Without vaccination against 10 diseases, mortality in children would be 45% higher: study

January 29 2021

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Vaccinations against 10 major pathogens have a substantial impact on public health in low-income and middle-income countries (LMICs),

according to new modelling research published in *The Lancet*. The study estimated that from 2000 to 2019 vaccinations have prevented 37 million deaths, and that this figure will increase to 69 million deaths for the period 2000-2030. Most of this impact is estimated to be among children younger than five years, most notably from measles vaccinations.

Vaccines are cost-effective health interventions that substantially reduce death and illness from a range of diseases. International programmes have increased the coverage of routine childhood vaccines in LMICs and descriptions of impact are needed to inform future investment. Direct measurement of impact is difficult due to limitations in data and disease surveillance systems. Mathematical models can provide valuable estimates of impact based on data on disease burden and vaccine coverage.

The new study involved 16 independent research groups modelling the impact of childhood vaccination programmes in 98 LMICs. The study assessed impact of vaccination programmes against ten pathogens: hepatitis B (HepB), Haemophilus influenzae type b (Hib), human papillomavirus (HPV), Japanese encephalitis (JE), measles, Neisseria meningitidis serogroup A (MenA), Streptococcus pneumoniae, rotavirus, rubella virus and yellow fever virus (YF).

Dr. Caroline Trotter from the University of Cambridge UK, and a co-author on the study, said: "There has been a much-needed investment in childhood vaccination programmes in low-income and middle-income countries (LMICs) and this has led to an increase in the number of children vaccinated. To inform future investment and ensure it continues we need to evaluate the impact of these programmes on public health. Our modelling has provided robust evidence on the effectiveness of vaccination programmes in LMICs and indicated what might be lost if current vaccination programmes are not sustained."

Multiple models were applied for each pathogen (20 models in all) [2]. Estimates of impact were based on past and future coverage of individual vaccines, vaccine effectiveness and data on deaths caused by the diseases, and on the years of healthy life lost due to premature death and disability from the diseases (DALYs). By comparing a scenario with no vaccination programmes in place to scenarios when vaccinations programmes had been implemented, the study estimated the impact on deaths and on DALYs.

The study used two methods to assess impact to provide both a cross-sectional (yearly) and longer-term (lifetime) view of impact. The first method assessed the difference in the number of deaths between the vaccination and no vaccination scenarios for each year and then totalled these annual results.

The second method assessed the long-term impact of vaccination by summarising impact over the lifetime for groups of people who were born in the same year between 2000 and 2030 and then calculated the difference between vaccination and no vaccination scenarios. This approach allowed for the inclusion of vaccination impact later in life, which is particularly relevant for diseases such as hepatitis B or HPV where there is a long delay between infection and severe outcomes. Most of the impact of hepatitis B vaccination will be seen after 2030 whilst for HPV impact will be seen after 2040.

Results demonstrated that between 2000 and 2019 there was an increase in the average number of vaccines received per child, both for existing vaccines such as measles, and for new vaccines such as rotavirus.

Considering impact per year, the study estimates that from 2000 to 2030, vaccination will have prevented 69 million deaths from the 10 diseases, 37 million of which were averted between 2000 and 2019. Vaccinations against measles had the biggest impact, preventing 56

million deaths between 2000 and 2030.

In terms of the impact of vaccination over the lifetime of people born between 2000 and 2030, the study estimated that vaccination will prevent 120 million deaths, of which 65 million are in children younger than five years. 58 million of deaths would be prevented by measles vaccines and 38 million by hepatitis B vaccines.

Considering those born in 2019 the study estimated that increases in vaccine coverage and introductions of additional vaccines resulted in a 72% reduction in lifetime mortality caused by the 10 pathogens. By taking this 2019 birth cohort and using UN World Population Prospects demographic estimates, the study estimated that mortality in children under five in the 98 countries would be 45% higher in the absence of vaccination against the 10 pathogens.

The study also examined the relative impact of each vaccine and demonstrated that measles, Hib and pneumococcal conjugate vaccines (PCVs) have the largest impact on deaths of children under five. Vaccines against HPV, hepatitis B and yellow fever have the largest impact per person vaccinated over lifetime.

Corresponding author, Professor Neil Ferguson from Imperial College London, UK said: "Our study signifies the huge public health benefits that can be achieved from vaccination programmes in low-income and middle-income countries. By projecting up until 2030 in these 98 countries we have provided insight on where investments in vaccine coverage should be directed to achieve further gains, for example increasing HPV coverage in girls and pneumococcal conjugate vaccines (PCV) coverage in children under five will have the most impact according to our modelling."

Co-author Dr. Katy Gaythorpe, also from Imperial College London, UK

added: "By estimating how much higher mortality levels would be if there were no vaccination programmes in place, our study has highlighted how crucial it is to maintain high coverage levels. This will require continuing political commitment, funding, public engagement to promote the benefits and safety of vaccinations, and programmes to deliver education, training and supervision on immunisation."

Researchers reported the level of uncertainty from data on disease burden and from the structural assumptions of the different models but they were unable to evaluate uncertainty in demographic estimates and estimates of past and future vaccine coverage. The study flagged a number of limitations, for example for those countries where certain vaccines were yet to be introduced the study assumed they will reach the same coverage as a reference vaccine, which may lead to an overestimation of impact. In addition, no models accounted for variation in vaccine coverage according to geographic region or clustering of hard-to-reach groups. Researchers highlighted the need for future models to stratify impact for different populations within countries to achieve more detailed estimates.

  More information: Xiang Li et al. Estimating the health impact of vaccination against ten pathogens in 98 low-income and middle-income countries from 2000 to 2030: a modelling study, *The Lancet* (2021). DOI: 10.1016/S0140-6736(20)32657-X

Provided by Lancet