

## Action needed now to prevent further increases in measles and measles deaths in the coming years



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Measles is a deadly disease that has killed or disabled millions of children over centuries.<sup>1</sup> In 1980, when most children in low-income countries did not have access to measles vaccine, it was estimated that measles led to the deaths of more than 2 million children.<sup>2</sup> Advances in child survival during the next two decades were partly due to the provision of measles vaccine for children in all countries through the Expanded Programme on Immunization.<sup>3</sup> By 2000, estimated global measles mortality was 539 000 deaths per year.<sup>4</sup> Further declines followed the introduction of catch-up vaccination campaigns to immunise children missed by routine immunisation. Measles cases declined through 2008, and regional elimination targets for measles were established thereafter.<sup>5</sup> In 2016, when measles elimination was verified for the Americas, the global number of reported measles cases reached a low of 132 490.<sup>4</sup> But measles is extremely infectious, with a basic reproduction number of 12–18.<sup>6</sup> At least 95% vaccination coverage is required for herd immunity. Globally, estimated measles vaccine coverage in 2019 was 85% and 71% for the first and second doses of measles-containing vaccine respectively,<sup>4</sup> which combined with poor immunisation campaign performance has left major immunity gaps likely to result in measles outbreaks. Non-uniform vaccination coverage, whether due to problems with accessing vaccination services or vaccine hesitancy, leads to clusters of non-immune individuals, even if overall vaccination coverage exceeds 95%.

In 2017–19, measles outbreaks increased worldwide. Measles re-emerged in Venezuela in 2017,<sup>7</sup> especially among Indigenous communities, and spread to neighbouring countries, leading to loss of elimination status in the region of the Americas. Major outbreaks occurred in all WHO regions in 2018, and in 2019, 869 770 measles cases were reported to WHO, the most since 1996.<sup>4</sup> Yet reported cases are always an underestimate. Patel and colleagues<sup>4</sup> estimate that in 2019 the number of measles cases was about 9·8 million worldwide and that there were 207 500 global deaths from measles—50% more deaths than in 2016.<sup>4</sup> Most measles deaths in 2019 have been in Africa, many associated with major outbreaks in Madagascar and the Democratic Republic of the Congo.<sup>4</sup>

Modelled mortality estimates are dependent on case fatality ratios (CFRs). Regional CFR estimates are based on a systematic review of published reports, adjusted for poverty, crowding, malnutrition, and immunisation coverage. Improvements in these factors have led the CFR estimates to trend downward over time.<sup>1,8–10</sup>

The COVID-19 pandemic has had a profound effect on global immunisation and control of vaccine-preventable diseases, with vaccination campaigns paused in the early months of 2020 and routine immunisation services greatly disrupted in many countries.<sup>11</sup> However, modelled evidence suggests that the potential risks of delaying vaccination outweigh the risks associated with COVID-19.<sup>12</sup> Since March, most countries have resumed routine immunisation and restarted preventive and outbreak response campaigns to reduce the number of children left susceptible to measles and other vaccine-preventable diseases.<sup>11</sup> Despite these efforts, WHO estimates that by the end of October, 2020, delays to vaccination campaigns in 26 countries have led to 94 million children missing scheduled measles vaccine doses, placing many of them at risk of measles.<sup>13</sup>

Surveillance data from the first 6 months of 2020 suggest that measles case numbers are down in most countries, but this decline is ominous rather than reassuring, portending future outbreaks.<sup>14</sup> The 2020 case reduction is typical of the epidemic cycle of measles, and



Surveillance and Immunisation Medical Officer (WHO) Sylhet City Corporation, Bangladesh, Dr Nafise Ahmed Najem/World Health Organization

probably also reflects reduced transmission of respiratory viruses due to COVID-19 control measures and reduced domestic and international travel. Compromised surveillance and reporting also have a role, with disruptions in many countries. Furthermore, the inadequate vaccination that was responsible for the 2019 measles outbreaks has not been adequately addressed, and the situation is now exacerbated by service disruptions during the COVID-19 pandemic so that high-risk, unimmunised children are clustered together in unreached communities.

The COVID-19 pandemic has adversely affected the economies of all countries. This economic impact is felt most strongly by families in the most deprived communities, where increased malnutrition is an inevitable consequence.<sup>15</sup> The relation between malnutrition and measles is complex.<sup>16,17</sup> Children who die from measles are often malnourished, but acute measles pushes many surviving children into malnutrition. The extent to which children with pre-existing malnutrition are more likely to die with measles is unclear. Malnutrition, along with measles-associated immune suppression, leads to delayed mortality, while co-existing vitamin A deficiency can also lead to measles-associated blindness.<sup>18</sup>

The coming months are likely to see increasing numbers of unimmunised children who are susceptible to measles, many living in poor, remote communities where health systems are less resilient, and malnutrition and vitamin A deficiency are increasing. All these factors are likely to increase measles CFRs, creating the environment for measles to return in 2021, accompanied by increased mortality and the serious consequences of measles that were common decades ago.<sup>9,14</sup> This is despite the fact that we have a highly cost-effective way to prevent this disease through measles vaccination.<sup>19</sup>

Three pillars of action are needed to address this concerning situation. First, urgent action is required to address the immediate risk of measles outbreaks by helping countries to reach unimmunised children through catch-up and campaigns. Second, countries need to prepare for the expected outbreaks. WHO and partners have developed a Strategic Response Plan to assist with measles outbreak prevention, preparedness, and response, and have launched a call to action and funding appeal.<sup>20</sup> These additional resources would complement the support from Gavi, the Vaccine Alliance, which does not extend to many middle-income countries. Finally, the international community must

not lose sight of measles and rubella elimination targets. The Measles & Rubella Initiative's new Measles and Rubella Strategic Framework 2021–2030,<sup>21</sup> aligned with WHO's Immunization Agenda 2030,<sup>22</sup> provides a plan for strengthening routine immunisation and surveillance. These are the solutions to end the cycle of inadequate immunisation and outbreaks of the past decade. Without concerted efforts now, it is likely that the coming years will see an increase in measles and its severe, frequently fatal, complications.

KM reports a grant from Pfizer as co-investigator for a study to evaluate the indirect impact of childhood PCV13 vaccination on adult pneumonia in Mongolia. KM is a member of the WHO Strategic Advisory Group of Experts (SAGE) on Immunization and Chair of the SAGE Measles and Rubella Working Group. KK and NC are co-authors and they contributed substantially to the following publications discussed in this Comment: the report by Patel and colleagues,<sup>4</sup> the WHO strategic response plan,<sup>20</sup> and the Measles and Rubella Strategic Framework 2021–2030.<sup>21</sup> LW declares no competing interests.

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\**Kim Mulholland, Katrina Kretsinger, Liya Wondwossen, Natasha Crowcroft*  
kim.mulholland@lshtm.ac.uk

Murdoch Children's Research Institute, Royal Children's Hospital, Melbourne, VIC 3051, Australia (KM); Department of Paediatrics, University of Melbourne, Melbourne, VIC, Australia (KM); London School of Hygiene & Tropical Medicine, London, UK (KM); Immunization, Vaccines and Biologicals, World Health Organization, Geneva, Switzerland (KK, NC); Human Papilloma Virus Vaccine Technical Assistance, PATH, Addis Ababa, Ethiopia (LW); and Centre for Vaccine Preventable Diseases, University of Toronto, Toronto, ON, Canada (NC)

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