Estimating the Efficacy of Adjuvanted Versus Standard Seasonal Influenza Vaccines in Older Adults Based on Anti-Haemagglutinin Antibody Titres

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BACKGROUND

- Haemagglutinin (HA) is a cell surface glycoprotein expressed by the influenza virus. Exposure to HA induces antibody responses associated with clinical protection against influenza disease.
- Influenza vaccine-induced HA-specific antibody titres are routinely measured by haemagglutination inhibition (HI) assay to assess vaccine immunogenicity. However, few attempts have been made to predict vaccine efficacy (VE) using HI antibody titres.
- Clinical data demonstrate the MF59®-adjuvanted trivalent influenza vaccine (Fluad™, Seqirus Inc.) (aTIV) to provide enhanced protection against influenza disease in older adults compared with standard influenza vaccine (TIV).

OBJECTIVES

- To predict the vaccine efficacy (VE) of aTIV compared to standard influenza vaccine using a Bayesian random-effects model.

METHODS

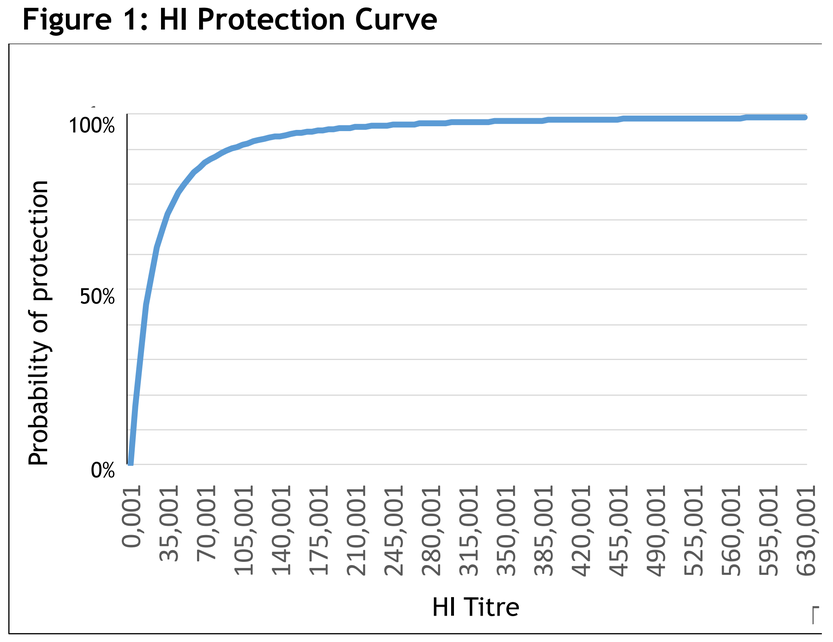
- Source data (anti-haemagglutinin antibody titres) derived from a Phase III randomized control trial comparing aTIV to TIV in older adults aged 65 years and above.[1]
- Antibody responses were examined against antigenically similar (homologous) and drifted (heterologous) strains using sera from subjects immunized with either aTIV or TIV comparator (Table 1)

Table 1: Homologous and Heterologous strains tested

Influenza Season	Strains tested in HI Assay	Influenza Strain		
		A/H1N1	A/H3N2	B
2010-2011	Homologous	A/California/2009	A/Perth/16/2009	Brisbane/16/2008
	Heterologous	-	A/Brisbane/10/2007 A/Wisconsin/67/2005	B/Malaysia/2506/2004

- The HI protection curve (Figure 1) was then generated, linking the level of clinical protection against lab-confirmed cases to the HI titres by deriving the previous work by Coudeville and al.[2]
- 95% Confidence intervals (CIs) were generated using the method described in Coudeville et al.[3] Briefly, a set of 10000 simulations were run where alpha and beta parameters were drawn from posterior distributions, estimated by Markov Chain Monte Carlo methods, with the immunogenicity data resampled using bootstrap method at the individual level to respect conditions of data collection and individual heterogeneity.
- Using this HI protection curve, absolute vaccine protection for aTIV and TIV against homologous and heterologous strains were computed and the aTIV relative vaccine protection was then calculated

Figure 1: HI Protection Curve



- Relative VE of aTIV was calculated by applying the relative aTIV vaccine protection to a sample population of 100,000 individuals ≥ 65 years of age with a 5% influenza attack rate.
- The results from the model were compared to aTIV effectiveness data.[4,5]

RESULTS

- Based on aTIV- and TIV-induced HI antibody titres, the model predicted the vaccine induced protection of aTIV to be greater than that of TIV in adults ≥ 65 years of age across all homologous and heterologous influenza strains tested (Table 2).

Table 2: Absolute predicted vaccine protection against PCR confirmed influenza by strain

		aTIV (95% CI)	TIV (95% CI)
Homologous	H1N1 (California)	75.73% [61.7% ; 85.47%]	65.03% [51.54% ; 75.79%]
	H3N2 (Victoria)	81.55% [67.94% ; 90.49%]	68.79% [54.35% ; 80.33%]
	B Strain (Brisbane)	41.06% [27.56% ; 54.18%]	33.21% [22.45% ; 44.31%]
Heterologous	H3N2 (Brisbane)	68.59% [54.66% ; 80.69%]	53.77% [40.21% ; 67.41%]
	H3N2 (Wisconsin)	79.79% [64.72% ; 90.6%]	65.83% [50.95% ; 79.46%]
	B Strain (Malaysia)	54% [38.53% ; 68.91%]	44.66% [31.28% ; 58.83%]

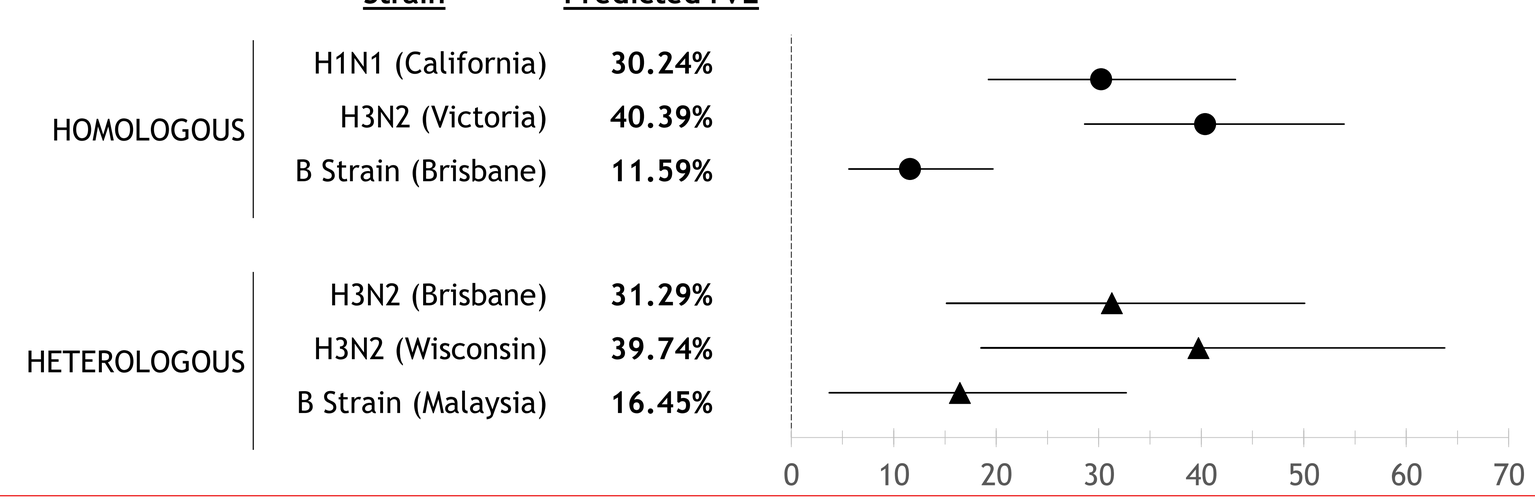
- The relative increase in the predicted vaccine protection by aTIV in older adults was high across all three homologous strains and is maintained against drifted H3N2 and B strains (Table 3).

Table 3: Relative predicted aTIV vaccine protection by influenza strain

Influenza Vaccine Strain	rVE (95% CI)
Homologous	
H1N1 (California)	16.34% [10.51% ; 23.1%]
H3N2 (Victoria)	18.27% [11.41% ; 27.3%]
B Strain (Brisbane)	23.58% [13.15% ; 34.78%]
Heterologous	
H3N2 (Brisbane)	27.33% [10.05% ; 49.06%]
H3N2 (Wisconsin)	20.73% [7.58% ; 37.98%]
B Strain (Malaysia)	20.76% [4.21% ; 40.88%]

- By applying the relative predicted aTIV vaccine protection in a sample population of older adults ≥ 65 years of age, the relative VE estimates for aTIV were globally similar for the two A strains with a higher increase for the H3N2 strain (40.39%) compared to the H1N1 strain (30.24%) (Figure 2)
- This high relative VE was stable against heterologous H3N2 strains (31.29%-39.74%) and the second B-strain lineage (16.45%) (Figure 2)

Figure 2: Relative vaccine efficacy (rVE) estimates, based on the number of influenza cases prevented, & corresponding 95% CIs.



CONCLUSIONS

- The results of this study predict that the heightened HA-specific antibody titres observed in response to aTIV against both homologous and heterologous strains result in a VE greater than that of TIV.
- These data predict that immunisation of older adults with aTIV rather than standard influenza vaccine would result in a significant reduction in the annual number of cases of influenza disease within this age group.
- The predicted relative VE results are consistent with the significantly improved effectiveness of aTIV against influenza and influenza related hospitalisations reported in the literature[4,5].
- Moreover, these results are comparable to the published relative vaccine efficacy of the other enhanced influenza vaccine (High Dose) for older adults[6].

REFERENCES

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