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CLINICAL EFFECTIVENESS AND USE OF THE LIVE ATTENUATED INFLUENZA VACCINE

Live attenuated influenza vaccine (LAIV)

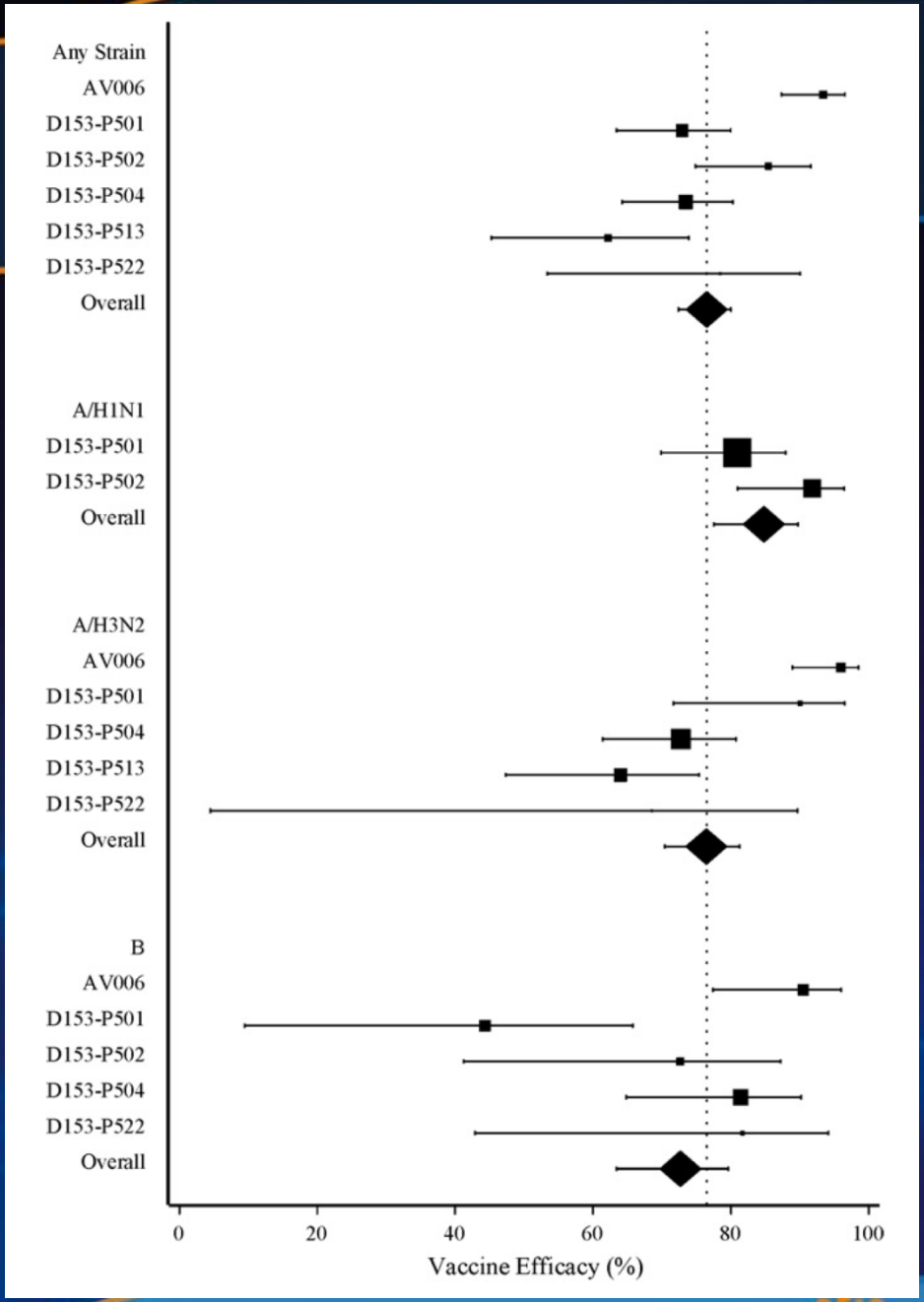
Approved for use in the United States in 2003

Indicated in the US for subjects 2-49 years of age

Efficacy in children: 2 doses

LAIV vs placebo

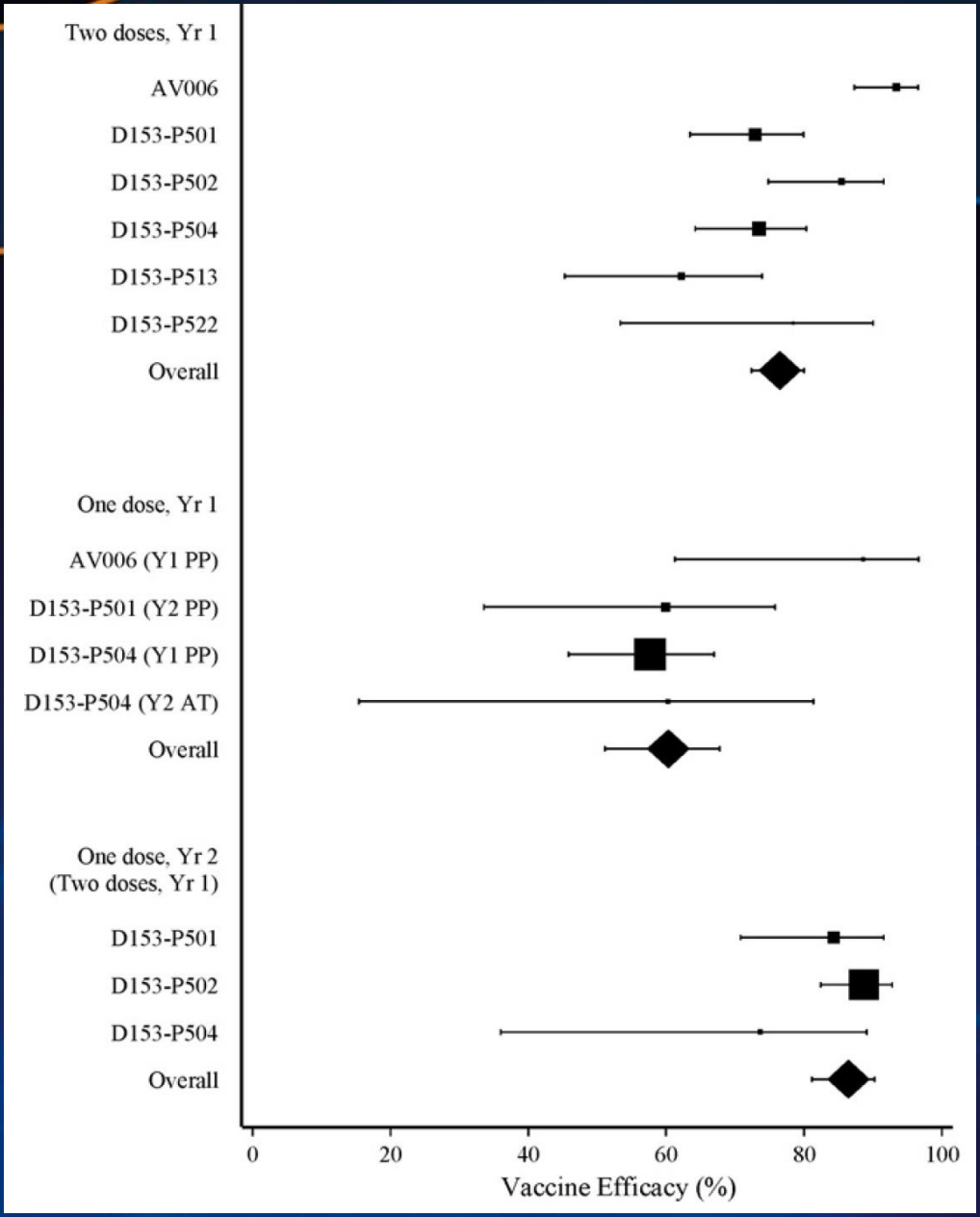
Overall vaccine efficacy:
- 77% against antigenically similar subtypes
- 72% against any strains



Rhorer et al, Vaccine 2009

Efficacy in children: 1 or 2 doses ?

LAIV vs placebo



Rhorer et al, Vaccine 2009

LAIV versus TIV in children 6-59 months of age

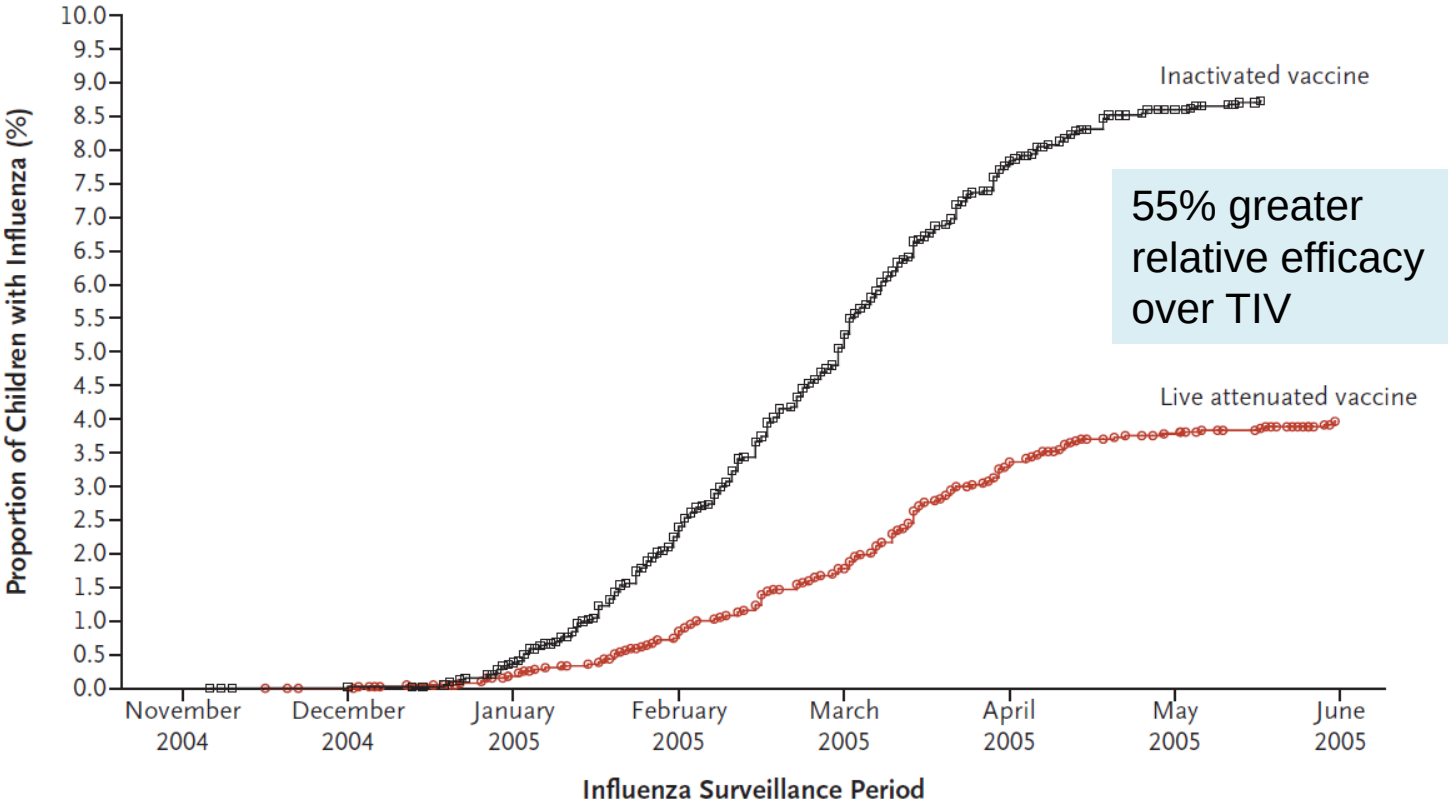
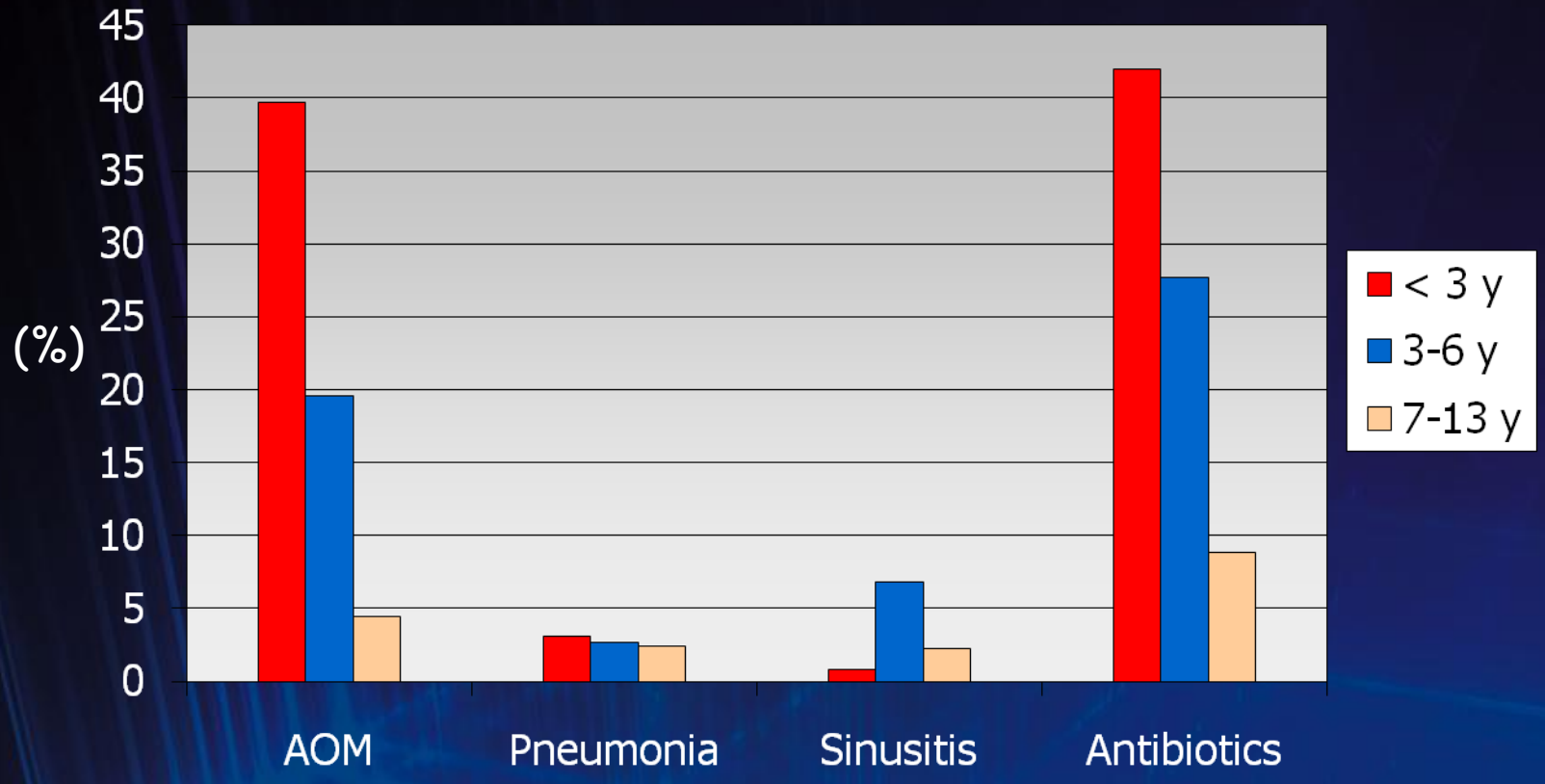


Figure 1. Kaplan–Meier Curves for the Time to the First Culture-Confirmed Report of Influenza in the Two Vaccine Groups.

Belshe et al., N Engl J Med 2007

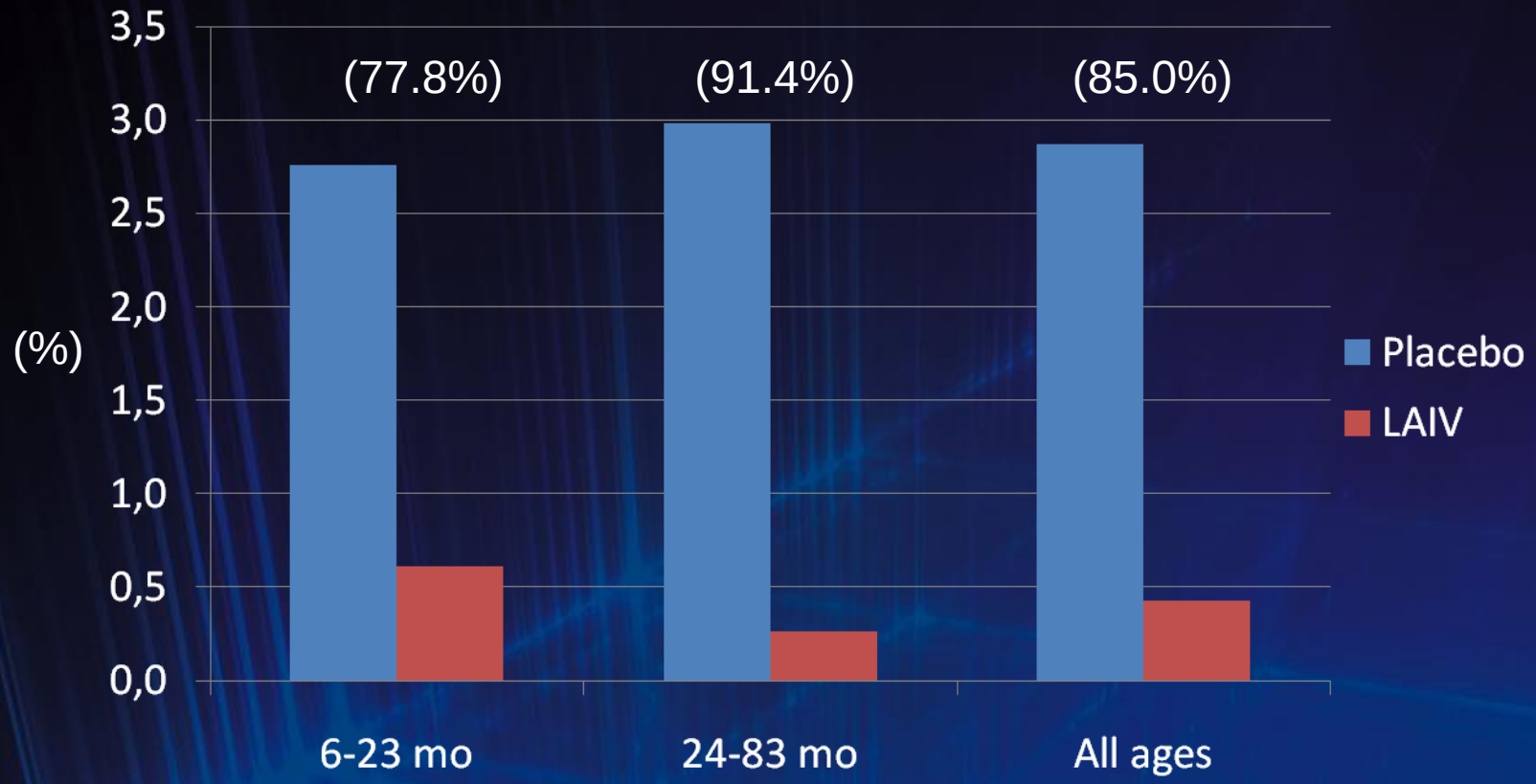
Complications of influenza in different age groups



Heikkinen et al., J Infect Dis 2004

Efficacy against influenza-associated AOM

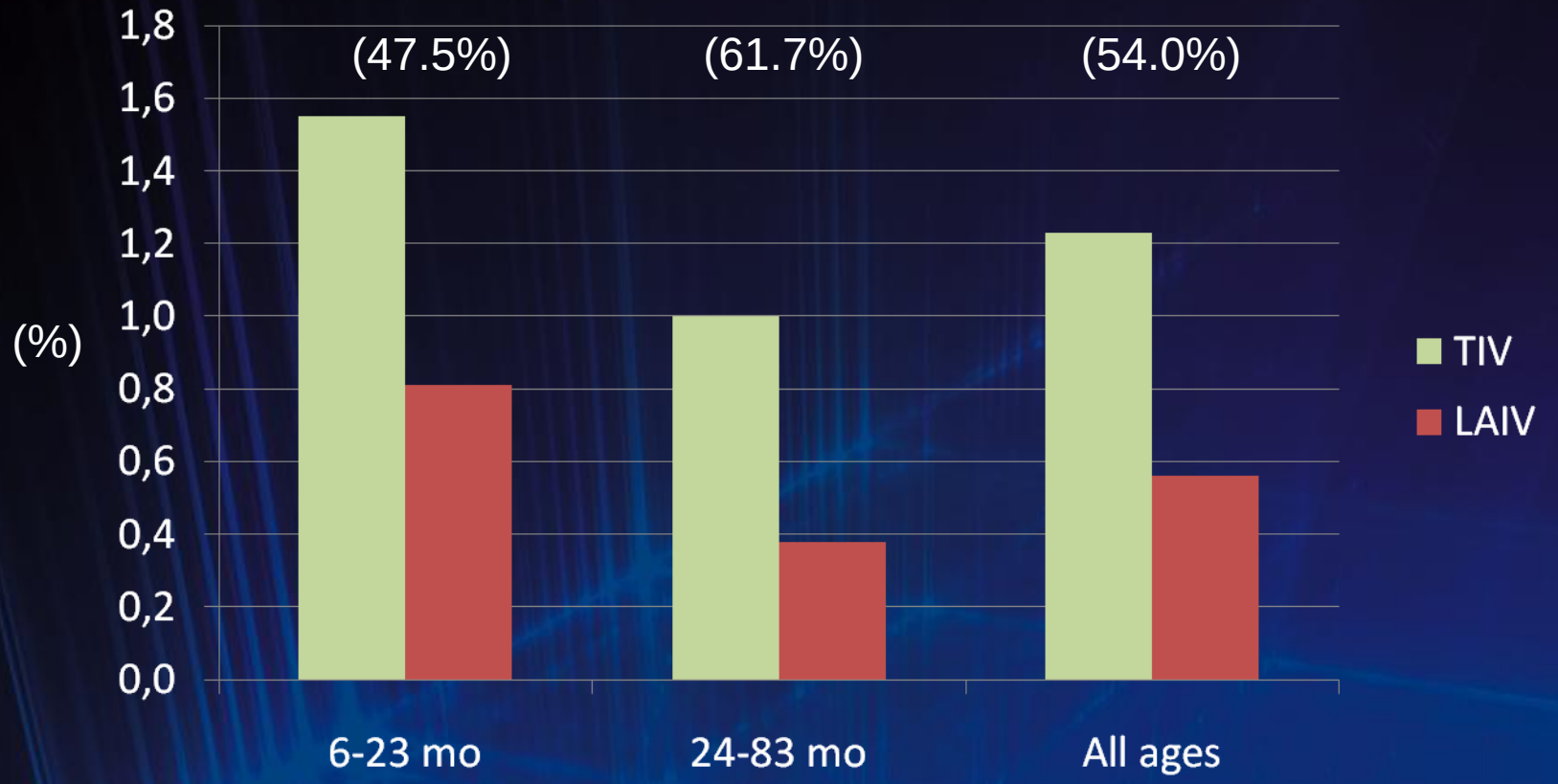
Placebo-controlled trials



Block et al., PIDJ 2011

Efficacy against influenza-associated AOM

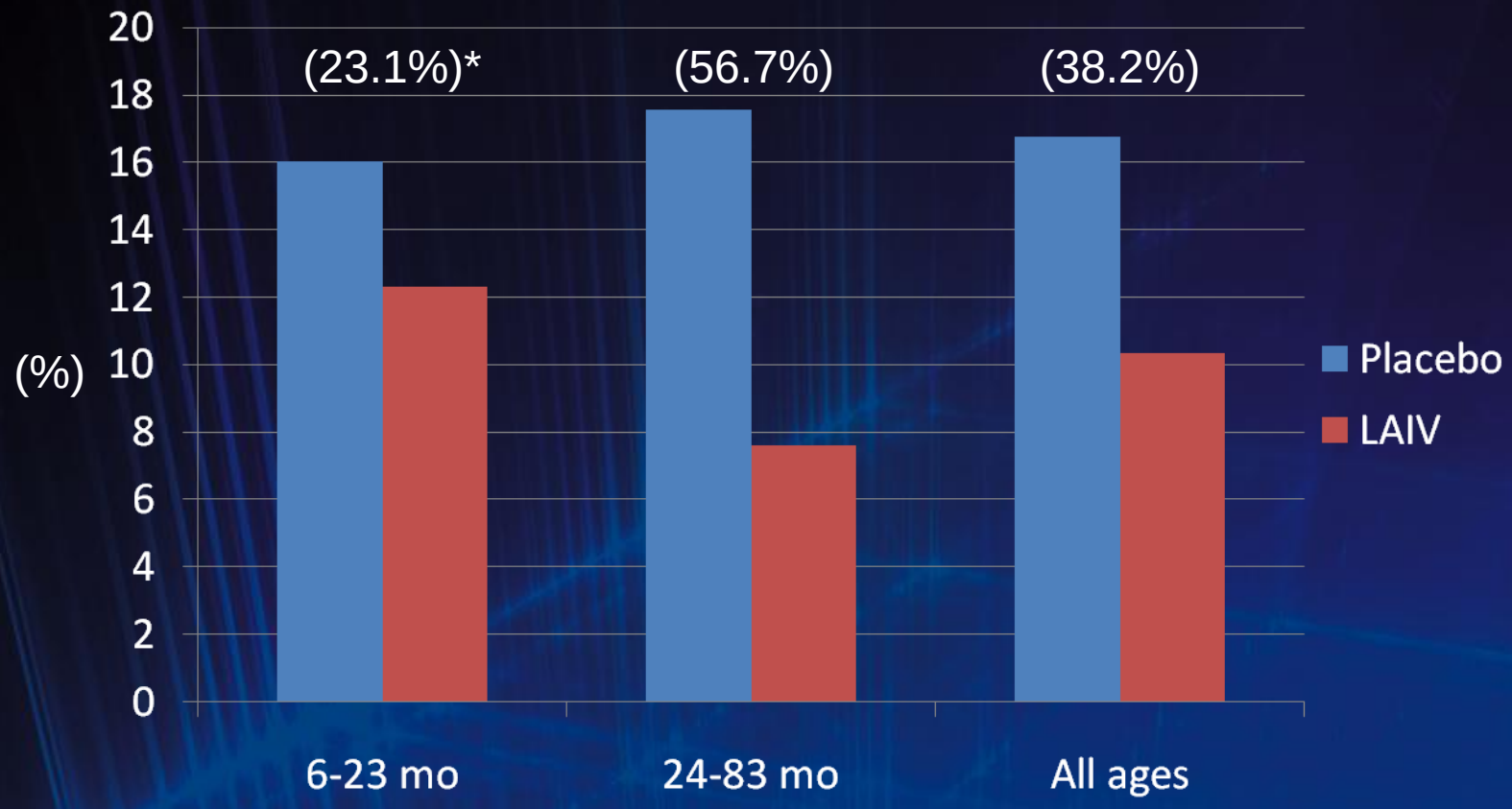
TIV-controlled trials



Block et al., PIDJ 2011

Proportion of AOM in influenza-positive children

Placebo-controlled trials

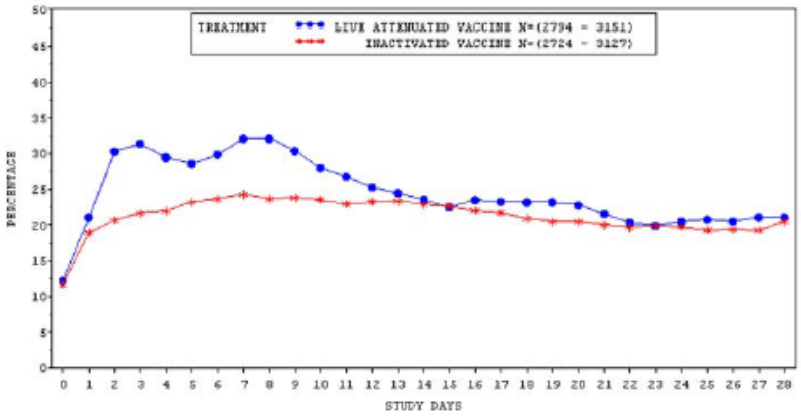


(* not significant)

Block et al., PIDJ 2011

Runny nose and fever: LAIV vs TIV

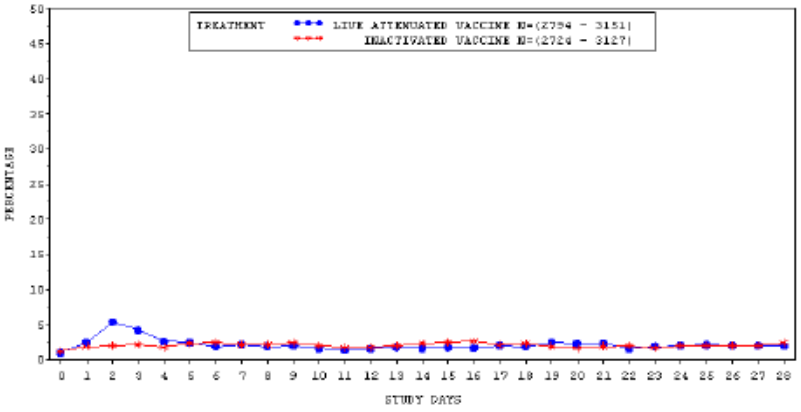
Runny/Stuffy Nose



Fever

(>100°F oral or

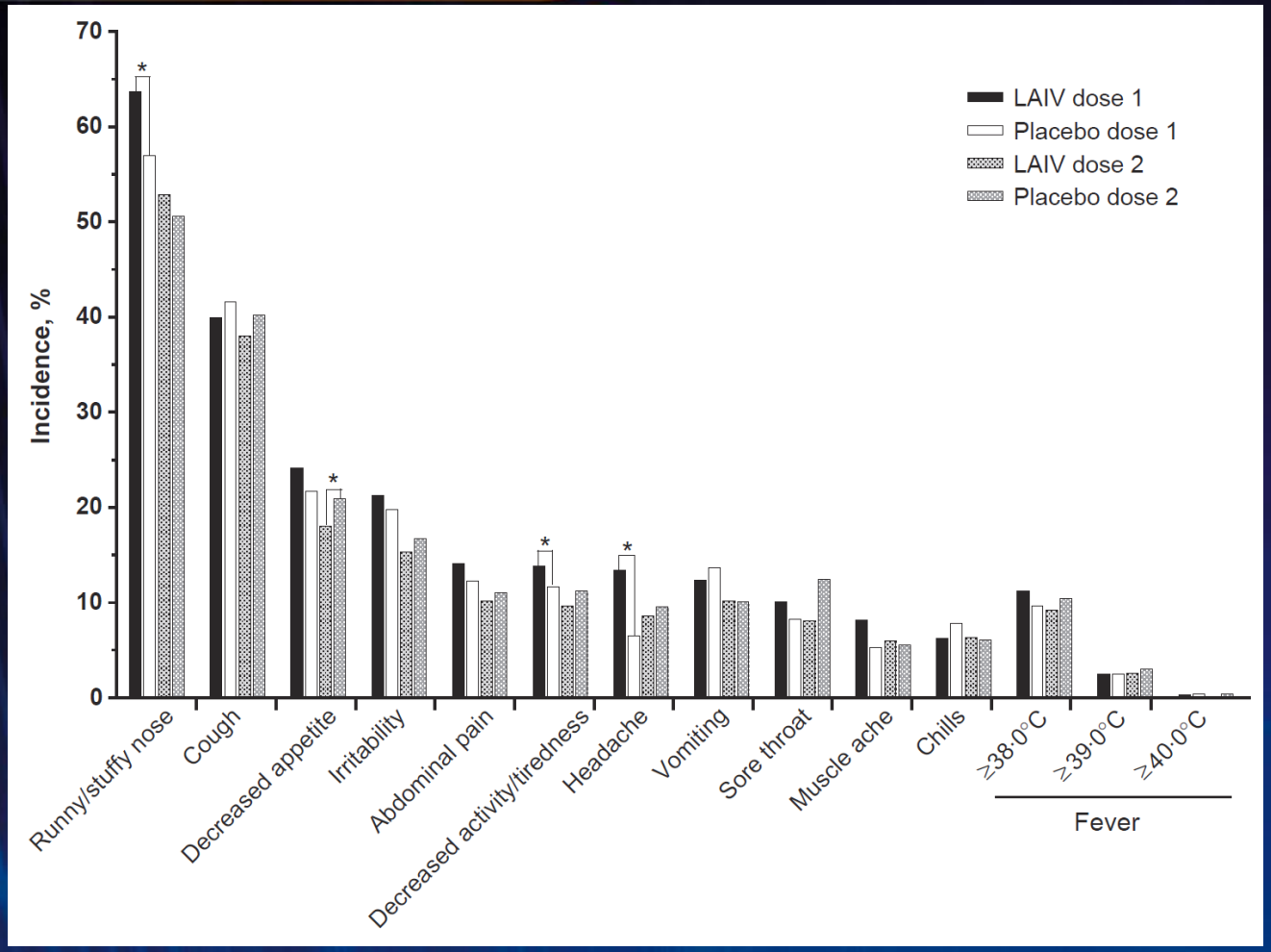
equivalent)



Belshe et al., N Engl J Med 2007

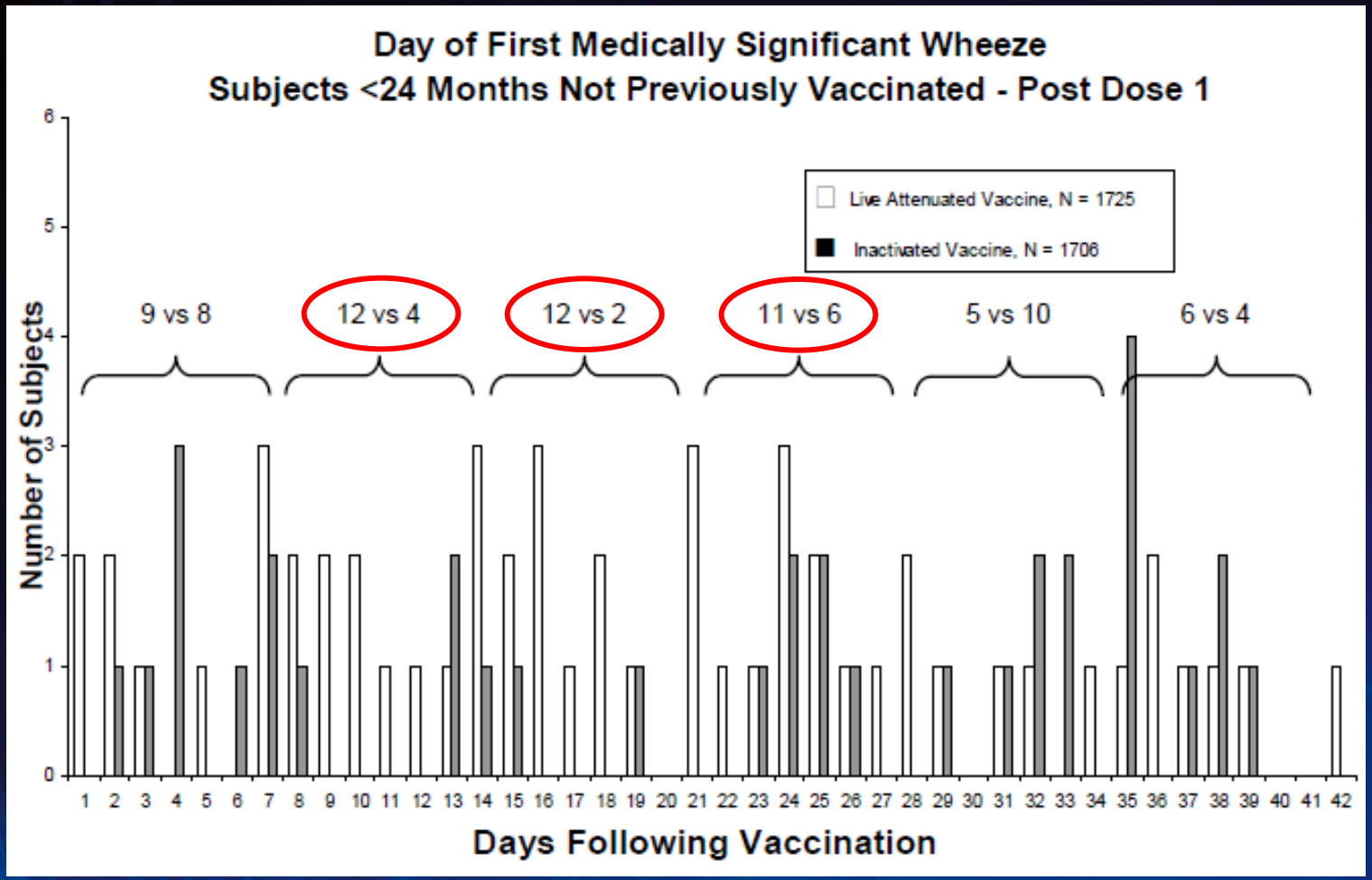
Solicited adverse events on days 0-10 post-vaccination

LAIV vs placebo



Ambrose et al, Influenza Other Respi Viruses 2011

Wheezing within 42 days after LAIV or TIV vaccination



Belshe et al., N Engl J Med 2007

Hospitalization for any cause within 180 days post-vaccination: LAIV vs TIV

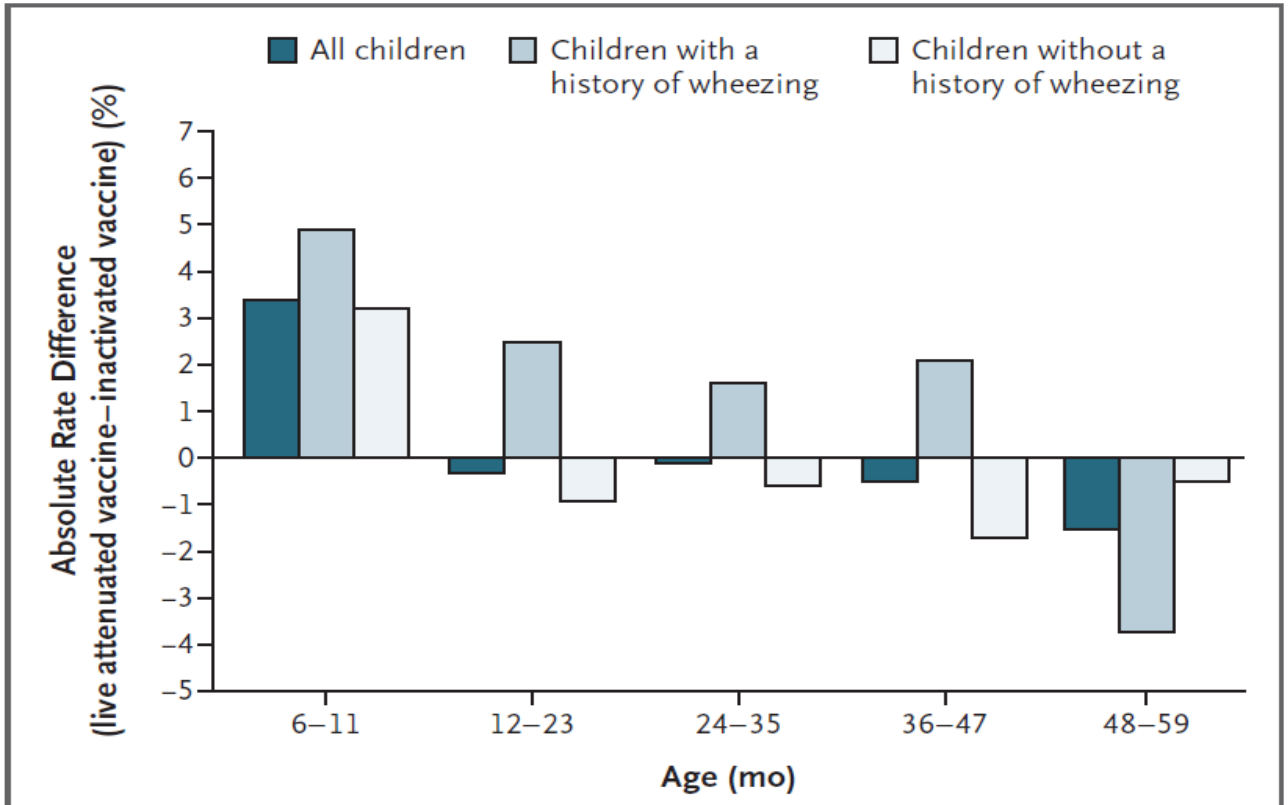


Figure 2. Difference in Rates of Hospitalization between the Two Vaccine Groups, According to Age and the Presence or Absence of a History of Wheezing Illness before Vaccination.

Belshe et al., N Engl J Med 2007

Efficacy of LAIV vs TIV vs placebo in adults

The NEW ENGLAND JOURNAL of MEDICINE

Table 2. Estimated Absolute and Relative Efficacies of the Trivalent Inactivated and Live Attenuated Influenza Vaccines.*

Confirmation of Symptomatic Influenza†	Cumulative Incidence of Influenza			Relative Risk (95% CI)			Percent Relative Reduction (95% CI)‡		
	TIV (N=813)	LAIV (N=814)	Placebo (N=325)	TIV vs. Placebo	LAIV vs. Placebo	TIV vs. LAIV	Absolute Efficacy, TIV vs. Placebo	Absolute Efficacy, LAIV vs. Placebo	Relative Efficacy, TIV vs. LAIV
	no. of participants (%)								
Positive culture	21 (2.6)	38 (4.7)	31 (9.5)	0.27 (0.15–0.49)	0.49 (0.30–0.81)	0.55 (0.31–0.97)	73 (51–85)	51 (19–70)	45 (3–69)
Positive PCR	28 (3.4)	56 (6.9)	35 (10.8)	0.32 (0.19–0.54)	0.64 (0.41–1.00)	0.50 (0.31–0.80)	68 (46–81)	36 (0–59)	50 (20–69)
Positive culture, positive PCR, or both	28 (3.4)	56 (6.9)	35 (10.8)	0.32 (0.19–0.54)	0.64 (0.41–1.00)	0.50 (0.31–0.80)	68 (46–81)	36 (0–59)	50 (20–69)

Monto et al., NEJM 2009

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Monto et al., NEJM 2009

Conclusions by the EMA

- ”Given the biological plausibility that pre-existing immunity may negatively affect the efficacy of LAIV, there are theoretical grounds that adults may not be optimal candidates for this vaccine”

- ”This concern is reinforced by the sharp distinction of the efficacy data in children and in adults”

- ”...an indication of this LAIV in adults could only be considered on the basis of an additional efficacy study versus TIV with an adequate sample size...”

EMA Assessment Report, 2010

The future of LAIV in Europe?

Indication for use: only in subjects 2-17 years of age

Commercially available in year .....(2013?)

Pros and cons of LAIV

- PROS
  - Easy way of administration
  - Higher clinical efficacy in children
  - Broad immunogenicity
  - Mimics natural infection
- CONS
  - Poorer efficacy in adults?
  - Slightly increased local reactions
  - Increased wheezing and hospitalization in children
  - Correlates of protection poorly defined
  - Price higher compared with TIV ??