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Implementation strategies for passive respiratory syncytial virus immunisation

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Respiratory syncytial virus (RSV) is one of the last remaining major causes of serious paediatric respiratory infection for which no vaccine or other wide-scale intervention is available. Although an effective prophylactic antibody (palivizumab) has been available for more than two decades,[1] its effect on the overall disease burden has been modest. The relatively high cost of palivizumab and its narrow indication to only a small proportion of infants who are at high risk of infection[1] has meant that the majority of infants at high risk from RSV do not receive palivizumab prophylaxis. Collectively, these shortcomings have translated into a large unmet burden of disease that puts millions of infants at risk of serious, life-threatening disease every year.[2] The mortality burden due to RSV is disproportionately borne by children from low-income countries; data from 2010 suggest that more than 99% of RSV-attributable deaths occur in low-income and middle-income countries (LMICs).[3]

Despite this bleak outlook, remarkable progress in the development of prophylactic interventions has been achieved in the past decade. Advances in vaccine antigen design[4] and delivery,[5] as well as bioengineering innovations that have led to a substantial increase in the serum half-life of prophylactic antibodies,[6] have greatly increased the prospect of achieving an effective combination of interventions in this decade.[7] The most advanced strategies for preventing serious RSV disease in infancy involve passive immunisation through maternal vaccination and neonatal administration of long-acting monoclonal antibodies. One candidate for maternal vaccination has reported phase 3 efficacy data (ResVax [Novavax]), which has an efficacy of 44·4% against hospital admission in the first 6 months of life.[8] There is also one monoclonal antibody prophylactic with reported phase 3 efficacy data (nirsevimab), which has an efficacy of 78·4% against hospitalisation within the first 6 months of life.[9] These encouraging signs suggest that the goal of preventing severe RSV disease in the clinically vulnerable first year of life is now within reach.

In LMICs, the success or failure of these preventive approaches will depend heavily on the strategies that are used to implement them. To be feasible, the cost of implementation will need to fit within already strained national health budgets and will have to compete with many other pressing health priorities. One of the main questions that policy makers in LMICs will face is whether to administer these interventions all year round or target only the RSV transmission season and the months of the year that immediately precede it.

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Although the targeted seasonal strategy would probably yield considerable cost savings and increase the long-term viability of its implementation, the effect of this approach on the overall disease burden relative to a year-round approach has, until now, been unclear.

In *The Lancet Infectious Diseases*, the study by You Li and colleagues[10] is the first major effort to address this question. Using data from 52 LMICs, Li and colleagues calculated the effectiveness (the proportion of the annual RSV incidence or hospital admissions averted) for both the year-round and targeted seasonal approaches, and the relative efficiency (the ratio of cases or hospital admissions averted per intervention dose between the seasonal approaches and the year-round approach). The results of their analysis show a striking pattern. Whereas the targeted seasonal approaches for both maternal vaccination and monoclonal antibody prophylaxis are only marginally less effective than a year-round approach, they are both substantially more efficient. For example, in countries where the annual RSV epidemic lasts for 5 or fewer months, administration of monoclonal antibody prophylaxis 3 months before the start of the epidemic resulted in a median 16% (IQR 13–18) reduced effectiveness in averting hospital admissions compared with year-round administration, but it was a median 70% (50–97) more efficient. Results were similar for maternal vaccination—administration of the vaccine 1 month before the start of the RSV season was associated with a median of 27% (25–33) reduced effectiveness in preventing hospital admission compared with year-round vaccination, but it was a median of 126% (87–177) more efficient. In other words, in countries with a clear seasonal transmission pattern, more cases of RSV were prevented per dose administered in the targeted seasonal approach than in the year-round approach. The results of this study suggest a potential pathway for achieving a cost-effective rollout of preventive RSV interventions in LMICs. A seasonal dosing strategy would cut the cost of rolling out these interventions to a fraction of the cost of year-round administration, and could substantially boost the prospect of cost-effectively implementing passive immunisation programmes in LMICs.

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