The Impact of 2-Dose Routine Measles, Mumps, Rubella, and Varicella Vaccination in France on the Epidemiology of Varicella and Zoster Using a Dynamic Model With an Empirical Contact Matrix

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ABSTRACT

Purpose: Varicella has a high incidence affecting the vast majority of the population in France and can lead to severe complications. Almost every individual infected by varicella becomes susceptible to herpes zoster later in life due to reactivation of the latent virus. Zoster is characterized by pain that can be long-lasting in some cases and has no satisfactory treatment. Routine varicella vaccination can prevent varicella. The vaccination strategy of replacing both doses of measles, mumps, and rubella (MMR) with a combined MMR and varicella (MMRV) vaccine is a means of reaching high vaccination coverage for varicella immunization. The objective of this analysis was to assess the impact of routine varicella vaccination, with MMRV in place of MMR, on the incidence of varicella and zoster diseases in France and to assess the impact of exogenous boosting of zoster incidence, age shift in varicella cases, and other possible indirect effects.

Methods: A dynamic transmission population-based model was developed using epidemiological data for France to determine the force of infection, as well as an empirically derived contact matrix to reduce assumptions underlying these key drivers of dynamic models. Scenario analyses tested assumptions regarding exogenous boosting, vaccine waning, vaccination coverage, risk of complications, and contact matrices.

Findings: The model provides a good estimate of the incidence before varicella vaccination implementation in France. When routine varicella vaccination is introduced with French current coverage levels, varicella incidence is predicted to decrease by 57%, and related complications are expected to decrease by 76% over time. After vaccination, it is observed that exogenous boosting is the main driver of change in zoster incidence. When exogenous boosting is assumed, there is a temporary increase in zoster incidence before it gradually decreases, whereas without exogenous boosting, varicella vaccination leads to a gradual decrease in zoster incidence. Changing vaccine efficacy waning levels and coverage assumptions are still predicted to result in overall benefits with varicella vaccination.

Implications: In conclusion, the model predicted that MMRV vaccination can significantly reduce varicella incidence. With suboptimal coverage, a limited age shift of varicella cases is predicted to occur post-vaccination with MMRV. However, it does not result in an increase in the number of complications.

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INTRODUCTION

Both varicella and herpes zoster diseases are expressions of the same pathogen—the varicella zoster virus (VZV), which is highly contagious and transmitted by inhalation of infectious particles or via person-to-person contact.[1,2] Varicella is a highly prevalent disease worldwide, affecting most of the population, typically young children. Besides substantial levels of varicella-associated morbidity and mortality, there is also an indirect burden on parents and caregivers.[2] In 2010, ~766,000 new cases of varicella were estimated to occur in France.[3] A seroprevalence study estimated that ~90% of children already had VZV antibodies by 8 years of age,[4] and a few studies reported the median age of varicella infection to be ~4 years.[5,6] Additionally, it has been reported that the risk of complications due to varicella is high in infants, children, and young adults.[7] In France, severe varicella complications lead to an estimated 20 deaths per year.[8]

Herpes zoster, which is characterized by a painful rash, mainly affects older individuals 50 to 60 years of age, and it appears that the risk of herpes zoster increases with age.[9] The VZV reactivates in this age group, possibly due to decreasing cell-mediated immunity that is associated with aging.[1] A sentinel survey in France estimated an annual incidence of 3.2 cases of herpes zoster (95% CI, 3.0–3.4) per 1000 inhabitants, 18.4% of whom reported chronic pain.[10] This chronic pain after zoster is known as postherpetic neuralgia, which is suggested to last for long periods of time and is reported to have a detrimental impact on the quality of life.[11,12] Zoster and postherpetic neuralgia are difficult to manage and treat; however, they can also be self-remitting.[12]

Effective prevention of varicella disease exists in the form of a vaccine against varicella, which is also suggested to result in a decrease in zoster disease incidence in vaccine recipients (attributed to a lower reactivation rate with the vaccine strain of the virus).[13,14] The World Health Organization recommends routine varicella vaccination in countries where high levels of coverage can be achieved and maintained.[2] Thus, using the combined measles, mumps, rubella, and varicella (MMRV) vaccine instead of the measles, mumps, and rubella (MMR) vaccine, which is presently used in routine immunization programs in the majority of countries worldwide, is suggested to be an efficient strategy to provide routine varicella vaccination at high levels of vaccination coverage.[2]

Varicella vaccination programs in Europe are aimed at high-risk groups, and routine varicella vaccination is not yet widely implemented, mainly due to concerns about the possible indirect effects of routine vaccination and its budget requirements. Further evidence is needed of the indirect effects of varicella vaccination such as the impact of herd immunity on the age of acquisition of varicella infection and the impact of the exogenous boosting on zoster disease incidence. It is widely suggested that the average age at which varicella infection occurs could increase due to the herd immunity effect, and this could result in a high risk of complications.[2] Conversely, if exogenous boosting of immunity exists, then zoster incidence could temporarily increase after vaccination due to fewer contacts with varicella cases.[15,16] It was first hypothesized by Hope-Simpson[17] in 1965 that re-exposure to a wild-type VZV might boost immunity against the reactivation of latent VZV and therefore would lower the probability of developing zoster diseases. This exogenous boosting hypothesis can imply that a vaccine-induced reduction in circulating wild-type VZV leads to a temporary increase in zoster incidence.[17–21] However, there is conflicting evidence of the existence of such an exogenous boosting effect that links an increase in the number of zoster cases and the adoption of routine varicella vaccination.[22] In a recent publication by Brisson et al,[23] the assumptions regarding exogenous boosting effects from previous models were updated to precise age-specific estimates (ie, the 100% input [percentage of effective varicella contacts that boost against zoster]) was now reduced to a maximum of 75% for individuals younger than 50 years of age and as low as 32% for those older than 80 years of age.[23]

Under these circumstances, the benefits of routine varicella vaccination on varicella incidence and potentially zoster incidence in vaccine recipients that would result in long-term benefits need to be weighed against the hypothetical increase in varicella and zoster cases due to indirect vaccination effects. The objective of this