Assessing the burden of congenital rubella syndrome in China and evaluating mitigation strategies: a metapopulation modelling study

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Summary

Background A rubella vaccine was licensed in China in 1993 and added to the Expanded Programme on Immunization in 2008, but a national cross-sectional serological survey during 2014 indicates that many adolescents remain susceptible. Maternal infections during the first trimester often cause miscarriages, stillbirths, and, among livebirths, congenital rubella syndrome. We aimed to evaluate possible supplemental immunisation activities (SIAs) to accelerate elimination of rubella and congenital rubella syndrome.

Methods We analysed residual samples from the national serological survey done in 2014, data from monthly rubella surveillance reports from 2005 and 2016, and additional publications through a systematic review. Using an age-structured population model with provincial strata, we calculated the reproduction numbers and evaluated the gradient of the metapopulation effective reproduction number with respect to potential supplemental immunisation rates. We corroborated these analytical results and estimated times-to-elimination by simulating SIAs among adolescents (ages 10–19 years) and young adults (ages 20–29 years) using a model with regional strata. We estimated the incidence of rubella and burden of congenital rubella syndrome by simulating transmission in a relatively small population lacking only spatial structure.

Findings By 2014, childhood immunisation had reduced rubella’s reproduction number from 7·6 to 1·2 and SIAs among adolescents were the optimal elimination strategy. We found that less than 10% of rubella infections were reported; that although some women with symptomatic first-trimester infections might have elected to terminate their pregnancies, 700 children could have been born with congenital rubella syndrome during 2014; and that timely SIAs would avert outbreaks that, as susceptible adolescents reached reproductive age, could greatly increase the burden of this syndrome.

Interpretation Our findings suggest that SIAs among adolescents would most effectively reduce congenital rubella syndrome as well as eliminate rubella, owing both to fewer infections in the immunised population and absence of infections that those immunised would otherwise have caused. Metapopulation models with realistic mixing are uniquely capable of assessing such indirect effects.

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Introduction

Rubella is a mild respiratory disease typically of unvaccinated children.1 Infections during pregnancy, especially the first trimester,2 however, often cause miscarriages, fetal deaths or stillbirths, and a constellation of severe birth defects—cataracts, congenital heart disease, hearing impairment, and developmental delay—collectively known as congenital rubella syndrome.

Because rubella is a mild disease, even in adults, with 20–50% of infections asymptomatic, maternal infections are under-ascertained even by active surveillance. Moreover, because causal relations between discrete phenomena that follow one another in close succession are most likely to be recognised, even symptomatic maternal infections might not be suspected of causing infant conditions, particularly those not diagnosed until long after birth (eg, hearing impairment, developmental delay). Finally, the spontaneous abortions, fetal deaths, and stillbirths that maternal rubella infections can cause are inestimable.

As rubella is a vaccine-preventable disease, during May of 2012, the World Health Assembly endorsed its elimination by 2020 as a goal for five of the WHO’s regions.3 Rubella has since been eliminated from the region of the Americas.4 More recently, the Western Pacific regional committee urged member states to establish target dates for rubella elimination.5 So far, cessation of endemic rubella transmission has been verified in Australia, Brunei, Macao, New Zealand, and South Korea. Rubella remains endemic in China, the largest country in the Western Pacific region with a mainland population of more than 1·38 billion and area of approximately 9·6 million km².6