

## When to have the Influenza vaccine?

There is clear evidence the influenza vaccine stops people getting sick, being hospitalised and dying from influenza, especially persons over 65 years of age (seniors), and those with other more serious medical problems.

However, the issue regarding TIMING of that vaccination is not so clear.

Recently there have been reports in the media<sup>1</sup> suggesting it is really dangerous to have the influenza vaccine “too early”. or “...The Australian Medical Association is urging people to hold off getting this year's flu vaccine<sup>2</sup>...”

I have been told a recent story of an elderly unwell patient presenting for their flu vaccine and being told by the GP to “come back in June, as to have it now is a waste of time and will have worn off”.

In my view, the data on the waning of the effectiveness of the influenza vaccine is not solid, and to delay vaccination is not the best course of action.

My reading of the scientific literature leads me to believe that timing of vaccination is an area that needs more research. The data suggests in *some previous influenza years*, and for *some strains* of influenza (particularly H3N2 strains), that seniors protection from influenza may decrease the longer it is from having the influenza vaccine.

The significance of any waning, if and when it does occur, is also uncertain. This editorial<sup>3</sup> stated “**Vaccination appeared to remain efficacious throughout an influenza season, despite a modest decrease in the inactivated influenza vaccine’s efficacy over time**”, according to this study.<sup>4</sup>

There are many variables and scientists have to use observational studies which give results that are not as accurate as the gold standard double blind placebo controlled trials which are not ethical to do in this circumstance. There are variables that may be hard to statistically account for, like the interaction between herd immunity and spread of the virus, the mutation of the virus as the season progresses, the difficulty of making a vaccine that exactly matches the current strain (let alone what the virus mutates into), an individuals’ medical history and ability to make antibodies, their degree of exposure to the virus or the flu vaccine this year or in previous years - to name a few.

Its is all a bit academic at the moment as there is no government flu vaccine yet available. Furthermore there are two ‘turbocharged’ vaccines that the seniors will be offered free by our “fearless leaders”.

These vaccines are meant to be better at helping seniors make antibodies, but there is no data yet which of the two ‘turbocharged’ vaccines is preferable.

Frankly its also a bit late into the season to be saying - “hold on, don’t have the vaccine yet” when all the systems are in place to get people vaccinated. Much of this data is not that new.

As I see it, the trouble with delaying having the influenza vaccine is:

- We do not know if this apparent waning is significant for all flu vaccines, people or circumstance
- We do not know if this degree of waning is enough to warrant exposing unvaccinated persons to the risk of full-blown influenza ie how significant is the waning.
- We do not know exactly when the 2018 influenza virus will arrive and peak - it may come early especially if no-one is vaccinated until later in the season.
- We do not know which strains are coming, and what mutations will occur during the season - we might be lucky and the arriving strains may indeed be a good match and there may be good protection from early vaccination.
- For the general public (and their GP’s) delaying the vaccine at this late stage in the season leads to a lot of difficulties with systems already in place,
- This kind of unclear communication may decrease confidence in vaccination, mean lost opportunities to vaccinate, and might even somehow give fodder for the anti-vaccine lobby.
- This may mean some persons miss out entirely on being vaccinated - which will be a much more significant problem than potential waning late in the season.

AND from my perspective (running a travel medicine clinic), travellers are leaving now and need the vaccine when they present for their other vaccines; Influenza is the number one vaccine-preventable disease of travellers.)

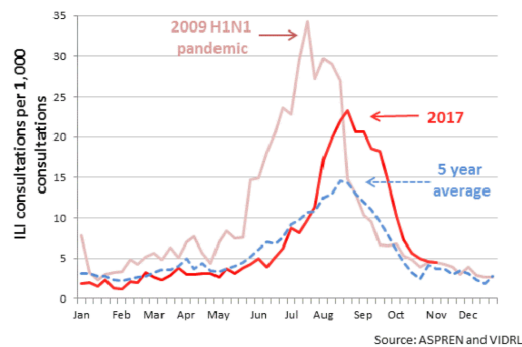
So in summary:

It is *way* better to have the influenza vaccine than not, it *might* be marginally better to have the influenza vaccine later in the season, but its a gamble - if the flu hits early you lose BigTime.

## More info and References

Somewhat variable timing of flu vaccine by week <sup>5</sup> Look at 2009 where influenza started in May.

Figure 1. ILI presentations to sentinel general practitioners, by week, 2009-2017, Australia



Study by Ferdinands <sup>6</sup> et al found decreasing vaccine effectiveness with increasing time since vaccination but concluded with saying that “This association is consistent with intra-season waning of host immunity, but bias or residual confounding could explain these findings. ...Evidence for intra-season waning of influenza vaccine protection is growing but inconsistent. The possibility of waning vaccine effectiveness merits further investigation; however, the current uncertainty in its nature and magnitude makes drawing conclusions difficult and suggests that careful **consideration of the risks and benefits of delaying vaccination is needed before contemplating changes to current vaccine recommendations.**”

Interestingly they also said their study “excluded adults who received >1 dose of influenza vaccine in a given season” Extra doses is rather like what we are doing this season with the ‘turbocharged’ new flu vaccines for seniors.

Sullivan et al <sup>7</sup> found in 2012, ( in Australia ) the trivalent influenza vaccine provided moderate protection against influenza and showed limited evidence for waning effectiveness: described as a non significant effect.

Eurosurveillance 2013 publication <sup>8</sup> found decreasing vaccine effectiveness for later vaccinated persons in Spain in 2011/12 year

Eurosurveillance April 2016 found “the pooling of our results across influenza seasons suggests a higher vaccine effectiveness against influenza A(H3N2) in the early than in the late phase among all ages and among those aged 60 years and older. This was not observed for influenza A(H1N1)pdm09 and only a small decline in vaccine effectiveness was observed against influenza B among all ages.<sup>9</sup>

Puig et al<sup>10</sup> found more risk for later vaccinated seniors in 2011/12 ( same year as the reference above in Spain ) and also 2014/15. They found no difference in later vaccinated persons in 2012/13 or 2013/14 They also report that 2011/12 and 2014/15 were H3N2 dominant, whereas in 2012/13 was strain pdm09 dominant and 2013/14 was Yamagata dominant. Which strain is dominant does matters.

CDC says Influenza vaccine is typically less effective against influenza A(H3N2) viruses<sup>11</sup>

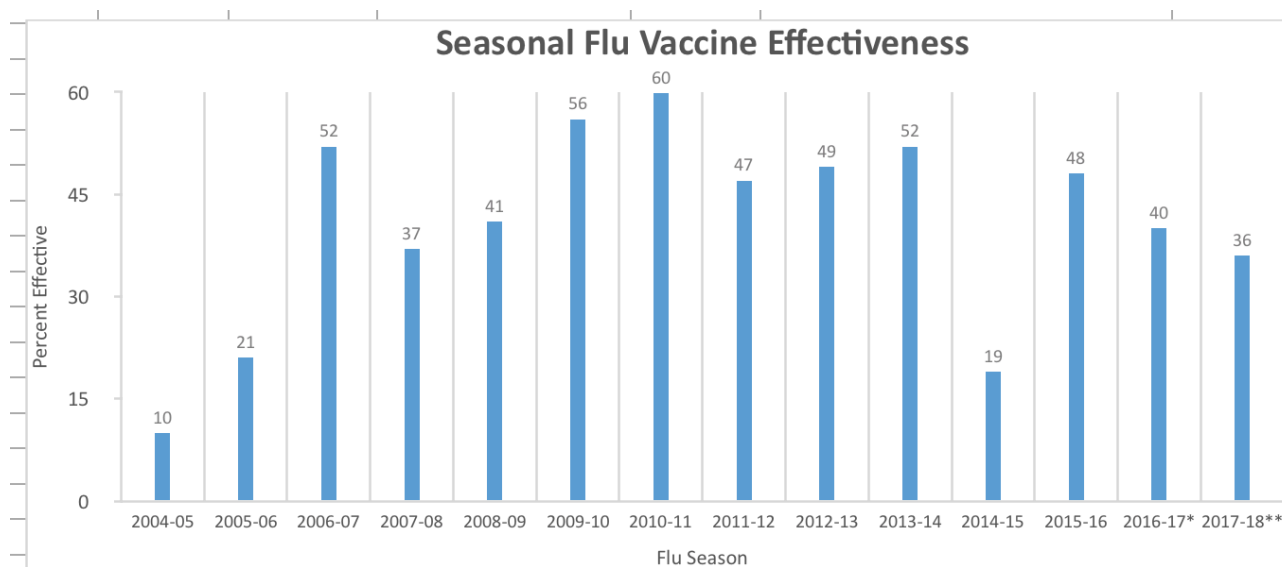
Belongia<sup>12</sup> found more infection with influenza A (H3N2) was associated with increasing time since vaccination among young children and older adults during a single influenza season in the 2007/8 season ( yes ten years ago).

CDC says : Some studies do suggest that flu vaccine effectiveness may be higher in people receiving flu vaccine for the first time compared to people who have been vaccinated more than once; other studies have found no evidence that repeat vaccination results in a person being less-protected against flu.

(If it were true that the influenza vaccine worked better the first time you had it, does that mean we don't give it at all until a bad year? So people die for want of an influenza vaccine? That would be perfectionism gone mad.)

The match<sup>13</sup> between the flu vaccines and the circulating strains is something that is always going to be important.

This graph from CDC <sup>14</sup> shows the wide variation in effectiveness of the vaccine per year. Make your own judgement about whether this changing virus might has a greater effect on influenza vaccine efficiency than waning of the vaccine antibodies.



Also all this means news about a new flu vaccine that will be more universally effective against all strains and not affected by the changing strains is a very hopeful development.<sup>15</sup>

I think the final word should go to this reference <sup>16</sup>

**Vaccination programs should balance maximizing the likelihood of persistence of vaccine-induced protection through the season, with avoiding missed opportunities to vaccinate or vaccinating after influenza virus circulation begins.**

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<sup>1</sup><http://www.news.com.au/lifestyle/health/health-problems/experts-say-timing-for-your-flu-shot-is-vital-this-season/news-story/f5a5397b076c9c108fc5aa7d2a9b6632#.ltxr>

<sup>2</sup> <http://www.abc.net.au/news/2018-03-25/flu-vaccines-should-be-delayed-ama-says/9585092>

<sup>3</sup> Muoio D. Despite waning efficacy, influenza vaccine protects throughout season. *Infectious Disease News; Thorofare*. 2016;29(5):29.

<sup>4</sup> Petrie JG, Ohmit SE, Truscon R, et al. Modest Waning of Influenza Vaccine Efficacy and Antibody Titers During the 2007–2008 Influenza Season. *Journal of Infectious Diseases*. 2016;214(8):1142-1149. doi:10.1093/infdis/jiw105

<sup>5</sup> [http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-ozflu-flucurr.htm/\\$File/2017-season-summary-22112017.pdf](http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-ozflu-flucurr.htm/$File/2017-season-summary-22112017.pdf)

<sup>6</sup> Ferdinands JM, Fry AM, Reynolds S, et al. Intraseason Waning of Influenza Vaccine Protection: Evidence From the US Influenza Vaccine Effectiveness Network, 2011–2012 Through 2014–2015. *Clin Infect Dis*. 2017;64(5):544-550. doi:10.1093/cid/ciw816

<sup>7</sup> Sullivan SG, Komadina N, Grant K, Jelley L, Papadakis G, Kelly H. Influenza vaccine effectiveness during the 2012 influenza season in Victoria, Australia: Influences of waning immunity and vaccine match. *Journal of Medical Virology; London*. 2014;86(6):1017-1025. doi:<http://dx.doi.org/10.1002/jmv.23847>

<sup>8</sup> <http://www.eurosurveillance.org/content/10.2807/ese.18.05.20388-en>

<sup>9</sup> <http://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2016.21.16.30201>

<sup>10</sup> Puig-Barberà J, Mira-Iglesias A, Tortajada-Girbés M, et al. Waning protection of influenza vaccination during four influenza seasons, 2011/2012 to 2014/2015. *Vaccine*. 2017;35(43):5799-5807. doi:10.1016/j.vaccine.2017.09.035

<sup>11</sup> <https://www.cdc.gov/flu/about/qa/vaccineeffect.htm>

<sup>12</sup> Belongia EA, Sundaram ME, McClure DL, Meece JK, Ferdinands J, VanWormer JJ. Waning vaccine protection against influenza A (H3N2) illness in children and older adults during a single season. *Vaccine*. 2015;33(1):246-251. doi:10.1016/j.vaccine.2014.06.052

<sup>13</sup> <http://blogs.plos.org/publichealth/2014/12/12/flu-shot-isnt-good-match-year-ever/>

<sup>14</sup> <https://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm>

<sup>15</sup> <https://www.cnn.com/2018/03/16/scientists-say-they-are-on-the-verge-of-creating-a-universal-flu-vaccine.html?sf86359039=1>

<sup>16</sup> [http://www.immunize.org/askexperts/experts\\_inf.asp](http://www.immunize.org/askexperts/experts_inf.asp)