Differential age susceptibility to influenza B/Victoria lineage viruses in the 2015 Australian influenza season

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Influenza B viruses make up an important part of the burden from seasonal influenza globally. The 2015 season in Australia saw an unusual predominance of influenza B with a distinctive switch during the season from B/Yamagata/16/88 lineage viruses to B/Victoria/2/87 lineage viruses. We also noted significant differences in the age groups infected by the different B lineages, with B/Victoria infecting a younger population than B/Yamagata, that could not be explained by potential prior exposure.

The 2015 season was notable for the predominance of influenza B in Australia. According to the Australian Influenza Surveillance Report [1] for the period 1 January to 9 October, 61% of cases were typed as influenza B and 38% influenza A (29% A (not subtyped), 7% A(H3N2) and 2% A(H1N1)pdm09). That season was also interesting due to the waxing and waning of the two B lineages over the season. Here, we summarise the lineage distribution using viruses submitted to the WHO Collaborating Centre for Reference and Research on Influenza in Melbourne for 2015 and compared these data with data from 2008, the last year when influenza B viruses predominated in Australia.

The 2015 influenza season in Australia

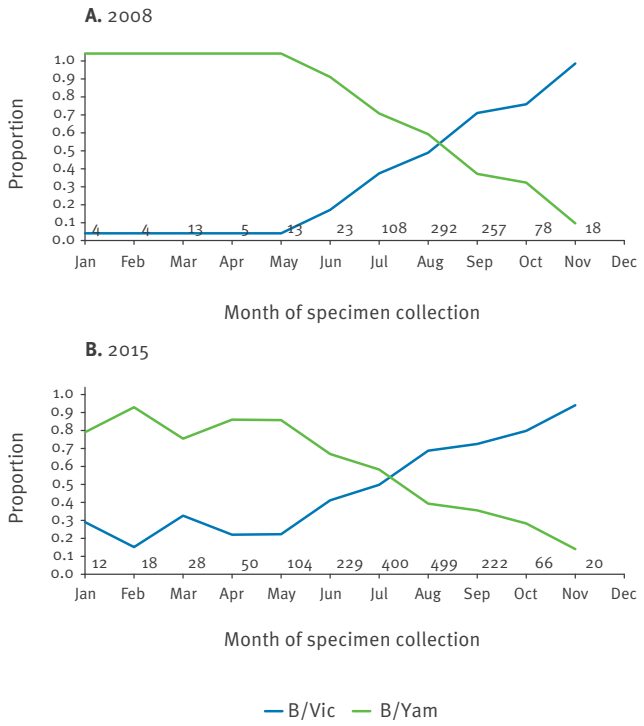
Lineage data was available for 816 influenza B viruses from 2008 and 1,648 from 2015 that were received by the Centre from all over Australia. The formal representativeness of these samples is unknown. Generally there is a bias towards sampling from children and this is seen in most years in most general and sentinel surveillance systems and was also seen in the 2008 [2] and 2015 [1] Australian influenza seasons. It is unlikely that any bias would exist in selecting patients with a particular B lineage, and given the size and the geographical diversity of the samples tested, it is likely these data will provide an accurate estimate of the overall situation with influenza B in Australia during these two years. During the 2015 pre-season period (January–April) and the early part of the influenza season (May–June), B/Yamagata/16/88 lineage (B/Yam) viruses predominated. However, from July to November, B/Victoria/2/87 lineage (B/Vic) viruses increased rapidly and were dominant from August (Figure 1). Notably, this same switch was seen during the 2008 season with similar timing although almost no B/Vic lineage viruses were detected in Australia before June (Figure 1). The distributions of lineages during 2015 were similar when individual Australian states were examined, with the exception of the Northern Territory, which has a small population largely situated in the tropics, that had an almost total B/Vic year (36/39 B viruses). Australia's most populous state, New South Wales, experienced an increase in the proportion of B/Vic viruses from low levels early in 2015 to 28% during the period from 15 June to 12 July 2015 [3] which according to our study continued to increase over the rest of the influenza season, and B/Vic viruses predominated from July onwards. Children and young adults carry a higher burden of influenza B disease than older adults and the elderly. According to the Australian Paediatric Surveillance Unit 2015 saw 88 children 15 years and younger (median: 3.3 years) hospitalised with severe complications of influenza between 1 July 2015 and 30 September 2015. Roughly two thirds (n = 59) were influenza B cases (lineage unknown) [1]. Overall, the average duration of hospitalisation was four days, 20 required an ICU admission, and there were three influenza-associated deaths, all associated with influenza B infections [1].

Antigenic and genetic drift

The move in dominance by the B/Vic viruses in 2015 was not accompanied by any major antigenic changes from the B/Vic viruses that circulated in smaller numbers in 2014. All Australian B/Vic viruses analysed by the Centre were antigenically B/Brisbane/60/2008-like as they were in 2014 (data not shown). Equally, the 2015 B/Yam viruses that were analysed remained

Figure 1

Relative frequency of influenza B subtypes received by month of specimen collection, Australia, 2008 (n = 816) and 2015 (n = 1,648)



B/Vic: B/Victoria/2/87 lineage; B/Yam: B/Yamagata/16/88 lineage.

Numbers at the bottom of the figure are the total number of B viruses tested for each month. Top panel: influenza B subtypes in 2008 (n=415 B/Vic, n=401 B/Yam); bottom panel: influenza B subtypes in 2015 (n=852 B/Vic, n=796 B/Yam).

antigenically B/Phuket3073/2013-like, similar to B/Yam viruses that circulated in Australia from mid-2014 (data not shown). However, subtle phylogenetic differences in the haemagglutinin (HA) genes of the two B lineages were apparent (Figure 2). The HA gene phylogeny revealed a greater diversity for B/Yam viruses isolated in Australia during 2015 (n=56) than during 2014 (n=42) (Figure 2, top panel). The mean time to most recent common ancestor (mTMRCA) extended beyond 2012 and the isolates belonged to three antigenic types (B/Wisconsin/1/2010, B/Massachusetts/2/2012 and B/Phuket/3073/2013), although the majority from 2015 (52 of the 56 viruses from 2015) belonged to the B/Phuket/3073/2013 clade (also known as group 3) with a mTMRCA in mid-2014. Reconstruction of non-synonymous changes along this phylogeny revealed an amino acid substitution (M267V) in the subclade of B/Phuket/3073/2013-like viruses that were dominant during the 2015 season, suggesting that this mutation may have contributed to increased viral fitness. All Australian B/Vic viruses from 2015 (n=54) were phylogenetically B/Brisbane/60/2008-like (also referred to as clade 1A) with an mTMRCA in 2013. This clade was made up of three distinct subclades (Figure 2, bottom panel) the largest of which had the non-synonymous amino acid substitutions V161I and I132V that may have also enhanced the fitness of these viruses.

Age distribution of influenza B infections

The age distribution of patients with confirmed B/Vic infections in 2015 was positively skewed, with a greater number of infections among the younger age groups (mean: 26.4 years, median: 19.9 years). For B/Yam infections, the age distribution was more even (mean: 42.4 years, median: 43.8 years; $p<0.001$ for Wilcoxon rank sum test). This age differential was less evident in 2008 where, despite the high proportion of viruses obtained from children younger than five years, the interquartile range indicated that B/Yam viruses affected a broader age range than the B/Vic viruses (Figure 3). This age difference between lineages has previously been reported from a household study in Hong Kong [4]. There, children younger than 15 years had a 13-fold increased risk of secondary influenza infection with a B/Vic virus than with a B/Yam virus, during a period when both lineages were co-circulating. Similar findings were reported in population studies in southern China during the 2009 and 2010 seasons [5], over three seasons in Slovenia (2010–13 [6]) and in our earlier studies from eastern Australia and New Zealand, where major differences in lineage distribution were observed in subjects older than five years [5,7].

Discussion

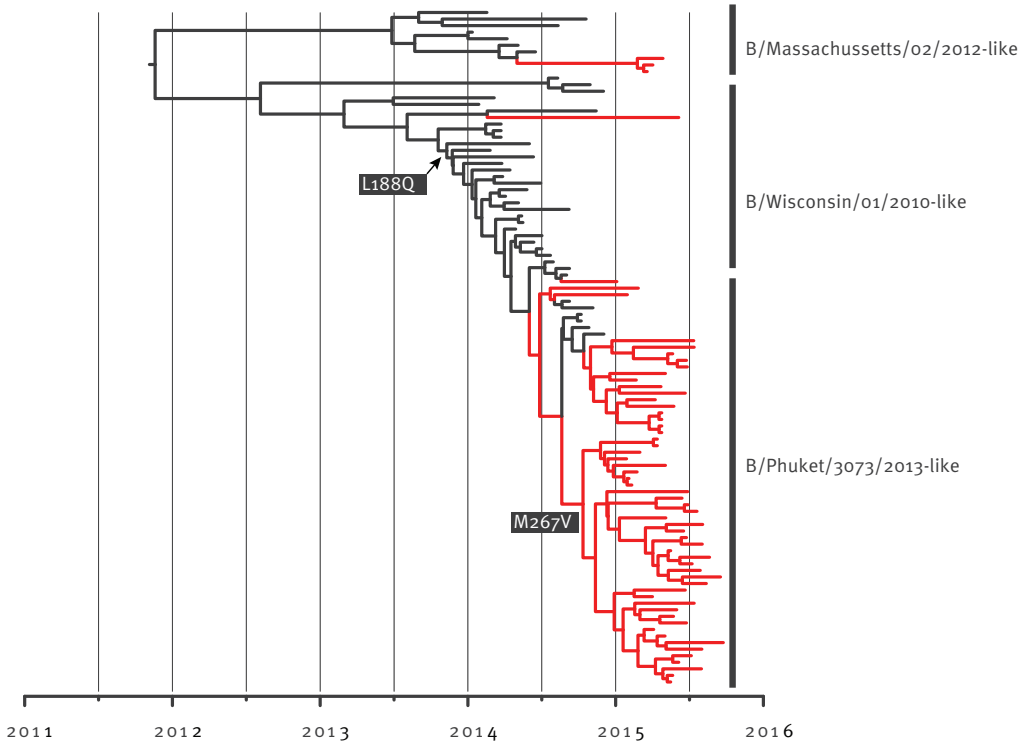
A predominance of influenza B viruses in an influenza season occurs infrequently, usually in the order of once every 10 years. Prior to 2015, it last occurred in Australia in the 2008 season, where 54% of typed viruses were influenza B, 43% were influenza A and 3% untyped [2]. Similarly in Europe for the seasons from 2001/02 to 2010/11, influenza B was the majority influenza type (59.1%) in only one season (2005/06). In the United States (US) over the same period, 2002/03 was the season with the highest proportion of influenza B (42.6%) among of all typed viruses [8]. The two antigenic and genetically distinct lineages of influenza B viruses (B/Yam and B/Vic) have co-circulated in various proportions since 2002 in most countries. Trivalent influenza vaccines (containing only one B virus lineage) used over this time have tried to match these changing lineage circulation patterns. Because of a number of poor matches during the 2000s, quadrivalent vaccines (containing viruses from both B lineages) were developed and have recently been introduced in order to improve vaccine effectiveness. The 2015 influenza vaccines licensed in Australia were all traditional inactivated virus vaccines (live attenuated influenza vaccines and recombinant vaccines were not available) with mostly trivalent vaccine containing only the B/Yam component being used along with low levels of quadrivalent vaccine.

The reasons for the apparent differential age susceptibility between the two B lineages described in this

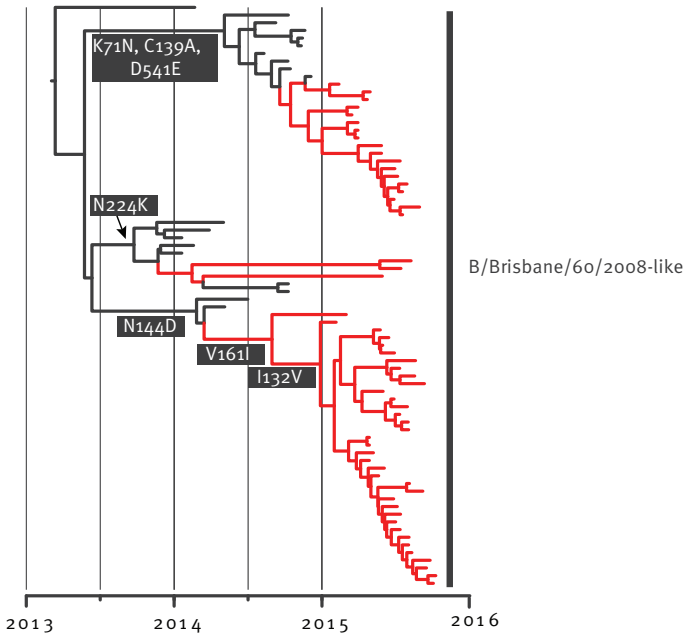
Figure 2

Maximum clade credibility trees showing the evolution of haemagglutinin genes of sequenced Australian influenza B viruses from 2014 and 2015 (n = 168)

A. Yamagata



B. Victoria



Phylogenies were inferred using a relaxed molecular clock model in a Bayesian Markov Chain Monte Carlo framework with the programme BEASTv1.8 [15].

Panel A: B/Yamagata/16/88 lineage viruses isolated in Australia in 2014 (n=42) and 2015 (n=56); Panel B: B/Victoria/2/87 lineage viruses isolated in Australia in 2014 (n=16) and 2015 (n=54). Red bars: Australian influenza B viruses from 2015; black bars: Australian influenza B viruses from 2014. Non-synonymous amino acid changes that occurred during the evolution of the lineages are shown adjacent to the nodes. All available haemagglutinin (HA) sequences were obtained from The Global Initiative on Sharing All Influenza Data (GISAID; http://platform.gisaid.org/epi3/frontend). See the Table at the end of the article for details of the source and details of the virus and the sequencing laboratory.

Table a

Australian influenza B viruses and haemagglutinin gene sequences used to construct Figure 2, obtained from The Global Initiative on Sharing All Influenza Data (GISAID)[a]

Segment ID	Collection date	Isolate name	Influenza B lineage	Originating laboratory	Authors[b]
EPI551283	2014-Aug-11	B/Newcastle/21/2014	Victoria	John Hunter Hospital	A
EPI561891	2014-Dec-05	B/Darwin/43/2014	Victoria	Royal Darwin Hospital	A
EPI541294	2014-Feb-18	B/Tasmania/1/2014	Victoria	Royal Hobart Hospital	A
EPI541365	2014-Feb-21	B/Perth/503/2014	Victoria	Pathwest	A
EPI529392	2014-Jan-20	B/Brisbane/3/2014	Victoria	QHSS	A
EPI540771	2014-Jan-20	B/Perth/501/2014	Victoria	Pathwest	A
EPI551321	2014-Jul-02	B/South Australia/20/2014	Victoria	IMVS	A
EPI540747	2014-Mar-29	B/Brisbane/12/2014	Victoria	QHSS	A
EPI551327	2014-May-03	B/Sydney/19/2014	Victoria	Clinical Virology Unit, CDIM	A
EPI541291	2014-May-06	B/Brisbane/13/2014	Victoria	QHSS	A
EPI562018	2014-Nov-14	B/Brisbane/71/2014	Victoria	QHSS	A
EPI561888	2014-Nov-20	B/Brisbane/74/2014	Victoria	QHSS	A
EPI561873	2014-Oct-09	B/Brisbane/62/2014	Victoria	QHSS	A
EPI561876	2014-Oct-10	B/Brisbane/63/2014	Victoria	QHSS	A
EPI561924	2014-Oct-15	B/Victoria/7/2014	Victoria	VIDRL	A
EPI551336	2014-Sep-09	B/Victoria/204/2014	Victoria	Royal Chidrens Hospital	A
EPI636426	2015-Apr-23	B/Darwin/9/2015	Victoria	Royal Darwin Hospital	B
EPI636340	2015-Apr-28	B/Brisbane/46/2015	Victoria	QHSS	B
EPI636409	2015-Apr-30	B/Darwin/11/2015	Victoria	Royal Darwin Hospital	B
EPI675691	2015-Aug-02	B/Victoria/849/2015	Victoria	Austin Health	B
EPI675652	2015-Aug-03	B/South Australia/1036/2015	Victoria	IMVS	B
EPI648854	2015-Aug-03	B/Victoria/847/2015	Victoria	Austin Health	B
EPI675636	2015-Aug-04	B/Newcastle/1012/2015	Victoria	IMVS	B
EPI675677	2015-Aug-05	B/Victoria/1009/2015	Victoria	IMVS	B
EPI675663	2015-Aug-09	B/Sydney/137/2015	Victoria	Westmead Hospital	B
EPI648856	2015-Aug-11	B/Victoria/861/2015	Victoria	Austin Health	B
EPI675694	2015-Aug-18	B/Victoria/898/2015	Victoria	Austin Health	B
EPI675672	2015-Aug-20	B/Tasmania/30/2015	Victoria	Royal Hobart Hospital	B
EPI675646	2015-Aug-30	B/Perth/201/2015	Victoria	Pathwest	B
EPI630025	2015-Feb-05	B/Brisbane/4/2015	Victoria	QHSS	A
EPI630050	2015-Feb-12	B/South Australia/3/2015	Victoria	IMVS	A
EPI636504	2015-Jul-02	B/South Australia/1015/2015	Victoria	IMVS	B
EPI648850	2015-Jul-06	B/Townsville/7/2015	Victoria	QHSS	B
EPI636421	2015-Jul-07	B/Darwin/17/2015	Victoria	Royal Darwin Hospital	B
EPI648882	2015-Jul-12	B/Victoria/524/2015	Victoria	Monash Medical Centre	B
EPI636621	2015-Jul-12	B/Victoria/525/2015	Victoria	Monash Medical Centre	B
EPI675604	2015-Jul-13	B/Brisbane/186/2015	Victoria	QHSS	B
EPI648868	2015-Jul-13	B/Canberra/27/2015	Victoria	Canberra Hospital	B
EPI648846	2015-Jul-14	B/Brisbane/185/2015	Victoria	QHSS	B
EPI675639	2015-Jul-15	B/Newcastle/28/2015	Victoria	John Hunter Hospital	B
EPI648870	2015-Jul-19	B/Canberra/29/2015	Victoria	Canberra Hospital	B
EPI636388	2015-Jul-19	B/Canberra/30/2015	Victoria	Canberra Hospital	B
EPI648848	2015-Jul-30	B/Darwin/22/2015	Victoria	Royal Darwin Hospital	B
EPI675688	2015-Jul-31	B/Victoria/843/2015	Victoria	Austin Health	B

IMVS: Institute of Medical and Veterinary Science; Pathwest: Pathwest QE II Medical Centre; QHSS: Queensland Health Scientific Services; VIDRL: Victoria Infectious Diseases Laboratory.

[a] All samples were sequenced and submitted by WHO Collaborating Centre for Reference and Research on Influenza, Melbourne, Australia, with the exception of B/Brisbane/47/2015 that was submitted by US Centers for Disease Control and Prevention.

[b] Authors: A: Deng Y-M, Iannello P, Spirason N, Jelley L, Lau H, Komadina N; B: Deng Y-M, Iannello P, Spirason N, Lau H, Komadina N; C: Tilmanis D, Hurt A, Komadina N.

Table B

Australian influenza B viruses and haemagglutinin gene sequences used to construct Figure 2, obtained from The Global Initiative on Sharing All Influenza Data (GISAID)[a]

Segment ID	Collection date	Isolate name	Influenza B lineage	Originating laboratory	Authors[b]
EPI636549	2015-Jun-01	B/Sydney/11/2015	Victoria	Clinical Virology Unit, CDIM	B
EPI636525	2015-Jun-04	B/South Australia/49/2015	Victoria	IMVS	B
EPI636567	2015-Jun-15	B/Tasmania/2/2015	Victoria	Royal Hobart Hospital	B
EPI636329	2015-Jun-27	B/Brisbane/136/2015	Victoria	QHSS	B
EPI636415	2015-Jun-28	B/Darwin/14/2015	Victoria	Royal Darwin Hospital	B
EPI636635	2015-Jun-28	B/Victoria/557/2015	Victoria	Monash Medical Centre	B
EPI636577	2015-Jun-29	B/Tasmania/5/2015	Victoria	Royal Hobart Hospital	B
EPI636465	2015-Jun-30	B/Newcastle/1005/2015	Victoria	IMVS	B
EPI636560	2015-Mar-02	B/Sydney/503/2015	Victoria	Prince of Wales Hospital	B
EPI636334	2015-Mar-16	B/Brisbane/15/2015	Victoria	QHSS	B
EPI636584	2015-Mar-31	B/Townsville/3/2015	Victoria	QHSS	B
EPI636605	2015-Mar-31	B/Victoria/502/2015	Victoria	Monash Medical Centre	B
EPI636354	2015-May-08	B/Brisbane/55/2015	Victoria	QHSS	B
EPI636361	2015-May-21	B/Brisbane/69/2015	Victoria	QHSS	B
EPI636363	2015-May-24	B/Brisbane/70/2015	Victoria	QHSS	B
EPI636369	2015-May-25	B/Brisbane/73/2015	Victoria	QHSS	B
EPI636485	2015-May-28	B/Perth/24/2015	Victoria	Pathwest	B
EPI636488	2015-May-28	B/Perth/25/2015	Victoria	Pathwest	B
EPI636658	2015-May-30	B/South Australia/48/2015	Victoria	IMVS	B
EPI636472	2015-May-31	B/Newcastle/7/2015	Victoria	John Hunter Hospital	B
EPI675619	2015-Oct-03	B/Darwin/65/2015	Victoria	Royal Darwin Hospital	B
EPI675622	2015-Oct-09	B/Darwin/70/2015	Victoria	Royal Darwin Hospital	B
EPI675660	2015-Sep-07	B/Sydney/1071/2015	Victoria	IMVS	B
EPI675655	2015-Sep-11	B/South Australia/118/2015	Victoria	IMVS	B
EPI675602	2015-Sep-16	B/Brisbane/1036/2015	Victoria	IMVS	B
EPI675686	2015-Sep-25	B/Victoria/700/2015	Victoria	Monash Medical Centre	B
EPI540782	2014-Apr-04	B/Newcastle/3/2014	Yamagata	John Hunter Hospital	A
EPI540744	2014-Apr-08	B/Darwin/35/2014	Yamagata	Royal Darwin Hospital	A
EPI540765	2014-Apr-15	B/Sydney/8/2014	Yamagata	Prince of Wales Hospital	A
EPI540762	2014-Apr-29	B/Sydney/7/2014	Yamagata	Prince of Wales Hospital	A
EPI551286	2014-Aug-11	B/Newcastle/22/2014	Yamagata	John Hunter Hospital	A
EPI551289	2014-Aug-12	B/Newcastle/25/2014	Yamagata	John Hunter Hospital	A
EPI561915	2014-Dec-02	B/Sydney/39/2014	Yamagata	Westmead Hospital	A
EPI562030	2014-Dec-03	B/Perth/579/2014	Yamagata	Pathwest	A
EPI529622	2014-Feb-17	B/Townsville/3/2014	Yamagata	QHSS	A
EPI540779	2014-Feb-25	B/Perth/505/2014	Yamagata	Pathwest	A
EPI529377	2014-Jan-12	B/Darwin/4/2014	Yamagata	Royal Darwin Hospital	A
EPI529619	2014-Jan-28	B/Brisbane/4/2014	Yamagata	QHSS	A
EPI551274	2014-Jul-03	B/Newcastle/12/2014	Yamagata	John Hunter Hospital	A
EPI540912	2014-Jul-03	B/South Australia/21/2014	Yamagata	IMVS	A
EPI551280	2014-Jul-24	B/Newcastle/19/2014	Yamagata	John Hunter Hospital	A
EPI551324	2014-Jul-31	B/Sydney/1002/2014	Yamagata	IMVS	A
EPI541331	2014-Jun-02	B/Brisbane/22/2014	Yamagata	QHSS	A
EPI541279	2014-Jun-12	B/South Australia/16/2014	Yamagata	IMVS	A
EPI541338	2014-Jun-13	B/Newcastle/8/2014	Yamagata	John Hunter Hospital	A

IMVS: Institute of Medical and Veterinary Science; Pathwest: Pathwest QE II Medical Centre; QHSS: Queensland Health Scientific Services; VIDRL: Victoria Infectious Diseases Laboratory.

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Table c

Australian influenza B viruses and haemagglutinin gene sequences used to construct Figure 2, obtained from The Global Initiative on Sharing All Influenza Data (GISAID)[a]

Segment ID	Collection date	Isolate name	Influenza B lineage	Originating laboratory	Authors[b]
EPI551277	2014-Jun-17	B/Newcastle/17/2014	Yamagata	John Hunter Hospital	A
EPI540909	2014-Jun-30	B/South Australia/1002/2014	Yamagata	IMVS	A
EPI541241	2014-Mar-07	B/Brisbane/8/2014	Yamagata	QHSS	A
EPI551249	2014-Mar-24	B/Brisbane/9/2014	Yamagata	QHSS	A
EPI540759	2014-Mar-26	B/Sydney/5/2014	Yamagata	Prince of Wales Hospital	A
EPI540785	2014-Mar-28	B/Newcastle/5/2014	Yamagata	John Hunter Hospital	A
EPI540906	2014-May-05	B/Sydney/13/2014	Yamagata	Westmead Hospital	A
EPI540768	2014-May-06	B/Sydney/9/2014	Yamagata	Prince of Wales Hospital	A
EPI540753	2014-May-14	B/South Australia/5/2014	Yamagata	IMVS	A
EPI540756	2014-May-17	B/South Australia/7/2014	Yamagata	IMVS	A
EPI541288	2014-May-27	B/South Australia/1000/2014	Yamagata	IMVS	A
EPI561918	2014-Nov-06	B/Victoria/512/2014	Yamagata	Monash Medical Centre	A
EPI561885	2014-Nov-11	B/Brisbane/70/2014	Yamagata	QHSS	A
EPI630034	2014-Nov-14	B/Canberra/20/2014	Yamagata	Canberra Hospital	A
EPI561870	2014-Oct-08	B/Brisbane/61/2014	Yamagata	QHSS	A
EPI561912	2014-Oct-08	B/Perth/569/2014	Yamagata	Pathwest	A
EPI561879	2014-Oct-20	B/Brisbane/65/2014	Yamagata	QHSS	A
EPI561882	2014-Oct-27	B/Brisbane/66/2014	Yamagata	QHSS	A
EPI561921	2014-Oct-30	B/Victoria/6/2014	Yamagata	VIDRL	A
EPI551820	2014-Sep-02	B/Victoria/804/2014	Yamagata	Austin Health	A
EPI551330	2014-Sep-08	B/Townsville/1000/2014	Yamagata	IMVS	A
EPI551264	2014-Sep-09	B/Darwin/38/2014	Yamagata	Royal Darwin Hospital	A
EPI551333	2014-Sep-09	B/Victoria/202/2014	Yamagata	Royal Chidrens Hospital	A
EPI636392	2015-Apr-02	B/Canberra/4/2015	Yamagata	Canberra Hospital	B
EPI636341	2015-Apr-03	B/Brisbane/33/2015	Yamagata	QHSS	B
EPI630067	2015-Apr-05	B/Victoria/500/2015	Yamagata	Monash Medical Centre	A
EPI636553	2015-Apr-09	B/Sydney/5/2015	Yamagata	Clinical Virology Unit, CDIM	B
EPI642630	2015-Apr-14	B/Brisbane/47/2015	Yamagata	WHO CC	NA
EPI636506	2015-Apr-23	B/South Australia/12/2015	Yamagata	IMVS	B
EPI636606	2015-Apr-25	B/Victoria/503/2015	Yamagata	Monash Medical Centre	B
EPI648860	2015-Apr-25	B/Victoria/530/2015	Yamagata	Monash Medical Centre	B
EPI636345	2015-Apr-28	B/Brisbane/50/2015	Yamagata	QHSS	B
EPI648852	2015-Aug-01	B/Victoria/845/2015	Yamagata	Austin Health	B
EPI675669	2015-Aug-02	B/Sydney/70/2015	Yamagata	Westmead Hospital	B
EPI675644	2015-Aug-03	B/Perth/166/2015	Yamagata	Pathwest	B
EPI675657	2015-Aug-04	B/Sydney/1031/2015	Yamagata	IMVS	B
EPI675666	2015-Aug-13	B/Sydney/153/2015	Yamagata	Westmead Hospital	B
EPI675675	2015-Aug-21	B/Tasmania/32/2015	Yamagata	Royal Hobart Hospital	B
EPI630031	2015-Feb-03	B/Canberra/1/2015	Yamagata	Canberra Hospital	A
EPI630047	2015-Feb-10	B/South Australia/2/2015	Yamagata	IMVS	C
EPI630053	2015-Feb-21	B/South Australia/4/2015	Yamagata	IMVS	A
EPI630055	2015-Feb-23	B/South Australia/5/2015	Yamagata	IMVS	C
EPI630064	2015-Feb-26	B/Townsville/1/2015	Yamagata	QHSS	A
EPI630016	2015-Jan-04	B/Brisbane/1/2015	Yamagata	QHSS	A

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Table d

Australian influenza B viruses and haemagglutinin gene sequences used to construct Figure 2, obtained from The Global Initiative on Sharing All Influenza Data (GISAID)[a]

Segment ID	Collection date	Isolate name	Influenza B lineage	Originating laboratory	Authors[b]
EPI630061	2015-Jan-28	B/Sydney/2/2015	Yamagata	Clinical Virology Unit, CDIM	A
EPI630058	2015-Jan-30	B/Sydney/1000/2015	Yamagata	IMVS	A
EPI636636	2015-Jul-07	B/Victoria/543/2015	Yamagata	Monash Medical Centre	B
EPI636618	2015-Jul-09	B/Victoria/519/2015	Yamagata	Monash Medical Centre	B
EPI636601	2015-Jul-13	B/Victoria/32/2015	Yamagata	VIDRL	B
EPI636387	2015-Jul-14	B/Canberra/28/2015	Yamagata	Canberra Hospital	B
EPI636627	2015-Jul-14	B/Victoria/532/2015	Yamagata	Monash Medical Centre	B
EPI636641	2015-Jul-21	B/Victoria/952/2015	Yamagata	Royal Chidrens Hospital	B
EPI675641	2015-Jul-29	B/Perth/136/2015	Yamagata	Pathwest	B
EPI636592	2015-Jun-01	B/Victoria/301/2015	Yamagata	Melbourne Pathology	B
EPI636531	2015-Jun-06	B/South Australia/50/2015	Yamagata	IMVS	B
EPI636566	2015-Jun-06	B/Tasmania/1/2015	Yamagata	Royal Hobart Hospital	B
EPI636313	2015-Jun-14	B/Brisbane/100/2015	Yamagata	QHSS	B
EPI636322	2015-Jun-18	B/Brisbane/118/2015	Yamagata	QHSS	B
EPI636460	2015-Jun-22	B/Newcastle/1003/2015	Yamagata	IMVS	B
EPI636468	2015-Jun-22	B/Newcastle/20/2015	Yamagata	John Hunter Hospital	B
EPI636326	2015-Jun-25	B/Brisbane/132/2015	Yamagata	QHSS	B
EPI636379	2015-Jun-25	B/Canberra/13/2015	Yamagata	Canberra Hospital	B
EPI636535	2015-Jun-25	B/South Australia/71/2015	Yamagata	IMVS	B
EPI636574	2015-Jun-27	B/Tasmania/4/2015	Yamagata	Royal Hobart Hospital	B
EPI636383	2015-Jun-28	B/Canberra/15/2015	Yamagata	Canberra Hospital	B
EPI636541	2015-Jun-29	B/Sydney/1013/2015	Yamagata	IMVS	B
EPI630019	2015-Mar-02	B/Brisbane/11/2015	Yamagata	QHSS	A
EPI630022	2015-Mar-20	B/Brisbane/19/2015	Yamagata	QHSS	A
EPI636455	2015-May-03	B/Newcastle/1/2015	Yamagata	John Hunter Hospital	B
EPI636349	2015-May-04	B/Brisbane/54/2015	Yamagata	QHSS	B
EPI636515	2015-May-04	B/South Australia/22/2015	Yamagata	IMVS	B
EPI636514	2015-May-05	B/South Australia/18/2015	Yamagata	IMVS	B
EPI636500	2015-May-17	B/South Australia/1000/2015	Yamagata	IMVS	B
EPI636611	2015-May-17	B/Victoria/507/2015	Yamagata	Monash Medical Centre	B
EPI636482	2015-May-22	B/Perth/21/2015	Yamagata	Pathwest	B
EPI636521	2015-May-22	B/South Australia/28/2015	Yamagata	IMVS	B
EPI636593	2015-May-25	B/Townsville/6/2015	Yamagata	QHSS	B
EPI675616	2015-Sep-17	B/Darwin/61/2015	Yamagata	Royal Darwin Hospital	B
EPI675683	2015-Sep-24	B/Victoria/698/2015	Yamagata	Monash Medical Centre	B

IMVS: Institute of Medical and Veterinary Science; Pathwest: Pathwest QE II Medical Centre; QHSS: Queensland Health Scientific Services; VIDRL: Victoria Infectious Diseases Laboratory.

[a] All samples were sequenced and submitted by WHO Collaborating Centre for Reference and Research on Influenza, Melbourne, Australia, with the exception of B/Brisbane/47/2015 that was submitted by US Centers for Disease Control and Prevention.

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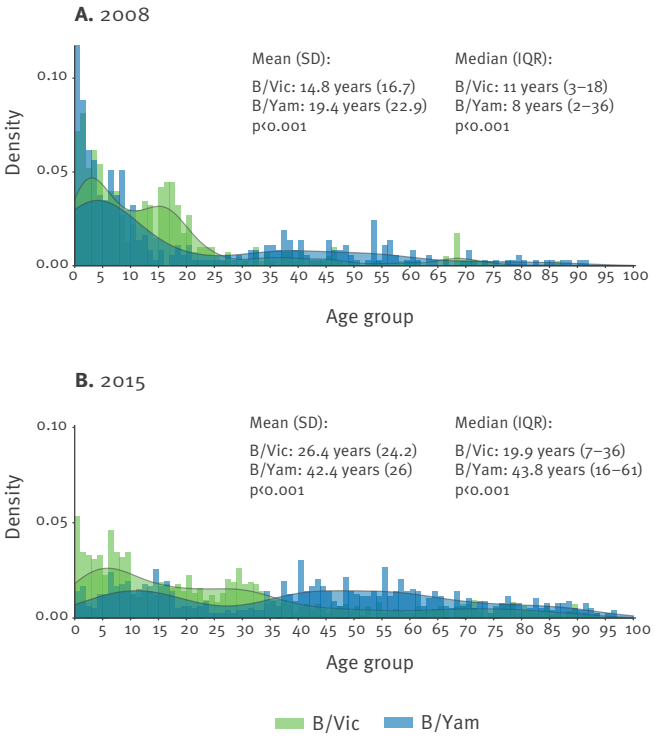
Figure 3

Age distribution of confirmed influenza B cases by lineage, Australia, 2008 (n = 780) and 2015 (n = 1,638)



IQR: interquartile range; SD: standard deviation.

Data shown are samples for which age data was available. Bars show the histogram in one-year age increments by lineage. The shaded areas indicate the smoothed density estimate of the age distribution. Values provided on the graphs for each lineage are mean (SD) or median (IQR). P values are for the t-test comparing mean age between the two lineages and the Wilcoxon rank-sum test for comparing medians.

study are unknown. It is, however, well known that the different influenza types/subtypes do affect different age profiles; both seasonal and 2009 pandemic A(H1N1) as well as influenza B viruses infect a younger population than A(H3N2) viruses [9], although in recent years, the median age of influenza A(H1N1)pdm09 cases has been increasing [6,10], again for unknown reasons. Studies to date have not shown differences in clinical presentation for the different B lineages [4,5], but long-term data on hospitalisations and deaths are lacking. In a study by Paddock et al. on deaths attributed to confirmed influenza B in the US from 2000 to 2010, the majority of subjects were 18 years and younger (34/45 cases), and a slightly higher proportion of infections were B/Vic compared with B/Yam (25 vs 17 deaths, respectively, in those cases that could be characterised) [11]. More studies are required to determine if there is indeed any difference in outcomes following severe infections with either of the B lineages in different age groups.

It is probable that the prior exposure history of the different age groups has influenced our observations. However, this is difficult to deduce from the present data. For example, five-year-old Australian children in 2015 were likely to have been exposed to a mixture of B/Yam viruses, which circulated in 2013 and 2014, and B/Vic viruses, which circulated from 2009 to 2012, as was the case in for five-year-olds in 2008. Possible exposure therefore fails to explain the elevated proportion of five year-old children infected with B/Yam viruses in 2008 or with B/Vic in 2015. In addition, it is unlikely given the low levels of childhood vaccination in Australia that this this would have significantly altered the circulation patterns of the influenza B lineages. Vaccination uptake is generally below 10% among Australian children [12]. Childhood influenza vaccination is only recommended for children of aboriginal descent five years and younger and for children six months and older with comorbidities [13].

We have suggested previously that there may be some fundamental differences in the receptor specificity of the different influenza B lineages and that the distribution or density of receptors for influenza B viruses in the respiratory tract of humans may differ with age [7]. Others have shown differential responses of children to B/Yam and B/Vic antigens contained in influenza vaccines that might also contribute to differential susceptibility to these two lineages 14]. Further work is needed to fully understand the basis of these observations and to determine if the differences are due to receptor variation or density during ageing or prior exposure history or a mixture of both. If indeed young children are at an elevated risk of infection with B/Vic viruses, then it may be prudent to prioritise distribution of quadrivalent vaccines (containing viruses from both B lineages) to this age group. This is relevant to the current northern hemisphere influenza season where the trivalent vaccine contains a B/Yam lineage virus, but B/Vic lineage viruses are in our view likely to increase substantially during the current season. Use of the quadrivalent vaccine for this subgroup (or preferably for the whole population) would be potentially advantageous in improving influenza vaccine effectiveness.

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Conflict of interest

None declared.

Authors' contributions

IB and SS wrote the manuscript, SS performed the epidemiological analysis, DV performed phylogenetic analyses, all authors revised the manuscript.

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