

Differences in Influenza Seasonality by Latitude, Northern India

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The seasonality of influenza in the tropics complicates vaccination timing. We investigated influenza seasonality in northern India and found influenza positivity peaked in Srinagar (34.09°N) in January–March but peaked in New Delhi (28.66°N) in July–September. Srinagar should consider influenza vaccination in October–November, but New Delhi should vaccinate in May–June.

Annual and pandemic influenza are sources of considerable illness and death worldwide (1). Human influenza infection rates peak during the winter months in temperate regions; however, the pattern of influenza is different in tropical and subtropical areas, with year-round circulation in some areas and biannual peaks in others (2–5). The complex seasonality of influenza in the tropics complicates appropriate vaccination recommendations, particularly the timing of vaccination campaigns in tropical regions (3,4).

India has discrete seasons that vary greatly from north to south. Jammu and Kashmir, the northernmost state of India, has severe winters from December to March, whereas Delhi, the capital region, has milder winters. Sentinel surveillance for influenza in India has shown distinct influenza peaks in India (6–8). We undertook influenza surveillance during 2011–2012 in 2 cities in northern India, Srinagar and New Delhi, which are ≈500 km apart, and found evidence for discrete seasonality related to the latitudes of these cities, a finding that has implications for influenza vaccination policy and timing.

The Study

For the study, we enrolled patients who attended the outpatient clinics at the All India Institute of Medical

Sciences, New Delhi, and Sheri-Kashmir Institute of Medical Sciences, Srinagar, during 2011–2012 who had influenza-like illness (ILI; defined as sudden onset or history of fever >38°C, cough or sore throat and/or rhinorrhea) (6). We collected 5–10 nasopharyngeal samples from these patients each week and tested them for influenza viruses by type and subtype (9,10). A confirmed case-patient was defined as a patient meeting the ILI case definition who had positive results for influenza by reverse transcription PCR. Sanger sequencing of the hemagglutinin and neuraminidase genes was completed, and consensus was used to construct a Kimura 2-parameter neighbor-joining tree (online Technical Appendix Figure 1, <http://wwwnc.cdc.gov/EID/article/20/10/14-0431-Techapp1.pdf>). Sequences from New Delhi and Srinagar were compared with those of vaccine strains and with published cognate sequences of corresponding genes (online Technical Appendix Table 1), including those from India (10).

Surveillance for influenza viruses revealed that overall influenza positivity was 17.6% (375 confirmed cases from 2,126 ILI patients) in Srinagar and 9.46% (239/2,526) in New Delhi (Table). Discrete winter time peaks were observed during January–March (epidemiologic weeks [EW] 1–12) in Srinagar, whereas New Delhi had peaks of influenza circulation during July 2011 and September 2012 (EW 26–36) (Figure 1). Influenza A was the predominant type in Srinagar (275/375; 72.9%), whereas influenza B dominated in New Delhi (154/239; 64.4%). Circulation of influenza A(H3N2) during the monsoon season of 2011 in New Delhi was followed by predominance of H3N2 during winter 2012 in Srinagar (Figure 1).

Phylogenetic analysis of the hemagglutinin and neuraminidase genes from selected samples from New Delhi and Srinagar revealed no notable differences between circulating viruses (online Technical Appendix Figure 1). Furthermore, circulating influenza strains were closely related to the selected influenza vaccine strains, A/California/7/2009 (H1N1), A/Perth/16/2009 (H3N2), and B/Brisbane/60/2008, which remained unchanged for 2011–2012 for the Northern and Southern Hemisphere formulations (online Technical Appendix Figure 2). The 2012–2013 Northern Hemisphere formulation changed the H3N2 strain to A/Victoria/361/2011 and the influenza B strain to B/Wisconsin/1/2010, but sequence information from 2013 circulating viruses from Srinagar was not available to assess vaccine similarity.

Analysis of meteorologic factors (i.e., rainfall, temperature, relative humidity, vapor pressure, and dew point)

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Table. Influenza surveillance, Srinagar and Delhi, India, 2011–2012

City	No. (%) persons		
	2011	2012	Total
Srinagar (34.09°N)			
Tested	768	1,371	2,139
Influenza positive	162 (21)	215 (15.7)	377 (17.6)
Influenza type*			
A(H1N1)pdm09	95 (58.6)	57 (26.5)	152 (40.3)
A(H3N2)	38 (23.5)	85 (39.5)	123 (32.6)
B	29 (17.9)	73 (34.0)	102 (27.1)
New Delhi (28.66°N)			
Tested	1,007	1,519	2,526
Influenza positive	74 (7.3)	165 (10.8)	239 (9.46)
Influenza type*			
A(H1N1)pdm09	3 (4.1)	44 (26.7)	47 (19.7)
A(H3N2)	38 (51.4)	0	38 (15.9)
B	33 (44.6)	121 (73.3)	154 (64.4)

*Percentages are of all influenza-positive test results in category.

showed that the monthly proportion of influenza positivity correlated with decreased temperature and dew point in Srinagar and with rainfall amount in New Delhi (data not shown). Cumulative data over the 2-year surveillance period revealed differences in seasonality by latitude; influenza

positivity peaked during December–February in Srinagar (34.09°N) but in July–September in New Delhi (28.66°N) (Figure 2). Influenza seasonality indicates that New Delhi would likely benefit from springtime vaccination (May–June), whereas vaccination in the fall (October–November) would be better for Srinagar (Figure 2). We recently illustrated that India and most other tropical countries in Asia exhibit influenza seasonality that coincides with the monsoon season, June–October (11).

Conclusions

We identified discrete patterns of influenza circulation in India. In Srinagar, a city in the northernmost region of India, influenza positivity rates peaked in winter (December–March), whereas in New Delhi, a city just ≈ 500 km south of Srinagar, influenza peaked during the monsoon season (July–September). The winter peak in Srinagar is similar to the timing of influenza circulation observed for most countries in Europe and United States in the Northern Hemisphere (4,5). By contrast, the data on influenza seasonality in New Delhi corroborate findings which showed

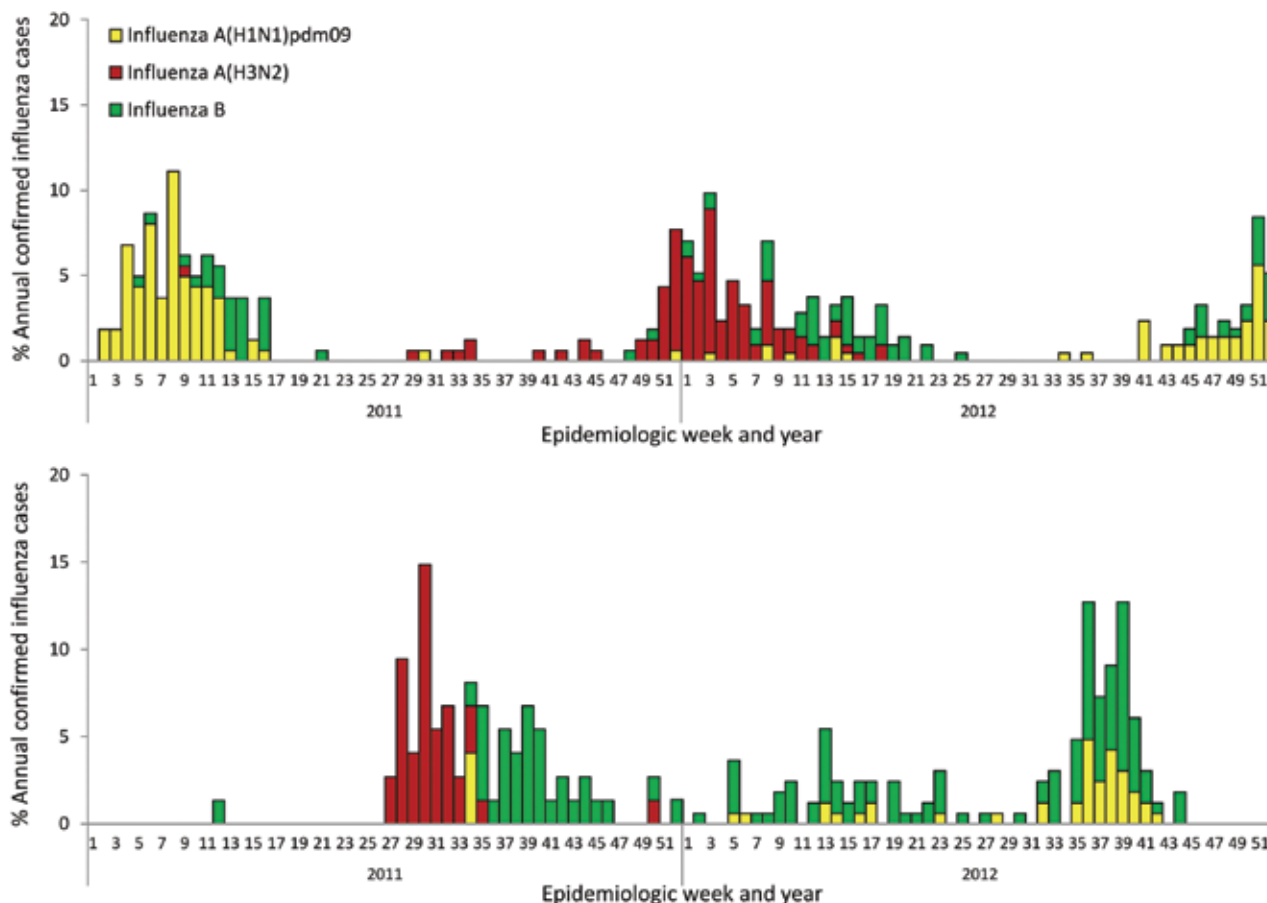


Figure 1. Weekly trends and proportion of annual numbers of positive influenza cases, by epidemiologic week and influenza type, Srinagar (A) and New Delhi (B), India, 2011–2012. Clear seasonal peaks are seen in January–March (weeks 1–16) for Srinagar and in July and September (weeks 28–40) for New Delhi.

that many countries in tropical regions (e.g., Brazil, India, Vietnam) experience high influenza transmission rates during the rainy season (6,11–13). Overall, influenza A and B viruses co-circulated throughout the surveillance period in Srinagar and New Delhi; however, the types and subtypes varied.

Peaks of influenza circulation in Srinagar and New Delhi show seasonal patterns that depend on factors such as temperature, rainfall, humidity, and latitude (2,3). Srinagar, at $>30^{\circ}\text{N}$ latitude, has influenza seasonality that coincides with lower temperature and low dew points during winter, whereas New Delhi, at $<30^{\circ}\text{N}$ latitude, has a peak of influenza circulation that coincides with the rainy season. Seasonal influenza activity coinciding with the humid, rainy season at lower latitudes has also been observed in large areas of Central and South America and southern Asia (11,13). In contrast, cold, dry weather was predictive of influenza peaks at higher latitudes, as observed for Srinagar. The latitude dependence of influenza circulation observed in this study is similar to such dependence observed in Brazil and China (13,14) and collectively suggests that decisions on the timing of influenza vaccination should not be based only on the hemisphere a country is in but also on the types of seasonal patterns that exist within a country (15). These latitudinal differences in influenza seasonality in India have implications for influenza vaccine timing and vaccine formulation.

Influenza vaccine induces a neutralizing antibody response that wanes over time. Thus, the timing of vaccination has a direct effect on vaccine effectiveness. In the northernmost part of India, peak influenza circulation occurs during the winter months; therefore, vaccination during October–November using the Northern Hemisphere vaccine formulation may be appropriate. However, this practice would not be appropriate in the Delhi metropolitan region, where influenza peaks in July–September. In addition, whereas our data points to an approximate latitude where temperate and tropical patterns for influenza peaks diverge, more robust data with multiple surveillance sites in tropical, subtropical, and temperate regions in India and China are needed to define the exact latitude points for influenza circulation patterns.

Our study has limitations. First, comparative data were available only for 2 years. Additional surveillance data for multiple years and many cities around the latitude gradient are required to further corroborate these observations. Furthermore, validation of vaccine formulation will require tracking of additional circulating influenza strains over several epidemic periods.

In summary, we identified 2 distinct seasons for influenza circulation in 2 cities in India. We recommend that policy makers in India review circulation patterns closely before implementing influenza intervention plans. Our data suggest that cities in India located north of 30°N latitude can continue vaccination in the winter, but those south of 30°N , including New Delhi, should consider vaccination in May–June (15). Collectively, these data should help decision makers, especially regulatory authorities, choose vaccines and vaccination schedules best suited for each region.

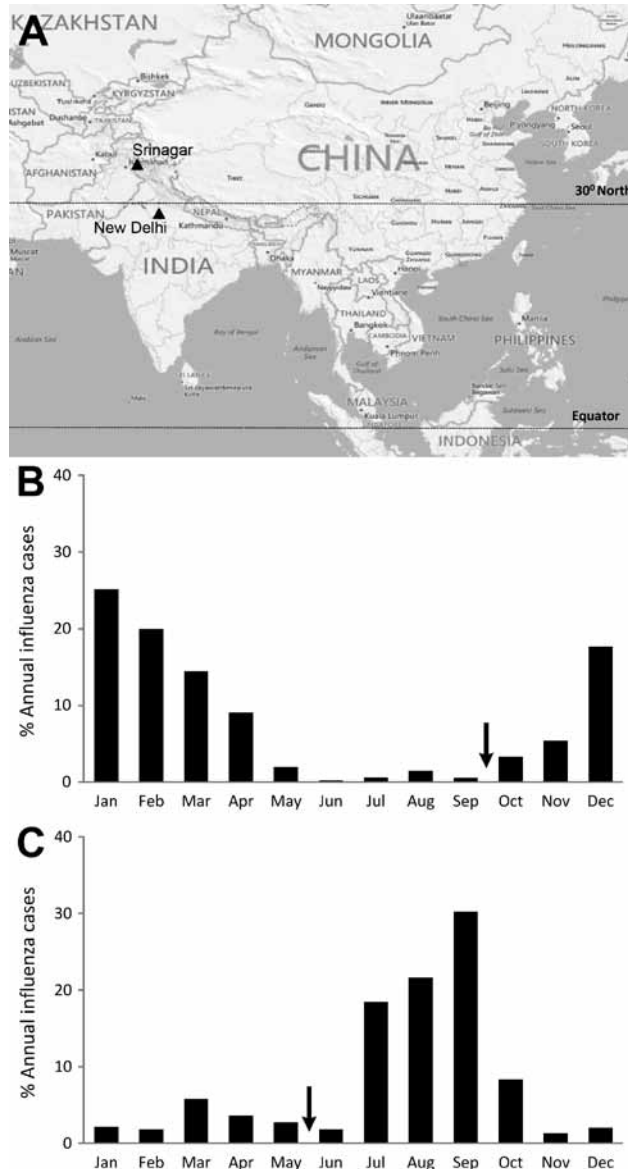


Figure 2. Comparison of latitudes of Srinagar and New Delhi, India, and distribution of influenza virus infections, 2011–2012. A) Locations of Srinagar and New Delhi (black triangles), with vertical lines indicating 30°N latitude and equator. B) Monthly distribution of cases of influenza virus infection in Srinagar (34.0°N latitude). C) Monthly distribution of cases of influenza virus infection in New Delhi (28.7°N latitude). Arrows indicate proposed vaccination timing; latitude of each city is shown. Map created in Epi-Map in Epi Info 7 (Centers for Disease Control and Prevention, Atlanta, GA, USA).

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Technical Appendix

Technical Appendix Table. Influenza strains and gene segments from GISAID EpiFlu database used in this study*

EPI-Segment-ID	Segment	Length	Strain
EPI332607	HA	1701	A/Alaska/14/2011
EPI215877	NA	1410	A/Alaska/14/2011
EPI325551	HA	1701	A/American Samoa/4520/2011
EPI325575	NA	1410	A/American Samoa/4520/2011
EPI404814	HA	1701	A/Argentina/1033/2012
EPI331203	NA	1410	A/Argentina/1033/2012
EPI267876	HA	1701	A/Argentina/19527/2009
EPI331206	NA	1410	A/Argentina/19527/2009
EPI331198	HA	1701	A/Argentina/63/2011
EPI273913	NA	1410	A/Argentina/63/2011
EPI335786	HA	1701	A/Argentina/8836/2011
EPI319996	NA	1410	A/Argentina/8836/2011
EPI330987	HA	1701	A/Arkansas/03/2011
EPI215722	NA	1410	A/Arkansas/03/2011
EPI331201	HA	1701	A/Bangladesh/8324/2011
EPI273910	NA	1410	A/Bangladesh/8324/2011
EPI215724	NA	1410	A/Barbados/104/2011
EPI194113	HA	1701	A/Bolivia/1263/2009
EPI319991	NA	1410	A/Bolivia/1263/2009
EPI341964	HA	1701	A/Bolivia/193/2011
EPI320120	NA	1410	A/Bolivia/193/2011
EPI404834	HA	1701	A/Bolivia/3040/2012
EPI325559	NA	1410	A/Bolivia/3040/2012
EPI280335	HA	1701	A/Brisbane/10/2010
EPI273896	NA	1410	A/Brisbane/10/2010
EPI273609	HA	1701	A/California/07/2009
EPI325587	NA	1410	A/California/07/2009
EPI316335	HA	1701	A/California/17/2011
EPI331040	HA	1701	A/Cape Town/60/2011
EPI325572	NA	1410	A/Cape Town/60/2011
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EPI325567	HA	1701	A/Chile/293/2011
EPI331041	NA	1410	A/Chile/293/2011
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EPI325578	NA	1410	A/Christchurch/16/2010
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EPI331215	NA	1410	A/Concepcion/16695/2011
EPI397078	NA	1410	A/Connecticut/08/2011
EPI537424	NA	1410	A/Delhi/1717/2012
EPI537425	NA	1410	A/Delhi/1938/2012
EPI537426	NA	1410	A/Delhi/1939/2012
EPI537428	HA	1701	A/Delhi/1966/2012
EPI537427	NA	1410	A/Delhi/1966/2012
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EPI370247	NA	1410	A/Dominican Republic/5059/2011
EPI271947	NA	1410	A/Dominican Republic/5145/2011
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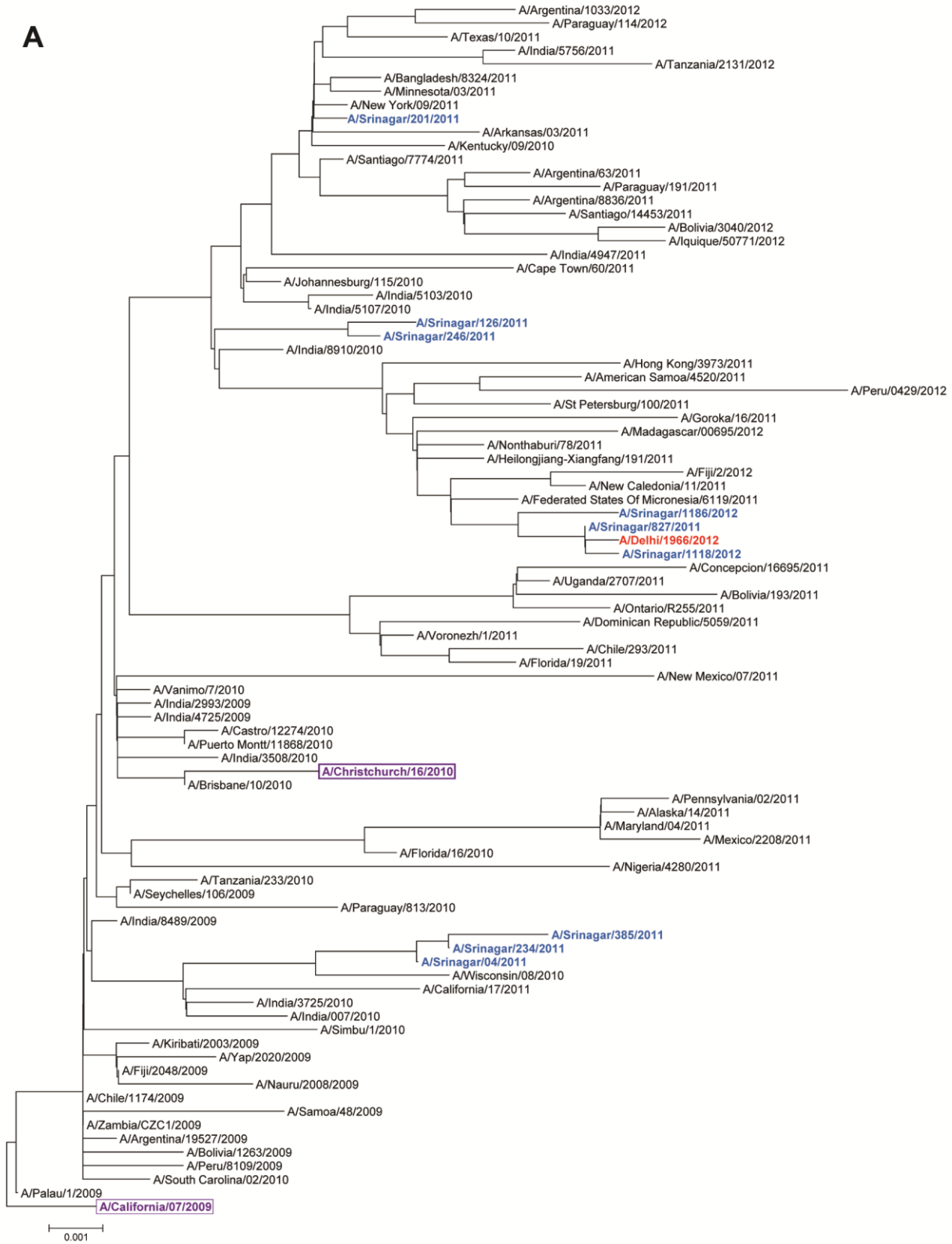
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EPI320013	NA	1410	A/Goroka/16/2011
EPI325576	HA	1701	A/Heilongjiang-Xiangfang/191/2011
EPI426452	NA	1410	A/Heilongjiang-Xiangfang/191/2011
EPI294253	NA	1410	A/Hong Kong/3962/2011
EPI331207	HA	1701	A/Hong Kong/3973/2011
EPI404813	NA	1410	A/Hong Kong/3973/2011
EPI194114	NA	1410	A/Hunan-Jishou/1116/2011
EPI278875	HA	1701	A/India/007/2010
EPI254552	NA	1410	A/India/007/2010
EPI227676	HA	1701	A/India/2993/2009
EPI280334	NA	1410	A/India/2993/2009
EPI295462	HA	1701	A/India/3508/2010
EPI353908	NA	1410	A/India/3508/2010
EPI273897	HA	1701	A/India/3725/2010
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EPI254551	HA	1701	A/India/4725/2009
EPI342419	NA	1410	A/India/4725/2009
EPI325579	HA	1701	A/India/4947/2011
EPI267878	NA	1410	A/India/4947/2011
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EPI278873	HA	1701	A/India/8910/2010
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EPI280325	NA	1410	A/India/8942/2012
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EPI342434	HA	1701	A/Kentucky/09/2010
EPI409911	NA	1410	A/Kentucky/09/2010
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EPI349352	HA	1701	A/Paraguay/191/2011
EPI316438	NA	1410	A/Paraguay/191/2011
EPI301698	HA	1701	A/Paraguay/813/2010
EPI316467	NA	1410	A/Paraguay/813/2010
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EPI272299	NA	1410	A/Pennsylvania/02/2011
EPI409912	HA	1701	A/Peru/0429/2012
EPI320094	NA	1410	A/Peru/0429/2012
EPI243881	HA	1701	A/Peru/8109/2009
EPI331212	NA	1410	A/Peru/8109/2009
EPI273911	HA	1701	A/Puerto Montt/11868/2010
EPI316334	NA	1410	A/Puerto Montt/11868/2010
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EPI194242	HA	1701	A/Seychelles/106/2009
EPI320097	NA	1410	A/Seychelles/106/2009
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EPI537432	HA	1701	A/Srinigar/201/2011
EPI537431	NA	1410	A/Srinigar/201/2011
EPI537435	NA	1410	A/Srinigar/226/2011
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EPI537440	NA	1410	A/Srinigar/410/2011
EPI537442	HA	1701	A/Srinigar/827/2011
EPI537441	NA	1410	A/Srinigar/827/2011
EPI316435	HA	1701	A/St. Petersburg/100/2011
EPI233071	NA	1410	A/St. Petersburg/100/2011
EPI215652	NA	1410	A/St. Petersburg/25/2011
EPI440929	HA	1701	A/Tanzania/2131/2012
EPI320021	NA	1410	A/Tanzania/2131/2012
EPI273851	HA	1701	A/Tanzania/233/2010
EPI332609	NA	1410	A/Tanzania/233/2010
EPI331216	HA	1701	A/Texas/10/2011
EPI301697	NA	1410	A/Texas/10/2011
EPI331219	HA	1701	A/Uganda/2707/2011
EPI243880	NA	1410	A/Uganda/2707/2011
EPI294254	HA	1701	A/Vanimu/7/2010
EPI342433	NA	1410	A/Vanimu/7/2010
EPI316468	HA	1701	A/Voronezh/1/2011
EPI215716	NA	1410	A/Voronezh/1/2011
EPI280326	HA	1701	A/Wisconsin/08/2010
EPI295461	NA	1410	A/Wisconsin/08/2010
EPI215878	HA	1701	A/Yap/2020/2009
EPI325544	NA	1410	A/Yap/2020/2009
EPI272184	HA	1701	A/Zambia/CZC1/2009
EPI331200	NA	1410	A/Zambia/CZC1/2009

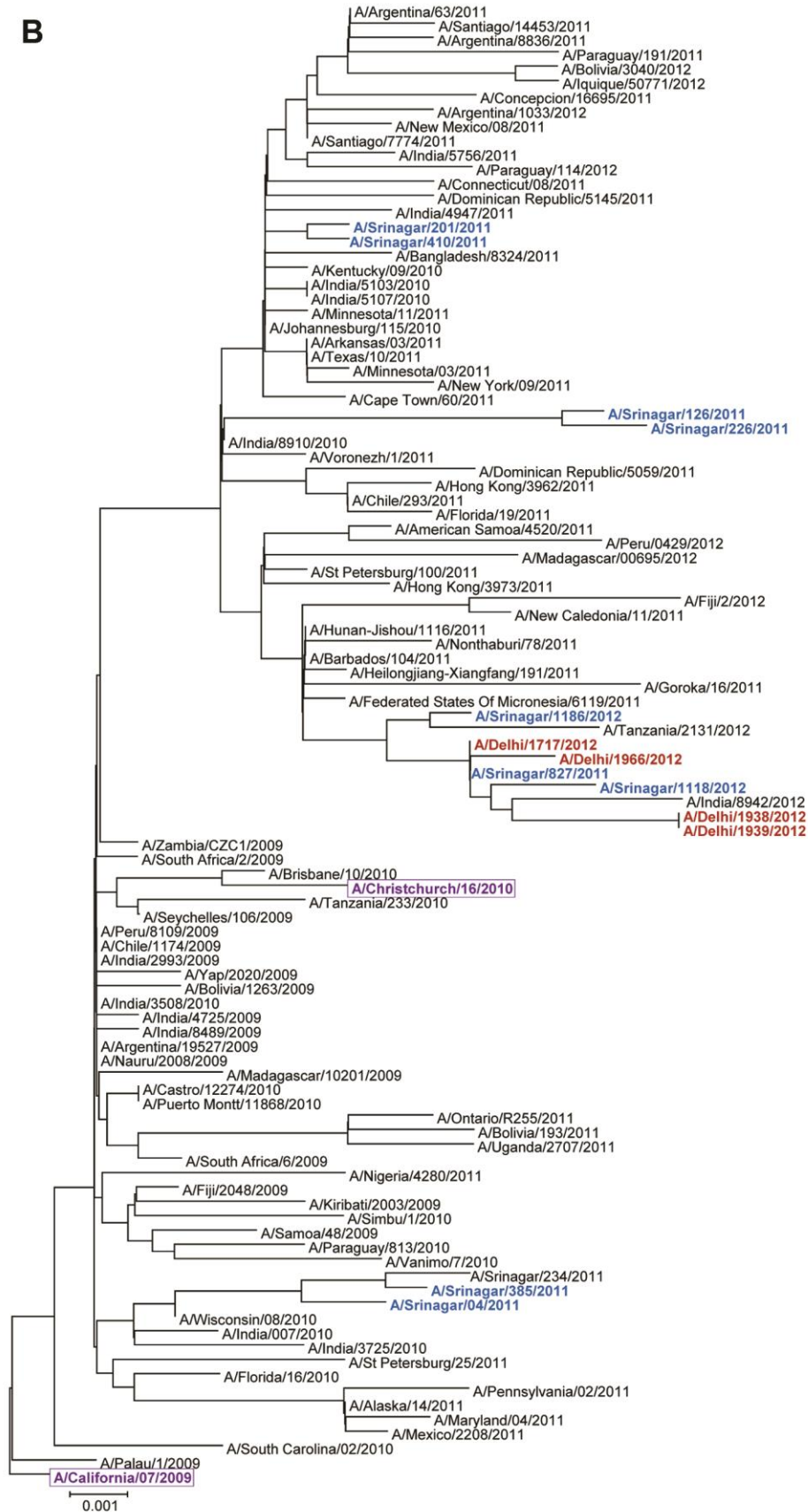
*<http://www.gisaid.org>.

Technical Appendix Figure 1 (following pages). Phylogenetic analysis of hemagglutinin (HA) and neuraminidase (NA) gene sequences of influenza virus strains from Srinagar and New Delhi, India, compared with published sequences and corresponding vaccine strains. Strains from Srinagar are shown in blue, from Delhi in red, and from influenza vaccine in purple; other strains are from published sequences, including those from India. A) Influenza A(H1N1)pdm09 HA gene; B) influenza A(H1N1)pdm09 NA gene; C) influenza A(H3N2) HA gene; D) influenza A(H3N2) NA gene; E) influenza B Victoria lineage HA gene; F) influenza B Victoria lineage NA gene; G) influenza B Yamagata lineage HA gene; and H) influenza B Yamagata lineage NA gene. HA-1 and NA genes were amplified and PCR products were sequenced using the dideoxynucleotides chain termination method using Big-Dye Terminator Chemistry (Life Technologies, Grand Island, NY, USA). A neighbor-joining tree was generated by using pairwise gap deletion and maximum composite likelihood using the Tamura-Nei nucleotide model in MEGA4 (<http://www.megasoftware.net>).

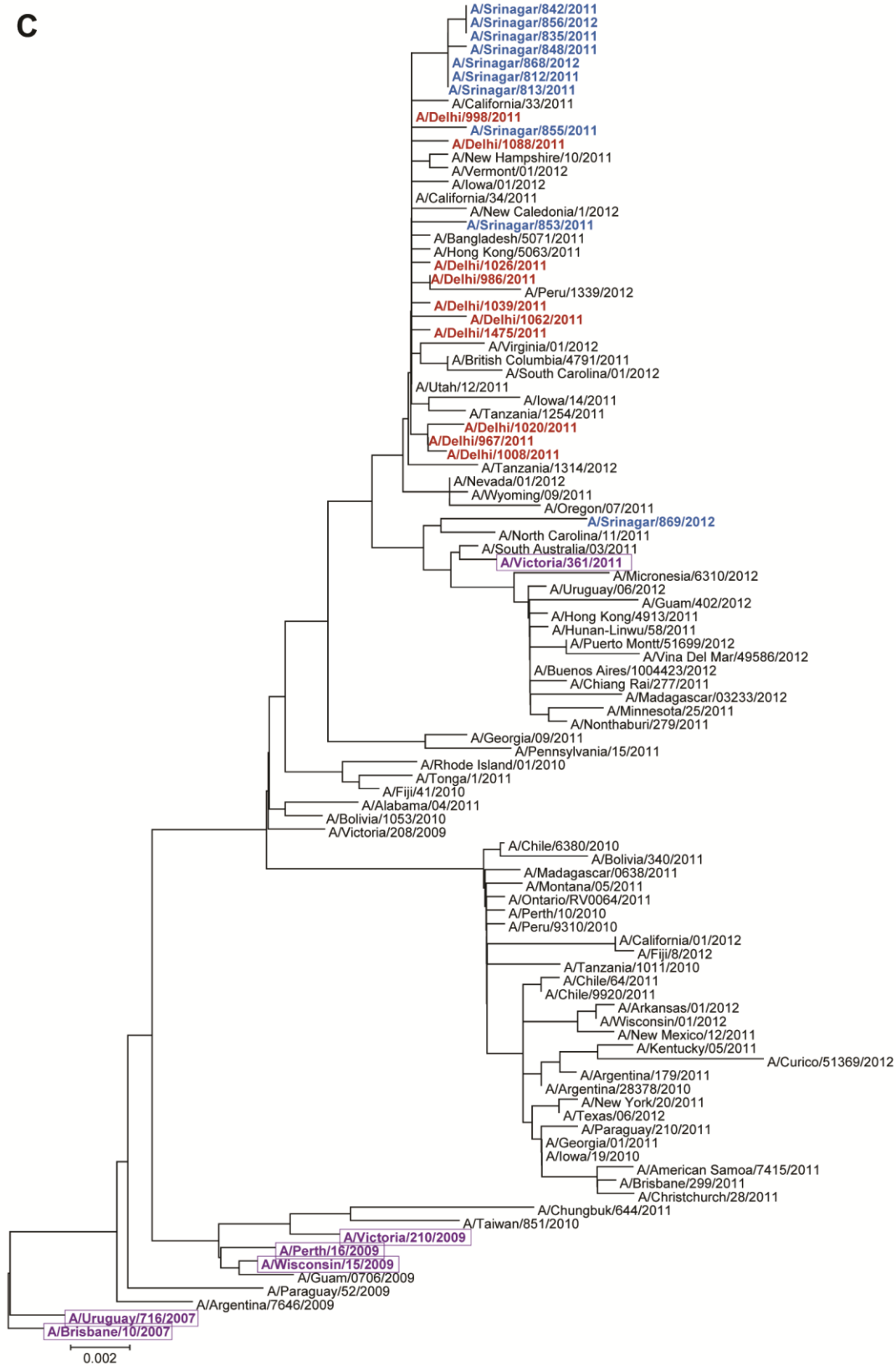
A



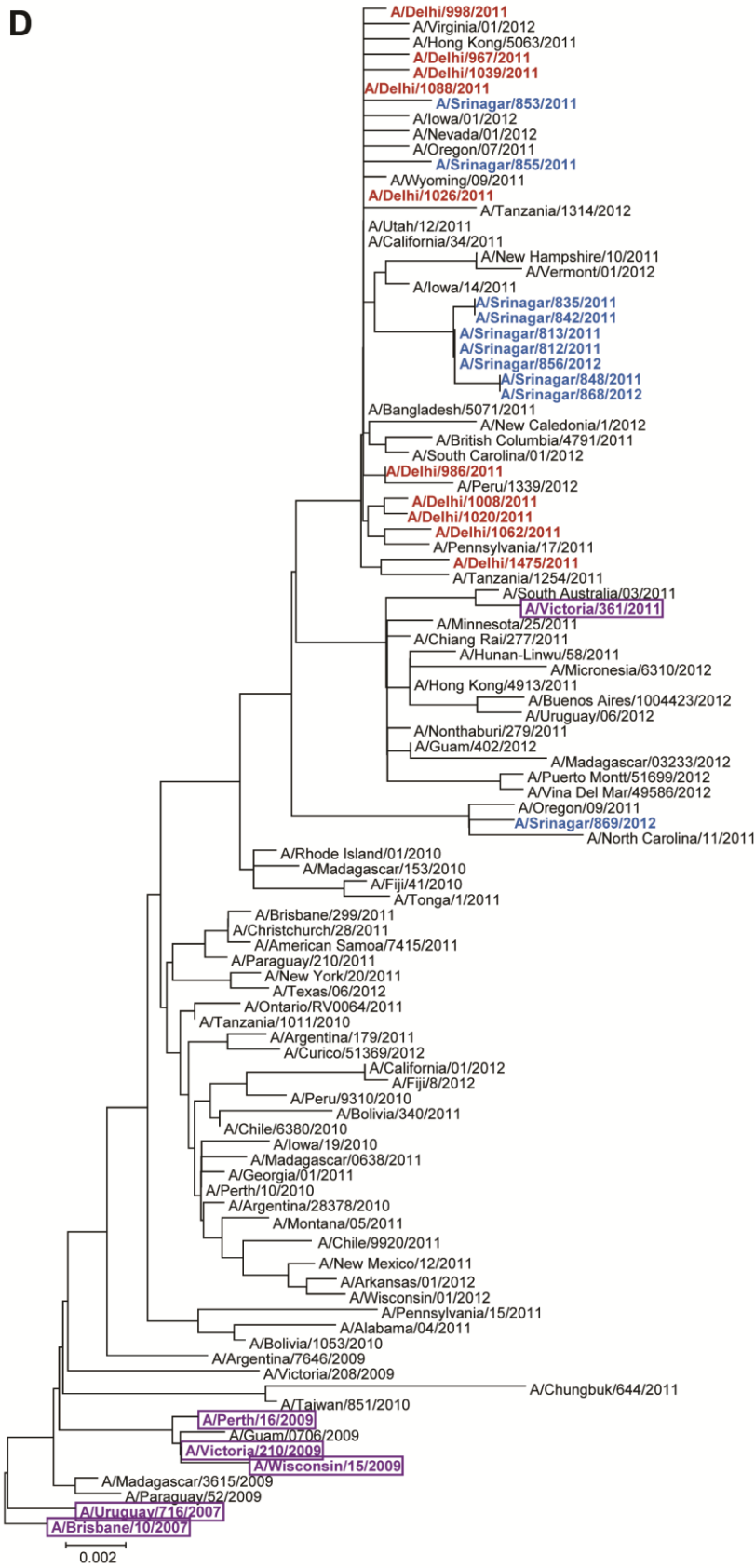
B



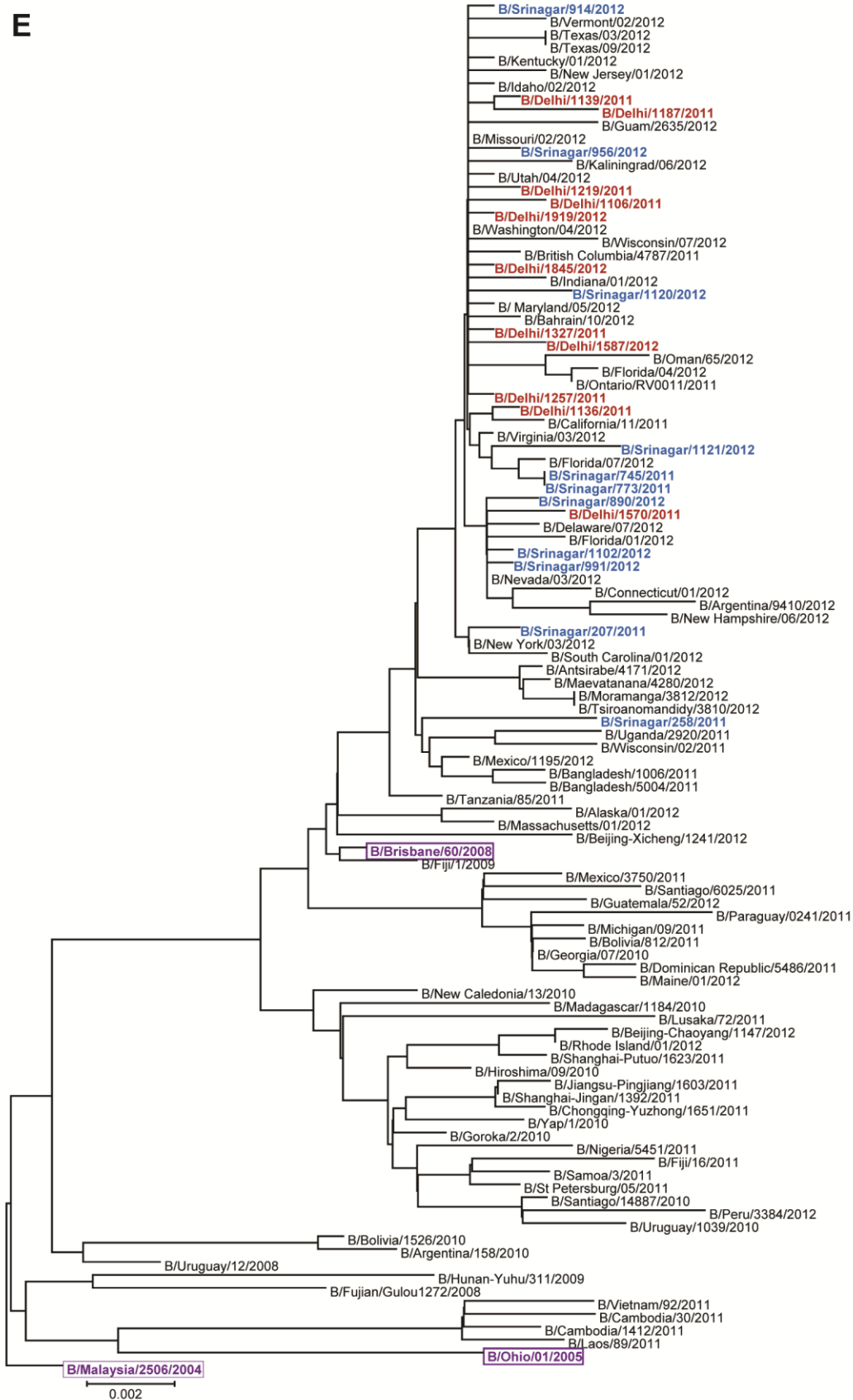
C



D



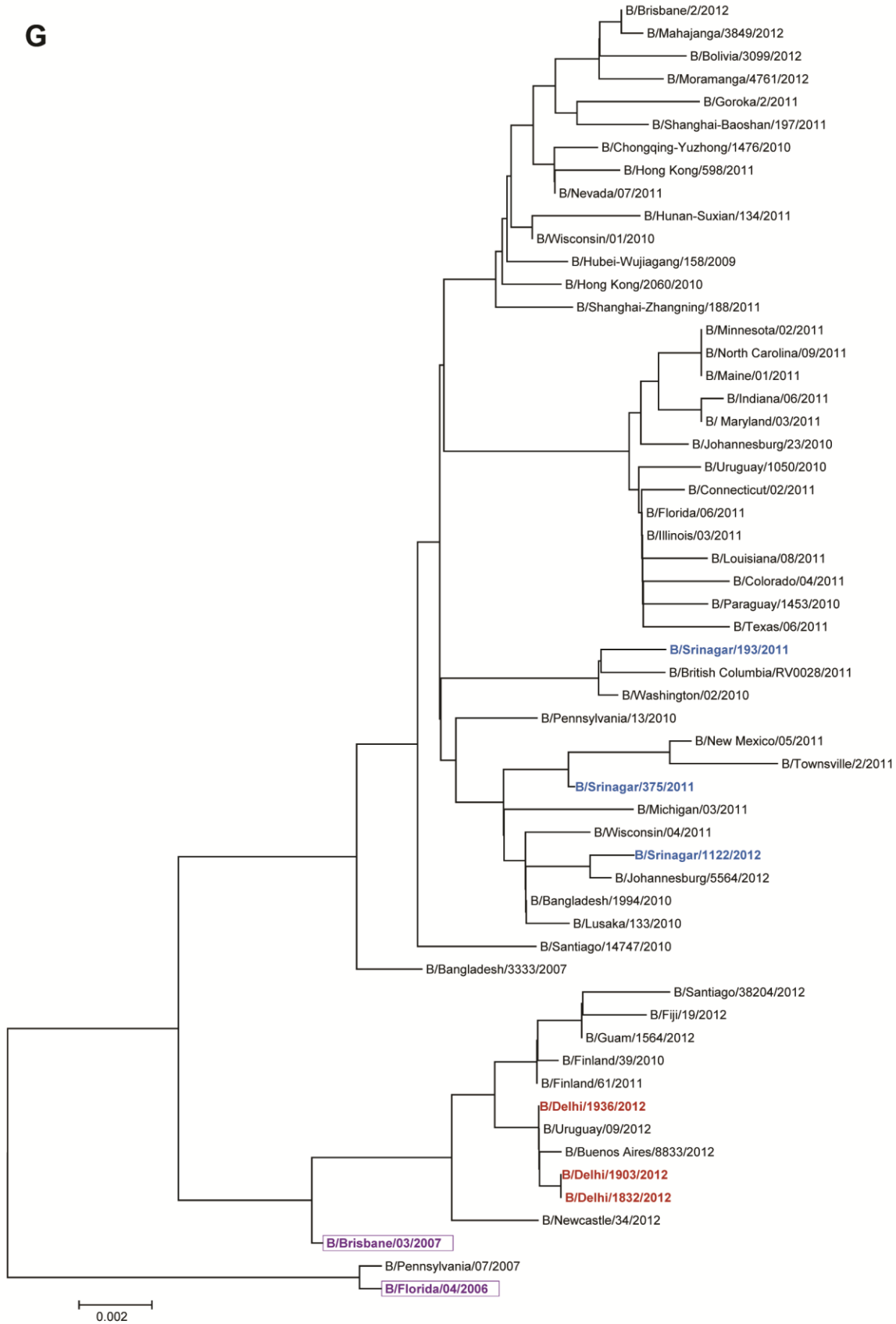
E



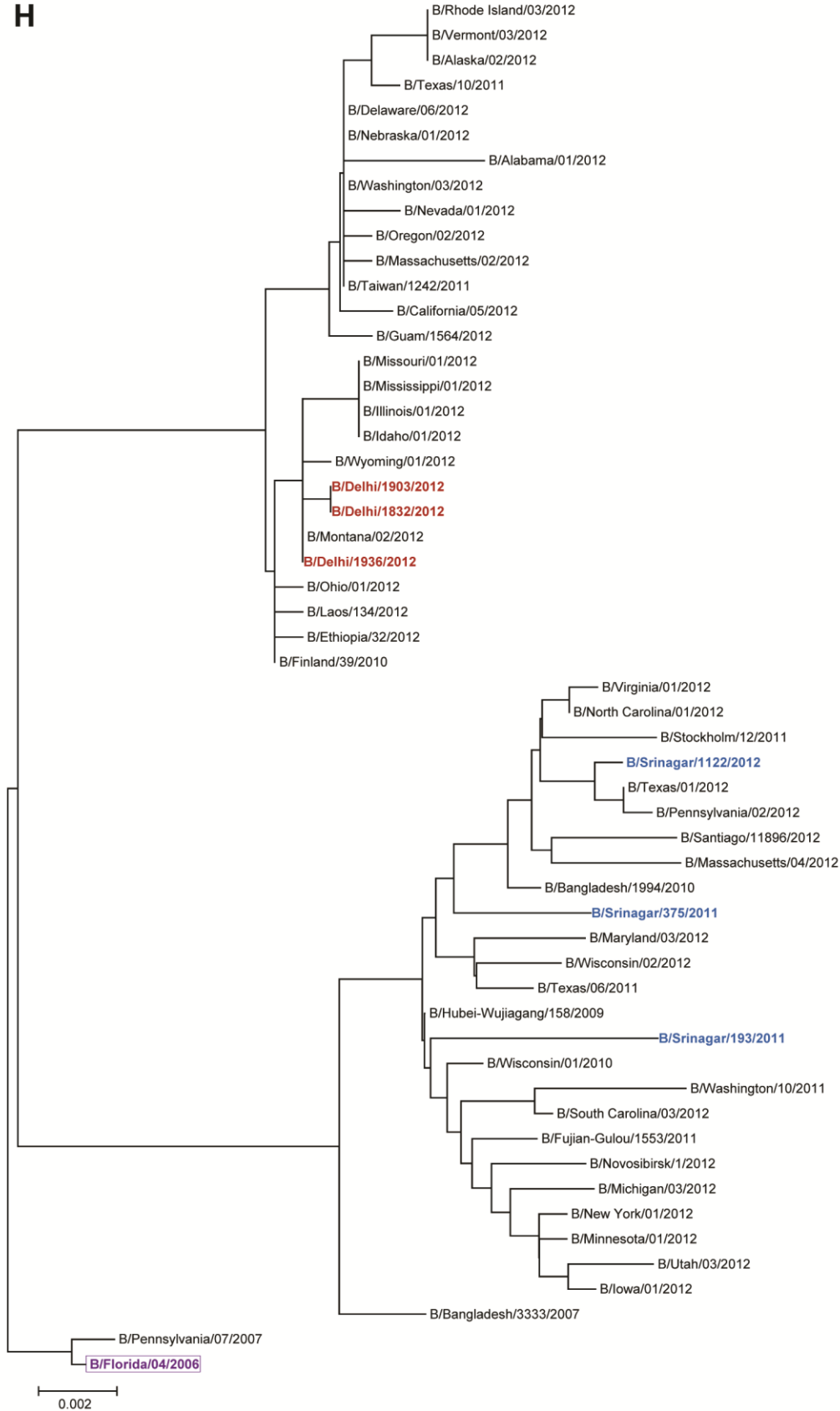
F



G



H



Technical Appendix Figure 2. World Health Organization recommended vaccines by season and hemisphere, 2006–2014.

Northern Hemisphere				Southern Hemisphere		
Season	Recommended Strain	alternates	Subtype	Season	Recommended Strain	alternates
2006-07	Wisconsin/67/2005	Hiroshima/52/2005	H3N2	2007	Wisconsin/67/2005	Hiroshima/52/2005
	New Caledonia/20/99		H1N1		New Caledonia/20/99	
	Malaysia/2506/2004	Ohio/1/2005	B Victoria		Malaysia/2506/2004	
			B Yamagata			
2007-08	Wisconsin/67/2005	Hiroshima/52/2005	H3N2	2008	Brisbane/10/2007	
	Solomon Islands/1513/2006		H1N1		Solomon Islands/1513/2006	
	Malaysia/2506/2004		B Victoria			
			B Yamagata		Florida/4/2006	
2008-09	Brisbane/10/2007		H3N2	2009	Brisbane/10/2007	Uruguay/716/2007
	Brisbane/59/2007		H1N1		Brisbane/59/2007	South Dakota/6/2007
			B Victoria			
	Florida/4/2006		B Yamagata		Florida/4/2006	Brisbane/3/2007
2009-10	Brisbane/10/2007	Uruguay/716/2007	H3N2	2010	Perth/16/2009	
	Brisbane/59/2007	South Dakota/6/2007	H1N1		H1pdm	California/7/2009
	Brisbane/60/2008	Brisbane/33/2008	B Victoria			Brisbane/60/2008
			B Yamagata			
2010-11	Perth/16/2009	Wisconsin/15/2009	H3N2	2011	Perth/16/2009	Wisconsin/15/2009 Victoria/210/2009
	California/7/2009		H1N1pdm		California/7/2009	
	Brisbane/60/2008		B Victoria		Brisbane/60/2008	
			B Yamagata			
2011-12	Perth/16/2009		H3N2	2012	Perth/16/2009	
	California/7/2009		H1N1pdm		California/7/2009	
	Brisbane/60/2008		B Victoria		Brisbane/60/2008	
			B Yamagata			
2012-13	Victoria/361/2011		H3N2	2013	Victoria/361/2011	Brisbane/6/2012 Ohio/2/2012 Maryland/2/2012 South Australia/30/2012 Brisbane/1/2012 Christ Church/16/2010
	California/7/2009		H1N1pdm		California/7/2009	
			B Victoria		Brisbane/60/2008	
	Wisconsin/1/2010		B Yamagata			
2013-14	Victoria/361/2011	Texas/50/2012	H3N2	2014	Texas/50/2012	
	California/7/2009	Christ Church/10/2010	H1N1pdm		California/7/2009	Christ Church/10/2010
	Brisbane/60/2008		B Victoria		Brisbane/60/2008	
	Massachusetts/2/2012		B Yamagata		Massachusetts/2/2012	