Joint Symposium on Closing Immunity Gaps in Older Children and Adults Towards Measles and Rubella Elimination: Lessons Learned and Challenges

Siena, Italy
10-11 May, 2016
Executive summary

The successful introduction and widespread use of measles containing vaccine (MCV) and rubella containing vaccine (RCV) has resulted in reduced measles and rubella transmission among young children but lower coverage levels in older children and lack of exposure to natural infection has led to an increasing number of susceptible adolescents and adults. The WHO Strategic Advisory Group of Experts (SAGE) has called for a mid-term review of the 'Global Measles and Rubella Strategic Plan 2012-2020' to be conducted in 2016 with the aim of refining the plans and monitoring and enhancing the quality of plan implementation. Experience from the Regional Verification Commissions (RVC) and regional activities towards elimination suggest achieving elimination may be difficult without strategies to close immunity gaps in older children and adult populations.

Although recent changes in measles epidemiology have been noted in several countries and in some recent measles outbreaks susceptible adolescents and young adults have represented a significant proportion of detected cases, their role in sustaining transmission has been difficult to fully determine. Recent evidence suggests that adolescents and young adults may form important links in chains of virus transmission, but evidence that susceptible adult populations can maintain virus transmission in the absence of susceptible childhood populations is, so far, inconclusive.

The level of priority that should be given to addressing immunity gaps in adolescents and young adults remains unclear. Although these gaps are known to exist in many countries, they do not necessarily pose the same level of risk. In countries with consistently high childhood vaccination coverage, moderate to low population density and a broad scattering of susceptibles, the risk of virus transmission posed by susceptible adult cohorts can probably be regarded as low. In countries with inconsistent or low childhood vaccination coverage, high population density and grouping of susceptible individuals into particular communities or areas, adolescents and young adults may play an important role in measles virus transmission to infants and young children.

Detection of immunity gaps relies on the effective collection, analysis and interpretation of high-quality data, an area that remains a challenge in many countries. In practice most countries use a process of triangulation of data from multiple sources to investigate population immunity and detect potential immunity gaps, or use dynamic modelling to predict potential immunity gaps. The specificity and accuracy of triangulation and modelling is dependent on the quality, extent and nature of data available, which can be problematic in some countries.

The many country presentations delivered during this symposium have illustrated a variety of approaches that can be taken to address immunity gaps among different age groups. Solutions to addressing country-specific issues often need to be tailor-made from more general strategies to fit the local context, and the use of micro-planning
based on detailed local knowledge that can be used to identify and address local barriers, is critical to the level of success that can be achieved.

Strategies specifically targeting adults in high risk groups and professions, such as health workers, teachers or students at schools and universities, staff in the travel and hospitality industries, members of the police and military forces and long-term residents of institutions may be an alternative to mass vaccination of all adults in a defined age group. Of increasing concern is the mass movement of migrants and refugees, their initial housing in refugee complexes and transit centres, and their longer-term integration and access to immunization services within host nations. Both immediate and longer-term strategies are required to specifically address the needs of these groups to ensure that they do not develop or maintain immunity gaps.

Developing and implementing a national plan of action for measles and rubella elimination is a key requisite for effectively closing immunity gaps. National health policies to address immunity gaps can be directive, such as demonstration of immunity or vaccination of health workers as a requirement for employment, or of students prior to school or university entry. Alternatively, health policies may incentivize behaviours, such as by providing additional payments for family doctors for giving vaccines, taxation relief or social benefits for families who ensure that their children, including teenagers, are fully vaccinated. In order to gain high-level political commitment for immunization services the positive public health benefits of vaccination need to be prioritized and effectively communicated and the cost-effectiveness of vaccination as a national investment needs to be promoted.

Professional societies, civil society and non-governmental organizations have an essential role to play in advocating for immunization, public education on vaccination, and social mobilization and communication. These groups are often well placed to actively participate in social mobilization, communication and monitoring activities before and during vaccination campaigns.

The window of opportunity for global eradication of measles, rubella and congenital rubella syndrome (CRS) may be closing as the epidemiology of measles and rubella continues to evolve with increasing numbers of susceptible adults and infants complicating established strategies for elimination. The cost effectiveness of measles eradication will be maximized if it can be accomplished sooner rather than later.
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<th>Abbreviations Used</th>
<th>Description</th>
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<tr>
<td>CRS</td>
<td>congenital rubella syndrome</td>
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<tr>
<td>GVAP</td>
<td>Global Vaccine Action Plan</td>
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<td>MCV</td>
<td>measles containing vaccine</td>
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<td>MCV1</td>
<td>first dose of measles containing vaccine</td>
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<td>MCV2</td>
<td>second dose of measles containing vaccine</td>
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<td>MMR</td>
<td>measles/mumps/rubella vaccine</td>
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<td>NIP</td>
<td>national immunization programme</td>
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<td>NGO</td>
<td>non-governmental organization</td>
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<td>PAHO</td>
<td>Pan American Health Organization</td>
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<td>RCV</td>
<td>rubella containing vaccine</td>
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<td>RVC</td>
<td>WHO Regional Verification Commission for measles and rubella elimination</td>
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<td>SAGE</td>
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<td>SIA</td>
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Background

All six WHO regions have goals for eliminating measles and three currently have goals for eliminating rubella. Three regions (Americas, European, and Western Pacific) have fully functional Regional Verification Commissions (RVC). The introduction and widespread use of measles containing vaccine (MCV) and rubella containing vaccine (RCV), but with inadequate coverage levels to guarantee elimination of transmission together with declining birth rates, has resulted in reduced measles and rubella transmission in young children and an increasing number of susceptible persons reaching adulthood without natural or vaccine-derived immunity. Experience from the RVC process and regional activities towards elimination suggest achieving elimination may be difficult without strategies to close immunity gaps in older children and young adult populations. For countries that do not rely on supplementary nationwide campaigns to target expanded age groups, including adolescents and adults, lack of an established infrastructure or mechanism to deliver adult vaccination services is a major challenge, and a common one among some countries in all WHO Regions.

A Joint Symposium was convened in Siena, Italy, 10 to 11 May 2016. The meeting was organized by the Sabin Vaccine Institute, the International Paediatric Associations (IPA), the American Academy of Pediatrics (AAP), the US Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO), and the Lions Clubs International, and hosted by the University of Siena. Participants included national immunization program managers, ministries of health, measles and rubella regional focal points, subject matter experts, and partners. This was the first global meeting held to address the recent shift seen in the age distribution of measles and rubella cases and the increasing problem of immunity gaps in adolescents and young adults.

Scope and purpose

The objectives of the meeting were to:

- Review the evidence regarding need to close immunity gaps in adolescents and adults, towards measles and rubella elimination
- Identify challenges and best practices for achieving high vaccination coverage among older children and adults
- Describe strategies and tactical measures to close immunity gaps
- Discuss experience with methods for obtaining high-quality data on coverage in all age groups, how to identify areas/groups at risk, and take effective action when gaps in immunity are identified
Session 1: Setting the scene

Status of measles and rubella elimination – Regions and Global

All six WHO Regions have established goals for measles elimination by 2020 at the latest, but only three have adopted targets for rubella elimination. The Global Vaccine Action Plan (GVAP) includes the goals of 4 WHO Regions having achieved measles elimination by 2015 and 5 by 2020; two WHO Regions to have eliminated rubella by 2015 and 5 by 2020. In 2002, the Americas became the first, and so far only, WHO Region to interrupt endemic measles transmission. The last confirmed cases of endemic rubella and congenital rubella syndrome (CRS) in the Americas Region were reported in 2008 and 2009 and the Region was declared rubella free in April 2015. In 2015, the WHO Strategic Advisory Group of Experts (SAGE) on immunization reviewed progress towards meeting mid-decade targets and concluded that most of the targets were significantly off track. Although there has been a 94% reduction in the global number of reported measles cases over the past 35 years, there continues to be approximately 250,000 cases reported each year. Global coverage with the first dose of measles containing vaccine (MCV1) rose to approximately 85% by 2010 but has not increased since that time. Global WHO/UNICEF estimates of MCV1 coverage in 2014 include 74 (37%) countries with coverage less than 90%. Coverage with the second dose of measles containing vaccine (MCV2) continues to lag at approximately 55% globally despite an additional 21 countries having introduced MCV2 to immunization schedules since 2007. Data available for 2010 to 2014 suggest that 2/3 of measles cases occurred in age-eligible children receiving fewer than 2 doses of MCV, a significant proportion of these having no history of receiving vaccine. As of March 2016, 5 WHO Regions continue to be endemic for measles.

Global coverage with rubella containing vaccine (RVC) has risen steadily since 1980, with 18 additional countries introducing RCV into immunization schedules since 2012, but over half of the world's children are still not vaccinated against rubella. Eleven countries plan to introduce RVC in 2016, including India, but a further 35 countries, have not provided information or have no plans to introduce the vaccine. The highest burden of CRS continues to be in Sub-Saharan Africa and South-East Asia, often in countries that do not include RCV in their schedules.

SAGE has called for a mid-term review of the global measles and rubella strategic plan to be conducted in 2016 with the aim of refining plans towards elimination, and monitoring and enhancing the quality of plan implementation. The changing epidemiology of measles has clearly demonstrated that further delays in achieving elimination goals increase the risk of creating population immunity gaps in older age groups missed by vaccination programmes during their childhood.
Overview of Progress by Region

**Americas Region**

This Region has provided proof of concept for measles and rubella elimination strategies. The Region was declared free from rubella and CRS in 2015 and is on track for verification of measles elimination in 2016. The main challenge faced by the Region is to maintain elimination in the face of ongoing importations through visitors from endemic countries in other Regions or travel of inadequately/un-vaccinated residents returning from overseas. Persistent importations into countries in the Region require intensive response efforts that incur significant financial costs.

**Western Pacific Region**

The Region as a whole has achieved high MCV1 and MCV2 coverage and conducted high coverage measles supplementary immunization activities. Seven countries or areas have been verified by the RVC to have eliminated endemic measles transmission. Despite the high vaccination coverage, the Region experienced resurgence in the number of reported measles cases in 2014 and 2015. There were large-scale measles outbreaks in Viet Nam, Papua New Guinea, the Solomon Islands and Mongolia. All countries have now introduced RVC and the Regional Technical Advisory Group (TAG) on Immunization has recommended adoption of a 2020 rubella elimination goal.

**European Region**

High overall coverage with 2 doses of MCV has been maintained for more than a decade, and 22 countries have interrupted endemic transmission of measles, but the Region continues to suffer large outbreaks with a significant number of cases among adolescents and young adults. Major challenges for the Region include the low political commitment to elimination, relatively high levels of vaccine decliners and reluctance to conduct mass immunization campaigns in some countries. In addition, the recent large influx of refugees and migrants into Europe has the potential to place strain upon immunization services in several countries.

**South-east Asian Region**

The Region has established a 2020 goal for the elimination of measles, but the current level of MCV1 coverage is approximately 84% with MCV2 coverage at approximately 60%. India began a monthly case-based reporting system for measles in 2014, leading to a large increase in the number of reported cases but more accurately reflecting the measles disease burden. Rubella containing vaccine will be introduced in India from 2016,
expecting to cover approximately 408 million children. The Region as a whole urgently needs to increase the level of routine immunization coverage and strengthen surveillance if it is to attain the 2020 goal.

**Eastern Mediterranean Region**

High levels of measles control have been achieved in 6 countries in the Region, and 3 of them are poised to verify elimination. However, MCV1 coverage in the Region as a whole remains below 80% while MCV2 coverage is below 70%. Many countries in the Region are affected by conflict and civil unrest, and persistent low vaccine coverage in some of these countries remains a major challenge. New strategies are urgently required to more effectively deliver immunization services in situations of conflict and civil war.

**African Region**

Twelve countries in the Region are near measles elimination and a further 14 are on track to meet the 2020 elimination goal. Overall MCV1 coverage, however, remains at below 75% and MCV2 coverage is below 15%. Seven countries have introduced RCV. There are weak and fragile health systems in many countries in the Region, easily disrupted by events such as the Ebola outbreak, and a continued need for periodic high quality SIAs in most countries to reach children missed by the routine immunization systems.

**Overview: Review of outbreak data and need to close gaps**

A review of case-based measles data from 2010 to 2014 representing all WHO Regions was undertaken to describe the distribution of cases across different age groups, specifically adolescent and adult populations. Only data on confirmed cases (laboratory confirmed, epidemiologically linked or clinically compatible) from countries experiencing ≥30 cases per year were considered. Available data show that while fewer than 20% of confirmed cases in the African and South-east Asian Regions were ≥15 years of age, in the Western Pacific Region the proportion rose to almost 30%, and in the European Region to 40%. Of the cases ≥15 years of age the highest represented age group was 15 to 24 years, followed by the 25 to 34 age group. Given the heterogeneous nature of the data it is very difficult to interpret it fully, but it does appear to confirm that as countries get closer to elimination status, but before elimination is achieved, the proportion of cases in older age groups increases.

A literature review of published reports on measles outbreaks involving adolescents and adults was conducted in an attempt to determine the impact of these age groups on sustaining measles transmission. Reports published between January 2010 and March 2016 were included if they described outbreaks of more than 50 cases with at least 25% of cases aged ≥15 years. A total of 25 reports were included in the review. In these reports the average age of cases was 22 years and the median age of cases was 11.8 years. Thirty-nine percent of reported cases
were of unknown vaccination status, while 64% of those of known status were unvaccinated. The reports suggest that areas with historically low MCV coverage are associated with disease in older age groups, but do not necessarily provide proof of adolescents and adults being the primary reason for the outbreaks or that they represent the primary source of transmission.

Furthermore, a report on the extensive measles outbreak in Malawi in 2010 suggested that while a large proportion of cases (28.6%) were ≥15 years of age, the outbreak was sustained by transmission in younger children and that targeting SIAs on children up to 15 years was sufficient to control the outbreak. There are several other examples where outbreaks involving a significant proportion of adult cases have been successfully controlled through SIAs targeted at children ≤15 years (Tanzania 2006/7, Vietnam 2008-2010, Ethiopia 2011, South Africa 2009-2010, and Namibia 2009-2010). In contrast, a report on an outbreak that occurred in a Kenyan refugee complex housing Somali refugees in 2011, where 60% of cases were >15 years of age, showed that the outbreak could only be controlled by vaccinating all adults (15 to 30 years of age) in the complex. The recent outbreak in Mongolia may provide another instance where adult immunization is necessary to halt transmission and control the outbreak.

An article currently in press1 provides a comprehensive assessment of measles transmission patterns during a measles outbreak in China in 2013-2014 where greater than 75% of reported cases occurred in persons ≥20 years of age. The outbreak started with adult-to-adult transmission in family and community settings, followed by a small number of young infants and children becoming infected. Nosocomial cases occurred one month after the first cases were reported. The first case led to at least 6 generations of infection. Among the 44 clearly determined transmission linkages, 37 (84.1%) were from adults to other age-groups (29 were adult to a different adult age group, seven were adult to children, and one was adult to a young infant), six were young infant to other age groups (4 were infant to adult, and 2 were infant to child transmission), and one was child-to-child transmission.

Data from modelling

There are four major factors believed to determine the age distribution in measles outbreaks: prevalence or force of infection; birth rate or population structure; target age for vaccination (SIAs); and age-dependent transmission. A reduced prevalence of infection results in a lower force of infection on each susceptible individual, resulting in a longer time elapsing until there is contact between infectious and susceptible individuals. This implies a higher mean age at infection. A declining birth rate decreases the proportion of potential susceptibles in the lowest age

groups, and SIAs targeted at the younger age groups further reduces the level of susceptibles in these groups, leaving a larger proportion of susceptibles in the older age groups. When outbreaks occur, virus transmission takes place among the very young, who are too young to have received vaccine, and older age groups, resulting in the classic bimodal age distribution of cases. The increase in the number of adult cases can be regarded as a natural consequence of a demographic transition in the population age structure and the protective effect of herd immunity.

The Issue: Country examples of outbreaks involving adolescents and adults

Romania

In 2011 and 2012, Romania experienced large concurrent outbreaks of rubella and measles. The most significantly affected age group for measles was those less than 1 year of age, and therefore not eligible for vaccination. The most significantly affected age group for rubella was the 15-19 years age group, both males and females, born between 1994 and 1997 and not included in the rubella vaccination programme. This age group was targeted in a SIA using measles/mumps/rubella vaccine (MMR) but with low coverage. Following the outbreak there has been a general loss of confidence in the immunization services, resulting in decreasing coverage of MCV1 (86%) and MCV2 (66%).

Italy

There is a high degree of autonomy within the provinces, resulting in a fragmented vaccination response. National MMR coverage is approximately 90% but has been declining since 2012 at least partially due to loss of confidence in immunization services. A change in measles epidemiology has been observed over the past 5 years, with the median age of cases rising to 23 years (the 15-39 years age group). Susceptible groups have been identified among health workers and vaccine decliner populations. There is evidence for a continued decline in vaccine coverage in 2016.

Morocco

Morocco introduced measles vaccine in 1987 and has achieved >90% coverage since then. The country has also conducted a series of targeted SIAs since 2003, achieving reasonably high coverage. A second dose of MCV (given at 18 months of age) was introduced into the immunization schedule in 2014. Despite the high vaccine coverage Morocco has continued to experience measles cases, although no outbreaks were reported in 2014 and 2015. From 2011 to 2013, 23% of cases were older than 20 years of age. In 2012, the Ministry of Health decided
to conduct a vaccination campaign against measles and rubella in 2 phases, the first phase targeted at those aged 9 months to 19 years, and the second phase targeted at those 20 to 35 years. The first phase was conducted in 2013 and achieved 91% coverage with apparent termination of the outbreak. The second phase remains in the planning stage, with multiple logistical and administrative challenges to successfully vaccinating healthy adult populations recognised.

**Mongolia**

In March 2014, Mongolia was verified as having interrupted endemic measles virus transmission for a period of at least three years since 2011. High coverage (>95%) with MCV2 in the routine immunization programme had reportedly been achieved for more than 10 years, supplemented with high coverage (93%-97%) SIAs in 2007 and 2012. There was no evidence of sustained measles virus transmission in the presence of high quality measles case-based surveillance since 2011.

A large outbreak with > 13,000 confirmed cases started in 2015 with all provinces affected but most cases occurring in the capital, Ulaanbaatar. A large proportion of cases were between 15-25 years, born 1990 to 2000 during the transition period following the breakup of the Soviet Union, with no history of vaccination. Many of the remaining cases were less than 1 year of age and ineligible for vaccine. An SIA was conducted in 2015 targeting the 6 months to 6 years age group and achieving 94% coverage. This was supplemented by a vaccination campaign targeting selected adult groups including HCWs, college and university students, high school students, members of the military and police services and prisoners. Despite these activities the outbreak continued into 2016 with a predominance of cases following the same bimodal distribution. The planned next step is to conduct a nationwide SIA targeting the 18-30 years age group starting in May 2016.

**Discussion**

There is clearly a role to be played by the international partners, including the various professional societies and associations, in harmonizing vaccination schedules for older children in different countries and in coordinating social mobilization activities. Due to the history and effectiveness of vaccination programmes in different countries, specificities with regard to potential age-related immunity gaps are different around the world, but all countries need to be aware of the problems posed by these gaps, and be prepared to take effective action to identify and close them.

Mass migration and the current surge of refugees fleeing from war and civil unrest, with the potential for these groups to present risk for transmission of measles and rubella, has in many countries led to a general policy to offer vaccination to all child migrants and refugees on entry. However given the transitory nature of their stay and
the pressures placed on immunization services, this policy is not always fully carried out. There is also a need to ensure that longer-term policies are put in place to ensure that migrants and refugees are not excluded from routine immunization activities.

Loss of public confidence in vaccination, and declining vaccine uptake, is a growing problem in some countries. This can probably be best tackled through careful diagnosis of the root cause of the problem and targeted strategies involving dedicated communications programs and social mobilisation. Professional associations and civic societies can facilitate and provide support for these activities. Greater use of social media to promote vaccination would be helpful, especially if a global resource base was available, providing generic examples, best practices and accounts of experience gained. In many countries there is reluctance among health workers to accept vaccination for themselves or promote vaccination for their patients. They clearly represent a high-risk profession that should be targeted with further training and education on the benefits of vaccination and the risks associated with susceptibility to measles and rubella.

Session 2A: Responses to fill immunity gaps: Experiences from the regions

Jordan

Although maintaining high vaccination coverage for many years, and being measles-free from 2010 to 2013, Jordan has faced recent challenges due to the influx of refugees from Syria. In 2013 an outbreak associated with refugees and nomadic communities occurred with a high proportion of adult cases. The immediate response was to launch a measles, polio and vitamin A campaign in the affected refugee camps, targeting all individuals up to 30 years of age. This was followed by a second campaign in Governorates bordering Syria and Iraq targeting children up to 16 years of age, and towards the end of 2013 by a national level campaign targeting all children. Lessons learned from this experience include the requirement for frequent advocacy meetings and effective coordination among all partners; close collaboration with the UN Humanitarian Commission for Refugees (UNHCR) and non-governmental organisations (NGOs) resulted in high coverage among refugees during the campaigns. There was a clear need for a strong supervisory structure for campaign monitoring and to provide rapid responses to dynamic developments, with daily supervisory tours providing transparency and accountability at all levels.

Routine immunization is now delivered to all children residing in Jordan regardless of their nationality and all refugees from Syria are given measles, polio vaccine and vitamin A at the entry points. Refugee camps are
included in all vaccination campaigns implemented in Jordan. The major challenge is one of sustainability as all activities are funded through the national health budget.

**Germany**

Germany has experienced a recent influx of refugees and asylum seekers with more than 1 million received in 2015 and more than 150,000 so far in 2016. The majority are from Syria, Iraq, Afghanistan and Pakistan. Upon arrival in reception centres all refugees and asylum seekers are given an initial mandatory screening to exclude infectious diseases and additional screening, vaccination and a first medical examination are offered, with treatment of ill individuals and pregnant women. No medical insurance for refugees is available in the first 15 months after arrival but medical treatment vouchers or electronic health care cards are provided for treatment of acute illness.

New arrivals are now entitled to receive the same vaccines as the German population, but many do not have vaccination cards or records of vaccines received, and thus are regarded as ‘unimmunized’. Children up to 13 years of age are offered measles/mumps/rubella/varicella vaccine (MMR-V), children older than 13 years and adults born after 1970 are offered MMR. An extensive information guide on health care in Germany has been provided by the Ministry of Health in 5 languages, and the Robert Koch Institute vaccination schedules and information materials are provided in 20 languages.

**Australia**

Australia was verified as having interrupted endemic measles transmission for at least 36 months in 2014, and is currently planning to provide evidence for having interrupted endemic rubella transmission and eliminated congenital rubella syndrome in 2017. In 1998 Australia introduced an incentivised system for families and family doctors, providing tax deductions to parents and payment to family doctors, in support of the national measles control programme. Results from serosurveys conducted before and after the main campaign in 1998 showed statistically significant closure of the immunity gap with immunisation coverage increasing from 80 to 90% in preschool children and 84% to 94% in primary school children. The policy was revised in 2016 so that only parents of children (less than 20 years of age) who are fully immunised or are on a recognised catch-up schedule can receive Child Care Benefits, a Child Care Rebate and the Family Tax Benefits. All vaccinations must be recorded on the Australian Childhood Immunisation Register. Children with medical contraindications or natural immunity for certain diseases continue to be exempt from the requirements based on standardised doctors’ reports. Conscientious objection and vaccination objection on non-medical grounds are no longer valid exemption from immunisation requirements. The system has been marketed as ‘no jab – no pay’.
Free catch-up with National Immunization Programmes (NIP) vaccines are offered to all children less than 10 years of age on an on-going basis, and free catch-up NIP vaccines are offered to all children 10 to 19 years of age until the end of December 2017. Some States provide free vaccination for adult international travellers who have not had two doses of MCV.

**Japan**

A large measles outbreak in Japan in 2007 and 2008, occurring mostly in adolescents and young adults, resulted in the closure of more than 250 high schools and universities around the country and the export of infection to many other countries. In response the Government developed a National Plan and Strategy to achieve and maintain 95% population immunity of each birth cohort in every district using measles-rubella vaccine. The Plan included recommendations for immunization strategies, implementation of case-based measles surveillance, and underscored the importance of epidemiological investigation. The Strategy placed local governments, schools, civil societies, parents and students at the centre of measles elimination activities. A catch-up vaccination campaign for older children was introduced in 2008, targeting specific school-aged cohorts, those aged 12 to 13 years and 17 to 18 years, and continued on an annual basis until 2013. Results of periodic national seroprevalence studies showed that by 2014 the immunity gap in older children and young adults had been closed. Japan was verified as having eliminated measles in 2015.

**Brazil**

Brazil has achieved and maintained high routine coverage with MCV and RCV for many years, supplemented with frequent campaigns targeted at specific groups, including catch-up campaigns. In 1998 and 2000 to 2001 MR vaccination campaigns targeted women of fertile age in support of the programme for prevention of rubella and congenital rubella syndrome. An analysis of vaccination opportunities by birth cohort showed that the majority of persons that had not been targeted by rubella vaccination strategies were males between 20 and 39 years of age, but there remained a small percentage of susceptible women that resulted in a number of children born with CRS. In 2008 a mass vaccination campaign with MR and MMR, targeting men and women aged 20 to 39 years, was conducted to contain an outbreak of rubella that had started in 2006. A total of 67 million doses were administered and although high overall coverage was achieved it was not homogeneous, with some areas achieving <95% coverage.

The last endemic measles case had occurred in 2002, but an outbreak in 2014-2015 revealed that vaccine coverage in the cohort aged 10 to 25 years was suboptimal. The outbreak started in Pernambuco but spread to Ceara. In Pernambuco the highest incidence was in those in < 1 year of age. In Ceara the highest incidence was also in infants < 1 year of age but the majority of cases occurred in adolescents and adults aged 15 to 30 years.
In response to the outbreak SIAs using MMR were conducted targeting infants and children aged 6 months to 4 years and children and adults aged 5 to 29 years in areas affected by the outbreak. Strategies for conducting the SIAs included establishing partnerships with the education sector and civic society, and extensive social mobilisation through the use of social and mass media. The campaign included house to house vaccination in areas considered to be at highest risk.

**The use of Speed-Up Campaigns in PAHO**

The Pan American Health Organization (PAHO) has designed and implemented a number of different vaccination and case based surveillance strategies towards measles and rubella elimination. The “Speed-Up” campaign was aligned with the “Catch-up” and “Follow-up” campaign strategies following the 2003 Regional resolution for the elimination of rubella and CRS. The experience in PAHO was driven initially by success achieved in a Caribbean-wide initiative. The Regional coordination led to improved surveillance and laboratory performance and results. Standardized case definitions and other surveillance procedures were implemented region-wide, benefitting cross-border disease control efforts. In addition, the use of Vaccination Week in the Americas allowed some groups of countries to coordinate vaccination campaigns across borders. Micro-plans were used at the community level only and rapid coverage monitoring helped improve coverage in many communities. It was estimated that the vaccination strategy for measles cost $1.10 per individual, but saved $280 million; the strategy for rubella and CRS saved $3 billion and has prevented >112,500 cases in Latin America and the Caribbean.

Implementing and monitoring high-quality Speed-Up Campaigns to vaccinate approximately 250 million adolescents and adults required careful planning and preparation. The first challenge was to establish the target population, and every country conducted an analysis of their susceptible population and the burden of disease. Some seroprevalence studies were implemented (Chile, Costa Rica, and Argentina) to complement the analysis. The target population for vaccination in most countries was adolescents and young adults aged 15-39 years. Each country could extend this range according to its own analysis of susceptibility and availability of financial resources, and each country was required to tailor strategies to address hard to reach areas and populations. A timeframe of nine months was established to conduct the Speed Up campaign, with the first three months used for national level planning, mobilizing resources and designing technical guidelines for training. The second three months were allocated for subnational and local level organization, including microplanning, logistics, training, and developing the social communication strategy. One and a half months were allocated to vaccination activities and one and a half months for evaluation of campaign effectiveness.

Greater than 60% of the Speed Up campaigns were conducted during the period 2004 – 2008. Between 1998-2008, Speed Up mass campaigns were conducted in 32 countries and 250 million adolescents and adults were
vaccinated, having a dramatic impact on both rubella and measles elimination. Three key factors in making Speed Up campaigns a success: the synchronised nature of the campaigns in Latin American countries; the large scale nature of activities targeting both men and women aged 15 to 39 years of age; and the short time-span in which these activities took place. Critical to achieving rubella and measles elimination has been the strong leadership provided at the highest political and scientific levels, and the spirit of Pan-Americanism that links the countries together.

Discussion

A common experience in several countries has been that academic and professional associations, together with civil society, have been developing the arguments and preparing for measles and rubella control activities in parallel of national health authorities. These groups can play a significant role in advocating, promoting and implementing national control policies when developed by the government. Although effectively used in the Americas, the relevance of Speed Up campaigns in other Regions will depend on the implementation of the above mentioned three key factors to vaccinate pockets of susceptible individuals in a wide age-range, in each country. The experience of the Americas has proof that Speed up campaigns are a cost-effective strategy to eliminate measles and rubella virus.

The Americas is a Region with some unique characteristics, including the revolving fund that has been essential for providing access to high volumes of low-cost vaccines, enabling member countries to successfully employ this strategy, but it is accepted that it may not be a feasible strategy for use in all countries.

Session 2B: Responses to fill immunity gaps: Experiences from the regions

Using routine immunization (RI) system capacity to address immunity gap

England (UK)

Following the loss of confidence in MR vaccine based on fraudulent “science” in late 1990s, England re-established measles transmission from 2005. The past 10 years, however, have seen strong growth in routine coverage with reestablishment of confidence in vaccination, but left a cohort susceptible to measles. In response to measles outbreaks in 2013 health authorities conducted an MMR catch-up campaign targeting unvaccinated 10 to 16 year olds. Although only 9 to 11% of the primary target group had received catch-up vaccine by August
2013, the decline in the number of reported measles cases was dramatic. In preparation for the campaign there was a requirement to engage and educate the media to guide public opinion and gain public support for vaccination. Considerable effort was expended in working with the media for developing effective communication and social engagement strategies. Press coverage of vaccination and immunization services have been monitored and work with the media undertaken to promote positive coverage of immunization services. To monitor the levels of public support and understanding of vaccination public opinion polls were undertaken, which were long-standing and are ongoing.

**Sri Lanka**

To guide the timing and selection of target populations for SIAs Sri Lanka has attempted to establish measles susceptibility profiles by age, using available surveillance and coverage data, serosurveillance data, and field-level vaccine efficacy studies. The country has achieved high coverage with MCV 1 and 2, but a large measles outbreak started in 2013 and, though now waning, continues. In 2014 an SIA was conducted, targeting infants 6 to 11 months of age. A campaign to vaccinate high risk populations, including university staff, health workers and prisoners was also undertaken.

**Chile**

Chile began using vaccination campaigns in 1992, and has continued with catch-up campaigns every 5 years. Although campaign coverage was initially high the campaigns in 2010 and 2015 only attained 75% and 82% coverage respectively. A National Record of immunization (RNI) was introduced starting in 2010 and is now the official source of data for vaccinations. With over 10 million people already registered, and 1,196 health facilities accessing the register, it is used by both public and private health sectors to provide timely information on the status of the immunization programme. Data analysis provides a detailed summary of routine vaccine coverage, and can be used to monitor and assess campaigns. The register is also used to record and report vaccine rejections and to identify unvaccinated and under-vaccinated children.

Chile has also developed a risk assessment matrix to monitor risk of reintroduction of measles, based on geographic location of susceptibles. To help identify potential immunity gaps a serosurvey was conducted in 2011 using serum samples collected during the 2009 National Health Survey. The serosurvey indicated a potential measles immunity gap in the 30 to 40 years age group and prompted attempts to target this age group for further serosurvey.

**Austria**

To control measles and rubella the vaccination recommendations in Austria have recently been changed to provide the first dose of MMR at 11 months of age with the second dose as early as possible, but not earlier than 4 weeks after the first dose. Missed doses of MMR should be caught up at any time and vaccination is
recommended for all adults lacking immunity and or missing documentation of 2 doses of MMR vaccine. Vaccination is free of charge for everyone.

In 2010 a survey was conducted on the attitudes of the population aged 16 years and above towards vaccination using a web-based questionnaire. Of the 1,000 respondents, 64% believed in the benefits of vaccination, while 35% were not convinced of the benefits of vaccination. When requested to imagine they were not vaccinated against measles, only 32% believed that measles represented a threat.

In 2013 a National Action Plan for the elimination of measles, rubella and CRS was published, accompanied by the launch of an extensive communications and social mobilization programme in January 2014. The annual number of distributed doses of MMR in 2014 increased by 19% over the number distributed in 2013, and in 2015 increased by 26% over 2014, with the result suggesting that vaccination rates among children of 1 year of age are now very high. In addition, 30,000 doses of MMR have been provided through the adult catch-up campaign. A publicity campaign on the benefits of vaccination has been launched, emphasising the importance of educating and vaccinating health workers.

A plan to accurately evaluate vaccine coverage rates is now being developed using a cohort model that considers the distributed, administered and total number of vaccine doses sold. The aim is to provide evidence-based data for the re-evaluation of current vaccination coverage rates in different age groups, taking the effects of migration into consideration, evaluating the effects of vaccination campaigns and identifying potential gaps in population immunity.

**Colombia**

The last measles endemic case in Colombia was reported in 2002 and the last rubella endemic case was reported in 2009. Catch-up vaccination campaigns for children and adolescents were conducted during the 1990s and a Speed Up campaign was conducted in 2005 targeting 14 to 39 year olds. Following an import-related measles outbreak in 2011 a cohort population analysis was conducted and susceptible individuals (almost 1 million) were identified in the 10 to 19 years age group. A strategy for closing this immunity gap was developed and implemented, by obtaining the highest level political commitment, and by securing $11.5 million for the vaccination campaign. There was also a call for mobilization of the entire country and from all communities. Due to limited vaccine availability, a roll-over vaccination strategy in three phases was developed. The first phase targeted the 3 departments involved in the measles outbreak, the second phase targeted 8 departments, and the final phase targeted 21 departments. The campaign was supported by a high level of social mobilization making use of all forms of media and support from religious and opinion leaders and celebrities. The epidemiological surveillance system was strengthened by improving and disseminating protocols for outbreak control, engaging the commitment of health personnel towards the sustainability of measles and rubella elimination. Inter-
institutional coordination with the education sector, health insurers, churches, NGOs, academic and scientific societies, and community groups, was also strengthened.

The campaign delivered approximately 7.7 million vaccine doses, resulting in 88.4% vaccination coverage. No additional measles cases were identified despite intensified surveillance and active case finding (institutional and community). A total of 1,122 rapid convenience monitoring surveys were implemented in each municipality, in which 218,611 adolescents and children were interviewed, and 97% were vaccinated.

**Malawi**

In Malawi, measles was a major childhood public health problem until 1998 when the first catch–up vaccination campaign, targeting all children ≤15 years, was conducted. Follow-up campaigns were conducted in 2002, 2005 and 2008 targeting children ≤5 years and achieving ≥95% coverage. A widespread measles outbreak occurred in 2010 with more than 118,000 reported cases. In response a second catch up measles campaign was conducted in 2010 targeting children ≤15 years with a follow up SIA in 2013 targeting children ≤5 years.

Malawi uses the Measles Risk Assessment Tool to determine susceptibility in adolescent and adult populations. The programme has mapped out hard to reach areas and socially isolated populations, deploying mobile teams to provide immunization services in hard to reach areas, and relying on updated micro-plans to ensure that all communities are included. Services have been prioritized to reach the largest number of unvaccinated individuals.

**Discussion**

Several countries already have sufficient data from surveillance activities, coverage estimates and knowledge of the history of introduction of vaccines into their schedules, to predict age-related immunity gaps. When this data has been cleaned, assessed and analysed it can show that potential immunity gaps are smaller than anticipated and identified gaps can be addressed through local catch-up campaigns. The availability of high-quality data from several countries has demonstrated that even small gains in the level of vaccine coverage (e.g., England) can have a dramatic effect in stopping virus transmission, although it may take considerable effort and investment to reach the groups that have historically missed out.
Session 3: Professional and civil societies in MR elimination activities B: Responses

There is a clear and growing need to develop and strengthen collaborative relationships between professional societies, such as the International Paediatric Associations (IPA) and the various national paediatric associations and academies, civil societies, such as the Lions Clubs International Foundation and the many country-based Lions Clubs, and the measles and rubella elimination programmes at global, regional and national levels. The professional and civil societies represent well-established and extensive organisations able to contribute both high-quality technical and scientific input and information, and a well-respected presence in-country that can be used for advocacy, social mobilisation and outreach activities. These societies are independent of governments and, as such, tend to be trusted by sectors of local populations that are wary of government interventions.

Session 4: Putting it all together

How big is the problem?

Although clearly an emerging phenomenon documented in several countries and Regions that have achieved high levels of coverage with childhood vaccination programmes, but with inadequate coverage levels to guarantee elimination of transmission, the scale of the problem of immunity gaps in adolescent and adult populations is difficult to assess at the global level. In some recent measles outbreaks susceptible adolescents and young adults have represented a significant proportion of detected cases, but their role in sustaining transmission has been difficult to determine. Recent evidence from a measles outbreak in China² demonstrates that adolescents and young adults can be important links in chains of virus transmission, but evidence that susceptible adult populations can maintain virus transmission in the absence of susceptible childhood populations is, so far, inconclusive.

A more comprehensive literature review of relevant published data, currently being undertaken, should provide further insight into the importance of susceptible populations of adolescents and young adults in maintaining virus transmission, and the level of challenge they pose to achieving measles and rubella elimination goals.

When is it necessary to fill immunity gaps?

While the focus of measles and rubella elimination programmes should be on preventing the further accumulation of susceptible age cohorts by ensuring timely high coverage with two doses of measles and rubella containing vaccines in each successive birth cohort, the presence of existing immunity gaps in older children, adolescents and young adults poses a potential threat that may challenge measles and rubella elimination goals. The level of priority that should be given to addressing these immunity gaps, however, remains unclear. Available evidence suggests that the continued existence of these immunity gaps poses a credible potential threat challenging the measles and rubella elimination goals.

Experience gained in Malawi where measles outbreaks included significant numbers of adolescent and adult cases, suggests that young adults may not need to be targeted in order to stop outbreaks. Successive high coverage SIAs targeting children <5 years failed to establish a level of herd immunity necessary to prevent a large-scale measles outbreak in 2010. A repeat “catch up” measles SIA targeting children <15 years old was effective in substantially reducing transmission. Other countries with similar experiences include Tanzania, Namibia, South Africa, and Viet Nam. In contrast, a nationwide outbreak response campaign in Mongolia targeting children 6 months to 6 years old and high risk adults during May 2015 appeared to stop a measles outbreak in spite of a large percentage of cases ages 18 – 25 years old. However, a resurgence of reported measles cases that began six months later, among which 27% were 10-19 years old, 32% were 20-29 years old and 14% were ≥ 30 years old, suggests that an SIA targeting a wider age group likely was needed.

Although immunity gaps in adolescents and adults are known or strongly suspected to exist in many countries, they do not all necessarily pose the same level of risk. Account must be taken of the level of childhood vaccine coverage, population density, migration and the geographical spacing of susceptible individuals. The level of vaccine coverage and virus transmission in neighbouring countries may also be a composite factor contributing to the risk posed by age-specific immunity gaps. In countries with consistently high childhood vaccination coverage, moderate to low population density and a broad scattering of susceptibles, the risk of virus transmission can probably be regarded as low. In countries with inconsistent or low childhood vaccine coverage, high population density and grouping of susceptible individuals into particular communities or areas, adolescents and young adults may play a role in in measles virus transmission to infants and children; closing immunity gaps in these adolescent and adult populations may therefore be desirable or even necessary.

How do we detect an immunity gap?

Detection of immunity gaps relies on the effective collection, analysis and interpretation of high-quality data, an area that remains a challenge in many countries. Effective data management, from collection to analysis, often
requires active participation of staff at subnational levels to ensure that data collected is both accurate and complete, and that any conclusions drawn from the analysis is valid within local contexts.

**Case-based surveillance data**

Analysis of the ages and vaccination status of reported measles and rubella cases remains a useful method for detecting immunity gaps where case-based surveillance and high quality reporting has been established.

**Outbreak data**

Determination of the age-specific population profile of cases detected during disease outbreaks is of increasing importance for accurately describing and targeting immunity gaps, particularly in countries that have achieved high childhood vaccination coverage. In countries with well-established childhood vaccination programmes, infants and persons ≥ 15 years old account for an increasing percentage of cases in disease outbreaks.

**Historical coverage data and coverage surveys**

Documented evidence on the date of introduction of vaccine into national immunization programmes, the target groups and coverage achieved in each birth cohort, and an indication of the burden of disease at the time of vaccine introduction can be used to predict potential immunity gaps. Most countries have this data, although its quality and completeness may be questionable, and data cleaning exercises may be required before the data can be used effectively.

Coverage surveys, using well-developed and widely available tools, such as the WHO Vaccination Coverage Cluster Survey, are usually employed to monitor routine childhood immunization programmes, supplementary immunization activities and campaigns targeted at younger age groups. As such, current surveys do not address the issue of immunity gaps in older children and adults, but the results of surveys conducted in previous decades may provide evidence of potential gaps in specific age cohorts and geographically identified sub-populations with recorded low coverage that have not been subsequently addressed through supplementary immunization activities.

**Serosurveys**

Direct determination of antibody prevalence in a population is an attractive and potentially powerful tool for revealing immunity gaps, but is fraught with technical and logistical problems. In countries with a well-developed health infrastructure and a documented history of conducting periodic cross-sectional serosurveys, seroprevalence data can reveal age-specific immunity gaps and provide health authorities with valuable information to target interventions as well as information used for advocacy to improve political commitment in
some situations. However, the cost effectiveness of conducting new serosurveys to specifically detect age-related immunity gaps in large populations is questionable and the technical resource requirements may overstretch national capacity to deliver results that can be accurately interpreted.

**Triangulation**

In practice most countries use a process of triangulation of data from multiple sources, such as surveillance and outbreak investigation data, coverage data and the history of vaccine introductions to investigate population immunity and detect potential immunity gaps. Dynamic modelling, using surveillance and outbreak data together with birth rate and coverage data has also been used to predict potential age-specific immunity gaps. The specificity and accuracy of triangulation and modelling is dependent on the quality, extent and nature of data available, which can be problematic in some countries.

**What strategies do we have to address the gaps?**

The many country presentations during this symposium have illustrated a variety of approaches that can be taken to address immunity gaps among different age groups. Solutions to address country-specific issues, such as age-related immunity gaps, often need to be tailor-made to fit the local context. The use of micro-planning, based on detailed local knowledge that can be used to identify and remove local barriers, is critical to the level of success that can be achieved.

Instead of very wide age range SIAs, a more selective adult strategy could be to specifically target higher risk groups and professions, particularly health workers, teachers and students at schools and universities, staff in the travel and hospitality industries, members of the police and military forces, long-term residents of institutions and workers or others that live in communal settings. Routine immunization and health services need to be structured to utilize opportunities to review vaccination status and, if needed, to vaccinate persons during any contact with the health services.

The "Guide to tailoring immunization programmes (TIP)", published by the WHO Regional Office for Europe in 2013, provides methods and tools to assist national immunization programmes (NIPs) in the design of targeted strategies that increase uptake of vaccinations. The Guide provides a systematic approach and tools to identify susceptible populations, determine potential barriers to vaccination and implement evidence-based interventions. Of increasing concern is the mass movement of migrants and refugees, their initial housing in refugee complexes and transit centres, and their longer-term integration and access to immunization services within host nations. Both immediate and longer-term strategies are required to specifically address these groups to ensure that they do not develop or maintain immunity gaps.
Developing and implementing a national plan of action for measles and rubella elimination is a key requisite for effective closure of immunity gaps. Establishing National Verification Committees to provide independent expert review and advise the NIPs is proving valuable in many countries. There is an increasing case to be made for regarding measles and rubella vaccines as ‘lifetime vaccines’ rather than ‘childhood vaccines’, and national health policies and strategies should reflect this. National health policies to address immunity gaps can be directive, such as making it necessary for all health workers to receive vaccine as a requirement for employment, or making it a requirement for day-care, school or university entry. Alternatively, health policies may incentivize behaviours by providing incentives, such as additional payments for family doctors for giving vaccines, and/or taxation breaks or benefits to parents for ensuring their children are fully vaccinated. Less directive policies, such as screening of immunization records at school entry and public reporting of vaccination rates at hospitals and other facilities can also be used to supplement surveillance information. In order to gain high-level political commitment for immunization services the positive public health benefits of vaccination need to be emphasized and the cost-effectiveness of vaccination as a national investment needs to be promoted.

Professional societies, civil society and NGOs have an essential role to play in advocacy for immunization, public education on vaccination, and social mobilization and promotion, particularly through the established media and social media. As well-respected, trusted multi-sectoral non-government agencies, these groups and societies can often have an impact on public opinion and acceptance that government agencies sometimes struggle to achieve. These groups are often well placed to participate in vaccination awareness campaigns with monitoring and follow-through.

There is now a unique opportunity to make best use of the polio eradication legacy to fully coordinate a global effort for measles and rubella elimination, through the establishment of a World Health Assembly (WHA) resolution on eradication and full alignment of the measles and rubella programmes of global partners. This would help persuade vaccine manufacturers to increase the global level of vaccine production, including the entry of new, licenced vaccine producers into the market, and persuade national governments and international partners on the need for further investment in vaccine cold chain and delivery systems. It would also emphasise the need for more comprehensive and accurate recording, reporting and analysis of vaccine coverage through the use of computerised national immunization registers and the greater use of available information technology and ‘smart tools’ to record and monitor vaccination events. The window of opportunity for global eradication of measles, rubella and CRS may be closing, as the epidemiology of measles and rubella continues to evolve with increasing numbers of susceptible adults and infants complicating established strategies for elimination. The cost effectiveness of measles eradication will be maximized if it can be accomplished sooner rather than later.