

FLUNITY^{DAN GAL}HD

United in Science

HD influenza vaccine is supported by extensive body of clinical evidence¹

Then why FLUNITY-HD?

Given the absence of an adequately powered individually randomized trial to assess hospitalization outcomes, there was a need to generate robust, evidence^{2,3}

Enrollment on an unprecedented scale would be needed to achieve this^{3,4}

Pragmatic trials allow for more inclusive, high-volume enrollment and improved generalizability vs. RCTs⁴

To address this evidence gap, two methodologically harmonized pragmatic, individually randomized trials (DANFLU-2, GALFLU) were conducted^{5,6}

FLUNITY-HD is the prespecified pooled analysis of DANFLU-2 and GALFLU trials with nearly half a million older adults across multiple seasons³

This study provides the first definitive evidence of HD-IIV's superior protection against hospitalization compared to SD-IIV*³

Findings were consistent across prespecified secondary analyses, including populations with CVD, ASCVD, or immunosuppression, as well as across age and sex groups⁷⁻¹⁰

Expanding influenza evidence to support public health and health care provider decision-making

*Comparator was SD-IIV (Vaxigrip Tetra [Sanofi] in DANFLU-2; Influvac Tetra [Viatris] in GALFLU)
Abbreviations: ASCVD, atherosclerotic cardiovascular disease; CVD, cardiovascular disease; HD-IIV, high-dose inactivated influenza vaccine; RCT, randomized controlled trial; SD-IIV, standard-dose inactivated influenza vaccine (egg-based unadjuvanted)
References: 1. Lee J, et al. *Vaccine*. 2023;41:100327; 2. Palmu AA, et al. *Influenza Other Respir Viruses*. 2024;18(4):e13270; 3. Johansen ND, et al. *Lancet*. 2025;406(10518):2425-2434; 4. Omerovic E, et al. *Trials*. 2024;25(1):80; 5. Johansen ND, et al. *N Engl J Med*. 2025;393:2291-2302; 6. Pardo-Seco J, et al. *N Engl J Med*. 2025;393:2303-2312; 7. Johansen ND, et al. *Circulation*. 2026;153:798-806; 8. Pareek M, et al. *J Am Coll Cardiol*. 2026;S0735-1097(25)10661-X; 9. Jensen AMR, et al. Presentation at ESCMID 2026, Munich, Germany; 10. Hosseini K, et al. Poster presented at ESCMID 2026, Munich, Germany

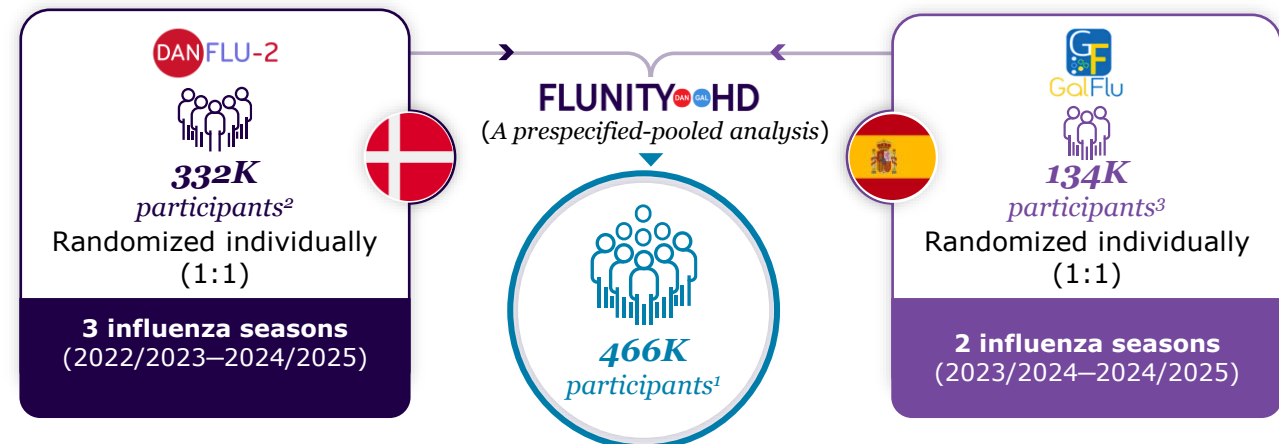
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FLUNITY^{DAN GAL}HD

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Pre-specified pooled analysis¹ of two methodologically harmonized, individually randomized pragmatic trials^{2,3}



Sanofi's high-dose influenza vaccine*, compared to standard-dose influenza vaccine†, demonstrated statistically significant superior protection (rVE [95% CI]) against hospitalization due to¹



Limitations: In the individual trials, potential limitations included the open-label nature of the trials, lack of systematic influenza testing, and lack of data on race or ethnicity. Reliance on routine health-care data might have introduced imprecision into the trial data. For the pooled analysis, despite harmonization of study protocols and endpoint definitions across trials, there was potential for heterogeneity between the trials, considering differences in regions, local epidemiology, enrolment ages, and local health-care practices (medical documentation, testing, diagnosis, coding, etc)^{2,3}

*Split-virion inactivated influenza vaccine (60 µg/strain); †Comparator was SD-IIV (Vaxigrip Tetra [Sanofi] in DANFLU-2; Influvac Tetra [Viatris] in GALFLU; †Primary endpoint
Abbreviations: CI, confidence interval; rVE, relative vaccine effectiveness

References: 1. Johansen ND, et al. *Lancet*. 2025;406(10518):2425-2434; 2. Johansen ND, et al. *N Engl J Med*. 2025;393:2291-2302; 3. Pardo-Seco J, et al. *N Engl J Med*. 2025;393:2303-2312

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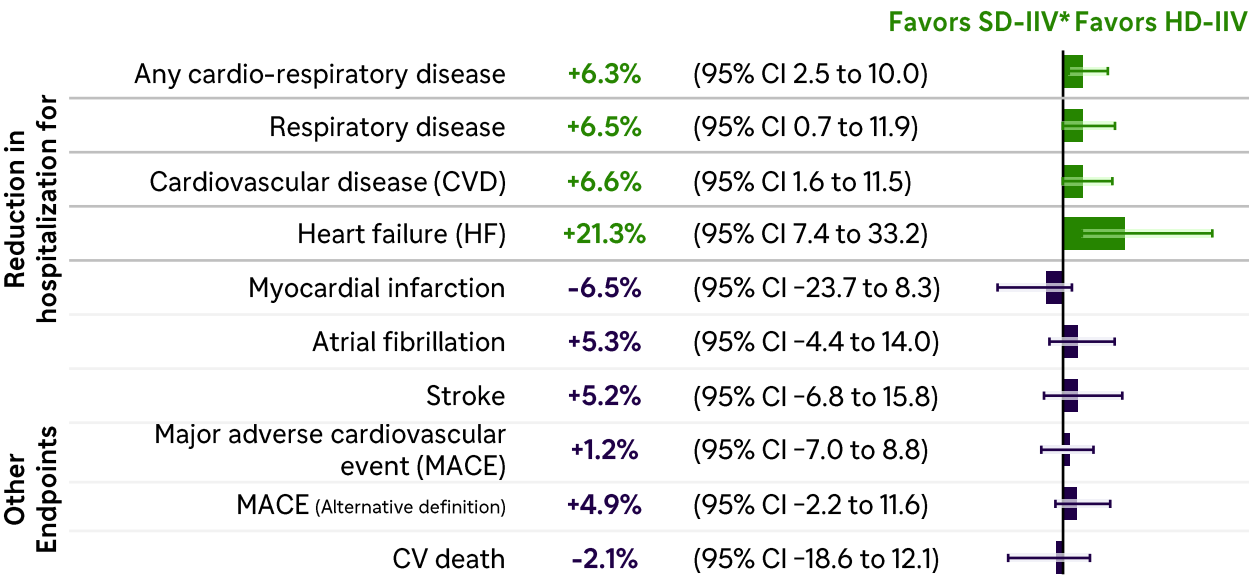
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CV OUTCOMES



466,320
participants

In this **prespecified secondary analysis of FLUNITY-HD**, investigators observed that HD-IIV vs. SD-IIV* reduced hospitalization for any CVD and HF by 6.6% and 21.3% respectively



CVD SUBPOPULATION

107,700
with history of CVD

HD-IIV
54,061



SD-IIV*
53,639



In this **prespecified secondary analysis of FLUNITY-HD**, investigators observed that HD-IIV vs. SD-IIV* showed consistent effectiveness among those with or without pre-existing CVD



HD-IIV consistently reduced severe hospitalization outcomes compared with SD-IIV* regardless of previous history of CVD



The consistent rVE findings resulted in larger absolute risk reductions in the population with history of CVD

*Comparator was SD-IIV (Vaxigrip Tetra [Sanofi] in DANFLU-2; Influvac Tetra [Viatris] in GALFLU)
Abbreviations: CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; HD-IIV, high-dose inactivated influenza vaccine; HF, heart failure; MACE, major adverse cardiovascular event; rVE, relative vaccine effectiveness; SD-IIV, egg-based unadjuvanted standard-dose inactivated influenza vaccine
Reference: Johansen ND, et al. *Circulation*. 2026;153:798–806



ASCVD SUBPOPULATION



466,320
participants



56,886
with history of ASCVD

HD-IIV
28,717



SD-IIV*
28,169



In this **prespecified secondary analysis of FLUNITY-HD**, investigators observed that HD-IIV vs. SD-IIV* showed consistent effectiveness among those with or without pre-existing ASCVD

Outcome	HD-IIV (n=233,311) n (%)	SD-IIV* (n=233,009) n (%)	NNV	rVE (95%CI)
Hospitalization for influenza or pneumonia [†]				
All	1312 (0.56)	1437 (0.62)	1667	8.82 (1.66 to 15.46)
No ASCVD	970 (0.47)	1069 (0.52)	2000	9.15 (0.81 to 16.80)
ASCVD	342 (1.19%)	368 (1.31)	833	8.84 (-5.91 to 21.55)



NNVs were overall lower with ASCVD as compared with those without ASCVD

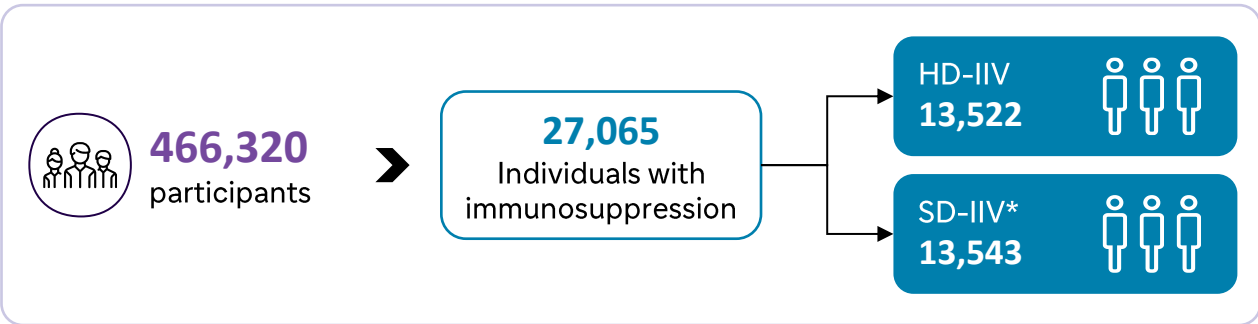


These findings support the use of HD-IIV for reducing both influenza specific and other hospitalization outcomes in older individuals both with and without preexisting ASCVD

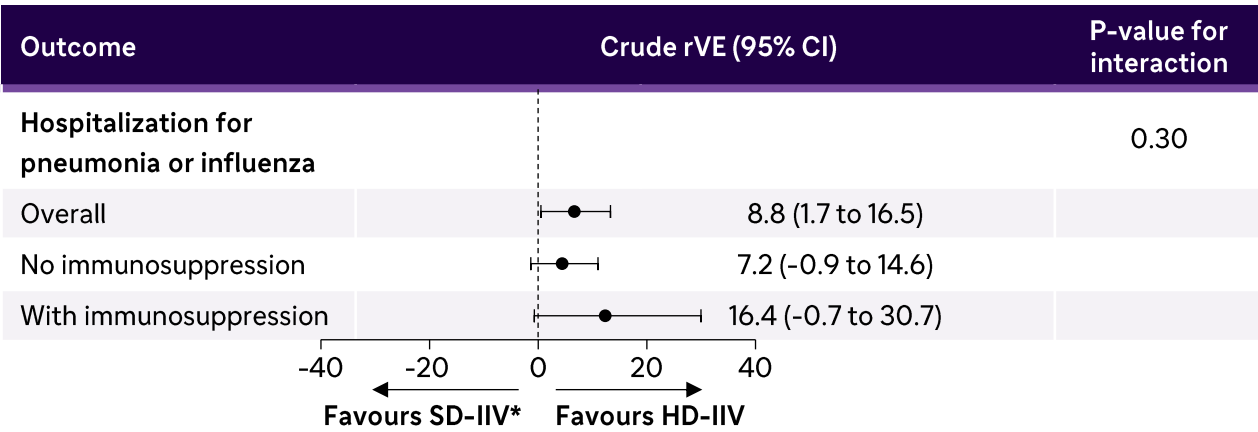
*Comparator was SD-IIV (Vaxigrip Tetra [Sanofi] in DANFLU-2; Influvac Tetra [Viatris] in GALFLU; [†]Primary Outcome
Abbreviations: ASCVD, atherosclerotic cardiovascular disease; CI, confidence interval; HD-IIV, high-dose inactivated influenza vaccine; NNV, number needed to vaccinate; rVE, relative vaccine effectiveness; SD-IIV, egg-based unadjuvanted standard-dose inactivated influenza vaccine
Reference: Pareek M, et al. *J Am Coll Cardiol*. 2026:S0735-1097(25)10661-X



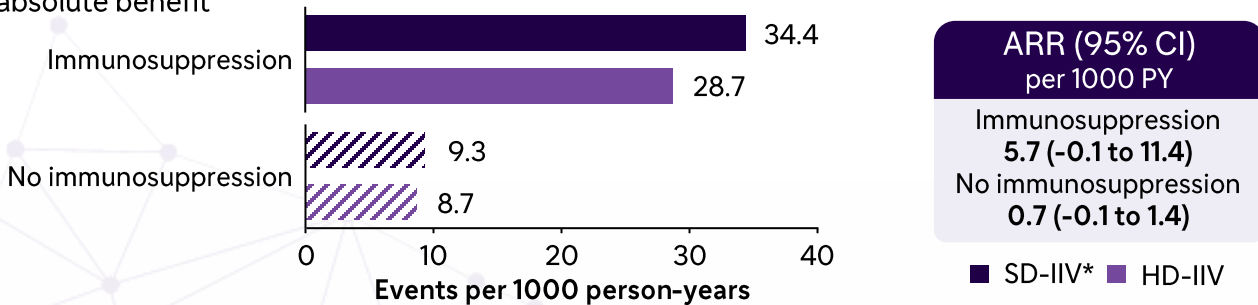
IMMUNOSUPPRESSED OLDER ADULTS



HD-IIV vs. SD-IIV* provided a significant reduction in hospitalization for influenza or pneumonia, with no effect modification by immunosuppression



High absolute risk was observed in immunosuppressed participants, with potentially greater absolute benefit



Definition of immunosuppression: Immunosuppressive conditions: Hematologic disease, solid organ transplant, HSCT, primary immunodeficiency, HIV and/or; Immunosuppressive treatment: chemotherapy, immunosuppressive agents, systemic glucocorticoids** Not mutually exclusive, based on registry data (ICD-10 codes, procedure codes, ATC codes**);

*Comparator was SD-IIV (VaxigripTetra [Sanofi] in DANFLU-2; InfluvacTetra [Viatris] in GALFLU;

†Only available in DANFLU-2; **Only available in GALFLU

Abbreviations: ATC, Anatomical Therapeutic Chemical; ARR, absolute risk reduction; CI, confidence interval; HD-IIV, high-dose inactivated influenza vaccine; HIV, human immunodeficiency virus; HSCT, hematopoietic stem cell transplantation; ICD-10, International Classification of Disease-10; PY, patient years; SD-IIV, standard-dose inactivated influenza vaccine (egg-based unadjuvanted)

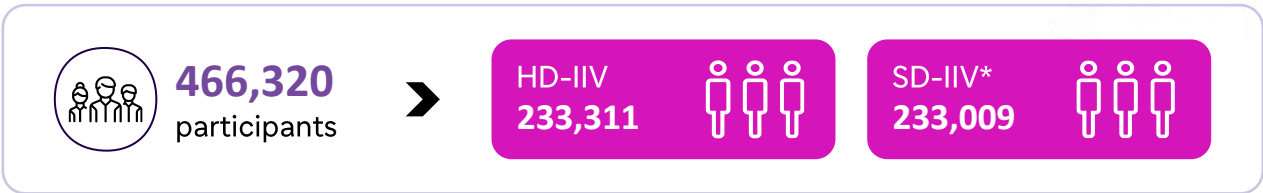
Study Limitation: Open-label design; heterogeneous immunosuppressed population; broad definition of systemic glucocorticoid use; registry-based data; secondary analysis

Reference: Jensen AMR, et al. Effectiveness of High-dose Versus Standard-dose Influenza Vaccine in Immunosuppressed Older Adults: A Prespecified Analysis of FLUNITY-HD. Presentation at ESCMID 2026, Munich, Germany

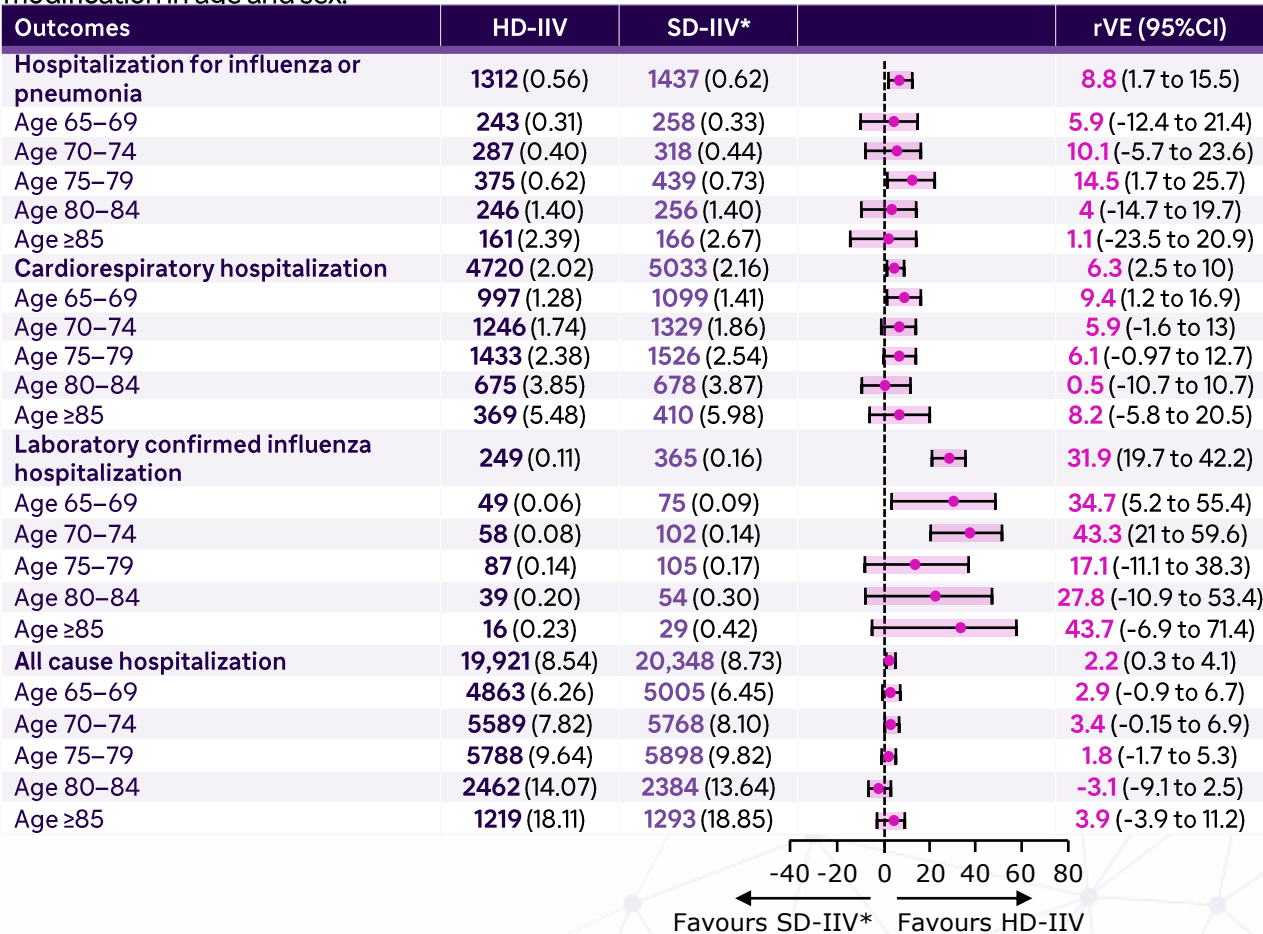
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AGE STRATIFIED



HD-IIV provided superior protection (overall rVE 8.8%, 95% CI (1.7 to 15.5), $P=0.0082$) compared with SD-IIV* against the primary endpoint of hospitalization for influenza or pneumonia with no effect modification in age and sex.



*Quadrivalent SD-IIV (VaxigripTetra [Sanofi] in DANFLU-2; InfluvacTetra [Viatris] in GALFLU)

Abbreviations: CI, confidence interval; HD-IIV, high-dose inactivated influenza vaccine; NNV, number needed to vaccinate; rVE, relative vaccine effectiveness; SD-IIV, egg-based unadjuvanted standard-dose inactivated influenza vaccine

Reference: Hosseini K, et al. E0738: A Bayesian Assessment of High-Dose vs. Standard-Dose Influenza Vaccine against severe outcomes in Older Adults: A prespecified analysis of FLUNITY-HD. Poster presented at ESCMID 2026, Munich, Germany

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