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# Flu in Elderly….

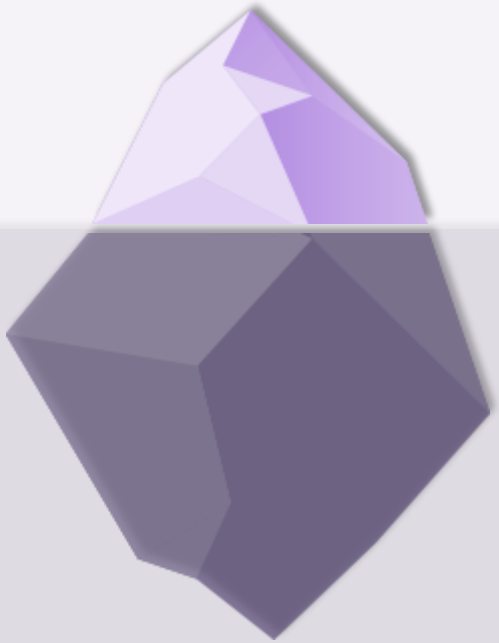
# Why it needs special consideration?!

MAT-AE-2400245 – April 2024 V1.0

# The true impact of influenza is under-recognized[1–3]

**Perceived impact**
Influenza is a simple respiratory infection that can resolve within a week

**Fever, headache, muscle pain, cough…**



**Actual impact**
True medical, economical and societal burden of influenza & complications

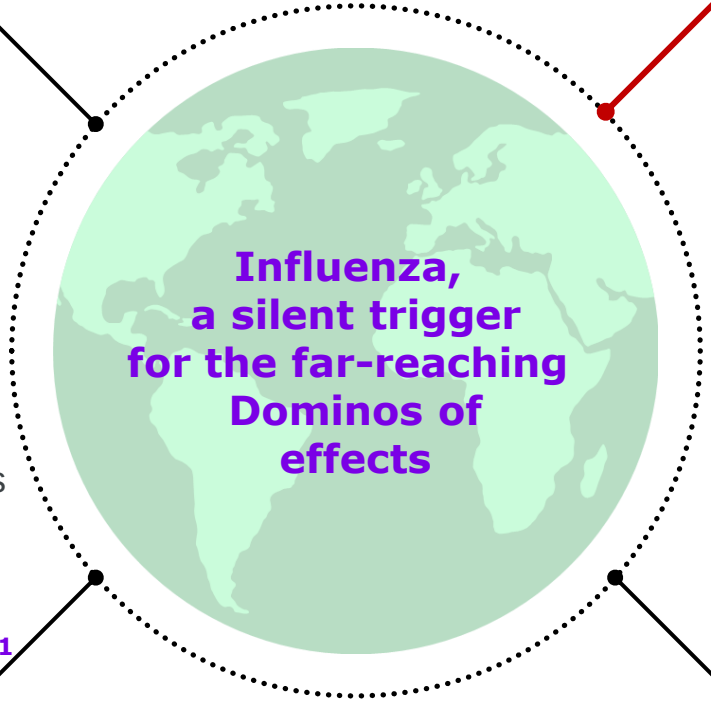
**Heart attack**
**Stroke**
**Pneumonia**
**Exacerbation of underlying chronic illnesses,**
**Diabetes,**
**Asthma,**
**COPD…**
**Death**

CDC: Centers for Disease Prevention and Control; COPD: chronic obstructive pulmonary disease; ECDC: European Centre for Disease Prevention and Control (ECDC).
**References:** 1. CDC. Frequently Asked Questions about Estimated Flu Burden. Available at: https://www.cdc.gov/flu/about/burden/faq.htm; 2. ECDC. Factsheet about seasonal influenza. Available at: https://www.ecdc.europa.eu/en/seasonal-influenza/facts/factsheet; 3. Macias AE, et al. *Vaccine*. 2021;39(Suppl 1):A6-A14. DOI: 10.1016/j.vaccine.2020.09.048

# Every year influenza is responsible for hundreds of thousands of deaths worldwide[1]

It has been estimated that influenza causes **290,000** to **650,000 respiratory deaths** annually worldwide[1]

Most deaths associated with influenza occur among older people **65+,** in industrialized countries[1,2]



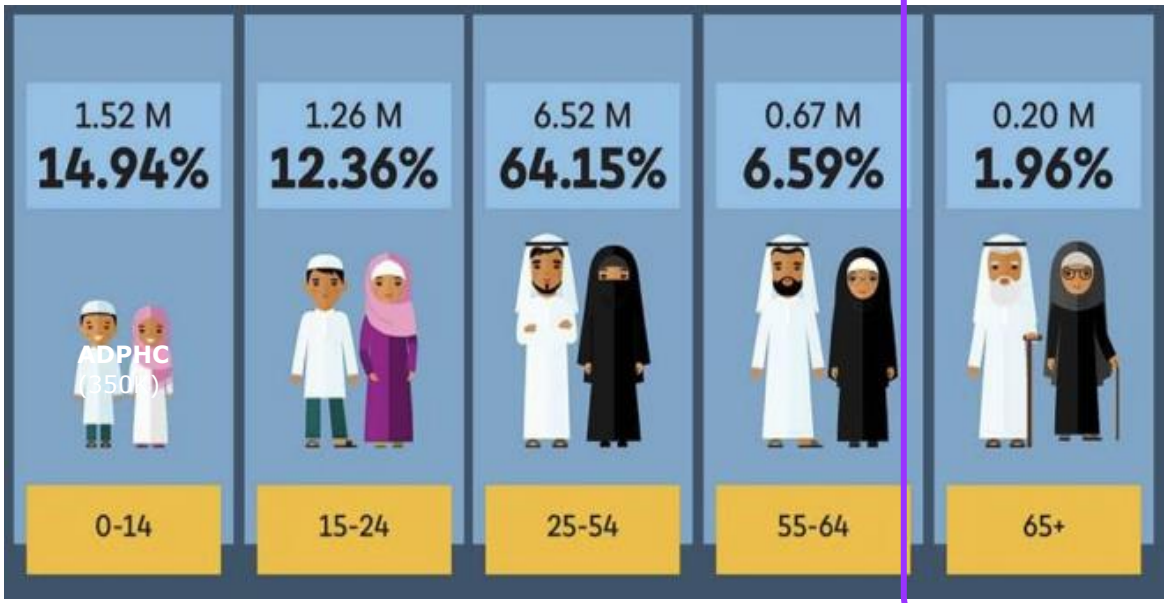

Annual global attack rate estimated at 5–10% in adults and 20–30% in children[4]
Worldwide influenza results in **3** to **5 million cases of severe illness**[1]

Approximately **4 people** die from influenza **every 5 minutes** around the world[3]

1. WHO: Seasonal Influenza Factsheet, 2023;
2. Thompson WW et al. 2009, doi:10.1111/j.1750-2659.2009.00073.x
3. Calculation from WHO: Seasonal Influenza Factsheet, 2018
4. WHO: Influenza (who.int)

# UAE populations 2023: 10,234,707

Tuesday, May 23, 2023

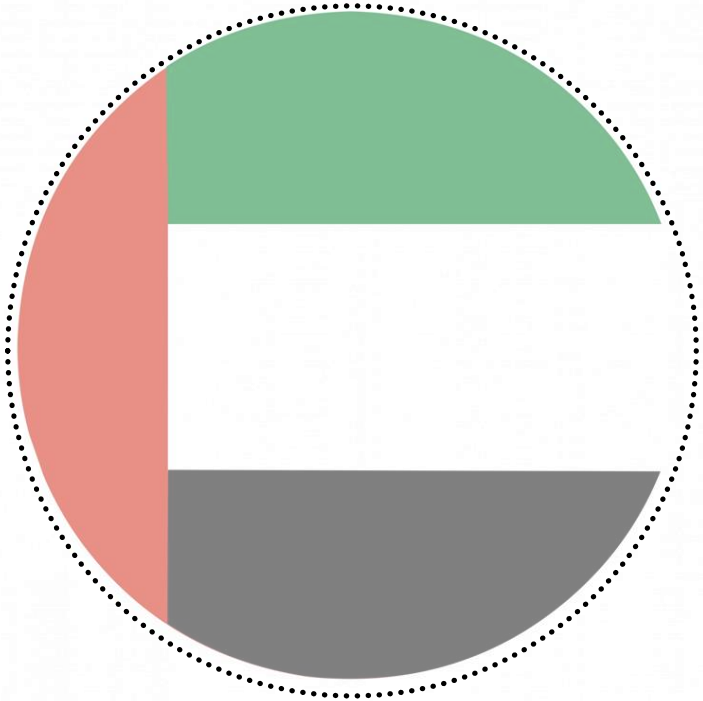



**Generally, Nationals represent: 12%**

**Adult older:200,000 subjects**

https://www.worldometers.info/world-population/united-arab-emirates-population/#:~:text=The%20current%20population%20of%20the,the%20latest%20United%20Nations%20data.

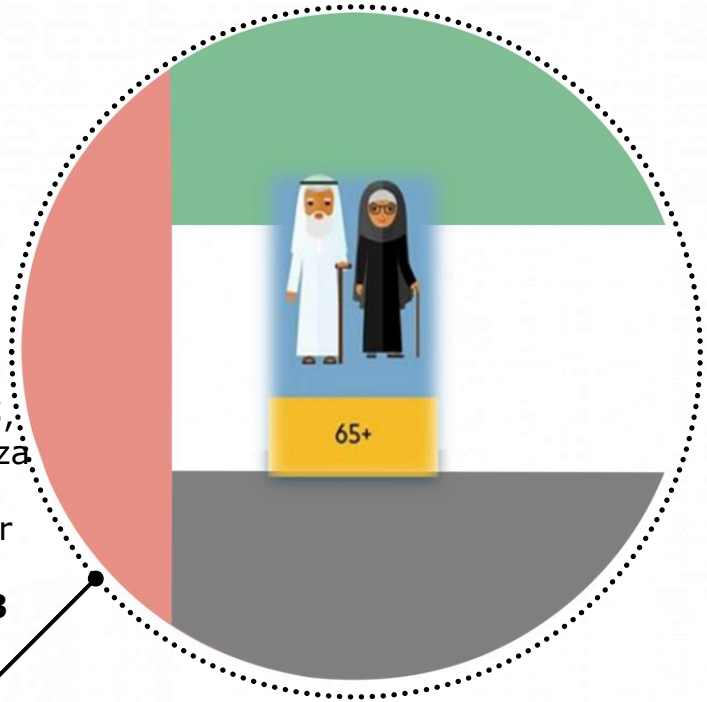
# Every year influenza is responsible for hundreds of thousands of deaths worldwide[1]





1. International Cardiovascular Forum Journal 11 (2017) DOI: 10.17987/icfj.v11i0.414
2. https://usuaebusiness.org/wp-content/uploads/2019/01/2021-U.A.E.-Healthcare-Report.pdf
3. https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death
4. Influenza Other Respi Viruses. 2018;12:146–152

# Every year influenza is responsible for hundreds of thousands of deaths worldwide[1]




The population aged over 65, a high-risk group for influenza and its complications, is projected to increase by over **262%** in the next two decades from **200K in 2023** to **643K in 2040**

1. International Cardiovascular Forum Journal 11 (2017) DOI: 10.17987/icfj.v11i0.414
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3. https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death
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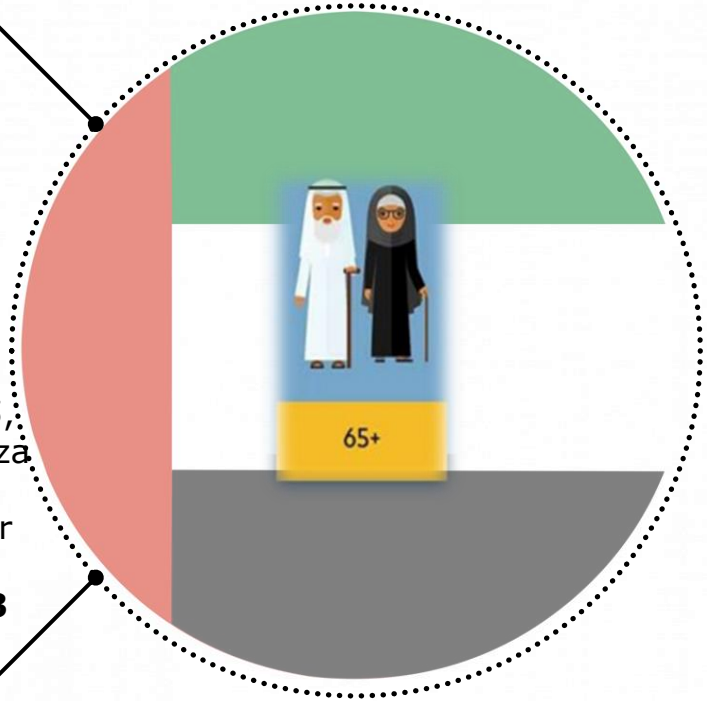
## Population structure and projections

| | | | | |
|---|---|---|---|---|
| Population over 65 years[1] | 177,543 (2023) | 643,142 (2040) | 262% growth | 2023 2040 |
| Total population[1] | 9,516,871 (2022) | 10,663,646 (2040) | 12% growth | 2022 2040 |

Economist Impact 2022

# Every year influenza is responsible for hundreds of thousands of deaths worldwide[1]

The CV risk factors are **highly dominated** in them vs. younger population[1]

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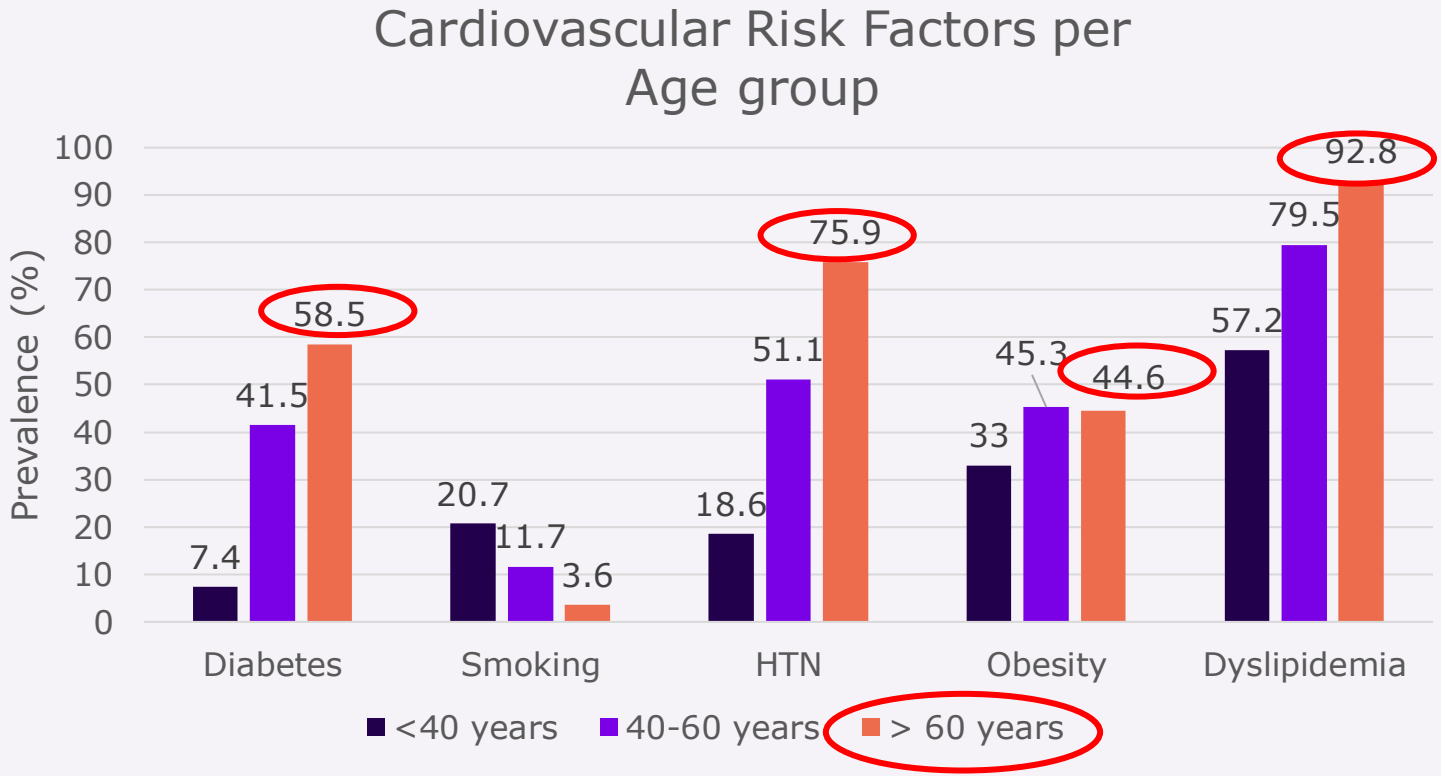
# ……. UAE Cardiovascular risk factors **predominant** among **older population**

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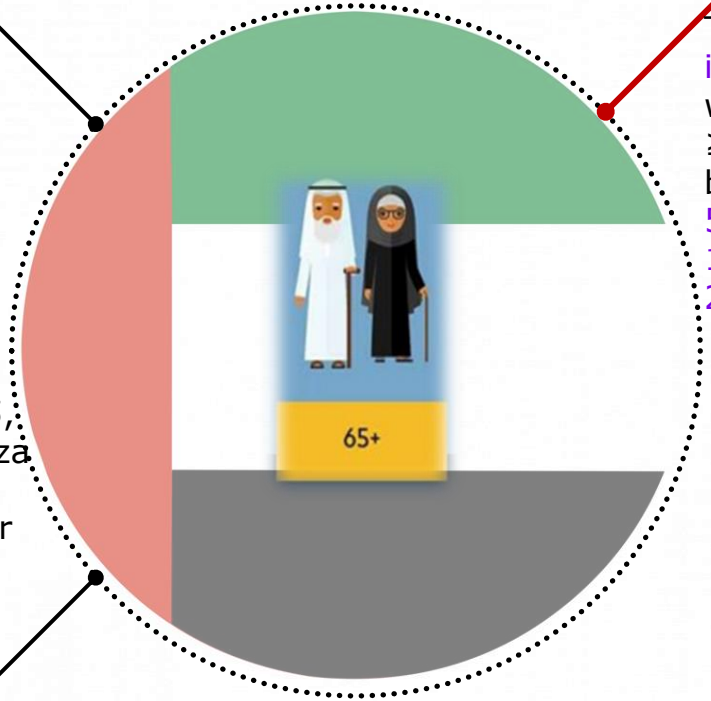
Cardiovascular Risk Factor Burden in the United Arab Emirates (UAE): The Africa Middle East (AfME) Cardiovascular Epidemiological (ACE) Study Sub-Analysis- International Cardiovascular Forum Journal 11 (2017) DOI: 10.17987/icfj.v11i0.414

# Every year influenza is responsible for hundreds of thousands of deaths worldwide[1]

The CV risk factors are **highly dominated** in them vs. younger population[1]

The population aged over 65, a high-risk group for influenza and its complications, is projected to increase by over **262%** in the next two decades and from **200K in 2023** to **643K in 2040**




The **highest** incidence of influenza-associated death was among those aged ≥65 years and ranged between 39.5 (95% CI: 27.3-51.8) per 100 000 in 2014 and 11.3 (95% CI: 7.5-15.1) in 2015.[4]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# Estimated National influenza- associated hospitalizations and deaths in Oman 2012- 2015

| Year | Age group (y) | Population size[a] | Severe acute respiratory infection | | Annual percentage of influenza positivity[d] | Estimated influenza-associated (per 100 000) | |
|---|---|---|---|---|---|---|---|
| | | | Hospitalizations[b] | Mortality[c] | | Hospitalizations[e] rate (95% CI) | Deaths[f] rate (95% CI) |
| 2012-2015 | <1 | 275 801 (1.7%) | 5374 (27.7%) | 48 (5.7%) | 5.9% | 121.3 (108.4-134.3) | 1.1 (−0.1-2.4) |
| | 1-<5 | 1 133 671 (7.2%) | 5834 (30.0%) | 20 (2.7%) | 13.2% | 71.7 (66.8-76.6) | 0.3 (0.0-0.6) |
| | 5-<15 | 2 038 237 (12.8%) | 1837 (9.5%) | 15 (1.7%) | 29.9% | 6.2 (5.3-7.2) | 0.4 (0.2-0.7) |
| | 15-<50 | 10 648 058 (67.4%) | 2232 (11.5%) | 96 (11.3%) | 25.7% | 5.3 (4.9-5.8) | 0.2 (0.1-0.3) |
| | 50-<65 | 1 130 319 (7.1%) | 1392 (7.2%) | 110 (13.0%) | 26% | 32.1 (28.8-35.4) | 2.2 (1.4-3.1) |
| | ≥65 | 591 638 (3.7%) | 2736 (14.1%) | 558 (65.8%) | 20.4% | 92.3 (84.6-100.1) | 18.6 (15.1-22.1) |
| | Total | 15 817 724 (100%) | 19 405 (100%) | 847 (100%) | 2862/17 141 (16.7%) | 20.6 (19.9-21.3) | 0.9 (0.7-1.0) |

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Influenza Other Respi Viruses. 2018;12:146–152

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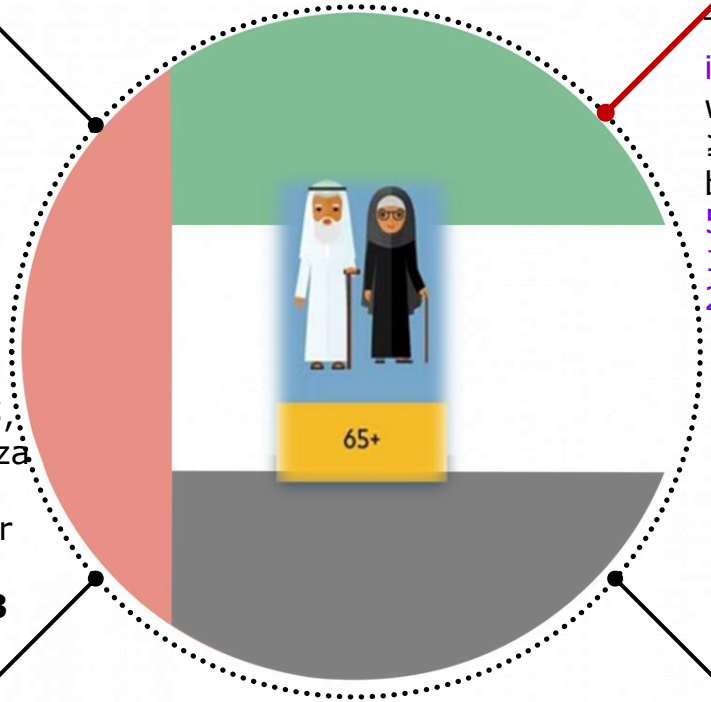


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In UAE, lower respiratory infections have been ranked among the top 10 leading causes of **premature deaths** in 2019 inUAE among 65+ years old [3]


1. International Cardiovascular Forum Journal 11 (2017) DOI: 10.17987/icfj.v11i0.414
2. Unmasking the risk and burden of seasonal influenza in the Middle East: Strengthening prevention and control strategies for a healthier tomorrow - Economist Impact. October 2023
3. https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death
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World Health Organization | Health Topics | Countries | Newsroom | Emergencies | Data | About WHO

# Top 10 causes of death in United Arab Emirates for both sexes aged 65 to 69 years (2019)

Hide filters | Top-10 deaths | Top-10 DALYs | Underlying data | Download with OData API

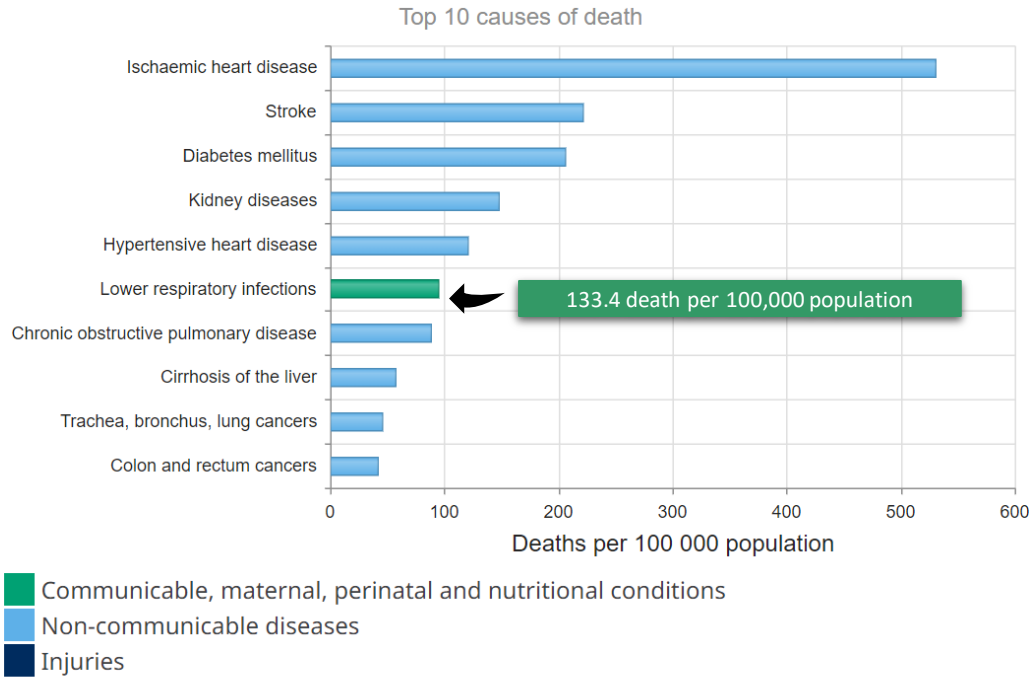
## Filters

**Country**
United Arab Emirates

**Year**
2019

**Sex**
Both sexes

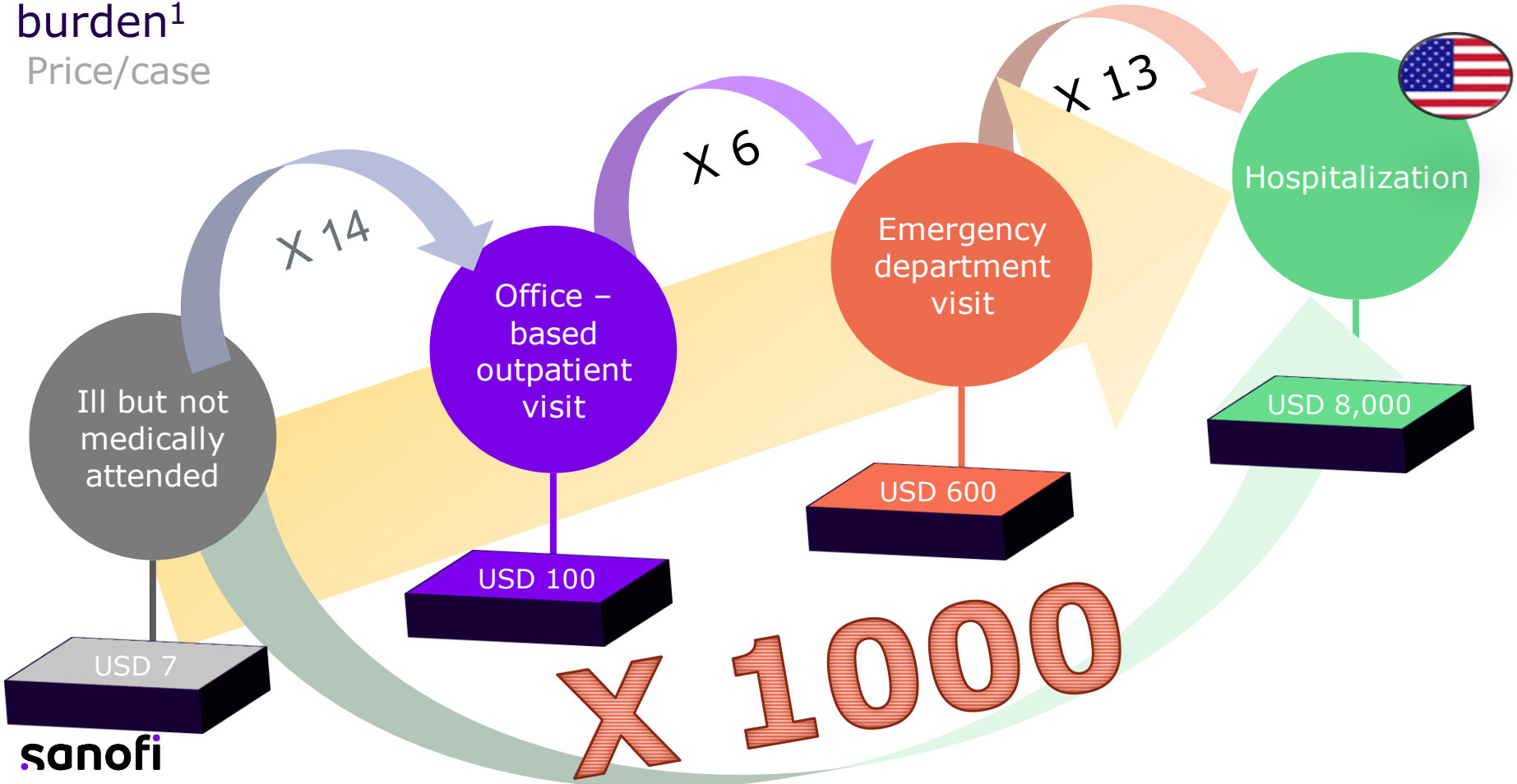
**Age group**
65 to 69 years




https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death

- **Influenza Economic Burden**

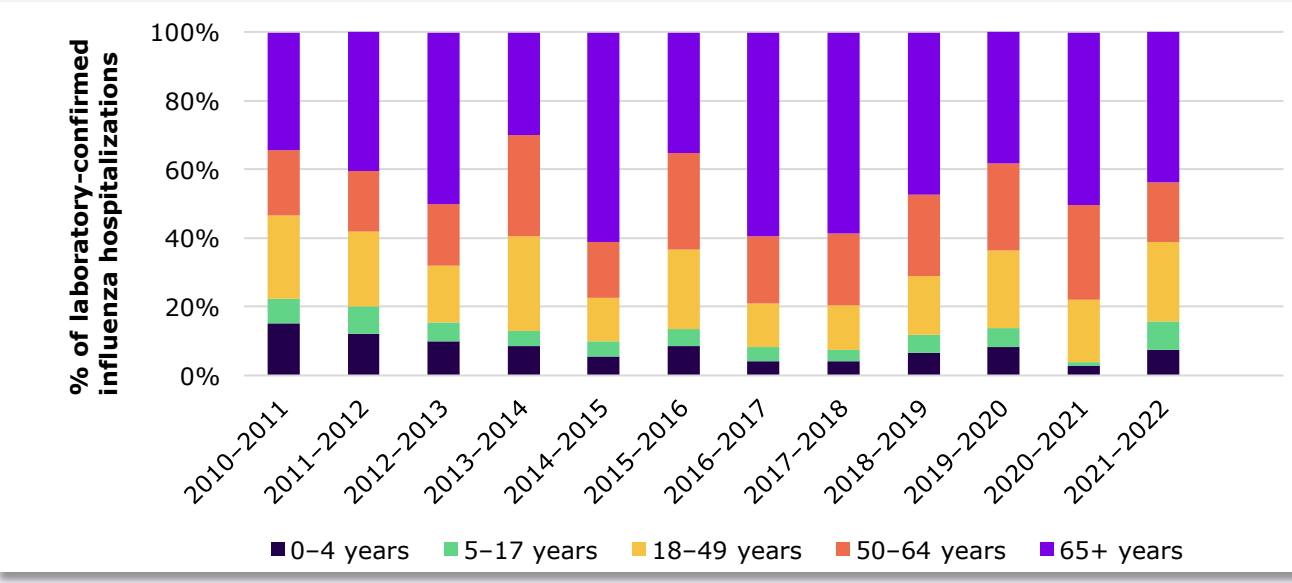
# In the USA, hospitalizations substantially contribute to influenza burden[1]




Putri *et al*. (2018). doi: 10.1016/j.vaccine.2018.05.057

# The burden of influenza in older adults – *United States Example*

Laboratory-confirmed influenza hospitalizations (2010 to 2022) by age group




Adults aged 65 years and older account for the *majority* of hospitalizations

Older adults need tailored influenza vaccines for better protection than standard dose inactivated vaccines

**References**: FluView - Weekly Surveillance Reports by season and by age. Available at: https://gis.cdc.gov/grasp/fluview/FluHospChars.html (Accessed April 2023).

Clinician Outreach and Communication Activity (COCA) Call Thursday, September 8, 2022

# 2022-2023 Influenza Vaccination Recommendations

**Centers for Disease Control and Prevention Center for Preparedness and Response**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# Influenza Vaccine Effectiveness Among Older Adults

| Season | Overall VE, % (all ages, viruses, and vaccine types) |
|---|---|
| 2022-23 | 54 (23,72) |
| 2021–22 | 36 (21, 48) |
| 2019–20 | 39 (32, 44) |
| 2018–19 | 29 (21, 35) |
| 2017–18 | 38 (31, 43) |
| 2016–17 | 40 (32, 46) |
| 2015–16 | 48 (41, 55) |
| 2014–15 | 19 (10, 27) |
| 2013–14 | 52 (44, 59) |
| 2012–13 | 49 (43, 55) |
| 2011–12 | 47 (36, 56) |

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Past Seasons' Vaccine Effectiveness Estimates
^Preliminary Flu Vaccine Effectiveness (VE) Data for 2022-2023 | CDC

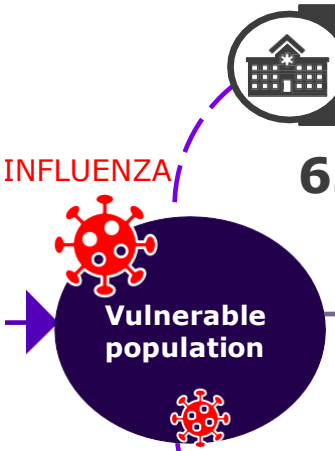
* Age ≥50 yrs

PowerPoint Presentation (cdc.gov);
https://emergency.cdc.gov/coca/ppt/2023/091923_slides.pdf

# Older adults are most at risk of influenza infection and serious outcomes

Influenza infection can contribute to functional decline, or a senior's inability to recover back to full prior functional capacity once the infection has passed

**Ageing**




**Increased Hospitalization**

**63%** of influenza related hospitalization[17]

**Increased Mortality**

**9/10** influenza-related deaths[18]

**Reduced Autonomy**

**1 in 3** hospitalized patients aged 70+ do not fully recover within a year[19]

**10%** experience loss of independence in more than 3 activities of daily living[15,16]

Source: Gozalo et al. [15], Andrew et al. [16], Thompson et al. [17], CDC [18], Boyd et al. [19], Global Medical Affairs – Fluzone HD Rationale
Note: *) Occurring in older adults 65+ in the USA, **) Defined as the loss of >3 basic functions, statistic true after influenza-linked hospitalisations

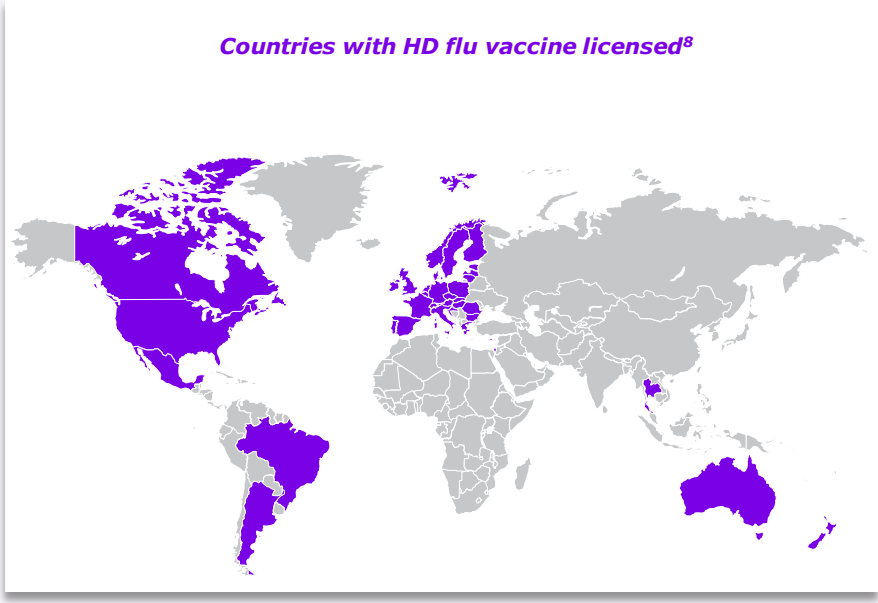
# High dose (HD) influenza vaccine has been developed to answer this medical need

**HD vaccine is a split inactivated influenza vaccine containing 60 µg of hemagglutinin (HA) per strain[1,2]**

- It contains 4× the amount of HA compared with standard-dose influenza vaccines
- It was first developed in a trivalent formulation (US license in 2009)
- It was then developed into a quadrivalent formulation (US license in 2019: Fluzone HD quadrivalent® and EU license in 2020: Efluelda®[3–5])

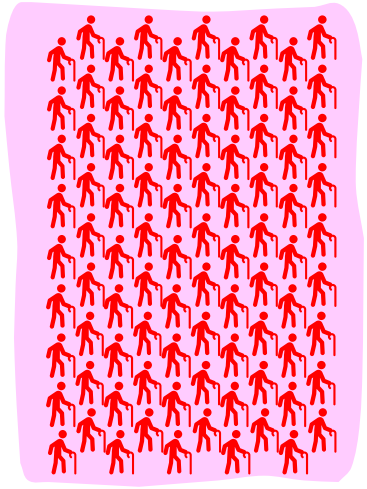
**HD vaccine is indicated for the prevention of influenza in people 60[7] or 65[2] years of age and older depending on the country**

**281 M doses of HD vaccine (including 142 M doses of QIV-HD) have been distributed, as of October 2023[6]**




EU: European Union; HA: hemagglutinin; HD: high-dose; M: million; QIV-HD: high-dose quadrivalent influenza vaccine; TIV-HD: high-dose trivalent influenza vaccine; US: United States.
References in slide notes.

# How 24.2% rVE Translates into Absolute Efficacy?



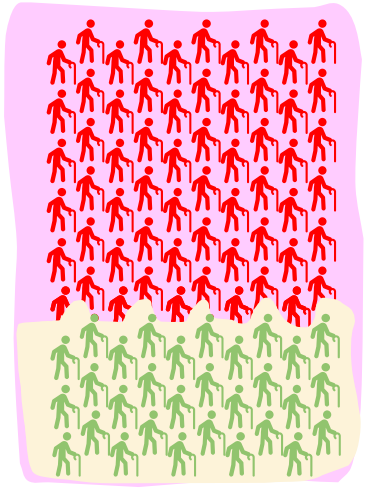
**100 influenza cases in adults 65 years of age if no one is vaccinated**

**Vaccinate with Vaccine A**
Hypothetical 30% Vaccine Efficacy

**100x30%=30**

30 out of 100 cases prevented by SD IIV

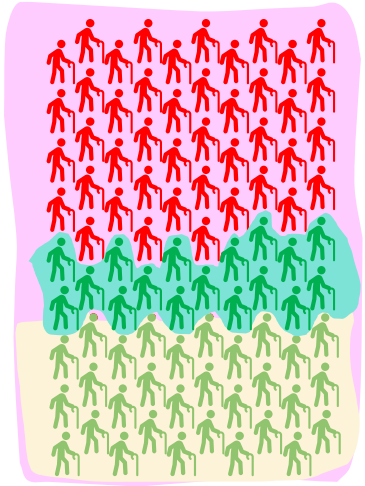
**Figure 1**
**70 out of 100 cases would still develop influenza despite standard-dose (SD) influenza vaccination**



**Vaccinate with Vaccine B**

24.2% rVE

Assuming 30% absolute efficacy for A in older adults (Figure 1), and using 24.4% relative efficacy B vs A (Figure 2), the absolute efficacy of B would be estimated at 47% (Figure 3)



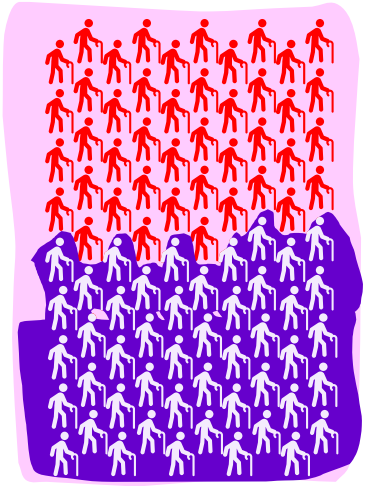
**70x24.2%≈17**

**17 cases out of 70 would be prevented**

**Figure 2**
**If everyone was vaccinated with B instead of A,**

**Total Number Protected if vaccine B used**

**Figure 3**



47 cases out of 100 Averted

47% Absolute Efficacy

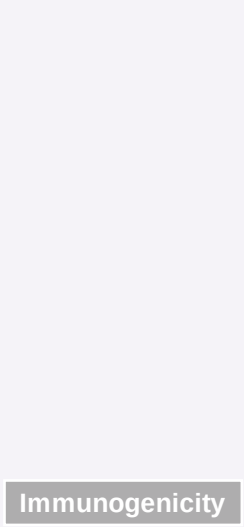
# Robustness of evidence

*Of a better flu vaccine for a better protection*

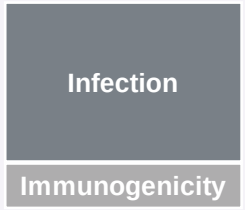
**….. Setting New Standard for Protection!**

# Immunogenicity trials alone are simply not enough

**Influenza vaccines must demonstrate protection beyond flu**




Current minimum for licensure[1,2]




Comparison between flu vaccines


**The new standard:**
***Protection Beyond Flu***

***Protection Beyond Flu***

- **High-quality study design**, including RCTs
- Multiple seasons of **consistent results vs. standard of care***
- **Cardiovascular & pneumonia** hospitalization endpoints, in addition to infection data

**standard of care is SD***



1. EMA Guideline on Influenza Vaccines. 16 July 2016.
2. FDA Guidance for Industry (Influenza Vaccines). May 2007

# HD vaccine's data generation plan has been built to ensure HD vaccine demonstrates *Protection Beyond Flu*

## *Protection Beyond Flu*

Our commitment to ensure people have access to influenza vaccines with proven better protection against flu infection and its severe complications

### CLINICAL OUTCOMES

**Infection data**
on lab-confirmed flu cases

**Hospitalization data**
to show impact on severe complications

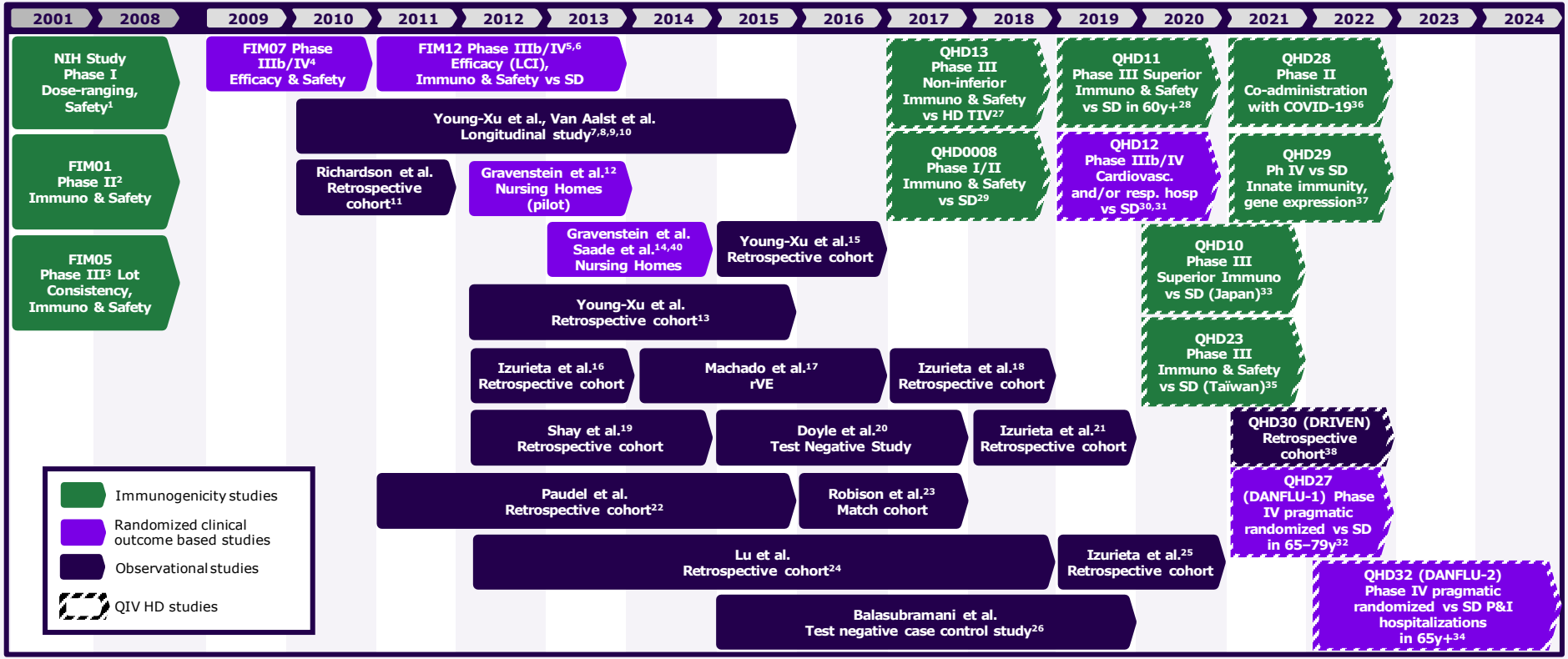
### ROBUST METHODOLOGY

**Randomized studies**
in clinical and real-world settings

**Standard dose**
as minimum comparator

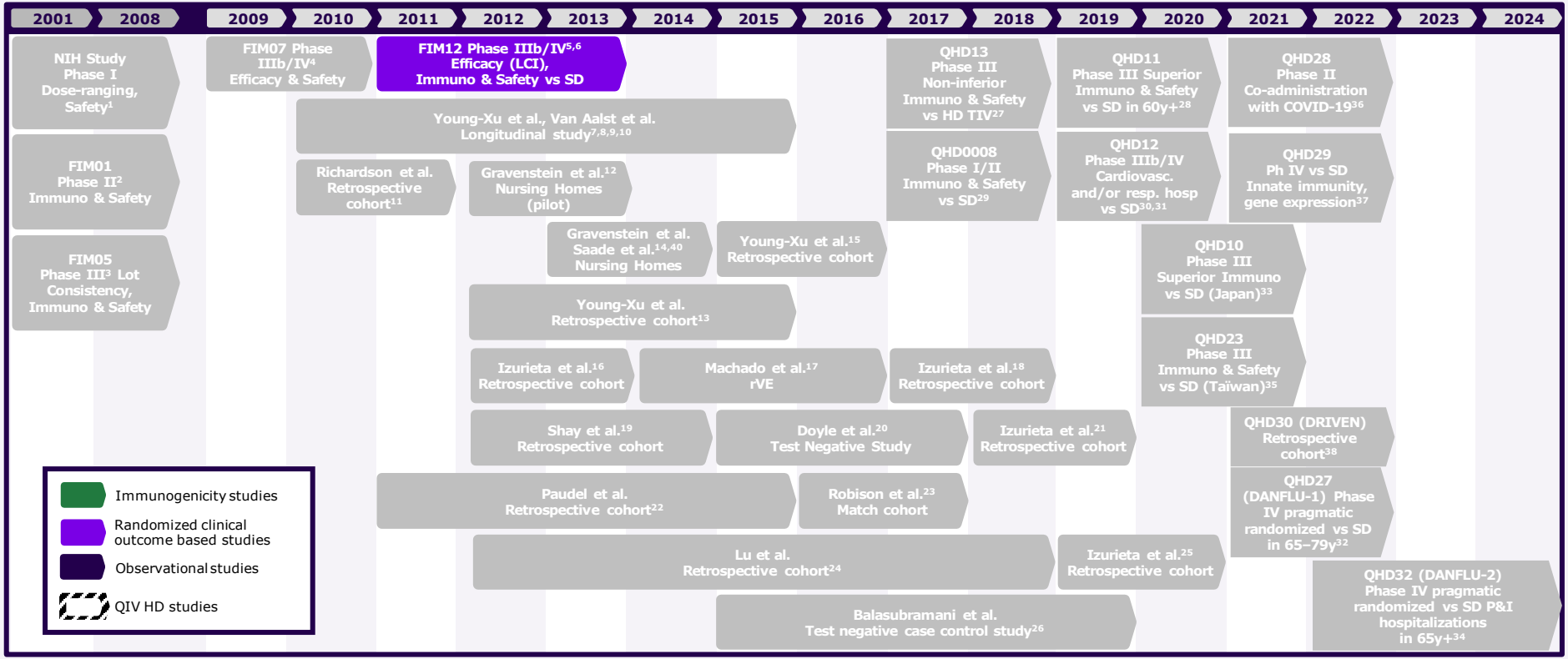
**Consistent results**
across multiple seasons and study designs

# Two Decades of Clinical Development and Post-licensure Evidence Generation*




*As of April 2023.
References in slide notes. The duration of the studies corresponds to the influenza season in which the study was conducted.

# Focus on RCT of High-dose vaccine Superiority vs. Standard-dose vaccine against laboratory-confirmed influenza




References in slide notes.

# *Trivalent HD vaccine* is the only influenza vaccine with *a proven superior efficacy* versus standard dose influenza vaccine in a randomized clinical trial in adults aged 65 years and older

**31,989**
***Adults ≥65 years old***

**Randomized 1:1**

**126**
***sites***

**2**
***Influenza seasons***
2011–12
2012–13

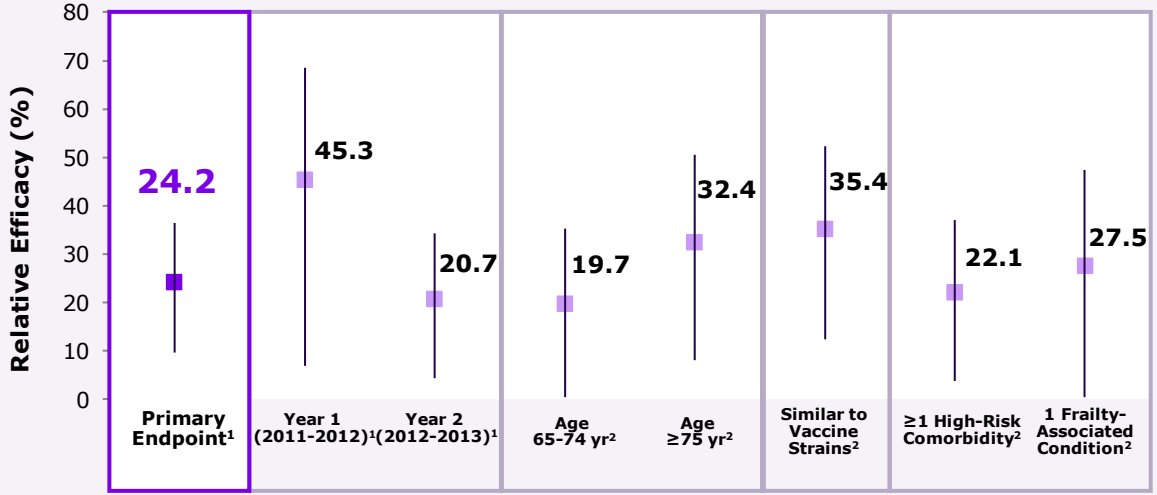
**High-dose trivalent influenza vaccine (TIV-HD)**

**or**

**Standard-dose trivalent influenza vaccine (TIV-SD)**

**Primary endpoint**

Laboratory-confirmed influenza associated with protocol defined influenza-like illness




**Compared with SD influenza vaccine, the benefit of HD vaccine was demonstrated across age groups, comorbidities/frailty conditions in community-dwelling seniors over 2 influenza seasons**

HD: high-dose; SD: standard-dose; TIV-HD: high-dose trivalent influenza vaccine; TIV-SD: standard-dose trivalent influenza vaccine.

**References**: 1. DiazGranados CA et al. *N Engl J Med* 2014;371:635-45. doi: 10.1056/nejmoa1315727. 2. DiazGranados CA et al. 2015 *Vaccine*;33:4565-71. doi: 10.1016/j.vaccine.2015.07.003.

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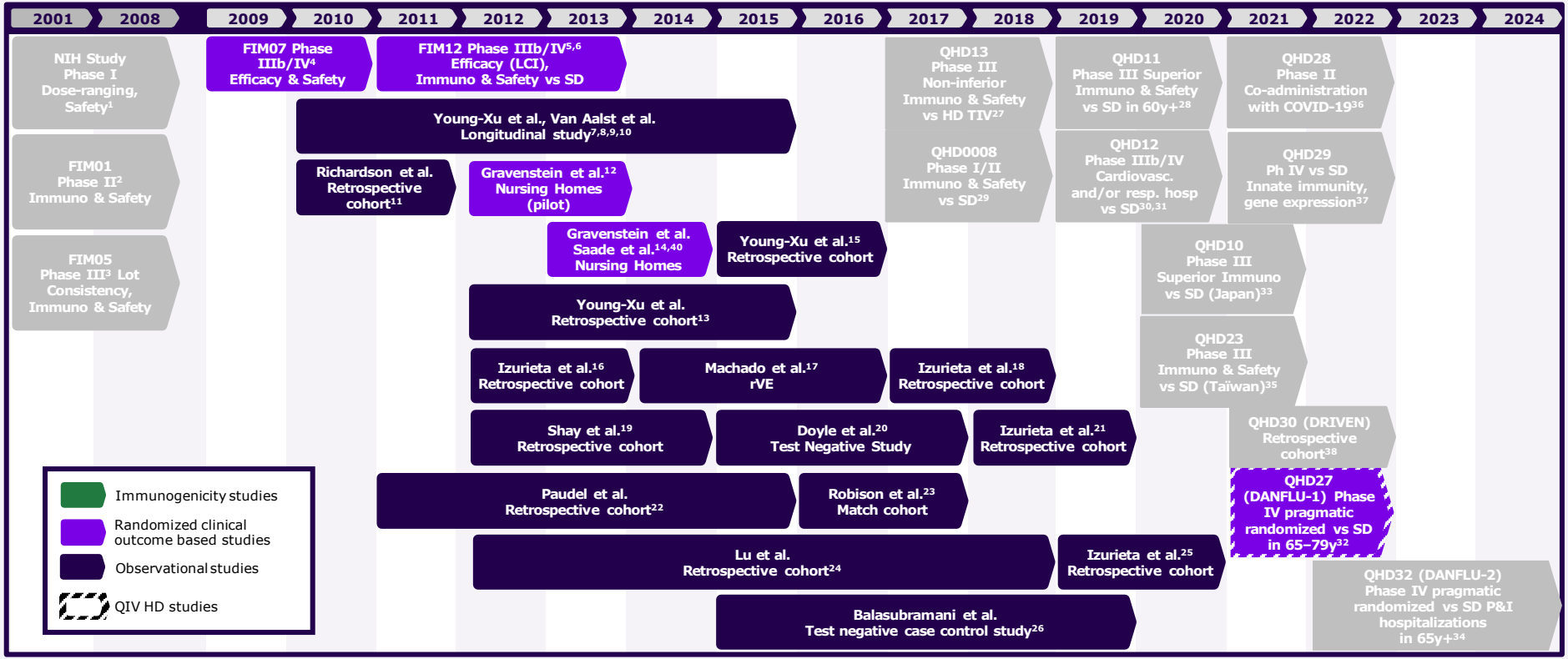
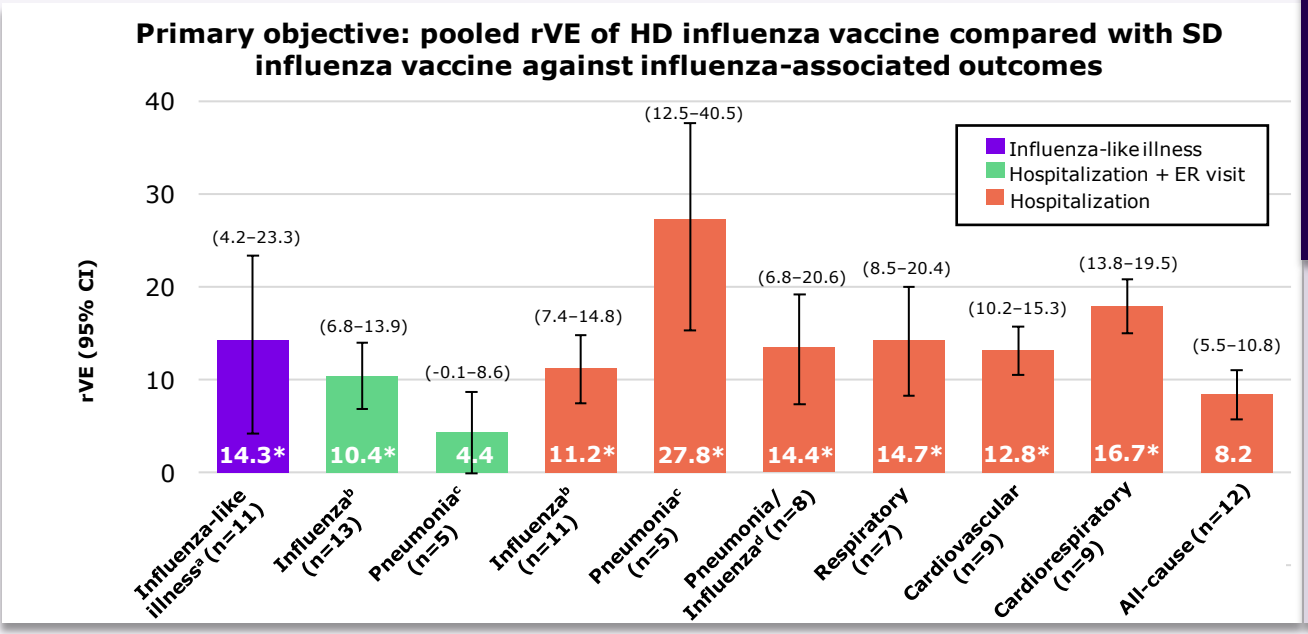
# Focus on 12-year HD efficacy/effectiveness meta-analysis[39]




References in slide notes.

# HD vaccine is consistently more effective than SD influenza vaccines at reducing the clinical outcomes associated with influenza infection in older adults




- **Literature search up to April 2023**
- **21 publications meta-analyzed**
  - 6 randomized studies
  - 15 observational studies
- **12 seasons, >45M people**

HD vaccine is **consistently** more effective than SD influenza vaccines at reducing the clinical outcomes associated with influenza infection in older adults **irrespective of outcome, season, circulating strain, antigenic match, study type, study setting and age subgroup.**

*p<0.05; [a]Probable/laboratory confirmed influenza like illness; [b]ICD-9-CM 487 coded hospitalizations; [c]ICD-9-CM 480–486 coded hospitalizations; [d]ICD-9-CM 480–488 coded hospitalizations.
CI: confidence interval; ER: emergency room; HD: high-dose; rVE: relative vaccine efficacy/effectiveness; RCT: randomized controlled trial; SD: standard-dose.
**Reference**: Lee J, et al. Vaccine: X. 2023 doi:10.1016/j.jvacx.2023.100327.

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# Efficacy and Effectiveness of HD Vaccine in Older Adults: An Updated Systematic Review and Meta Analysis

**A:** All seasons and sub-analyses by season type

| Outcome<br>*rVE (95% CI);n; p-value* | All Seasons | A/H3N2-dominant Seasons[a] | A/H1N1 Se |
|---|---|---|---|
| Influenza-like Illness[d] | **14.3%**<br>(4.2 - 23.3%)<br>n=11; p=0.007 | **16.3%**<br>(2.5 – 28.2%)<br>n=7; p=0.022 | 8<br>(-3.7<br>n=4; |
| *Hospitalization+ER Visit* | | | |
| Influenza[e] | **10.4%**<br>(6.8 – 13.9%)<br>n=13; p<0.001 | **10.3%**<br>(5.4 – 15.0%)<br>n=8; p<0.001 | 1<br>(3.8 -<br>n=5; |
| Pneumonia[f] | 4.4%<br>(-0.1 - 8.6%) | 2.2%<br>(-2.8 – 6.9%) | 8<br>(-0.7 |
| Cardiovascular | (10.5 – 15.7%)<br>n=7; p<0.001 | (10.1 – 15.7%)<br>n=6; p<0.001 | |
| Cardiorespiratory | **17.9%**<br>(15.0 - 20.8%)<br>n=7; p<0.001 | **17.7%**<br>(14.5 - 20.8%)<br>n=6; p<0.001 | |
| All-cause | **8.4%**<br>(5.7 - 11.0%)<br>n=11; p<0.001 | **8.3%**<br>(4.5 - 12.0%)<br>n=8; p<0.001 | 8<br>(5.4 -<br>n=3; |

**B:** Sub-analyses by study type

| Outcome | Randomized Studies[h] | | | Observational Studies | | |
|---|---|---|---|---|---|---|
| | n | rVE[c] (95%CI) | p-value | n | rVE[c] (95%CI) | p-value |
| Influenza-like Illness | 3 | **24.1%** (10.0 – 36.1%) | 0.002 | 8 | 11.1% (-0.1 – 21.0%) | 0.051 |
| *Hospitalization+ER Visit* | | | | | | |
| Influenza | - | - | - | 13 | **10.4%** (6.8 – 13.9%) | <0.001 |
| Pneumon | | | | | | |
| *Hospitali* | | | | | | |
| Influenz | | | | | | |
| Pneumo | | | | | | |
| Pneumo | | | | | | |
| Respirat | | | | | | |
| Influenz | | | | | | |

[a] Determine
characteriza
15, 2018–19) as well as seasons where egg-adapted vaccine strains may have affected vaccine effectiveness (2012–13, 2016–17, 2017–18); [c] A random-effects model with DerSimonian-Laird estimators was used to calculate the pooled OR across multiple studies and influenza seasons; [d] Probable/laboratory confirmed influenza-like illness; [e] ICD-9-CM 487 coded hospitalizations; [f] ICD-9-CM 480–486 coded hospitalizations; [g] ICD-9-CM 480–488 coded hospitalizations; [h] Includes both individual-level randomized and cluster-randomized studies.
CI, confidence interval; rVE, relative vaccine efficacy/effectiveness

**Study results suggest that irrespective of study type, study setting, age of vaccine recipients, circulating strains or antigenic match, HD IIV is expected to be more effective than SD IIV**

***Continues to highlight breadth of published literature on HD IIV efficacy/effectiveness:***

- Studies in 12 consecutive influenza seasons
- Diversity in study design and outcomes
- Large sample size (>29 million HD recipients, >45 million total)

***Use of clinical outcomes that are relevant to clinicians and decision makers***

Lee J, et al. Options XI. P-336 10183_ABSTRACTS_POSTER+SESSION+II++++27+SEPT+22.PDF (AMAZONAWS.COM)

# *No safety concerns* identified during clinical development nor post-marketing surveillance (>243M doses distributed)

Both the clinical trial and post-licensure data demonstrate that the safety profile of HD in adults 65 years of age and older is acceptable[1,2]

### *Independent ECDC and CDC data:*

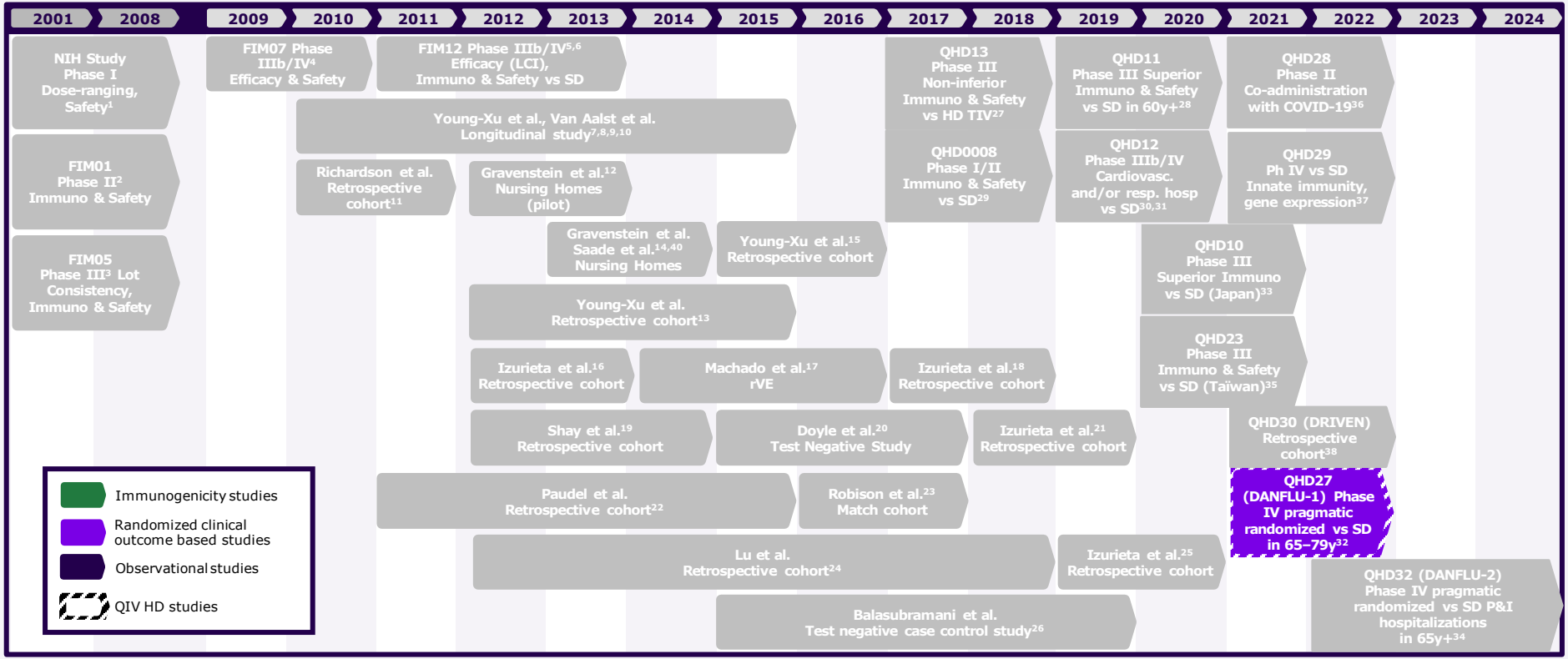
- HD vaccines are likely associated with a higher frequency of local and systemic reactions […] Notably these symptoms are typically reported as mild and transient in nature[5]
- Studies conducted using VAERS demonstrate no new or unexpected safety concerns among individuals aged≥65 years[3–5]

| Solicited local reactions[1] n (%) | TIV-HD (n=2572) | TIV-SD (n=1260) |
|---|---|---|
| Pain | 915 (**36%**) | 306 (**24%**) |
| Erythema | 384 (**15%**) | 136 (**11%**) |
| Swelling | 165 (**9%**) | 45 (**6%**) |

CDC: Centers for Disease Control and Prevention; ECDC: European Centre for Disease Prevention and Control; HD: high-dose; SD: standard dose; TIV: tetravalent influenza vaccine; VAERS: Vaccine Adverse Event Reporting System.

**References**: 1. Falsey A, et al. *J Infect Dis*. 2009 200:172-80. doi: 10.1086/599790.; 2. Kaka et al. *Open Forum Infect Dis*. 2017;4:ofx001. doi: 10.1093/ofid/ofx001.; 3. Moro PL et al. *Infect Dis*. 2012; 54:1608-14. doi: 10.1093/cid/cis256.; 4. Moro PL et al. *Vaccine.* 2020; 38:5923-26. doi: /10.1016/j.vaccine.2020.07.007.; 5. ECDC. Seasonal influenza vaccines systematic review. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/seasonal-influenza-vaccines-systematic-review-efficacy.pdf (Accessed April 2023).

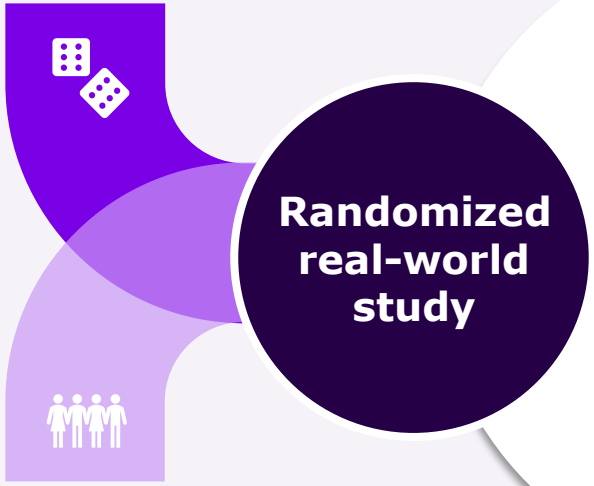
# Focus on Randomized Real-world study of HD-QIV vs. SD-QIV against hospitalizations and deaths




References in slide notes.

# DANFLU-1 study: An innovative way to randomize people in the real world

Randomization




- Randomized to demonstrate causal relationship
- Large populations to study many outcomes, across different seasons & settings

**Impact on critical *public health endpoints***

NEJM Evidence

Published January 23, 2023
NEJM Evid 2023; 2 (2)
DOI: 10.1056/EVIDoa2200206

ORIGINAL ARTICLE

## A Pragmatic Randomized Feasibility Trial of Influenza Vaccines

Niklas Dyrby Johansen, M.D.,[1,2] Daniel Modin, M.B.,[1,2] Joshua Nealon, Ph.D.,[3] Sandrine Samson, Ph.D.,[4] Camille Salamand, M.Sc.,[4] Matthew M. Loiacono, Ph.D.,[5] Carsten Schade Larsen, M.D., D.M.Sc.,[6] Anne Marie Reimer Jensen, M.D.,[1,2] Nino Emanuel Landler, M.D.,[1,2] Brian L. Claggett, Ph.D.,[7] Scott D. Solomon, M.D.,[7] Martin J. Landray, Ph.D.,[8,9] Gunnar H. Gislason, M.D., Ph.D.,[1,10,11,12] Lars Køber, M.D., D.M.Sc.,[10,13] Jens Ulrik Stæhr Jensen, M.D., Ph.D.,[14] Pradeesh Sivapalan, M.D., Ph.D.,[14] Lasse Skafte Vestergaard, M.D., Ph.D.,[15] Palle Valentiner-Branth, M.D., Ph.D.,[15] Tyra Grove Krause, M.D., Ph.D.,[15] and Tor Biering-Sørensen, M.D., Ph.D., M.P.H.[1,2]

**Reference**: Johansen ND, et al. *NEJM Evid* 2023;2. doi: 10.1056/EVIDoa2200206.

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# DANFLU-1 study overview

| Description | | | Study characteristics |
|---|---|---|---|
| **Study Population** | **Age:** | 65 to 79 years* | **NCT number**: NCT05048589<br>**EudraCT number**: 2021-003170-31<br><br>**Sponsor:** Copenhagen University Hospital-Herlev and Gentofte (Danmark)<br><br>**Principal Investigator:**<br>Dr. Tor Biering-Sorensen<br><br>*Conducted collaboratively with Sanofi* |
| | **Number of subjects:** | 12,477 randomly assigned participants | |
| **Interventions** | **Group 1** | Randomly assigned to quadrivalent high dose influenza vaccine (QIV-HD; Fluzone High-Dose); n = 6281 | |
| | **Group 2** | Randomly assigned to quadrivalent standard dose influenza vaccine (QIV-SD; Influvac Tetra); n=6270 | |
| **Study Design** | Phase II, pragmatic, open-label, active-controlled, individually-randomized feasibility trial in Denmark<br>Randomly assigned 1:1 | | |
| **Enrollment** | Electronic invitation & consent (or consent at vaccination) | | Link to primary paper<br>Link to study design paper<br>Link to Q&A |
| **Duration** | 2021/2022 flu season (start: October 1st 2021; follow-up period: 14 days after vaccination to May 31st 2022) | | |
| **Location** | Denmark (>1,000 decentralized vaccination sites across the country) | | |
| **Objectives** | 1. Assess feasibility, reliability, and validity of the proposed pragmatic randomized study design<br>2. Demonstrate comparability of the QIV-HD vs QIV-SD cohorts to the overall Danish population<br>3. Assuming adequate influenza circulation**, validate the feasibility conditions above by describing event rates in the QIV-HD and QIV-SD participants and calculating rVE for respiratory endpoints<br>• ICD-coded hospitalization for pneumonia/influenza, respiratory disease, and cardio-respiratory disease<br>4. Validate the feasibility conditions above by describing event rates in the QIV-HD and QIV-SD participants and calculating rVE for cardiovascular disease, all-cause hospitalization, all-cause mortality, and COVID-19 | | |

*QIV-HD was preferentially recommended for those 80+ during the 2021/22 season; ** >4 weeks (consecutive or non-consecutive) of ≥10% influenza test positivity in national Danish surveillance data.
ICD: International Classification of Diseases; QIV-HD: high-dose quadrivalent influenza vaccine; QIV-SD: standard-dose quadrivalent influenza vaccine; rVE: relative vaccine effectiveness.
**Reference:** Johansen N, et al. *NEJM Evidence.* 2023;2(2); doi: 10.1056/EVIDoa2200206.

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# The first and only published data from a randomized real-world study comparing QIV-HD to QIV-SD in 2021–22 in Europe

**12,477** participants (mean age: 71.7 years; 5877 [47.1%] were women) with 99.9% complete follow-up data

| Outcome | Events QIV-HD (n=6245) n, (%) | Events QIV-SD (n=6232) n, (%) | rVE (95% CI) |
|---|---|---|---|
| **Hospitalization for influenza or pneumonia** | **10 (0.2)** | **28 (0.4)** | **64.4 (24.4 to 84.6)** |
| Hospitalization for respiratory disease | 24 (0.4) | 40 (0.6) | 40.1 (-1.8 to 65.5) |
| Hospitalization for cardiorespiratory disease | 103 (1.6) | 117 (1.9) | 12.1 (-15.5 to 33.3) |
| Hospitalization for cardiovascular disease | 82 (1.3) | 81 (1.3) | -1.0 (-39.1 to 26.6) |
| Hospitalization for COVID-19 | 15 (0.2) | 12 (0.2) | -24.7 (-191.9 to 45.5) |
| Hospitalization for any cause | 513 (8.2) | 550 (8.8) | 6.9 (-5.2 to 17.6) |
| **All-cause death** | **21 (0.3)** | **41 (0.7)** | **48.9 (11.5 to 71.3)** |

## *Conclusions*

This study showed:

- A **pragmatic randomized trial** of QIV-HD vs QIV-SD using existing infrastructure and registry-based data was **feasible**
- **Lower incidence of hospitalization** for **influenza or pneumonia** and **all-cause mortality** in the QIV-HD group compared with the QIV-SD group
- Positive rVE trends provide new high-quality evidence for QIV-HD, however, findings require confirmation in an adequately powered trial to confirm exact magnitude of effect size → DANFLU-2

CI: confidence interval; QIV-HD: high-dose quadrivalent influenza vaccine; QIV-SD: standard-dose quadrivalent influenza vaccine; rVE: relative vaccine effectiveness.

**Reference**: Johansen ND, et al. *NEJM Evid* 2023;2. doi: 10.1056/EVIDoa2200206.

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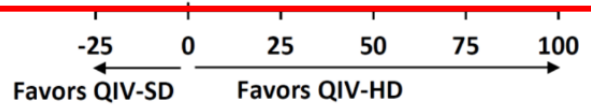
# DANFLU-1: post-hoc analysis of recurrent hospitalizations

| | QIV-HD | QIV-SD | Relative vaccine effectiveness (%) (95% CI) | p-value |
|---|---|---|---|---|
| | No. of events | | | |
| Hospitalizations for pneumonia or influenza | 10 | 33 | 70 (36 to 86) | 0.002 |
| Respiratory hospitalizations | 30 | 46 | 37 (-9 to 63) | 0.10 |
| Cardio-respiratory hospitalizations | 118 | 147 | 21 (-6 to 41) | 0.12 |
| Cardiovascular hospitalizations | 90 | 102 | 12 (-22 to 37) | 0.44 |
| All-cause hospitalizations | 647 | 743 | 13 (1 to 24) | 0.032 |




- In a post-hoc analysis, QIV-HD was associated with lower incidence rates of hospitalizations for pneumonia or influenza and all-cause hospitalizations compared with QIV-SD, with trends evident independent of influenza circulation levels.
- Our exploratory results correspond to **a number needed to treat of 65** (95% CI 35-840) **persons vaccinated with QIV-HD compared with QIV-SD to prevent one additional all-cause hospitalization per season**
- Further research is needed to confirm these hypothesis generating findings.

Johansen ND et al., Effectiveness of high-dose versus standard-dose quadrivalent influenza vaccine against recurrent hospitalizations and mortality in relation to influenza circulation: A post-hoc analysis of the DANFLU-1 randomized clinical trial, Clinical Microbiology and Infection, (https://doi.org/10.1016/j.cmi.2024.01.017).

# High-dose flu vaccine sets the bar for Protection Beyond Flu

## CLINICAL OUTCOMES

### INFECTION DATA[1]

Randomized clinical trial

vs standard dose (SD)

32,000 subjects aged 65+ years across two seasons

Lab-confirmed influenza

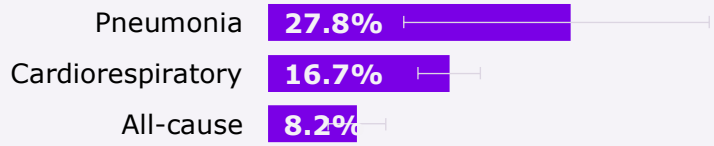
**+24.2%**

(95% CI: 9.7–36.5)

relative efficacy

### HOSPITALIZATION DATA[2]

Reduction in hospitalizations vs SD




## ROBUST METHODOLOGY

**RANDOMIZED STUDIES**

*Clinical* settings

*Real-world* settings

**VS STANDARD DOSE**

All results

*over and above*

standard dose

**CONSISTENT RESULTS**

**12** seasons[2]

**>45M** older adults[2]

DANFLU-1 **Randomized real-world study** *Season 2021-22* QIV HD associated with **64.4%** (95% CI: 24.4–84.6) lower rates of flu and pneumonia hospitalizations vs QIV SD[3]

CI: confidence interval; M: million; QIV-HD: high-dose quadrivalent influenza vaccine; QIV-SD: standard-dose quadrivalent influenza vaccine; SD: standard-dose.

**References**: 1. DiazGranados CA, et al. *N Engl J Med*. 2014; 371:635-45. doi: 10.1056/nejmoa1315727; 2. Lee J, et al. Vaccine: X. 2023 doi:10.1016/j.jvacx.2023.100327. ; 3. Johansen ND, et al. *NEJM Evid* 2023;2. doi: 10.1056/EVIDoa2200206.

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# Acknowledgement of high quality of evidence and recommendations by scientific societies/HCPs associations

## France[1–2]

- SFGG Geriatricians preferential recommendations LTCF **February 2021**
- SFGG preferential recommedations 65+ years **October 2022**
- 20 scientific societies **November 2022**

## Spain[3–4]

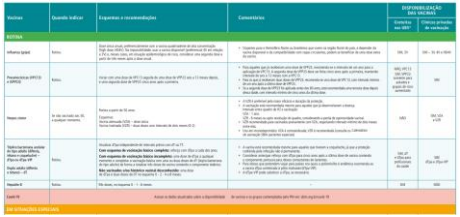
- Neumo Experto en Prevencion **June 2021**
- 8 scientific societies **October 2021**
- SEGG Geriatricians preferential recommendations **March 2023**

## Italy[5-6]

- GIMBE foundation **November 2021**
- AIOM Oncologist **May 2023**

## Brazil[7]

- ID society preferential recommendations 60+ years **March 2023**



GIMBE: Gruppo Italiano per la Medicina Basata Sulle Evidenze; HCP: health care professional; LTCF: Long Term Care Facility; SBIM: Sociedade Brasileira de Imunizações; SEGG: Spanish Society of Geriatrics and Gerontology; SFGG: Société Française de Gériatrie et Gérontologie. AIOM:Italian Association of Medical Oncology
References in slide notes.

# "Grade-like" analyses on HD and "related" recommendations

## NACI 2018

- "There is good evidence that the Fluzone® HD vaccine provides superior protection[1] (e.g., decrease in ILI, influenza-related death and all-cause hospitalization compared with SD-TIV in the elderly (Grade A Evidence)"[1]

**Recommendation season 2022–2023[6]**
- HD-IIV should be used over SD-IIV (Individual recommendation)
- Any available influenza vaccine (Public level)

## ECDC 2020

- "Overall, HD influenza vaccines may provide better protection against laboratory-confirmed influenza and proxy outcome measures"[2]

## STIKO 2021

- "Evidence of relative efficacy/effectiveness and safety is better for HD than for the three other enhanced vaccines"
- "HD shows small but significant superiority against lab-confirmed influenza and not lab-confirmed endpoints. For the other vaccines, this statement can not be made with such certainty currently"[3]

**Recommendation season 2022–2023[7]**
Preferential recommendation for all persons ≥60 years of age with inactivated, high-dose quadrivalent influenza vaccine

## US CDC 2022

"HD-IIV, RIV, and aIIV have shown relative benefit compared with SD-IIVs in certain studies, with the most evidence available for HD-IIV3."[4]

**ACIP**

**Recommendation season 2022–2023[4]**
- "ACIP recommends that adults aged ≥65 years preferentially receive any one of the HD or adjuvanted influenza vaccines HD-IIV4, RIV4, or aIIV4"

## NCIRS 2022

- For HD-IIV vs SD-IIV in people aged 65+, the overall certainty of evidence in GRADE was rated as "moderate"
- For the MF59 vaccine vs the SD-IIV vaccine in people aged 65+, the overall certainty of evidence in GRADE was rated as "low"[5]

**ATAGI**

**Recommendation season 2022–2023[5]**
- "HD-IIV is recommended in preference to SD-IIV in adults aged ≥65 years"
- Same for adjuvanted
- "Neither adjuvanted nor HD IIV is recommended in preference to the other in 65+"

ACIP: Advisory Committee on Immunization Processess; aIIV: adjuvanted inactivated influenza vaccine; ATAGI: Australian Technical Advisory Group on Immunisation; ECDC: European Centre for Disease Prevention and Control; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HD: high-dose; HD-IIV: high-dose inactivated influenza vaccine; ILI: influenza-like illness; NACI: National Advisory Committee on Immunization; NCIRS: National Centre for Immunisation Research and Surveillance; RIV: recombinant influenza vaccine; SD-IIV: standard-dose inactivated influenza vaccine; STIKO: Standing Committee on Vaccination; TIV: trivalent influenza vaccine, US CDC: United States Centers for Disease Control and Prevention.
References in slide notes.

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**Acknowledgement of high quality of evidence and recommendations by scientific societies/HCPs associations**

**….. Led to what**

# Efficacy of influenza vaccines for reducing cardiovascular deaths after myocardial infarction

**The IAMI trial** evaluated the effect of in-hospital influenza vaccination on death and cardiovascular outcomes in patients with STEMI or non-STEMI (NCT02831608)*

- 1:1 double-blind, placebo-controlled, multi-centre RRCT, across 30 centres in 8 countries
- 28% (95% CI : 0.01-0.48) efficacy of flu vaccines (TIV & QIV) vs. placebo against the composite of all-cause death, MI and stent thrombosis
- 41% efficacy against cardiovascular deaths (95% CI : 0.1-0.61) and all-cause deaths (95% CI : 0.11-0.61)

Table 2. Primary, Key Secondary, and Other Secondary Endpoints[2]

| | Vaccine (N = 1272) | Placebo (N = 1260) | Hazard Ratio (95% CI) | P-value | efficacy |
|---|---|---|---|---|---|
| **Primary Endpoints, no (%)** | | | | | |
| All-cause death, myocardial infarction, stent thrombosis | 67 (5.0) | 91 (7.2) | **0.72 (0.52-0.99)** | 0.040 | 28% |
| **Key Secondary Endpoints, no (%)** | | | | | |
| All-cause death | 37 (2.9) | 61 (4.9) | **0.59 (0.39-0.89)** | 0.010 | 41% |
| Cardiovascular death | 34 (2.7) | 56 (4.5) | **0.59 (0.39-0.90)** | 0.014 | 41% |
| Myocardial infarction | 25 (2.0) | 29 (2.4) | 0.86 (0.50-1.46) | 0.57 | 16% |
| Stent thrombosis | 6 (0.5) | 3 (0.2) | 1.94 (0.48-7.76) | 0.34 | -0.94% |

**"Influenza vaccination should be considered as part of in-hospital treatment after MI"**

*There were grants provided from Sanofi for the study and Sanofi also provided the vaccine but had no role in the design or conduct of the study.

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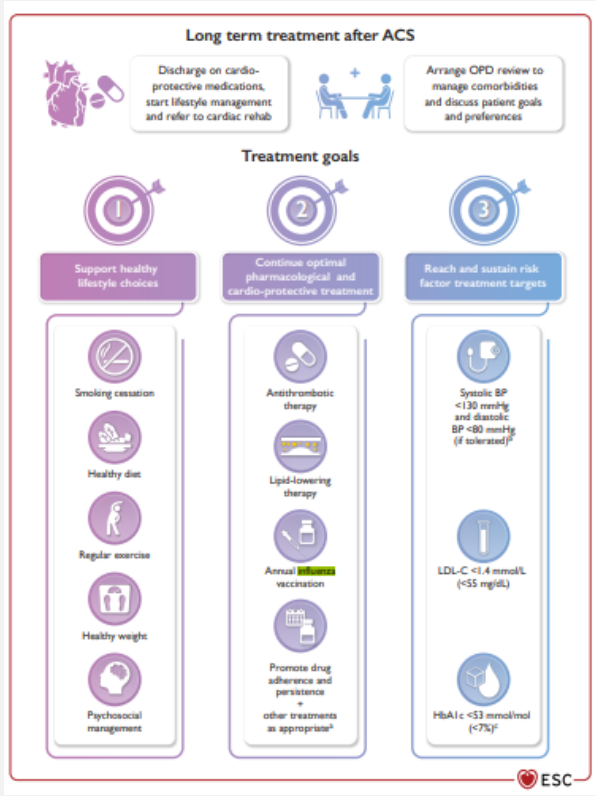
1. Fröbert O, Götberg M, Angerås O, et al. Design and rationale for the Influenza vaccination After Myocardial Infarction (IAMI) trial. A registry-based randomized clinical trial. Am Heart J. 2017;189:94-102.
2. Frøbert O, Götberg M, Erlinge D, et al. Influenza Vaccination after Myocardial Infarction: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. Circulation. 2021 Nov 2;144(18):1476-1484.

# ESC Updated Guidelines: Influenza Vaccine Recommendation Update: Class I, Grade A Evidence




**Quality of evidence upgraded from B level to A Level IAMI TriaL!**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Vaccination | | |
| Influenza vaccination is recommended for all ACS patients.[843,845–847] | I | A |

### 13.3.8. Vaccination

An annual influenza vaccination in patients with stable ASCVD appears to be associated with reduced incidence of MI, an improved prognosis in patients with HF, and decreased CV risk in adults aged 65 years and older.[843,844] In addition, influenza vaccination given early after an MI or in high-risk CAD has been shown to result in a lower risk of all-cause death and CV death at 12 months.[845–847] Therefore, influenza vaccination is recommended for all ACS patients and should be given preferentially during index hospitalization during influenza season for those not protected by a seasonal influenza vaccination.

https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehad191/7243210?login=true

INFLUENZA VACCINATION

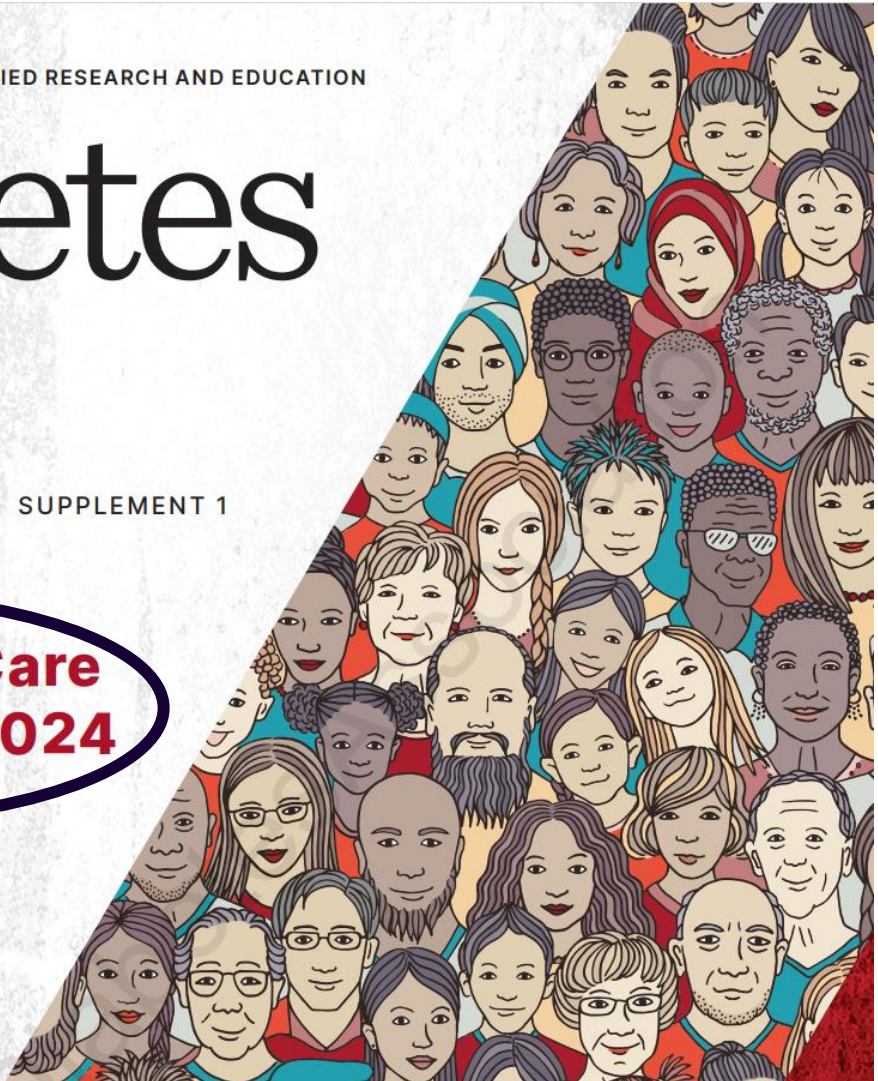
THE JOURNAL OF CLINICAL AND APPLIED RESEARCH AND EDUCATION

# Diabetes Care®

JANUARY 2024 | VOLUME 47 | SUPPLEMENT 1

WWW.DIABETESJOURNALS.ORG/CARE

## Standards of Care in Diabetes—2024



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American Diabetes Association.

# Influenza vaccination in diabetes is a well-established recommendation

2024

## Annual influenza vaccination is recommended for people with diabetes by health authorities and associations worldwide[1]

- Influenza vaccination in people with diabetes has been found to significantly reduce influenza and diabetes related hospital admissions. In people with diabetes and cardiovascular disease, influenza vaccine has been associated with lower risk of all-cause mortality, cardiovascular mortality, and cardiovascular events.

- Given the benefits of the annual influenza vaccination, it is recommended for all individuals > 6 months of age who do not have a contraindication. The live attenuated influenza vaccine, which is delivered by nasal spray, is an option for people who are 2–49 years of age and who are not pregnant, but people with chronic conditions such as **diabetes are cautioned against taking the live attenuated influenza vaccine and are instead recommended to receive the inactive or recombinant influenza vaccination.**

- **For individuals > 65 years of age, there may be additional benefit from the high- dose quadrivalent inactivated influenza vaccine.**

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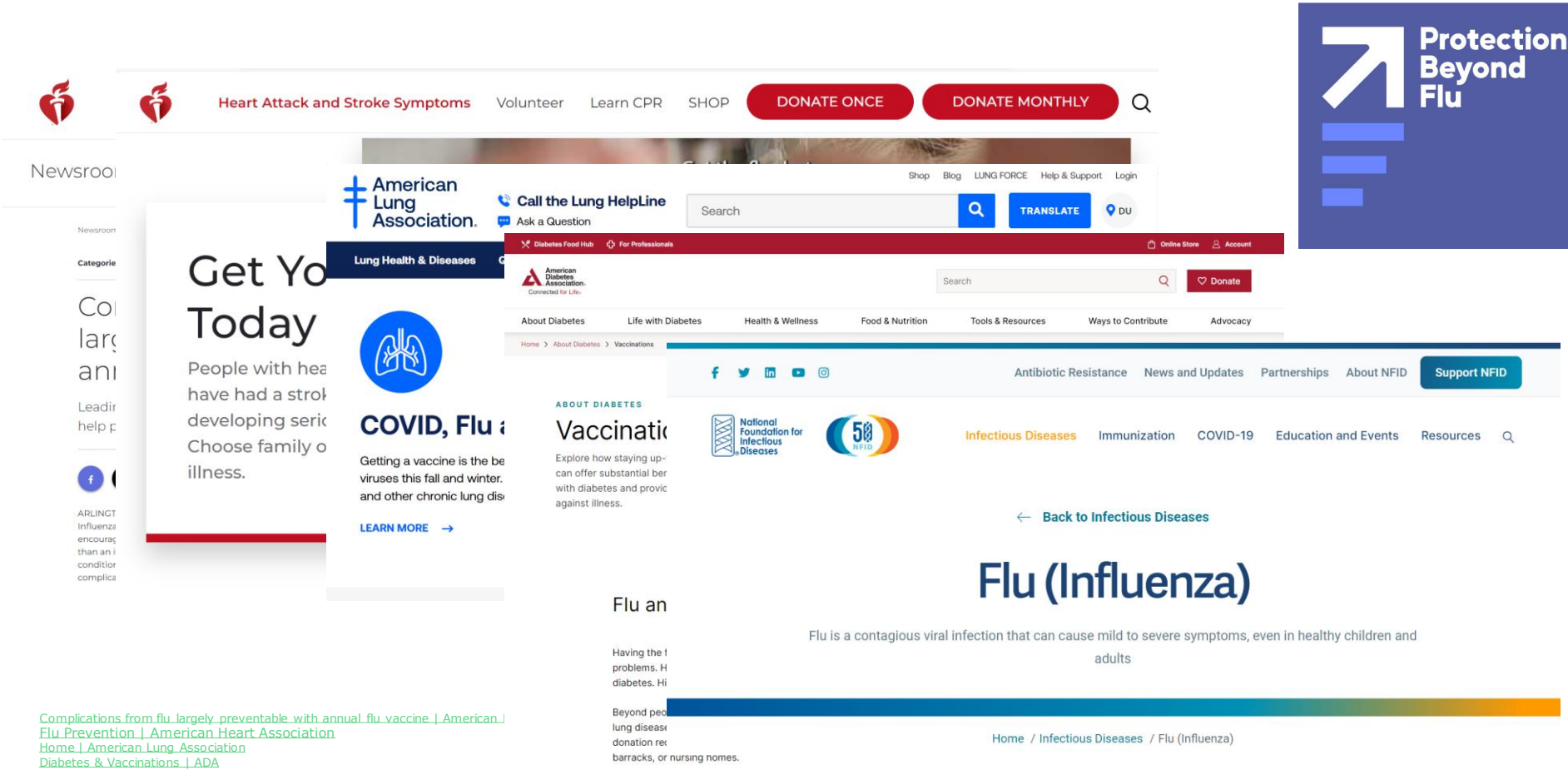
WHO, World Health Organization
standards-of-care-2024.pdf (silverchair-cdn.com)

# Dec 2023, During the National Influenza Vaccination Week, four leading public health organizations have encouraged everyone to get an influenza vaccine.

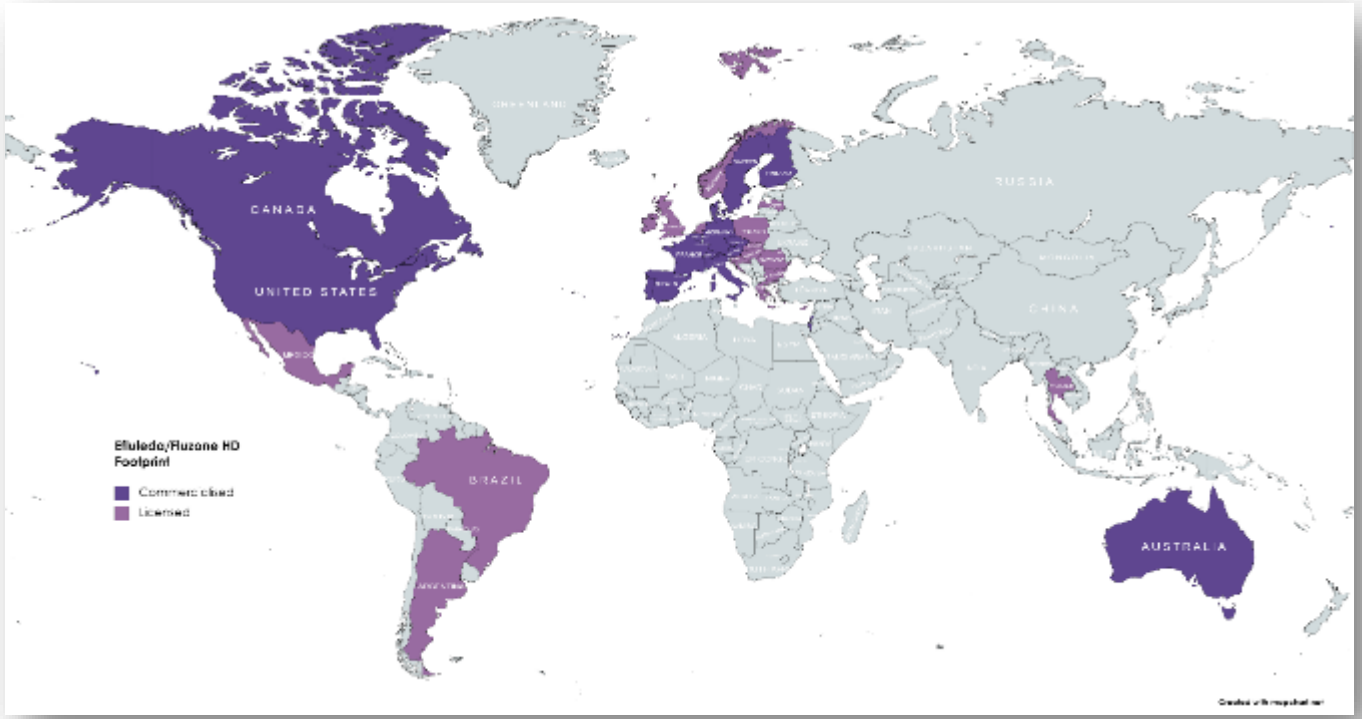



Complications from flu largely preventable with annual flu vaccine | American
Flu Prevention | American Heart Association
Home | American Lung Association
Diabetes & Vaccinations | ADA
Flu (Influenza) – NFID

# High-dose flu vaccine Global Footprint

## High-dose flu vaccine *has a global footprint in 18+ countries with >281M doses distributed worldwide as of October 23*[1]

| COUNTRY | STATUS |
|---|---|
| Argentina | Licensed |
| Australia | Commercialised |
| Austria | Commercialised |
| Belgium | Commercialised |
| Brazil | Licensed |
| Canada | Commercialised |
| Croatia | Licensed |
| Czech Rep. | Commercialised |
| Denmark | Commercialised |
| France | Commercialised |
| Finland | Commercialised |
| Germany | Commercialised |
| Greece | Licensed |
| Israel | Commercialised |
| Ireland | Licensed |
| Italy | Commercialised |
| Latvia | Licensed |
| Mexico | Licensed |
| Netherlands | Licensed |
| Norway | Licensed |
| Poland | Licensed |
| Portugal | Commercialised |
| Romania | Licensed |
| Slovakia | Licensed |
| Slovenia | Licensed |
| Spain | Commercialised |
| Sweden | Commercialised |
| Switzerland | Commercialised |
| Thailand | Licensed |
| United States of America | Commercialised |
| United Kingdom | Licensed |




Source: Sanofi Vaccines Data on File 2022
1. Internal Data

**What about our International recommendations?**

# Preparing for the Upcoming Respiratory Virus Season: Recommendations for Influenza, COVID-19, and RSV Vaccines for Older Adults

Clinician Outreach and Communication Activity (COCA) Call

Tuesday, September 19, 2023

PowerPoint Presentation (cdc.gov);
https://emergency.cdc.gov/coca/ppt/2023/091923_slides.pdf

## Influenza Vaccination of Persons Aged ≥65 Years

**"ACIP recommends that adults aged ≥65 years preferentially receive any one of the following higher dose or adjuvanted influenza vaccines:**

1. **Quadrivalent high- dose inactivated influenza vaccine (HD-IIV4),**
2. Quadrivalent recombinant influenza vaccine (RIV4),
3. or Quadrivalent adjuvanted inactivated influenza vaccine (aIIV4).

→ If none of these three vaccines is available at an opportunity for vaccine administration, then any other age-appropriate influenza vaccine should be used."



https://www.cdc.gov/flu/pdf/professionals/acip/acip-2023-24-Summary-Flu-Vaccine-Recommendations.pdf

# Key Information for Clinicians for Fall/Winter Viral Respiratory Season

| | |
|---|---|
| **Influenza** | • Vaccination of all persons aged ≥6 months who do not have contraindications is recommended.<br>• **Changes**: Updated U.S. influenza vaccine composition for 2023–2024<br>  • **Adults 65+ should get a high-dose or adjuvated flu vaccine**<br>  • Persons with egg allergy: Should receive influenza vaccine, no additional safety measures required |
| **COVID-19** | • Updated COVID-19 vaccines recommended for everyone aged ≥6<br>• The vaccines are **covered by insurance**. Uninsured and underinsured children and adults have access to vaccines through **VFC** or **Bridge Program**.<br>• Everyone ages **5 years** and older recommended for a single 2023 – 2024 dose<br>• No additional dose for age 65+ recommended **at this time** |
| **RSV** | • RSV can cause serious illness in older adults. Certain underlying medical conditions and advanced age are associated with increased risk of severe RSV.<br>• Adults 60+ may receive an RSV vaccine based on shared clinical decision- making with a healthcare provider. |

PowerPoint Presentation (cdc.gov);
https://emergency.cdc.gov/coca/ppt/2023/091923_slides.pdf

# All published "GRADE-like" analyses of benefit-risk of influenza vaccines in older adults acknowledge the highest level of evidence for HD

## GRADE

### ECDC 2020

"High-dose trivalent influenza vaccination was shown to have higher relative vaccine efficacy in preventing influenza compared with standard-dose trivalent influenza vaccines in older adults ≥ 65 yo (VE=24%, 95%CI 10 to 37, one RCT, moderate-certainty evidence)."

"HD may provide better protection against laboratory-confirmed influenza and proxy outcome measures"[2]

### NACI 2018

For 65+: "There is good evidence that the Fluzone® HD vaccine provides superior protection (e.g., decrease in ILI, influenza-related death and all-cause hospitalization compared with SD-TIV in the elderly (Grade A Evidence)"[1]

### RKI 2021

"For 60+: "Evidence of relative efficacy/effectiveness and safety is better for HD than for the three other enhanced vaccines"[3]

"HD shows small but significant superiority against lab-confirmed influenza and not lab-confirmed endpoints. For the other vaccines, this statement can not be made with such certainty currently"[3]

### US CDC 2022

For 65+: "HD-IIV, RIV and aIIV have shown relative benefit compared with SD-IIVs certain studies, with the most evidence available for high dose vaccine"[5]

### NCIRS 2022

"For HD-IIV vs SD-IIV in people aged 65+, the overall certainty of evidence in GRADE was rated as "moderate""

"For the MF59 vaccine vs the SD-IIV vaccine in people aged 65+, the overall certainty of evidence in GRADE was rated as "low""[4]

## RECO

### NACI

**Recommendation season 2023–2024**[6]

- "IV-HD should be used over IIV-SD, given the burden of influenza A(H3N2) disease and the good evidence of IIV3-HD providing better protection compared to IIV3-SD in adults 65 years of age and older" (Individual recommendation)
- Any available influenza vaccine (Public level)

### STIKO

**Recommendation season 2023–2024**[7]

- Preferential recommendation for all persons ≥60 years of age with inactivated, high-dose quadrivalent influenza vaccine

### ACIP

**Recommendation season 2023–2024**[9]

- "ACIP recommends that adults aged ≥65 years preferentially receive any one of the HD or adjuvanted influenza vaccines: HD-IIV4, RIV4, or aIIV4"
- ***"HD-IIV4 was associated with lower risk for diagnostic pneumonia and influenza hospitalizations (rVE 64.4; 95% CI = 24.4–84.6)"***

### ATAGI

**Recommendation season 2023**[8]

- "For adults aged ≥65 years, both the adjuvanted (Fluad® Quad) and high dose influenza vaccine (Fluzone High Dose Quadrivalent) are preferentially recommended over standard influenza vaccine."

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Reference in the footnotes

VACCINES

# The Flu Vaccine Works—In a Way Most People Don't Appreciate

## The CDC is emphasizing how the flu vaccine can turn the virus from "Wild to Mild"


The Flu Vaccine Works--In a Way Most People Don't Appreciate - Scientific American
lion-wild-to-mild-200x675-1.png (1200×675) (cdc.gov)

# CDC Interim Vaccine effectiveness for this season 2023- 2024

# Interim Vaccine effectiveness for this season: Did we go from WILD to MILD?


# Did the preferential recommendation do any good this year?

**Interim vaccine effectiveness estimates 2023-24**

- Flu vaccines have worked!
- Substantial reduction in medical visits and hospitalizations
- Benefit across all age groups
- Some estimates are even higher than observed before during well-matched seasons

**Vaccine effectiveness (VE)**



This Season's Flu Vaccines Reduced Flu Medical Visits and Hospitalizations Across All Ages | CDC

Interim Estimates of 2023–24 Seasonal Influenza Vaccine Effectiveness — United States | MMWR (cdc.gov)

# What about our Regional recommendations?

# The number of national authorities recommending HD for older adults is expanding


- *Recommended as any other available flu vaccines*
- *Recommended to be used preferentially over the conventional SD vaccine*

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**Cut of date: December 2023**
**References** in the notes

# GCC Health Authorities updates

MOH Flu- HD recommendation

MOH circular with targeted VCR

# GCC Health Authorities updates

MOH Flu- HD recommendation

MOH circular with targeted VCR

وزارة الصحة
Ministry of Health

**KSA MOH Circular**

The committee recommends the **preference for giving high-dose influenza vaccines to people in the age group 65 years or older**. If high-dose influenza vaccines are not available, other influenza vaccines should be given

الحملة الوطنية للتطعيم

تاريخ بدء الحملة

مدة الحملة
4 أشهر.

التغطية المستهدفة

- ✓ 100٪ من النساء الحوامل خلال موسم الإنفلونزا الموسمية.
- ✓ 100٪ من مرضى فشل الكلى (غسيل الكلى).
- ✓ 100٪ من الممارسين الصحيين الذين يقدمون الرعاية الصحية للمرضى بشكل مباشر.
- ✓ 60٪ من كبار السن من هم ٦٥ سنة فما فوق.
- ✓ أكبر عدد ممكن من بقية الفئات.

اللقاحات

- لقاح نصف الكرة الشمالي ٢٠٢٣/٢٠٢٤
  - an A/Victoria/4897/2022 (H1N1)pdm09-like virus;
  - an A/Darwin/9/2021 (H3N2)-like virus;
  - a B/Austria/1359417/2021 (B/Victoria lineage)-like virus;
  - a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.
- لقاح نصف الكرة الجنوبي 2023
  - an A/Sydney/5/2021 (H1N1)pdm09-like virus;
  - an A/Darwin/9/2021 (H3N2)-like virus;
  - a B/Austria/1359417/2021 (B/Victoria lineage)-like virus;
  - a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.
- لقاح الإنفلونزا عالي الجرعة Fluzone High-Dose Quadrivalent ٢٠٢٣/٢٠٢٤ . (فقط لكبار السن بعمر ٦٥ عام و أكبر)
  - an A/Victoria/4897/2022 (H1N1)pdm09-like virus;
  - an A/Darwin/9/2021 (H3N2)-like virus;
  - a B/Austria/1359417/2021 (B/Victoria lineage)-like virus;
  - a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

**QIV-HD** is recommended for 2023/2024 Flu season for only **65 years and above**

With target of coverage rate of **60%**

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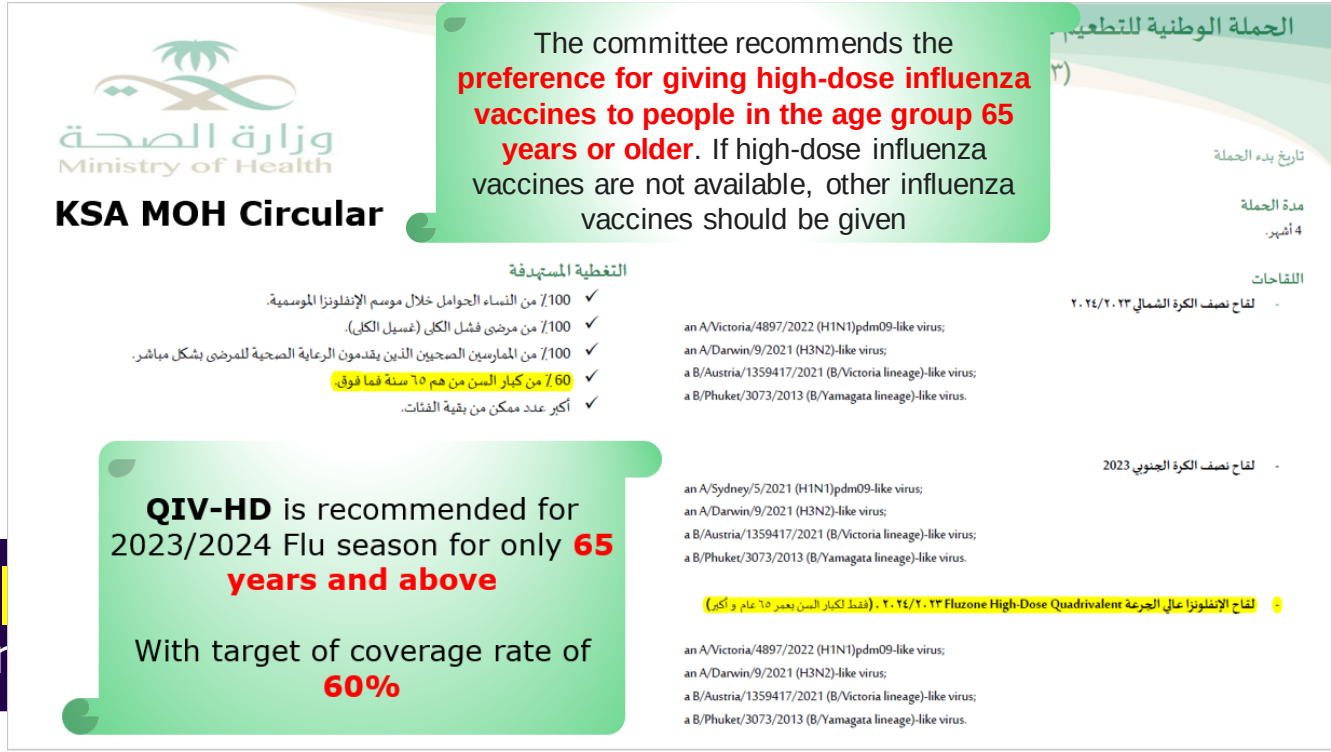
# GCC Health Authorities updates

MOH Flu- HD recommendation

MOH circular with targeted VCR

The Flu-HD is
Yet registered in

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# GCC Health Authorities updates

MOH Flu- HD recommendation

MOH circular with targeted VCR

DOH HD recommendation

Flu- HD is **officially Registered**

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# GCC Health Authorities updates

MOH Flu- HD recommendation

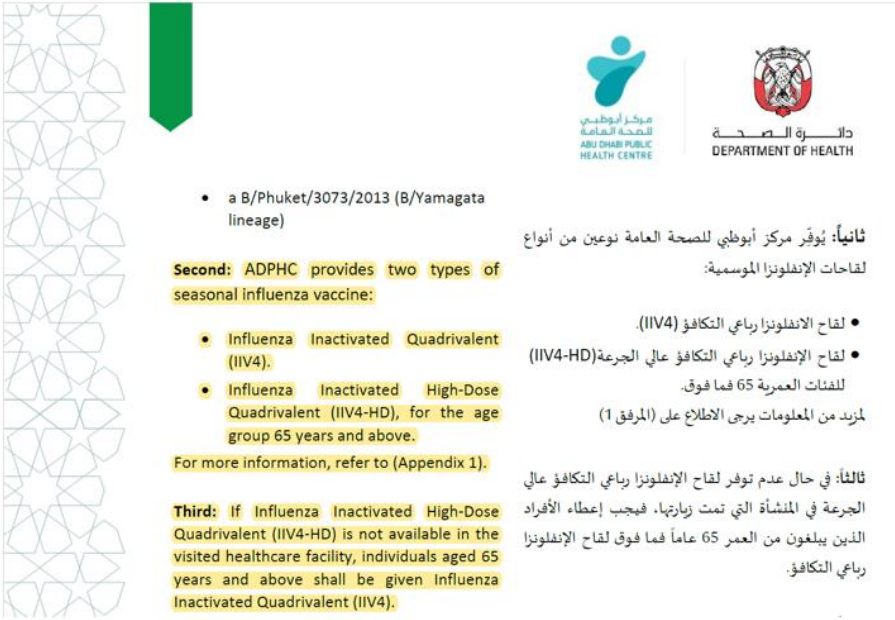
MOH circular with targeted VCR

DOH HD recommendation

Flu- HD is **<u>officially Registered</u>**

Internal

## DOH announce their Flu-HD recommendation



- a B/Phuket/3073/2013 (B/Yamagata lineage)

**Second:** ADPHC provides two types of seasonal influenza vaccine:

- Influenza Inactivated Quadrivalent (IIV4).
- Influenza Inactivated High-Dose Quadrivalent (IIV4-HD), for the age group 65 years and above.

For more information, refer to (Appendix 1).

**Third:** If Influenza Inactivated High-Dose Quadrivalent (IIV4-HD) is not available in the visited healthcare facility, individuals aged 65 years and above shall be given Influenza Inactivated Quadrivalent (IIV4).

مركز أبوظبي للصحة العامة
ABU DHABI PUBLIC HEALTH CENTRE

دائرة الصحة
DEPARTMENT OF HEALTH

**ثانياً:** يُوفّر مركز أبوظبي للصحة العامة نوعين من أنواع لقاحات الإنفلونزا الموسمية:

- لقاح الانفلونزا رباعي التكافؤ (IIV4).
- لقاح الإنفلونزا رباعي التكافؤ عالي الجرعة(IIV4-HD) للفئات العمرية 65 فما فوق.

لمزيد من المعلومات يرجى الاطلاع على (المرفق 1)

**ثالثاً:** في حال عدم توفر لقاح الإنفلونزا رباعي التكافؤ عالي الجرعة في المنشأة التي تمت زيارتها، فيجب إعطاء الأفراد الذين يبلغون من العمر 65 عاماً فما فوق لقاح الإنفلونزا رباعي التكافؤ.

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# GCC Health Authorities updates

MOH Flu- HD recommendation

MOH circular with targeted VCR

DOH HD recommendation

Flu- HD is **<u>officially Registered</u>**

Internal

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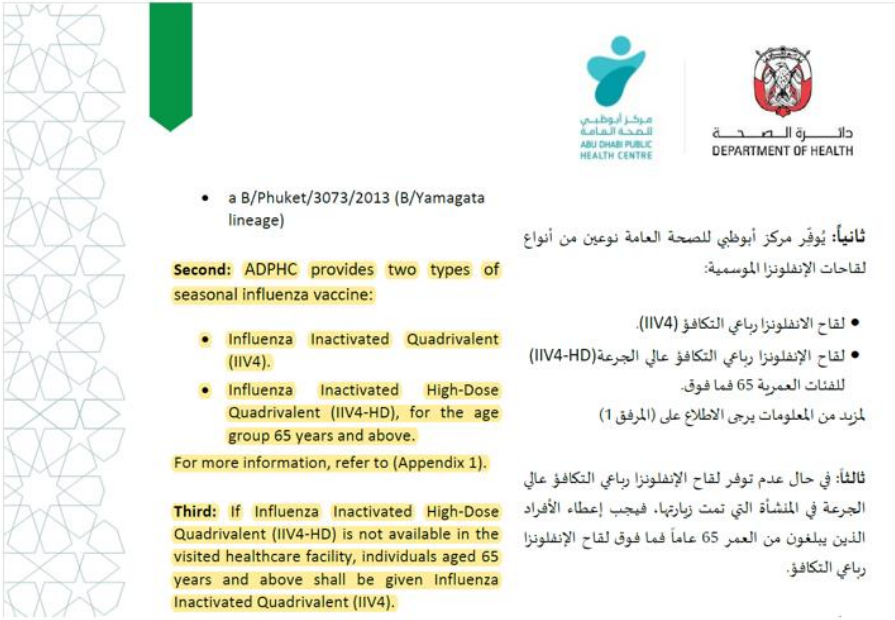

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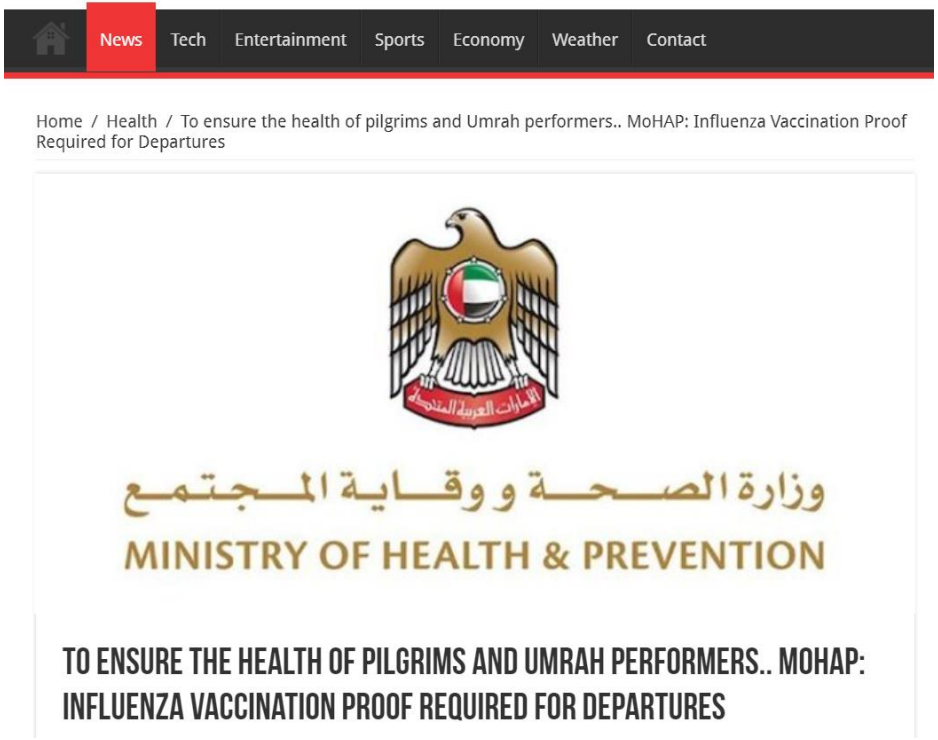
# MOHAP recommendation for Hajj and Umrah

UAE BARQ
برق الإمارات




The Ministry emphasizes the **mandatory requirement** of receiving all necessary doses of vaccinations, **especially the influenza vaccine**

The **elderly** are advised to receive the necessary vaccinations **10 days prior to traveling**, to ensure optimal effectiveness. Those who have received influenza vaccination within less than a year do not require a new dose.

Vaccination cards can be obtained from public and private healthcare facilities upon receiving the vaccination, and records will also be available at **"Al Hosn" app.**

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To ensure the health of pilgrims and Umrah performers.. MoHAP: Influenza Vaccination Proof Required for Departures – UAE BARQ

# GCC Health Authorities updates

MOH Flu- HD recommendation

MOH circular with targeted VCR

DOH HD recommendation

Flu- HD is **officially Registered**

In Jan 2024, it is **officially registered**

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# The evidence for HD in the *older population* demonstrates *Protection Beyond Flu*

- The ONLY superiority RCT vs SD in those aged 65+ with LCI as a primary endpoint[1]
- Benefits beyond influenza: notably regarding influenza-associated hospitalizations[2]
- Consistent efficacy/effectiveness data in 12 influenza seasons: meta-analyzed, >45 M subjects[2]
- The 1st and only published data from a randomized real-world study comparing QIV-HD to QIV-SD in 2021–22[3]
- No safety concerns[4], with more than 243M doses distributed as of season 2022/23*
- Concomitant administration with mRNA-COVID vaccine safe and immunogenic[5]

Quality of evidence acknowledged by ALL the five independent critical appraisals publicly available (GRADE-like analyses)[6-10]

*Sanofi data on file; GRADE: Grading of Recommendations, Assessment, Development and Evaluation; LCI: laboratory-confirmed influenza; M: million; QIV-HD: high-dose quadrivalent influenza vaccine; QIV-SD: standard-dose quadrivalent influenza vaccine; RCT: randomized controlled trial; SD: standard-dose.
References in slide notes.

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**pigeonhole.at**

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**SANOFIVACCINES**

# Q & A

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# Thank You

# Thank you

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To Report adverse events please call: +971 561747001 or email Gulf.Pharmacovigilance@sanofi.com www.sanofi.com

To report any side effect(s): Saudi Arabia: The National Pharmacovigilance and Drug Safety Centre (NPC)" SFDA call center: 19999
- E-mail: npc.drug@sfda.gov.sa
- Website: https://ade.sfda.gov.sa/

Full Prescribing Information is available upon request: SANOFI, Kingdom of Saudi Arabia, P.O. Box 9874, Jeddah 21423, K.S.A. Tel: +966-12-669-3318, Fax: +966-12-663-619.
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