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Protecting young children from influenza

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Take-home strategies: Evidence-based strategies are needed to ensure children targeted by influenza programmes get vaccinated.

Influenza is a major global cause of childhood morbidity and mortality [1, 2], straining healthcare resources particularly during epidemics and pandemics [3, 4]. Annual seasonal influenza vaccination programmes were launched to help reduce the burden of influenza but there is variation between countries on which children are targeted. Certain national programmes (e.g. Canada and the United States) recommend universal influenza vaccination [5, 6] while most European countries still focus mainly on groups considered to be at greater risk of influenza-related complications [7]. These include children with certain known underlying medical conditions and children under two years of age [8, 9].

In this issue of the *European Respiratory Journal*, Hardelid *et al.* provide evidence to inform influenza vaccine strategies by identifying risk factors for influenza-related hospital admission in children younger than two years of age [10]. The cohort study of 402,762 singleton livebirths in Scotland from 2007 and 2015 used data linkages between birth and death registration, hospital administrative data and influenza laboratory reports from 2009 to 2015 (six influenza seasons). They identified 1019 influenza-confirmed hospital admissions during the study period, or 2.57 per 1000 child years in children under 6 months and 2.07 per 1000 child years in children 6-23 months [10]. The study findings highlight several limitations of current influenza immunisation programmes.

Problems with current vaccination strategies

Targeting 'at-risk' groups is likely to have limited impact on hospitalisations. Hardelid and colleagues found that 85% of influenza-related hospital admissions in children aged 6 to 23 months occurred in children who were not known to be in a clinical risk group [10]. Additionally, targeting preventative strategies at these risk groups would only prevent between 3% and 6% of hospital admissions. Nevertheless, targeting 'at-risk' groups may be of value in prioritising resources during periods of high

influenza activity, and in reducing burden of illness associated with other outcomes not examined by Hardelid *et al.*, including complications managed in the community and prolonged hospital admissions.

Guidelines for vaccination of household contacts are inconsistent. Hardelid *et al.* found the strongest predictor for hospital admission in infants under 6 months of age was having one or more siblings [10]. Infants under 6 months of age are at particularly high risk of influenza-related complications as no influenza vaccines are currently licensed for use in this age group [11], and vaccinating pregnant women has only a limited protective effect [12, 13]. However, unlike in Canada and the US [5, 6], only 7 of 30 EU member states recommend influenza vaccination for household contacts of infants under 6 months of age [7]. The findings reported by Hardelid *et al.* therefore suggest that more widespread adoption of strategies involving vaccination of older siblings of young infants should be considered.

Delays incorporating new risk factors. Hardelid and colleagues also found that children aged 6 to 23 months born prematurely had a 47% increased risk of influenza-related hospitalisations [10]. This is consistent with the findings of a systematic review of published and unpublished data, which found that premature birth was a risk factor for hospitalisation in children presenting with influenza or influenza-like illness (ILI) in community-based clinical settings (mainly hospital ambulatory care) [8]. Yet, children born prematurely are still not targeted by most influenza vaccine programmes [6, 7] even though an estimated 15 million children are born prematurely each year, ranging from 5% in several European countries to 12% in the US [14].

Implications for future research

Hardelid and colleagues’ study is one of the largest to date of influenza-confirmed hospital admissions in young children and the first to examine influenza risk factors in children under 6 months of age [10]. The

study demonstrates the power of data linkage studies, with 596,174 person child-years of follow-up spanning six influenza seasons. However, by only evaluating hospitalised children with confirmed influenza, the study did not address the potential impact of influenza vaccination on burden of illness in primary care (e.g. number of GP visits) or the impact of illness on families (e.g. workplace leave for parents). Further data are therefore needed on risk factors relevant to primary care, and risk factors for influenza-related complications managed in the community.

It is likely that Hardelid *et al.* would have underestimated the number of influenza cases in their study population given that most hospitalised children with suspected respiratory infections are not tested for viruses [10]. Clear consensus on who and when to test for influenza (or other viruses) are lacking, including the role of point-of-care tests. One approach, as suggested in a recent review of paediatric respiratory virus testing, is to reserve influenza testing for children at increased risk of influenza-related complications [15]. Most clinicians use diagnostic tests to identify a subset of children who may benefit from the efficient use of antiviral medications. While the neuraminidase inhibitor oseltamivir has limited effectiveness in otherwise healthy children [16, 17], most guidelines recommend oseltamivir in 'at-risk' children due to the increased risk of influenza-related complications and death in this population [8, 9, 18]. However, more recent data from 1725 children included in an individual participant data meta-analysis found no survival benefit in 'at-risk' children [19]. High quality randomised controlled trials are needed to define the populations that would benefit the most, if at all, from viral testing and antiviral therapy.

Controversy also still exists regarding the effectiveness of universal versus targeted vaccination programmes. Which one is more effective? Is effectiveness defined by reduced number of cases, reduced complications, or cost? There is a clear tension between targeting 'at-risk' children and

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reducing the overall burden of influenza on the healthcare system. Universal vaccination may draw attention away from greater resources spent focusing on a smaller number of ‘at-risk’ patients, who have a greater risk of influenza-related complications. A policy of universal vaccination may only be worthwhile if influenza vaccination is effective at reducing complications and hospitalisations from influenza. Findings from a recent systematic review suggest that influenza vaccination of children may be effective at reducing rates of laboratory-confirmed influenza infection in some community settings, but more evidence is needed to determine which settings are most suitable for this strategy and whether targeting these settings would also result in reduction in complications and hospitalisations from influenza/ILI [20].

For both universal and targeted vaccination strategies, influenza vaccination uptake rates are much lower than those observed in relation to other childhood vaccinations, ranging from 24% to 52.5% [21, 22]. Reasons for poor uptake are multifactorial, relating to caregiver priority, access, perceived importance, understanding of indication, and health beliefs, amongst others [23]. Evidence-based strategies to improve implementation of vaccination programmes are therefore needed to address these potential barriers, particularly in high priority and ‘difficult to reach’ groups.

Conflict of interest

None of the authors have a conflict of interest to declare.

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Take-home strategies: Evidence-based strategies are needed to ensure children targeted by influenza programmes get vaccinated.

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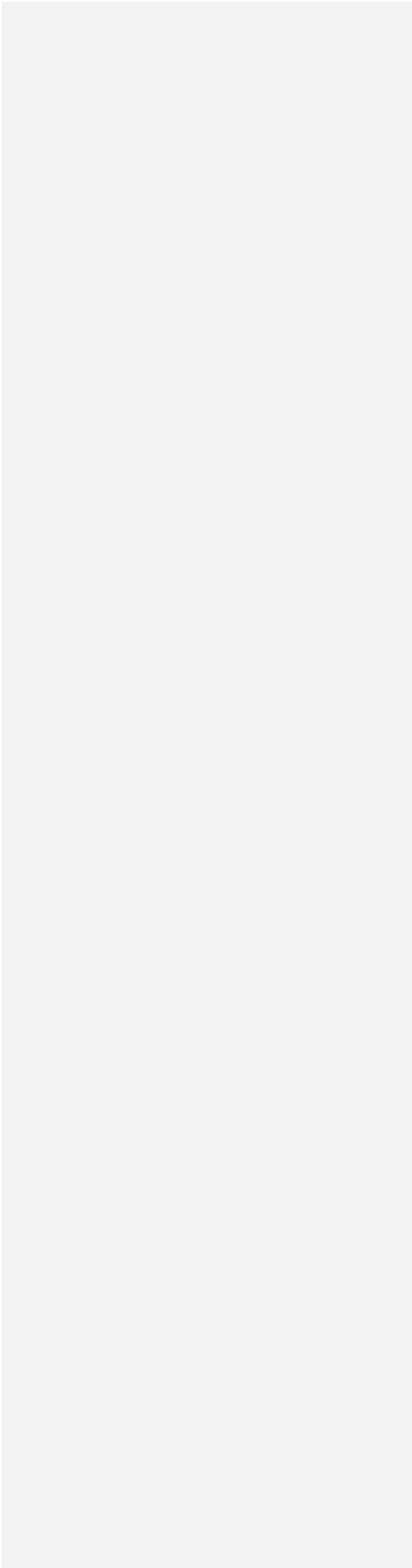
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Conflict of interest

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