# Assessing High Dose Versus Standard Dose Influenza Vaccine Protection Against Severe Disease Outcomes

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## FLUNITY-HD*: A LARGE TRIAL WITH INNOVATIVE DESIGN

**Largest individually randomized influenza vaccine effectiveness trial**

**466,320 participants** enrolled across Denmark (three flu seasons) and Spain (two flu seasons)[1-4]

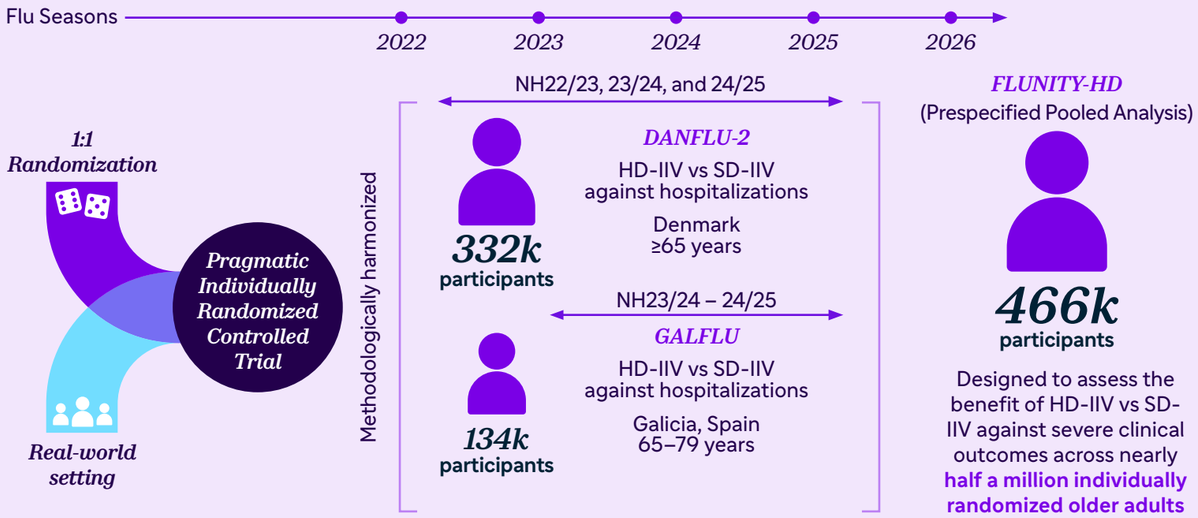
**Innovative pragmatic design**

- **Digital** invitation letters and e-consent[1]
- Vaccination through **standard healthcare systems** (no trial sites)[1]
- Outcomes assessed via national EHRs[1]

**High statistical power**

Powered to study the rVE of HD-IIV versus SD-IIV against **severe outcomes** (i.e., hospitalizations) in older adults[1,4]

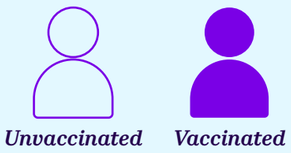
### Largest ever analysis of influenza vaccine effectiveness among individually randomized older adults[1-4]



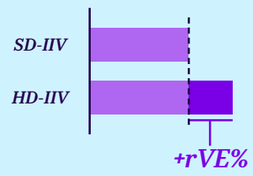

## Study Strengths

- Prospective methodological harmonization of the underlying DANFLU-2 and GALFLU trials to minimize heterogeneity across trials and regions[1]
- Consistency in findings across seasons, regions, and age ensures greater reliability and generalizability of results[1]
- FLUNITY-HD is the largest ever individually randomized influenza vaccine effectiveness study and the first of its kind for an influenza vaccine.[1]
- Pragmatic design ensures results reflect real-world clinical practice[9]

**aVE:**
Outcomes in a vaccinated cohort compared to those in an unvaccinated or placebo cohort[6]




**rVE:**
Additional benefit of high-dose vaccine compared to standard-dose vaccine, not absolute protection rates[6]




## KEY RESULTS FROM FLUNITY-HD

*HD-IIV demonstrated additional protection over SD-IIV across a range of severe influenza outcomes*

### Primary endpoint[1]

***+rVE 8.8%*** (CI: 1.7–15.5) for **influenza/pneumonia hospitalization**

### Secondary endpoints[1]

***+rVE 6.3%***
(CI: 2.5–10.0) for **cardio-respiratory hospitalization**

***+rVE 31.9%***
(CI: 19.7–42.2) for **LCI hospitalization†**

***+rVE 2.2%***
(CI: 0.3–4.1) for **all-cause hospitalizations**

***515=NNV***
for **all-cause hospitalization**

## Study Limitations

- Open label trial design and did not employ systematic influenza testing[1]
- Potential imprecision and misclassification of data in EHRs[5]
- Potential for heterogeneity between the trials, considering differences in regions, local epidemiology, enrollment ages, and local healthcare practices, despite harmonization of study protocols and end points[1,‡]
- The standard of care with respect to hospitalization in Denmark and Spain may differ from that in the United States[1]

**Abbreviations:**

aVE: absolute vaccine efficacy; EHR: electronic health record; HD-IIV: high-dose inactivated influenza vaccine; LCI: laboratory-confirmed influenza; NNV: number needed to vaccinate; rVE: relative vaccine effectiveness; SD-IIV: standard-dose inactivated influenza vaccine; vs: versus.

**References:**

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*The comparator standard-dose vaccine used in the trial is not licensed in the U.S.
†LCI hospitalization was a secondary outcome in FLUNITY-HD, exploratory in the individual studies due to uncertainty in adequate testing to accrue cases.
‡However, no statistically significant heterogeneity was detected.

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