Seasonal Influenza Vaccine Selection Using the Crossmatch Test

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How effective is the yearly vaccine against seasonal influenza predicted to be?

Virus Biology

- Two types of human influenza viruses -- type A and B, cause seasonal epidemics of disease almost every year.
- A flu vaccine is made up from a collection of strains of virus observed in previous years that are predicted to circulate in the upcoming flu season.
- This season's recommended flu shot is composed of: A/Brisbane/02/2018 (H1N1)pdm09-like, A/Kansas/14/2017 (H3N2)-like and B/Colorado/06/2017-like (Victoria lineage) virus.
- To what extent the vaccine is effective depends on whether there is a good match between the strains selected as vaccine component and the current circulating strain.
- Virus strains are characterized both genetically and antigenically. Our method specifically focuses on genetic characterization through phylogenetic trees.
- Higher genetic difference is characterized by longer branch on the phylogenetic tree.

References

Phylogenet







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Is there a good match between circulating virus and vaccine component? (i.e. Are they genetically and antigenically close?) Is there a significant discrepancy between phylogenetic trees constructed under two different mechanisms?

ic trees		Crossmatch Test	
Circulating Virus A ₂		N ₁ Tree I	N_2 Tree II
culating Virus D ₂		$N_1 + N_2$ total trees	
Circulating Virus C ₂	Trees I: All tips are from randomly	Given $\binom{N}{N}$	$\binom{N_1+N_2}{2}$ pairwise distances
Circulating Virus A ₄	selected circulating H1N1-pdm09 strains in season	Group data po Minimize the	oints into pairs sum of within pair distances
Circulating Virus D_4 Circulating Virus C_4	2012-13	A crossmatch a pair come fr	n occurs if two components in com different populations
Circulating Virus A' ₂		The test statis	tics is the number of crossmatches
lifornia/07/2009	The crossmatch test:		
/irus C' ₂	<u>Trees II</u> : One tip is vaccine strain A/California/07/2 009, and all rest are from randomly	•	preserves more information from the data Applies beyond standard Euclidean space, as long
Circulating Virus A' ₄	selected circulating H1N1-pdm09		as distance metrics are available
Circulating Virus C' ₄ Virus B' ₄	strains in season 2012-13	•	Does not assume a specific distribution of the original data



Goodness of Match by Year

Consecutive years with good match between vaccine and virus:

Season	Pooled VE (%)	Number of Crossmatch out of 100 Pairs	P-val
2010-11	60% (54 to 65)	50	0.56
2011 - 12	68% (50 to 80)	56	0.91
2012 - 13	55% (41 to 66)	52	0.71
2013-14	$62\%~(52~{\rm to}~70)$	62	0.99

Number of Crossmatches with N=200 under Null



A recent year with bad match between vaccine and virus:

Season	Pooled VE $(\%)$	Number of Crossmatch out of 100 Pairs	P-val
2018-19	9% (-4 to 20)	22	9.95e-09

Time series analysis would help explore the dynamics of the changing virus make–up from season to season and make future predictions.

Geographical variation would also be of interest, Since the virus strains included are from all over the world and the WHO makes generic vaccine component recommendations for southern and northern hemisphere