Vaccine availability in 2017 & the vaccine pipeline

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https://www.youtube.com/watch?v=Eihfaq58wfo

"Which kind of Flu?"

Quadrivalent vaccines for use in the 2017 southern hemisphere influenza season

- **an A/Michigan/45/2015 (H1N1)pdm09-like virus;**
- **an A/Hong Kong/4801/2014 (H3N2)-like virus;**
- **a B/Brisbane/60/2008-like virus.**
- **a B/Phuket/3073/2013-like virus.**

Who can receive funded influenza vaccine?

- ✓ Pregnant women (in any trimester)
- ✓ Indigenous children aged 6 months to <5 years
- ✓ Indigenous people aged ≥15 years
- ✓ Any person aged >65 years
- ✓ Any person aged ≥6 months with a medical condition that places them at increased risk of complications from influenza.

Table 1: Influenza vaccines for particular age groups

Registered age group	Vaccine name			
	FluQuadri Junior 0.25mL Sanofi Pasteur	**FluQuadri** 0.50mL Sanofi Pasteur	**Fluarix Tetra** 0.50mL GSK	**Afluria Quad** 0.50mL Sequirus
<6 months	***NB: No influenza vaccine is registered for use in this age group***			
6 to 35 months	✓	✗	✗	✗
≥3 to 18 years	✗	✓	✓	✗
≥18 years	✗	✓	✓	✓

NB: Afluria Quad is not registered for use in anyone under 18 years of age.

Only Flu Quadri Junior (0.25mL) can be used for children aged 6 to 35 months. A 0.50mL vaccine dose **cannot** be halved for a paediatric 0.25mL dose.

Astra Zeneca

The wistful ferret

Updates tomorrow

Sanofi

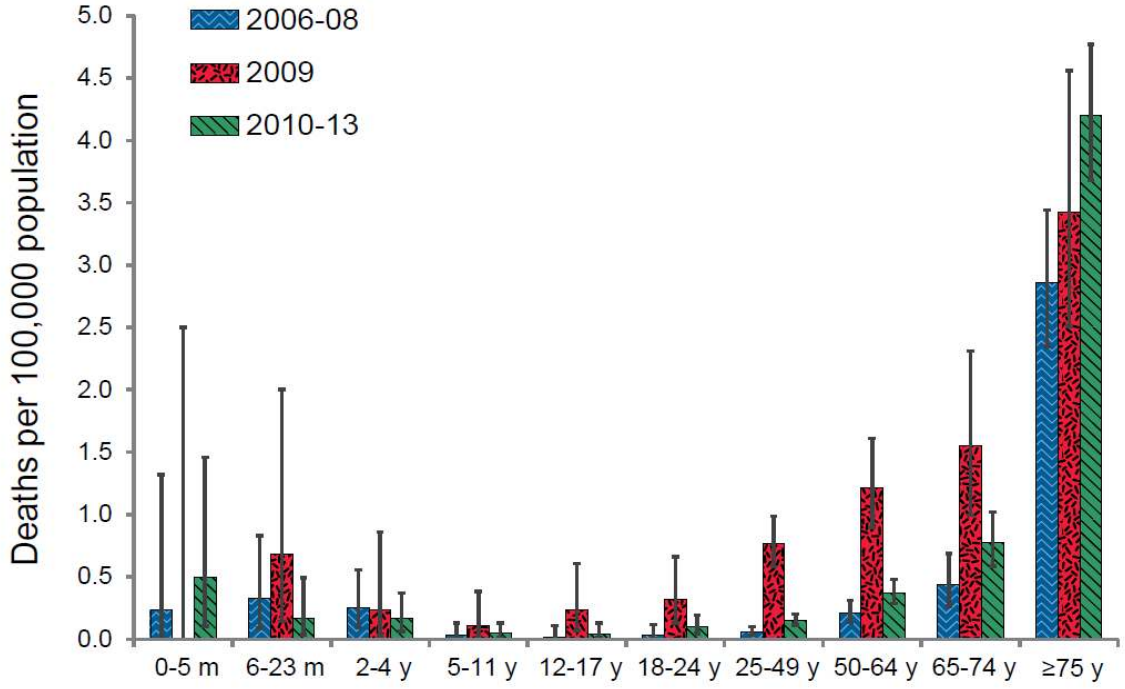
"Hi! I'm the Flu! Do you have a couple of weeks free?"

Substantial influenza burden in ≥65 years old despite 75% uptake *(AIHW 2011)*: better vaccine is needed

- **≥65 years old**
  - Population: 25m in 2017 → 44m in 2067 *(ABS 2013)*
  - % comorbidity = 38% *(Li-Kim-Moy et al. 2016)*

- **Majority of influenza-attributable deaths in ≥65 years old**

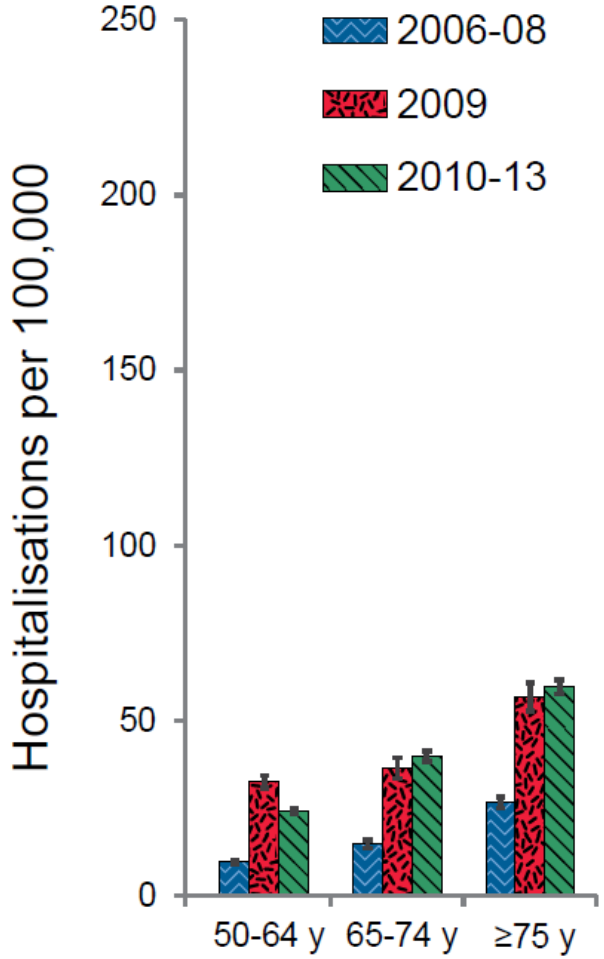
Incidence of ABS* certified death due to influenza *(Li-Kim-Moy et al. 2016)*



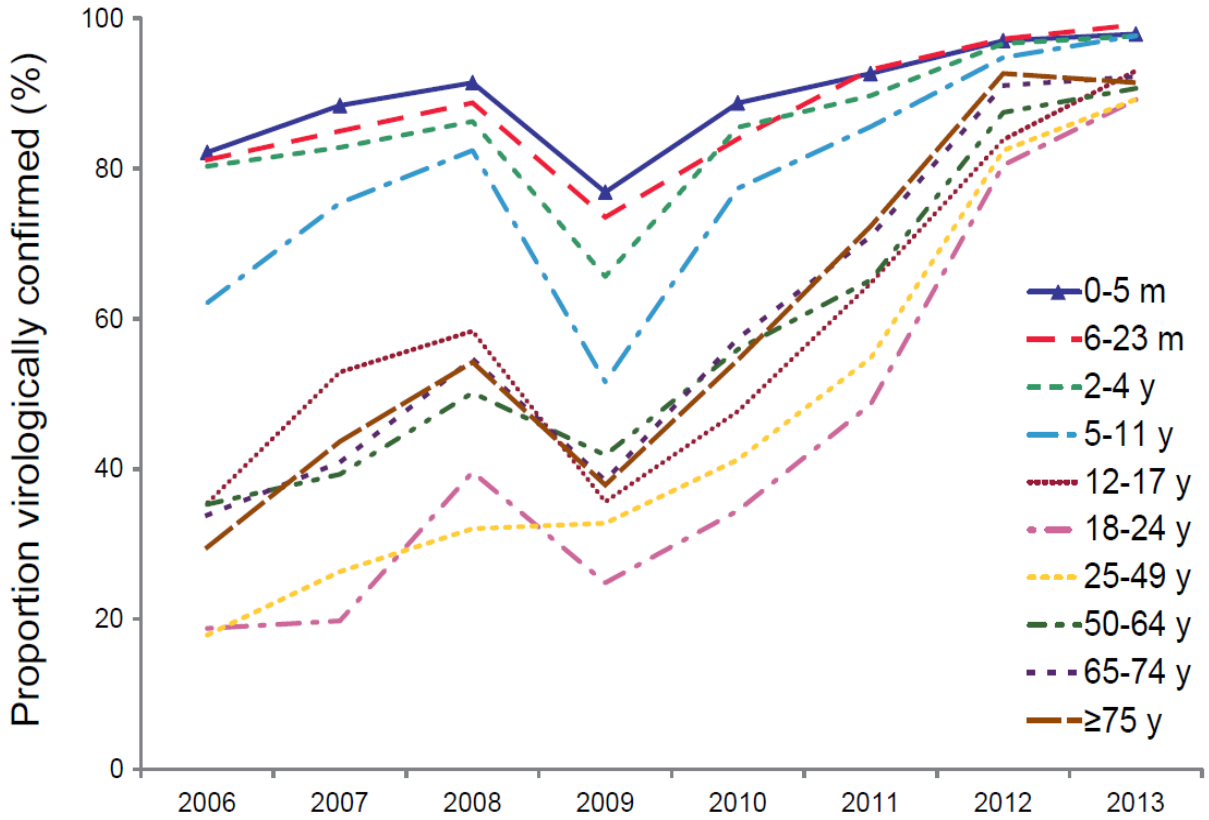
** Australian Bureau of Statistics*

↑ hospitalisation incidence in adults post 2009: more testing complicates the interpretation

Incidence of ICD-coded influenza hospitalisation



Proportions of ICD-coded influenza hospitalisation recorded as virologically confirmed (J9-10) of total (any diagnosis: J09-J11)



Reference: Li-Kim-Moy et al. 2016

High dose TIV (Fluzone® High-Dose)
4 times HA content of standard-dose vaccine

- **HD-TIV has <u>superior</u> efficacy relative to standard dose TIV** *DiazGranados et al. NEJM 2014*

Laboratory-confirmed influenza caused by any viral type or subtype (regardless of similarity)

	Fluzone High-Dose N=15,892 n (%)	Fluzone N=15,911 n (%)	Relative Efficacy % (95% CI)
Associated with influenza-like illness	228 (1.4)	301 (1.9)	24.2 (9.7; 36.5)

- **Lower limit of the 95% CI of relative efficacy = 9.7%**
- **Pre-specified lower limit required by FDA to demonstrate superior clinical benefit > 9.1%**
- **This is the only analysis for which the study was powered**

GSK

Fluarix® Tetra [Quadrivalent influenza vaccine (split virion, inactivated)]

2017 availability and presentations

***Fluarix Tetra* is indicated for adults and children 3 years of age and older**

Available on the National Immunisation Program (NIP) and private market in 2017

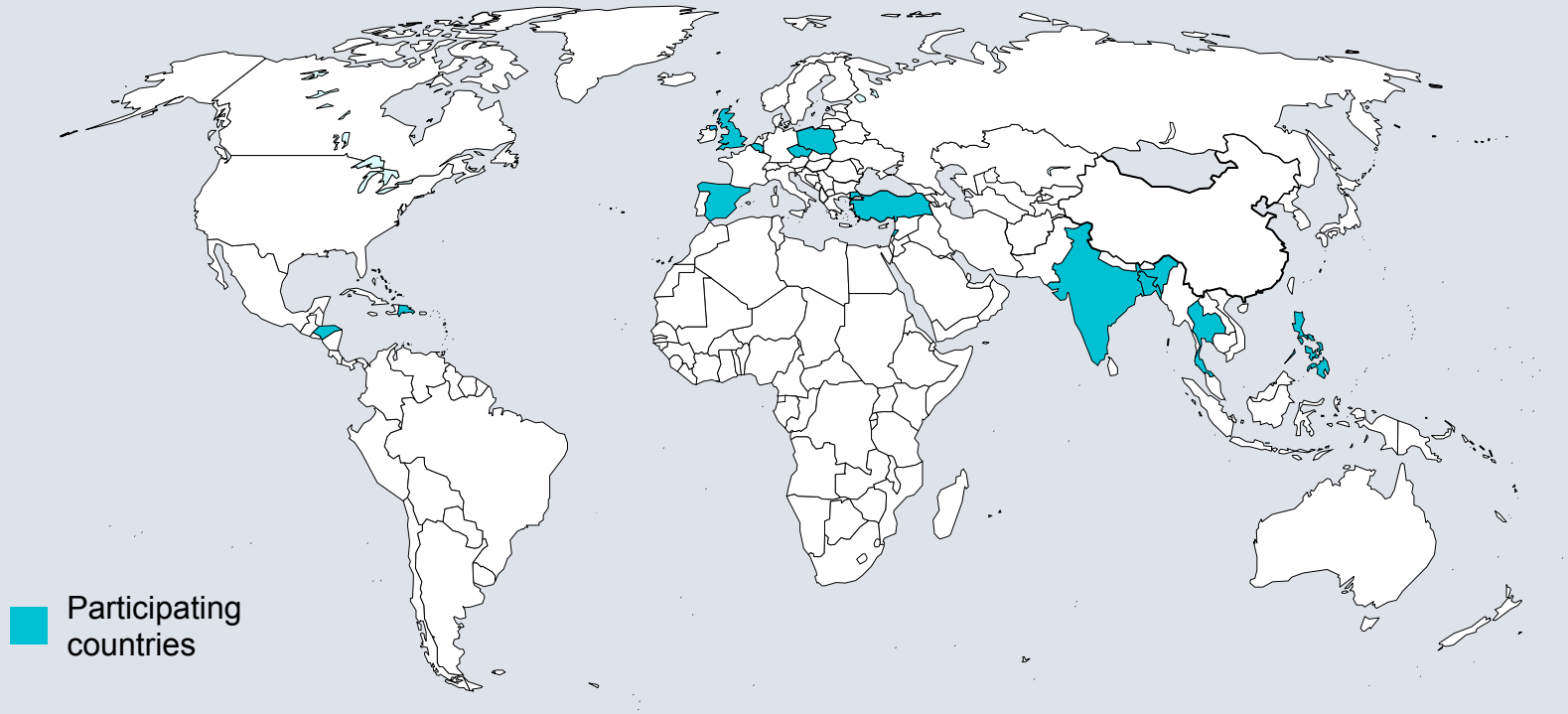
10-packs and single packs available

Note: NIP packs shown. Packs for the private market do not state 'Government Funded Program'

Separate needle/s included in the packs

FLU-D-QIV-004, *Fluarix Tetra* efficacy trial in children aged 6-35 months

Conducted over 5 Northern and Southern hemisphere seasons in > 12,000 subjects

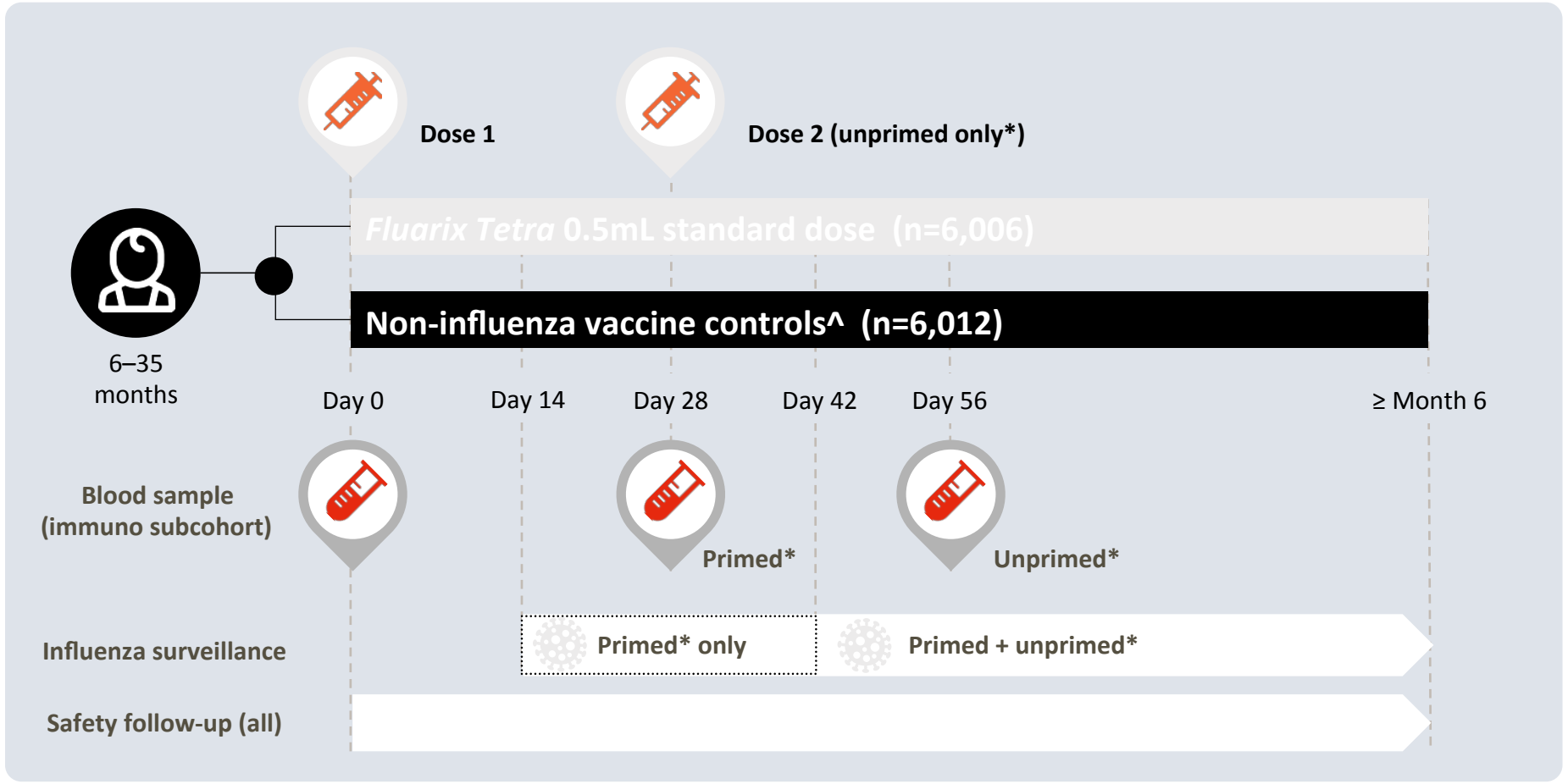


2011-12	2012	2012-13	2013	2014
Cohort 1 N=1777 Belgium, Czech Republic, Poland, Spain, UK	Cohort 2 N=2526 Bangladesh, Dominican Republic, Honduras	Cohort 3 N=1564 Belgium, Czech Republic, Lebanon, Poland, Spain, Turkey, UK	Cohort 4 N=1501 Bangladesh, Dominican Republic, Honduras, Philippines, Thailand	Cohort 5 N=4650 Bangladesh, Dominican Republic, Honduras, Philippines, Thailand, India

Approval date: J Approval Date: January 2017 AUS/FLU/0004/17

FLU-D-QIV-004: Design

Phase III observer-blind, randomised, comparator-controlled clinical trial



*Children were considered vaccine-primed if they had previously received ≥2 doses of seasonal influenza vaccine, separated by ≥28 days. All other subjects, including infants aged <12 months, were considered vaccine-unprimed.
^Vaccine controls: 13-valent pneumococcal conjugate vaccine (PCV13); GSK hepatitis A vaccine; Varicella vaccines

Approval date: J Approval Date: January 2017 AUS/FLU/0004/17

FLU-D-QIV-004: Co-Primary efficacy objectives

To evaluate the **efficacy** of *Fluarix Tetra* in the prevention of RT-PCR confirmed **influenza A and/or B disease**…

…due to **any seasonal influenza strain**, compared with **non-influenza vaccine controls**, in children aged 6 to 35 months

Moderate to severe influenza

Efficacy demonstrated if the lower limit of 97.5% CI for vaccine efficacy is >25%

Any severity of influenza

Efficacy demonstrated if the lower limit of 97.5% CI for vaccine efficacy is >15%

RT-PCR, reverse transcription polymerase chain reaction; CI, confidence interval

FLU-D-QIV-004: Secondary efficacy objectives

	Influenza		
	Severe*	Moderate-to-severe	Any
Influenza-associated **lower respiratory illness**			
Influenza due to **vaccine-matching** influenza strains			
Influenza due to **any seasonal** influenza strain			
Influenza-associated **acute otitis media**			
Influenza A and/or B disease			

*Any influenza with a physician-diagnosed serious extra-pulmonary complication, hospitalisation in intensive care , or requiring supplemental O_2 for > 8 hours

Approval date: J Approval Date: January 2017 AUS/FLU/0004/17 https://www.gsk-clinicalstudyregister.com/study/115345

Seqirus

UPDATE ON AFLURIA CLINICAL PROGRAM

6 Feb 2017

Background

- 2010: unexpected increase in fever and febrile seizures reports in children <5 years; increased reports of fever also reported in children 5-8 years
- Manufacturing method results in more residual lipid and RNA components: lipid-mediated delivery of fragmented viral RNA induced a stronger than expected pro-inflammatory signal in *in vitro* assays (Maraskovsky et al 2012, Rockman et al 2014)
- Increasing concentration of the splitting agent, sodium taurodeoxycholate (TDOC), significantly reduced lipid levels and release of pro-inflammatory cytokines

TDOC Study
CSL TIV
N=120, 18-60 years
Phase 4
Immunogenicity

QIV-01 Adults
N=3484 ≥18 years
CSL QIV:TIV1:TIV2
Randomised, DB, comparator-controlled immunogenicity and safety

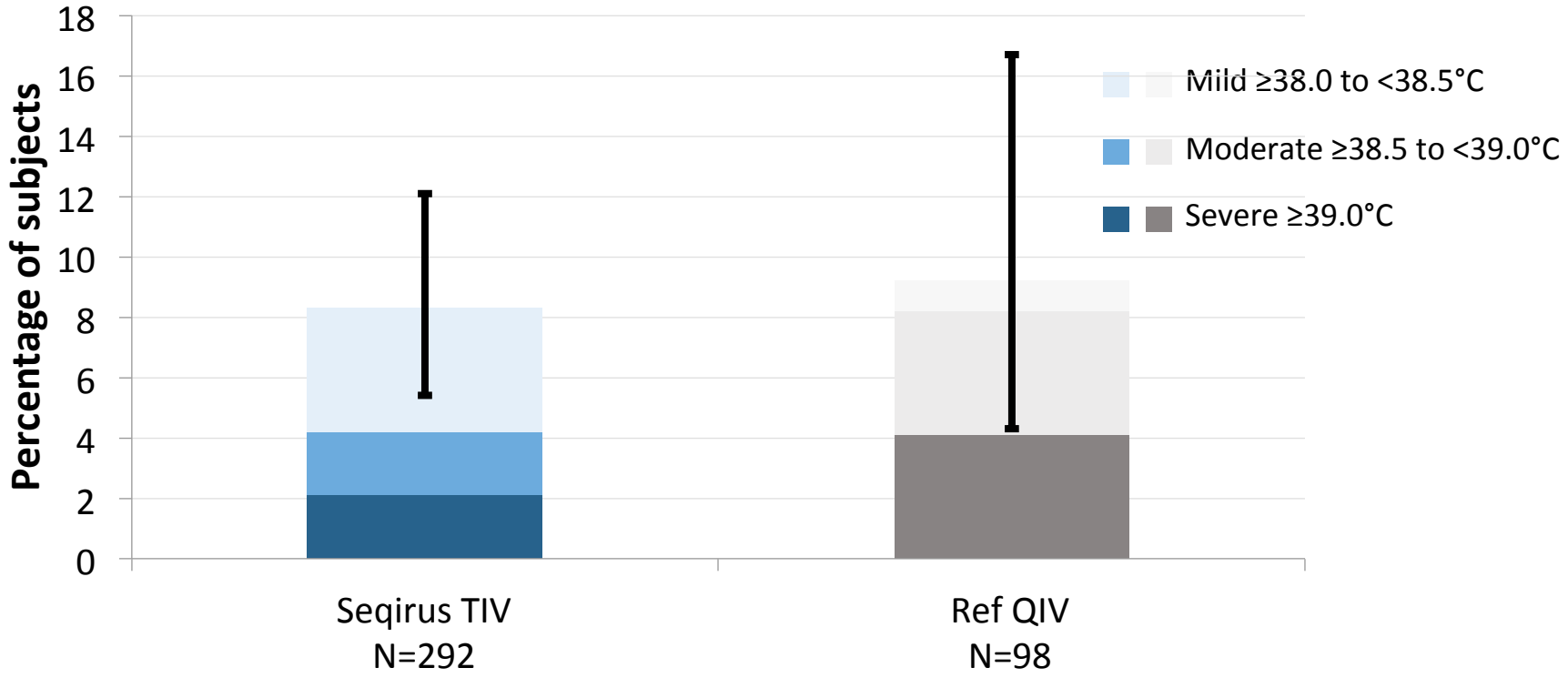
TIV 10-69
CSL TIV:QIV Ref Vax
N=402, 5-8 years
Randomised, observer-blinded, comparator-controlled safety

QIV-02 Paediatric
N=2222 5-17 years
CSL QIV:Comparator QIV
Randomised, observer-blinded, comparator-controlled immunogenicity and safety

QIV-03 Paediatric
N=2220 6 mth-4 years
CSL QIV:Comparator QIV
Randomised, observer-blinded, comparator-controlled immunogenicity and safety

Study TIV-10-69 (NH 2014/15)
Fever rates following vaccination in children aged 5 through 8 years

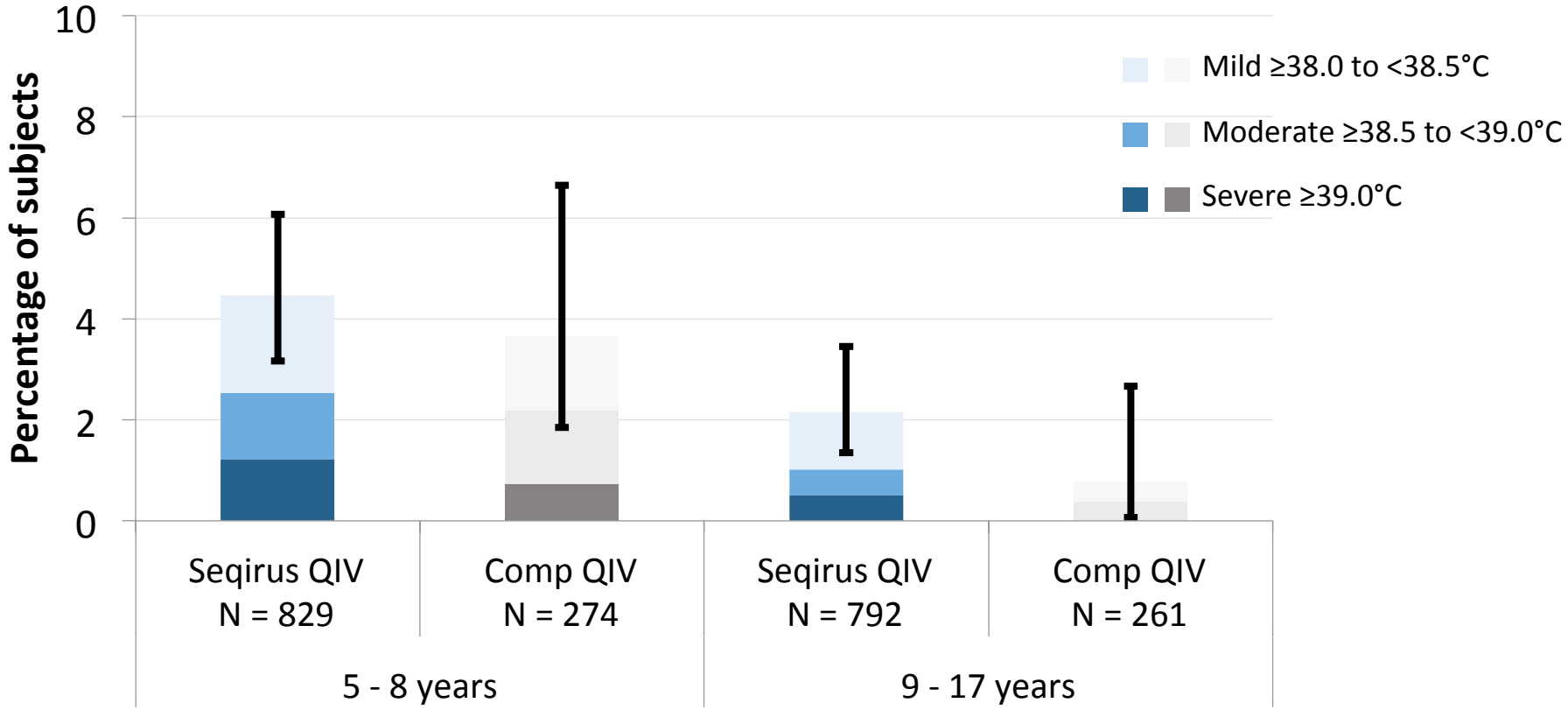
Previous TIV: B strain split at 0.6% TDOC, H3N2 at 1.5% TDOC, H1N1 at 0.9% TDOC
Study TIV: B strain split at 1.5% TDOC, H3N2 at 1.5% TDOC and H1N1 at 0.9% TDOC (within registered conditions)



- **Seqirus TIV fever rate similar to Reference QIV**
  - **Seqirus TIV: 8.2% (95% CI: 5.3, 12.0), Reference QIV: 9.2% (95% CI: 4.3, 16.7)**
- **Fever rate for Seqirus TIV in Study 07-36 (Brady *et al,* 2014) in children 5-8 years was 16%**
  - **Similar observation for severe fever: 10-69 (TIV): 2.1%: Study 07-36: 5%**

QIV-13-02: Paediatric 5-17yrs
Fever rates following vaccination in children 5 through 17yrs

Previous TIV: B strain split at 0.6% TDOC, H3N2 at 1.5% TDOC, H1N1 at 0.9% TDOC
Study 10-69 TIV: B strain split at 1.5% TDOC, H3N2 at 1.5% TDOC and H1N1 at 0.9% TDOC
QIV 13-02 with all strains split at 1.5% TDOC (within registered conditions)



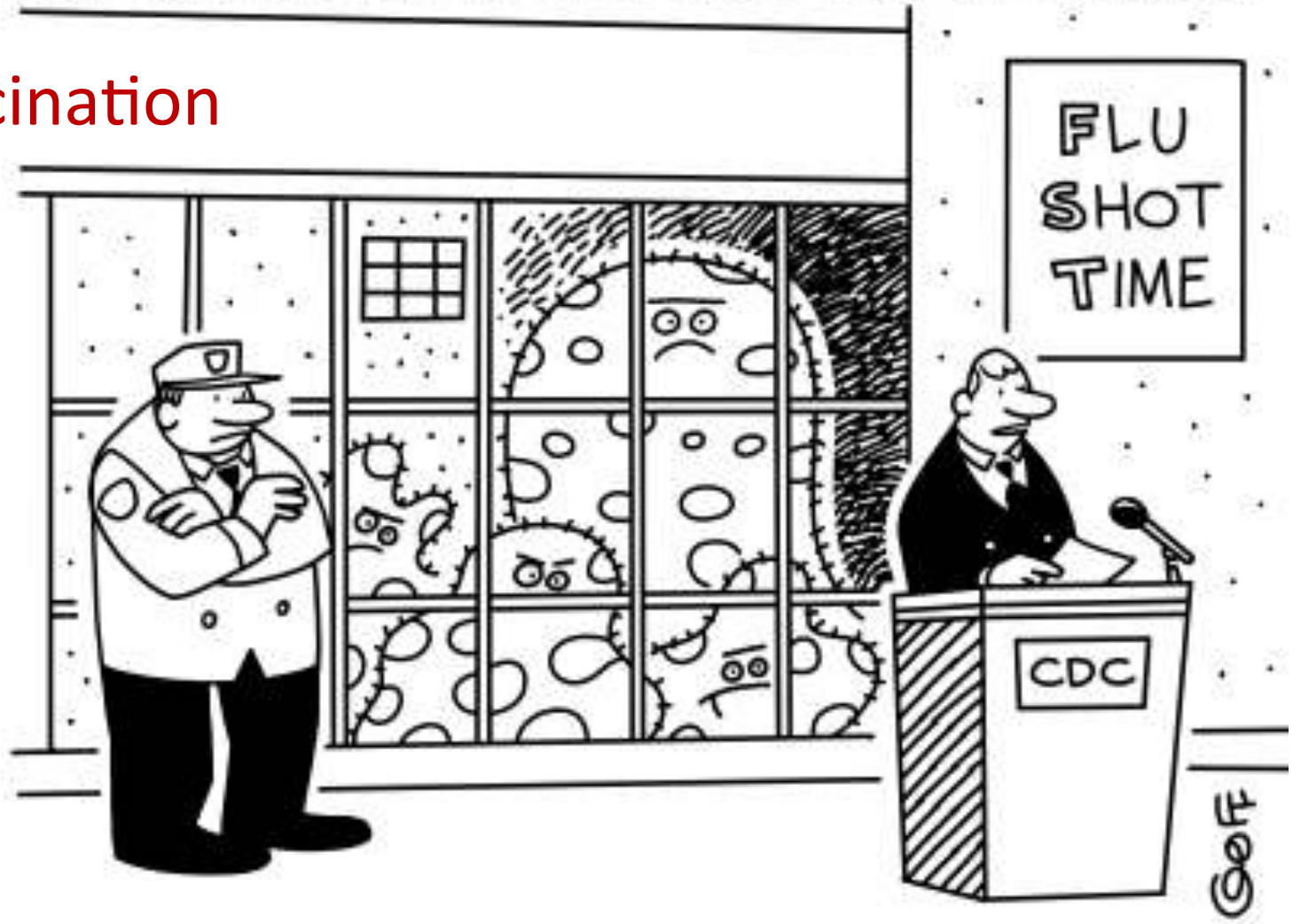
Seqirus QIV fever rate similar to Comparator QIV in both age groups

- **5 – 8 years: 4.5% (95% CI: 3.2, 6.1) vs 3.6% (95% CI: 1.8, 6.6)**
- **9 – 17 years: 2.1% (95% CI: 1.3, 3.4) vs 0.8% (95% CI: 0.1, 2.7)**

Summary

- Afluria QIV for 18 years and above: approved in USA and Australia
- 2 paediatric clinical studies demonstrate that the safety and tolerability profile of Seqirus' vaccine is similar to comparator vaccines
- Substantial attenuation of the fever response compared to previous Seqirus TIV formulations
- Safety and tolerability profile acceptable in children 5 through 8 years
- Proceed with a study in children 6m through 4 years: commenced in September 2016 (NH 2016/17)

Timing of Vaccination



"We all have less than a month before they are let out."

Children bring joy into our lives..

Sir Muir Gray, NHS Chief Knowledge Officer

Children bring joy into our lives..

and viruses.

Sir Muir Gray, NHS Chief Knowledge Officer