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Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance

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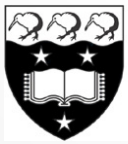
Feb 2012



THE UNIVERSITY OF AUCKLAND
FACULTY OF MEDICAL AND HEALTH SCIENCES

Aims

- Robust estimation of the protective effect of seasonal influenza vaccine in the prevention of:
  - Hospitalised influenza
  - community influenza (presenting to General Practice)
- Investigate over 5 different seasons
- Investigate differential protective effects among subpopulations
  - Age
  - Co-morbidities
  - Ethnicity

Vaccine Effectiveness : Project Team

- ESR: lead
  - Sue Huang PI
- University of Auckland
- University of Otago

VE Study team

- Nikki Turner(UoA) PI.
- Nevil Pierse (UoO) and Ange Bissielo (ESR) bio-stats and analysis
- Heath Kelly (Australian epidemiologist, influenza VE expert) mentoring/advisory
- Epidemiology support: Don Bandaranayke (ESR), Michael Baker (UoO)
- CDC support: Marc-Alain Widdowson, Dianne Gross, David Shay

Tools: Two surveillance systems

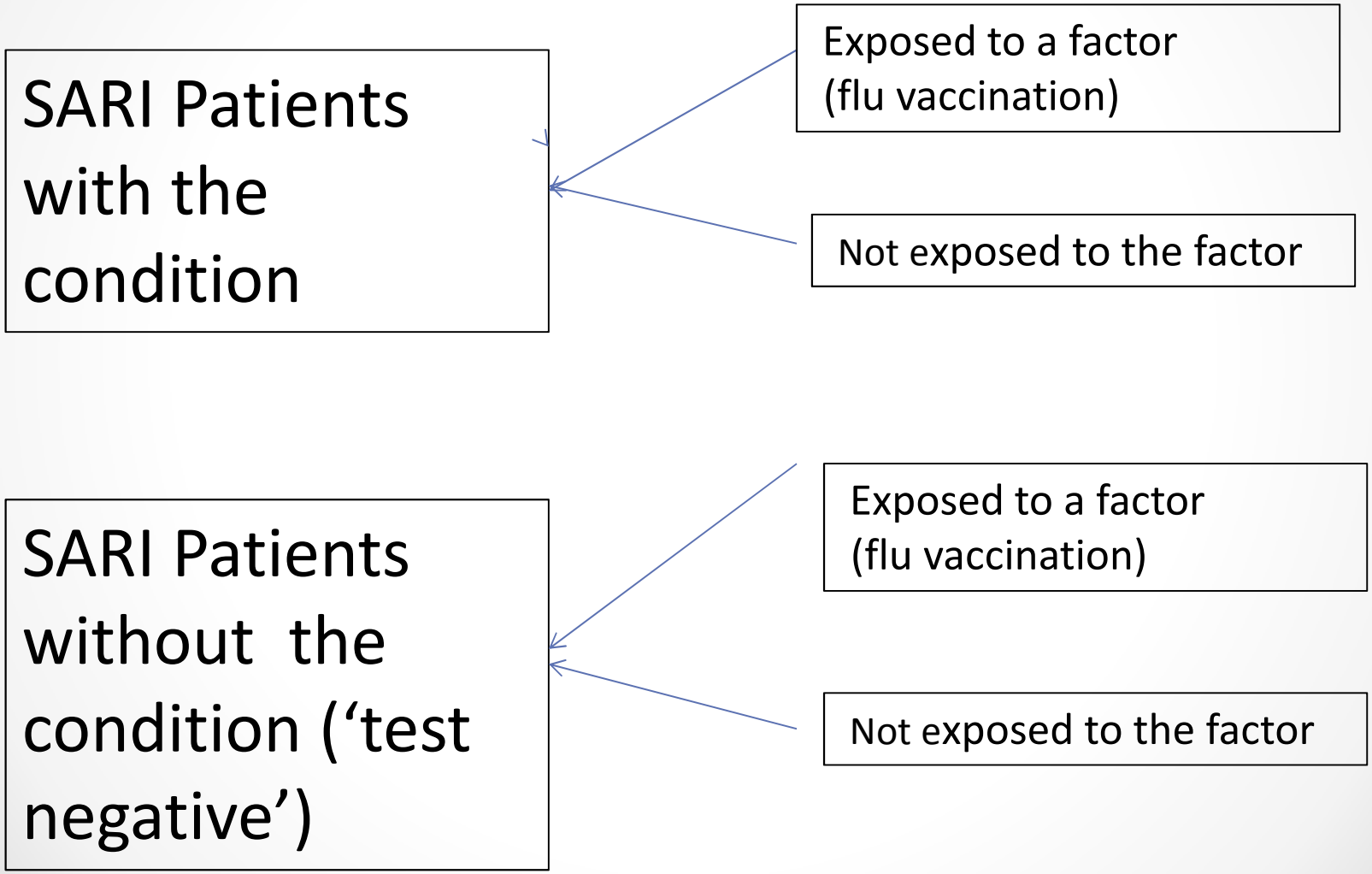
- **Hospital-based surveillance**: enhanced, active, year-round (5 yrs), population based surveillance for hospital SARI (sudden acute respiratory) cases
  - Auckland and Middlemore Hospitals

- **Community-based surveillance**: enhanced, active, (4 yrs), population based surveillance for community ILI (Influenza-like illness) cases caused by influenza
  - Recruitment of 50 – 100 'sentinel' General Practices in greater Auckland (200,000 – 400,000 patients)

Study One: Case Control

- Case-control study, test negative variant to estimate Vaccine Effectiveness (VE) in patients hospitalised for a febrile respiratory illness (SARI) due to laboratory confirmed influenza

Case-control



Study population

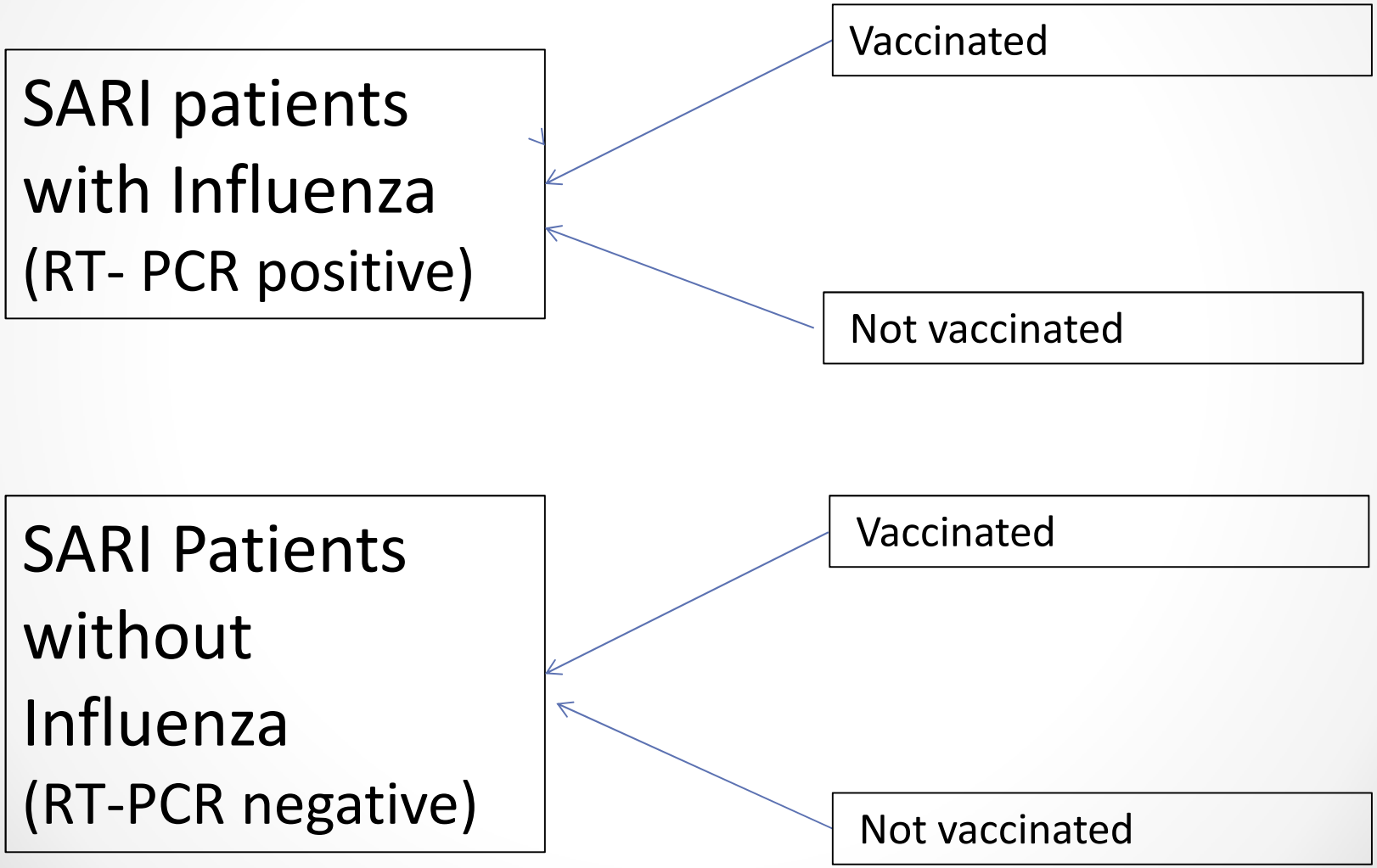
- All patients admitted to Auckland and Middlemore Hospital with a ‘SARI’

Sudden Acute Respiratory Illness (SARI)

- An acute respiratory illness with
  - A history of fever or measured fever ≥38°C
  - Cough AND
  - Onset within the past 7 or 10 days

NB modify the fever definition for elderly residential care patients

Case-control VE



VE Population	Description
Source population	All those residing in the Auckland metropolitan region
Study population	Patients from the source population admitted to any of the two Auckland hospitals with a diagnosis that is covered by the definition of SARI during the study period
Case	Any SARI patient from the study population who is influenza positive (RT-PCR)
Control	1. Any influenza negative (RT-PCR) patient from the study population 2. For children under 5 years: Any influenza negative (PCR) from the study population with evidence of another respiratory virus
Exposed	1. Received seasonal vaccine at least 14 days prior to onset of SARI 2. Children 6 months to ≤ 9 years: Received seasonal vaccine at least 14 days prior to onset of SARI and have had a previous vaccine in any year AND at least 28 days prior to the second dose
Unexposed	Not vaccinated with current seasonal vaccine or received vaccine less than 15 days prior to onset of SARI

Data collection

- Patient questionnaire and hospital data
  - Demographics
  - Medical history
  - Vaccination history
- GP PMS
  - Medical history
  - Vaccination record
- Occupational health flu vaccinators
  - Vaccination record

Analysis

- VE = 1-OR (odds ratio)
- OR = odds of being a vaccinated case divided by the odds of being a vaccinated control
- Multivariable conditional logistic regression model used
- Covariates to be included
  - Anything likely to be associated with the vaccine update
  - Anything likely to be association with catching flu
  - Anything likely to affect vaccine effectiveness

Study Two – Case Control

Test-negative design case-control to estimate influenza vaccine effectiveness in patients presenting to General Practice with a febrile respiratory illness (ILI)

Study population

- All patients enrolled with ‘sentinel’ General Practices

Cases obtained from nasopharyngeal swabbing of all presenting with **Influenza-like illness (ILI)**

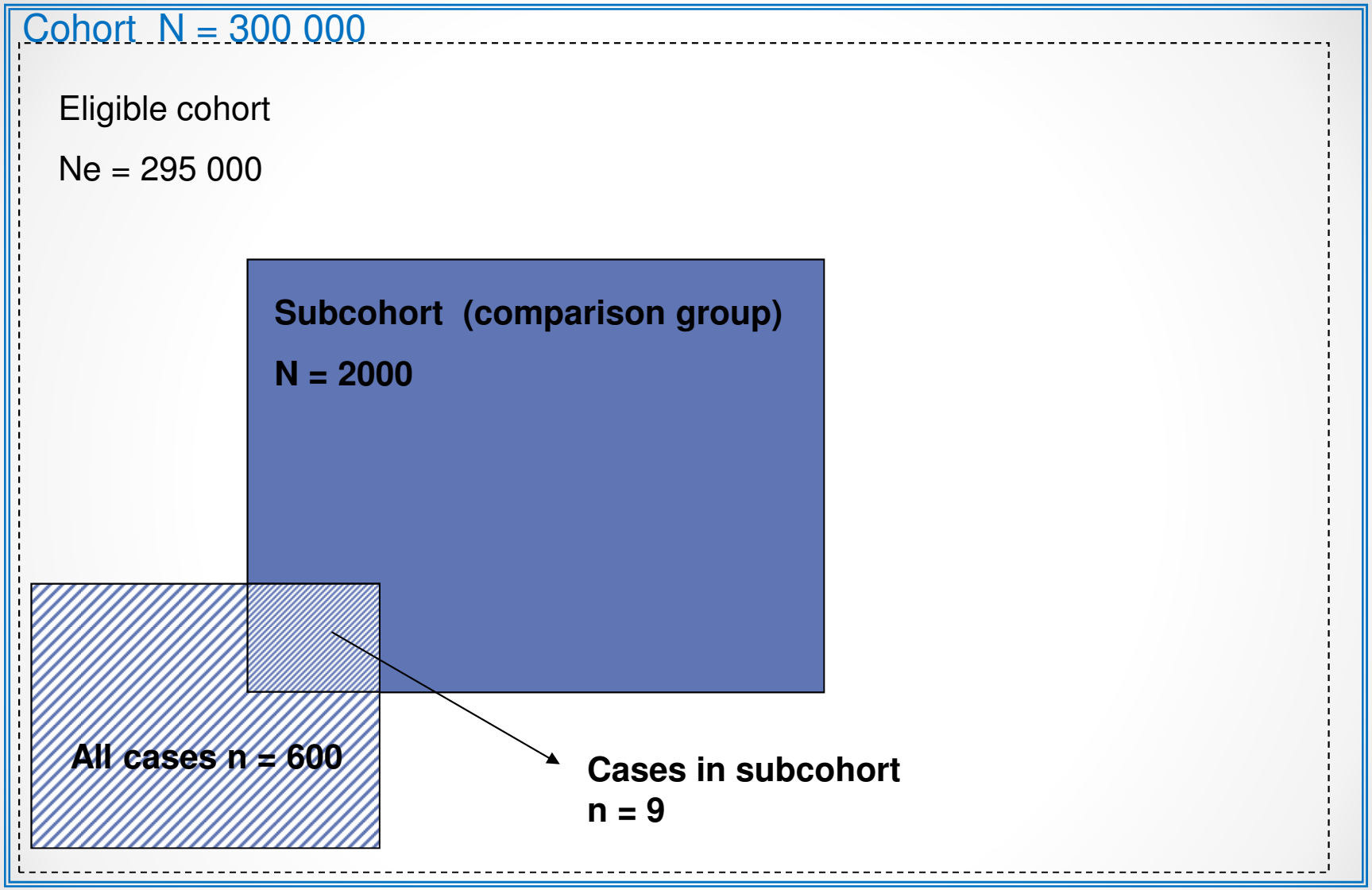
- An acute respiratory illness with
  - A history of fever or measured fever ≥38°C
  - Cough AND
  - Onset within the past 7 or 10 days

  NB modify the fever definition for elderly residential care patients

Study Three: Case cohort

A prospective case cohort to estimate Vaccine Effectiveness in patients presenting to primary care in the greater Auckland region with a febrile respiratory illness due to laboratory confirmed influenza.

Conceptual illustration of the case-cohort design (Adapted from Ulithian et al, 2007)



Courtesy of Ange Bissielo, numbers for illustration only

VE Population	Description
Source population	All those residing in the Auckland metropolitan region
Study population	All patients enrolled with the sentinel general practices
Case	Any of the study population who presents to the general practice in the time frame with an ILI which is influenza positive (RT-PCR)
Subcohort	A stratified random sample of patients from the same sentinel general practices
Exposed	1. Received seasonal vaccine at least 14 days prior to onset of ILI 2. Children 6m to < 9 years: Received seasonal vaccine at least 14 days prior to onset of ILI and have had a previous vaccine in any year and ≥ 28 days apart
Unexposed	Not vaccinated with current seasonal vaccine or received vaccine < 15 days prior to onset of ILI

Data collection

- Patient questionnaire
  - Medical history
  - Vaccination history
- GP PMS
  - Demographics
  - Medical history
  - Vaccination record
- Occupational health flu vaccinators
  - Vaccination record

Analysis

- Cohort sampled at start of the flu season
- Exposure compared between cases and the cluster random sample from the cohort with adjustment for signifcant co-variates in a logistic regression model
- Analysis takes into account the cluster sampling and stratification used for control sampling

- Controls selected through a random cluster sampling frame

- VE = 1-OR (odds ratio)

The OR for a case-cohort study is an estimate of the risk ratio from the cohort

Limitations: examples

- VE measures very specific and limited:
  - Not a full measure of VE against all influenza illness in the community
- Potential biases – some examples
  - Incomplete data collection - Flu vaccination history, obesity measurements
  - Accuracy of sample collection
    - Are all hospitalised flu cases identified by the SARI definition e.g. elderly without a fever
  - Accuracy of the control group
    - e.g. SARI positive but PCR negative ?had flu earlier
  - Have we considered all covariates that are potential confounders
    - e.g. Vaccination bias – are we less likely to vaccinated frail elderly
- Sample size for subpopulations likely to be inadequate for differential VE measurements