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**Effectiveness of 10- and 13-valent  
pneumococcal conjugate vaccines against  
invasive pneumococcal disease in children <5 years:  
lessons learnt from SpIDnet multicentre study**

# SpIDnet network

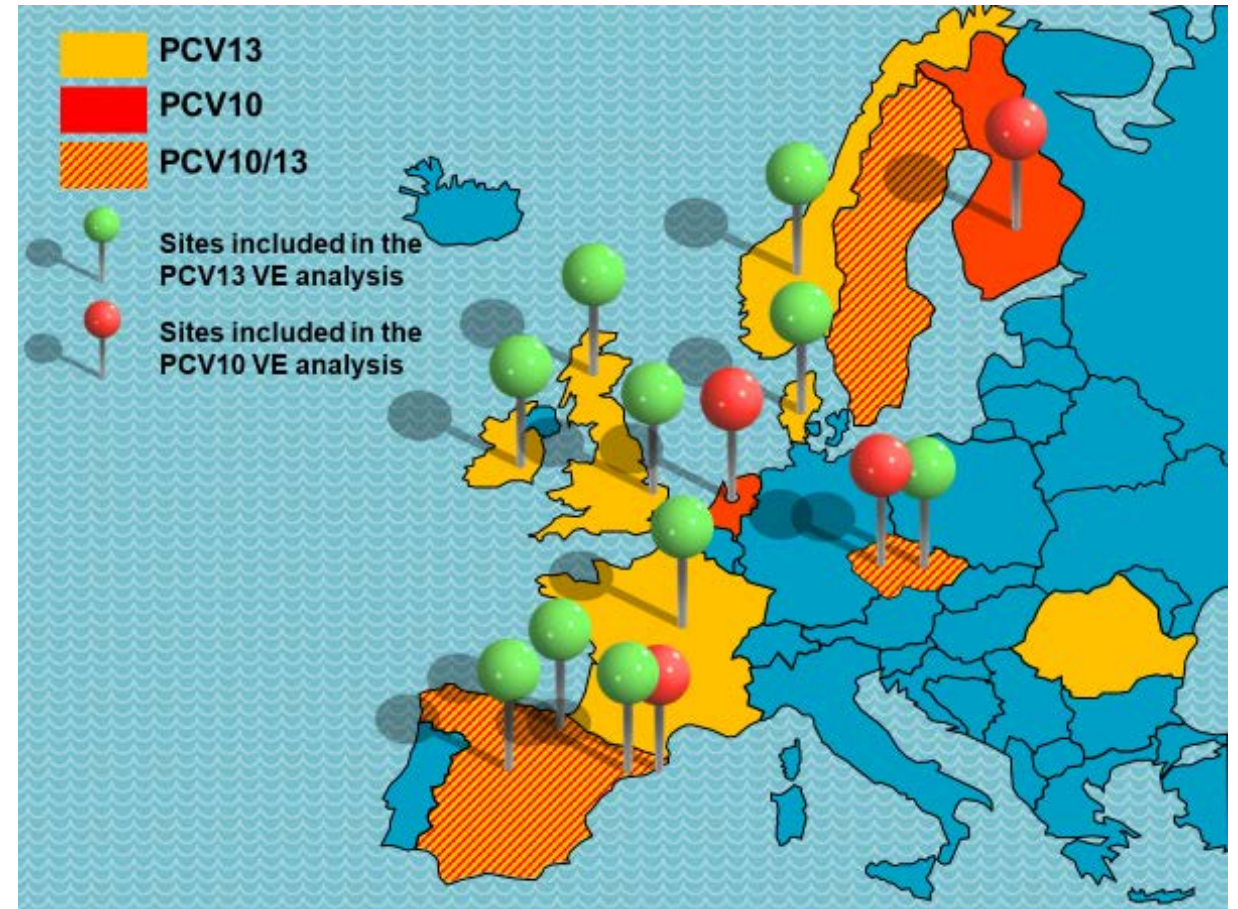
## Background and objective

### Enhanced Invasive Pneumococcal Disease (IPD) surveillance

- Since 2012
- 7.2 mil. children <5 years (2018)

### Objective

- To measure vaccine **effectiveness** of **PCV10** and **PCV13** and summarise lessons learnt from pooling surveillance data from the sites using these vaccines



- 2+1 (9 sites)/ 3+1 (4 sites up to 2016 and 1 site after)
- VC > 90% (11 sites) / VC=67-77% (2 sites)

# PCV13 effectiveness: **Methods**

**Study data:** SpIDnet surveillance (10 sites) using a common protocol

## Study design

- Indirect cohort method

**Cases by** serotype categories: PCV13st, PCV7st, PCV13non7st, PCV13-related (VRT)

**Controls:** nonPCV13 IPD excluding vaccine-related serotypes (VRT: same serogroup as the vaccine serotypes)

## Exposure

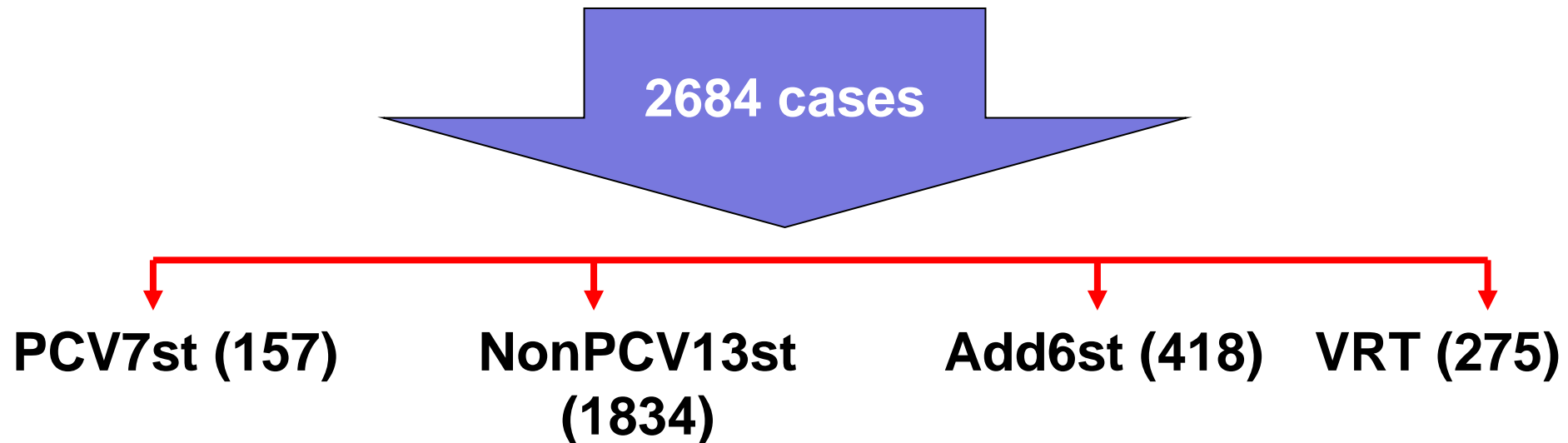
- **At least one dose** vaccination PCV13
- **Fully vaccinated** PCV13 (3 or 4 doses in children > 1 year old)

## Analysis

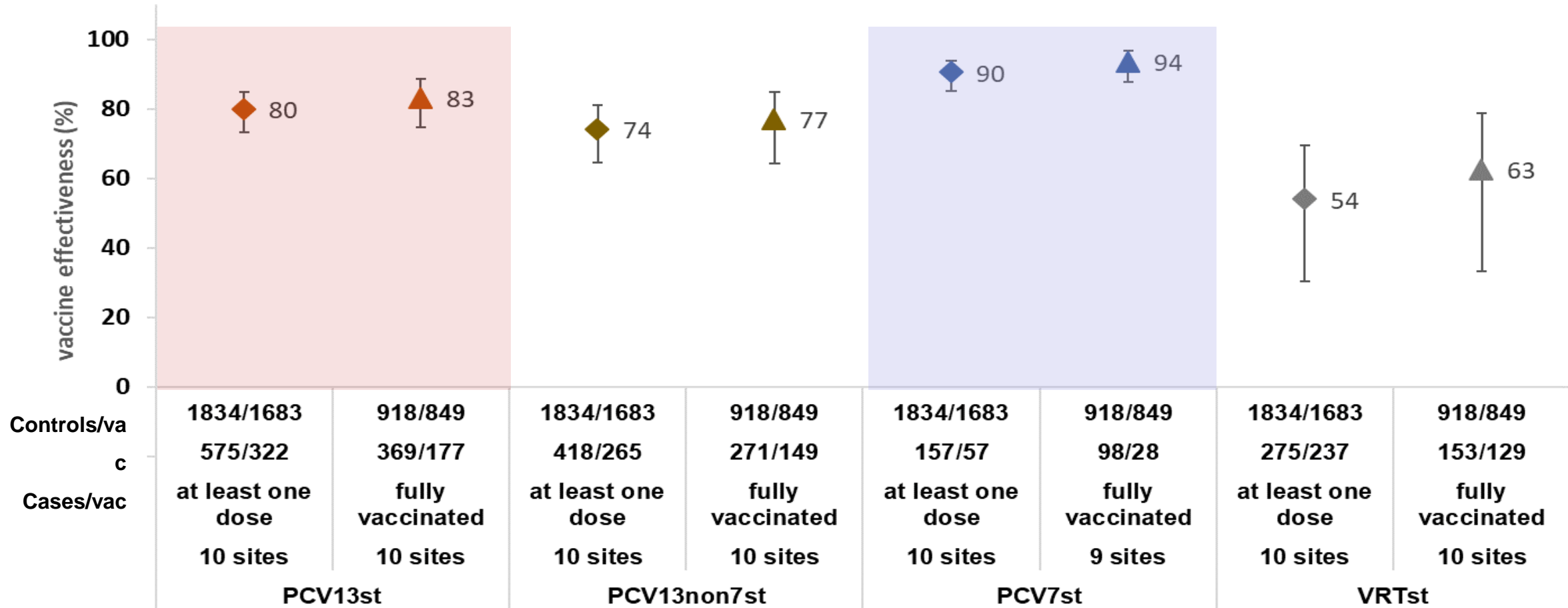
- $VE=(1-OR)*100$ ; site as fixed effect
- Logistic regression/penalized logistic regression with event / parameter = 10 →  
adjustment for: site, age, at least one underlying disease and year of notification

# Data inclusion and exclusion for complete case PCV13 effectiveness study – at least one dose PCV

- 4649 children <5 years
- 4119 children in sites using PCV13 (10 sites)
- 3700/ 4119 (90%) hospitalized children eligible for PCV13 vaccination with brand available
- 3374/ 3700 (91%) children 2/3mo-4y
- 2940/ 3374 (87%) with serotype available (excluding not-typable and serotype stated as “others”)
- 2883/ 2940 (98%) with vaccination data available
- 2684/2883 (93%) with underlying condition available



# Adjusted **PCV13 VE** against categories of IPD serotypes by vaccination status, SpIDnet multicentre study, 2012-18



Adjusted for site, age, underlying conditions, year of notification

# Conclusions and lessons learnt (1)

- High VE overall for both vaccines
  - point estimates > 80% for most analyses

## **Advantages** of indirect cohort method

- Use of **surveillance data** only
- **Laboratory-confirmed** outcome: > 87% IPD with serotype available
- **Design** minimises bias due to health seeking behaviour and IPD severity
- **Validated** against matched case control studies (*De Serres, 2012*)

# Lessons learnt (2)

## Limitations

- **Observational study:** unmeasured confounders
- **High vaccine uptake** → Small sample size

## Assumptions

- **Fixed effect:** similar vaccine effect in all sites
  - **Statistical heterogeneity:**  $I^2=27%$  (crude VE) /  $39.5%$  (adjusted VE) for at least one dose PCV13 VE
- Check **VE of serotypes with the same groups as vaccine** → excluded from analysis
- **Effect of vaccine in carriage**
  - complete serotype replacement in carriage → increased risk for non-vaccine types IPD
  - VE overestimated by 2-5%, *Andrews 2011*

# SpiDnet team

## At the surveillance sites:

### Professionals from participating hospitals and laboratories in each site

**Czech Republic:** P. Krizova, J. Kozakova, H. Sebestova, M. Maly

**Denmark:** P. Valentiner-Branth, T. Dalby, Z. Harboe, HC Slotved, K. Fuursted

**France:** K. Danis, S. Georges, C. Levy, R. Cohen, E. Varon, M.C. Ploy, J. Gaillat, D. Levy-Bruhl

**Finland:** H. Rinta-Kokko, P. Nuorti

**Ireland:** J. Mereckiene, S. Cotter, M. Corcoran, H. Humphries

**Netherlands:** M. Knol, L. Mollema, A. Van der Ende, W. van der Hoek, G. Berbers, H. de Melker, E. Sanders

**Norway:** B. Winje, D. Vestrheim, M. Bergsaker

**Romania:** M. Pana, V. Alexandrescu

**Sweden:** B. Henriques Normark, E. Morfeldt, J. Darenberg, T. Lepp, A. Lindstrand

**Scotland, UK:** L. Macdonald, A. Smith, B. Denham, B. Jones, C. Cameron

**England and Wales, UK:** S. Ladhani, Z. Amin, N. Fry

**Spain:** R. Cano, M. Viarce Torres (national level)

- **Catalonia:** P. Ciruela, C. Izquierdo, C. Muñoz-Almagro, S. Broner, R. Pallarés
- **Madrid:** S. De Miguel, L. Garcia, J. C. Sanz, M. Ordobas
- **Navarre:** M. Guevara, J. Castilla, M.E. Portillo, C. Ezpeleta, A. Gil-Setas

**At the ECDC:** E. Colzani, P. Naucler, L. Pastore Celentano

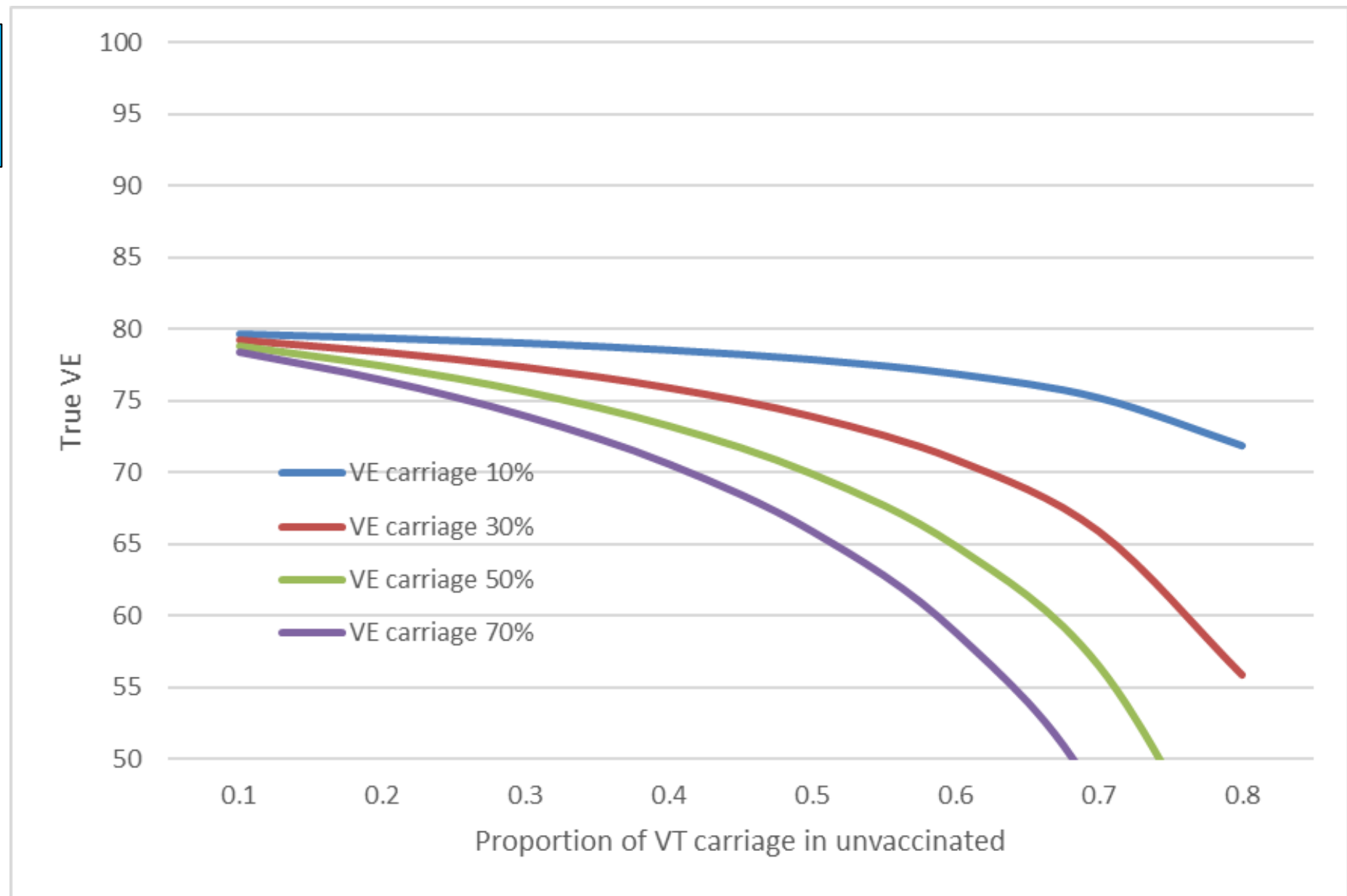
**At the coordination:** C. Savulescu, G. Hanquet, E. Kissling, M. Valenciano, A. Moren – EpiConcept



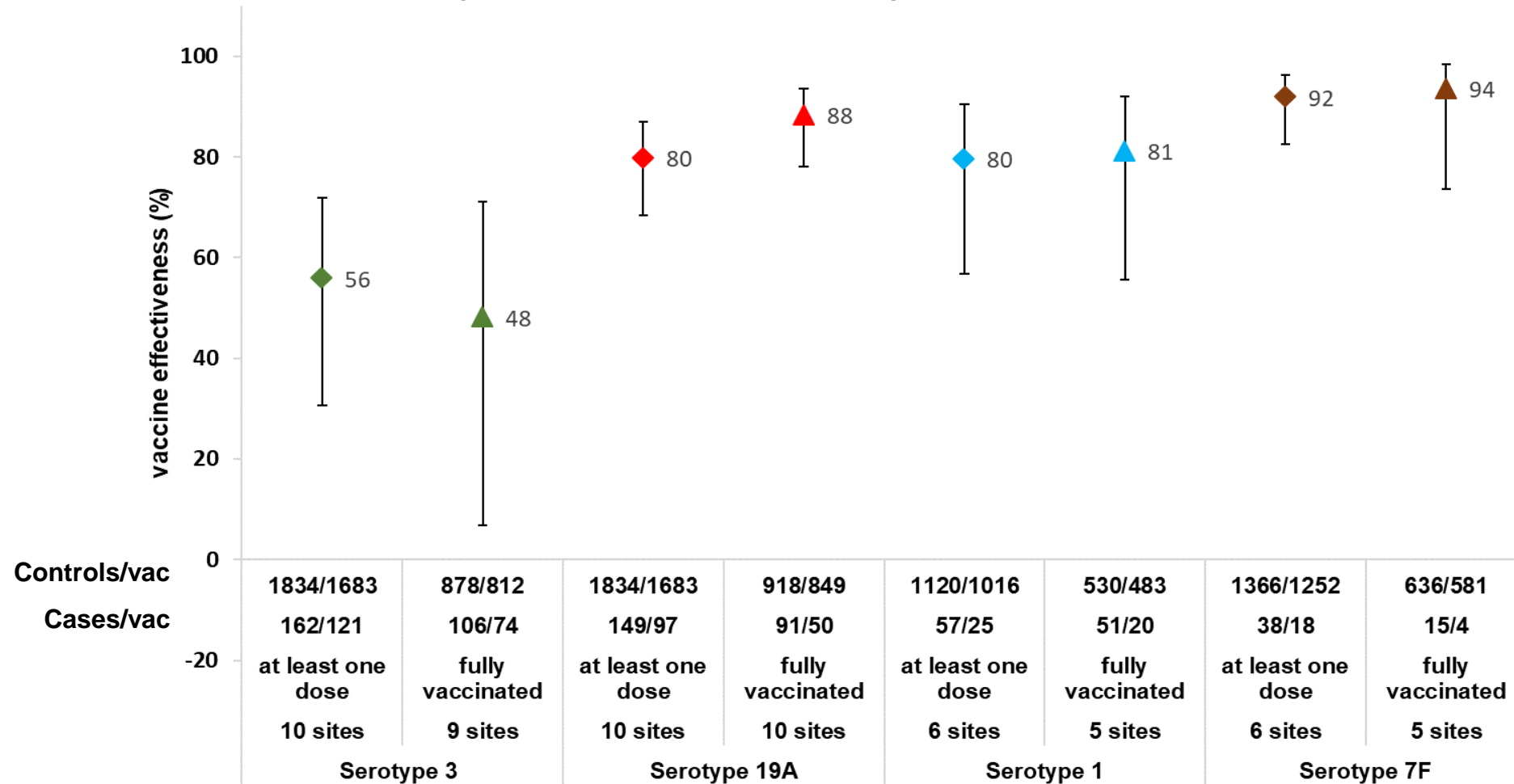
**Thank you!**  
**Děkuji!**  
**Tak!**  
**Merci!**  
**Takk!**  
**Dank je!**  
**Multumesc!**  
**Gracias!**  
**Tack!**  
**Kiitos!**

Extra slides

$VE_{\text{Broome}} = 0.79$   
9  
 $P_u(\text{IPD}) = 0.44$

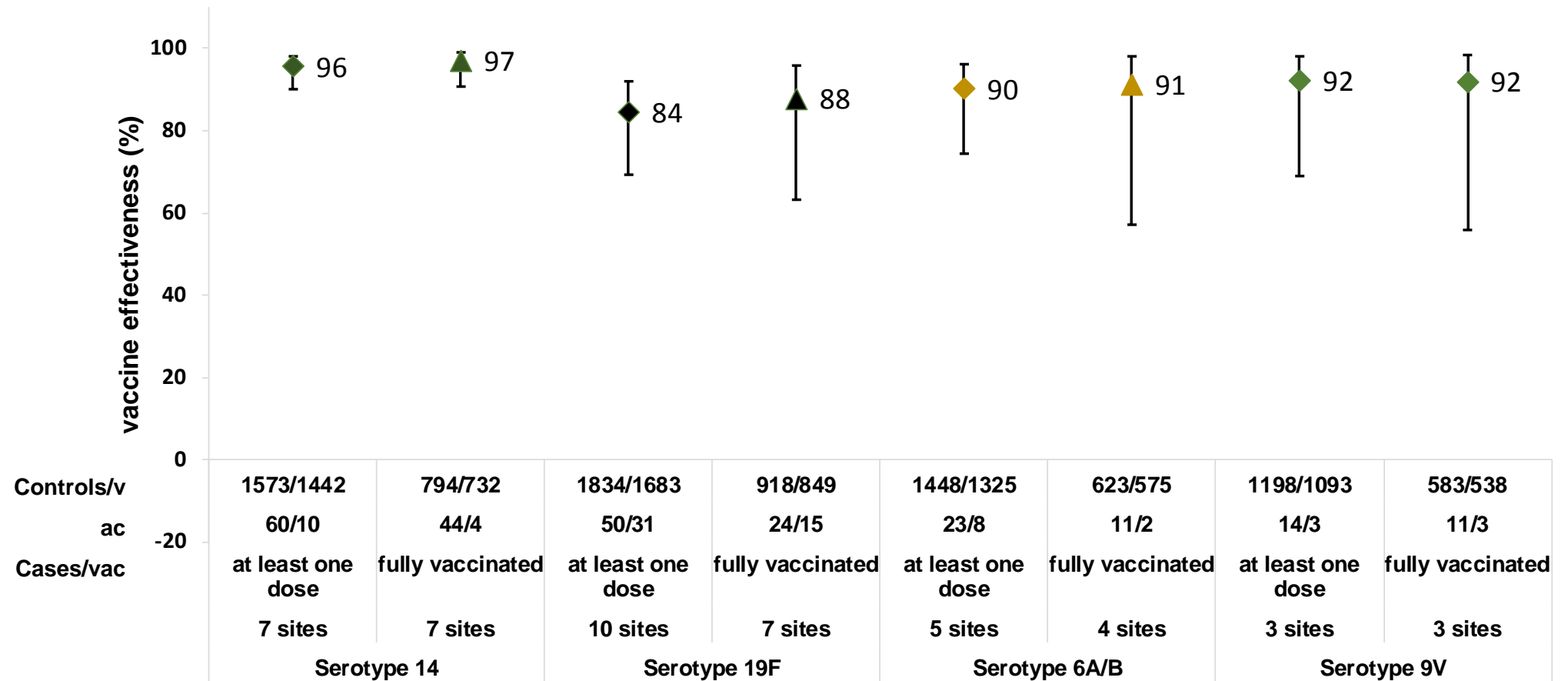


## Adjusted PCV13 VE against PCV13 specific serotype IPD by vaccination status, SpIDnet multicentre study, 2012-2018



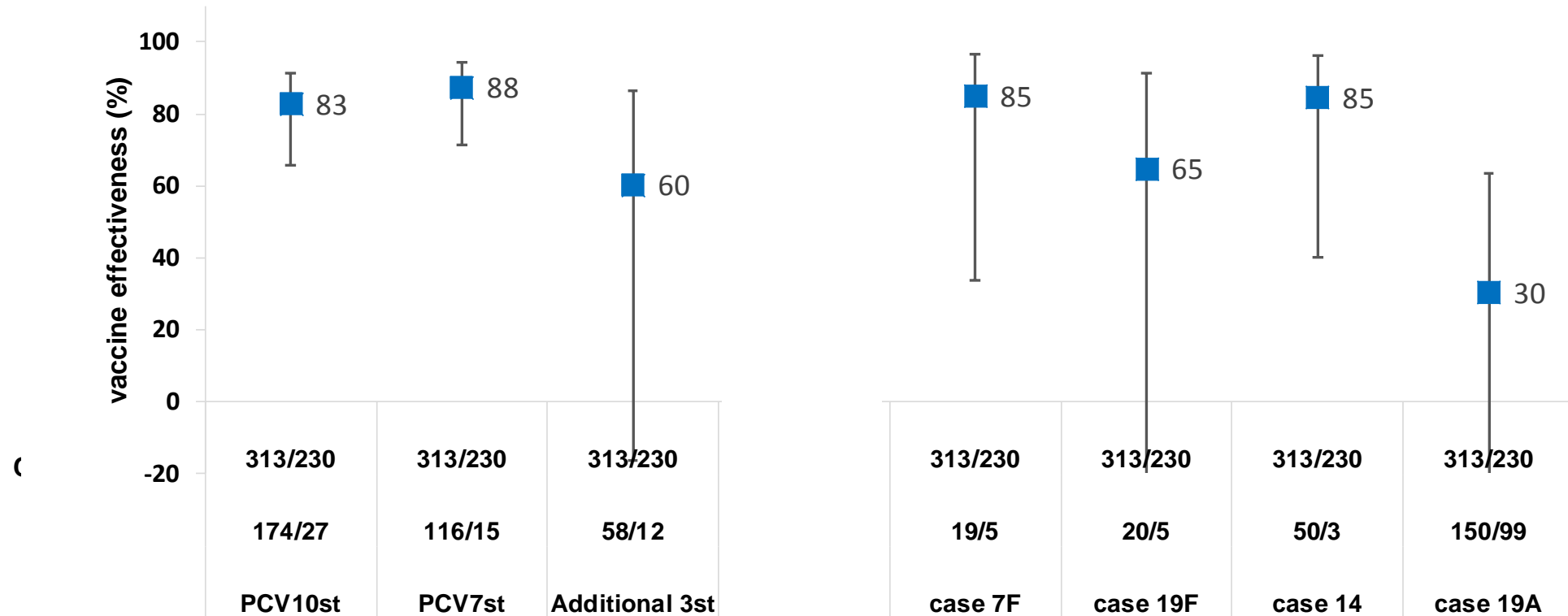
Adjusted for site, age group, underlying conditions, year of notification

## Adjusted **PCV13** VE against **specific serotype IPD** by vaccination status, SpIDnet multicentre study, 2012-2018



Adjusted for site, age, underlying conditions, year of notification

# Adjusted VE of **at least one dose PCV10** against **IPD serotypes**, SpIDnet2 multicentre study, 2011/2-2018 (n=4)



Adjusted for site, age group, year of notification