Targeting respiratory syncytial virus vaccination using individual prediction

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Now that respiratory syncytial virus (RSV) prevention for all infants is within reach with a long-acting monoclonal and a maternal prefusion F protein-based vaccine approved by the US Food and Drug Administration and European Medicines Association,[1–4] countries will have to decide whether one or both prevention strategies will be implemented in a national immunisation programme, offering protection for all infants or only certain subgroups. An important question is whether there is a reliable prediction model to select groups with a higher risk that could therefore make a prevention strategy more cost-effective.

In this issue of the *Lancet Digital Health*, Pekka Vartiainen and colleagues[5] used the extensive nationwide registries of Finland and Sweden to develop a clinical prediction model for risk of RSV hospital admission in infants (younger than 1 year). The authors used the Finnish nationwide registry between June 1, 1997, and May 31, 2020, as the derivation cohort (infants born until May 31, 2017) and internal validation cohort (infants born between June 1, 2017, and May 31, 2020) and validated the outcomes in a Swedish birth cohort (infants born between June 1, 2006, and May 31, 2020. They found an overall yearly incidence of RSV bronchiolitis hospital admission of 1·5% in Finland and 1·4% in Sweden. This result is similar to a recent prospective birth cohort study in Europe.[6] The authors tested a comprehensive set of 1510 candidate predictors, of which 15 were predefined known risk factors. They included an impressive number of 2·72 million infants in their analysis. Reassuringly, they found that the predefined predictors from literature were significantly associated with RSV hospital admission. In addition, Vartiainen and colleagues found that, among medical conditions, esophageal malformation was strongly correlated with severe RSV infection. The 16 variables they finally used for their prediction model were selected based on how easily they could be ascertained and whether they would be generalisable to other countries. The model includes infant variables (eg, gestational age, Down syndrome and congenital heart disease) and external variables (eg, age at next epidemic peak and presence of siblings). The performance was good in the Finish derivation cohort (C statistic 0·744), in the Finnish internal validation cohort (0·766), and in the Swedish external validation cohort (0·729).

This study is impressive and contributes to our knowledge of individual RSV prediction. RSV prediction studies have mainly been done in late preterm infants with small sample sizes, showing that a young age during RSV season is the most constant predictor of hospital admission[7] but also in healthy term infants.[8] Larger studies, which aimed to define disease burden also found young age to be an important risk factor for RSV hospitalisation,[9] but the number of included infants are significantly lower than in the current study.

The question arises of whether this model is sufficiently reliable to use in the coming years when RSV immunisation will be introduced in many countries. Criteria for the implementation of a prediction model have previously been described.[10,11] First the model has to be appropriate for the intended purpose and generalisable to the population where the model will be implemented. We believe Vartiainen and colleagues' model is derived from and validated in large populations representative for upper-middle-income or high-income countries with seasonal RSV incidence, which will apply to the majority of European countries. Second, the accuracy of the model has to be acceptable for its intended use. C-statistics are frequently used to establish accuracy, with a value higher than 0·7, which is the case in this study, indicating a reasonable model, while models with a C-statistics above 0·8 are considered strong.[10] There is no commonly accepted criterium for a prediction model of RSV infection. Application of a risk threshold, below which children would not receive immunisation, must be carefully considered as even in the lower risk groups hospital admission with RSV could be realistic. The next step before implementation will be a clinical impact study to evaluate the cost-effectiveness of this model compared with general immunisation introduction to all children. Impact studies will also help to identify factors (such as ease of use and acceptability) that can affect implementation. We hope the authors or others are able to carry out such a challenging study.

In conclusion, Vartiainen and colleagues[5] developed a robust novel prediction model to estimate an infant's risk of hospital admission with RSV at an individual level. If accuracy could be further increased, this model seems promising and easy to use, with the ability to guide decision making both for policy makers and parents.

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