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Short communication

Evaluation of Southern Hemisphere influenza vaccine recommendations

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ABSTRACT

In 1999, the World Health Organization switched from annual to semi-annual recommendations for influenza vaccine composition. We compared the antigenic match between recommendations and circulating viruses before and after 1999, in the Northern and Southern Hemispheres. Vaccine match proportion for A/H3N2 viruses increased from 31% to 59% in the Southern Hemisphere ($P < 0.05$), and is now comparable to that in the Northern Hemisphere. Vaccine match for influenza B decreased from ~100% to 33–54% in both hemispheres ($P < 0.05$), following the unexpected resurgence of influenza B/Victoria in 1997. No estimate was available for influenza A/H1N1. We conclude that semi-annual vaccine recommendations are useful overall and discuss potential ways forward, including a recommendation for the improvement of vaccination policy and influenza surveillance in tropical areas.

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1. Introduction

Large-scale influenza vaccination programs have been in place for many years in Europe, Japan, and the US. Annual immunization is the most widespread strategy to prevent influenza morbidity and mortality, especially in those at highest risk of complications, including seniors, children, and those with certain chronic conditions [1]. Three influenza subtypes circulate in the population (A/H3N2, A/H1N1 and B) and most commercial influenza vaccines include one representative strain for each of these subtypes. Gradual changes in the virus surface antigens generate new influenza strains that evade population immunity, and influenza vaccine composition must be updated periodically to reflect these changes [2,3]. Occasionally, a novel influenza virus, such as the 2009 A/H1N1pandemic virus, emerges from the animal reservoir of influenza viruses and becomes transmissible among humans, requiring rapid development of a new pandemic vaccine and later incorporation of a new antigen into the seasonal influenza vaccine.

Since 1973, the World Health Organization (WHO) has issued annual recommendations for the influenza A/H3N2, A/H1N1 and B strains to be included in trivalent seasonal influenza vaccines [4]. The annual vaccine composition recommendations were based on surveillance of circulating strains in the previous 12 months, considerations regarding potential epidemic drift strains, vaccine strain production potential, and existing immunity within the population [5]. Until 1998, an annual recommendation was made every February, just in time for the vaccine to be produced and distributed for the following Northern Hemisphere influenza season (October–April). While the Northern Hemisphere population received a vaccine based on recommendations that were approximately eight months old, by the time the Southern Hemisphere received the same vaccine, around March or April of the following year, the vaccine recommendations were over 13 months old. Therefore, it was thought that the match between the strains included in the vaccine and the circulating strains was better in the Northern Hemisphere than in the Southern Hemisphere, although this was not formally evaluated. As a response to this perceived Northern Hemisphere bias, Southern Hemisphere-specific vaccine recommendations were implemented in October 1998 [6], and semi-annual influenza vaccine recommendations have been made since that time.

Despite these efforts, no published study has evaluated how well the WHO vaccine composition recommendations have matched the circulating strains worldwide, before or after the semi-annual vaccine recommendations were implemented in 1999. In this study, we quantify the match between vaccine composition and circulating strains during seasonal epidemics in both Hemispheres, based on publicly available surveillance reports between 1991 and 2008.

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2. Methods

We conducted a literature search to identify reports containing information on national or regional influenza virus surveillance (Pubmed search terms: national, regional, influenza, activity, surveillance, report), and perused publicly available data from national surveillance websites maintained by health authorities. Influenza virus surveillance data were collected for 1991–2008 for the United States (US) [7–16], Canada [17–31], and Europe [32], representing the Northern Hemisphere, and for Australia [33], New Zealand (1999, 2000 [34,35]; 2001–2007 [36]), Latin America [37], and general global reports [38–48], representing the Southern Hemisphere. These data were collected separately for each location, year, and influenza subtype. This report presents primarily data for the A/H3N2 and B subtypes due to limited available surveillance data and less rapid antigenic change over the years for the A/H1N1 subtype.

To evaluate the match between influenza vaccine strains and circulating strains, we recorded the prevalence of each strain(s) within each subtype circulating in each season and location. Occasionally the reports did not specify the exact number or percent of the influenza isolates that matched a given strain, in which case the information was considered missing.

For influenza A/H3N2, we categorized strains (either naturally circulating or included in the vaccine) based on the antigenic clusters defined by Smith et al. [2] and Russell et al. [49] For recent years when A/H3N2 antigenic clusters are less well defined, we considered that A/Fujian/411/2002, A/California/7/2004, and A/Wisconsin/67/2005 were distinct clusters, that strains A/Wellington/1/2004 and A/California/7/2004 belonged to the same cluster, as well as A/Brisbane/10/2007 and A/Wisconsin/67/2005. If a circulating A/H3N2 strain was in the same cluster as the vaccine strain, it was considered a match.

For influenza B, we considered two classically distinct virus lineages, Yamagata and Victoria, which are associated with different genetic and antigenic characteristics [50,51]. If the circulating B strain was in the same lineage as the vaccine strain, it was considered a match. We note that our definitions of vaccine match for both influenza B and A/H3N2 are similar to those used in a recent Canadian study evaluating influenza vaccine effectiveness by subtype [52].

To evaluate vaccine recommendations, we estimated the match proportion between circulating strains and vaccine strains by subtype, season and country. To compare vaccine match proportion between seasons and hemisphere, while taking into account potential geographical differences in sampling and vaccine match between countries, we used weighted *t*-tests for which weights were based on the number of influenza samples typed in each location and each season. We also conducted sensitivity analyses with a method that puts more emphasis on locations but disregards sampling issues (unweighted *t*-tests applied to average vaccine match proportion by hemisphere), and a method that disregards potential geographical heterogeneity but heavily relies on sampling (chi-square tests of aggregated virus surveillance data at the hemisphere and season level).

3. Results

3.1. Description of WHO influenza vaccine recommendations, 1990–2008

Table 1 lists the subtype-specific influenza vaccine composition recommendations issued by the WHO between 1990 and 2008. Nine recommendations were issued during the early part of our study period, 1990–1998, when influenza vaccine composition recommendations were made annually. Twenty recommendations (10 in the Northern Hemisphere and 10 in the Southern Hemisphere) were issued by the WHO during 1999–2008, when semi-annual composition recommendations were in place. Recommendations for vaccine composition in the Northern Hemisphere have been made between February 10 and March 1 since 1990, and between October 1 and 24 for the Southern Hemisphere since 1999. In three cases, incomplete recommendations were initially issued, twice without an A/H3N2 strain recommendation, and once with-

Table 1
Influenza vaccine recommendations issued by WHO, 1990–2008. Changes in vaccine composition are highlighted when they correspond to a change in vaccine strain (A/H1N1), antigenic cluster (A/H3N2), or lineage (B; Yamagata (Yam) vs Victoria (Vic)). N = Northern Hemisphere, S = Southern Hemisphere.

Hemisphere	Year	A/H1N1	A/H3N2	B
N	1990	A/Singapore/6/86	A/Guizhou/54/89	B/Yamagata/16/88 **(Yam)**
N	1991	A/Singapore/6/86	**A/Beijing/353/89**	B/Yamagata/16/88 or B/Panama/45/90 **(Yam)**
N	1992	A/Singapore/6/86	A/Beijing/353/89	B/Yamagata/16/88 or B/Panama/45/90
N	1993	A/Singapore/6/86	**A/Beijing/32/92**	**B/Panama/45/90 (Yam)**
N	1994	A/Singapore/6/86	A/Shangdong/9/93	B/Panama/45/90
N	1995	A/Singapore/6/86	A/Johannesburg/33/94	**B/Beijing/184/93 (Yam)**
N	1996	A/Singapore/6/86	**A/Wuhan/359/95**	B/Beijing/184/93
N	1997	**A/Bayern/7/95**	A/Wuhan/359/95	B/Beijing/184/93
N	1998	**A/Beijing/262/95**	**A/Sydney/5/97**	B/Beijing/184/93
S	1999	A/Beijing/262/95	A/Sydney/5/97	B/Beijing/184/93
N	1999	A/Beijing/262/95	A/Sydney/5/97[3]	B/Beijing/184/93
S	2000	**A/New Caledonia/20/99**	A/Moscow/10/99	B/Beijing/184/93
N	2000	A/New Caledonia/20/99	A/Moscow/10/99	B/Beijing/184/93
S	2001	A/New Caledonia/20/99	A/Moscow/10/99	**B/Sichuan/379/99 (Yam)**
N	2001	A/New Caledonia/20/99	A/Moscow/10/99	B/Sichuan/379/99
S	2002	A/New Caledonia/20/99	A/Moscow/10/99	B/Sichuan/379/99
N	2002	A/New Caledonia/20/99	A/Moscow/10/99	**B/Hong Kong/330/2001 (Vic)**
S	2003	A/New Caledonia/20/99	A/Moscow/10/99	B/Hong Kong/330/2001
N	2003	A/New Caledonia/20/99	A/Moscow/10/99	B/Hong Kong/330/2001
S	2004	A/New Caledonia/20/99	**A/Fujian/411/2002**	B/Hong Kong/330/2001
N	2004	A/New Caledonia/20/99	A/Fujian/411/2002	**B/Shanghai/361/2002 (Yam)**
S	2005	A/New Caledonia/20/99	**A/Wellington/1/2004**	B/Shanghai/361/2002
N	2005	A/New Caledonia/20/99	A/California/7/2004	B/Shanghai/361/2002
S	2006	A/New Caledonia/20/99	A/California/7/2004	**B/Malaysia/2506/2004 (Vic)**
N	2006	A/New Caledonia/20/99	**A/Wisconsin/67/2005**	B/Malaysia/2506/2004
S	2007	A/New Caledonia/20/99	A/Wisconsin/67/2005	B/Malaysia/2506/2004
N	2007	**A/Solomon Islands/3/2006**	A/Wisconsin/67/2005	B/Malaysia/2506/2004
S	2008	A/Solomon Islands/3/2006	A/Brisbane/10/2007	**B/Florida/4/2006 (Yam)**
N	2008	**A/Brisbane/59/2007**	A/Brisbane/10/2007	B/Florida/4/2006