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

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") (Gershon, Takahashi et al. 2008). 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 (Bilcke, Ogunjimi et al. 2012).

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 (Hope-Simpson 1965). 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. (Schuette and Hethcote 1999; Brisson, Edmunds et al. 2000; Van Hoek, Melegaro et al. 2012; Bilcke, van Hoek et al. 2013)]. 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 (Ogunjimi, Van Damme et al. 2013).

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 (Ogunjimi, Van Damme et al. 2013). 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 (Taylor 2001; Beutels, Scuffham et al. 2008; Luyten, Vandeveldde et al. 2011; Bilcke, Van Hoek et al. 2013). 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 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 (Kymlicka 1990). 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. (Sinnott-Armstrong 2014)) 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: hospitalisation reduction up to 88%, mortality reduction more than 74% (Marin, Meissner et al. 2008). 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 (Ogunjimi, Van Damme et al. 2013). 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 (Brisson and Edmunds 2003). These findings were confirmed in later studies that also use QALYs as an outcome (not with life-years gained as an outcome) (Bilcke, Van Hoek et al. 2013). Shingles vaccination of older adults could only in some scenarios fix this problem and yield gains in total net QALYs (Bilcke, Van Hoek et al. 2013) (Van Hoek, Melegaro et al. 2012).

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 (Kymlicka 1990), ranging from 17-18th century theories from philosophers such as Hobbes, Locke and Rousseau to late 20th century authors such as Rawls (Rawls 1971) or Scanlon (Scanlon 1998). 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.

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 (Oxman, Levin et al. 2005; Schmader, Oxman et al. 2012). Importantly, shingles vaccination can be deemed safe (Oxman, Levin et al. 2005).

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. (Rawls, 1971, p. 19-30)]. 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 (Bilcke, Ogunjimi et al. 2012). In other contexts (e.g. traffic, energy-use, food safety) similar risks are often considered acceptable.

Uncertainty. An impartial contractor will value prudence and risk-aversion, especially in health matters. Although the literature suggests that exogenous boosting exists, its effects on the incidence of shingles remain more uncertain than the effects of vaccination on the disease burden of chickenpox. If a preventive program will produce protection with (close to) certainty, but has uncertain externalities, then it seems reasonable to demand a more favourable weighing of those health outcomes of which we can be sure and to discount those with more uncertainty. This speaks in favour of vaccinating children, as here uncertainties are lower.

Age. Some authors argue that age can be a "morally-relevant" personal characteristic in setting health priorities (Callahan, 1987, Daniels 1988; Williams 1997). However, in the present context, we would judge that an impartial person would not consider VZV-related disease occurring in children as intrinsically more valuable than disease occurring in older generations. The negative effects of chickenpox vaccination on shingles incidence would already occur in young individuals, far below a possible threshold to speak of a 'fair innings' (Williams, 1997), i.e. an age after which someone may be considered as having received his/her fair share of life. Moreover, VZV infections rarely lead to permanent disability or mortality but mostly to transient illness, which is less relevant for a fair innings argument. In fact, one might even speculate that young individuals have more resilience in coping with physical annoyances than old people.

Acts and omissions. A final consideration may be that letting VZV infections run their natural course leads to harm resulting from an omission (not introducing vaccination) whereas changing the natural epidemiology by introducing childhood chickenpox vaccination causes

harm that is more 'man-made' or 'policy-induced'. People indeed judge harms following from actions and omissions differently (Spranca, Minsk et al. 1991) and also in ethics the duty of avoiding actions that bring harm is often held to be stronger than the duty of doing good (Beauchamp and Childress 2001). However, in this case the nuance seems to be of lesser relevance. First, redistributing health risks from children to older generations through vaccination could still qualify as an omission (allowing harm to occur) rather than as an act of doing harm. Second, a preference for the 'natural' epidemiology of VZV over an 'artificial' one is based upon a contestable and non-universally shared metaphysical view about nature, i.e. about the moral value and authority of its natural order.

These considerations allow us to frame the VZV vaccination issue from a different perspective than the utilitarian one. If we force ourselves to think in terms of a social contract, the case *against* chickenpox vaccination for children becomes unconvincing. It is hard to motivate with principles why children should protect older generations through experiencing chickenpox instead of protecting themselves through vaccination. The fact that adults and the elderly can to a substantial extent avoid shingles infection themselves, that risks of disability and mortality from shingles remain all-in-all relatively limited and that the effect size of exogenous boosting remains uncertain are important arguments to the benefit of children. Arguments about age and about the natural vs. man-made origins of VZV-infections are open for discussion, but even if they would be to the advantage of older generations they seem to be outweighed by the above other claims.

4. Conclusion

Evidence increasingly suggests that chickenpox vaccination of children risks redistributing health risks towards older generations. Next to a need for more conclusive data, there is also a need for further ethical discussion on the justifiability of this program. We discussed the case pro and contra widespread childhood chickenpox vaccination from two different ethical perspectives. In the current state of knowledge on VZV, classic utilitarianism, highlighting aggregate health and wellbeing, seems to support the case against introducing universal childhood chickenpox vaccination because the exogenous boosting effect on older generations would outweigh the total health benefits of the program for children (when it is valued in QALYs). However, this claim is largely based upon the yet available empirical studies and new evidence on the effect size of exogenous boosting effects could alter this conclusion. The contractualist view, however, highlights impartial *a priori* rules instead of a

posteriori consequences, and is therefore less dependent on quantitative estimates of consequences. This perspective offers a basis to justify the introduction of a chickenpox program for children. We conclude that discussions, and eventually decisions on VZV-policy not only require using quantitative data (e.g. studies estimating the effect size on disease burden) but that they also require specification of the ethical framework in which terms the discussion is implicitly held, and consideration and discussion of alternative ethical perspectives.

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