

Safety of Live-Attenuated vs. Inactivated Influenza Vaccines for Healthy Children (GRADE)

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Overview

❑ Three outcomes

- Fever
- Medically-attended wheezing
- Serious adverse events (SAEs)

❑ Safety analyses focus upon younger children

❑ Observational studies excluded

- Differences in health status of underlying populations may affect interpretation of safety outcomes

EVIDENCE PROFILE

2—8 YEARS

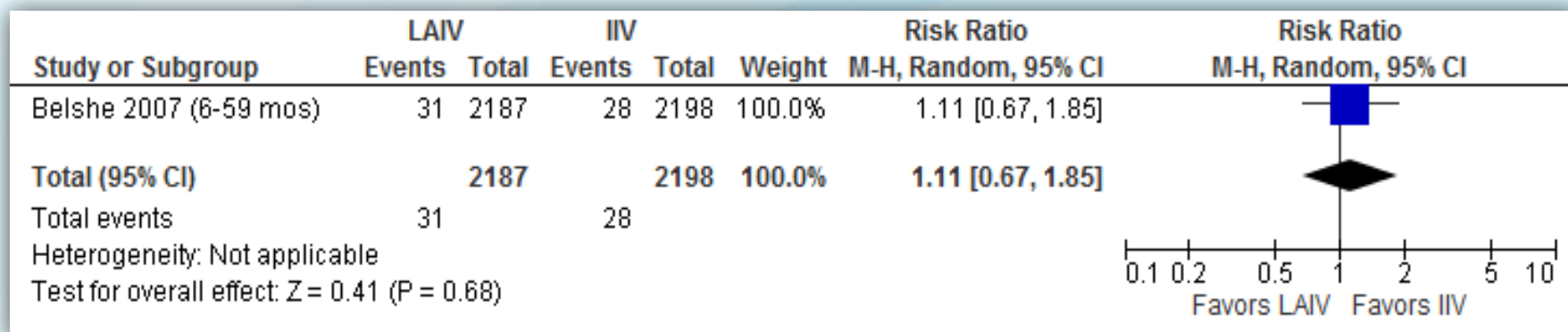
Evidence Profile—LAIV vs. IIV—2-8-year-olds

Medically-attended wheezing

(CRITICAL)

Studies (n)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Effect		Quality
					RR[95% CI]	Risk Difference with LAIV [95% CI]	
1	Not Serious	Not Serious	Not Serious	Serious	1.11 [0.67 – 1.85]	1 more per 1000 [4 fewer – 11 more]	2 (Moderate)

- Protocol-defined “medically significant wheezing”
- Follow-up 42 days.
- Data limited to children aged 24 through 59 months.
- Following dose 1; without regard to previous vaccination.



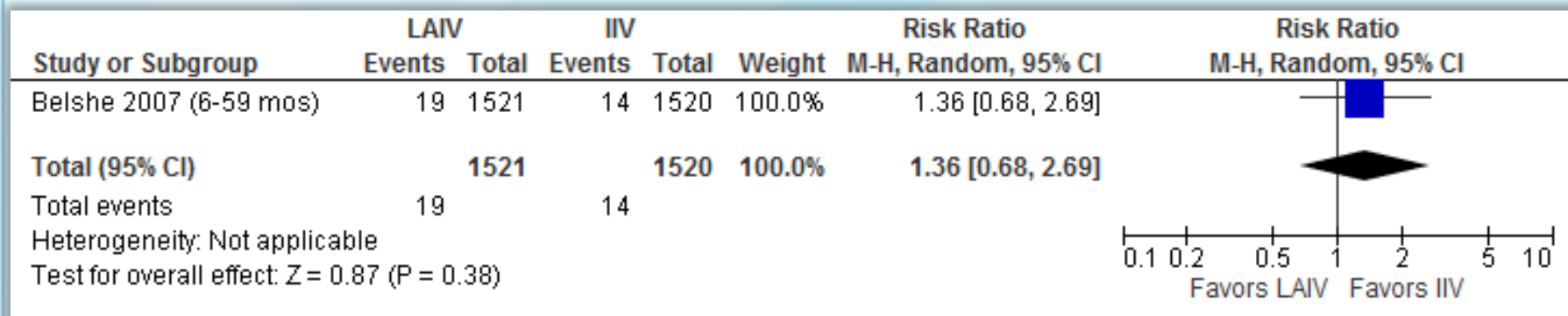
Evidence Profile—LAIV vs. IIV—2-8-year-olds

Medically-attended wheezing

(CRITICAL)

Studies (n)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Effect		Quality
					RR[95% CI]	Risk Difference with LAIV [95% CI]	
1	Not Serious	Not Serious	Not Serious	Serious	1.36 [0.68 – 2.69]	3 more per 1000 [3 fewer – 16 more]	2 (Moderate)

- Protocol-defined “medically significant wheezing”
- Follow-up 42 days.
- Data limited to children aged 24 through 59 months.
- Following dose 1; NOT previously vaccinated.



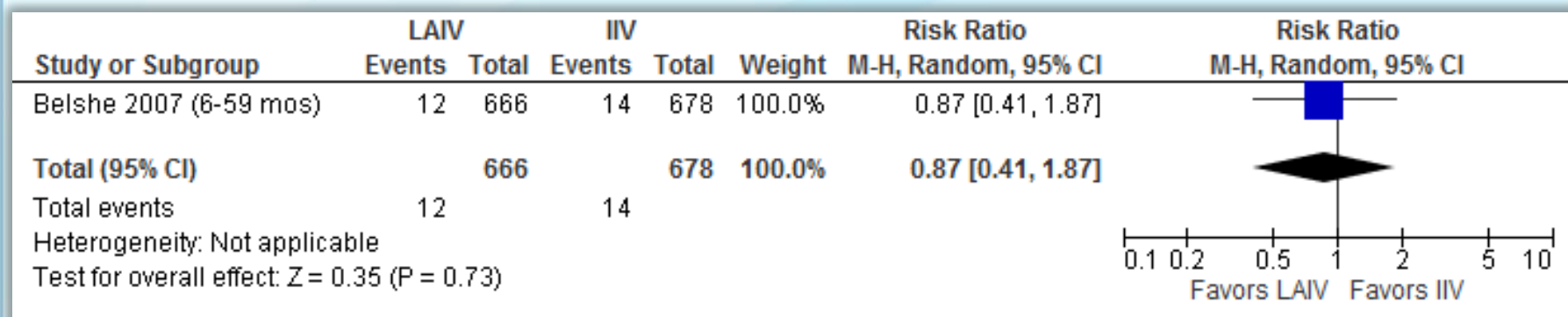
Evidence Profile—LAIV vs. IIV—2-8-year-olds

Medically-attended wheezing

(CRITICAL)

Studies (n)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Effect		Quality
					RR[95% CI]	Risk Difference with LAIV [95% CI]	
1	Not Serious	Not Serious	Not Serious	Serious	0.87 [0.41 – 1.87]	3 fewer per 1000 [12 fewer–18 more]	2 (Moderate)

- Protocol-defined “medically significant wheezing”
- Follow-up 42 days.
- Data limited to children aged 24 through 59 months.
- Following dose 1; previously vaccinated.



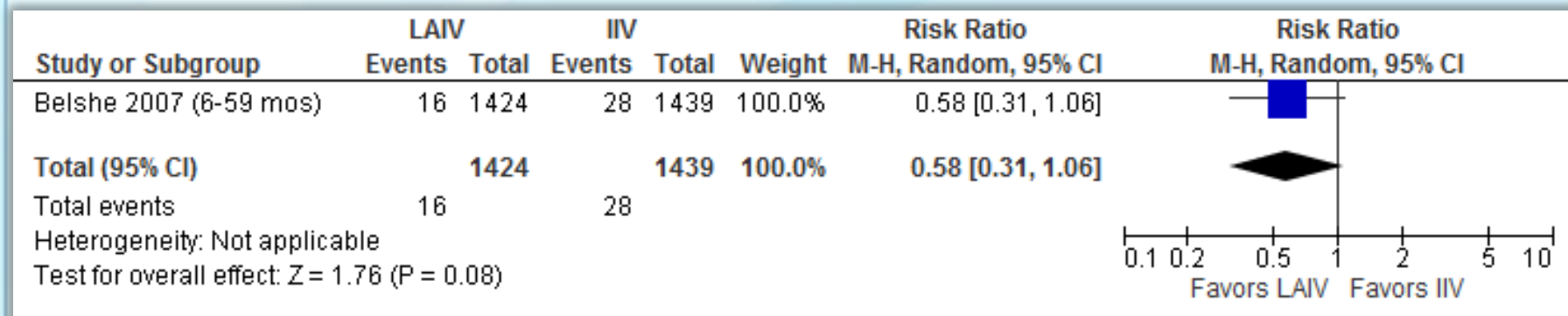
Evidence Profile—LAIV vs. IIV—2-8-year-olds

Medically-attended wheezing

(CRITICAL)

Studies (n)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Effect		Quality
					RR[95% CI]	Risk Difference with LAIV [95% CI]	
1	Not Serious	Not Serious	Not Serious	Serious	0.58 [0.31 – 1.06]	8 fewer per 1000 [13 fewer – 1 more]	2 (Moderate)

- Protocol-defined “medically significant wheezing”
- Follow-up 42 days.
- Data limited to children aged 24 through 59 months.
- Following dose 2; NOT previously vaccinated.



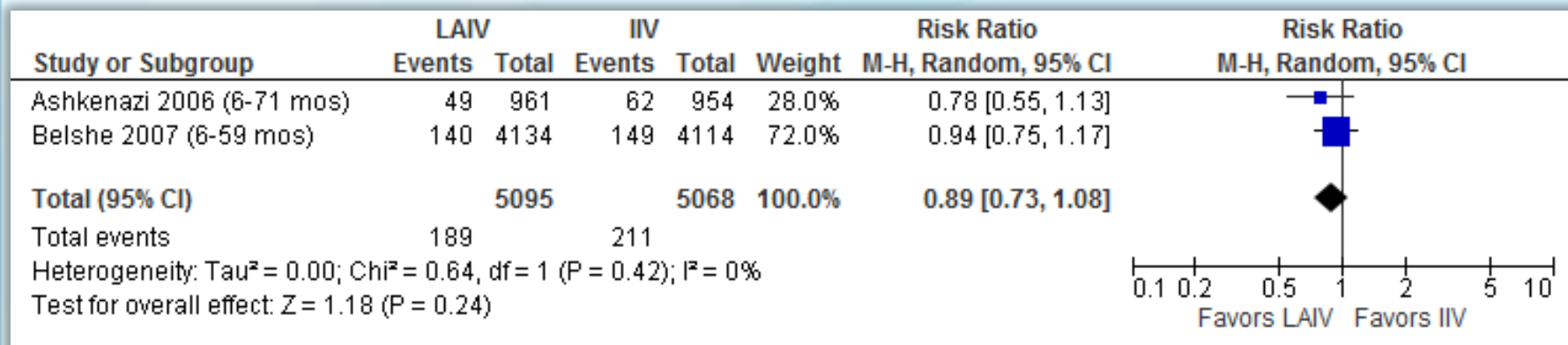
Evidence Profile—LAIV vs. IIV—2-8-year-olds

Fever, $\geq 38.6^{\circ}\text{C}$ or $\geq 38.9^{\circ}\text{C}$ —Randomized Studies

(IMPORTANT)

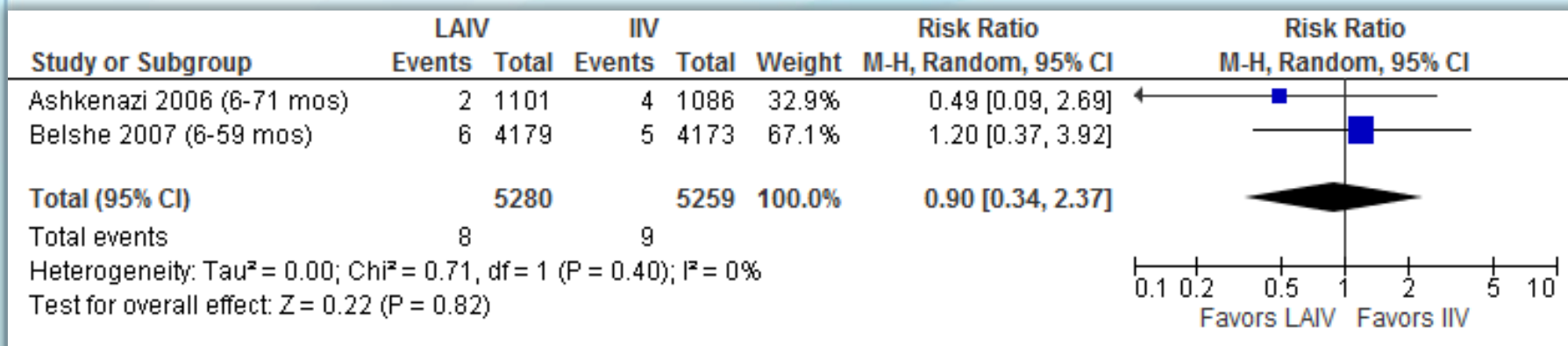
Studies (n)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Effect		Quality
					RR [95% CI]	Risk Difference with LAIV [95% CI]	
2	Not Serious	Not Serious	Not Serious	Serious	0.89 [0.73 – 1.08]	5 fewer per 1000 [11 fewer – 3 more]	2 (Moderate)

- Follow-up days 0-10.
- Following dose 1.
- Data for Belshe et al. from sBLA .
- Temperature thresholds differed slightly between studies: 38.6°C (Ashkenazi) vs. 38.9°C (Belshe).



Evidence Profile—LAIV vs. IIV—2-8-year-olds Related SAEs

Studies (n)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Effect		Quality
					RR[95% CI]	Risk Difference with LAIV [95% CI]	
2	Not Serious	Not Serious	Not Serious	Serious	0.90 [0.34 – 2.37]	0 fewer per 1000 [1 fewer – 2 more]	2 (Moderate)



Evidence Summary: Safety

2-8 year olds	Study Design (n)	Findings	Quality
Medically attended wheezing (Critical)	RCT (1)	No difference	2 (Moderate)
Fever (Important)	RCT (2)	No Difference	2 (Moderate)
Related SAE	RCT (2)	No difference	2 (Moderate)

Limitations

- ❑ Definitions of outcomes of interest not standardized across studies.
- ❑ Studies not adequately powered to detect differences in rare but serious outcomes (e.g., Guillain-Barré; anaphylaxis).
- ❑ All data pertain to trivalent vaccines (LAIV3 and IIV3).

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Thank You!

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