University of Copenhagen - Herlev and Gentofte Hospital

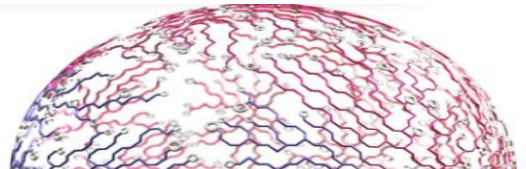
High-Dose vs. Standard-Dose Influenza Vaccine in Older Adults According to Diabetes status, A Prespecified Analysis of the FLUNITY-HD study

Kaveh Hosseini, MD-MPH, Cardiologist
Senior Researcher
Copenhagen University Hospital – Herlev and Gentofte, Denmark

On behalf of the FLUNITY-HD study group:

K. Hosseini, ND Johansen, AB Nielsen, J Pardo-Seco, C Rodriguez-Tenreiro-Sánchez, MM Loiacono, RC Harris, K Sharff, JA Hill, Y Huang, R van Aalst, A Chit, CS Larsen, L Larsen, L Wiese, M Dalager-Pedersen, BL Claggett, KH Janstrup, C Duran-Parrondo, M Piñeiro-Sotelo, M Cribeiro-González, M Conde-Pájaro, S Mirás-Carballal, J-M González-Pérez, SD Solomon, P Sivapalan, CJM Martel, JUS Jensen, F Martinón-Torres, T Biering-Sørensen

ESC Congress 2026
28 Aug 2026 - 31 Aug 2026
Munich, Germany



CIRL
CARDIOVASCULAR NON-INVASIVE IMAGING RESEARCH LABORATORY

CTCPR
CENTER FOR TRANSLATIONAL CARDIOLOGY AND PRAGMATIC RANDOMIZED TRIALS

Disclosure

- I have no personal disclosure
- The DANFLU-2 & GALFLU trials received funding from Sanofi

Background

Individuals with **diabetes** are at increased risk of severe influenza-related complications[1-2]

Immune responses and clinical protection may be attenuated in **older and metabolically vulnerable individuals with diabetes** [3]

High-dose influenza vaccine*

↑ Protection vs standard-dose against severe respiratory and cardiovascular hospitalization in the general older population[3]

Knowledge gap

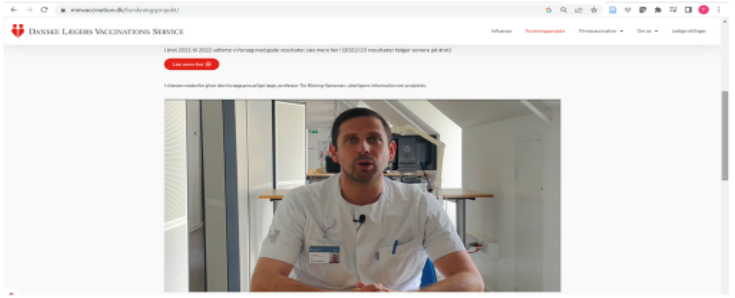
Limited evidence in diabetic populations

[1] Danielle Iuliano A et al. The Lancet 2017
[2] Modin D et al. Diabetes Care 2020
[3] Nielsen AB et al. et al. JAMA internal Medicine 2026

*Fluzone® High-Dose Quadrivalent/Efluelda®/Efluelda Tetra®[Sanofi] containing 60 µg of haemagglutinin antigen per strain;
VaxigripTetra [Sanofi] in DANFLU-2;InfluvacTetra [Viatris] in GALFLU containing 15 µg of haemagglutinin per strain









Vaccination clinic network:
- Open year-round – not just for flu vaccination
- Vaccinates >200,000 persons/year and rapidly upscaling
- Inclusion and randomization
- Administration of study drug

Initial participant data

UNIVERSITY OF COPENHAGEN

REGION H Gentofte Hospital

Center for Pragmatic Randomized Trials

- Central trial site
- Study oversight
- Database management
- Nationwide access to all medical records and lab results

Participant SSN

Baseline characteristics and outcomes



Registry data:
- Nationwide tax-funded public health system
- Nationwide registries can be crosslinked using social security numbers (SSN)
- Every hospital contact, death, redeemed prescription is captured in the registries

[1] Johansen ND et al. N Engl J Med 2025

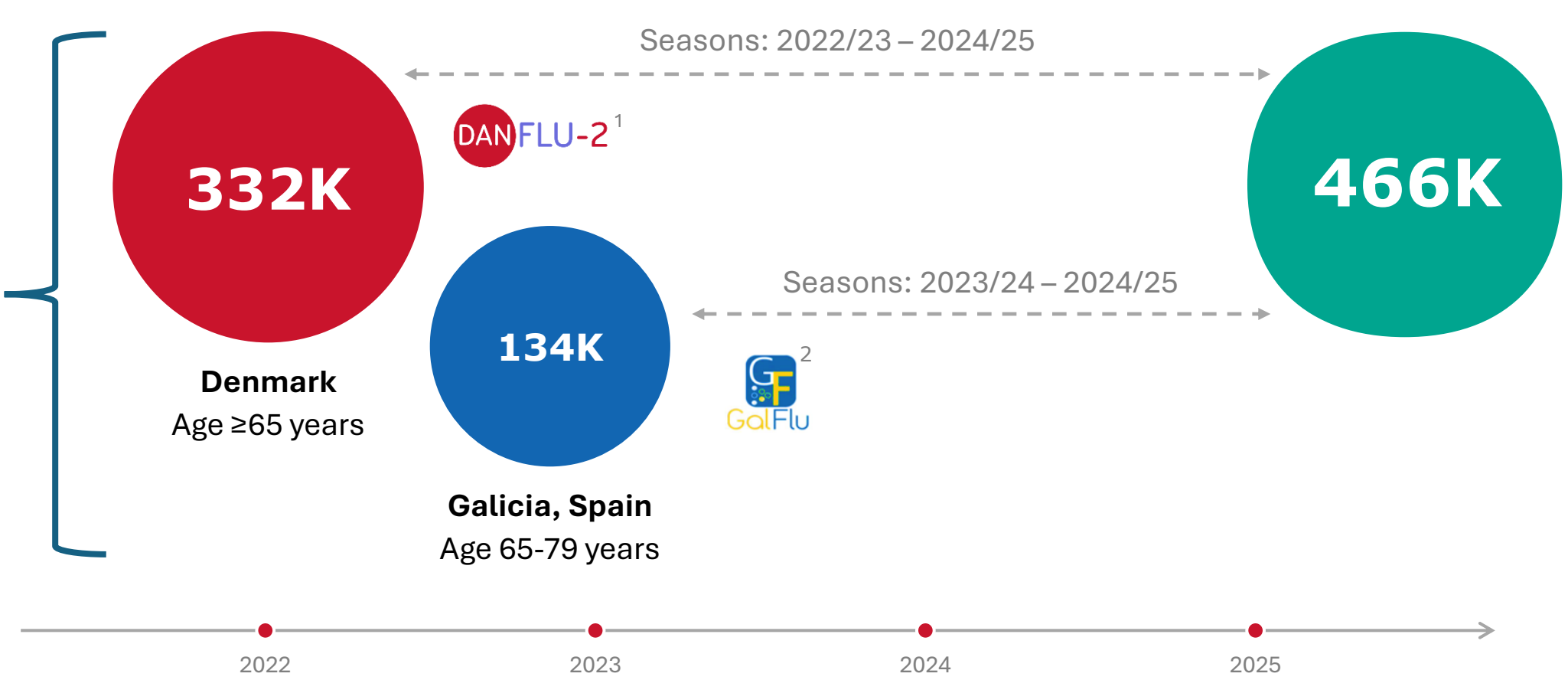
ESC Congress 2026
28 Aug 2026 - 31 Aug 2026
Munich, Germany

Internal

Study population

FLUNITY DAN GAL HD

Pre-specified individual-level analysis
of the harmonized DANFLU-2 and GALFLU trials



[1] Johansen ND et al. N Engl J Med 2025

[2] Pardo-Seco J et al. N Engl J Med 2025

Articles

Effectiveness of high-dose influenza vaccine against hospitalisations in older adults (FLUNITY-HD): an individual-level pooled analysis

Niklas Dyrby Johansen, Daniel Modin, Jacobo Pardo-Seco, Carmen Rodriguez-Tenreiro-Sánchez, Matthew M Loiacono, Rebe
Marine Dufournet, Robertus van Aalst, Ayman Chit, Carsten Schade Larsen, Lykke Larsen, Lothar Wiese, Michael Dalager-P
Brian L Claggett, Kira Hyldekær Janstrup, Carmen Duran-Parrondo, Marta Piñeiro-Sotelo, Martín Cribeiro-González, Mónic
Susana Mirás-Carballal, Juan-Manuel González-Pérez, Scott D Solomon, Pradeesh Sivapalan, Cyril Jean-Marie Martel, Jens
Federico Martinón-Torres, Tor Biering-Sørensen, for the DANFLU-2 Study Group* and the GALFLU Trial Team*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

High-Dose Influenza Vaccine to Reduce Hospitalizations

J. Pardo-Seco,[1-5] C. Rodríguez-Tenreiro-Sánchez,[1-3,6,7] I. Giné-Vázquez,[1-3] N. Mallah,[1,2,8,9] S. Mirás-Carballal,[10] M. Piñeiro-Sotelo,[10] M. Cribeiro-González,[11] M. Conde-Pájaro,[10] J.-M. González-Pérez,[12] I. Rivero-Calle,[1-3,6,7] X. Bello,[1-5] J.L. Razzini,[1-3,6,7] A. Dacosta-Urbieta,[1-3,6,7] A. Salas,[1,3-5] R.C. Harris,[13] M.M. Loiacono,[14,15] R. van Aalst,[14] J.M. Farre,[16] M. Dufournet,[17] N.D. Johansen,[18,19] D. Modin,[18,19] T. Biering-Sørensen,[18-21] C. Durán-Parrondo,[10] and F. Martinón-Torres,[1-3,6,7] for the GALFLU Trial Team*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

High-Dose Influenza Vaccine Effectiveness against Hospitalization in Older Adults

N.D. Johansen,[1,2] D. Modin,[1,2] M.M. Loiacono,[3,4] R.C. Harris,[5] M. Dufournet,[6] C.S. Larsen,[7,8] L. Larsen,[9] L. Wiese,[10] M. Dalager-Pedersen,[11,12] B.L. Claggett,[13] K.H. Janstrup,[1,2] K.V. Bartholdy,[1,2] K.F. Bernholm,[1,2] J.I.-M.H. Borchsenius,[1,2] F.S. Davidovski,[1,2] L.W. Davodian,[1,2] M. Dons,[1,2] L.S. Duus,[1,2] C. Espersen,[1,2] F.H. Fussing,[1,2] A.M.R. Jensen,[1,2] N.E. Landler,[1,2] A.C.F. Langhoff,[1,2] M.C.H. Lassen,[1,2] A.B. Nielsen,[1,2] C.I. Ottosen,[1,2] M. Sengeløv,[1,2] K.G. Skaarup,[1,2] S.D. Solomon,[12] M.J. Landray,[14] G.H. Gislason,[1,15,16] L. Køber,[15,17] L. Ralfkiaer,[18] J. Nealon,[19] P. Sivapalan,[15,20] C.J.-M. Martel,[21] J.U.S. Jensen,[15,20] and T. Biering-Sørensen[1,2,17,22]

Fluzone® High-Dose Quadrivalent/Efluelda®/Efluelda Tetra®[Sanofi] containing 60 µg of haemagglutinin antigen per strain; VaxigripTetra [Sanofi] in DANFLU-2;InfluvacTetra [Viatris] in GALFLU containing 15 µg of haemagglutinin per strain

ESC Congress 2026
28 Aug 2026 - 31 Aug 2026
Munich, Germany

Endpoints

PRIMARY ENDPOINT

Hospitalization for influenza or pneumonia

Defined by ICD-10 codes

OTHER MAIN ENDPOINTS

- Cardio-respiratory hospitalization
- Lab-confirmed influenza hospitalization
- All-cause hospitalization
- All-cause mortality
- Exploratory endpoints: CV endpoints

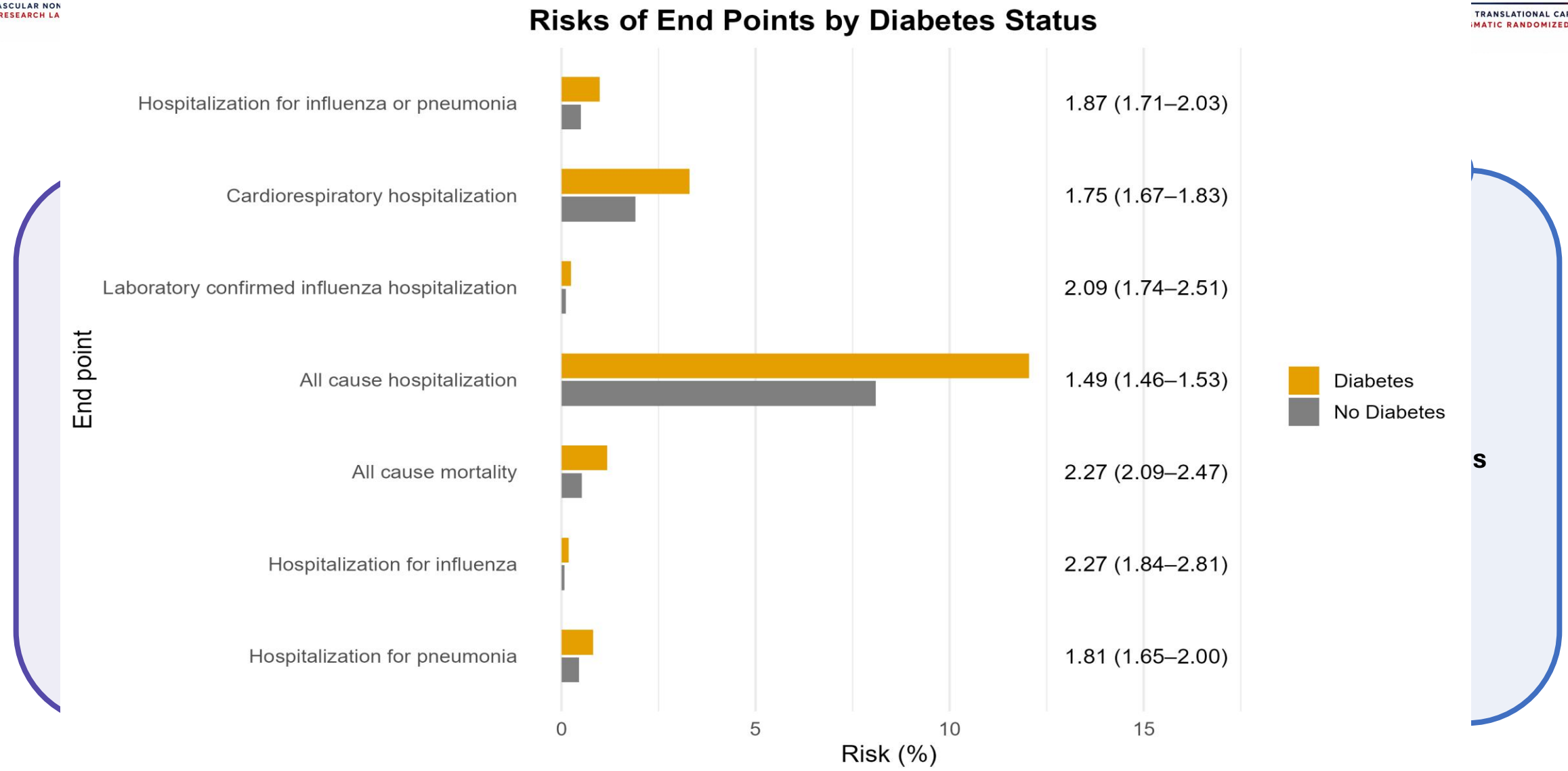


Analysis

Relative vaccine effectiveness (rVE)*, absolute risk reduction (ARR) and Number Needed to Vaccinate (NNV) per endpoint averted

Stratified by diabetes status with test for interaction (p interaction in forest plots)

$$*\text{rVE} = 1 - \frac{Risk\ in\ HD{-}IIV\ group}{Risk\ in\ SD{-}IIV\ group} = \text{relative risk reduction}$$

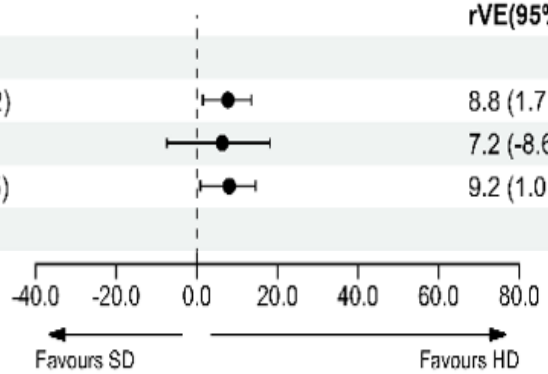


*Diabetes definition : ICD-10 E10–E14 diagnosis, glucose-lowering medication (A10), or HbA1c ≥48 mmol/mol (6.5%) before randomization

ESC Congress 2026
28 Aug 2026 - 31 Aug 2026
Munich, Germany

Primary Endpoint

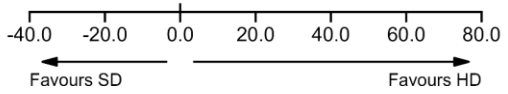
Outcome	HD-IIV	SD-IIV	rVE(95%CI)	NNV	P-interaction
Hospitalization for influenza or pneumonia					
All participants	1312 (0.56)	1437 (0.62)	8.8 (1.7 to 15.5)	1839 (1041-9488)	0.81
Diabetes	307 (0.94)	331 (1.02)	7.2 (-8.6 to 20.8)	1114 (633-5767)	
No diabetes	1005 (0.50)	1106 (0.55)	9.2 (1.0 to 16.7)	2066 (1173-10695)	



Fluzone® High-Dose Quadrivalent/Efluelda®/Efluelda Tetra®[Sanofi] containing 60 µg of haemagglutinin antigen per strain; VaxigripTetra [Sanofi] in DANFLU-2;InfluvacTetra [Viatris] in GALFLU containing 15 µg of haemagglutinin per strain

Cardiovascular Endpoints (Exploratory)

Outcome	HD-IIV	SD-IIV	rVE(95%CI)	NNV	P-interaction
Hospitalization for any cardiovascular disease					
All participants	2692 (1.15)	2880 (1.24)	6.6 (1.6 to 11.5)	1217 (706 to 5126)	0.33
Diabetes	566 (1.74)	637 (1.96)	11.1 (0.3 to 20.7)	773 (444 to 3189)	
No diabetes	2126 (1.06)	2243 (1.12)	5.3 (-0.4 to 10.8)	1353 (776 to 5580)	
Hospitalization for heart failure					
All participants	267 (0.11)	339 (0.15)	21.3 (7.4 to 33.2)	3221 (2067 to 9308)	0.72
Diabetes	90 (0.28)	119 (0.37)	24.3 (-0.3 to 43.1)	1269 (814 to 3652)	
No diabetes	177 (0.09)	220 (0.11)	19.6 (1.6 to 34.4)	4268 (2738 to 12285)	
Hospitalization for myocardial infarction					
All participants	369 (0.16)	346 (0.15)	-6.5 (-23.7 to 8.3)		0.75
Diabetes	78 (0.24)	70 (0.22)	-11.4 (-56.1 to 20.3)		
No diabetes	291 (0.14)	276 (0.14)	-5.2 (-24.5 to 11.0)		
Hospitalization for atrial fibrillation					
All participants	812 (0.35)	856 (0.37)	5.3 (-4.4 to 14.0)		0.05
Diabetes	112 (0.34)	148 (0.46)	24.3 (2.6 to 41.3)		
No diabetes	700 (0.35)	708 (0.35)	1.2 (-9.7 to 11.2)		
Hospitalization for stroke					
All participants	545 (0.23)	574 (0.25)	5.2 (-6.8 to 15.8)		0.29
Diabetes	110 (0.34)	102 (0.31)	-7.8 (-42.6 to 18.3)		
No diabetes	435 (0.22)	472 (0.24)	8.0 (-4.8 to 19.3)		
MACE					
All participants	1227 (0.53)	1240 (0.53)	1.2 (-7.0 to 8.8)		0.14
Diabetes	284 (0.87)	257 (0.79)	-10.5 (-31.3 to 6.9)		
No diabetes	943 (0.47)	983 (0.49)	4.2 (-4.8 to 12.4)		
Cardiovascular death					
All participants	360 (0.15)	352 (0.15)	-2.1 (-18.6 to 12.1)		0.08
Diabetes	114 (0.35)	91 (0.28)	-25.2 (-66.8 to 5.7)		
No diabetes	246 (0.12)	261 (0.13)	5.8 (-12.4 to 21.2)		



Strengths and limitations

STRENGTHS

- Pre-specified analysis of two large, methodologically harmonized, individually randomized trials
- Broad, real-world population
- Near-complete follow-up
- **> 60K diabetes participants**

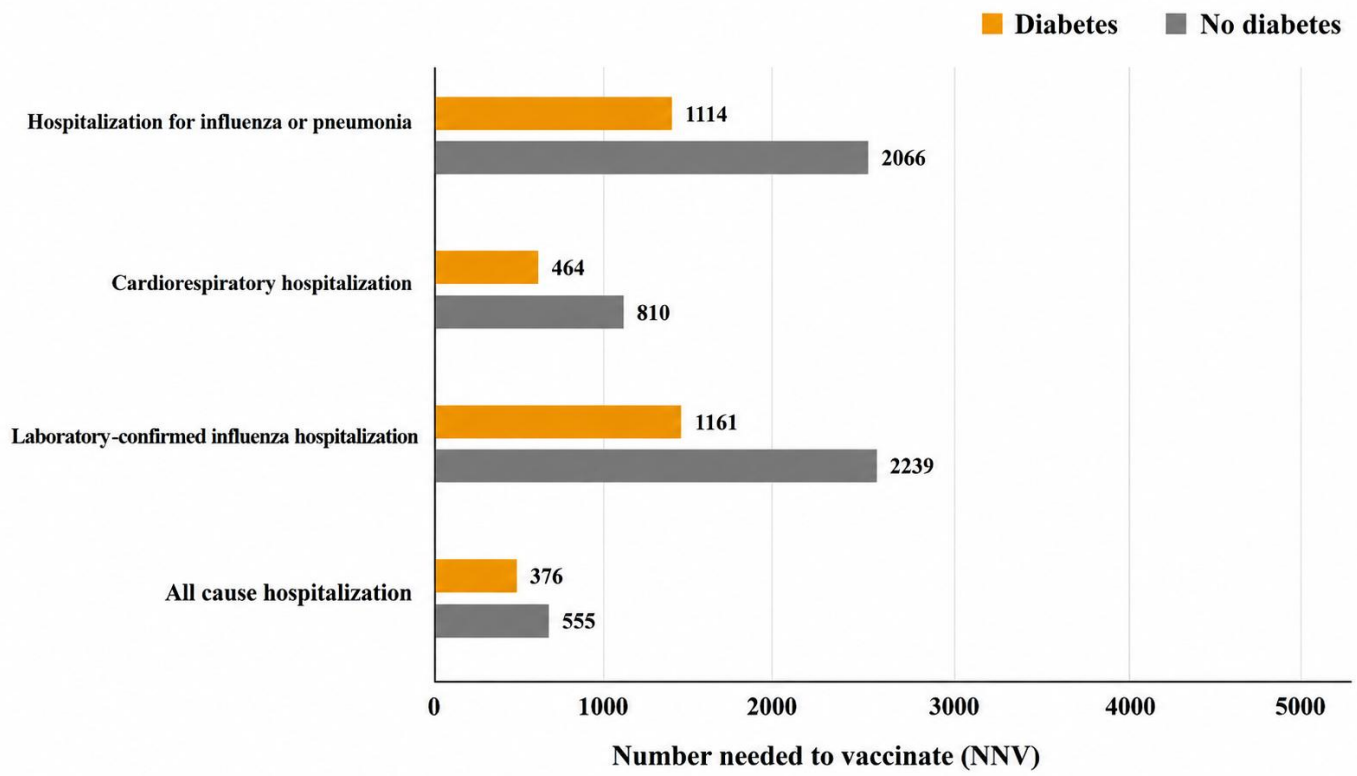
LIMITATIONS

- Open-label design
- Registry-based data
- Secondary analysis

Conclusions

- HD-IIV compared to SD-IIV provided a modest but ***superior protection against hospitalization for influenza or pneumonia*** and ***significant reduction*** in many severe hospitalization causes, **regardless of diabetes status.**

Diabetic participants had markedly ***higher absolute risk***, with **potentially greater absolute benefit** and **lower NNV**



Thank you to the

Audience, Chairpersons and Jury members

now I'm happy to take your questions ☺