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Vaccination against varicella as post-exposure prophylaxis in adults: A quantitative assessment

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ABSTRACT

Background: Varicella can be severe in adults. When universal vaccination is not adopted, post-exposure prophylaxis has been recommended in adults with uncertain history of varicella to reduce the burden of the disease in adults, however its impact is not quantified.
Methods: We developed a Bayesian probabilistic framework to estimate the impact of post-exposure prophylaxis in adults. We hypothesized that post-exposure vaccination would be proposed only after varicella exposure in close relatives. Information regarding the nature of the culprit exposure was obtained from a sample of 221 adult varicella cases. The lifelong probability that adults aged 18 would be infected with varicella was determined using data from the French *Sentinelles* surveillance network. Estimates of post-exposure vaccination efficacy were then used to compute the number of cases and hospitalizations prevented in adults.
Results: Familial exposure to varicella was reported by 81 adult cases out of 221. The probability of infection after exposure was 32%, so that six exposures on average were necessary to explain the observed cumulated lifetime incidence of varicella in non-immune 18 years old and over adults. Among the 35% of the 18 years old population with uncertain history of varicella, 11% would truly be non-immune. Post-exposure vaccination would prevent 26% of the cases (13 cases prevented per 100,000 adults per year) and 31% of the hospitalizations (0.2 hospitalizations prevented per 100,000 adults per year) if vaccination acceptance was 70%. An average of 16 adults would be vaccinated to avert one varicella case.
Conclusions: Post-exposure vaccination is associated with a substantial decrease in the burden of the disease in adults in a country where universal vaccination is not recommended. This quantitative information may help inform professionals to uphold the recommendation.

1. Introduction

Varicella is a ubiquitous, highly contagious childhood disease due to the varicella zoster virus. In western countries, nine teenagers out of 10 have evidence of past infection in the absence of vaccination [1,2]. In those who are infected in adulthood, the disease is usually more severe with complications including death [3–7]. Adults account for 26% of hospitalizations and 69% of deaths related to varicella, although they are only 10% of the cases [3].

To reduce the burden of disease when universal vaccination is not recommended, targeted primary vaccination of non-immune adolescents and adults as well as post-exposure vaccination may be considered [8–10]. However, recommendation for vaccination in adolescents have been poorly followed by general practitioners and the public, mostly due to ignorance or opposition [11].

Post-exposure vaccination, in the 3 days following exposure, prevents up to 90% infections and reduces severity [12–14]. A quantified assessment of the benefit of this recommendation may help inform professionals and patients and allow effectiveness analysis.

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We therefore set out to estimate the number of cases of varicella that could be avoided if a recommendation of post-exposure varicella vaccination was applied.

2. Methods

To estimate the impact of post-exposure prophylaxis in adults, we modeled the risk of varicella during the lifetime of a non-immune adult aged 18. In case of identified exposure to varicella, adults with a negative or unknown history of varicella would be proposed vaccination, irrespective of their real immunity as no time would be spent for serotesting. We assumed that identification of varicella exposure would be possible only in case of infection in close relatives, for example in the household, classified as "familial" exposure.

The framework for assessing the risk was therefore described along the following steps:

- Determine the percentage of 18 years-old with uncertain history of varicella (unknown or negative) and the percentage of non-immune among them.
- Determine the lifelong number of varicella exposures and the probability of infection after each exposure.
- Determine the probability that a familial exposure occurs before infection in non-immune subjects.
- Determine the eventual number of avoided cases taking into account acceptance of vaccination and subsequent protection.

The main ingredients to the calculation are summarized below and parameters reported in Table 1, while detailed calculations are deferred to the appendix A. All data are illustrative of the epidemiology of varicella in France. Number of cases were estimated based on the size of a French birth cohort at age 18 (n = 761,482 [20]).

2.1. Non immune and uncertain history of varicella in adults

Approximately 4.2% of subjects aged 18 are non-immune to varicella [1]. The sensitivity and specificity of the reported history of varicella in relation to actual immunity is 68% and 87% respectively [15]. This allowed estimating the number of people with uncertain history (negative or unknown) from the total population aged 18.

2.2. Exposure to varicella and infection in adults

Exposures were categorized as "familial", i.e. with close relatives, or not. The probability of infection after a familial exposure was given by the secondary attack rate (SAR) of varicella in households (SAR_F = 70–80%). The probability of infection after non-familial exposure was assumed to be smaller (SAR_{NF} = 10–35%) [16,17]. Combining these two values with the (unknown) probability p_F that an exposure is familial yielded an average probability of infection after exposure of $p_V = p_F \times SAR_F + (1 - p_F) \times SAR_{NF}$.

2.3. Lifelong number of varicella exposures in adults and familial exposure first

We assumed that the number of lifelong varicella exposures in adults was Poisson distributed with mean μ_E. The eventual probability of infection during one's lifetime, due to repeated exposures to varicella, therefore evaluates at $p_L = 1 - \exp(-\mu_E \times p_V)$; it is estimated to be approximately 80% in non-immune adults [15]. We computed the probability that a familial exposure would occur before the culprit exposure (leading to infection) as $p_{F1} = (p_F + p_V \times (1 - p_F) \times \exp(-P \times \mu_E))/P$ where $P = p_F + p_V \times (1 - p_F)$.

In immune subjects with an unknown history of varicella, we assumed the same distribution of exposures, and computed the probability of at least one familial exposure during the lifetime to determine the percentage offered vaccination.

2.4. Vaccination and protection

Regarding vaccination, we assumed that 70% of adults would undergo vaccination when proposed; that, if declined once, vaccination would be declined for all subsequent exposures; and that upon acceptance, protection would be lifelong effective, avoiding 75% of infections and 95% of severe diseases in those infected [12–14,18,19]. Vaccination would also be proposed to immune people with unknown history after a familial contact, with the same acceptance pattern.

The lifetime number of varicella cases avoided was computed as the percentage of non-immune adults that would be vaccinated before having varicella, discounted for vaccine effectiveness. The number of avoided hospitalizations was computed likewise considering a risk of hospitalization at 1.46% in adults varicella cases [3]. The yearly absolute reduction in varicella incidence and hospitalization was computed by dividing the number of cases avoided each year in adults by the total adult population (n = 49,637,690 [20]).

We also computed the "number needed to vaccinate" (NNV) as the number of adults with uncertain history that are needed to be vaccinated to prevent one varicella case during their lifetime [21]: NVV = N/P, where N is the number of adults with uncertain history that would be vaccinated and P the potential number of varicella cases avoided.

2.5. Sensitivity analysis

We performed a sensitivity analysis using partial rank correlation coefficients (PRCC) [22] to identify input parameters that were the most influential on the following outcome variables: "number of varicella cases avoided" and "number needed to vaccinate". Larger PRCCs indicated more influential parameters.

2.6. Computational details

All computations were performed using WinBugs software (v1.4) [23] and the R2WinBUGS package [24] of R software [25]. Three parallel MCMC chains were used, each consisting of 100,000 iterations of which the first 2000 were discarded. After this "burn-in" period the remaining chains were thinned by saving every 10th parameter to reduce the MCMC sampling autocorrelation. The code is available at RunMyCode (http://www.runmycode.org/companion/view/887).

3. Results

Between 2011 and 2013, 221 cases of varicella were reported to the *Sentinelles* network in adults aged more than 18. Among those, 81 (37%) reported a familial contact prior to infection. Using this data in our Bayesian framework led to estimate that an average number of μ_E = 6 (95% CI [2; 13]) varicella exposures during one's lifetime were necessary to reach a lifetime varicella risk of 80% in non-immune adults. The risk of infection after an exposure was 32% (95% CI [16%; 43%]). One varicella exposure out of 6 was familial (16%, 95% CI [8%; 24%]) (Table 2).

Approximately 35% (95% CI [24%; 47%]) of the population of age 18 had an uncertain history of varicella (unknown or negative) of which 11% were truly non-immune. In the absence of vaccination, 52 adults out of 100,000 (95% CI [16; 109]) were eventually infected with varicella and 0.8 hospitalized (95% CI [0.2; 1.6]) per year.