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EDITORIAL COMMENTARY

If Influenza Vaccines Wane, Can We Delay Vaccination Without Compromising Coverage?

Nicola P. Klein and Bruce Fireman

Kaiser Permanente Vaccine Study Center and Division of Research, Kaiser Permanente Northern California, Oakland

(See the Major Article by Ferdinands et al on pages 1550–59.)

In this issue of *Clinical Infectious Diseases*, following reports that the effectiveness of influenza vaccines wane within months of vaccination, Ferdinands et al [1] evaluated the potential benefits and harms of a modest delay in the timing of influenza vaccination. If vaccine effectiveness (VE) starts waning within a month or two, then people who delay vaccination from September to October would be better protected in the winter when seasonal influenza peaks, but this benefit could be offset if delays to vaccination campaigns reduce the number of people vaccinated.

Ferdinands et al [1] modelled the consequences of different shifts in the timing of vaccination. Featuring a scenario that delays vaccinations until October, they found that the harms would exceed the benefits if delay reduced vaccinine coverage by 14% or more. Their model used inputs based on 2012–13 data on vaccine coverage, the timing of vaccination, and the incidence of influenza-associated hospitalizations among U.S. adults aged 65 and above. Although they focused only on the consequences of vaccination timing for hospitalization rates among the elderly, their reasoning is relevant to a broader assessment of the consequences of shifts in vaccination timing for the overall burden of influenza.

We commend them for tackling the difficult question of how best to balance the potential benefits and downsides of delaying influenza vaccination. Hospitals, clinics, workplaces, and public health professionals and clinicians devote significant resources every year to influenza vaccination campaigns, and any shift in vaccination timing will have substantial policy and logistical implications for many stakeholders. The timing of iinfluenza vaccination should not be revised without careful consideration of potential unintended consequences. This study seeks to do just that and is a welcome step.

The authors found wide variation in the expected consequences of delayed vaccination, depending on how much VE wanes and how much vaccine coverage is reduced by delay. Considering the uncertainties, they concluded that it would be premature to revise our current recommendations. We agree. But it is not premature to undertake a randomized study of waning, nor would it be too soon to pilot ways to shift vaccination timing without attenuating coverage.

A randomized controlled trial (RCT) could enlighten us considerably about how much VE wanes (if at all) and the trajectory of VE over time. Consenting patients could be randomized to weekly or bi-weekly intervals from early August to mid-November. The ethical concerns that preclude placebo-controlled influenza RCTs would be mitigated both because this RCT would vaccinate all enrollees and because there is now a reasonable amount of equipoise between earlier versus later vaccination. Influenza strains vary from year to year, and incidence can peak at different times of the winter; thus, it would be worthwhile to conduct such a trial over several years, with an interim analysis after each influenza season. Such an RCT could yield a reasonable estimate of how many influenza-associated events would be prevented per 100 vaccinees, on average, by vaccinating a month closer to when influenza circulates.

Ferdinands et al [1] did not provide convincing evidence for their expectation that coverage would decrease substantially if recommendations for early vaccination are revised. We concur that vaccine coverage would suffer if patients come for an influenza vaccine in September and are simply advised to return in October. But instead, patients can be counseled well in advance that they may be better protected if vaccinated in October. A pilot study could explore how best to do this. For some patients, a shared decision-making approach could be appropriate: they are provided information on what is known and what is still uncertain about the best time for vaccination, while emphasizing to them that it is better to get vaccinated early than not at all. If done the wrong way, this approach could waste time and sow doubt and confusion. However, if done appropriately, it may walk the fine line between addressing the evidence that VE wanes without prematurely undermining well-established public health campaigns and recommendations.

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Correspondence: N. P. Klein, Kaiser Permanente Vaccine Study Center, 1 Kaiser Plaza, 16th Floor, Oakland, CA 94612 (Nicola.Klein@kp.org).

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If VE really does wane substantially, then evidence of this will continue to accumulate. More patients will want later vaccination and more clinicians will recommend it. While it is appropriate for public health authorities to prioritize vaccine coverage, it may become problematic for them to stand by the current recommendations. They would have to devise ways to facilitate later vaccination while sustaining vaccine coverage.

With this in mind, we recommend that, in the meantime, pilot efforts be undertaken to learn how to optimize vaccination timing without attenuating coverage. We might suggest delaying vaccination to patients who can be counted on not to forego vaccination altogether. Patients who have been hard to reach for vaccination would be encouraged to receive an influenza vaccine at any opportunity. Maybe predictive algorithms could help discern hard-to-reach patients from those who would reliably get vaccinated later.

This study by Ferdinands et al [1] nicely examines the tradeoffs that might occur by delaying the timing of influenza vaccination, and appropriately highlights the potential reductions in vaccine coverage. It warns us that, even if the evidence becomes compelling that vaccination in October or November confers more protection than vaccination in August or September, we should be concerned that delaying immunizations could reduce coverage. We are suggesting two next steps: (1) an RCT that could yield a reasonable estimate of the increase in VE that could be achieved by vaccinating closer to when influenza circulates, and (2) pilot studies of how to optimize the timing of vaccination without decreasing coverage. And of course, work should continue on the ideal solution: a universal influenza vaccine that confers lifelong protection against all strains of influenza.

Note

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Reference

1. Ferdinands et al.