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Brief Report

Reducing Hospital Capacity Needs for Seasonal Respiratory Infections: The Case of Switching to High-Dose Influenza Vaccine for Dutch Older Adults

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ABSTRACT

Objectives: Influenza is responsible for considerable health and economic burden every year. Especially older adults are vulnerable for influenza infection and its complications due to immunosenescence and often-underlying medical conditions. Recently, the innovative quadrivalent high-dose influenza vaccine (QIV-HD) has become available in Europe. Through its enhanced immunogenicity, QIV-HD offers improved protection for older adults against respiratory as well as cardiovascular complications. We estimated the potential impact—specifically in terms of hospital admissions and related costs—of a hypothetical past switch from QIV-Standard dose (SD) to QIV-HD in The Netherlands.

Methods: Estimates of hospitalizations for the older adults vaccinated with QIV-SD were derived from the seasons 2010/2011–2017/2018. Subsequently, the number of respiratory infections and cardiovascular complications of influenza were estimated for the year 2019/2020 for both QIV-SD and QIV-HD. To calculate the overall corresponding savings, costs for hospital complications, derived from literature, were used.

Results: When QIV-HD would have been used instead of QIV-SD during the season 2019/2020, an additional 220 hospitalizations would have been averted among older adults of 60 years and older in the Netherlands. This corresponds to savings of €1 219 779 (uncertainty interval: 1 089 813–1 348 549), of which 69% is attributable to cardiovascular-related hospitalizations.

Conclusions: We demonstrate that a relevant improvement in influenza vaccination among older adults in The Netherlands can be achieved by switching from the current QIV-SD to QIV-HD. Not only comes a switch from QIV-SD to QIV-HD with a significant reduction in pressure on hospital capacity but also with notable cost savings.

Keywords: cardiovascular-related hospitalizations, hospital capacity, hospital costs, influenza, quadrivalent influenza vaccine high dose, vaccination

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Optimal protection against influenza is more important than ever, because, with COVID-19 restrictions being lifted, severe seasonal influenza epidemics are to be expected. Indeed, immunity in the population has lacked regular boosting because of social distancing and other restrictions, resulting in increased risks for seasonal influenza epidemics.¹ Such epidemics will come with additional pressure on hospital and intensive care unit capacity and corresponding societal costs, especially among adults 60 years and older (60+). For this risk group, the quadrivalent influenza vaccine (QIV) has been in use since 2019/2020 in The Netherlands. Nevertheless, the vaccine effectiveness of QIV remains suboptimal in elderly individuals. Notably, we demonstrated that even if the 60+ group in The Netherlands had been vaccinated with QIV during the 2010/2011 through 2017/2018 seasons, on an average, hundreds of influenza-associated respiratory disease hospitalizations would still have occurred among these senior individuals on an annual basis.² Ergo, despite vaccination with QIV, there remains

a considerable burden of influenza among older adults with a corresponding need for healthcare capacity. With ongoing developments in the area of influenza vaccines, further improvements in vaccination programs might therefore be considered. Potential improvements include, for example, a switch from the standard-dose (SD) to a high-dose (HD) vaccine formulation for the 60+ population. Current SD inactivated influenza vaccines contain 15 μg ³ of the hemagglutinin antigen per virus strain included in the vaccine. By contrast, the HD vaccine contains 60 μg ⁴ hemagglutinin per strain. HD influenza vaccine has been shown to be superior compared with SD in various studies,^{5–7} with improved vaccine effectiveness and no increase in serious adverse events. QIV-HD is available for older adults in the United States since 2020, and its use has been recommended in countries such as Canada, Germany, Italy, and the United Kingdom.^{8–12} Recently, the potential benefit of a switch from SD to HD to further reduce hospitalizations has been demonstrated in

Table 1. Estimated remaining hospitalizations after vaccination of senior Dutch citizens with QIV-SD or QIV-HD, showing hospitalizations additionally averted by QIV-HD (including the uncertainty interval), during the 2019/2020 influenza season, taking the estimated average level of influenza-related respiratory hospitalizations with the use of QIV-SD during the 2010/2011 through 2017/2018 seasons² and 2019/2020 vaccine coverage rates as the baseline.^{19,20}

Age category in years	Complication	QIV-HD	QIV-SD	Difference
60-64	Respiratory	30	34	5
	Cardiovascular	56	66	10
	All	86	101	15
65+	Respiratory	405	471	66
	Cardiovascular	765	905	140
	All	1170	1375	205
Total (60+)	All	1256	1476	220 (197-244)

HD indicates high dose; QIV, quadrivalent influenza vaccine; SD, standard dose.

retrospective database analyses in the United States.^{13–15} Here, we estimated the potential impact—specifically in terms of hospital admissions and related costs—of a switch from QIV-SD to QIV-HD in The Netherlands. Hospital capacity has emerged as a crucial factor in infectious disease control during the COVID-19 pandemic, justifying the focus of our study.

The remaining burden of influenza in The Netherlands among the 60+ group can be estimated at approximately 61 500 influenza cases annually, over the period of 2010/2011–2017/2018 (with assumed QIV-SD coverage rates of 50% and 70% among 60- to 65-year-old people and 65+, respectively).² This remaining burden is largely due to immunosenescence contributing to the modest vaccine effectiveness of QIV-SD in this specific group. As indicated above, QIV-HD, because of its 4 times higher dose of antigen than QIV-SD, induces a stronger immune response and therefore overcomes part of the immunosenescence effects and provides older adults with improved protection against influenza. Specifically, the HD vaccine has been shown to provide superior protection against cardiovascular complications of influenza and corresponding hospitalizations.⁶ Cardiovascular complications have been found to occur from days up to months after the actual influenza infection.^{16–18}

We estimated the number of hospitalizations in the 60+ population that could have been additionally avoided with the use of QIV-HD instead of QIV-SD in the season 2019/2020. In this season, QIV-SD was used for the first time and the epidemiology was not influenced yet by the COVID-19 restrictions, potentially enhancing representativeness for the coming years. The hospitalization estimates for the 60+ population vaccinated with QIV-SD over the period 2010–2018 by Zeevat et al² were used as a starting point (Appendix Table 1 in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2022.11.020>), reflecting hospitalizations of both vaccinated and nonvaccinated individuals. Subsequently, we related the average number of hospitalizations and vaccination coverage rates over the period 2010–2018 to the vaccine effectiveness rates of QIV-SD with regard to respiratory, as well as cardiovascular complications of influenza and the most recent coverage rates for the 2019/2020 season as indicated in Appendix Table 2 in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2022.11.020>.^{2,13,19–21} Also, in Appendix Table 3 in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2022.11.020>, we provide the baseline costs for complications as used to estimate overall corresponding savings.^{2,5,22–25} Uncertainty intervals for hospitalizations averted and corresponding cost savings were taken into the analysis using 95% confidence intervals on the vaccine effectiveness estimates for the 2019/2020 season.^{13,20,21}

Using the average hospitalization data during the seasons 2010/2011–2017/2018 as baseline, it follows that in a scenario in which during the season 2019/2020 QIV-HD would have been used instead of QIV-SD, 220 hospitalizations among the 60+ group would have been additionally averted (Table 1^{2,19,20}). Of these averted hospitalizations, 150 were cardiovascular-related hospitalizations using the assumption that there is a 1:1.89 ratio between respiratory and cardiovascular-related hospitalizations caused by influenza for vaccinating with QIV-HD and 1:1.92 with QIV-SD.²¹ These additional hospitalizations, which could have been avoided by the use of the HD vaccine, represent a total expenditure of €1 219 779 (uncertainty interval: 1 089 813–1 348 549) of which €841 531 (ie, 69% of the total costs) is attributable to the aversion to cardiovascular-related hospitalizations.

As exemplified by the COVID-19 pandemic, outbreaks of respiratory infections pose a significant pressure on hospital capacity in The Netherlands, as well as elsewhere. Nevertheless, this pressure is by no means restricted to the current COVID-19 crisis. For example, influenza regularly poses strains on hospital capacity during annual winter epidemics. In addition, increased influenza-related cardiovascular events may put an even higher pressure on hospital capacity. For the coming years, it is to be anticipated that epidemics of respiratory infections, influenza, and coronavirus alike will coincide during winter seasons.²⁶ Therefore, maximal control of these seasonal epidemics is crucial to avoid hospital capacity overload. Optimization of influenza vaccination represents one measure to achieve such maximal control. In the present study, we demonstrate that a relevant improvement in influenza vaccination among older adults in The Netherlands can be achieved by switching from the current QIV-SD to QIV-HD. Indeed, based on the 2019/2020 influenza season, we estimate that such a switch could avert an additional 220 cardio-respiratory hospitalizations annually, corresponding to almost €1.22 million in terms of cost savings in hospitals. This demonstrates that not only can a significant reduction in pressure on hospital capacity be achieved but also that a switch from QIV-SD to QIV-HD comes with notable cost savings as well. The significance of our results is further illustrated by comparing the 71 respiratory hospitalizations avoided in this analysis with previously published results,² where it was estimated that switching from trivalent influenza vaccine to QIV (ie, SD) could result in 84 avoided respiratory-related hospitalizations. These published results were based on a slightly broader population of those aged 60+, as well as high-risk individuals < 60 years. Notably, these earlier findings gave rise to the switch from trivalent influenza vaccine to QIV (ie, SD) in The Netherlands.

As indicated above, a major share of the benefits of the switch from QIV-SD to QIV-HD come from cardiovascular-related hospital admissions (68% of hospitalizations avoided). This logically derives from our assumption that for every respiratory hospitalization, almost 2 cardiovascular hospitalizations occur.²¹ In general, it can be concluded that including cardiovascular-related hospitalizations in a cost-effectiveness analysis may have a major impact on the favorability of the result compared with when respiratory-related hospitalizations alone are included.

Against the perspective of a potential resurgence of influenza, now that COVID-19 control measures are relaxed after 2 years of lockdowns and social distancing and in view of the recurrent pressure on hospital capacity within the broader context of winter peaks in respiratory infections, including not only influenza but also coronavirus, respiratory syncytial virus, and pneumococcal infections, further improvement in the Dutch influenza vaccination program by a switch to QIV-HD appears not only timely but also urgent.

Supplemental Material

Supplementary data associated with this article can be found in the online version at <https://doi.org/10.1016/j.jval.2022.11.020>.

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