Influenza B-Associated Pediatric Mortality in the US Between 2010 and 2019

Allyn Bandell,[1] Pedro A. Piedra,[2] Christopher S. Ambrose,[1] Ravi Jhaveri[3]

[1]Medical Affairs, AstraZeneca, Gaithersburg, MD, USA; [2]Baylor College of Medicine, Houston, TX, USA; [3]Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Background

- Influenza causes substantial illness among children and is associated with high healthcare use in this age group.[1]
  - There were 675 influenza-associated deaths in the US pediatric population between 2010 and 2016, with half occurring in healthy children.[2]
- Although influenza A accounts for the majority of influenza cases each season,[2,3] there is increasing evidence that influenza B places a considerable health burden on the pediatric population.[2,4–9]

Objectives

- To assess the contribution of influenza B to influenza-associated mortality in the US pediatric population using national surveillance data from nine influenza seasons between 2010/11 and 2018/19.
- To assess the effectiveness of live attenuated influenza vaccine (LAIV) and inactivated influenza vaccine (IIV) against influenza B.

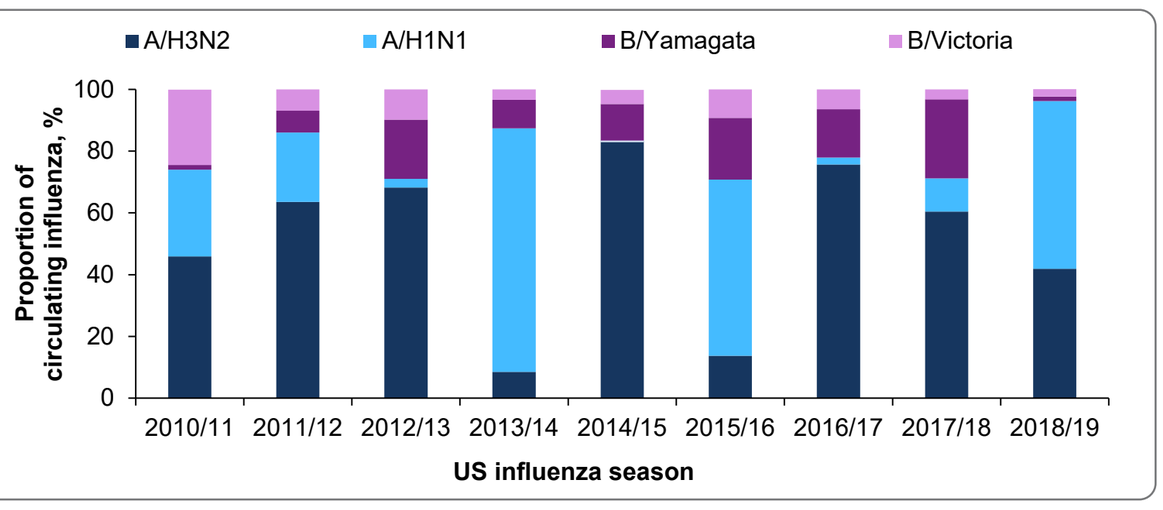
Methods

- The pediatric population comprised children aged 0–17 years.
- Data on circulating strains and influenza-associated pediatric mortality for each season were obtained from Centers for Disease Control and Prevention (CDC) Morbidity and Mortality Weekly Reports (MMWR).[10–18]
  - The CDC receives influenza surveillance data from public health and clinical laboratories in all 50 states, Puerto Rico, and the District of Columbia via US World Health Organization Collaborating Laboratories and the National Respiratory and Enteric Virus Surveillance System.
  - Surveillance periods were between September and May each year, with the start and end weeks varying slightly between years.
  - The contribution of each influenza subtype (A/H1N1pdm09, A/H3N2, B/Yamagata, and B/Victoria) to overall influenza circulation was calculated from MMWR data based on the proportion of circulating A and B subtypes and lineages, respectively.
- The proportion of overall pediatric mortality due to influenza B versus A was calculated using mortality data from the published MMWR reports.
  - Chi-squared test with Yates' correction was used to assess the contribution of influenza B to pediatric mortality relative to its overall circulation among influenza viruses in the general population.
  - Statistical significance was assessed based on $P<0.05$.
- Annual estimates of influenza vaccine coverage were obtained from the CDC via FluVaxView Interactive.[19]
- Consolidated vaccine effectiveness (VE) against influenza B for IIV between the 2010/11 and 2017/18 seasons and for LAIV between the 2010/11 and 2015/16 seasons were obtained from a published meta-analysis[20] and annual US Flu VE Network studies.[21]
  - VE estimates for LAIV were not available for the 2016/17 and 2017/18 seasons as the CDC Advisory Committee on Immunization Practices (ACIP) did not recommend use of LAIV during these seasons.[22]
  - From the 2013/14 season onwards, quadrivalent LAIV was available for use.[23] Trivalent (IIV3) and quadrivalent (IIV4) IIV have been used since 2013, with no preferential recommendation for IIV4 use over IIV3.[24,25]

Results

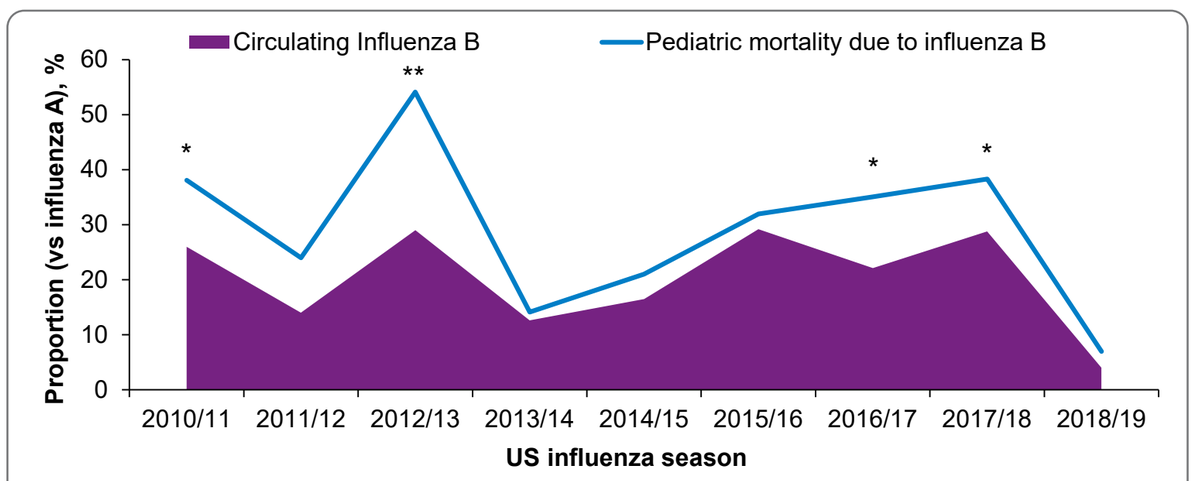
- Between the 2010/11 and 2018/19 seasons, influenza B accounted for 4.0–29.2% of circulating influenza in all ages (**Figure 1**).
  - During all seasons except for 2010/11 and 2018/19, B/Yamagata viruses circulated in greater proportions than B/Victoria viruses, while A/H3N2 viruses were the predominant circulating strain in most seasons.

Figure 1. *Proportion of circulating influenza A and B between the 2010/11 and 2018/19 influenza seasons*



- Influenza B accounted for 7.0–54.1% of all influenza-associated deaths in the US pediatric population between 2010 and 2019 (**Figure 2**).
  - Influenza B-associated deaths were disproportionately and significantly higher overall ($P<0.001$), and during the 2010/11, 2012/13, 2016/17, and 2017/18 seasons relative to the proportion of circulating influenza B.
  - There were almost 50% more influenza B-associated deaths than expected during the 2012/13 season.

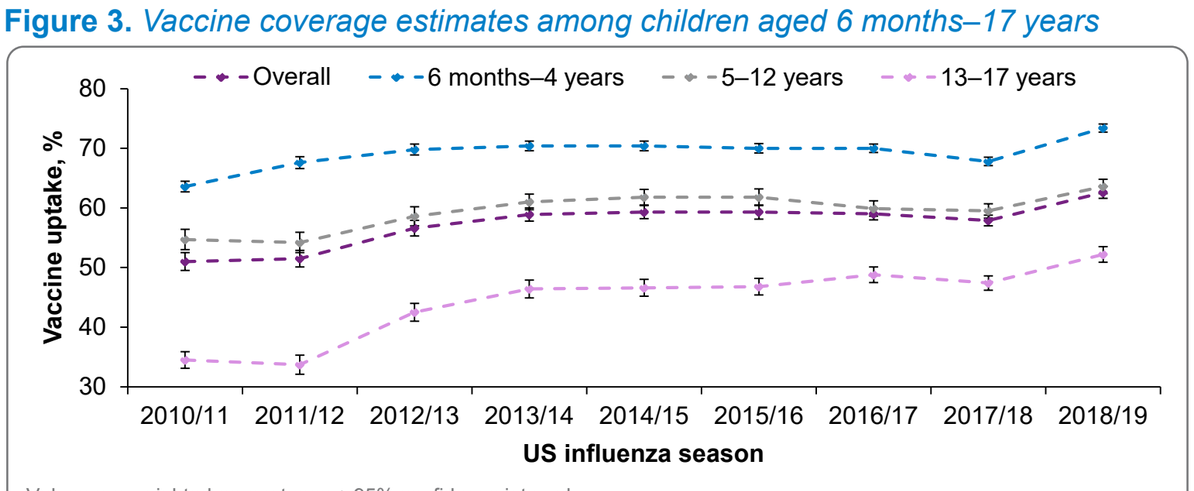
Figure 2. *Disproportionate influenza B-associated pediatric deaths relative to circulating influenza B in the US between the 2010/11 and 2018/19 influenza seasons*



*P<0.01 or **P<0.001 for the difference between the contribution of influenza B to mortality versus its overall circulation.

- Estimated vaccine coverage among US children aged 6 months–17 years ranged from 51.0% in 2010/11 to 62.6% in 2018/19 and was highest in the 6 months–4 years age group versus older pediatric age groups (**Figure 3**).
  - The mean age of children who died from influenza during this period ranged from 6.0 years in 2013/14 to 8.2 years in 2012/13.[10–18]

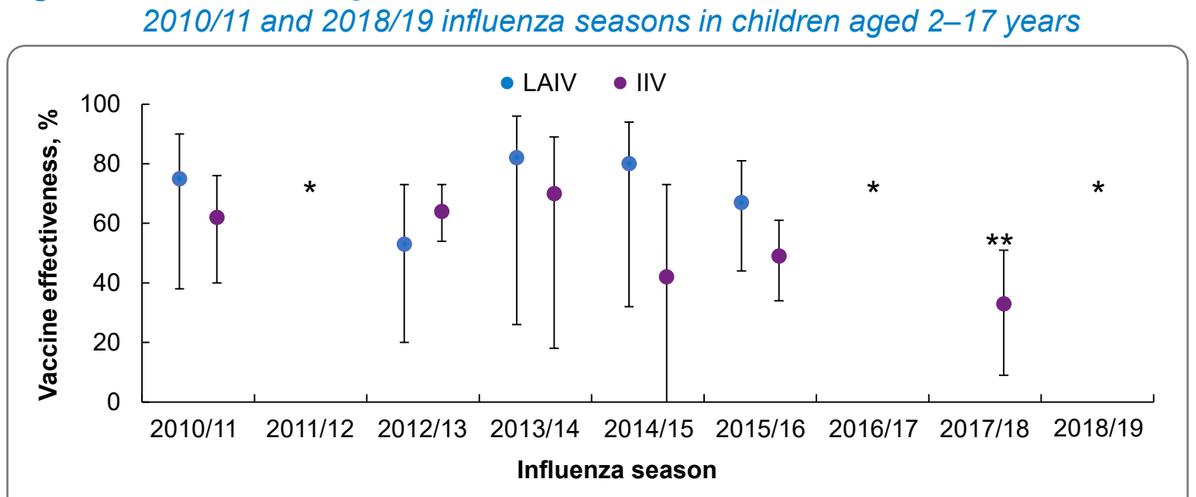
Figure 3. *Vaccine coverage estimates among children aged 6 months–17 years*



Values are weighted percentages ± 95% confidence interval.
Percentages are weighted to the non institutionalized, US civilian population.

- Point estimates of VE against influenza B for children aged 2–17 years were 33–70% for IIV between the 2010/11 and 2017/18 seasons and 53–82% for LAIV between the 2010/11 and 2015/16 seasons (**Figure 4**).
  - In seasons with infrequent circulation of influenza B, VE estimates had wide confidence intervals.

Figure 4. *VE estimates against influenza B for LAIV and IIV between the 2010/11 and 2018/19 influenza seasons in children aged 2–17 years*



*VE estimates for influenza B are not available for the 2011/12, 2016/17, and 2018/19 influenza seasons due to low circulating influenza B, and are not available for the pediatric age group during the 2016/17 season;
**For children aged 5–17 years. Confidence intervals truncated at 0 to enable graphical display.

Conclusions

- Influenza B accounted for a disproportionate percentage of the total influenza-associated pediatric deaths in the US relative to its overall circulation between the 2010/11 and 2018/19 influenza seasons.
- These data highlight the high burden of influenza-attributable illness in the US pediatric population, and counter the perception that influenza B is less severe than influenza A in children.
- With ~80% of influenza-associated pediatric deaths occurring in unvaccinated children, these data highlight the importance of vaccination for preventing influenza and its complications.[26]

References

1. Poehling KA, et al. *N Engl J Med* 2006;355:31–40; 2. Shang M, et al. *Pediatrics* 2018;141:e20172918; 3. Caini S, et al. *Influenza Other Respir Viruses* 2015;9:3–12; 4. Tran D, et al. *Pediatrics* 2016;138:e20154643; 5. Glezen WP, et al. *Am J Public Health* 2013;103:e43–51; 6. Yan S, et al. *Hum Vaccin Immunother* 2017;13:2041–2047; 7. Matias G, et al. *Influenza Other Respir Viruses* 2014;8:507–15; 8. Matias G, et al. *BMC Public Health* 2017;17:271; 9. PHE. Surveillance of influenza and other respiratory viruses in the UK: Winter 2017 to 2018. 2018. Accessed August 27, 2020; 10. CDC. *MMWR Morb Mortal Wkly Rep* 2011;60:705–712; 11. CDC. *MMWR Morb Mortal Wkly Rep* 2012;61:414–420; 12. CDC. *MMWR Morb Mortal Wkly Rep* 2013;62:473–479; 13. Epperson S, et al. *MMWR Morb Mortal Wkly Rep* 2014;63:483–490; 14. Appiah GD, et al. *MMWR Morb Mortal Wkly Rep* 2015;64:583–590; 15. Davlin SL, et al. *MMWR Morb Mortal Wkly Rep* 2016;65:567–575; 16. Blanton L, et al. *MMWR Morb Mortal Wkly Rep* 2017;66:668–676; 17. Garten R, et al. *MMWR Morb Mortal Wkly Rep* 2018;67:634–642; 18. Xu X, et al. *MMWR Morb Mortal Wkly Rep* 2019;68:544–551; 19. CDC. https://www.cdc.gov/flu/fluvaxview/earlier-seasons.htm. Accessed August 27, 2020; 20. Caspard H, et al. *Open Forum Infect Dis* 2017;4:ofx111; 21. Rolfes MA, et al. *Clin Infect Dis* 2019;69:1845–1853; 22. Grohskopf LA, et al. *MMWR Morb Mortal Wkly Rep* 2018;67:643–645; 23. Rodgers L, et al. *Vaccine* 2015;33:6517–6518; 24. CDC. *MMWR Morb Mortal Wkly Rep* 2013;62:1–43; 25. Committee on Infectious Diseases. *Pediatrics* 2017;140:e20172550; 26. CDC. Frequently Asked Questions about Estimated Flu Burden. 2018. Accessed August 27, 2020.

Acknowledgements

Medical writing support, data collection, and figure preparation was undertaken by Matthew Young, DPhil, and Lucy Ambrose, DPhil, and editing support was provided by Sinead Stewart, BSc (Hons), all of Core, London, UK and supported by AstraZeneca according to Good Publication Practice guidelines (GPP3).

Disclosures

Allyn Bandell and Christopher S. Ambrose are employees of AstraZeneca.

Poster presented virtually at IDWeek, October 21–25, 2020, Philadelphia