



# Challenges when measuring Influenza Vaccine Effectiveness In Europe

Collaboration between

- I-MOVE, Europe
- EU-Member states
- EU CDC
- REVELAC
- Australia
- Canada

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*On behalf of*

*The I-MOVE network*





# The I-MOVE network 2007 – 2015

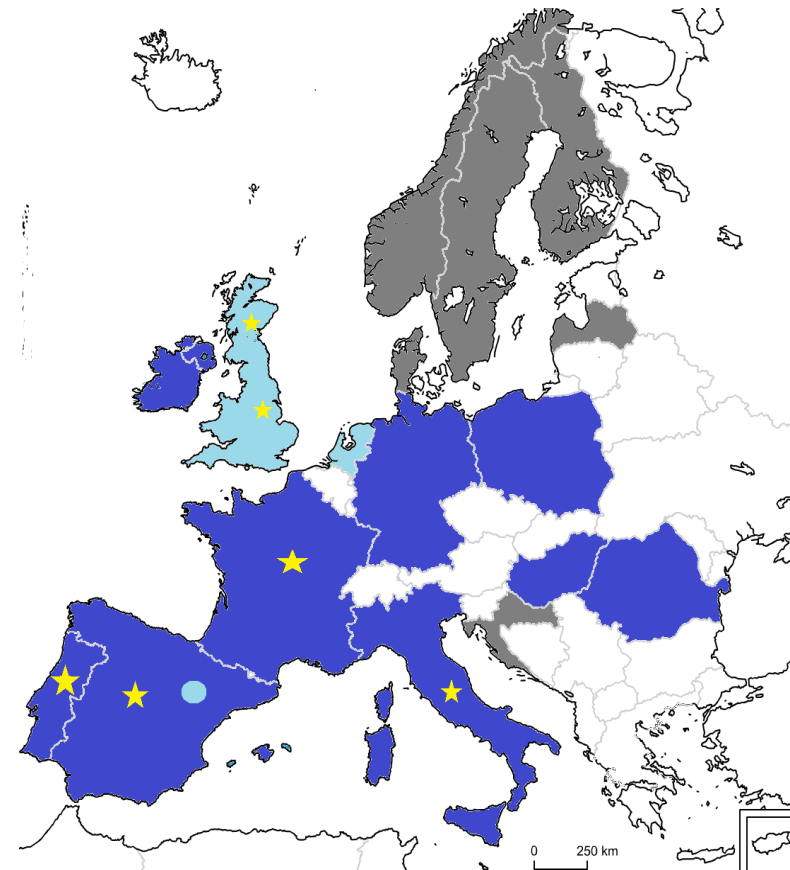
## ■ I-MOVE network

- ✓ 24 institutes + ECDC
- ✓ 17 Member States in EU / EEA
- ✓ Collaboration with:
  - WHO, WHO-EURO, EMA, USA, Canada,
  - Australia, Latin America

## ■ Studies in 15 sites since 2007

- ✓ Generic protocols
- ✓ National test negative design (TND) studies based on GP sentinel networks
- ✓ **Multicentre TND in up to 10 countries**
- ✓ Cohorts based on computerised registers
- ✓ Rapid case coverage VE estimates

-  Test negative design (TND)
-  Cohort with nested TND
-  Case coverage method
-  Partner institutes



# Influenza vaccine effectiveness

## Unanswered questions

- What is the average VE for H1N1, H3N2 & B over time?
- Is immunity waning in the season?
- What is the role of vaccinations in previous seasons?
- Can we / should we measure VE by vaccine type / brand?
- Can we provide robust VE results to guide WHO Committee on vaccine content?

# Methods: Multicentre test negative design study

## I-MOVE network, 8 EU countries, 2008-15

### ■ Study population

Patients consulting for ILI/ARI in >1000 GP practices

- ✓ **Systematic statistical sampling** of ILI/ARI patients to swab
- ✓ Confirmation with RT-PCR or culture
- ✓ EU ILI, swabbed <8 days after symptom onset

### ■ Test-negative design (sub type-specific analysis)

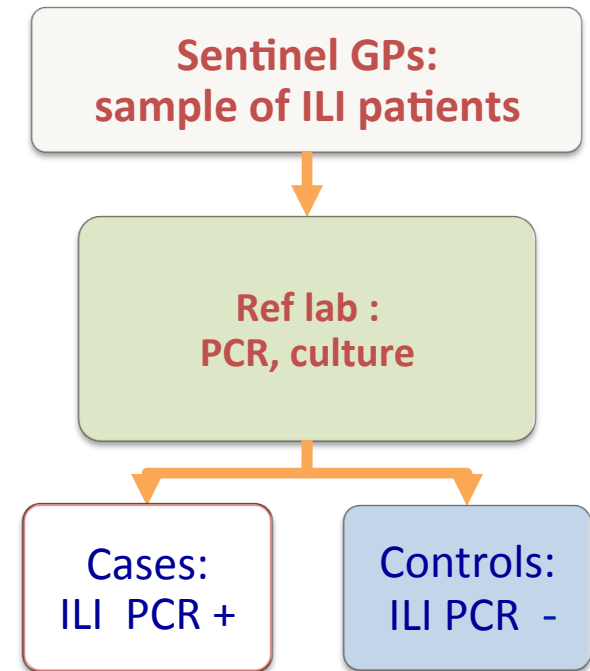
Case	Influenza (type/subtype) positive
Control	Influenza negative

### ■ Study period

Start	>14 days after vaccination campaign begin
End	Two weeks after last case

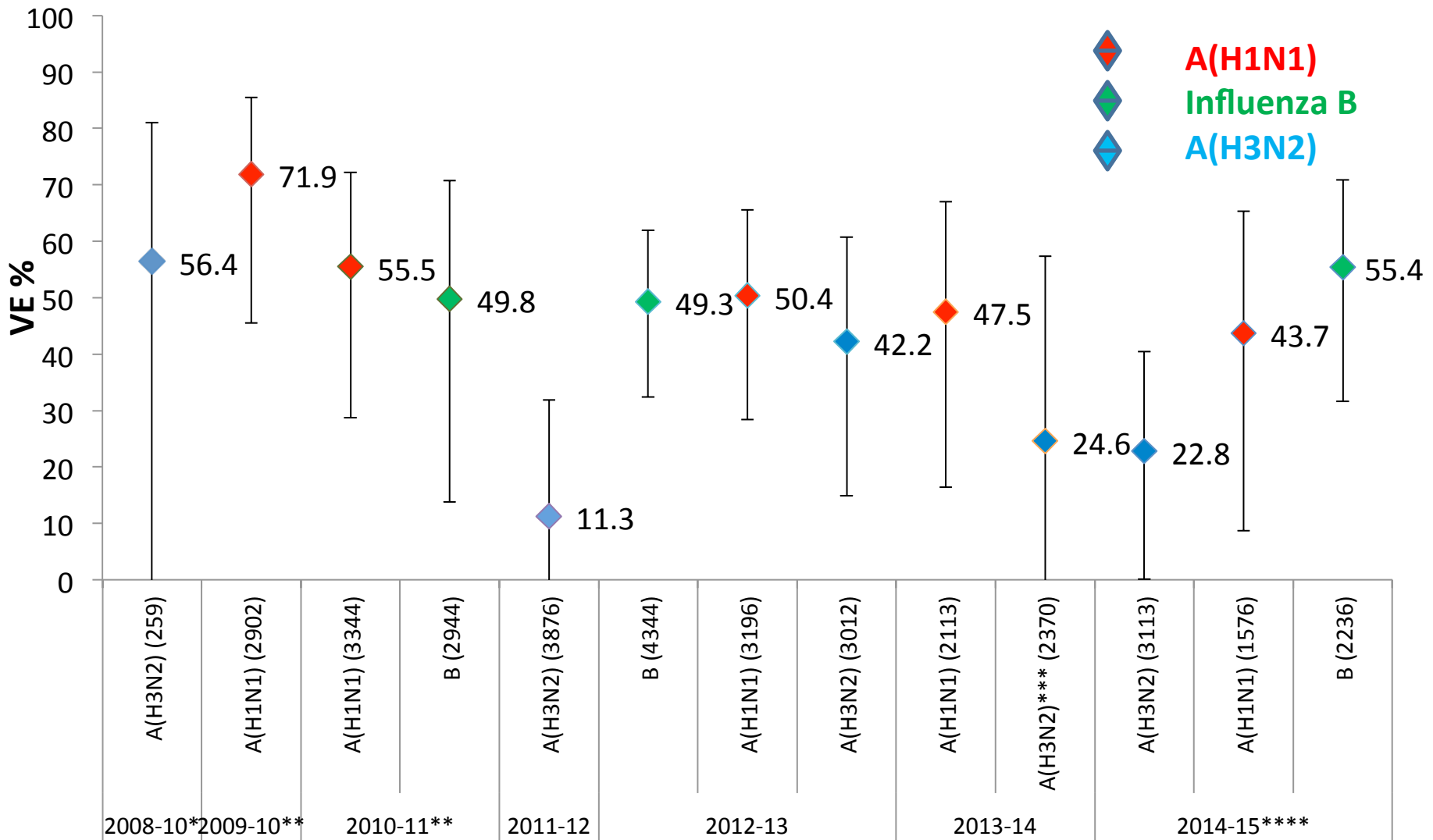
### ■ Vaccinated

Onset	>14 days after vaccination
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# Adjusted VE, all ages, by type/subtype and season

## I-MOVE 2008/9-2014/15



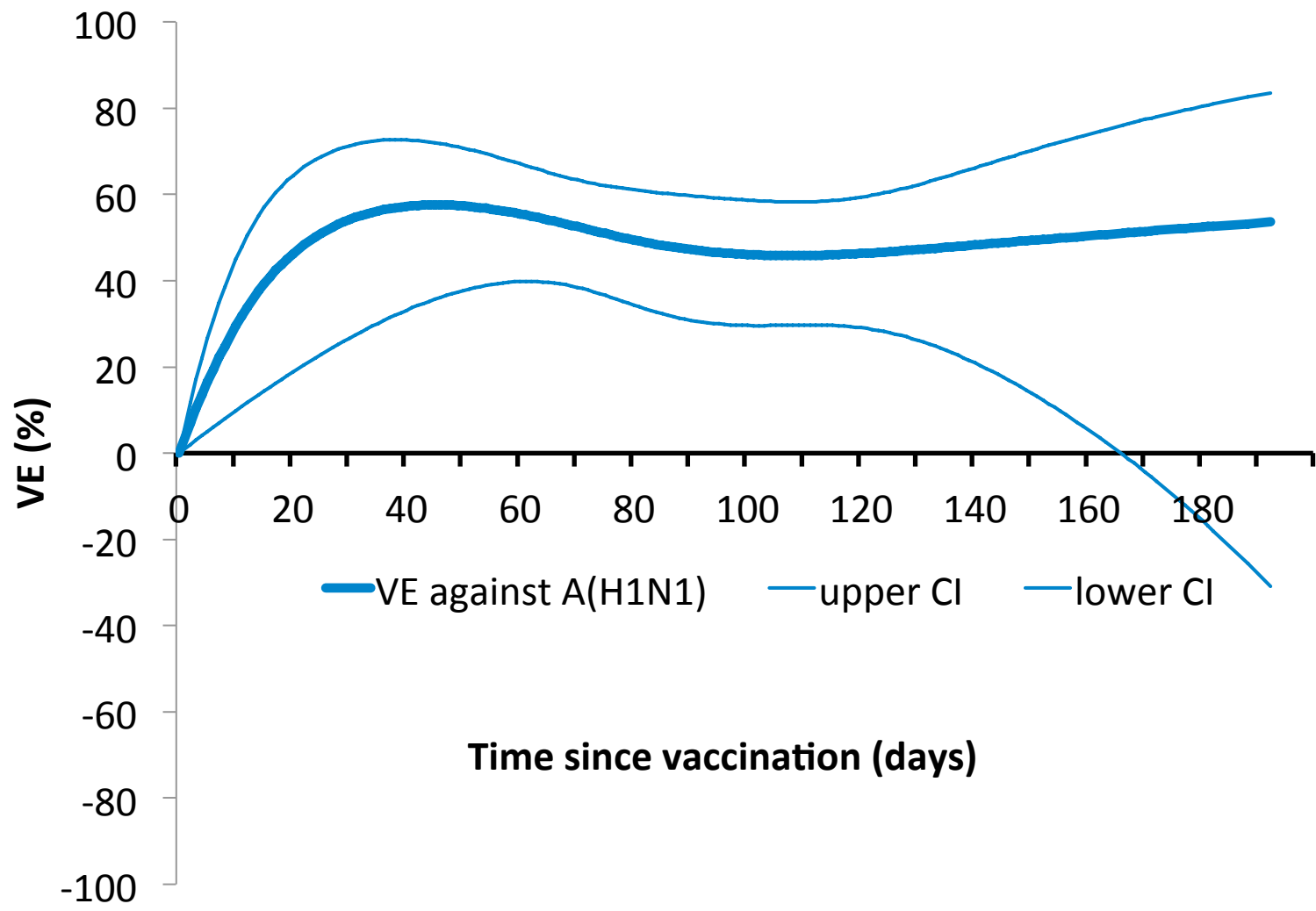
\* Among those ages 65 and older; \*\* Imputed analysis, \*\*\* 2-stage model, \*\*\*\* Estimates up to w9, 2015

## Pooled VE over 5 seasons, I-MOVE, 2011-2015

Type/ sub-type	Sample size Cases/controls	VE%	Lower limit	Upper limit
<b>A(H1N1)</b>	10193 (3013;7180)	<b>50.5</b>	39.1	59.7
<b>Influenza B</b>	9406 (3195;6211)	<b>52.0</b>	40.9	61.0
<b>A(H3N2)</b>	12477 (4437;8040)	<b>20.5</b>	8.1	31.3

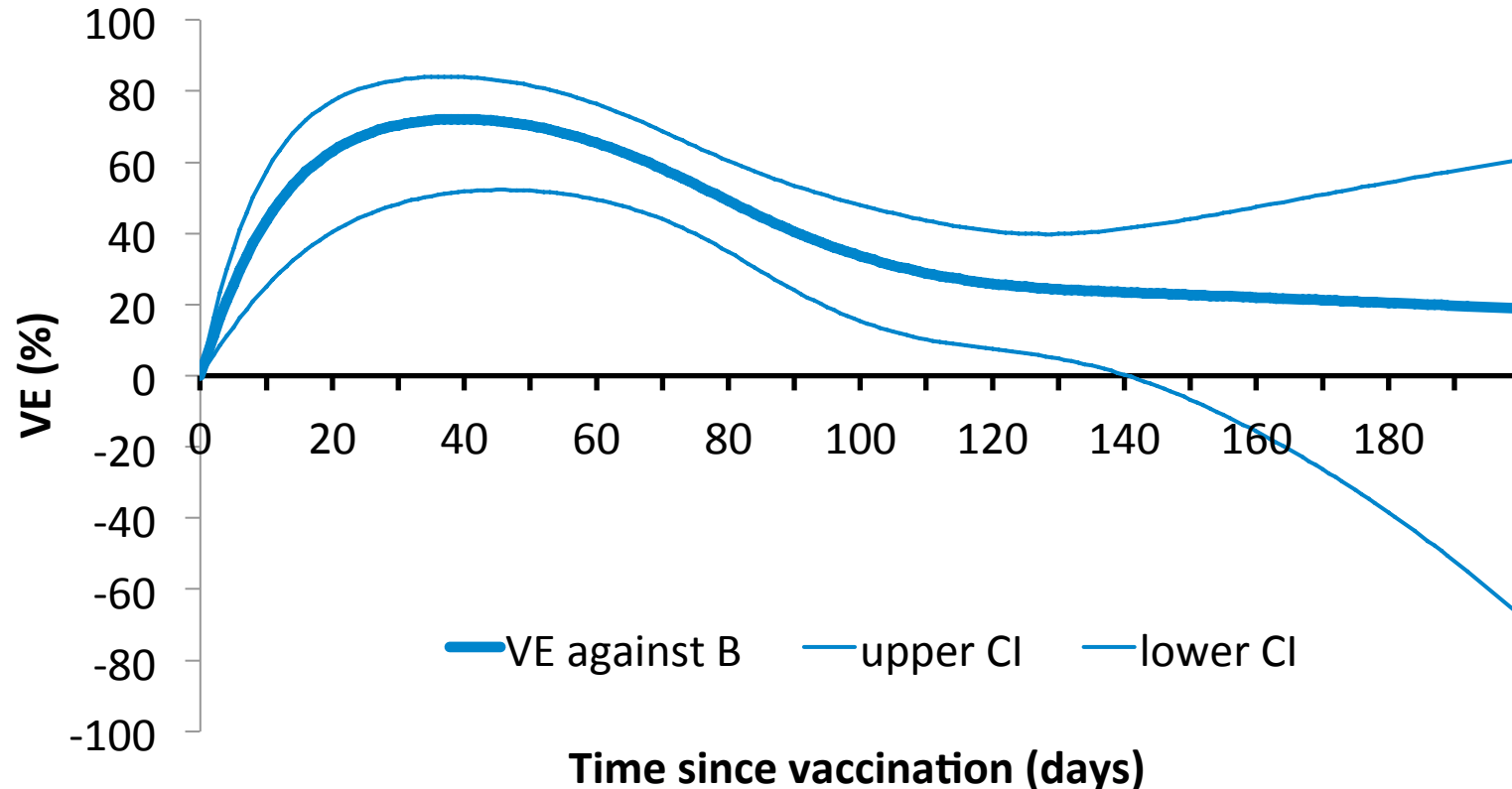
# Waning immunity?

VE against **A(H1N1)** by time since vaccination (days), all ages, **whole season**, I-MOVE 2010-11 to 2014-15



# Waning immunity?

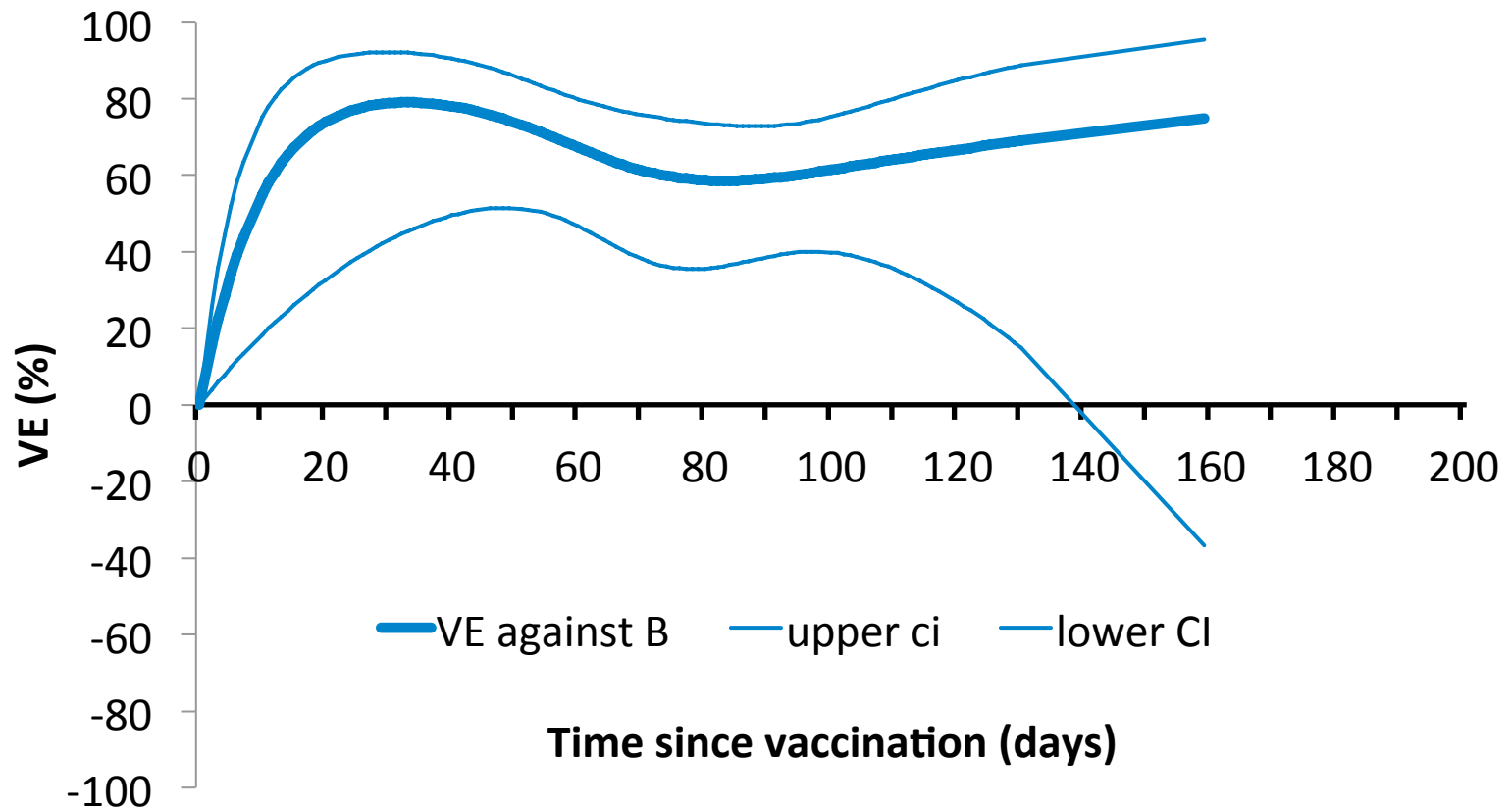
VE against **influenza B** by time since vaccination (days), all ages, **overall season**, I-MOVE 2010-11 to 2014-15





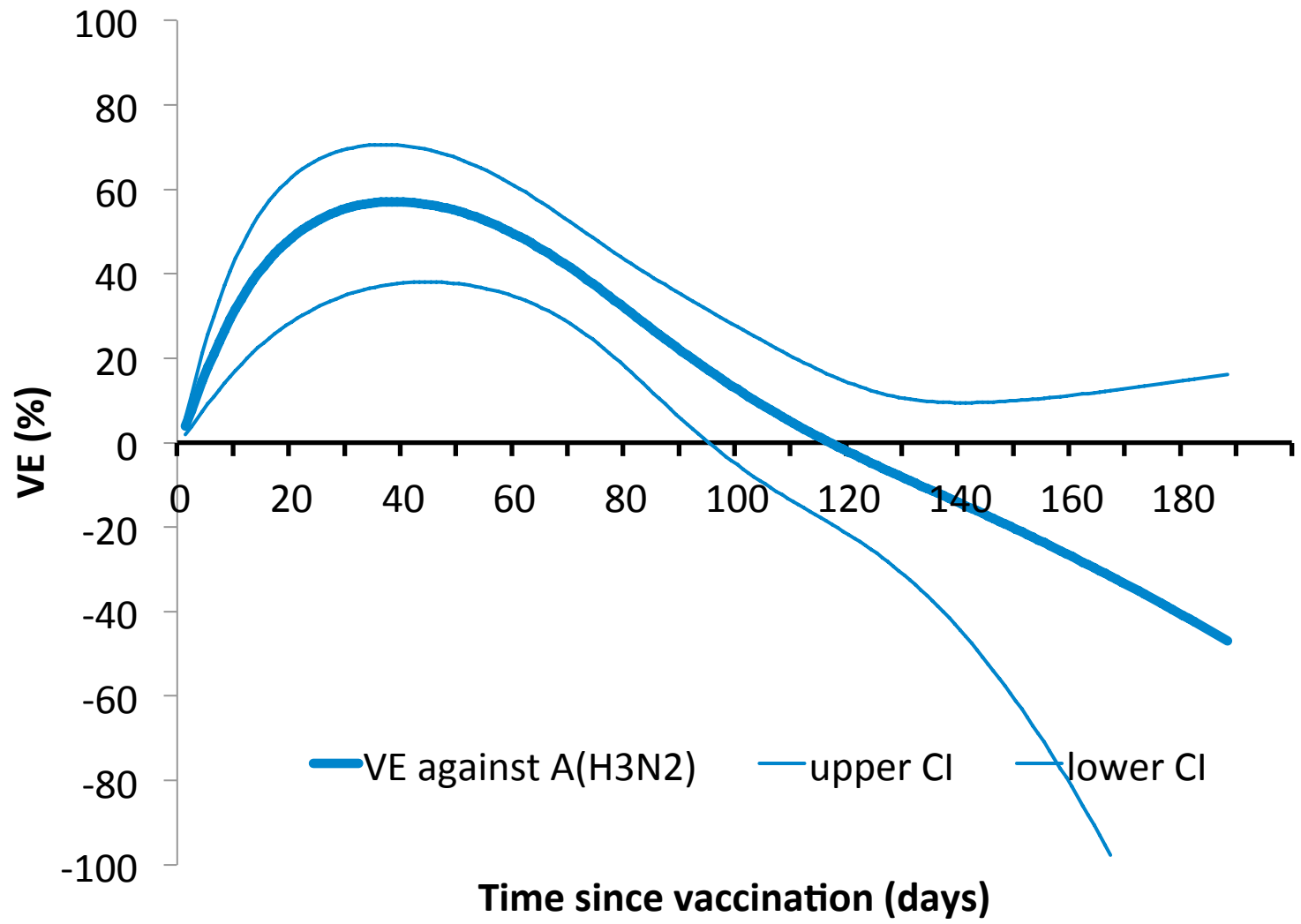
# Waning immunity?

VE against **influenza B** by time since vaccination (days),  
all ages, **early season**, I-MOVE 2010-11 to 2014-15



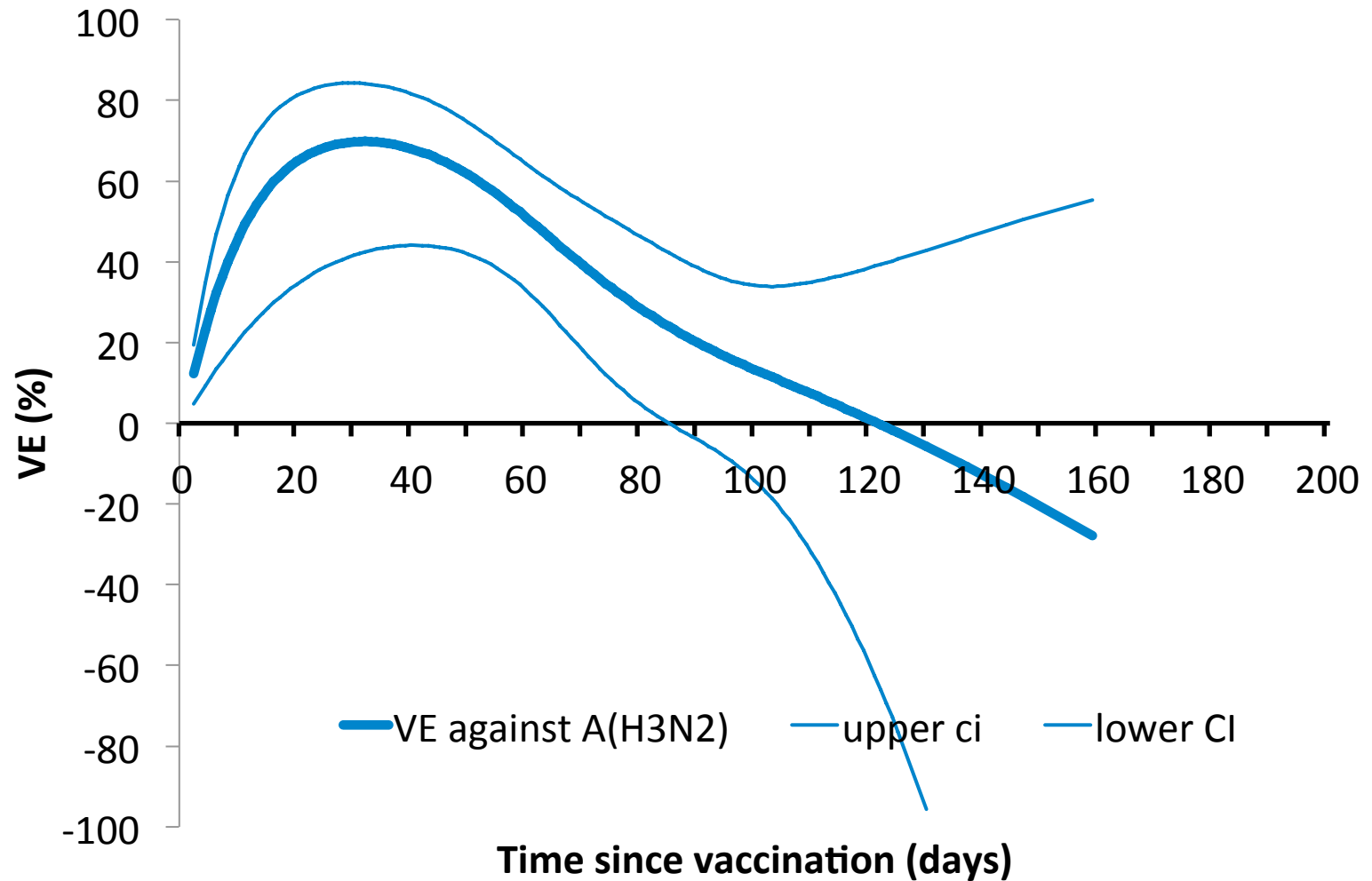
# Waning immunity?

VE against **A(H3N2)** by time since vaccination (days), all ages, **overall season**, I-MOVE 2010-11 to 2014-15



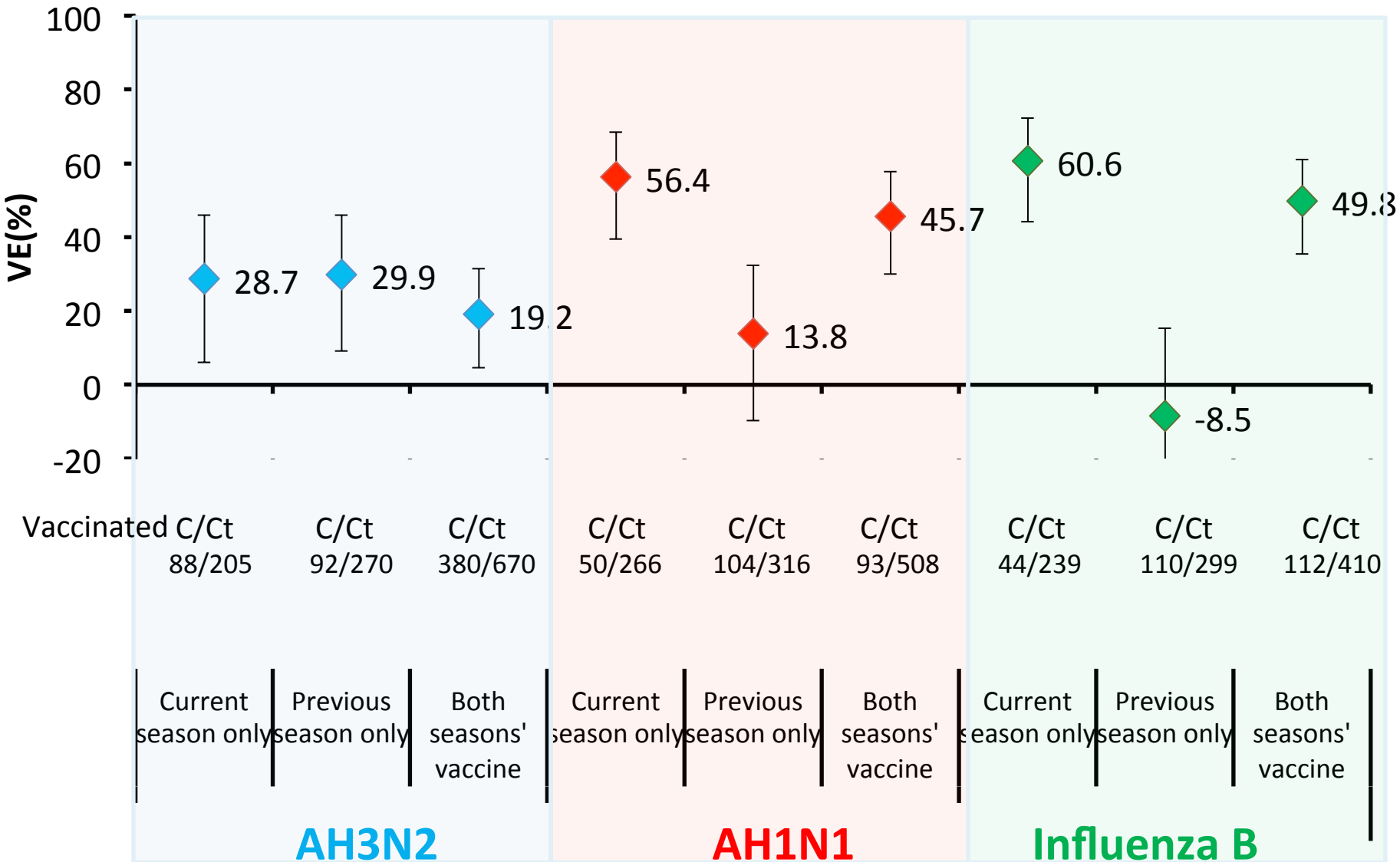
# Waning immunity?

VE against **A(H3N2)** by time since vaccination (days),  
all ages, **early season**, I-MOVE 2010-11 to 2014-15



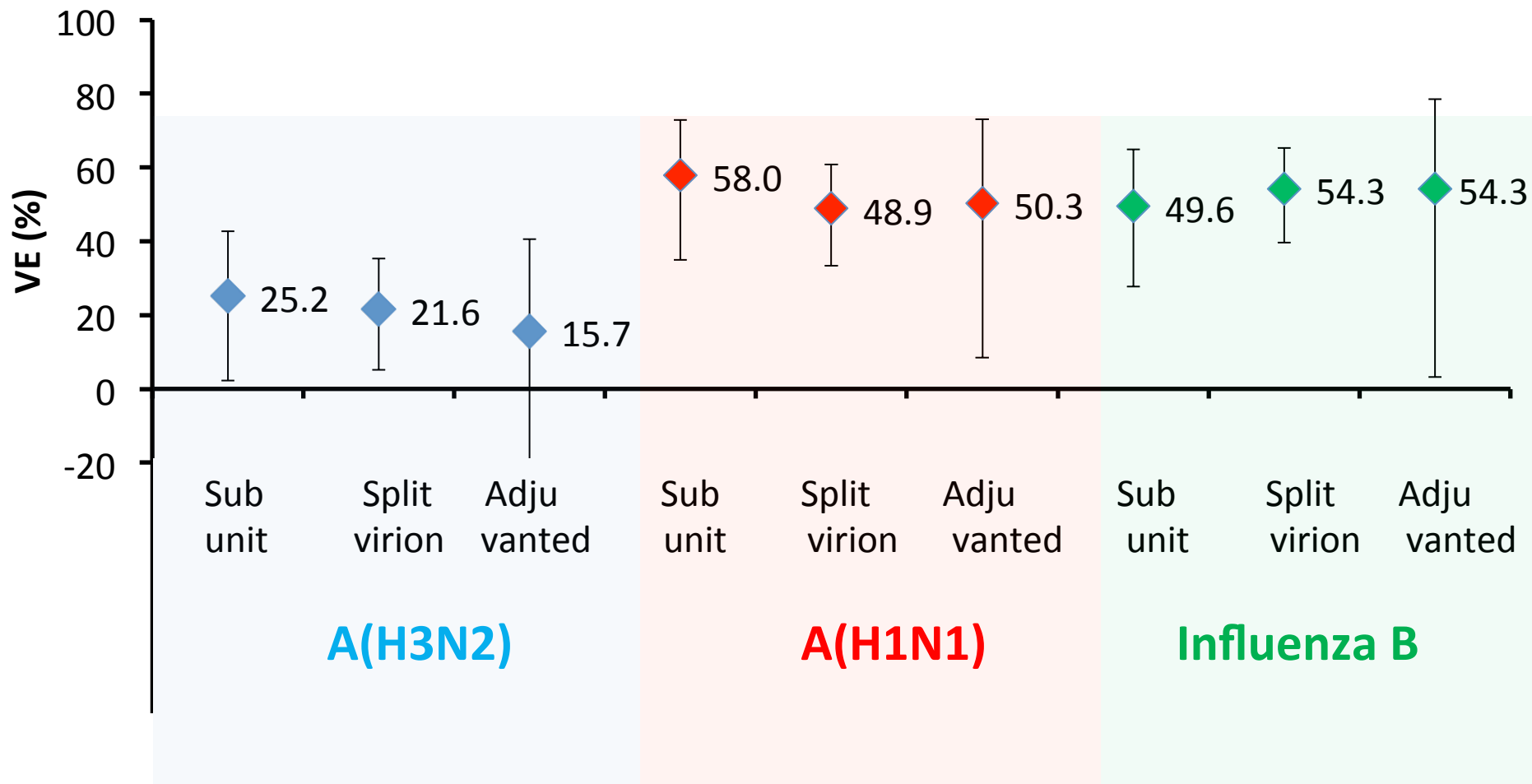
# Is former vaccination affecting current VE?

Adjusted VE by **current and previous season** vaccination status, by type/subtype, I-MOVE 2010-11 to 2014-15



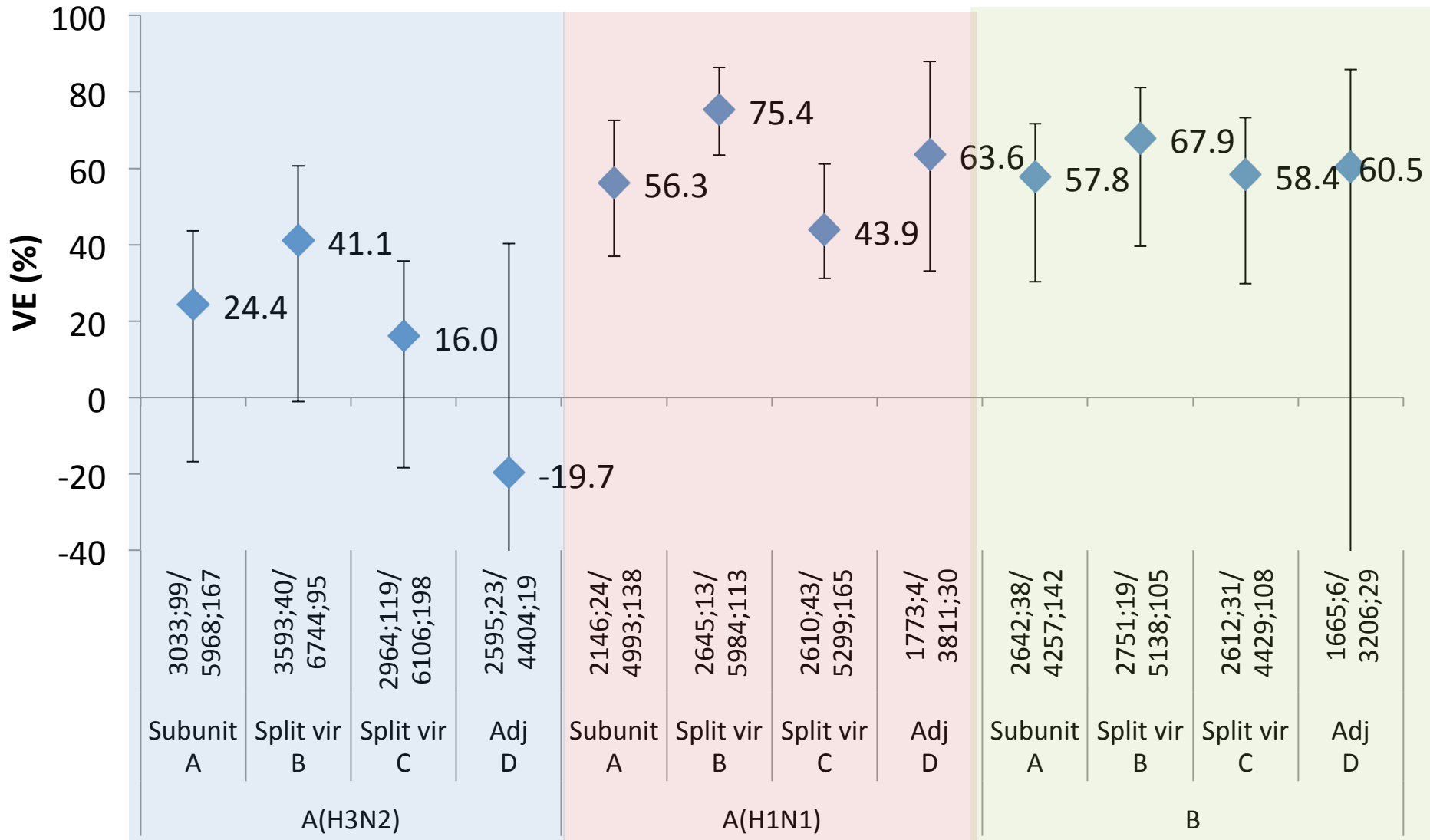
# Does VE vary by vaccine type?

## Adjusted **vaccine type**-specific VE, by type/subtype, I-MOVE 2010-11 to 2014-15

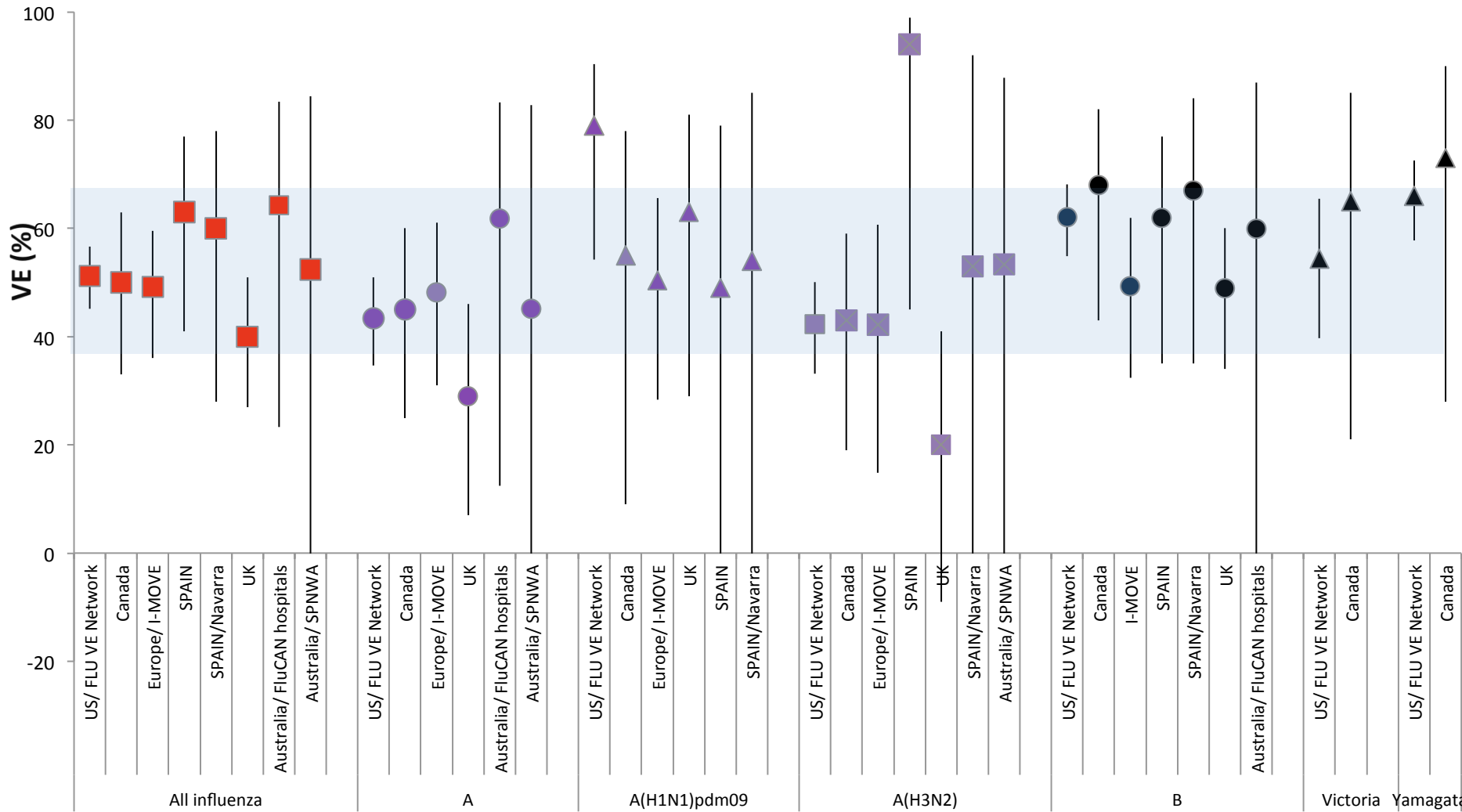


# Does VE vary by vaccine brand?

## Adjusted **vaccine brand**-specific VE, by type/subtype, I-MOVE 2010-11 to 2014-15



# GIVE: Estimates of influenza vaccine effectiveness all age groups provided to WHO by virus type/subtype, 2013 season, eight study sites (six North & two South hemisphere)



Source: United Kingdom National; Canada National, Europe I-MOVE network, Navarra Spain, Spain National, UK National, USA Flu VE Network; Denmark National; Australia GP network..

# How can we respond to the challenge?

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- Larger sample size
- Multicentre studies / Pooling countries & years?
- Joint large laboratory and VE studies
  - ✓ Increase number and representativeness of strains characterised
  - ✓ **Quantified** viral change in season
  - ✓ Robust vaccine effectiveness results early in season
- International collaboration
- Sustainable national & international funding



- **Patients**
- **Influenza Sentinel networks**
- **Study sites I-MOVE**



Thanks

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USA, Canada & Australia  
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