Slide 1

Curtin University

The Pregnancy Vaccine Effectiveness Network (PREVENT): a multi-country cohort study estimating influenza vaccine effectiveness

Dr Annette Regan
16th National Immunisation Conference
5 June 2018

A global university   Perth | Kalgoorlie | Dubai | Malaysia | Singapore

---

Slide 2

Influenza vaccination in pregnancy

- Pregnant women are at higher risk of serious complications from influenza infection – particularly in later stages of pregnancy[1]
- Maternal vaccination can offer protection to 1) women during pregnancy[2] and 2) their infants in the first six months of life
- Pregnant women are listed by WHO as the highest priority group for influenza vaccination
- Clinical trial data showing vaccination during pregnancy can prevent 63% of infant infections and 36% of febrile respiratory illnesses in mothers
- Previous studies estimate 53-65% effective against ARI illness and hospitalization during pregnancy

Dauble et al., CMAJ, 2007
Regan et al., Vaccine, 2016

Curtin University 1

Slide 3
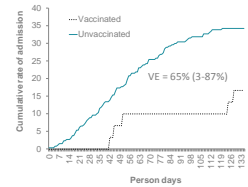
Gaps in Current Knowledge

1. Majority of maternal vaccine effectiveness studies focus on VE among infants
2. Much of the existing evidence is restricted to a) pandemic influenza; or b) ARI/ILI – limited data describing intra-pandemic influenza infections during pregnancy
3. Limited data on VE in pregnant women against severe laboratory-confirmed influenza infections (e.g., those resulting in admission to hospital)

To address these gaps, the Pregnancy Influenza Vaccine Effectiveness Network (PREVENT) was established in April 2016

Curtin University 2

Slide 4

PREVENT Network Aims

PRIMARY:
- Estimate the effectiveness of inactivated seasonal influenza vaccine against hospitalised influenza during pregnancy

SECONDARY:
- Describe epidemiological characteristics associated with influenza and respiratory syncytial virus infection during pregnancy
- Estimate incidence of influenza hospitalization during pregnancy
- Compare vaccination rates across countries
- Compare birth outcomes among pregnant women hospitalised with laboratory-confirmed influenza to non-hospitalised women

Curtin University 3

Slide 5

PREVENT Network
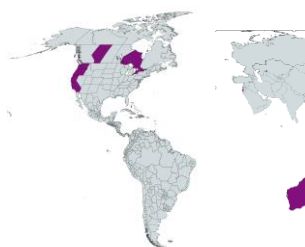
- Recruitment of sites by CDC in 2016
- Criteria for participation:
  - Ability to identify pregnant women hospitalized with acute respiratory or febrile illness (ARFI)
  - Ability to measure influenza vaccination and laboratory testing results for influenza
- 7 sites from four countries: US, Canada, Israel, and Australia

Curtin University 4

Slide 6

Methods
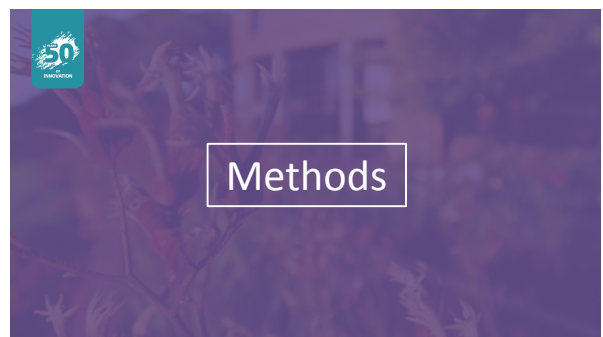
PREVENT Network Sites

Description	US (CA, OR, WA)	Israel	Alberta	Ontario	Australia (WA)
Sponsoring institution	Kaiser Permanente	Clalit Health Services	Alberta Health	Institute for Clinical Evaluative Sciences	Department of Health WA
Local population	6.2m	4.4m	4.1m	6.2m	2.6m
Influenza seasons contributed	2011-16	2010-11, 2012-2016	2011-2015	2011-2016	2012-15
Method of identifying hospitalized pregnant women	Local pregnancy registry	Hospital EMR; Demographic registry	National Discharge Abstract Database; Provincial Vital Statistic Registry	National Discharge Abstract Database	State Perinatal Data collection; Hospital Morbidity Data system
Method of identifying vaccination status	EMR; State immunisation registries	EMR	Provincial vaccination registry	Billing claims to provincial health system	State immunisation registry

Curtin University 5

Data Analysis

- ❑ Data sources:
  - Acute respiratory or febrile illnesses - Diagnosis codes from hospital discharge data and EMRs
    - ICD-10 codes adapted from previous similar work conducted by US CDC
    - Converted to ICD-10-AM for Australia and ICD-10-CM for Canada
  - Laboratory testing data - EMR or linked pathology records
    - Any test for influenza data obtained
    - Test date ±3 days from admission date = influenza hospitalisation
    - Only testing by RT-PCR included in final analysis
- ❑ Test-negative design to estimate VE:
  - Included only women hospitalised with ARFI and tested for influenza by RT-PCR
  - Aggregate data combined across sites and logistic regression model used to estimate odds of influenza in vaccinated and unvaccinated women
  - Model adjusted for site, season/year, season period, presence of high-risk medical condition
- ❑ Descriptive analyses of clinical characteristics of antenatal infections
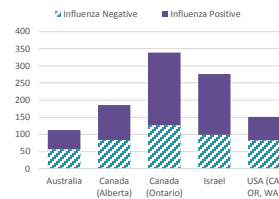- ❑ Additional analyses conducted for secondary network objectives
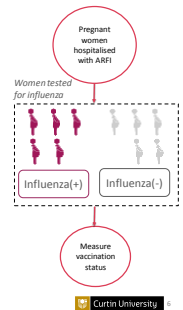
Curtin University 6

Results

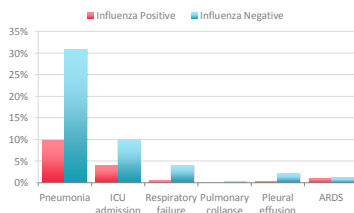## Influenza testing among pregnant women

- ❑ Total of 1,065 pregnant women were tested for influenza (5% of those hospitalised with ARFI)
- ❑ 450 influenza negative and 615 influenza positive pregnant women included in sample (58% positive)
- ❑ Positivity ranged by site (45% in US – 65% in Israel)

Curtin University 7
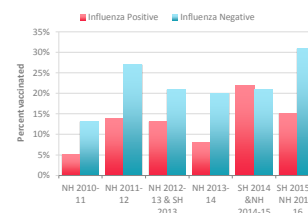
Clinical characteristics

- ❑ Severe complications uncommon
- ❑ Overall, 5% pregnant women admitted to ICU
- ❑ 71% discharged ≤3 days
- ❑ No cases identified requiring ECMO
- ❑ No maternal deaths identified

Curtin University 8

Vaccination Effectiveness

- ❑ 13% of cases and 22% controls vaccinated
- ❑ Overall estimate (2010-2016): 40% (95% CI: 12-59%)
- ❑ First and second trimester: 55% (95% CI: 10-78%)
- ❑ Third trimester: 35% (95% CI: -3-59%)
- ❑ Expected variation by season
  - If exclude 2014 SH and 2014-15 NH mismatch season: VE 49% (95% CI: 22-67%)

Curtin University 9

Conclusions

Conclusions & Lessons Learnt

❑ Difficult combining large datasets from different health systems
   • Investment in homogenizing data across health systems
   • Issues with data sharing and local privacy laws

❑ Hospital admission with laboratory-confirmed seasonal influenza during pregnancy was a relatively low-frequency event
   • Low proportion of women tested for influenza across all sites
   • Even starting with population coverage of 2 million pregnant women – small numbers available for estimating annual VE and certain sub-analyses
   • Analyses by site are unlikely to be informative (advantages of pooling)

❑ In pooled analyses, inactivated influenza vaccine was effective in reducing influenza hospitalization in pregnant women

Curtin University 10

Secondary Analyses

❑ RECENTLY PUBLISHED:
   • *Description of patient and clinical factors associated with RSV hospitalization during pregnancy (Regan et al., Clin Infect Dis, 2018)*

❑ IN PROGRESS:
   • *Description of clinical factors of seasonal influenza-associated hospitalization during pregnancy*
   • Estimating seasonal influenza incidence among pregnant women
   • CART (classification and regression tree) analysis of factors associated with clinical testing during pregnancy
   • Patterns of vaccination coverage across sites and countries
   • Examining birth outcomes of influenza hospitalized pregnancies

Curtin University 11

Acknowledgements

Influenza Division, US CDC
• Mark Thompson (PI)
• Eduardo Azziz-Baumgartner
• Fatimah Dawood
• Shikha Garg

Clalit Research Institute
• Becca Feldman
• Mark Katz

Institute for Clinical Evaluative Sciences
• Jeff Kwong
• Deshayne Fell
• Hannah Chung
• Sarah Buchan

Abt Associates
• Sarah Ball
• Brandy Wyant
• Pat Shifflett

WA Department of Health
• Paul Effler

PathWest Laboratory Medicine WA
• Avram Levy

Alberta Ministry of Health
• Kimberly Simmonds

University of Alberta
• Steven Drews

Kaiser Permanente NW
• Allison Naleway
• Stephanie Irving
• Bradley Crane
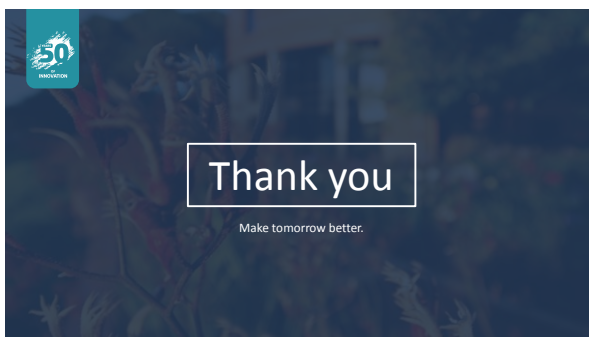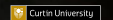• Matthew Slaughter

Kaiser Permanente NC
• Nicola Klein
• Edwin Lewis
• Sharareh Modaressi

Kaiser Permanente WA
• Michael Jackson
• Kristin Goddard

University of Calgary
• Stephanie Booth
• Margaret Russell

Curtin University

Thank you

Make tomorrow better.