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# Varicella-zoster virus vaccination under the exogenous boosting hypothesis: Two ethical perspectives

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ABSTRACT

The varicella-zoster virus (VZV) causes two diseases: varicella ('chickenpox') and herpes zoster ('shingles'). VZV vaccination of children reduces exposure to chickenpox in the population and it has been hypothesized that this could increase the prevalence of shingles. This 'exogenous boosting' effect of VZV raises an important equity concern: introducing a vaccination program could advance the health of one population group (children) at the expense of another (adults and elderly). We discuss the program's justifiability from two ethical perspectives, classic utilitarianism and contractualism. Whereas the former framework might offer a foundation for the case against introducing this vaccination, the latter offers a basis to justify it.



## 1. Introduction

The varicella-zoster virus (VZV) causes two distinct diseases: varicella (i.e. "chickenpox") and herpes zoster (i.e. "shingles") [1]. Chickenpox, which primarily occurs during childhood, causes an itchy rash for about a week. Complications from chickenpox are relatively infrequent and include pneumonia, bacterial surinfection and encephalitis. Shingles predominantly occurs at older age. It is the result of a reactivation of VZV, which after chickenpox remains latently present in neural ganglia. This reemergence of the virus can be assumed to be a consequence of waning cellular immunity. Shingles is characterized by a painful rash on the body and causes on average a more severe and longer-lasting loss of quality of life than chickenpox [2].

Already in 1965 it was postulated that occasional re-exposure to VZV through chickenpox could boost VZV-specific immunity of adults, and consequently avoid reactivation of VZV [3]. Older generations may thus require the occasional proximity of children infected with VZV in order to keep their protection against shingles up to date. A consequence of this so-called "exogenous boosting hypothesis" would be an increase in shingles cases in the decades following the introduction of a universal childhood chickenpox (or VZV) vaccination program. Indeed, many simulation studies on the incidence of VZV predicted an increase in shingles incidence after introduction of widespread childhood chickenpox vaccination due to the loss of protection from exposure to chickenpox [e.g. [4–7]]. A systematic review of the scientific literature on shingles risk reduction through chickenpox exposure concluded that exogenous boosting exists, although the true effect size is yet to be determined [8].

Evidently, this vaccination program raises an equity concern: the health prospects of one population group could be advanced to the detriment of another group. Several countries (e.g. USA, Germany, Australia, Japan, Taiwan, Greece) have introduced widespread childhood vaccination against chickenpox [8]. Many others are considering doing the same thing but are awaiting more conclusive data on the duration and magnitude of the exogenous boosting effect. However, the program's justifiability cannot only be determined by data. This, as several researchers have urged, also requires ethical discussion [7,9–11]. Nonetheless, hitherto, in-depth analysis remains lacking from the literature.

The VZV issue cannot be settled by simply adhering to fixed ethical rules such as respecting autonomy (to become vaccinated) or 'do no harm to others' (i.e. do not become vaccinated). It necessitates balancing of different groups' competing basic interests and therefore it requires a more complex ethical framework. The objective of this paper is to structure and clarify ethical reflection on the issue

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by framing it from two fundamental ethical perspectives: classic utilitarianism and contractualism. Whereas there exist other perspectives from which the issue can be approached, in our opinion the two perspectives we discuss give an intuitive and consistent foundation to the case pro and contra. The first framework, classic utilitarianism, would, in the present state of knowledge on VZV-related risks, serve as a normative basis to oppose childhood vaccination. The second framework, contractualism, is a completely different ethical starting point. It offers a foundation to argue why childhood VZV vaccination would be justified.

We do not discuss here whether VZV vaccination is a good use of health care resources. Whether the program is cost-effective or not, and whether cost-effectiveness warrants funding or not, is a more general issue of resource allocation, which is not of particular relevance to this specific ethical dimension of VZV vaccination (i.e. the redistribution of disease between the age groups affected by the program). Instead we will only consider the health effects of implementing the program.

## 2. Utilitarianism

From the 18th century onwards, largely through the works of philosophers such as Bentham, Mill and Sidgwick, utilitarianism became a highly influential theoretical framework that was able to approach complex societal issues in a transparent and straightforward way [12]. Up to today it has had a profound impact on both ethical discourse and public policy. By now there exist many interesting versions and adaptations of utilitarianism, (see e.g. [13]) but in its most classic form it starts from two premises: (1) when difficult ethical decisions need to be made, ultimately, the available choice-alternatives' effect on wellbeing (or one of its related forms, e.g. happiness or health) is the only aspect that really matters and (2) everyone's wellbeing is equally important. Consequently, policy choices are justifiable depending solely on the fact whether they – compared to the alternatives – contribute most to total (or average) wellbeing. It appeals to the intuition that wellbeing (or in our case health) is of such an essential importance that it should not be 'wasted' by choosing for suboptimal courses of action, motivated by e.g. misguided moral principles, intentions or religious beliefs.

In the specific case of VZV, the relevant ethical question from a classic utilitarian perspective is thus whether introducing childhood chickenpox vaccination diminishes the total burden of disease. Existing empirical evidence from the USA shows that universal chickenpox vaccination is a success related to chickenpox: hospitalization reduction up to 88%, mortality reduction more than 74% [14]. However, such assessments are partial, as they exclude the shingles-effects in adults and the elderly. The exact magnitude of the exogenous boosting effect is still a matter of discussion [8]. Nonetheless, several modeling studies have indicated that chickenpox vaccination is not attractive anymore after accounting for the redistributive effect on older generations. Brisson and Edmunds estimated that routine infant vaccination against chickenpox will produce an increase in overall morbidity in England and Wales, as the QALYs lost to shingles (induced by exogenous boosting) are greater than those won by averting chickenpox [15]. These findings were confirmed in later studies that also use QALYs as an outcome (not with life-years gained as an outcome) [7]. Shingles vaccination of older adults could only in some scenarios fix this problem and yield gains in total net QALYs [6,7].

The overall potential negative health impact of a universal childhood vaccination program raises serious questions about the program's net effect on wellbeing. The ethical objection against this is coherently expressed through a classic utilitarian perspective. Awaiting more conclusive evidence, it would offer a basis to prescribe policy measures that limit or discourage childhood vaccination for VZV.

## 3. Contractualism

Contractualism is a completely different ethical approach and it offers a different perspective on the VZV-case. Again, many influential variants exist [12], ranging from 17 to 18th century theories from philosophers such as Hobbes, Locke and Rousseau to late 20th century authors such as Rawls [24] or Scanlon [16]. From the contractualist viewpoint, the moral justifiability of a decision is not determined by weighing consequences (e.g. health effects), but by its justifiability in terms of principles and rules, resulting from a hypothetical 'social contract'. This contract is laid out between all individuals and in this they decide which fundamental rules ought to govern society. Requirements for establishing the contract are that the agreement is made between equals in power (freedom from domination) and that contracting parties are rational and reasonable. If so, they can come to a consensus about which rules and arrangements are fair and acceptable, and which ones not. This initial contract serves as a moral benchmark to evaluate policy options and measures.

If we apply such a contractualist perspective to the VZV problem, the relevant issue is not whether the aggregate benefit of the vaccination program quantitatively outweighs the required sacrifice, but whether its introduction can be justified in terms of universally acceptable principles, i.e. principles that are also acceptable to those who stand to lose: the adults and the elderly. The following considerations would become relevant.

### 3.1. Freedom and responsibility

Contractants would grant each other extensive autonomy, especially in matters of the body and health. This entails the freedom to protect one's own health by becoming vaccinated. Moreover, if those who risk to undergo the negative externalities of a chickenpox vaccination program (adults and elderly) can be expected capable of protecting themselves, e.g. by becoming vaccinated against shingles themselves, but refuse or neglect to do so, their demand for solidarity may lose universal appeal. Shingles vaccination of elderly reduces shingles' incidence by 50% and its burden of disease by 60% in adults aged 60 years and older [17,18]. Importantly, shingles vaccination can be deemed safe [17].

### 3.2. Unacceptable sacrifices

Reasonable contractants would never agree on a principle that justifies big losses concentrated in a small number of individuals in exchange for a benefit spread out thinly over a large group. This is a main point where contractualism differentiates itself from utilitarianism [for discussion of this point, see e.g. [24]]. In the VZV case, some members of older generations will not be able to protect themselves against shingles (because of ineffective vaccine, medical reasons to avoid vaccinations, etc.). These individuals would be 'sacrificed' for the benefit of a large group of children. However, the difference in severity between shingles and chickenpox might not be big enough to call this sacrifice an unreasonable demand. Despite shingles presenting on average a more severe clinical image than chickenpox, the effects are only rarely leading to fatalities or permanent disability [2]. In other contexts (e.g. traffic, energy-use, food safety) similar risks are often considered acceptable.

### 3.3. Uncertainty

An impartial contractor will value prudence and risk-aversion, especially in health matters. Although the literature suggests that