficient to achieve and maintain high population immunity. In certain circumstances, one-time SIAs may need to be conducted to close existing immunity gaps in the population, for example immunity gaps among adults.
- Efforts to enhance measles and rubella prevention should take into account the importance of strengthening the overall immunization delivery system. For example,
 - delivery of MCV2 can be used as a platform to deliver other health interventions (i.e., helping to establish a second-year-of-life platform);
 - in planning SIAs, the enumeration of high-risk communities can be focused to also improve delivery of routine immunization services to these same populations.
- A standardized method to categorize countries based on their level of disease control and likelihood of achieving and sustaining achievement of measles and rubella elimination goals should be developed. The major purpose of such a categorization is to tailor outbreak response

and surveillance strategies appropriately. Large countries in which measles epidemiology is not uniform should adjust their measles control and elimination strategies to subnational settings.

- The current approach for determining the target age range for measles vaccine (M) and measles-rubella vaccine (MR) SIAs should be re-evaluated. This includes the potential for developing new guidelines based on more detailed analysis (including mathematical modelling) of sub-national coverage/disease incidence data to guide vaccination strategies.
- Approval of financial support from international partners for preventive SIAs should be conditional on country commitment to meet minimum standards of readiness as articulated in the SIA readiness checklist.
- Non-Gavi-eligible countries should take advantage of strategies being developed by WHO, Gavi and the United Nations Children's Fund (UNICEF) to address financing of vaccines in these settings.
- Efforts should be made to determine key reservoirs for measles and rubella that have proven to be exporting disease and take remedial action to terminate transmission in those areas/populations.
- The accuracy, completeness and timeliness of administrative coverage data must be improved to increase their usefulness both at national and sub-national level.
- Use of the district level program risk assessment tool, which takes into account reported or evaluated coverage, surveillance data, and program performance data to identify areas requiring special efforts, should be encouraged.
- All countries should institute a school entry check for immunization, including vaccination against measles and rubella as well as against other VPDs. Vaccination should be provided to children who have not received vaccine.
- Every opportunity should be taken to vaccinate people not adequately vaccinated, particularly those under 15 years of age. Policies which prohibit use of vaccine in children >1 year of age, older children and teenagers should be changed to allow these individuals to be vaccinated.
- In view of the changing epidemiology of measles, immunity gaps among adolescents and adults need to be addressed by removing regulatory and policy barriers and promoting effective strategies for vaccinating older children, adolescents, and adults if they are believed to be susceptible to measles and/or rubella.
- Quality of SIAs should be systematically and rapidly assessed. In the case of underperformance, remedial action should be taken immediately. Campaign planning and budgeting should always include "mopping-up" activities in poor performing areas.
- The current criterion recommended by WHO for introduction of MCV2 into the routine schedule, i.e., WHO/UNICEF estimates of MCV1 coverage greater or equal to 80% for three consecutive years, should be re-assessed.
- In principle, all doses of vaccine delivered (including through SIAs) should be documented, for example in the home-based record and, in those countries introducing computerized record systems, in the patient's electronic record.

Strategy 3. Develop and maintain outbreak preparedness, respond rapidly to outbreaks and manage cases.

- Emphasis should be placed on prevention of outbreaks through monitoring of risk status, for example through the use of risk assessment tools, and increased attention to vaccination in high risk settings.

- All measles outbreaks should be promptly investigated and used to develop a susceptibility profile of the population to better inform measles control and elimination strategies, including outbreak prevention and response immunization.
- Countries should develop national measles outbreak preparedness and response plans and build national capacity to investigate and respond to such outbreaks. A clear definition of what constitutes a measles outbreak that can be used to prompt outbreak investigation and control measures is required. Country ownership with regards to rapidly investigating and responding to measles and rubella outbreaks should be encouraged.
- Based on existing experience, training materials should be developed for use at global, regional and country levels to perform outbreak investigations as well as to understand the underlying reasons that outbreaks are occurring and disseminate results of these investigations to all levels of the system. Protocols should guide critical data to be collected as well as guidelines for analysis, interpretation of analysis results, and presentation of the data (see Strategy 1 above).
- Guidance should be developed to allow countries to assess the economic burden of outbreaks. Information on the cost and disruptiveness of outbreaks, including the costs incurred in controlling outbreaks, should be collected to use as an advocacy tool and to encourage preventive action.
- There is need for global guidelines for outbreak investigation and response for elimination settings, including contact tracing and the identification of population immunity gaps.
- There must be adequate financial, human and laboratory resources to conduct adequate measles and rubella outbreak investigations. Gavi-eligible countries should consider using HSIS funds for this.
- Financial resources should be urgently mobilized to support outbreak investigation and control in non-Gavi eligible countries. Countries should develop national Measles Outbreak Preparedness and Response Plans. Outbreak preparedness and response capacity should be assessed by Regional Verification Commissions (RVCs) or by Regional Immunization Technical Advisory Groups (RITAGs)
- When measles and rubella outbreaks are detected, in addition to investigation, countries should take steps to mitigate the outbreak through vaccination. The magnitude of the response should be based on the characteristics of the outbreak, the stage of measles and rubella control, and the category to which countries belong. The more rapid the response, the more likely it is to mitigate the impact of the outbreak.
- In countries that have introduced rubella-containing vaccines, outbreak immunization measures should be based on the susceptibility profile of the population, the groups affected, and the availability of vaccine.
- During and following a rubella outbreak, pregnant women should be registered and followed according to existing guidelines.
- When massive outbreaks occur, minimal information can be collected on all cases, but intensive investigations of a representative subset should be carried out to determine the underlying causes of the outbreak so that actions can be taken to prevent similar outbreaks in the future.
- When conducting case-based surveillance, at least twelve core⁵ elements should be investigated for each case as well as a classification of whether or not the case is preventable. The outbreak investigation response should be tailored to the classification of countries.

⁵ World Health Organization. Framework for verifying elimination of measles and rubella. *Weekly Epidemiological Record*, 2014, 88(9):89–100.

Strategy 4. Communicate and engage to build public confidence and demand for immunization.

- Increased resources are needed for communication to raise the visibility of VPDs and the importance of ongoing immunization services, with a focus on measles and rubella.
- Creating and promoting demand for immunization requires long term investment and should be an integral part of routine immunization strategy.
- Communication plans may target many different audiences (e.g., politicians, public health leaders and workers, healthcare providers, caregivers, etc.). Plans targeting each of these audiences should be developed and audience-specific messages developed and tested.
- Communication research science should be used to identify the most effective means of communication; these data should inform the communication strategies selected.
- Outbreaks of measles or rubella should be recognized as opportunities to promote the importance of immunization in preventing outbreaks, with particular focus on measles and rubella vaccination.
- Messages specific to rubella need to be developed, tested, and used.
- Data on measles incidence, including complications and deaths, as well as information on the costs associated with outbreaks, should be the focus of educating various audiences about the importance of preventing the illness. Data should be supplemented by stories of actual cases to illustrate the statistical data. Collection of information on cases of CRS can also be a powerful advocacy tool.
- Outbreaks should be an opportunity to sensitize medical professionals about the risk of nosocomial transmission of infectious diseases and take proper preventive measures.
- In advocating for improved prevention of measles and rubella, it will be important to collect stories of how a focus on those diseases not only improved their control but also helped to enhance overall immunization and health systems (see Resource Mobilization Section below).
- Communications plans should address hesitancy toward vaccination and building confidence in vaccines. This should include risk communication following publicized adverse events following immunization (AEFI), and promotion of the safety of vaccines.

Strategy 5. Perform the research and development needed to support cost effective operations and improve vaccination and diagnostic tools

- Programmatically-oriented operations research, in addition to technologically-oriented research such as the development of new vaccine delivery or antibody testing methods, should be used to determine how to best interrupt measles transmission. Such operations research should include achieving optimal uptake of vaccination in populations, which populations should be targeted for special immunization efforts, how to optimize surveillance systems, and the economic impact of disease.
- Sustained commitment to adequately funding measles and rubella research is required. An advocacy plan to secure funding for research should be developed.
- A measles and rubella research committee focusing in a sustained fashion on advocating for, promoting, and prioritizing measles and rubella research, similar to the Polio Research Committee (PRC), is critical. The natural home for this working group is WHO.
- Research should be conducted to determine the impact at the country level of measles and rubella control and elimination efforts on the overall immunization system.

Building on the Polio Transition

- Given the imminent reduction in polio eradication resources, which can have an adverse impact on both measles and rubella control/elimination efforts, a focus on transition of GPEI funded

immunization program capacity (including surveillance capacity) is urgent and needs to be a top priority.

- All stakeholders involved in control and elimination of measles and rubella (national governments, the M&RI, Gavi, etc.) as well as those involved in immunization system strengthening (Bill & Melinda Gates Foundation (BMGF), John Snow Incorporated (JSI), Centers for Disease Control and Prevention (CDC), WHO, UNICEF, the World Bank, etc.) should engage in polio transition planning (at all levels) to leverage the opportunity and avoid the risks of the end of the GPEI.
- Strengthening immunization systems and the control and elimination of measles and rubella should be designated as high priorities for polio transition planning and implementation.
- Polio assets should be re-purposed in such a way as to sustain essential polio functions (surveillance, lab network, communications, social mobilization, etc.) as well as the measles, rubella and other immunization functions that they have been supporting. At minimum, there should be no weakening of non-polio activities currently supported by polio assets.
- As part of the country planning framework for immunization and in support of the GVAP goals, a concrete plan with an earmarked budget should be developed and implemented for transitioning essential polio assets to immunization system strengthening and measles and rubella elimination. Under the leadership of the ministries of health, this plan should aim to include the participation of other ministry and all partners with an interest in health system strengthening.

Governance

- It is imperative that there be close collaboration and coordination between Gavi and the M&RI, as a central element in building the overall immunization system and in order to ensure that measles and rubella control and elimination efforts are coordinated and efficient.
- Efforts to control and eliminate measles and rubella should be integrated with the general immunization system (including surveillance) and should be used to build and enhance the overall immunization system.
- All countries should establish National Verification Committees (NVCs) to review national progress toward elimination goals, and make recommendations as to how these goals may be met.
- RVCs should be established in all regions where they do not exist and their efforts strengthened in regions in which they do exist. The RVCs should serve as independent reviewers of progress toward measles and rubella elimination and make region and country-specific recommendations to overcome impediments to measles and rubella elimination.

Resource Mobilization

- A multi-year Financial Resource Requirements (FRR) document for measles and rubella in the context of the overall immunization system should be revised. The FRR should include demand-driven, country -driven projections on need, and reflect funding from Gavi, the M&RI, other partners and domestic financing. This document should be complemented by yearly work plans with detailed national partners' financial contributions.
- The recent welcome support from Gavi for measles and rubella activities provides a major step forward for achieving measles and rubella goals. However, it is not, in itself, sufficient to provide adequate assistance globally, as many countries are not Gavi-eligible or are graduating from Gavi-eligibility. Consequently, there is a need for additional funding.
- The five M&RI founding partners should have adequate staff capacity to identify and align the resources needed and mobilize additional donors and resources to fill the funding gap for

- immunizations overall and measles and rubella surveillance and vaccination in particular.
- Country co-financing for measles and rubella activities should increase as countries move along the development continuum. Country financial commitments should be closely followed through the annual work plan budget.
 - Efforts should be made to identify examples of when a focus on measles and rubella elimination has led to building of the overall immunization system (e.g., where a focus on measles and rubella led to a school entry check for those vaccines as well as other vaccines recommended for children, leading to improved coverage for all recommended vaccines). In addition, it is important to remain open to examples of when a focus on measles and rubella has had a negative impact on overall healthcare and immunization systems, and learn from any such examples how such a situation can be avoided.

SECTION 1. BACKGROUND, CONTEXT AND RATIONALE FOR MIDTERM REVIEW

Disease and Vaccines

Measles, a viral illness, is one of the most highly infectious diseases known to man. Complications of measles include pneumonia, diarrhea and encephalitis. Case fatality rates from measles vary from 0.1% in the developed world to 15% in the less developed world,⁶ with death usually caused by pneumonia or diarrhea. Population immunity of 92% – 95% is considered necessary to stop measles transmission.⁷ A highly-effective measles vaccine has existed since 1963. Nonetheless, in 2014, an estimated 114,900 people, mostly children, died from the disease⁸. Due to its highly infectious nature, measles effectively seeks out unvaccinated individuals. For this reason, it is often considered to be the indicator disease or the ‘canary in the coal mine’, able to identify individuals and subpopulations who remain unreached by immunization programs. Measles vaccination coverage serves as an indicator of the quality of immunization programs,⁹ while the epidemiology of measles cases highlights specific geographic areas and populations in which immunization services require further strengthening.

Rubella, another vaccine-preventable viral disease, is primarily a concern because infection during pregnancy can result in severe congenital defects in the baby. These congenital defects include heart defects, cataracts, deafness, and cleft palate among others. In 2010, more than 100,000 babies with congenital rubella syndrome (CRS) were estimated to be born globally.¹⁰

The concept of measles eradication has been reviewed by the International Task Force for Disease Eradication (ITFDE), as well as by an independent group of experts and the World Health Organization’s (WHO’s) Strategic Advisory Group of Experts on Immunization (SAGE), resulting in the affirmation of the feasibility and desirability of eventual eradication of measles. The ITFDE also reviewed progress towards rubella eradication, concluding that this was technically feasible and that the economic literature demonstrated that eradication of both measles and rubella was more cost effective than indefinite high level control of either of these diseases.^{11 12 13}

⁶ Strebel PM, Papania MJ, Fiebelkorn AP, Halsey N. Measles vaccine. In Plotkin SA, WA Orenstein, PA Offit (Eds.), *Vaccines*, 6th Edition, China: Elsevier Saunders 2013.

⁷ Orenstein WA, Gay NJ. The Theory of Measles Elimination: Implications for the Design of Elimination Strategies. *Journal of Infectious Diseases*, 2004, 189(Suppl 1): S27-S35. doi: 10.1086/381592

⁸ CDC. Progress toward Regional Measles Elimination – Worldwide. 2000-2014. *MMWR* 2015; 64(44):1246-1251

⁹⁹ <http://www.gavi.org/results/goal-level-indicators/health-systems-goal-indicators/> Accessed July 10 2016

¹⁰ Vynnycky E, Adams EJ, Cutts FT, Reef SE, Navar AM, Simons E et al. Using seroprevalence and immunisation coverage data to estimate the global burden of congenital rubella syndrome, 1996-2010: a systematic review, 2016 (<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0149160>)

¹¹ World Health Organization. Meeting of the international task force for disease eradication, November 2015.

Weekly Epidemiological Record, 2016, 91:61-71.

¹² World Health Organization. World Health Organization global technical consultation to assess the feasibility of measles eradication. 2010

http://www.who.int/immunization/sage/1_Global_Technical_Consultation_Assess_Feasibility_Measles_Erad_8_sept_2010.pdf?ua=1. Accessed September 18, 2016

¹³ World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, November 2010. Summary, conclusions and recommendations. *Weekly Epidemiological Record*, 2011,86:1-16

When the Expanded Programme on Immunization (EPI) was launched in 1974, measles vaccine was one of the six vaccines included in the basic package of vaccines recommended for all children in developing countries. As injectable vaccines recommended at either 9 months or 12-15 months of age, measles containing vaccines (MCV) (measles (M), measles rubella (MR), measles mumps rubella (MMR), and measles mumps rubella varicella (MMRV) are currently part of the schedule of childhood vaccinations in all countries. Mass vaccination campaigns against measles (also called supplementary immunization activities, or SIAs, because they aim to reach children missed by routine immunization activities) targeting all persons in a given age group (usually children ≥ 9 months of age) regardless of prior vaccination status were pioneered by the Pan American Health Organization (PAHO) in Latin America. These SIAs have remained an integral part of national and global immunization program activities but should be regarded as truly supplemental, with primary emphasis on delivering two doses of MCV to all children through ongoing services.

Relationship of measles and rubella control and elimination to other global health initiatives

The control and elimination of measles and rubella contribute directly to achieving the goals of numerous global health initiatives. Programs to eliminate measles and rubella are significant contributors to achieving the health-related Sustainable Development Goals and targets.¹⁴ The World Health Assembly (WHA) in May 2016 (Resolution WHA 69.11) recognized that universal health coverage includes access to essential vaccines, and it reaffirmed the commitment to accelerate progress in reducing newborn, child and maternal mortality by ending all such preventable deaths before 2030.

This report's emphasis on the need to improve surveillance should serve to strengthen national surveillance and response capacities in line with requirements in the International Health Regulations (2005) (IHR)¹⁵ A fundamental aspect of the IHR is the obligation for all 196 countries that are party to the Regulations (i.e., two countries beyond the 194 Member States of WHO) to develop, strengthen and maintain core public health capacities for surveillance and response in order to be able to detect, assess, notify and report events and respond to public health risks and emergencies of international concern.

The effort to eliminate measles and rubella, which builds on and enhances the overall immunization system, also serves to enhance global health security. At the Ise-Shima Summit in May 2016, the G-7 countries repeated their commitment to advancing compliance with WHO's IHR objectives including through the Global Health Security Agenda (GHSa).¹⁶ GHSa measures progress for its Immunization Action Package by achieving at least 90% coverage of the country's fifteen-month-old population with at least one dose of MCV, as demonstrated by coverage surveys or administrative data.¹⁷ The desired national impact is to have effective protection through achievement and maintenance of immunization against measles and other epidemic-prone vaccine preventable diseases (VPDs). Measles immunization is emphasized because it is widely recognized as a proxy indicator not only for overall immunization coverage levels, but also of the level of effectiveness of the primary health care system in general. While implementing the recommendations made in this report most obviously supports the

¹⁴ United Nations. Sustainable development knowledge goals- Transforming our world- the 2030 agenda for sustainable development (<https://sustainabledevelopment.un.org/?menu=1300> Accessed July 10 2016).

¹⁵ World Health Organization. International Health Regulations 2005. Second edition.(http://apps.who.int/iris/bitstream/10665/43883/1/9789241580410_eng.pdf)

¹⁶ G7 Ise-Shima vision for global health 2016 (<http://www.g8.utoronto.ca/summit/2016shima/health.html>) Accessed July 26 2016. Accessed August 15 2016.

¹⁷ Global Health Security Agenda (<https://ghsagenda.org/>, Accessed July 26, 2016).

implementation of the GHSA's Immunization Action Package, it also supports a number of other GHSA Action Packages. High levels of measles control contribute to combating antimicrobial resistant bacteria, one area of focus of the GHSA, by decreasing the inappropriate use of antibiotics and the need to appropriately use antibiotics to treat measles complications caused by secondary bacterial infections, such as bacterial pneumonia. This report's focus on laboratory-supported surveillance and appropriate interpretation and use of surveillance data is aligned with the GHSA's efforts to increase laboratory capacity at national, provincial and district levels while linking to national disease reporting frameworks, as well as with the GHSA's Real-Time Surveillance Action Package and the GHSA's Workforce Development Action Package.¹⁸

Other relevant international frameworks are the Convention for the Rights of Children,¹⁹ and the Sphere project (Sphere) recommendations.²⁰ Sphere articulates measles vaccination as one of the highest priorities in humanitarian emergencies due to the deadly nature of outbreaks in these settings. Recent data from the United Nations Children's Fund (UNICEF) indicate that almost two-thirds of the world's under- or unvaccinated children now live in conflict zones.²¹

Development and Implementation of the *Global Measles and Rubella Strategic Plan 2012-2020*

In 2001, the Measles Initiative, a coalition led by UNICEF, WHO, the US Centers for Disease Control and Prevention (CDC), the United Nations Foundation (UNF), and the American Red Cross (ARC), was formed, spearheading a more aggressive approach to measles control based on the PAHO strategy of wide age-range national SIAs and regular follow-up SIAs as supplementary strategies to increasing routine first and second dose coverage with MCV. This strategy was initially highly successful and resulted in a reduction of estimated measles mortality by 74% in 2010 relative to 2000.²² However, since that time, gains have slowed with a plateauing of global coverage with the first dose of measles containing vaccine (MCV1) and SIA coverage inadequate to stop the accumulation of individuals susceptible to measles, reflected in a plateauing of the number of reported cases globally (Figure 1).

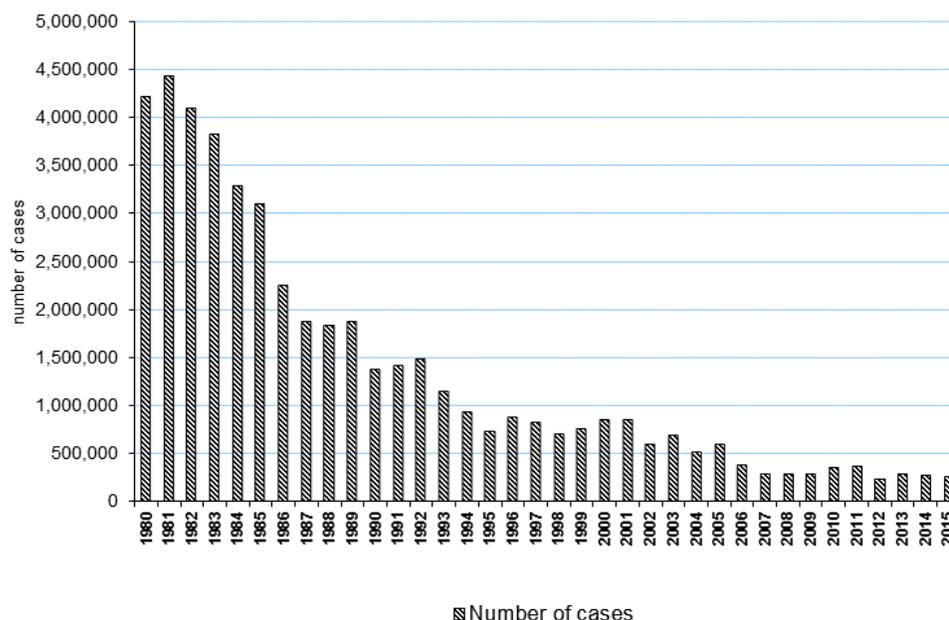
¹⁸ Global Health Security Agenda: Action Packages. Available at <https://ghsagenda.org/packages.html> Accessed Sept 8 2016.

¹⁹ United Nations Human Rights- Convention of the Rights of the Child. 1989 (<http://www.ohchr.org/EN/ProfessionalInterest/Pages/CRC.aspx>. Accessed July 10 2016.

²⁰ The SPHERE Project. Humanitarian Charter and Minimum Standards in Humanitarian Response <http://www.sphereproject.org/handbook/>. Accessed July 10 2016.

²¹ UNICEF- Two-thirds of unimmunized children live in conflict-affected countries – UNICEF, 2016 http://www.unicef.org/media/media_90987.html, Accessed July 10 2016.

²² Simons E, Ferrari M, Fricks J, Wannemuehler K, Anand A, Burton A et al. Assessment of the 2010 global measles mortality reduction goal: results from a model of surveillance data. *Lancet*, 2012, 379:173-2178.



Source: WHO/IVB database, 2016
194 WHO Member States.
Data as of 15 July 2016

Figure 1. Number of measles cases reported to WHO by year, 1980 – 2015. Data as of 9 July 2016

In 2012, the Initiative, now targeting both measles and rubella and renamed the Measles and Rubella Initiative (M&RI), published the ‘*Global Measles and Rubella Strategic Plan 2012-2020*’.²³ This document had, as a goal for end-2020, to achieve measles and rubella elimination in at least five WHO regions. Five core strategies to reach this goal were articulated, as follows:

- Achieve and maintain high levels of population immunity by providing high vaccination coverage with two doses of measles- and rubella-containing vaccines;
- Monitor disease using effective surveillance and evaluate programmatic efforts to ensure progress;
- Develop and maintain outbreak preparedness, respond rapidly to outbreaks and manage cases;
- Communicate and engage to build public confidence and demand for immunization;
- Perform the research and development needed to support cost-effective operations and improve vaccination and diagnostic tools.

To measure progress toward the 2020 goal, specific milestones for 2015 were established. These were to:

- Reduce annual measles incidence to less than five cases per million and maintain that level;
- Achieve at least 90% coverage with the first routine dose of measles-containing vaccine (or measles-rubella-containing vaccine as appropriate) nationally, and exceed 80% vaccination coverage in every district or equivalent administrative unit;
- Achieve at least 95% coverage with M, MR or MMR during SIAs in every district;

²³ World Health Organization. *Global Measles and Rubella Strategic Plan: 2012-2020* (http://apps.who.int/iris/bitstream/10665/44855/1/9789241503396_eng.pdf).

- Establish a rubella/CRS elimination goal in at least three additional WHO regions (i.e., in addition to the AMR and EUR that had established goals before 2012);
- Establish a target date for the global eradication of measles.

Figure 2 summarizes the status of these milestones based on 2015 data.

2015 Milestone	2015 Data	Evaluation
Reduce annual measles incidence to less than five cases per million and maintain that level	Global incidence of 39.3 per million	
Achieve at least 90% coverage with measles vaccine (or measles-rubella-containing vaccine as appropriate) nationally, and exceed 80% vaccination coverage in every district or equivalent administrative unit.	119 (61%) countries have coverage with first dose of measles containing vaccine exceeding 90% at national level.	
Achieve at least 95% coverage with measles, measles rubella (MR) or measles mumps rubella (MMR) vaccine during supplementary immunization activities (SIAs) in every district.	Of 34 countries conducting SIAs between 2012 and 2014 and conducting coverage evaluations of the SIA, 16 (47%) reached 95% national coverage	
Establish a rubella/congenital rubella syndrome elimination goal in at least three additional World Health Organization regions (i.e., in addition to the Region of the Americas and the European Regions that had established goals before 2012).	One additional region, the Western Pacific Region, has established a rubella elimination goal but no date is associated with it	
Establish a target date for the global eradication of measles.	No target date for global measles eradication established	

Figure 2. Status of Global Measles and Rubella Strategic Plan: 2012-2020 2015 Milestones

Legend: Black: Little or no progress.

Gray: Moderate progress but inadequate to meet 2015 milestone

Recommendation for Midterm Review

In 2015, WHO's SAGE recommended a midterm review (MTR) of the *Global Measles and Rubella Strategic Plan*. The objectives of the MTR are to:

- provide a candid review of progress towards, and key political, financial and technical reasons for not attaining, 2015 World Health Assembly targets and regional elimination goals;
- assess the quality of implementation of the *Global Measles and Rubella Strategic Plan's 2012-2020's* five key strategies and provide recommendations on how the strategies and principles should be

refined to address weaknesses in immunization systems and to accelerate progress towards the global and regional goals;

- formulate a set of lessons learned, risks, and financial, political and programmatic priorities over the next five years (2016-2020) for countries and partners in order to execute the work.

The request for the MTR reflects the urgency of re-setting the course to reach the 2020 goals. This urgency is dictated by the fact that Global Polio Eradication Initiative (GPEI) assets, which have been pivotal in the gains made toward measles and rubella elimination through the contribution of human resources and infrastructure, will decrease rapidly as of 2017 (Figure 11, page 68) if concrete and funded plans for transition are not made. Furthermore, the current status of measles control leads to a situation in which susceptibility to measles is distributed across increasingly wide age groups, which will make eventual elimination both more expensive and more technically difficult. Incomplete control allows persons to grow to older ages still susceptible as they have neither been vaccinated nor exposed to measles because while not eliminated, measles incidence is decreased. This can lead to outbreaks which have wider age ranges of cases than in the pre-vaccine era.

SECTION 2. METHODOLOGY OF MIDTERM REVIEW

The MTR was conducted by a project team of five individuals. The team undertook a comprehensive document review, and conducted interviews with and received presentations from a broad range of stakeholders. Each individual (with the exception of the chairperson) was tasked with contacting specific Regional Offices of WHO to develop an in-depth understanding of the Region's experiences in pursuing measles elimination and rubella control. Each Office also selected one or two countries from its region to illustrate the diverse faces of measles elimination and rubella control. A brief summary of regional findings is given below, in Section 4. Detailed regional and country reports are available in the web-based version of this report.

This report examines each of the *Plan's* five strategies. For each strategy, the report summarizes relevant background, progress and challenges to date, the deliberations of the MTR team, and recommendations for mid-term corrections. In addition, in the context of measles and rubella elimination, the report addresses the critical questions of building on the polio transition, governance, and resource mobilization.

SECTION 3. OVERARCHING CONCLUSIONS

This review reached a number of overarching conclusions, articulated below.

- The *Global Measles and Rubella Strategic Plan, 2012 – 2020* set the ambitious goal of achieving measles and rubella elimination in at least five World Health Organization (WHO) regions by 2020 through the implementation of five core strategies. Significant gains toward measles elimination have been made in the past 15 years with an estimated 79% reduction in global measles mortality between 2000 and 2014 resulting in over 17 million measles-related deaths averted. From 2012 – 2014, alone, over four million measles-related deaths are estimated to have been averted through measles vaccination. During 2012-2015, the number of WHO Member States providing a second dose of measles containing vaccine (MCV2) nationally through routine immunization services increased from 131 (68%) to 154 (79%) and estimated global MCV2 coverage increased from 48% to 56%. By end 2015, Regional Verification Commissions (RVCs) in the American, European and Western Pacific Regions had verified elimination of

measles in 61 Member States (34/35 Member States in the Americas; 21/53 Member States in Europe; and 6/27 Member States in the Western Pacific) and elimination of rubella in 67 Member States (35/35 Member States in the Americas; 20/53 Member States in Europe).

- Although all six regions now have measles elimination goals by 2020 and two have rubella elimination goals by this date, recent years have seen a slowing of progress. No region except the Americas has yet achieved its 2015 milestones. All countries should continue to work toward these elimination goals with a particular focus on strengthening routine immunization systems.
- The basic strategies—i.e., surveillance, achieving high levels of population immunity, outbreak prevention and control, research, and communications -- articulated in the *Plan* are sound, however these require full implementation, and, at times, adaptation to the local context. The main impediments to full implementation have been inadequate country ownership and global political will, reflected in inadequate resources.
- Despite the recent, welcome increase in funding for measles and rubella vaccination from Gavi, The Vaccine Alliance (Gavi), the measles and rubella program remains under-resourced both from the financial and the human resource perspectives, both at global and at regional level.
- Although both the tools and the strategies to reach the 2020 goals currently exist, the further development of certain tools, e.g., microarray patches (MAPs), could enhance the likelihood of success.
- Although all six regions have measles elimination goals and three regions have rubella elimination goals²⁴ with the ultimate vision of a world free of measles and rubella, it is premature to set a timeframe for eradication of either disease at this point. Instead, the annual review of progress toward the Global Vaccine Action Plan (GVAP) goals²⁵ should be used to assess progress toward measles elimination. A determination should be made, not later than 2020, whether formal global goals for measles and rubella eradication should be set with timeframes for achievement. In the meantime, all regions should work toward achieving the regional elimination goals.
- Strengthening of immunization systems is critical to achieving regional elimination goals. Working to achieve measles and rubella elimination can help strengthen health systems in general and immunization systems in particular – this should be carefully documented. Measles and rubella vaccination programs should be considered ‘indicator programs’ for immunization systems, and the incidence of measles and rubella and coverage with measles and rubella vaccines should be considered among the primary indicators of immunization system performance. Coverage with the first dose of measles containing vaccine (MCV1) should be adopted as an indicator in the Global Vaccine Action Plan (GVAP) to align with the prioritizing of this indicator by the International Health Regulations, Global Health Security, and Gavi, The Vaccine Alliance.

²⁴ Two of these regions have a rubella elimination date by 2020 while one does not yet have a date associated with the goal.

²⁵ GVAP has as measles and rubella targets to achieve measles elimination in four WHO regions and rubella elimination in two WHO regions by 2015, and to achieve measles and rubella elimination in five WHO regions by 2020. World Health Organization. *Global Vaccine Action Plan 2011-2020*. Available at http://www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/ Accessed September 18 2016.

- Measles and rubella elimination efforts should be aligned with and take advantage of changing global priorities and opportunities, for example the transition of polio assets (see below).
- Measuring coverage with measles and rubella containing vaccines, while important, is not the best indicator of progress towards measles/rubella control/elimination. Disease incidence, in the presence of an effective surveillance system, is the most important indicator of progress. The presence or absence of measles is one of the best indicators of overall immunization program performance.
- There is an urgent need to strengthen the collection and use of surveillance data to better guide program strategy and implementation.
- An implementation plan in response to these recommendations should be developed not later than twelve months after the release of this report.

SECTION 4. REGIONAL SUMMARIES

Table 1 summarizes regional incidence of measles reported through the Joint Reporting Form (JRF) for the period 2013 – 2015, as well as presenting data on 2010 as a baseline. Table 2 presents similar data for rubella. A brief summary of the current status of measles and rubella control in each of WHO's regions follows these Tables.

WHO region	MCV1 national coverage (%)					% of Member States reporting measles in their JRF				Measles incidence per million population					% of Member States with incidence greater than 5 per million population			
	2015	2014	2013	2010	% change 2010–2015	2015	2014	2013	2010	2015	2014	2013	2010	% change 2010–2015	2015	2014	2013	2010
African Region	74	72	71	73	+1.4	98	100	100	98	115.3	76.7	182.5	233.0	-51	51	51	53	30
Region of the Americas	94	93	92	92	+1.1	97	100	97	100	0.6	2.0	0.5	0.3	+100	94	97	97	100
Eastern Mediterranean Region	76	76	76	81	-6.6	95	90	86	100	33.5	28.9	34.7	17.5	+91	38	24	24	38
European Region	94	94	95	93	+1.1	77	77	87	98	36.3	19.2	33.6	34.2	-6	53	45	58	68
South-East Asia Region	85	85	84	83	+2.4	91	81	100	100	17.4	17.9	16.0	29.9	-42	45	45	45	36
Western Pacific Region	96	97	97	96	0	59	63	74	93	35.4	71.6	17.5	27.6	+28	33	22	48	63
Total	85	84	84	85	0	86	87	91	97	39.3	39.8	40.2	50.0	-21	55	51	58	59

Table 1. Number of measles cases and incidence by WHO region, 2013 - 2015 and baseline 2010.

^a List of Member States not reporting JRF measles data: Albania, Andorra, Cook Islands, Fiji, Finland, Greece, Indonesia, Kiribati, Libya, Marshall Islands, Mauritius, Monaco, Montenegro, Nauru, Netherlands, Niue, Oman, Poland, Portugal, Samoa, San Marino, Singapore, Solomon Islands, Turkey, Tuvalu, Ukraine, United States of America. (NB: Turkey, Ukraine and Tuvalu submitted their JRF after the 24th June 2016, date of GVAP report).

Source: JRF (as of 24 June 2016) and WHO-UNICEF estimates, 1980–2015, revision July 2016.

WHO region	National rubella coverage (%)				Member States reporting rubella cases (%) ²⁶				Rubella incidence per million population			
	2015	2014	2013	2010	2015	2014	2013	2010	2015	2014	2013	2010
African Region	12	9	4	0	94	94	91	79	5.6	7.8	15.1	3.9
Region of the Americas	94	93	92	93	97	100	97	100	0.0	0.0	0.0	0.0
Eastern Mediterranean Region	45	42	38	38	86	90	86	81	3.0	4.7	6.6	3.5
European Region	94	94	95	93	72	72	81	92	0.6	1.0	62.8	14.3
South-East Asia Region	14	12	12	3	82	91	100	82	2.6	5.0	5.5	26.1
Western Pacific Region	89	90	88	61	56	59	67	85	5.1	7.0	18.5	27.1
Total	46	44	42	35	81	84	86	88	3.3	4.8	14.9	15.0

Table 2. Rubella cases and incidence by WHO region, 2013 - 2015 and baseline year 2010.

Note: MCV1 was used as a proxy in the Member States that have introduced rubella vaccine.

Source: JRF (as of 24 June 2016) and WHO-UNICEF estimates, 1980–2015, revision July 2016.

²⁶ This percentage is of all countries (with or without rubella surveillance) who report rubella cases.

African Region (AFR)

Status

Regional measles mortality reduction activities began in AFR in 2001 and, ten years later, all 47 countries adopted the target of measles elimination by 2020. Although there is no target date set for rubella elimination, countries are introducing rubella containing vaccine (RCV) and conducting surveillance for rubella and CRS.

Significant progress has been achieved to date. The number of countries achieving MCV1 coverage of 90% or more increased from 4 in 2000 to 16 in 2009, leading to an increase in regional MCV1 coverage from 53% to 74% during the same period. As of 2014, 14 countries had maintained > 90% coverage with MCV1. Nonetheless, regional coverage has stagnated around 75% since 2009. Introduction of MCV2 and RCV has also made progress: by December 2015, 23 (48.9%) of 47 countries had introduced MCV2 and 9 (19%) had introduced RCV in their routine immunization programs. In response to higher vaccination coverage, reported cases of measles declined > 90% from more than half a million annually in 2000 to fewer than 50,000 in 2008. Despite this progress, 2010 and 2011 saw sharp increases in reported cases due to outbreaks. These outbreaks were predominantly in Southern African countries with transmission primarily in older age groups. Further increases in cases in 2013 represented large outbreaks occurring in the Democratic Republic of the Congo and Nigeria which, between them, accounted for 83% of the 171,178 cases reported in AFR that year. Overall, the average incidence for the period 2012-2014 of reported cases was less than 1 per million population in 11 countries, between 1 and 5 per million in another 11, between 5 and 9 in 6 countries, and between 10 and 49 in 12 countries. Four countries (Ethiopia, Nigeria, Angola, and Namibia) had an average annual incidence above 50 per million. During the period reviewed, the larger countries have faced outbreaks of varying magnitude almost annually. In Africa, no RVC currently exists.

By 2015, case-based surveillance had been implemented in 44 countries. AFR does not monitor the percentage of districts reporting at least two cases of non-measles rash fever cases. However, it does monitor other indicators of surveillance quality. These include the percentage of cases with adequate specimens collected (2012: 91%; 2013: 78%; 2014: 85%; 2015: 82%). As case-based surveillance has improved throughout the continent, the number of specimens received in the network laboratory has steadily increased.

Despite great progress in vaccination coverage and surveillance since 2000, substantial challenges to reaching elimination remain. The major challenges are gaps in population immunity at subnational levels, immunity gaps among older children, lack of resources to fully implement recommended strategies, suboptimal performance during SIAs and lack of political commitment and competing priorities at national level. In addition, because of the large contribution that polio funding makes to supporting measles and rubella activities in AFR, this region is particularly vulnerable to decreases in GPEI funding.

Conclusions and Recommendations

The diverse socio-economic development levels, political structures, and health system challenges in AFR influence immunization program performance overall as well as the ability to achieve measles elimination. Twelve (25.7%) of 47 countries with strong programs have sustained very low incidence of measles and are nearing measles elimination while 16 (34%) countries have immunity and surveillance gaps at subnational level but are on track for elimination. Eight (17%) countries with a variety of

program gaps, including large population immunity gaps and poor surveillance (including lack of program ownership) are not on track for measles elimination. Lastly, there are 11 (23%) countries with major challenges such as large populations, insecurity, high incidence of measles, frequent outbreaks and leadership gaps. These countries pose the biggest challenge to reaching elimination in the region.

While the strategies for measles elimination are appropriate, the failure to meet the set mid-term goals is due to incomplete implementation of the strategies. Technical issues, such as improved surveillance, higher quality SIAs and better monitoring, can be addressed. However, addressing technical issues alone is not adequate: an enabling environment, with local and national commitment, improved health systems performance and adequate resources will be required. Region-specific recommendations are as follows:

- Give priority to the introduction of MCV2 in all countries;
- Establish and maintain elimination level surveillance at subnational level in all countries;
- Make financial support for all SIAs in the region contingent on the ability to meet minimum standards of readiness to ensure the highest quality of activity;
- Continue to make outbreak investigation a priority with the objective of identifying the reasons for the outbreak and the chains of transmission so as to guide local strategies;
- Systematically use surveillance data and outbreak investigation findings for advocacy with local and national stakeholders and
- Undertake an in-depth review of program activities for the coming years to define the most appropriate strategy and the technical and financial support needed in the countries identified as presenting the biggest challenge to meeting the regional elimination goal.

Americas Region (AMR)

Status

AMR achieved measles elimination in 2002 and rubella/CRS elimination in 2009, convincingly demonstrating the feasibility of eliminating these conditions across a large and diverse region. Elimination was achieved through strong political commitment and leadership, regional cohesion, effective disease surveillance, and a combination of strong routine immunization programs and mass vaccination campaigns. In 2014, in addition to the U.S. and Canada, 23 (70%) of the other 33 countries in AMR reached national coverage of $\geq 90\%$ with the first dose of measles mumps rubella vaccine (MMR1), with 18 (78%) of those 23 countries reporting that $\geq 80\%$ of districts achieved $\geq 90\%$ coverage. The second dose of measles mumps rubella vaccine (MMR2) has been introduced into 30 of the 35 countries in the region, and in 2014, 15(55%) of 27 countries submitting data using the WHO/UNICEF Joint Reporting Form achieved national coverage of $\geq 90\%$, with 12 countries reporting that $\geq 80\%$ of districts achieved $\geq 90\%$ coverage with MMR2. Sensitive and timely case-based surveillance for measles, rubella, and CRS is in place in all countries in AMR, although a decrease in performance with regard to various indicators was observed between 2014 and 2015, and the quality of the active epidemiological surveillance is not homogenous at the sub-national and local levels.

Since elimination of measles was achieved in 2002, importations of measles virus have led to multiple outbreaks, producing a total of 5,277 cases between 2003 and 2014 and an additional 614 cases in 2015. Large outbreaks with multiple generations of cases have occurred in Canada, the U.S., and Brazil. The outbreak in Brazil lasted a total of 28 months, ultimately resulting in 1,052 reported cases in 38 municipalities. As endemic measles transmission is defined as the existence of any continuous

indigenous chain of transmission of measles virus that persists for >1 year in any defined geographic area,²⁷ this outbreak in Brazil was considered re-establishment of endemic measles. Of the cases in Brazil, 73% were in unvaccinated individuals and 9% were in individuals of unknown vaccination status; of the vaccinated individuals who contracted measles, only 7% had received two doses of vaccine. Almost half (44%) of the persons with measles who had not been vaccinated against measles were 15-39 years of age. On July 6th 2015, Brazil reported the last endemic measles case. One year later, following a review of data, the RVC declared Brazil free of endemic measles virus. This outbreak demonstrated that low levels of measles virus transmission can persist in populations with high reported vaccination coverage and that importations of measles virus remain a threat

The RVC for AMR, known as the International Expert Committee for Measles and Rubella Elimination in the Americas, initially met in Dec. 2010. Annual meetings were held after that with the last meeting to date held in 2015. An ad hoc meeting was held in September, 2014.

Conclusions and Recommendations

The current status of AMR documents that the region continues to lead in the global effort to eliminate measles and rubella, demonstrating the feasibility of global eradication. Although the components required to achieve regional elimination are in place, threats to maintaining a region free of measles and rubella in our interconnected world, such as the importations of both viruses, are certain to continue to occur for years to come. The recent measles outbreaks in the region demonstrated that immunity gaps persist, despite high reported vaccine coverage. Simultaneously, new threats (e.g. Zika virus) are competing for limited public health and clinical resources, adding to the difficulty of maintaining strong population-wide immunization programs. Other problems alluded to by AMR Office (AMRO) staff include high turnover of staff, inadequate planning and supervision of vaccination campaigns, difficulties and delays in providing laboratory supplies and reagents and growing vaccine hesitancy.

Priority activities for the region include ongoing work to ensure a high level of country ownership of and political support for immunization activities, including routine immunization, strengthened surveillance for measles, rubella, and CRS and well-planned and well-executed follow up vaccination campaigns to help reduce or eliminate immunity gaps. In addition, the region needs to maintain the capacity to detect and respond rapidly and aggressively to all suspected cases of measles, rubella, and CRS, increasing the quality of surveillance indicators, guarantee sufficient availability of laboratory supplies and reagents to maintain the quality of its network of laboratories, continue to develop new surveillance tools, and disseminate technical guidelines and training materials throughout the region.

PAHO's Member States have recently submitted updated data regarding measles to the RVC. The region hopes to be declared measles-free by end -2016.

Eastern Mediterranean Region (EMR)

Status

EMR initially set 2010 as a target date for elimination of measles and has subsequently revised that date twice, to 2015 and then 2020; it is not likely to meet the current target. EMR has yet to set a target date for the elimination of rubella, but has proposed setting one in 2020.

²⁷ Orenstein WA, Papania MJ. Defining and Assessing Measles Elimination Goals. *Journal of Infectious Diseases*, 2004, 189(Suppl 1):S23-S26.

In 2015, the reported incidence of measles in EMR remained high. WHO's joint reporting form gives a regional incidence of 33.5 cases per million. In 2015, only eight (38%) of the 21 countries in the region had met the indicator of a reported measles incidence of < 5 cases/million population. The number of estimated measles deaths in the region in 2014, while 74% lower than in 2000, was 13,900. Reliable information concerning rubella and CRS cases in the region is not available, although some countries do have case-based surveillance for these conditions.

As summarized in their status report, of the 22 countries in EMR, only 11 (50%) had achieved MCV1 coverage of $\geq 90\%$ nationally and in $\geq 80\%$ of districts in 2014. MCV1 coverage for the region has been stagnant over the past decade at approximately 75-80%. MCV2 coverage has been steadily rising since 2000, but was still under 70% in 2014. All but five countries in the region have introduced RCV.

Despite high coverage with MCV1 and MCV2 (based on administrative data) and repeated earlier measles SIAs, Egypt experienced a drop in routine immunization coverage and population immunity, and as a result experienced a small measles outbreak in 2012 and a large measles outbreak in 2014-15, with the latter outbreak persisting for > 18 months. The vast majority of the cases in 2014-15 were in unvaccinated children < 5 years of age, reflecting a drop in routine immunization coverage due to a combination of a shortage of MMR vaccine and civil unrest, together with a six-year interval since the last SIA in 2009.

In 2014, relatively few countries in EMR had met all of the measles and rubella surveillance indicators.

Despite substantial problems with security in a number of countries in EMR, many countries in the region conducted measles SIAs in 2014 and 2015, often co-administering Vitamin A and occasionally offering other interventions. Approximately two-thirds of countries in the region provide at least 80% of operational costs for SIAs, although the quality of the SIAs has been variable.

There is currently no RVC in EMR.

Conclusions and Recommendations

The report from EMR demonstrates the very difficult hurdles to achieving measles and rubella elimination in this region of the world. While some small and relatively wealthy countries in the region have achieved national elimination of measles, rubella, and CRS, other countries have found it difficult to achieve and sustain high levels of population immunity through a combination of a strong routine immunization program and well-organized SIAs. Many of the same countries have been unable to achieve targets concerning surveillance indicators. In most of the countries in the region that have not been able to achieve and sustain high levels of MCV1 and MCV2 (and RCV) coverage, diverse societal problems make it difficult to reach all segments of the population on a regular basis. These problems include war, civil unrest, political and economic instability, ethnic and religious strife, and migration of a large number of migrants and internally displaced persons, among others. In such settings, the obstacles to the elimination of measles, rubella and CRS are formidable.

Despite the many challenges, as EMR Office (EMRO) staff understands, there needs to be ongoing commitment to improving the quality and reach of routine immunization services, linking them to other infant and child health programs whenever possible. At the same time, the planning, implementation, and follow-up assessment of well-targeted and timely SIAs need to be supported technically and financially in high priority countries in the region. In addition, impediments to the availability of MRCV and of laboratory supplies and reagents need to be minimized and case-based surveillance systems

improved, so as to ensure timely detection of and response to outbreaks. Finally, renewed political commitment to and visibility of measles and rubella elimination goals is needed in multiple countries.

European Region (EUR)

Status

EUR set the goal of reaching measles and rubella elimination and prevention of CRS by 2015. All 53 countries in the Region have two doses of MRCV in their routine immunization schedules. In 2015, reported regional coverage with MCV1 was 94% with little change in the past four years. District level data are not currently available from all countries.

Significant measles outbreaks were reported in 2013 and in 2014 in Azerbaijan, Bosnia and Herzegovina, Georgia, Germany, Italy, Latvia, the Netherlands, Russian Federation, Turkey, Ukraine and the United Kingdom. There is a continuing large outbreak of rubella in Poland, although the number of cases began to decline in 2014. Most recent outbreaks of measles and rubella have occurred among the general population but some have been focused on recognized under-vaccinated groups. The EUR uses indicators which differ from those used in other regions to monitor the quality of surveillance. The RVC in EUR was first convened in 2012 and held annual meetings in 2013, 2014 and 2015, for a total of four meetings to date. A fifth meeting is scheduled for October 2016. The RVC meeting of October 2015 concluded that 21 (40%) of 53 Member States had eliminated measles and 20 (38%) had eliminated rubella.

Conclusions and Recommendations

Discussions with EUR Office (EURO) staff identify the following three main barriers to achieving measles and rubella objectives: 1) inadequate political commitment – both at the national (Presidential or Ministerial) level and at the health system level; 2) population attitudes to immunization – most are not against immunization but are apathetic about immunization, and do not perceive any personal risk from VPDs; and, 3) diversity of population and health systems in the Region. The 5 – 10% of the population that remains susceptible to measles appears to be sufficient to sustain transmission. This population is very diverse in the Region and requires different approaches to reach with vaccination. Elimination of measles and rubella transmission by 2020 is feasible in the European Region, but it seems unlikely it will be achieved.

- Sixty percent of countries in the region have achieved interruption of measles and rubella transmission in 2015.
- Some of the largest and most developed countries (e.g., France, Germany, Italy, Russian Federation, and Switzerland) have not achieved interruption of measles and rubella transmission. In some of these countries major problems relate to political/societal will rather than technical or financial issues. In other EUR countries, for example Turkey and Ukraine, security and other concerns impede progress.
- Overall MCV1 immunization coverage in the region is stagnant (at 90-94%) or decreasing, and MCV2 coverage is 10% lower than MCV1.
- In some countries, groups of unimmunized persons (e.g. Roma, certain religious groups, and groups with certain philosophic beliefs) pose major programmatic challenges.
- Varied population/political situations within the region and even within certain countries necessitate development of tailored approaches to interrupt transmission.
- Case and outbreak investigation needs to be strengthened, as does the exchange of data among countries; In particular, rubella and CRS surveillance needs to be strengthened.

- Improved approaches need to be developed to identify and reach “new susceptible” populations such as adolescents and adults.

South East Asian Region (SEAR)

Status

With the establishment in 2013 of a measles elimination goal for 2020 and a rubella/CRS control target for the same date, all countries within SEAR have developed national plans of action to address measles and rubella/CRS either as a stand-alone plan or as part of National Health plans or National Immunization Program Plans. Despite this, at regional level, MCV1 coverage has stagnated at 84% since 2012. This figure hides inter-country variation: 6 (55%) of 11 countries sustained MCV1 coverage > 90% for the period 2010 to 2015. Except for Indonesia, India and Timor-Leste, all countries (with the exception of Thailand, which does not collect these data) reported over 80% of districts with MCV1 coverage > 80% in 2014. All countries have introduced MCV2 and regional MCV2 coverage was estimated at 59% in 2014. Nonetheless, measles continues to circulate widely in most countries of the region, primarily due to underutilization of measles vaccine. RCV is given in all SEAR countries with the exception of DPR Korea, India, and Indonesia. However, these three countries account for 87% of children < 1 year of age in the region.

Laboratory-supported case-based surveillance for all sporadic cases of measles is performed by all countries in the region except India and Indonesia. India and Indonesia limit the use of case-based surveillance to outbreaks, as the current incidence of measles is too high for the existing laboratory network to support case-based surveillance on an ongoing basis. CRS surveillance is routinely conducted in three countries: Bangladesh, Nepal and Sri Lanka. The RVC has recently been established with its first meeting having taken place in August. Ten out of 11 countries have a National Verification Committee. Significant challenges exist in surveillance for sample collection and transportation for laboratory confirmation of measles and rubella.

Conclusions and Recommendations

In spite of gradual increases in both MCV1 and MCV2 coverage, challenges to achieving measles elimination exist in SEAR. This is particularly true as India was estimated to have had 3.23 million children not receiving MCV1 in 2015 while Indonesia had 1.52 million. Apart from strengthening routine vaccination systems in the region (and particularly in these two countries) the following issues should be addressed:

- Closing the immunity gaps for measles and rubella in countries with large birth cohorts (India and Indonesia) through nationwide wide age range measles and rubella SIAs;
- Addressing gaps in surveillance for measles, rubella and CRS, including use of more sensitive case definitions. Only Maldives and Sri Lanka have achieved the desired non-measles-non-rubella discard rate of more than 2 per 100 000 population. In addition, most countries have difficulties with sample collection and transportation as well as inadequate linkage between case-based surveillance and laboratory data;
- Developing communication strategies to address issues with measles programming as well as care seeking behavior at various levels from community to policy makers;
- Developing guidelines to reduce nosocomial transmission of measles;
- Securing adequate MR supply to enable India and Indonesia to conduct nationwide SIAs and introduce MR in routine immunization.

If accelerated progress can be made in India and Indonesia and if these two countries close the population immunity gap for measles and rubella by 2018, the region has the possibility of achieving the

regional goal of eliminating measles by 2020; however, aggressive and innovative approaches are required.

Western Pacific Region (WPR)

Status

WPR set the goal of achieving measles elimination by 2012. Although it has a goal to eliminate rubella and prevent CRS, there is currently no target year associated with this goal.

In the region, 34 (92%) of 37 countries, (i.e., all except the Lao People's Democratic Republic, Solomon Islands and Vanuatu) have two doses of MCV in their routine immunization schedules and as of 2016 all countries and areas routinely provide at least one dose of RCV. Since 2009, both MCV1 and MCV2 coverage have been over 90% at regional level but variation exists between and within countries for which data are available, with only 33% of countries having both MCV1 >90% nationally and >80% in all districts. However, district-level data are not available in three countries: Fiji, Japan and New Zealand.

WPR's RVC was first convened in 2012, held annual meetings in 2013, 2014 and 2015 (i.e., four to date) and is scheduled to hold a fifth meeting in September 2016. As of end-2015, 7 countries and areas (Australia, Brunei Darussalam, Cambodia, Japan, Macao SAR (China), Mongolia and the Republic of Korea) have been verified as having interrupted endemic transmission of measles for more than 36 months, as determined by the RVC. The historic lowest regional measles incidence was experienced in 2012. From 2013, resurgence of endemic transmission occurred in China and the Philippines and large scale outbreaks followed importations in the Federated States of Micronesia, Malaysia, Mongolia, New Zealand, Papua New Guinea, Solomon Islands, and Viet Nam. Recent outbreaks of measles have occurred primarily among unvaccinated children less than 5 years of age (especially among those too young to be eligible for their first dose of MCV) and adolescents and young adults.

Although measles case-based surveillance is functioning in all countries/areas, rubella case based surveillance is less wide spread. CRS surveillance is being rolled out at sentinel sites in some countries (e.g., Papua New Guinea, and Viet Nam).

WPR provides an example of how a focus on measles elimination can improve coverage for some vaccines included in the country's recommended vaccination schedule. In China, a pilot project looking to assess the feasibility of measles elimination included a school entry check to make sure that children were vaccinated against measles. This was expanded to include a check to verify that children were up to date with all vaccines recommended by China's EPI. This system was then further expanded to other provinces in China. A graph depicting the impact of this school check on children's vaccination status is found below, as an inset box under Strategy 2, page 54.

Conclusions and Recommendations

WPR has all the ingredients to succeed in eliminating measles and rubella: high reported MCV1 and MCV2 coverage, high reported coverage with MCV delivered through SIAs, good case based and laboratory-supported surveillance and strong support of the RVC. However, some issues remain to be addressed:

- Resurgence of endemic transmission has occurred in countries with the largest populations in the Region: China, Philippines, Viet Nam and Malaysia;
- Reliance on "reported coverage" over measuring population immunity and thus underestimating the true number of susceptible individuals;
- Not routinely disaggregating coverage to lower administrative levels;

- Frequently leaving organization of follow up until too late, and not targeting a wide enough age group when SIAs are conducted;
- SIAs in priority countries (e.g. Lao PDR, Philippines, Viet Nam) often planned, prepared and implemented without effective strategies to identify and vaccinate children who had been missed and unvaccinated in the routine immunization program and/or previous SIAs, resulting in repeatedly missing the same children;
- Not systematically pursuing case- and laboratory based surveillance systems for early case detection and detailed analysis of outbreaks, although this is improving in China;
- Increased infection and transmission of measles virus among people outside the target age range of current immunization strategies (i.e., infants aged ≤ 8 months, adolescents and adults);
- In countries with large populations (e.g. China, Philippines, Viet Nam), the need to adjust the SIA target age groups to provincial age-specific attack rates;
- In contrast to polio, the lack of a major donor to the program and, with rapid economic development, the ability of fewer and fewer countries to avail themselves of Gavi funding;
- The lack of full implementation of infection control measures to prevent nosocomial transmission of measles when outbreaks occur;
- De-centralization and lack of commitment to the regional goal of elimination at the state or provincial level, particularly in priority countries such as China, the Philippines and Viet Nam.

The region is currently revising its *Regional Strategies & Plan of Action* and it is expected that the revised version will address these challenges.

SECTION 5. CORE STRATEGIES, BUILDING ON THE POLIO TRANSITION, GOVERNANCE AND RESOURCE MOBILIZATION

Strategy 1. Monitor disease using effective surveillance and evaluate programmatic efforts to ensure progress.

Background

Surveillance data are critical to guiding measles and rubella control and eradication efforts. Surveillance enables the establishment of burden of disease and mortality, and thus plays an important role in advocacy for and prioritization of activities targeting measles and rubella. Measles cases detected by surveillance identify un- or under-vaccinated populations, highlighting geographic areas or sub-populations in which vaccination programs overall – not only those targeting measles and rubella – require further support. Surveillance measures the best outcome indicator of disease control and eradication programs: disease incidence.

Well-done outbreak investigations are an important aspect of surveillance. Such investigations are invaluable to allow understanding of who is giving disease to whom. This information is critical to formulating effective vaccine strategy. For example, if, in families with multiple measles cases, the first case in the family is commonly found in a school-aged child and the second case is found in an infant, we may understand that transmission is from the school child to the infant and that breaking the chain of transmission will require vaccinating the school-aged child, not only the infant. Well-done outbreak investigations can also provide information to be used for economic analyses of the societal impact of measles or rubella.

Investigation identifies unvaccinated Amish at heart of outbreak

In 2014, the United States of America experienced a large outbreak of 383 measles cases. Outbreak investigations allowed these cases to be identified as occurring predominantly among unvaccinated Amish communities in Ohio.

<http://www.cdc.gov/measles/cases-outbreaks.html> Accessed July 10 2016

Investigation shows role of Apostolic Sect in large Zimbabwean outbreak

In 2009-2010, Zimbabwe experienced a large outbreak of measles with more than 2,000 cases. Outbreak investigations showed that approximately 75% of the cases were from the Apostolic Sect. This Sect refuses immunization based on religious beliefs.

UNICEF, WHO. Measles Outbreak Response in Zimbabwe. A proposal to respond to and control the ongoing measles outbreak in Zimbabwe. Harare, 2010.

Investigation demonstrates nosocomial infection in 45% of measles cases in S. Korea outbreak

In 2007, South Korea experienced an outbreak of 180 confirmed cases of measles. Eighty-one (45%) cases resulted from nosocomial transmission at six hospitals.

Choi WS, Sniadack DH, Jee Y, Go UY, So JS, Cho H et al. Outbreak of Measles in the Republic of Korea, 2007: Importance of Nosocomial Transmission. *Journal of Infectious Diseases*. 2011 204 (Suppl 1): S483-S490.

For all of these reasons, the MTR considers improving the quality of surveillance and outbreak investigations for measles and rubella over the next five years to be of primary importance. Because of this primacy, this report presents findings and recommendations related to surveillance and outbreak investigation before those related to immunization strategies.

WHO recognizes three levels of measles control associated with different incidences of measles: control in highly endemic settings of more than 5 cases per million population; accelerated control and mortality reduction in endemic settings with fewer than 5 cases per million; near elimination and elimination settings where cases are sporadic and outbreaks very small, with less than 1 case per million. WHO recommends, that the attributes of measles and rubella surveillance should change as countries progress toward elimination. WHO has also recommended the use of measles and rubella surveillance indicators to describe the quality of the surveillance being conducted. The indicators currently in use by WHO Regions are generally similar, although not identical.

Progress and challenges

Case-based²⁸ surveillance for measles exists in 188 (97%) of 194 countries. However, the quality of case-based surveillance is highly variable and the percentage of cases investigated varies a great deal among and within countries. Eight of 12 core data elements recommended for measles case investigations are common among regions (see paragraph below for listing of 12 data elements). Of WHO Member States, 94% report data monthly to regional offices. However, at present, 88 (45%) of 194 countries do not report case-based data to WHO Headquarters. Furthermore, data on age, vaccination status, and final case classification are often incomplete. The current data reporting cycle results in at least a two-month lag of data availability at global level. All regions use indicators to evaluate the quality of surveillance, although these vary slightly from region to region.

Case-based surveillance for rubella exists in 189 (97%) of 194 countries. However, currently, the quality of case-based rubella surveillance cannot be assessed at the global level as data have not been officially requested from regions. Not unexpectedly, given the fact that a global focus on rubella is relatively recent, surveillance for rubella remains weaker than that for measles. Nonetheless, in 2015, 164 (85%) countries reported testing at least 1 specimen for rubella in the measles rubella lab network.

Global measles surveillance guidelines were developed in 2003.²⁹ These guidelines were updated with the publication of WHO's Framework for verification of elimination of measles and rubella which recommends collecting 12 core variables.³⁰ These variables are: name or identifiers; place of residence; place of infection (at least to district level); age (or date of birth); sex; date of rash onset; date of specimen collection; measles-rubella vaccination status; date of last measles/rubella or measles-mumps-rubella vaccination; date of notification; date of investigation; and travel history.

Integrating rubella and measles surveillance is recommended in the three WHO Regions with a rubella elimination goal (AMR, EUR, WPR), as well as in SEAR which has established a rubella/CRS control goal.³¹ Surveillance and outbreak investigations are underpinned by the diagnostic services of the Global Measles and Rubella Laboratory Network (GMRLN). This network of 723 labs provides confirmation of suspected measles and rubella cases by serologic and molecular methods, as well as providing information on global genotype distribution and evidence of interruption of transmission of endemic genotypes. The data that it provides support verification of elimination of measles and rubella.

²⁸ Case-based surveillance refers to surveillance systems that collect information about each case at the individual level. Murray J, Cohen AL. Infectious Disease Surveillance, Chapter in International Encyclopaedia of Public Health. In press, to be published 2017.

²⁹ World Health Organization WHO- Recommended Surveillance Standard of Measles.

(http://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/active/measles_standards/en/, Accessed July 9 2016).

³⁰ World Health Organization. Framework for verifying elimination of measles and rubella. *Weekly Epidemiological Record*, 2014, 88(9):89–99.

³¹ SEAR defines control as a 95% reduction in estimated rubella/CRS cases relative to 2008 estimates both nationally and for the region. World Health Organization. Regional Office for South-East Asia Region. Regional plan for measles elimination and rubella and congenital rubella syndrome control. 2014-2020. Available at http://www.searo.who.int/entity/immunization/documents/sear_mr_strategic_plan_2014_2020.pdf Accessed August 10 2016.

Measles and rubella surveillance has taken advantage of existing, polio-funded surveillance personnel. Globally, of support provided by international donors, approximately 80% of surveillance personnel (including data managers, field surveillance staff and laboratory staff) are paid for by polio funds and the remaining 20% paid by a combination of US CDC, BMGF and Gavi funding.

Discussion

From 2001 – 2015, substantial gains were made in measles surveillance. During 2004–2011, the number of countries using case-based surveillance, increased from 120 (62%) to 182 (94%); by 2015 this had increased to 189 countries. Expansion in case-based surveillance has been supported by expansion in the GMRLN. The GMRLN is a highly proficient laboratory network with a strong emphasis on quality control. It provides timely and accurate surveillance data to national programs, and has successfully introduced molecular methods for detection of measles and rubella, and genotyping. Laboratory testing has also successfully been integrated with that for other VPDs, such as yellow fever and Japanese encephalitis. The global sequence databases established for measles and rubella provide models for data sharing.

Despite these successes, the global measles and rubella surveillance system now faces four types of challenges. The first is that the system, as it currently exists, has not yet met its full potential. The second is the need to expand the system in order to better inform and guide disease control and eradication efforts as well as advocacy for these. The third challenge is to ensure that data are used to the fullest extent possible. The final challenge is to ensure that funding is adequate to meet programmatic needs particularly in an environment where measles activities supported by GPEI will be reduced.

The sensitivity of surveillance is assessed using an indicator of at least two discarded measles cases/100,000 population annually. This indicator is based upon limited data derived largely from a 2004 study which recommended 1/100,000 population as a minimum standard against which to compare the sensitivity of measles surveillance.³² In contrast, enhanced surveillance for all rash and fever illness in Campinas Brazil, (a setting with high vaccination coverage against both measles and rubella), found an incidence of 181/100,000 population aged < 40 years.³³ Whether the current indicator is sufficiently sensitive to assure surveillance systems would detect circulating measles, if present, is unclear and requires further validation.

Other challenges exist. The extent to which the private sector is incorporated into the surveillance network is highly variable. Despite the existence of alternative specimen collection methodologies, traditional venipuncture remains the most frequent methodology used to collect specimens for laboratory confirmation. Most importantly, there is limited evidence that surveillance and outbreak investigation data are locally-owned and used to improve program management and guide disease control strategy. In terms of rubella, most countries in regions with rubella/CRS control or elimination goals have not yet integrated rubella and measles surveillance.

³² Harpaz R, Papania MJ. Can a Minimum Rate of Measles-like Illnesses Serve as a Standard for Evaluating Measles Surveillance? *Journal of Infectious Diseases*, 2004, 189(Suppl 1): S204-S209.

³³ de Moraes JC, Toscano CM, de Barros EN, Kemp B, Liviano F, Jacobson S et al. Etiologies of rash and fever illnesses in Campinas, Brazil. *Journal of Infectious Diseases*, 2011; Sep 1; 204(Suppl 2):S627-S636.

Although case-based surveillance for measles is now very widespread, it does not capture critical aspects of measles disease, such as complications and death. Inadequate surveillance data force estimates of disease burden and death to be mathematically modelled rather than being derived from real data. This limits the credibility and the value for advocacy of burden data.

The relatively sparse data collected during outbreaks do not permit a good understanding of who is transmitting measles to whom, thus limiting the extent to which outbreak investigations can guide strategy. These data are also too sparse to form the basis for such powerful advocacy tools as studies of the economic burden of an outbreak.

Enhancing surveillance will require investing more resources. However, even in its current state, the surveillance program has recently suffered serious financial setbacks linked to the decreased funding available to the M&RI, historically the major funder of measles and rubella surveillance networks. Networks are further threatened because they depend heavily on polio-funded staff and infrastructure. Funding for GPEI will decrease as of January 2017; unless polio assets are transitioned, existing measles and rubella surveillance networks will be seriously impacted. This is an urgent problem needing to be addressed.

Recommendations

- A top priority for achieving the goals of the *Measles Rubella Strategic Plan* is to enhance integrated case-based, laboratory-supported surveillance for measles and rubella. All countries must implement case-based surveillance for measles and rubella, and report case information to the WHO Regional Office on a weekly basis.
- A working group on surveillance and outbreak investigation and response should be developed at global level; this group should also provide guidance on linking surveillance findings with programmatic changes.
- Protocols should be updated or, when necessary, developed, to guide:
 - how to conduct outbreak investigations including: critical data to be collected; criteria for laboratory confirmation, guidelines for analysis, interpretation of analysis results, and presentation of the data (see Strategy 3 below);
 - setting up and strengthening surveillance systems to detect and investigate cases of rash illness and fever which could be measles or rubella, analyze the data, and interpret and disseminate the results of analysis for action and policy. For example, analysis should identify who is transmitting disease to whom, the role of failure to vaccinate versus vaccine failure, and in what settings exposure is occurring; and
 - selecting a representative subset of cases to be studied in-depth in settings of very high transmission where it may not be feasible to examine all cases in such detail.
- Sera collected to investigate cases of rash illness with fever to diagnose measles should be tested for rubella if found to be negative for measles, or tested for both measles and rubella at the same time. The results of laboratory testing should routinely be fed back to the original health care provider and the caregiver.
- Training materials should be developed based on existing experience for use at global, regional and country levels to design and improve systems to collect surveillance data, as well as to understand the underlying reasons that cases are occurring and disseminate results to all levels of the system.
- It is critical that there be country and local level ownership and use of surveillance and outbreak data for program improvement and advocacy.
- Countries need to dedicate resources for surveillance and partners need to supplement resources as needed, including resources for staffing, laboratory support, training, and other operational costs.

Countries eligible for funding from Gavi (Gavi-eligible countries) should take advantage of Health System and Immunization Strengthening (HSIS) funding to build the surveillance infrastructure which serves to optimize immunization program performance. Where appropriate, measles and rubella surveillance systems should look for opportunities to also support surveillance for other diseases, for example dengue or yellow fever.

- Countries should take advantage of opportunities from the IHR review and national implementation of WHO evaluation of core capacities and lab surveillance strengthening to strengthen surveillance for measles and rubella.
- CRS surveillance, either sentinel or national level, should be implemented, especially in countries using MR.
- As the GPEI winds down, at a minimum the current level of measles and rubella surveillance should be maintained. Wherever possible, the polio transition should be capitalized on to further strengthen measles and rubella surveillance, as well as surveillance for other VPDs.
- The current measures to evaluate the quality of surveillance systems should be reviewed. Specifically, efforts should be made to determine if the indicator “occurrence of 2 cases of rash illness with fever per 100,000 children per year shown not to be measles or rubella” is adequate to say that measles would be detected if present in a given country.
- Both in outbreak investigations as well as in routine surveillance, all cases should be classified to determine the proportion of cases attributable to program failure – that is, that should have been vaccinated according to the national schedule, but were not. Remedial actions need to be tailored depending on the distribution of cases in this classification. For example, remedial action for cases attributable to program failure would be to improve coverage in groups with these same characteristics. Detailed case investigation becomes ever more important as case counts are driven down. Persons of unknown vaccine status should be considered unvaccinated and thus attributable to program failure.
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Strategy 2. Achieve and maintain high levels of population immunity by providing high vaccination coverage with two doses of measles- and rubella-containing vaccines.

Background

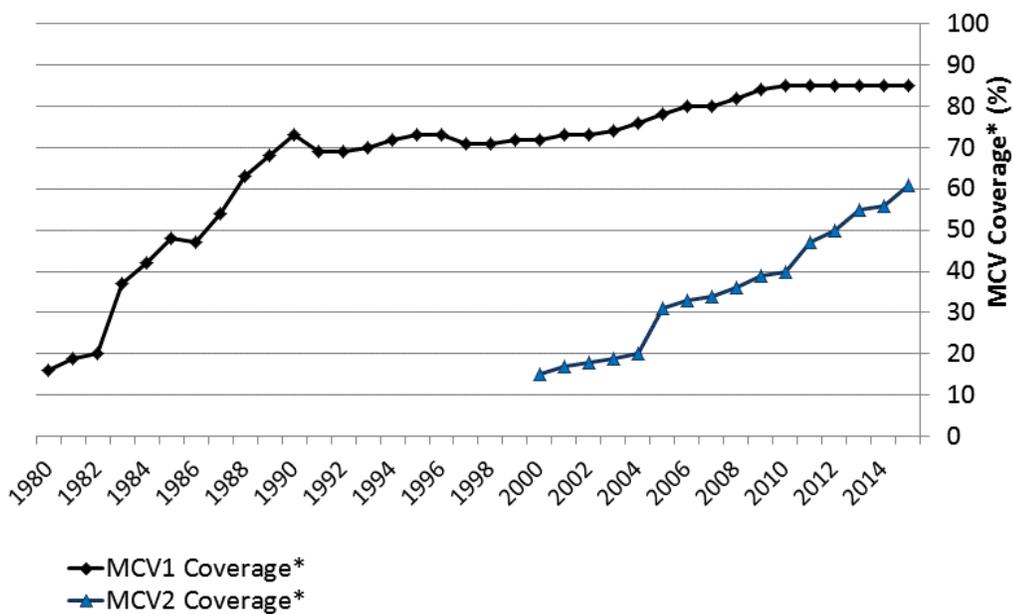
The extremely infectious nature of measles mandates very high levels of population immunity, generally considered to be 92 – 95 % in order to assure transmission³⁴ is stopped. Such levels of population immunity require delivery of two doses of MCV. Measles and rubella vaccines are routinely administered in the same syringe as MR. Current WHO policy is that two doses of vaccine can be administered through the routine immunization system, which is the preferred approach, or one dose can be administered through the routine immunization system while the second is administered through SIAs. Target age groups for SIAs are selected based upon the age distribution of susceptibility to measles in the population.

Progress and challenges

Globally, coverage with MCV1 has largely stagnated since 2008 (Figure 3). This figure hides heterogeneity in administrative MCV1 coverage among and within WHO regions, as well as within large countries such as China and India. Between 2010 and 2015, three regions sustained MCV1 above 90% (AMR, EUR and WPR), one maintained coverage between 80% and 90% (SEAR), and two regions

³⁴ Orenstein WA, Gay NJ. The Theory of Measles Elimination: Implications for the Design of Elimination Strategies. *Journal of Infectious Diseases.* (, 2004), 189(Suppl 1):S27-S35.

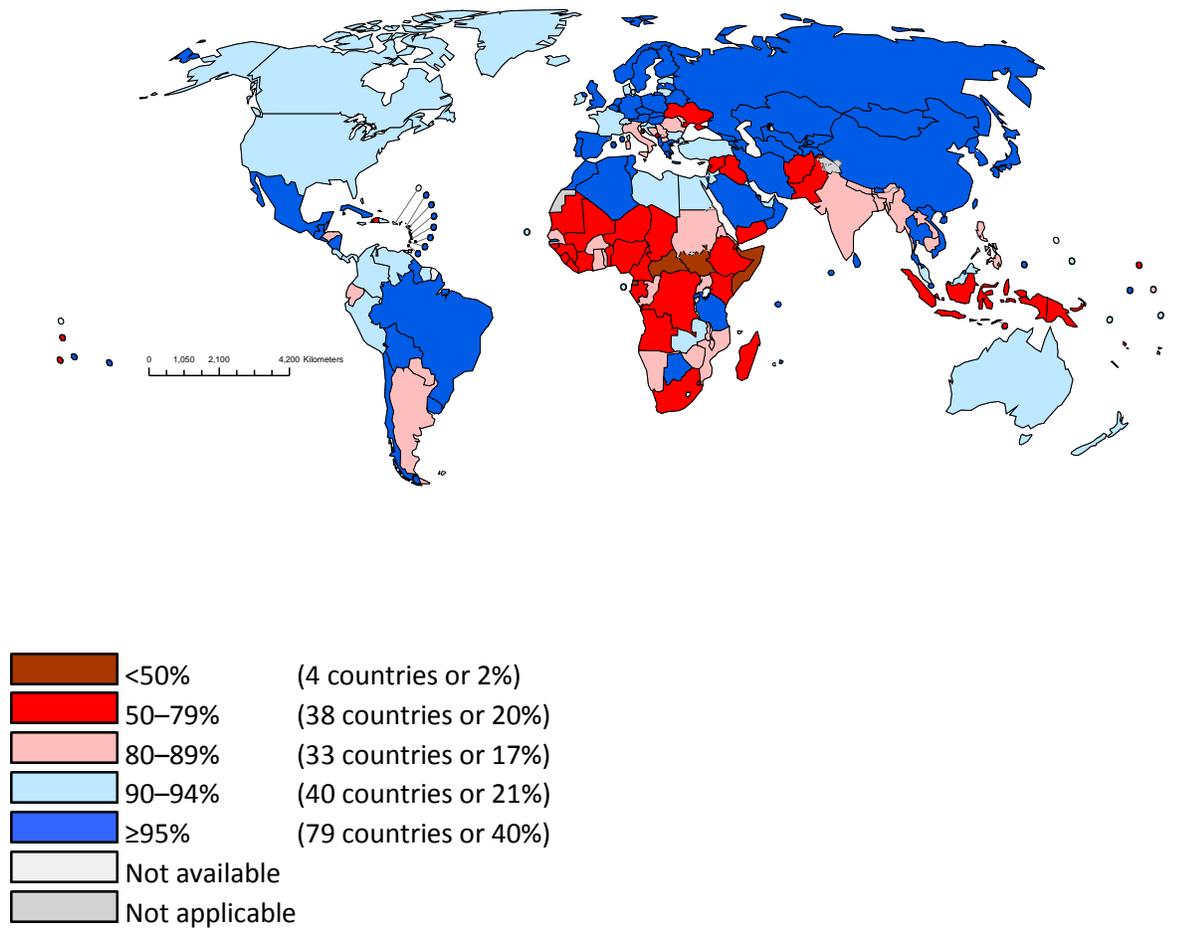
maintained coverage below 80% (AFR and EMR). In 2015, 119(61%) of 194 Member States had achieved the $\geq 90\%$ MCV1 national coverage target. By 2015, MCV2 was offered in 160(82%) of 194 Member States, up from 136 (70%) in 2010. Global coverage with MCV2 has continued to rise from 40% in 2010 to 61% in 2015.



* MCV1 coverage: coverage with first dose of measles-containing vaccine as estimated by WHO and UNICEF.
 **MCV2 estimates is only available from 2000 when global data collection started, however some countries have introduced the vaccine earlier.

Source: WHO/IVB database, 2016; 194 WHO Member States; Updated on July 2016

Figure 3. Coverage with first dose of measles-containing vaccine (MCV1) and second-dose of measles-containing vaccine (MCV2) as estimated by WHO and UNICEF, 1980 - 2015.



Map production: Immunization Vaccines and Biologicals (IVB), WHO.

Date of slide: 16 July 2016

Source: WHO–UNICEF coverage estimates, 2016 revision.

Figure 4. Immunization coverage (%) with first dose of measles-containing vaccines in infants per country, 2015

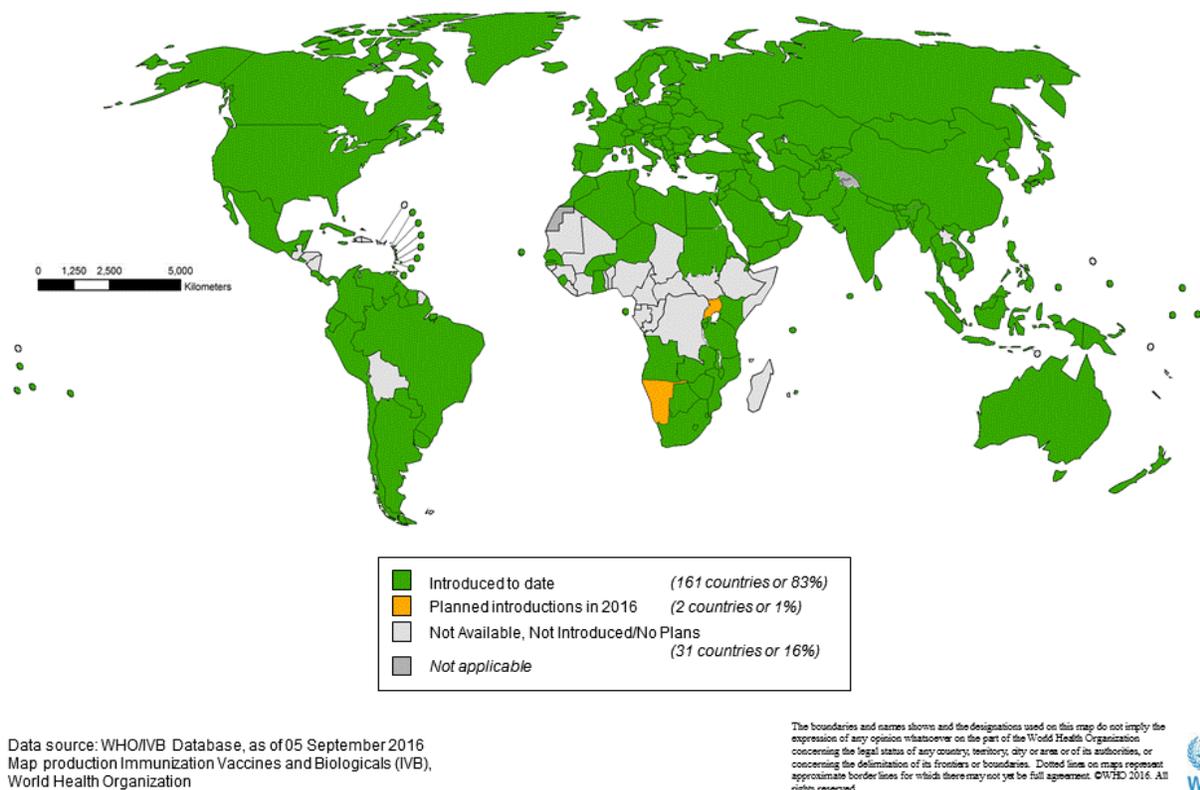


Figure 5. Countries that have introduced a second dose of measles-containing vaccine in the routine immunization system and those that plan to do so in 2016. Data as of September 2016

In many countries, the routine immunization system has been bolstered by SIAs. However, among 34 countries that conducted SIAs between 2012 and 2014 and that conducted a coverage evaluation survey of the SIA, less than half (16 Member States) were able to reach the target of 95% national coverage. At times, SIAs have also been delayed due to funding gaps.

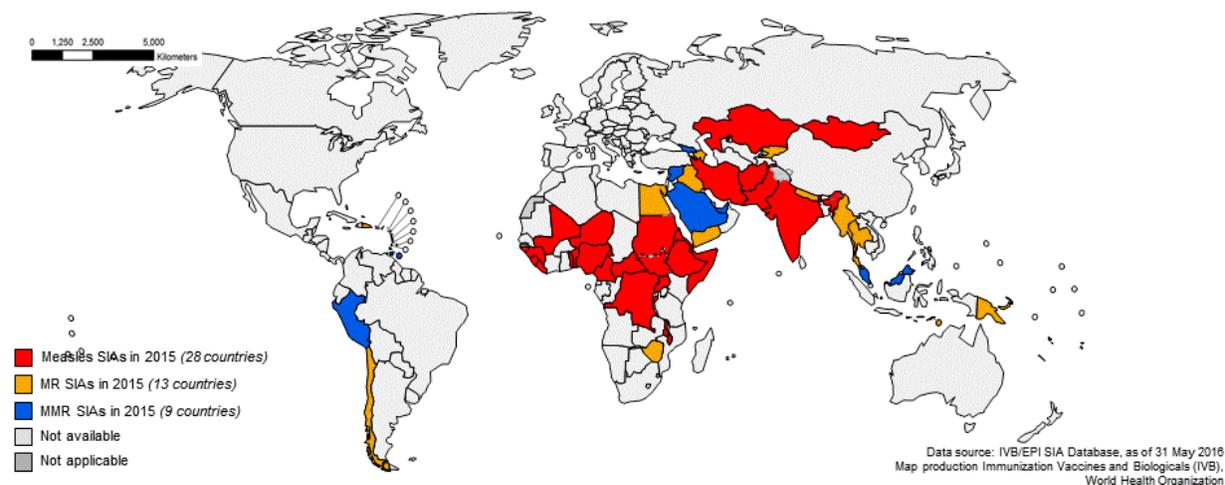
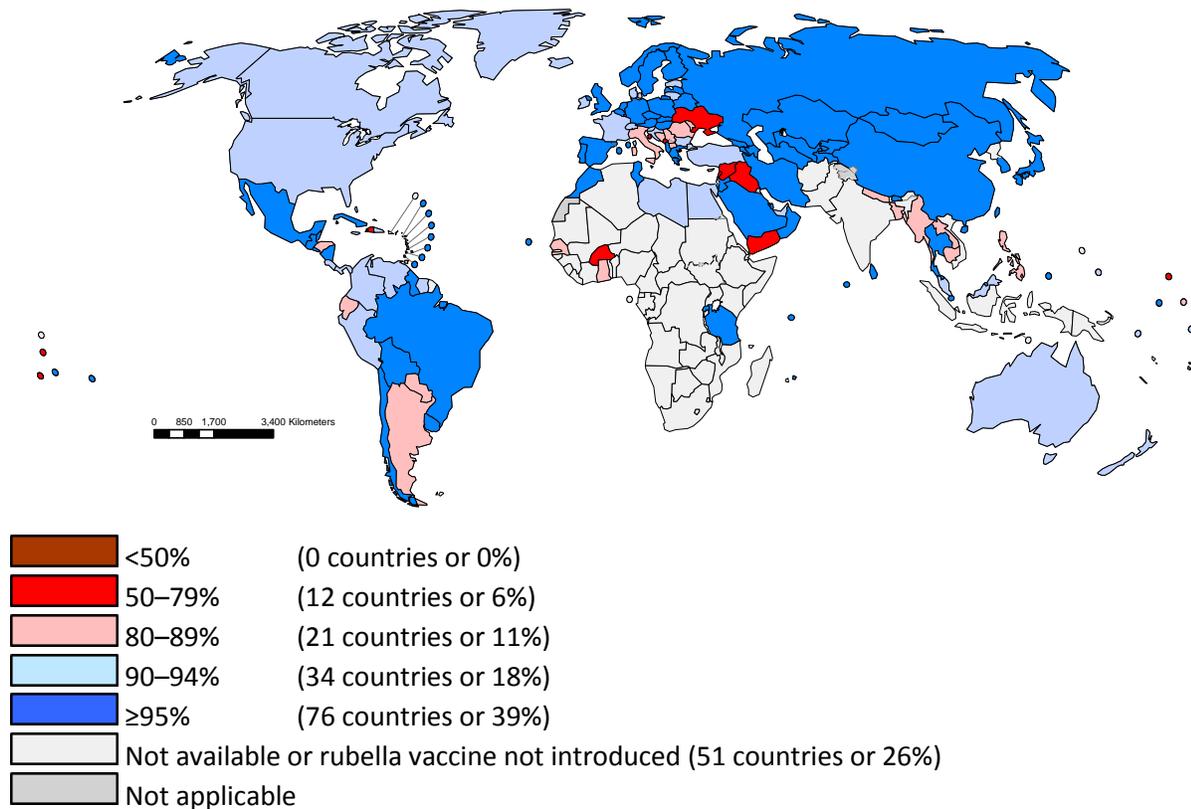


Figure 6. Measles, Measles-Rubella, or Measles-Mumps-Rubella SIAs conducted in 2015

Measles Rubella Midterm Review Report

Since 2012 (inclusive), 18 countries have introduced rubella containing vaccine.. From 2012 to 2014, global coverage with RCV rose from 42% to 46%.



Coverage estimates for the 1st dose of rubella containing vaccine are based on WHO and UNICEF estimates of coverage of measles containing vaccine.

Map production: Immunization Vaccines and Biologicals (IVB), WHO.

Date of slide: 16 July 2016

Source: WHO-UNICEF coverage estimates, 2016 revision.

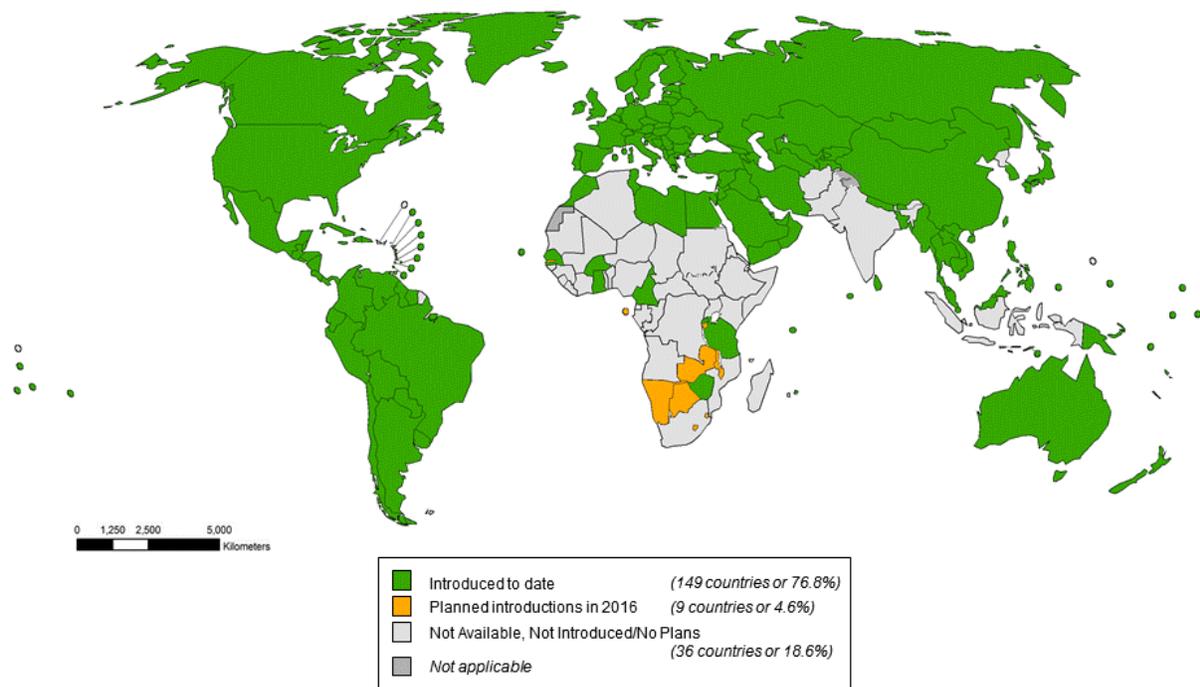
Figure 7. Immunization coverage with rubella-containing vaccines in infants, 2015

The Democratic Republic of the Congo’s experience: Poor MCV1 coverage and delayed SIAs lead to outbreak

During 2004 – 2010, national MCV1 coverage in the Democratic Republic of the Congo (DRC) increased from 57% to 73%. During the same period, the country conducted phased SIAs, at times with coverage < 95%. In 2010, SIAs in 5 of 11 provinces were not implemented as planned resulting in a prolonged interval between SIAs. In addition, a birth cohort was missed for vaccination in one province. A massive measles resurgence in DRC began in 2010 with 4,250 confirmed measles cases reported in 2010-2011. An investigation concluded that the outbreak was caused by an accumulation of unvaccinated, measles-susceptible children due to low MCV1 coverage and suboptimal SIA implementation.

Scobie HM, Ilunga BK, Mulumba A, Shidi C, Coulibaly T, Obama R et al. Antecedent causes of a measles resurgence in the Democratic Republic of the Congo. *Pan African Medical Journal*. 2015;21:30 doi:10.11604/pamj.2015.21.30.6335

Since 2012 (inclusive), eighteen countries have introduced rubella containing vaccine (RCV). From 2012 to 2015, global coverage with RCV rose from 42% to 46%.



Data source: WHO/IVB Database, as of 05 September 2016
Map production Immunization Vaccines and Biologicals (IVB),
World Health Organization

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. ©WHO 2016. All rights reserved.



Figure 8. Countries that have introduced rubella-containing vaccine in the national vaccine program and those that plan to introduce in 2016-2017. Data as of September 2016

Kenya's experience: SIA delayed to allow concurrent distribution of bed nets leads to outbreak

In 2002, Kenya conducted a nationwide, wide-age-range measles SIA resulting in a > 99% reduction in reported measles deaths. A follow-up measles SIA was initially scheduled for July 2005, but was delayed until 2006 following a decision to distribute insecticide treated bed nets concurrently with administering measles vaccine, as funding needed to be mobilized for the bed nets. After the introduction of measles virus in Sept. 2005, a large outbreak with 2544 reported measles cases during Sept. 2005 – May 2007 and 24 measles deaths occurred. This outbreak was attributed to the accumulation of children susceptible to measles due to the delayed SIA.

Centers for Disease Control and Prevention. Progress in Measles Control – Kenya 2002 – 2007. *Morbidity and Mortality Weekly Report*, 2007, 56(37); 56: 969-972.

Discussion

After substantial gains in the first decade of the century, increases in coverage with MCV1 have slowed. Gavi funding for RCV introduction has facilitated progress in rubella introduction in Gavi-eligible countries which has, in turn, raised global rubella coverage. Nonetheless, in 2014 less than half of the global birth cohort was vaccinated against rubella.

Review of country-specific measles incidence and MCV1 coverage shows a strong link between high quality routine immunization programs (assuming reliable coverage reporting) and sustained high levels of measles control.³⁵ A strong routine immunization program allows timely delivery of MCV1 and MCV2 as well as the full range of other immunizations to the entire birth cohort. Conversely, the very high levels of coverage required to stop measles transmission can motivate identification of and attention to unvaccinated populations and missed opportunities for vaccination, which can benefit coverage of all vaccines and promote equity. For these reasons, and most critically, the measles and rubella control and eradication program must be fully integrated into the immunization program at every level – global, regional, national and local.

Measles SIAs and Gavi funds as catalysts for improving injections safety in Africa

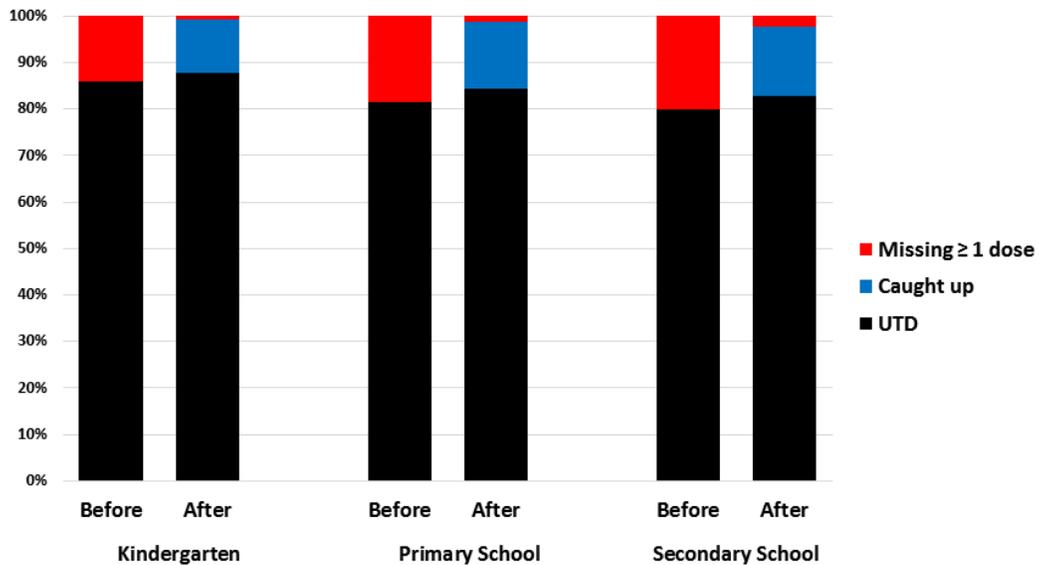
'In 2000, reuse of disposable syringes and inadequately sterilized syringes resulted in 39% of all infections being unsafe...In 19 (49%) of 39 countries, the measles program catalyzed the introduction of injection safety equipment, including (auto disable) AD syringes and safety boxes, training, and procurement of safety equipment during SIAs. Gavi was catalytic through financial support in 14 countries (36%) for including safe injection equipment in routine immunization. Additionally, Gavi funded 21 countries that had already introduced AD syringes in their national program...The measles mortality reduction program and Gavi complemented each other in improving injection safety. All countries continued with AD syringes for immunization after measles catch-up SIAs and Gavi funding ended'

Hoekstra EJ, van den Ent MMVX, Deo H, Salovaara A. Measles supplementary immunization activities and Gavi funds as catalysts for improving injection safety in Africa. *Journal of Infectious Diseases*, 2011;204 (Suppl 1): S190 –S197.

School entry vaccination checks in China increase coverage for all vaccines

As part of a pilot project to look at the feasibility of measles elimination in China, the country implemented school entry checks for measles vaccination. Other vaccines were also checked. The school entry check has been expanded within China. A recent study of the impact of school entry checks in Ninyang County, Shandong Province showed how they detected students that had been missed through routine services and increased coverage for all vaccines.

Impact of School Entry Vaccination Record Check, Ninyang County, Shandong Province, 2015



Vaccines that are needed for the child to be considered up-to-date (UTD) and that are checked as part of the school-entry check:
 Kindergarten (age 3 yr): 1 BCG; 3 HepB; 1 or 2 HepA (depending on the vaccine); 3 DTaP; 3 tOPV; 2 JEV; 2 M/RCV; and meningococcal vaccine.
 Primary (elementary school) and secondary (middle and high school): same as kindergarten, but 4 doses of tOPV instead of 3 doses

YIN Xiu-wang, et al. *Chinese Journal of Vaccines and Immunization* 2016;13(5): in press

Measles elimination plays a key role in building the National Immunization Program of the United States of America

'In 1966....the Centers for Disease Control and Prevention began an effort to eliminate measles within the United States....With measles elimination as the primary driver, fundamental components of today's immunization program were built that affected not only measles, but all of the vaccines and vaccine-preventable diseases of childhood. Some of the major contributions were the enactment and enforcement of immunization requirements for school attendance in all 50 states, enactment of an entitlement program for vaccine purchase, the Vaccines for Children Program, support for health services research to determine reasons for non-immunization and interventions to improve coverage, development of standards for immunization practices and the measurement system for immunization coverage in all 50 states and 28 major urban areas. Key lessons have been: (1) the program must rest on a sound base of vaccine science and health services science; (2) having a limited number of measurable goals allows program focus, but consider strategies that have crosscutting impact; (3) accountability is critical to program performance at all levels – state, local and individual practice; and (4) establishing and maintaining political support is essential.'

Orenstein WA. The role of measles elimination in development of a national immunization program, *Pediatric Infectious Disease Journal*, 2006, Dec; 25(12): 1093 –1 101.

Both the epidemiology of measles and the challenges faced by programs vary within regions and, in some settings, within countries. An increasing problem in some settings has been the rising incidence of measles outside the target age group of current immunization strategies (i.e., infants aged < 8 months, adolescents and adults). Four of the six WHO regions have recognized the need to tailor recommendations for measles control to the local setting by grouping countries into categories, and making recommendations by category. Developing globally standardized criteria for grouping countries as well as globally standardized recommendations by group (neither of which currently exists) would recognize the reality of differing program performance and allow specific but globally-standardized guidance to be offered to countries. This type of grouping would also allow a more nuanced description of the world's progress with regard to measles and rubella eradication than is currently possible. The review team has selected country examples from each WHO Region to illustrate successful, fragile, and seriously-challenged programs. Program performance is reflected in disease incidence and age and vaccination status of measles cases. More information on each region and selected countries is found in the Appendix (available for the web-based report).

An important programmatic consideration is how best to achieve very high two-dose coverage. Approaches may include school entry checks for measles and rubella (as well as other) vaccines, provider-based record review and catch-up vaccination, and SIAs. However, the challenge of reaching consistently high SIA coverage in the face of funding gaps and increasing complacency with falling disease incidence is underlined by the percentage of SIAs with measured coverage less than 95%.

The traditional emphasis placed on vaccination coverage as opposed to incidence should be reconsidered. Conceptually, incidence is an outcome indicator, whereas coverage is an intermediate indicator. In addition, administrative coverage is plagued by unreliable denominator data while precisely measuring coverage at the very high levels of coverage required to stop transmission is also

technically difficult. Nonetheless, to the extent possible, coverage should be validated, and differences in coverage between MCV1 and MCV2 should be monitored. The most effective way of achieving and maintaining very high dose coverage is through the routine immunization system.

Recommendations

- Measles and rubella control and elimination activities at national level should be located within the overall immunization program.
- The incidence of measles and rubella and coverage with measles and rubella vaccines should be considered among the primary indicators of immunization system performance.
- Two doses of MCV or MRCV delivered through ongoing services is the standard for all national immunization programs. Preventive SIAs should be conducted on a regular basis, if routine two dose coverage is insufficient to achieve and maintain high population immunity. In certain circumstances, one-time SIAs may need to be conducted to close existing immunity gaps in the population, for example immunity gaps among adults.
- Efforts to enhance measles and rubella prevention should take into account the importance of strengthening the overall immunization delivery system. For example,
 - delivery of MCV2 can be used as a platform to deliver other health interventions (i.e., helping to establish a second-year-of-life platform);
 - in planning SIAs, the enumeration of high-risk communities can be focused to also improve delivery of routine immunization services to these same populations.
- A standardized method to classify countries based on their level of disease control and likelihood of achieving and sustaining achievement of measles and rubella elimination goals should be developed. The major purpose of such a classification is to tailor outbreak response and surveillance strategies appropriately. Large countries in which measles epidemiology is not uniform should adjust their measles control and elimination strategies to subnational settings.
- The current approach for determining the target age range for M and MR SIAs should be re-evaluated. This includes the potential for developing new guidelines based on more detailed analysis (including mathematical modelling) of sub-national coverage/disease incidence data to guide vaccination strategies.
- Approval of financial support from international partners for preventive SIAs should be conditional on country commitment to meet minimum standards of readiness as articulated in the SIA readiness checklist.
- Non-Gavi-eligible countries should take advantage of strategies being developed by WHO, Gavi and UNICEF to address financing of vaccines in these settings.
- Efforts should be made to determine key reservoirs for measles and rubella that have proven to be exporting disease and take remedial action to terminate transmission in those areas/populations.
- The accuracy, completeness and timeliness of administrative coverage data must be improved to increase their usefulness both at national and sub-national level.
- Use of the district level program risk assessment tool, which takes into account reported or evaluated coverage, surveillance data, and program performance data to identify areas requiring special efforts, should be encouraged.
- All countries should institute a school entry check for immunization, including vaccination against measles and rubella as well as against other VPDs. Vaccination should be provided to children who have not received vaccine.
- Every opportunity should be taken to vaccinate people not adequately vaccinated, particularly those under 15 years of age. Policies which prohibit use of vaccine in children >1 year of age, older children and teenagers should be changed to allow these individuals to be vaccinated.

- In view of the changing epidemiology of measles, immunity gaps among adolescents and adults need to be addressed by removing regulatory and policy barriers and promoting effective strategies for vaccinating older children, adolescents, and adults if they are believed to be susceptible to measles and/or rubella.
- Quality of SIAs should be systematically and rapidly assessed. In the case of underperformance, remedial action should be taken immediately. Campaign planning and budgeting should always include "mopping-up" activities in poor performing areas.
- The current criterion recommended by WHO for introduction of MCV2 into the routine schedule, i.e., WHO/UNICEF estimates of MCV1 coverage greater or equal to 80% for three consecutive years,³⁶ should be re-assessed.
- In principle, all doses of vaccine delivered (including through SIAs) should be documented, for example in the home-based record and, in those countries introducing computerized record systems, in the patient's electronic record.

Strategy 3. Develop and maintain outbreak preparedness, respond rapidly to outbreaks and manage cases

Background

Outbreaks provide important opportunities to gather data on who is susceptible to measles or rubella, and how this susceptibility may reflect program weaknesses. Outbreak investigations allow determination of whether the outbreak is due to vaccine failure, or failure to vaccinate. In addition, data gathered in outbreaks (e.g., deaths, economic costs) can be critical for political advocacy.

Prior to 2008, outbreak response immunization (ORI) was discouraged in lower and lower middle income countries.³⁷ Global outbreak response guidelines were modified in 2009 to facilitate outbreak response, in recognition of the fact that outbreaks in certain settings last for many months and that the length of these outbreaks provides opportunities for morbidity and mortality reduction through vaccination response.³⁸ Global rubella outbreak investigation and response guidelines have recently been published by WHO.³⁹

Progress and challenges

At present, global guidelines for measles and rubella outbreak investigations exist, but the measles guidelines are basic and do not provide guidance on collecting much of the information that is needed both to understand disease transmission patterns and for advocacy (see Strategy 1). A specific measles outbreak-related challenge is to develop an appropriate algorithm which allows for adequate laboratory testing without overwhelming the laboratory with samples.

³⁶World Health Organization. Measles vaccines: WHO position paper. *Weekly Epidemiological Record*, 2009,84:349-360.

³⁷Aylward RB, Clements J, Olive JM. The impact of immunization control activities on measles outbreaks in middle and low income countries. *International Journal of Epidemiology*, 1997, 26 (3):662-669.

³⁸World Health Organization. *Response to measles outbreaks in measles mortality reduction settings*. Geneva, World Health Organization, 2009, i-36 (WHO/IVB/09.03, http://apps.who.int/iris/bitstream/10665/70047/1/WHO_IVB_09.03_eng.pdf accessed 8 August 2016).

³⁹World Health Organization. *Introducing rubella vaccine into national immunization programs. A step-by-step guide*. WHO/IVB/15.07 Geneva, World Health Organization, 2015 (WHO/IVB/15.07, http://apps.who.int/iris/bitstream/10665/184174/1/9789241549370_eng.pdf).

Since 2013, a Gavi-funded measles outbreak response fund of USD 10 million annually has existed, administered by the M&RI through WHO. This fund has recently become available for rubella outbreaks as well. The goal of this funding is to enable countries experiencing measles or rubella outbreaks to rapidly respond to these while they are still relatively small and localized, thus preventing them from developing into large and widespread outbreaks. Funding is restricted to Gavi-eligible countries. The age groups that can be targeted may also be restricted. Once the M&RI receives a completed request for funding for ORI, funds can be disbursed to the national government within 48 hours. However, vaccination response within country may be slowed by the need to decide what geographic areas and age groups to target for vaccination. No external funding for ORI is available for non-Gavi eligible countries.

Discussion

The existence of measles and rubella outbreak investigation and response guidelines as well as funding for measles and rubella ORI in Gavi-eligible countries reflects progress in outbreak investigation and control. However, the full potential of outbreak investigations to inform and advocate for the program has not been met. Outbreaks result in increased morbidity and mortality as well as disruptions of and expenses to health care services. Outbreaks should be used as opportunities to sensitize policy makers and the public to the importance of preventing, rather than responding to, outbreaks. From a technical perspective, measles outbreak investigation guidelines need to be updated, should provide guidance on what outbreaks to investigate and how, and should reinvigorate efforts to prevent nosocomial transmission. For example, investigation of outbreaks should attempt to determine in families or household settings where there is more than one case, the characteristics of the index case (e.g., age, vaccination status, attendance at a school, prior visit to a healthcare setting, etc.).

Experience with the Gavi ORI fund has seen some countries delay response to measles outbreaks for months, both while preparing a request for funding and after receiving vaccine. The reasons for such delays can be complex, including the political ramifications of declaring an outbreak, lack of awareness of how to apply for ORI funding, and uncertainty as to who to vaccinate. Prompt response would diminish the mortality and morbidity associated with the outbreak, but requires strong country ownership.

The ORI fund currently available is also limited because it cannot be used for non-Gavi countries (including those that have recently graduated). Although the M&RI responds rapidly to requests for ORI funding for Gavi-eligible countries, the time-to-request as counted from the beginning of the outbreak may be months. In addition, once funding has been released it may take months before ORI occurs, resulting in the opportunity for the outbreak to spread widely and decreasing the extent to which ORI can mitigate morbidity and mortality associated with the outbreak. Furthermore, although the ORI fund is substantial, some populous countries with poor measles control (e.g., DRC and Pakistan) have had financial requirements which surpass the magnitude of available funding.

The need for outbreak response may depend upon the background immunity in the population (i.e., in countries with very high background immunity outbreaks may be expected to die out, whereas in countries with low background immunity outbreaks may continue for many months). Recommendations regarding response may vary accordingly.

Recommendations

- Emphasis should be placed on prevention of outbreaks through monitoring of risk status, for example through the use of risk assessment tools, and increased attention to vaccination in high risk settings.
- All measles outbreaks should be promptly investigated and used to develop a susceptibility profile of the population to better inform measles control and elimination strategies, including outbreak prevention and response immunization.
- Countries should develop national measles outbreak preparedness and response plans and build national capacity to investigate and respond to such outbreaks. A clear definition of what constitutes a measles outbreak that can be used to prompt outbreak investigation and control measures is required. Country ownership with regards to rapidly investigating and responding to measles and rubella outbreaks should be encouraged.
- Based on existing experience, training materials should be developed for use at global, regional and country levels to perform outbreak investigations as well as to understand the underlying reasons that outbreaks are occurring and disseminate results of these investigations to all levels of the system. Protocols should guide critical data to be collected as well as guidelines for analysis, interpretation of analysis results, and presentation of the data (see Strategy 1 above).
- Guidance should be developed to allow countries to assess the economic burden of outbreaks. Information on the cost and disruptiveness of outbreaks, including the costs incurred in controlling outbreaks, should be collected to use as an advocacy tool and to encourage preventive action.
- There is need for global guidelines for outbreak investigation and response for elimination settings, including contact tracing and the identification of population immunity gaps.
- There must be adequate financial, human and laboratory resources to conduct adequate outbreak investigations. Gavi-eligible countries should consider using HSIS funds for this.
- Financial resources should be urgently mobilized to support outbreak investigation and control in non-Gavi eligible countries. Countries should develop national Measles Outbreak Preparedness and Response Plans. Outbreak preparedness and response capacity should be assessed by RVCs or by regional immunization Technical Advisory Groups (RITAGs).
- When outbreaks are detected, in addition to investigation, countries should take steps to mitigate the outbreak through vaccination. The magnitude of the response should be based on the characteristics of the outbreak, the stage of measles control, and the category to which countries belong. The more rapid the response, the more likely it is to mitigate the impact of the outbreak.
- In countries that have introduced rubella-containing vaccines, outbreak immunization measures should be based on the susceptibility profile of the population, the groups affected, and the availability of vaccine.
- During and following a rubella outbreak, pregnant women should be registered and followed according to existing guidelines.
- When massive outbreaks occur, minimal information can be collected on all cases, but intensive investigations of a representative subset should be carried out to determine the underlying causes of the outbreak so that actions can be taken to prevent similar outbreaks in the future.

- When conducting case-based surveillance, at a minimum, twelve core⁴⁰ elements should be investigated for each case as well as a classification of whether or not the case is preventable. The outbreak investigation response should be tailored to the classification of countries.

Strategy 4. Communicate and engage to build public confidence and demand for immunization.

Background

Communication is critical to make populations aware of where, when and why they should be vaccinated – both routine immunization and SIAs. It is also critical to help policy makers and health workers understand why and how to support immunization programs. Communication is also critical to build and maintain public confidence in immunization. This is particularly the case in the wake of adverse events following immunization (AEFI) or other events that raise concerns about the safety of immunization.

Progress and challenges

The Gavi Secretariat has the strongest communications team for supporting all its immunization activities including measles and rubella. In addition, each of the five M&RI founding partners has communications specialists. However, with the exception of UNICEF which has hosted a communication specialist focusing on measles and rubella activities since 2013, these specialists handle a broad range of topics. In 2014, communication specialists from all M&RI core partner agencies developed a strategic communications plan for the M&RI. The objective of this plan was to support achievement of the 2015 and 2020 goals of the *Global Measles and Rubella Strategic Plan 2012-2020*.

The ARC focuses on social mobilization for immunization by mobilizing and training volunteers from national Red Cross and Red Crescent societies for house-to-house visits. However, financial constraints limit this service to approximately 500,000 children per country. Although house-to-house mobilization could be used to sensitize populations to the need for routine immunization as well as awareness of SIAs, a desire to optimize the impact of the limited funds available has led to a focus on SIAs and urban populations. A small, unpublished study comparing coverage achieved during an SIA in districts without house-to-house mobilization to that achieved in districts with house-to-house mobilization showed that the districts with house-to-house mobilization showed an increase of 6-12 percentage points in vaccination coverage. However, lack of funding has limited the ability of ARC to conduct larger studies on this topic.

UNICEF plays a lead role in communications. This includes channeling and/or adding resources to the UNICEF Communications for Immunization (C4I) initiative at country level to be used for measles and rubella immunization activities and technical assistance. However, there remains an emphasis on traditional approaches to social mobilization such as printed materials and television spots despite unpublished recent data indicating the success of less traditional methods, for example town criers.

⁴⁰ World Health Organization. Framework for verifying elimination of measles and rubella. *Weekly Epidemiological Record*, 2014, 88(9):89–100.

Relatively few communications messages specifically target rubella. Resources have not been adequate to target the multiple audiences implicated in immunization programs, such as politicians, public health leaders and workers, public and private healthcare providers and parents.

Discussion

Since 2012 there has been an increased emphasis on the importance of communications, as evidenced by the creation of a dedicated post in UNICEF and the development of a strategic communications plan. While many activities demonstrate dedication and creativity, the scope of these activities – in terms of numbers reached and breadth of focus – appears limited by resources. The ability to argue for more resources based on the impact of communications activities is limited by a lack of data; the ability to generate such data is, in turn, limited by lack of resources.

Communications teams need to have the resources to craft and test messages aimed at particular target audiences, such as politicians, public health leaders and workers, health care providers, and parents. In selecting media to reach target audiences, existing information on what media are most effective should be carefully considered. In keeping with the concept that measles and rubella immunization needs to remain firmly embedded in the routine immunization program, in communications the importance of immunizations overall should be emphasized with a particular focus on measles and rubella immunization.

Information on incidence, burden of mortality and vaccination coverage are critical. However, it is important not to overlook the role that anecdotes play in illustrating statistical data and capturing the attention of policy makers and the public. The mortality and morbidity as well as the disruption and expense associated with outbreaks provide opportunities to remind policy makers and the public of the importance of preventive vaccination.

Rubella and its sequelae remain poorly known in much of the world. As the implications of rubella infection are substantially different from those of measles infection, it is important to develop messages specifically focused on the importance of immunization against rubella.

Recommendations

- Increased resources are needed for communication to raise the visibility of VPDs and the importance of ongoing immunization services, with a focus on measles and rubella.
- Creating and promoting demand for immunization requires long term investment and should be an integral part of routine immunization strategy.
- Communication plans may target many different audiences (e.g., politicians, public health leaders and workers, healthcare providers, caregivers, etc.). Plans targeting each of these audiences should be developed and audience-specific messages developed and tested.
- Communication research science should be used to identify the most effective means of communication; these data should inform the communication strategies selected.
- Outbreaks of measles or rubella should be recognized as opportunities to promote the importance of immunization in preventing outbreaks, with particular focus on measles and rubella vaccination.
- Messages specific to rubella need to be developed, tested, and used.
- Data on measles incidence, including complications and deaths, as well as information on the costs associated with outbreaks, should be the focus of educating various audiences about the importance of preventing the illness. Data should be supplemented by stories of actual cases to

illustrate the statistical data. Collection of information on cases of CRS can also be a powerful advocacy tool.

- Outbreaks should be an opportunity to sensitize medical professionals about the risk of nosocomial transmission of infectious diseases and take proper preventive measures.
- In advocating for improved prevention of measles and rubella, it will be important to collect stories of how a focus on those diseases not only improved their control but also helped to enhance overall immunization and health systems (see Resource Mobilization Section below).

Communications plans should address hesitancy toward vaccination and building confidence in vaccines. This should include risk communication following publicized adverse events following immunization, and promotion of the safety of vaccines.

Strategy 5. Perform the research and development needed to support cost-effective operations and improve vaccination and diagnostic tools.

Background

Experience with smallpox and polio has shown the disease control gains that can be made by targeted and programmatically –driven research. Research can be critical to breaking through periods of program stagnation, particularly if it results in the dissolution of barriers limiting program performance.

Progress and challenges

Since 2005, six global meetings focused on measles and rubella research have been held, with the most recent in 2015. A further meeting to prioritize research topics is proposed for the fourth quarter of 2016. An independent survey of individuals working programmatically or in academia on measles and rubella control was conducted with the goal of identifying gaps in essential evidence and program barriers to achieving measles and rubella/CRS elimination; the results of this survey were endorsed by the SAGE in 2014. This survey indicated that the most important areas for research were considered to be developing novel ways to optimize vaccine delivery and assess vaccination coverage (Table 3). To promote and advocate for measles and rubella research, the M&RI has established a Research and Innovation Working Group, chaired by CDC. Total funding available annually, primarily from CDC and BMGF, is approximately USD 1 million. At present, there is no standard approach to prioritizing research topics or to ensuring ongoing funding of research.

Measles Rubella Midterm Review Report

Research Topics	Status of progress as of July, 2016*
Global Measles and Rubella Research priorities for MR control and eradication identified at WHO meeting of experts held at CDC, and published in Vaccine (2012;30(32):4709-16	
Measles Epidemiology	
<i>Measles epidemiology in various settings in India</i>	*
<i>Causes of measles outbreaks in high vaccination coverage settings</i>	**
<i>Adult measles susceptibility in suboptimal vaccination coverage settings</i>	*
<i>Adult vaccination needed to reach and maintain elimination</i>	*
<i>Need for measles vaccination prior to 9 months of age</i>	**
<i>Measles susceptibility among HIV-infected adults</i>	**
Vaccine Development and Effectiveness, and Alternative Vaccine Delivery Methods	
<i>Measles vaccine effectiveness in densely-populated settings</i>	*
<i>Thermo-stable vaccines, alternative delivery methods (needle-free devices, aerosol, dry powder, microneedles)</i>	**
Surveillance and Laboratory Methods	
<i>Global distribution of measles virus genotypes</i>	***
<i>Rapid diagnostic tests to detect cases in the field</i>	**
<i>High throughput tests to accurately measure neutralizing antibodies</i>	*
<i>High resolution molecular sequencing methods</i>	**
<i>Assays to differentiate vaccine-acquired immunity and immunity from exposure to wild-type viruses</i>	*
Immunization Strategies	
<i>Second year of life strategies for increasing vaccination coverage</i>	**
<i>Strategies to maximize SIA coverage</i>	**
<i>Methods for monitoring vaccination coverage through routine and SIAs</i>	**
<i>Strategies for identifying, vaccinating nomadic populations, migrants, refugees</i>	**
<i>Communication messages and strategies that increase demand for vaccination in various settings</i>	*
<i>Strategies for outbreak response immunization activities</i>	*
Mathematical Modeling and Economic Analyses	
<i>Modeling progress toward measles eradication</i>	**
<i>Modeling approaches to estimate population size and susceptible density required to sustain transmission</i>	*
<i>Economic burden of measles outbreaks in low and middle income countries</i>	**
Rubella/CRS Control and Elimination	
<i>Epidemiology of rubella/CRS in settings with varying birth rates</i>	**
<i>Optimal methods and corresponding costs for CRS surveillance, in areas with weak health systems</i>	**
<i>Global distribution of rubella virus genotypes</i>	*
<i>Economic burden of rubella and CRS at global, regional and national levels</i>	***
SAGE MR Work Group prioritized 12 research topics by a survey of experts, and endorsed by SAGE in 2014	
<i>Strategies to increase coverage in difficult populations</i>	**
<i>Novel strategies to increase vaccine coverage</i>	**
<i>Strategies to address confidence gaps</i>	*
<i>Outbreaks in settings with high coverage</i>	*
<i>Optimal age of measles vaccination</i>	**
<i>Reasons for low confidence in vaccines</i>	**
<i>Outbreak response strategies</i>	*
<i>Strengthen routine immunization & surveillance</i>	**
<i>Susceptibility profiles to measles and rubella</i>	**
<i>Measures of vaccine coverage</i>	**
<i>Epidemiology & surveillance for rubella & CRS</i>	**
<i>Point of care diagnostics</i>	**

*not adequately being addressed, **somewhat being addressed, ***well addressed

Table 3. Measles and rubella research priorities and status of implementation

Discussion

The Research and Innovation Working Group has been instrumental in raising the profile of measles and rubella research, and promoting a coordinated approach to prioritization of research projects. Potentially ‘game-changing’ advances are in development, with the most critical likely to be administration of vaccine through microarray patches (MAPs) (also known as ‘microneedles’). This

technology would allow non-medically trained personnel to administer vaccine, which would be of critical importance in countries with limited human resources. In addition, it would allow house-to-house administration of vaccine, potentially increasing coverage to levels high enough to achieve herd immunity. Such innovations would enhance the likelihood of success in reaching regional elimination goals.

While research is often seen in terms of technology, equally important is operations research. Operations research can assist in appropriately guiding the implementation of basic strategies, and the tailoring of approaches to local contexts. Programmatic questions that should be addressed include the best ways of reaching hard-to-reach populations, how to enhance disease surveillance, and the best approaches to measuring vaccination coverage. At times, this research may be context-specific. Country-led research would benefit from further emphasis. Research targeting programmatic and, at times, country-specific challenges, as has been done in the polio program, is likely to yield the most programmatic gains and should be prioritized.

Progress has been made in exploring topics identified as priorities at previous measles and rubella research meetings (Table 3). However, measles and rubella research activities remain under-funded and without dedicated staff. Attempts to identify funding for research have focused on a small number of donors and could be expanded to a much broader group. Measles and rubella research is also a natural successor to the Polio Research Committee (PRC). Transitioning the PRC to measles and rubella research should be considered part of the overall polio transition.

Recommendations

- Programmatically-oriented operations research, in addition to technologically-oriented research such as the development of new vaccine delivery or antibody testing methods, should be used to determine how to best interrupt measles transmission. Such operations research should include achieving optimal uptake of vaccination in populations, which populations should be targeted for special immunization efforts, how to optimize surveillance systems, and the economic impact of disease.
- Sustained commitment to adequately funding measles and rubella research is required. An advocacy plan to secure funding for research should be developed.
- A measles and rubella research committee focusing in a sustained fashion on advocating for, promoting, and prioritizing measles and rubella research, similar to the PRC, is critical. The natural home for this working group is WHO.
- Research should be conducted to determine the impact at the country level of measles and rubella control and elimination efforts on the overall immunization system.

Building on the Polio Transition

Background:

Pursuing the goal of poliomyelitis eradication has led to the commitment of vast human and financial resources. The *Polio Eradication and Endgame Strategic Plan (PEESP) 2013 – 2018* articulates ‘Transition Planning’ as its fourth Objective, stating that (governments should) “...ensure that the investments made to eradicate poliomyelitis contribute to future health goals, through a program of work to systematically document and transition the knowledge, lessons learned and assets of the Global Polio Eradication Initiative... and establishment of a comprehensive polio transition strategic plan by no later than end-2016”.⁴¹

Progress and challenges

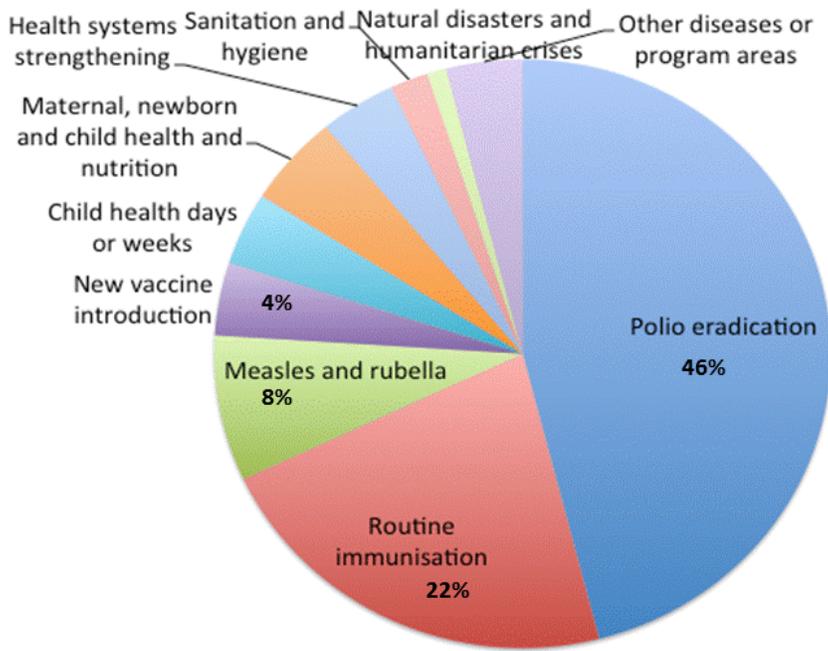
A subcommittee of the GPEI has been tasked with Polio Legacy Transition Planning. This subcommittee has defined the three key components of polio legacy transition planning as:

- Maintaining and mainstreaming essential polio functions (e.g., immunization, surveillance);
- Sharing knowledge and lessons learned from GPEI to improve child health globally;
- Transitioning polio capacities, infrastructure and assets to support other public health priorities, where appropriate.

At present, more than 30,000 individuals comprise the internationally-supported GPEI workforce, while more than 700 laboratories form the Polio Laboratory Surveillance Network. In addition to performing their polio functions, these 30,000 individuals provide support to a broad array of immunization and health initiatives which will not phase out with GPEI. A survey of polio-funded staff done by the Boston Consulting Group indicated that approximately 46% of the staff’s time was spent on polio eradication, 22% on routine immunization, 8% on measles elimination, rubella control and 4% on new vaccine introduction, and the remainder on a variety of other health initiatives (Figure 9)⁴². Working toward polio eradication has taught the immunization community many lessons including how to access insecure and hard-to-reach areas, accountability, the importance of communications, how to optimize social mobilization and community engagement, how to achieve and maintain political commitment, and how to operate global disease surveillance networks. These lessons are relevant to a broad swathe of disease control initiatives.

⁴¹The Global Polio Initiative. *Polio Eradication & Endgame Strategic Plan 2013-2018*. 2013, Geneva, World Health Organization (WHO/POLIO/13.02, <http://www.polioeradication.org/resourcelibrary/strategyandwork.aspx>, accessed 9 July 2016).

⁴² Boston Consulting Group. Polio funded personnel’s involvement in routine immunization and broader immunization goals. Final report, May 2015, 1-82.



Boston Consulting Group study in Afghanistan, Angola, Chad, DR Congo, Ethiopia, India, Nigeria, Pakistan, Somalia, South Sudan

Figure 9. Allocation of polio staff time

Sixteen priority countries (Figure 10) have been identified for polio transition planning with the goal that 14 of these countries develop polio transition plans by end-2016. The plans should provide a roadmap for the transition which should occur during 2017 – 2019 of essential polio functions, resources and lessons learned. These polio transition plans should also include budget commitments from governments and donors to enable the implementation of the plans beginning in 2017.

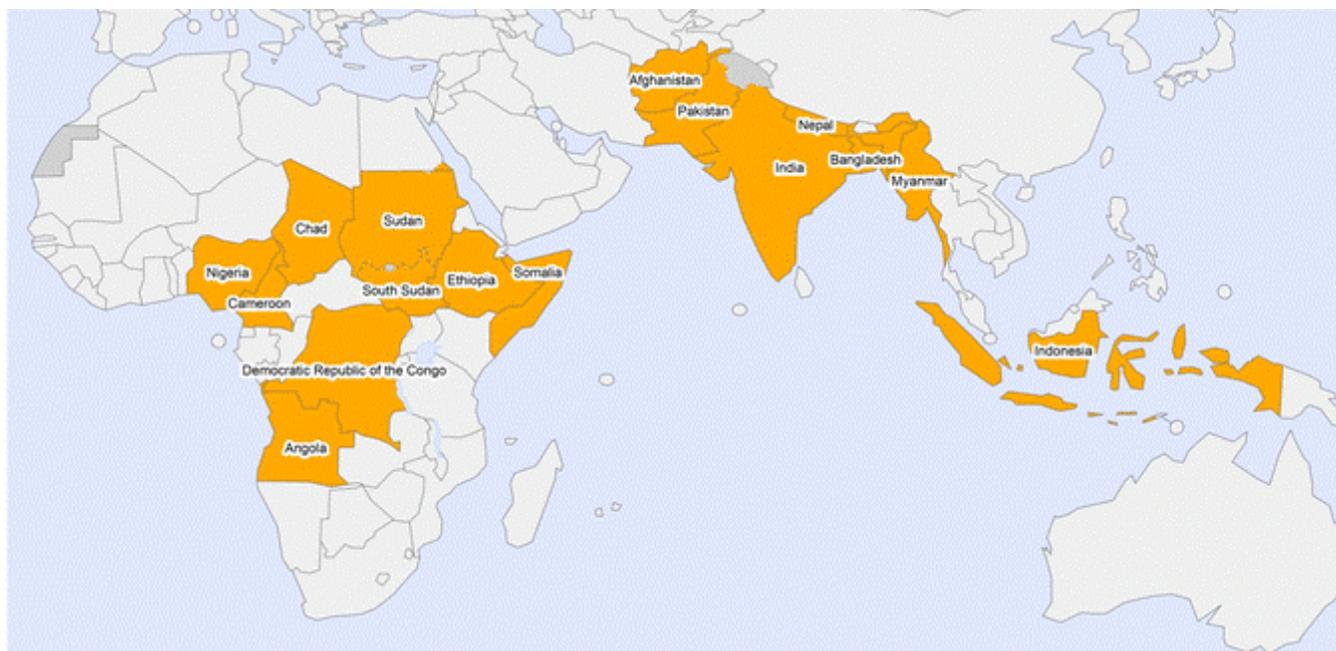


Figure 10. Sixteen priority countries for polio transition planning

Cochi SL, Hegg L, Kaur A, Pandak C, Jafari H. The global polio eradication initiative: progress, lessons learned, and polio legacy transition planning, *Health Affairs*, 2016;35:277-83.

Discussion

The 16 priority countries selected for polio transition planning contain most of the world's unvaccinated and under-vaccinated children, as well as most of the world's measles cases and deaths and most of the world's rubella and CRS cases. Immunization system strengthening and measles and rubella elimination are obvious candidates for the transitioning of polio assets. Currently, the polio infrastructure is concentrated in countries with the lowest-performing immunization systems which would benefit from pivoting polio eradication assets to strengthening routine immunization. Many of the strategies used to reach polio eradication are broadly applicable across immunization systems, for example the importance of surveillance laboratory networks, the use of communications and social mobilization, the importance of micro-planning, and the importance of management and accountability. Strategies for measles and rubella control and eradication have other similarities to those for polio eradication, including the importance of outbreak preparedness and response and the need for periodic SIAs to reach inaccessible children. Despite advances, measles and rubella remain high burden diseases: measles is an important cause of deaths in children aged less than five years, and rubella remains the leading infectious cause of birth defects. The ITFDE explicitly recommended that 'countries should adapt infrastructure and resources developed for polio eradication to measles and rubella eradication'.¹¹

At country level, it is important to conduct an inventory of current polio functions and ensure that governments and partners are aware of the possibility of the loss of these functions if they are not transitioned in a timely fashion. The comprehensive multiyear plan (cMYP) should be used as a vehicle for in-country legacy planning and should ensure that there is no weakening of overall immunization programs as a result of the transition. There is a short window of time as polio assets are already beginning to decrease (Figure 11). Although the details of this graph are difficult to see, it clearly demonstrates the marked fall off in overall polio assets anticipated to occur over the next decade.

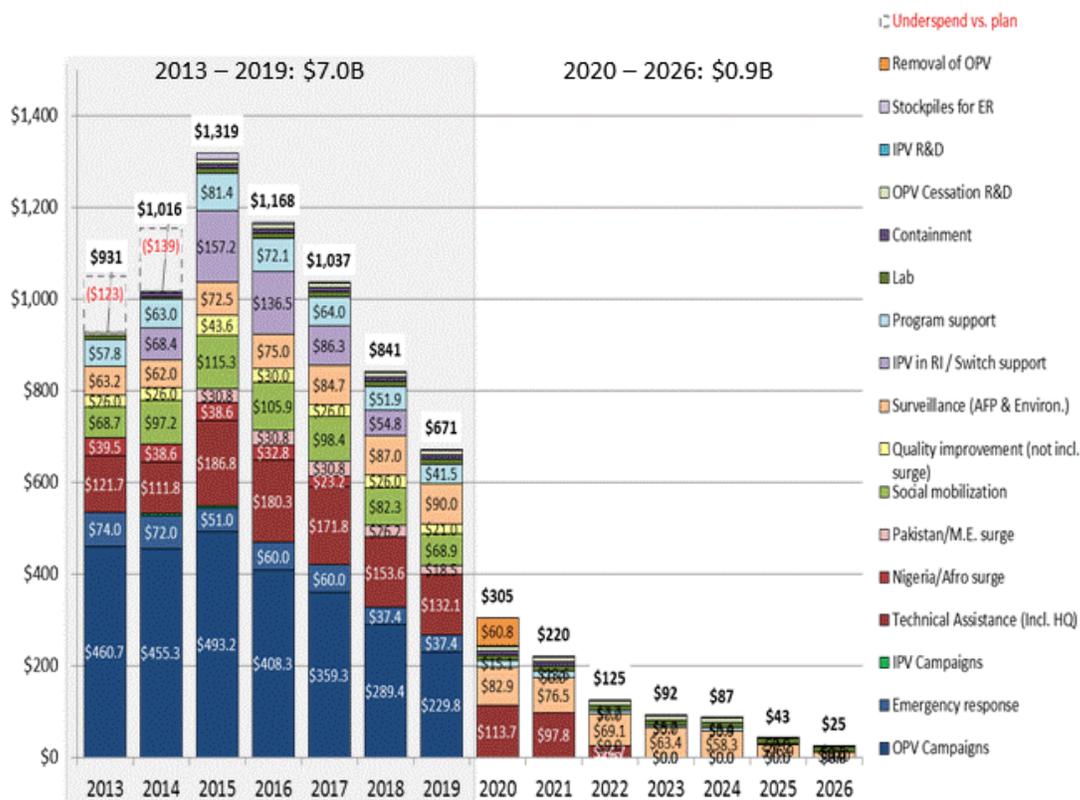


Figure 11. Estimated Costs for Polio Eradication by Activity (USD, not including India self-funded costs). 2013 – 2023

Source: Unpublished data, Financial Resource Requirements, Financial Management Team, Global Polio Eradication Initiative, 2016.

Recommendations

- Given the imminent reduction in polio eradication resources, which can have an adverse impact on both measles and rubella control/elimination efforts, a focus on transition of GPEI funded immunization program capacity (including surveillance capacity) is urgent and needs to be a top priority.
- All stakeholders involved in control and elimination of measles and rubella (national governments, M&RI, Gavi, etc.) as well as those involved in immunization system strengthening (BMGF, JSI, CDC, WHO, UNICEF, the World Bank, etc.) should engage in polio transition planning (at all levels) to leverage the opportunity and avoid the risks of the end of the GPEI.
- Strengthening immunization systems and the control and elimination of measles and rubella should be designated as high priorities for polio transition planning and implementation.
- Polio assets should be re-purposed in such a way as to sustain essential polio functions (surveillance, lab network, communications, social mobilization, etc.) as well as the measles, rubella and other immunization functions that they have been supporting. At minimum, there should be no weakening of non-polio activities currently supported by polio assets.
- As part of the country planning framework for immunization and in support of the GVAP goals, a concrete plan with an earmarked budget should be developed and implemented for

transitioning essential polio assets to immunization system strengthening and measles and rubella elimination. Under the leadership of the ministries of health, this plan should aim to include the participation of other ministry and all partners with an interest in health system strengthening.

Governance

Background:

National governments have the primary responsibility for management and governance of their national immunization programs. Interagency Coordinating Committees also play a central role in ensuring strong governance of immunization programs in low and lower-middle income countries that rely on external partner support. At regional and national levels, important roles are played by National Verification Committees (NVCs) and RVCs. NVCs scrutinize and monitor progress toward measles and rubella elimination. Annual reports from NVCs are reviewed and feedback provided by independent RVCs. As yet, no global verification committee has been established.

Internationally, two major groups have played critical roles in measles and rubella control and elimination efforts since 2000: the M&RI, originally called the Measles Initiative, and Gavi. The M&RI, formed in 2001 and made up of the UN Foundation, WHO, UNICEF, CDC and ARC, originally aimed to accelerate reduction in measles deaths by expanding the PAHO mass campaign strategies to other regions starting in Africa, where the burden was highest. The M&RI's mission is to globally lead and coordinate efforts to achieve a world without measles and rubella.

Gavi was also formed in 2001 with four founding partners: the Bill & Melinda Gates Foundation, the World Bank, UNICEF and WHO. In contrast to the M&RI, which focuses on measles and rubella, Gavi's mission is to save children's lives and protect people's health by increasing equitable use of vaccines in lower-income countries. Although Gavi's initial focus was introduction of new vaccines, it supported measles control activities from 2004-2008 with US\$176 million channeled through the M&RI together with support for introduction of a routine measles second dose.

Progress and challenges:

Since its inception, the M&RI has provided more than US\$1.1 billion for measles and rubella control and elimination activities contributing to reduction of measles deaths by 79% by 2014 compared with 2000. In 2013, after a hiatus of five years, Gavi re-engaged in measles and rubella control with support for introduction of rubella vaccine. Gavi's commitment to measles and rubella control was further strengthened when, in December 2015, the Gavi Board approved a new comprehensive measles and rubella strategy with approximately USD 800 million available to Gavi-eligible countries over the period 2016-2020.

Despite the investments made to date in reaching measles and rubella elimination, the 2014 Annual Report on the GVAP concluded that progress towards regional measles and rubella elimination goals was off track and that *"A huge amount of work and political commitment lies ahead if their elimination goals are to be achieved"*⁴³. To build country commitment, the SAGE recommended that each country

⁴³ World Health Organization. *Global vaccine action plan 2011-2020*. Geneva, World Health Organization (www.who.int/immunization/global_vaccine_action_plan/en, Accessed July 11 2016....).

establish an NVC. RVCs have been actively working in three WHO Regions (Americas, European and Western Pacific) and the SE Asian Region held its first RVC meeting in August 2016. The Table below shows data as of December 2015 summarizing progress towards measles and rubella elimination goals as determined by these RVCs.

WHO Region	Regional Verification Commissions Established	Elimination Achieved	
		No. of Countries	% of Countries
Americas	Yes	Measles: 34 Rubella: 35	97 100
Europe	Yes	Measles: 21 Rubella: 20	40 38
Western Pacific	Yes	Measles: 6	22
Eastern Mediterranean	No	-	-
South East-Asia	No	-	-
Africa	No	-	-

Table 4. Regional Verification Commissions and number of countries verified to have eliminated measles or rubella by WHO Region as of December 2015.

Discussion

In view of the complementary but sometimes overlapping roles of partners in the M&RI and Gavi, effective mechanisms for coordinating the support provided by global partners to countries are clearly needed to avoid duplication and maximize efficiency. Country ownership is a critical success factor for measles and rubella elimination; examples of such ownership have been shown by the multiple countries within AMR that have largely self-funded measles SIAs in a proactive move to prevent measles outbreaks. Governments have primary responsibility for achieving their measles and rubella goals and must demonstrate this responsibility by providing domestic resources. NVCs and RVCs play an important role in promoting country ownership and accountability. Identifying resources to fill national resource gaps for realistic objectives is a shared responsibility between countries and other stakeholders, including the M&RI and Gavi.

The M&RI has championed measles and rubella vaccination activities globally, advocated for eventual eradication, and while it received funding in the past from donors primarily for mass campaigns and surveillance, funding has dropped dramatically as most donors prefer to give their support for all immunization-related activities to Gavi which is a single agency which can distribute funds to support a range of antigens. Gavi, in turn, has become increasingly supportive of measles and rubella control and the new Gavi measles and rubella strategy offers comprehensive, multi-year support to low income countries that aims to build financial sustainability through increasing country co-financing. However, Gavi's focus is on reduction in morbidity and mortality from measles and rubella and not elimination. This has resulted in differences between Gavi and the M&RI regarding the size and scope of mass vaccination activities (e.g., target age groups for SIAs). In the past, although M&RI may have channeled most of its funding to low-income countries, if needed these funds could, in principle, be available for

other countries. The redistribution of funding between the M&RI and Gavi has resulted in this option no longer being available, as Gavi is limited in the countries that it is able to fund.

Recommendations

- It is imperative that there be close collaboration and coordination between Gavi and the M&RI, as a central element in building the overall immunization system and in order to ensure that measles and rubella control and elimination efforts are coordinated and efficient.
- Efforts to control and eliminate measles and rubella should be integrated with the general immunization system (including surveillance) and should be used to build and enhance the overall immunization system.
- All countries should establish NVCs to review national progress toward elimination goals, and make recommendations as to how these goals may be met.
- RVCs should be established in all regions where they do not exist and their efforts strengthened in regions in which they do exist. The RVCs should serve as independent reviewers of progress toward measles and rubella elimination and make region and country-specific recommendations to overcome impediments to measles and rubella elimination.

Resource Mobilization

Background

In addition to the resources provided by national governments, funding for measles and rubella control at global level currently has two streams: funding to the M&RI and funding to Gavi. The history of this funding is illustrated in Figure 12.

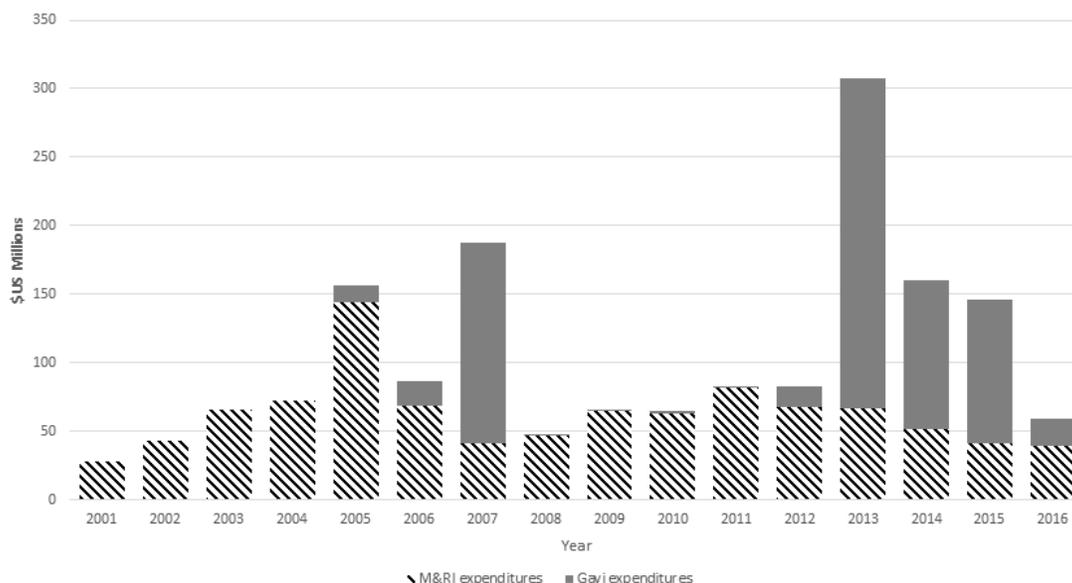


Figure 12. Annual Measles & Rubella Initiative (M&RI) and Gavi Expenditures for Measles and Rubella Control and Elimination Activities, 2001- mid 2016. ⁴⁴

Funding to the M&RI began in 2001 and increased annually until 2004. A sharp increase occurred in 2005 due to funds brought in by ARC following the Southeast Asian tsunami. In 2004-8, Gavi contributed > USD 175 million through the International Finance Facility for Immunisation. However, in recent years the M&RI has seen a steady decline in funding as donors increasingly seek to consolidate all funding given for immunization by giving to a single agency rather than to multiple disease-specific initiatives. The United Kingdom’s Department for International Development in its Multilateral Aid Review also cited Gavi’s effectiveness in increasing access to immunization, its focus on results, as well as its financial management, accountability checks, and promotion of country ownership.⁴⁵ In contrast to funding through the M&RI, funding from Gavi has recently increased substantially. The spike in Gavi funding in 2013 and the subsequent Gavi funding through 2015 reflects Gavi’s commitment to rubella introduction as well as funding for measles-specific activities in six large countries not yet ready to

⁴⁴ Graph compiled from publicly available web sites.

⁴⁵ Department for International Development. Multilateral Aid Review. March 2011.

www.gov.uk/government/uploads/system/uploads/attachment_data/file/67583/multilateral_aid_review.pdf

introduce rubella. The graph shown above reflects expenditures through mid-2016, and, as a result, most of the funding pledged by Gavi in December 2015 is not reflected.

Progress and challenges

In addition to the funding currently received from national governments, the M&RI partners and Gavi, estimates by the M&RI in October 2015 showed a projected budget shortfall of USD 431 million for the six-year period 2015 – 2020, for an annual average of USD 71 million. This figure includes SIAs and ORI for non-Gavi countries, and surveillance, research and other core functions for both Gavi and non-Gavi countries, but is based on maintaining high level measles control rather than achieving elimination. Since October 2015 when these figures were developed, Gavi has pledged an additional USD 220 million towards these activities.

Discussion

Funding for measles and rubella activities through Gavi for Gavi-eligible countries has increased markedly. However, as noted above, the focus of this funding remains mortality reduction. There remains a need for funding to vaccinate age groups outside of those targeted through Gavi funding. In addition, financing for non-Gavi eligible countries is declining rapidly. Although many countries are able to fund their own measles and rubella control activities, others that have recently graduated from Gavi may be unable to afford the costs of large scale ORI or SIAs. Given the extremely infectious nature of measles, it is very easily transmitted across borders, rendering a global approach to disease control particularly important. If the recommendations from this report are implemented, further funding for strengthening surveillance, research, communications and resource mobilization will be required. In order to advocate for these funds, better estimates of what it would cost to implement these recommendations are required. Initial work on costing the needs for surveillance has begun.

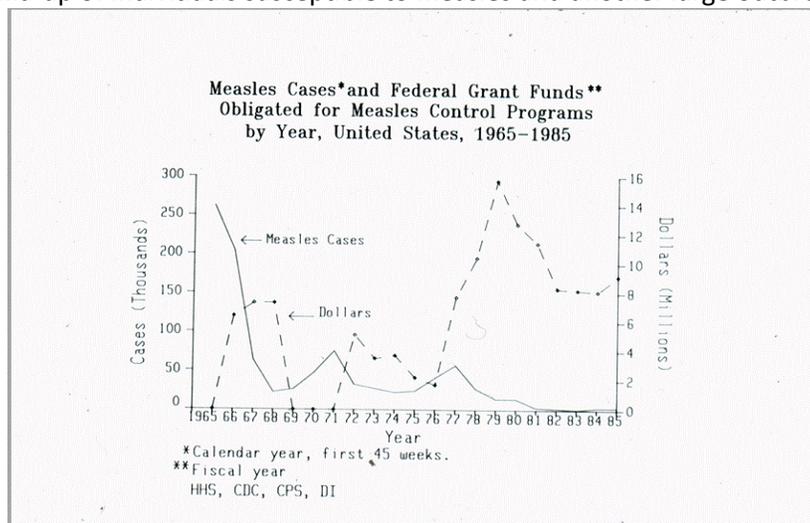
Funds are more likely to be mobilized for measles and rubella elimination if the measles and rubella community can demonstrate how a measles and rubella focus can strengthen health systems overall, and immunization systems in particular. It is also important to remain open to instances in which measles and rubella elimination activities may have been detrimental to health systems overall, and use these situations as opportunities to learn how to avoid such negative interactions in the future.

Stable and predictable funding is important to running effective and efficient immunization programs. Frequently, funding for measles and rubella control is most available immediately during and after large outbreaks. However, this funding could usually have been better spent in advance of the outbreak for preventive vaccination. Preventing the outbreak not only prevents the morbidity and mortality as well as the disruption associated with outbreaks, but vaccination activities in non-outbreak settings have more opportunity than those conducted in outbreak settings to be carefully planned, usually resulting in higher coverage and a better return on investment.

In order to mobilize funds, it may be necessary to look beyond the traditional donors to an expanded donor base. This requires investing in adequate staffing for resource mobilization.

Lack of stable funding leads to recurrence of disease

In the United States of America, a recurrent funding and disease cycle occurred before funding was stabilized and dependably available for adequate preventive vaccination. In this cycle, measles outbreaks led to increased funding for measles control which then resulted in decreased measles cases and a perception by policy makers that funding could be decreased. This decrease in funding in turn led to a build-up of individuals susceptible to measles and another large outbreak.



Source: Orenstein WA. The role of measles elimination in development of a national immunization program. *Pediatric Infectious Disease Journal* 2006 Dec;25(12):1093-101

Recommendations

- A multi-year Financial Resource Requirements (FRR) document for measles and rubella in the context of the overall immunization system should be revised. The FRR should include demand-driven, country driven projections on need, and reflect funding from Gavi, the M&RI, other partners and domestic financing. This document should be complemented by yearly work plans with detailed national partners' financial contributions.
- The recent welcome additional support from Gavi for measles and rubella activities provides a major step forward for achieving measles and rubella goals. However, it is not, in itself, sufficient to provide adequate assistance globally, as many countries are not Gavi-eligible or are graduating from Gavi-eligibility and key global strategies such as surveillance and research are under-resourced. Consequently, there is a need for additional funding.
- The five M&RI founding partners should have adequate staff capacity to identify and align the resources needed and mobilize additional donors and resources to fill the funding gap for immunizations overall and measles and rubella vaccination in particular.
- Country co-financing for measles and rubella activities should increase as countries move along the development continuum. Country financial commitments should be closely followed through the annual work plan budget.
- Efforts should be made to identify examples of when a focus on measles and rubella elimination has led to building of the overall immunization system (e.g., where a focus on measles and rubella led to a school entry check for those vaccines as well as other vaccines recommended for

children, leading to improved coverage for all recommended vaccines). In addition, it is important to remain open to examples of when a focus on measles and rubella has had a negative impact on overall healthcare and immunization systems, and learn from any such examples how such a situation can be avoided.

SECTION 6. SUMMARY

In summary, tremendous progress has been made towards both measles and rubella elimination since 2001. Significant gains have also been made during the period 2012 – 2015. However, despite these advances, neither measles nor rubella elimination are on track to achieve the ambitious goals laid out in the *Global Measles and Rubella Strategic Plan, 2012-2020*. The basic strategies articulated in this document are sound, but full implementation of them has been limited by lack of country and global political will and country ownership, reflected in insufficient resources. 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 SIAs. Elimination, once achieved, would be difficult to sustain without more robust routine immunization systems than currently exist in much of the world. This report recommends focusing on improving ongoing immunization systems --although this may delay reaching measles and rubella elimination goals -- in order to ensure that gains in measles and rubella control can be sustained. Re-orienting the measles and rubella elimination program to increase emphasis on surveillance so that programmatic and strategic decisions can be guided by data is critical.

The inextricable linkage between achieving and maintaining measles and rubella elimination and strong immunization systems is also repeatedly underlined in this report. Measles incidence is recognized as a marker of the health of immunization systems, and of health systems overall. Because of its ability to detect unreached populations and program weaknesses, measles also serves as an indicator disease, or the ‘canary in the coal mine’, a characteristic whose importance has recently been highlighted in the context of global health security.⁴⁶ A focus on measles and rubella elimination can result in gains across the immunization system, as is well described by Orenstein^{47,48} and as occurred in China where school entry –checks to ensure measles vaccination were expanded to check all recommended vaccines.⁴⁹

⁴⁶ Berkley S. Measles – the canary in the coal mine. 27 April 2016. Devex. (<https://www.devex.com/news/measles-the-canary-in-the-coal-mine-88044>, Accessed July 9 2016).

⁴⁷ Orenstein WA. The role of measles elimination in development of a national immunization program, *Pediatric Infectious Disease Journals*, 2006, 25(12):1093 –1101.

⁴⁸ Orenstein WA, Seib K. Beyond Vertical and Horizontal Programs: a Diagonal Approach to Building National Immunization Programs through Measles Elimination. *Expert Review of Vaccines*, 2016, 15(7):791-793 (<http://www.tandfonline.com/doi/full/10.1586/14760584.2016.1165614>. Accessed 8 August 2016).

⁴⁹ Zuo S, Cairns L, Hutin Y, Liang X, Zhu Q, Lee LA, et al. Accelerating measles elimination and strengthening routine immunization services in Guizhou Province, China, 2003-2009. *Vaccine*, 2015, Apr 21; 33(17):2050-2055.