



# COVID-19, seasonal influenza and measles: potential triple burden and the role of flu and MMR vaccines

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Policy interventions aimed at reducing person-to-person transmission of SARS-CoV-2 (such as hand hygiene, physical distancing and wearing face coverings) were implemented globally to minimise healthcare burden, and to allow more time for an effective treatment and successful vaccine.<sup>1,2</sup> After months of ‘lockdown’, many countries started to ease these measures recently only to see a surge in COVID-19 cases and deaths. During the winter of 2020–2021, we face the prospect of a dual burden of a COVID-19 pandemic and a seasonal influenza epidemic.<sup>3</sup> However, what’s not being currently discussed is that the burden on healthcare could be further compounded by a potential surge of measles and rubella cases. This is due to: (1) a declining trend in Measles-Mumps-Rubella vaccine coverage accompanied by an increasing trend in Measles-Mumps-Rubella cases since 2016;<sup>4</sup> and (2) disruption and suspension of Measles-Mumps-Rubella vaccination campaigns in 23 countries to cope with the COVID-19 pandemic.<sup>5</sup>

Each of these diseases can result in life-threatening illnesses and death: more than 685,000 COVID-19 deaths (as of 2 August 2020), an estimated 291,243–645,832 influenza-associated respiratory deaths per year (1999–2015), and approximately 9,769,400 cases and 142,300 deaths from measles in 2018 alone.<sup>4,6</sup> Moreover, these diseases disproportionately affect certain vulnerable populations, including the elderly, ethnic minorities and people from lower socioeconomic status.<sup>7,8</sup> While we wait for an effective vaccine against SARS-CoV-2, the influenza and Measles-Mumps-Rubella vaccine with proven safety and efficacy profile can play critical role in reducing the healthcare burden.

First, an increase in the coverage of influenza and Measles-Mumps-Rubella vaccines will decrease the

number of cases and the need for hospitalisations for severe illnesses due to these diseases. It will, thereby, reduce the burden on healthcare providers and facilities, which will be particularly crucial in resource-poor settings in making the scarce resources (e.g. hospital beds) allocated to those who need them the most. A lower rate of hospitalisation from influenza and Measles-Mumps-Rubella will also help reduce the transmission of COVID-19 by decreasing the exposure to SARS-CoV-2 of the at-risk population, patients and their caregivers, such as parents of young children.<sup>9</sup>

Second, live attenuated vaccines such as Measles-Mumps-Rubella and Bacillus Calmette–Guérin have been reported to provide non-specific protection against lethal infections including pneumonia and sepsis, especially in low-income settings.<sup>10</sup> The precise mechanisms by which these vaccine-related non-specific protections work are not completely understood, but at least two mechanisms have been documented: vaccine-induced trained immunity and emergency granulopoiesis (more technical details are available in Aaby et al.<sup>10</sup>). Moreover, SARS-CoV-2 is a single-stranded positive-sense RNA virus, which shares similarity in structure with the yellow fever virus and murine Mengo virus. The Bacillus Calmette–Guérin vaccine was found to reduce the severity of infections due to yellow fever and murine Mengo viruses showing the potential that the Bacillus Calmette–Guérin vaccination may reduce COVID-19 severity as well. However, further empirical research is required to confirm the role of the Bacillus Calmette–Guérin and Measles-Mumps-Rubella vaccines on COVID-19 disease burden and outcomes.

Third, infection with measles has been shown to increase children’s susceptibility to other infections

by reducing the immune system's memory against other pathogens including the influenza virus.<sup>11</sup> Therefore, infection with measles may also increase the susceptibility to SARS-CoV-2 even though it is yet to be empirically tested. Nevertheless, an expanded Measles-Mumps-Rubella vaccine coverage will certainly reduce the number of cases with measles and potentially other diseases through non-specific protection, as described above, and will decrease the exposure to SARS-CoV-2 for at-risk children and their parents by reducing the need for hospitalisations.

Therefore, as we wait for a successful vaccine for COVID-19, we can minimise winter pressures on health systems and societies by maximising the uptake of influenza and Measles-Mumps-Rubella vaccines (and potentially Bacillus Calmette–Guérin vaccines, especially in tuberculosis-endemic areas). It is to be noted that the proposal for expanding the vaccine coverage is for the intended purpose of protecting the at-risk population in which the vaccines have an established efficacy and safety profile. From the implementation perspectives, however, these actions come with some potential challenges. For example, uptake of the flu vaccine has often been low in younger at-risk patients (those aged <65 years) and among health and care staff in many countries, including the UK.<sup>12</sup> Even though many governments plan an expanded flu vaccination programme, the concurrent COVID-19 pandemic will make it challenging due to the need for good infection control (e.g. maintaining social distancing during the vaccination program, scarcity of personal protective equipment by the healthcare professional carrying out the vaccination campaign in resource-poor settings). Therefore, it is imperative that the planning for these vaccination programmes starts sooner to ensure a high coverage and uptake by the at-risk populations, including the healthcare providers.

### Declarations

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