Real-World Effectiveness of Inactivated and Live Attenuated Influenza Vaccines in Children During Three Recent Seasons: 2016–2019

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Background

- Influenza causes a substantial global burden of disease, with approximately 3–5 million cases of severe illness and 290,000 to 650,000 influenza-associated respiratory deaths each year.[1]
- With the pediatric population having the highest risk of contracting and transmitting influenza,[2] vaccination is being recommended for healthy children in an increasing number of countries.[3–5]
- Vaccine types available for use in children include:[3–5]
  - intranasal live attenuated influenza vaccine (LAIV) for those aged ≥2 years;
  - injectable inactivated influenza vaccines (IIVs) for those aged ≥6 months.
- Real-world influenza vaccine effectiveness (VE) against circulating strains has been variable.[6]
  - In the 2013/14 and 2015/16 influenza seasons, LAIV demonstrated reduced VE against A/H1N1 strains in children,[7,8] although strains with enhanced replicative fitness have been used since the 2018/19 season.[9]
  - All influenza vaccine formulations have demonstrated variable VE against A/H3N2 strains in recent years, possibly due to antigenic drift and/or egg adaptations during vaccine growth eliciting immune responses that are not directed at circulating strains.[6,10]

Objective

- This study evaluated LAIV and IIV VE in children between the 2016/17 and 2018/19 influenza seasons.

Methods

- Quadrivalent LAIV (LAIV4) and IIV VE studies in children aged 6 months–17 years conducted from the 2016/17 to the 2018/19 influenza seasons were identified from published literature, congress presentations, public health websites, and personal communications with national investigators.
  - Studies were excluded if they were from countries where Ann Arbor-backbone LAIV was not available for at least one season during the study period, if they were randomized interventional studies, or if they contained duplicate data from other publications.
- VE and 95% confidence intervals (CIs) were reported for all influenza strains, influenza A subtypes A/H1N1 and A/H3N2, and influenza B.
- Statistical comparisons of LAIV4 and IIV VE were not feasible due to the multivariate nature of each study cohort.

Results

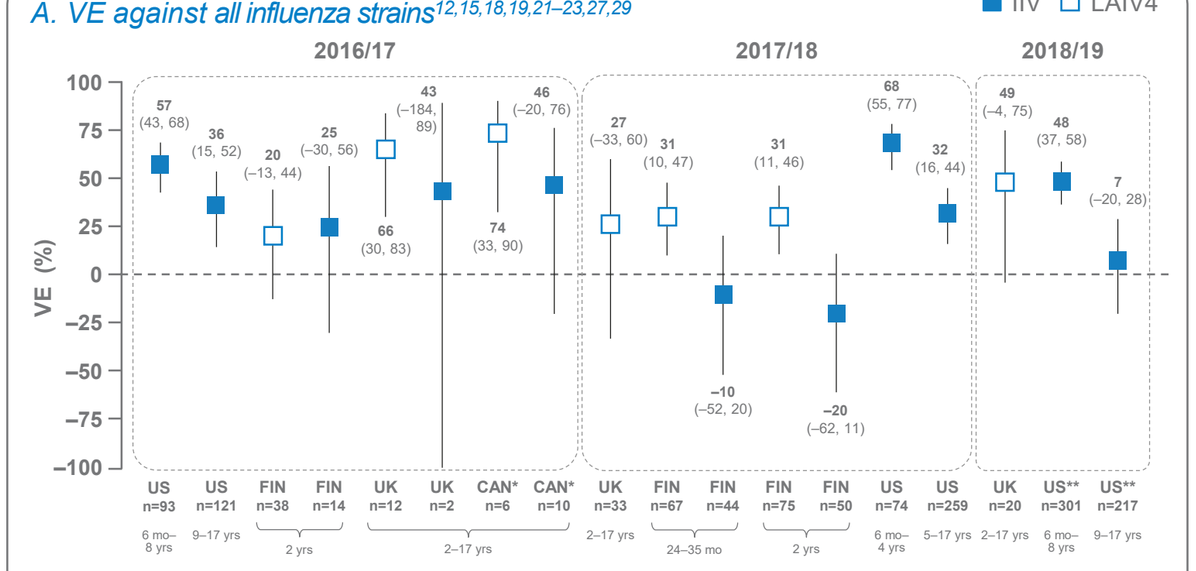
- Data on LAIV4 and IIV VE in the pediatric population were identified from studies conducted in Canada, Finland, Germany, the UK, and the US.
- Five studies for the 2016/17 season and three studies for each of the 2017/18 and 2018/19 seasons met the inclusion criteria **(Table 1)**.
- Point estimates of IIV and LAIV4 VE in children are shown in **Figure 1A** for all influenza strains and **Figure 1B–D** for influenza A/H3N2, A/H1N1, and B.

Table 1. *Characteristics of included studies*

	Location	Study design	Age (years)	Primary endpoint	Dose	Vaccine
2016/17	Canada[11,12]	TNCC	2–17	PCR-confirmed influenza[13]	1 or 2[a]	LAIV4, IIV4, or IIV3
	Finland[14]	Register-based nationwide cohort	2	PCR, culture- or antigen-confirmed[10,b]	1	LAIV4 or IIV3
	Finland[15]	Register-based nationwide cohort	2	Laboratory-confirmed influenza	1 or 2[c]	LAIV4 or IIV3
	Germany[16,17]	TNCC	2–17	PCR-confirmed influenza	1 or 2[d]	LAIV4, IIV4, or IIV3
	UK[18]	TNCC	2–17	PCR-confirmed influenza	1 or 2[e]	LAIV4 or IIV4
	US[19]	TNCC	0.5–17	PCR-confirmed influenza	1 or 2[20,a]	IIV4 or IIV3
2017/18	Finland[21]	Register-based nationwide cohort	24–35 months	Laboratory-confirmed influenza	NR	LAIV4 or IIV3
	Finland[15]	Register-based nationwide cohort	2	Laboratory-confirmed influenza	1 or 2[c]	LAIV4 or IIV3
	UK[22]	TNCC	2–17	PCR-confirmed influenza	1 or 2[e]	LAIV4 or IIV4
	US[23]	TNCC	0.5–17	PCR-confirmed influenza	1 or 2[24,a]	IIV4 or IIV3
2018/19	Finland[25,26]	Register-based nationwide cohort	2–6	Laboratory-confirmed influenza	NR	LAIV4 or IIV4
	UK[27,28]	TNCC	2–17	PCR-confirmed influenza	1 or 2[e]	LAIV4
	US[29]	TNCC	0.5–17	PCR-confirmed influenza	1 or 2[9,a]	LAIV4,[9] IIV4, or IIV3

IIV3, trivalent inactivated influenza vaccine; IIV4, quadrivalent inactivated influenza vaccine; LAIV4, quadrivalent live attenuated influenza vaccine; NR, not reported; PCR, polymerase chain reaction; TNCC, test-negative case–control.
[a]Children aged ≤8 years, not previously vaccinated against influenza were recommended to receive two doses of vaccine; children aged ≥9 years were recommended to receive a single dose; [b]Specific antigen test varied by hospital/clinic; [c]Children due to receive IIV3 who had not received LAIV4 or two doses of IIV3 in previous seasons were recommended to receive two doses of vaccine; [d]Children not previously vaccinated against influenza were recommended to receive two doses of vaccine; previously vaccinated children were recommended to receive a single dose; [e]Healthy children were recommended to receive a single dose of LAIV; children in a clinical risk group aged <9 years, not previously vaccinated, were recommended to receive two doses of vaccine.

Figure 1. *VE of IIV and LAIV4 against all influenza strains, influenza subtypes A/H3N2 and A/H1N1, and influenza B*



CAN, Canada; FIN, Finland; GER, Germany; IIV, inactivated influenza vaccine; LAIV4, quadrivalent live attenuated influenza vaccine; UK, United Kingdom; US, United States; VE, vaccine effectiveness.
*Unadjusted estimates; **Data for all vaccines, but little use of LAIV in 2018/19 season in the US; ***Against B/Yamagata.
n = number of vaccinated cases. CIs truncated at –100 to enable graphical display.

Conclusions

- During three recent seasons, LAIV4 and IIV showed similar moderate VE against all influenza strains, A/H1N1 strains, and B strains.
  - Influenza B accounted for a minority of circulating strains during the 2016/17 season,[11] which likely contributed to the wide CIs observed.
  - IIV demonstrated reduced VE among older versus younger pediatric age groups irrespective of influenza strain, and particularly during the 2017/18 and 2018/19 US influenza seasons.
- VE against A/H3N2 for LAIV4 and IIV was good in 2016/17, but decreased during the 2017/18 and 2018/19 seasons.
- VE estimates for LAIV4 and IIV VE overlapped for all strains and each subtype, suggesting that LAIV4 and IIV VE were generally comparable during the seasons between 2016 and 2019.

References

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Disclosures

Allyn Bandell, Raburn Mallory, and Christopher S. Ambrose are employees of AstraZeneca.

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