## When to have the Influenza vaccine?

Will the influenza vaccine protection really run out before the end of the season? Short answer - we don't really know. The optimal TIMING for influenza vaccination is not clear. However, there is clear evidence that the influenza vaccine stops people getting seriously sick and even dying from influenza. This is especially true for persons over 65 years of age (seniors), and those with other medical problems.

## Its all about Timing

Recently there have been reports in the media¹ reporting waning influenza vaccine effectiveness and suggesting it is even dangerous to have the influenza vaccine "too early". or "...The Australian Medical Association is urging people to hold off getting this year's flu vaccine²....."

I have been told a recent story of an elderly unwell patient presenting for their flu vaccine. He was told by the GP to "come back in June, as to have it now is a waste of time".

## What does the data say?

In my view, the data on the waning effectiveness of the influenza vaccine toward the end of the season is still shaky. Delaying influenza vaccination may not be a good idea.

My reading of the scientific literature is that more research is needed. The data suggests that in *some* previous influenza years, and for some strains of influenza (particularly H3N2 strains), and for some groups eg seniors, the protection from influenza may decrease the longer it is from the date the influenza vaccine was given.

The significance of this waning influenza vaccine effectiveness, if and when it does occur, is also uncertain. This editorial<sup>3</sup> said "Vaccination appeared to remain efficacious throughout an influenza season, despite a modest decrease in the inactivated influenza vaccine's efficacy over time".

There are many variables. Scientists have to use observational studies for this research. These studies are not as accurate as the gold standard double blind placebo controlled trials. Some variables may be hard to statistically account for. [Issues 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 amount of exposure to the flu virus or the flu vaccine, this year or in previous years - to name a few.]

Waning influenza vaccine effectiveness is a bit academic at the moment. There is no government free influenza vaccine available yet anyway (2.4.18). Furthermore, there are two new 'turbocharged' vaccines that the seniors will - in due course - be offered free.

These newer vaccines are supposedly better at helping seniors make antibodies. Unfortunately, there is no data yet which of the two 'turbocharged' vaccines is the better of the two, or even which one wanes or does not.

Frankly, it is also a bit late in the season to be saying "hold on - don't have the vaccine yet". All the systems are in place to get people vaccinated. Much of the 'waning data' is a few years old. Problems with delaying influenza vaccination

As I see it, the problems with delaying the influenza vaccine are:

- 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 balance the risk of exposing unvaccinated persons to the risk of full-blown influenza. How significant really is this waning influenza vaccine effectiveness?
- 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.
- This kind of last minute, negative communication may decrease confidence in vaccination, mean lost opportunities to vaccinate, and might even somehow give fodder to the anti-vaccine lobby.

• Patients may be sent away and not come back. Not having a flu vaccine will definitely mean a greater risk than any potential waning influenza vaccine effectiveness late in the season.

AND from my perspective (running a travel medicine clinic), travellers are going overseas *now*. So they need the vaccine now; Influenza is the number one vaccine-preventable disease of travellers.) In Summary

It is better to have the influenza vaccine than not, especially if you are over 65 years or have medical problems. It *might* be marginally better to have the influenza vaccine later in the season, but it's a bit of a gamble - if the flu hits early, you lose BigTime.

## More info and References

Somewhat variable timing of flu vaccine by week 4 Look at 2009 where influenza started in May.

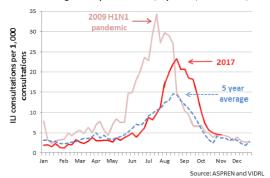


Figure 1. ILI presentations to sentinel general practitioners, by week, 2009-2017, Australia

Study by Ferdinands <sup>5</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>6</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>7</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.8

Puig et al<sup>9</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 pmd09 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>10</sup>

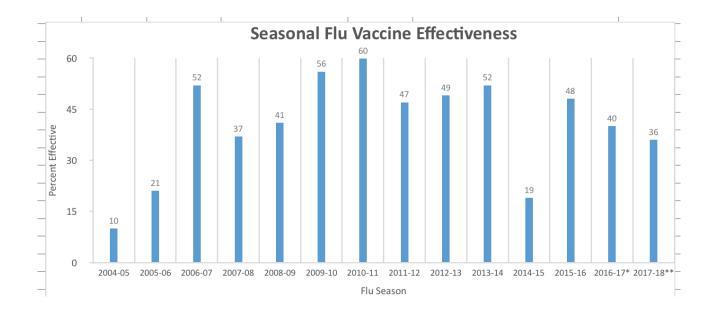
Belongia<sup>11</sup> found more infection with influenza A (H3N2) was associated with increasing time since vaccination among young children and older adults during a single influenza season in the 2007/8 season (yes ten years ago).

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>12</sup> between the flu vaccines and the circulating strains is something that is always going to be important.

This graph from CDC <sup>13</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>14</sup>

I think the final word should go to this reference 15

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.

<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#.ltxer

- <sup>3</sup> Muoio D. Despite waning efficacy, influenza vaccine protects throughout season. *Infectious Disease News; Thorofare*. 2016;29(5):29.
- <sup>4</sup> http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-ozflu-flucurr.htm/ \$File/2017-season-summary-22112017.pdf
- <sup>5</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>6</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
- 7 http://www.eurosurveillance.org/content/10.2807/ese.18.05.20388-en
- 8 http://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2016.21.16.30201
- <sup>9</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
- 10 https://www.cdc.gov/flu/about/ga/vaccineeffect.htm
- <sup>11</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
- 12 http://blogs.plos.org/publichealth/2014/12/12/flu-shot-isnt-good-match-year-ever/
- 13 https://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm
- <sup>14</sup> https://www.cnbc.com/2018/03/16/scientists-say-they-are-on-the-verge-of-creating-a-universal-flu-vaccine.html?sf86359039=1
- <sup>15</sup> http://www.immunize.org/askexperts/experts inf.asp

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