

A Bayesian Assessment of High-Dose vs. Standard-Dose Influenza Vaccine against severe outcomes in Older Adults: A prespecified analysis of FLUNITY-HD

Key Takeaways

HD-IIV showed high posterior probabilities of benefit across severe hospitalization outcomes, with the strongest effect for laboratory-confirmed influenza hospitalization.

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BACKGROUND

- DANFLU-2 and GALFLU were pragmatic RCTs comparing high-dose (HD-IIV) vs. standard-dose (SD-IIV) influenza vaccine in older adults
- A pooled analysis (FLUNITY-HD) demonstrated superior protection of HD-IIV against severe outcomes including influenza/pneumonia and cardiorespiratory hospitalizations
- This pre-specified Bayesian re-analysis assessed the robustness of FLUNITY-HD findings using non-informative, evidence-based, and skeptical priors

METHODS

- Pooled data from DANFLU-2 (Denmark) and GALFLU (Galicia, Spain), two harmonized pragmatic trials randomizing older adults 1:1 to HD-IIV or SD-IIV with register-based follow-up
- Primary outcome: influenza/pneumonia hospitalization. Secondary: cardiorespiratory hospitalization, LCI hospitalization, all-cause hospitalization, and all-cause death
- Bayesian log-binomial regression applied with three priors: non-informative, evidence-based, and skeptical (10% prior probability of rVE >5%)

RESULTS

- A total of 466,320 participants were included across DANFLU-2 and GALFLU
- Influenza/pneumonia hospitalization: median rVE 8–9% across all priors, >99% probability of any benefit (Table)
- Cardiorespiratory hospitalization: median rVE ~6.3%, >99.9% probability of benefit across all priors
- LCI hospitalization: median rVE ~32%, 100% probability of exceeding both 5% and 10% thresholds under all priors
- All-cause mortality: median rVE ~1.2%, 62–63% probability of any benefit

OBJECTIVE

To assess the robustness of the FLUNITY-HD findings using Bayesian re-analysis with non-informative, evidence-based, and skeptical priors.

CONCLUSIONS

- HD-IIV showed high posterior probabilities of benefit across multiple severe hospitalization outcomes, with the strongest effect for LCI hospitalization
- Bayesian re-analysis further strengthened the original FLUNITY-HD findings
- Results support the added value of HD-IIV in older adults

Bayesian Posterior Estimates of Relative Vaccine Effectiveness of HD-IIV vs. SD-IIV

Outcome and prior	Posterior median rVE [95% CrI]	Probability of rVE > 0%	Probability of rVE > 5%	Probability of rVE > 10%
Hospitalization for influenza or pneumonia				
Non informative prior	8.68% [1.69%;15.65%]	99.3%	85.9%	36.7%
Evidence-based prior	9.15% [2.18%;15.46%]	99.5%	87.9%	39.2%
Skeptical prior	8.27% [1.80%;14.67%]	99.2%	83.6%	31.3%
Hospitalization for any cardio-respiratory disease				
Non informative prior	6.26% [2.46%;9.88%]	99.9%	76.1%	2.1%
Evidence-based prior	6.39% [2.56%;9.83%]	99.9%	77.0%	1.8%
Skeptical prior	6.37% [2.48;9.89%]	99.9%	75.7%	2.2%
Laboratory-confirmed influenza hospitalization*				
Non informative prior	32.02% [20.33%;42.62%]	100.0%	100.0%	100.0%
Evidence-based prior	32.04% [20.10%;42.21%]	100.0%	100.0%	100.0%
Skeptical prior	32.03% [20.12%;42.19%]	100.0%	100.0%	100.0%
All-cause mortality				
Non informative prior	1.27% [-5.74%;7.91%]	62.4%	13.3%	0.5%
Evidence-based prior	1.25% [-5.91;8.01%]	63.2%	14.1%	0.6%
Skeptical prior	1.13% [-6.04%;7.86%]	62.6%	13.7%	0.6%

Non-informative prior: rVE = 0, SD = 100 (log RR scale). Skeptical prior: rVE = 0, SD = 0.0312 (10% prior probability of rVE ≥ 5%). Evidence-based priors per outcome: flu/pneumonia hosp. (rVE 23.5%, 12.3–33.2%), cardiorespiratory hosp. (18.2%, 6.8–28.1%), LCI hosp. (11.7%, 7.0–16.1%), all-cause mortality (1.6%, –2.0 to 5.0%).

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