# Pregnancy and Influenza vaccination.



# **Paul Van Buynder**

# Professor Griffith University







#### **Disclosures**

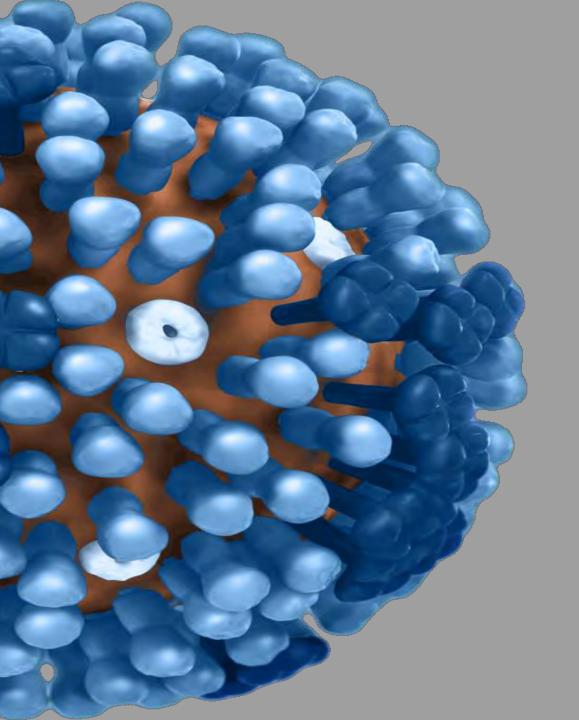
I have received research support, travel support or attended Adboards for Novartis, Sanofi, CSL, Seqirus and GSK

# I am an advocate

# Acknowledgements

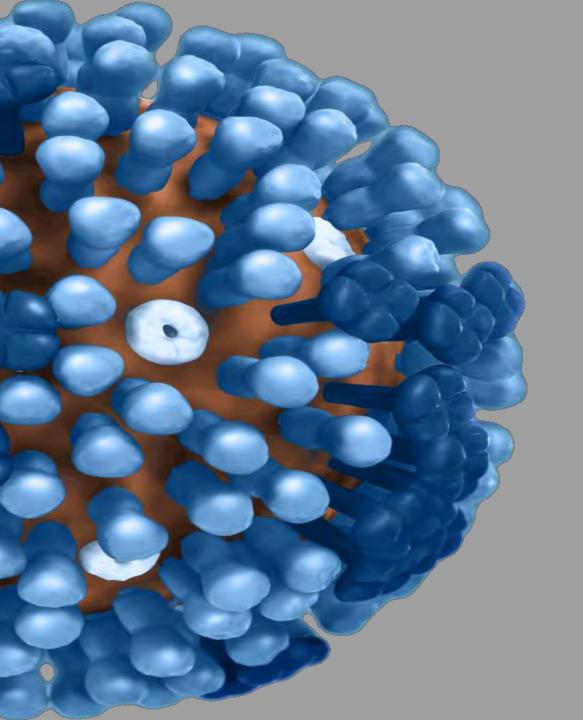
#### I have received slides from

- Dr Deshayne Fell
- Prof Paul Effler
- Prof Ross Andrews
- Stacey Rowe
- Michelle Giles
- Numerous Others



# Outline

- 1. Who recommends Flu vaccine?
- 2. Is Flu vaccine safe
- 3. How are we doing with this
- 4. Why?
- 5. What next



Who recommends influenza vaccine in pregnancy?



# Immunization, Vaccines and Biologicals

# WHO recommends seasonal influenza vaccination to pregnant women as the highest priority

23 NOVEMBER 2012 - In an updated position paper, published in the Weekly Epidemiological Record today, WHO recommends that countries considering the initiation or expansion of seasonal influenza vaccination programmes give the highest priority to pregnant women. Additional risk groups to be considered for vaccination, in no particular order of priority, are: children



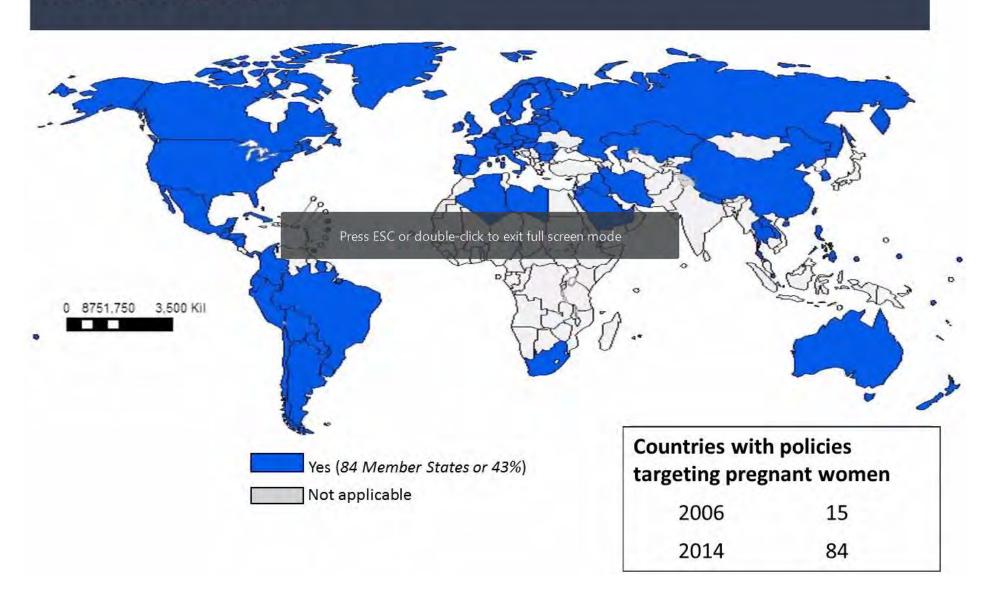
aged 6-59 months; the elderly; individuals with specific chronic medical conditions; and healthcare workers.



# College Policy Statement

- Influenza vaccination is recommended for all pregnant women regardless of gestation, and in women planning pregnancy.
- Vaccination early in the season and regardless of gestational age is optimal, but unvaccinated pregnant women should be immunised at any time during influenza season as long as the vaccine supply lasts.
- The Royal Australian and New Zealand College of Obstetricians and Gynaecologists strongly endorse routine vaccination of obstetric and midwifery staff, both to protect these individuals as well as their families, close contacts and patients.

# National policies for maternal influenza immunization



# Influenza Vaccine



#### Protects mum

Immunisation against flu not only protects mum from this season's flu but it provides ongoing protection to baby after birth and into the first six months of life.



#### Protects baby

Babies born to mothers who have been vaccinated against influenza in pregnancy have more antibodies against the disease than babies whose mothers weren't vaccinated.

Mum provides protection to baby through the placenta soon after she is vaccinated. The vaccination protects baby after birth, when they are most vulnerable, until they are old enough to be vaccinated at 6 months of age.

















# Are Vaccines Safe During Pregnancy?



CDC FAILED to tell Pregnant Mothers
Of THE INCREASE CHANCE OF

MISCARRIAGE & STILLBIRTH

after receiving CDC recommended FLU VACCINE

tinyurl.com/FluShotCausesFetalDeath

CDC has decided to recommend a potentially unsafe and ineffective vaccination for use in pregnancy, even though they cannot provide any convincing data to reassure mothers that it cannot harm their unborn child.

**RETHINK VACCINES** 





influenza deaths not only rank lower than the major killers such as heart disease and cancer but also are lower down in the mortality rankings than ulcers and hernias. Incredibly, even though most "flu" is not



New Flu Vaccine Made with Armyworms and Insects Claims to be "Pure"



Science vs. CDC: Is the Flu Vaccine More Dangerous than the Flu?

Study: Vitamin D Is More Effective Than Flu Vaccine



Friends, Romans, countrymen, lend me your ears; I come to bury Caesar, not to praise him. The evil that men do lives after them; The goo is oft interred with their bones.

(William Shakespeare)

So let it be with flu vaccine



Hi, I'm Carrie Vitt, NTP Welcome to Deliciously Organic

Through unprocessed, organic food and detox I've reversed Hashimoto's disease, chronic migraines, IBS and eczema.

Read the insert before you get the vaccine

Fluarix flu vaccine insert via Glaxo Smith Kline – "There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, FLUARIX should be given to a pregnant woman only if clearly needed."

FluZone flu vaccine insert via the FDA – "There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, Fluzone Quadrivalent should be given to a pregnant woman only if clearly needed."

Agriflu flu vaccine insert via the FDA – "There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, AGRIFLU should be given to a pregnant woman only if clearly needed."

## Flu vaccinations 'do little', wear face mask inste says health expert

By Sarah Wiedersehn
4 June 2018 — 4:47pm

A A A

A push to protect people against the flu with a "weak" vaccine is overshadowing effect methods such as hand-washing and mask-wearing, a public health expert has warned

Dr Chris Del Mar, Professor of Public Health at Bond University has challenged the val influenza vaccinations while speaking at the GPs Down Under Conference on the Gold

## Is Vaccination Safe?

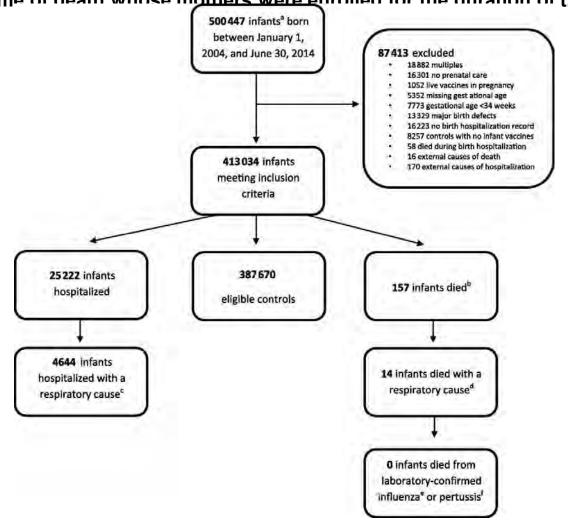
#### **Pediatrics**

February 2018
From the American Academy of Pediatrics
Article

### Infant Hospitalizations and Mortality After Maternal Vaccination

Lakshmi Sukumaran, Natalie L. McCarthy, Elyse O. Kharbanda, Gabriela Vazquez-Benitez, Heather S. Lipkind, Lisa Jackson, Nicola P. Klein, Allison L. Naleway, David L. McClure, Rulin C. Hechter, Alison T. Kawai, Jason M. Glanz, Eric S. Weintraub

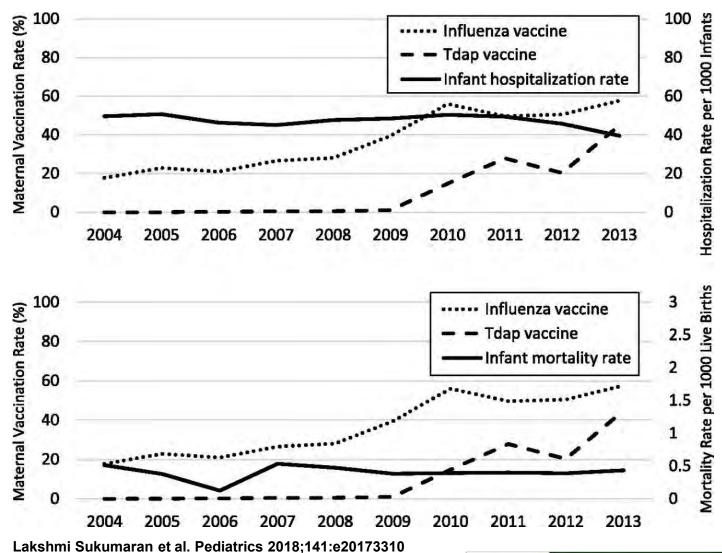
Study population of infants with hospitalization or death in the first 6 months of life in the VSD, 2004–2014. a Infants with continuous enrollment in the VSD until 6 months of age or until the time of death whose mothers were enrolled for the duration of t...



Lakshmi Sukumaran et al. Pediatrics doi:10.1542/peds.2017-3310



Rates of maternal influenza and Tdap vaccination, infant hospitalization, and infant mortality in the VSD, 2004–2013.



Authors found infants did not have an increased risk of hospitalization or death when their mother had been vaccinated. Adjusted odds ratios for hospitalization and maternal influenza and Tdap vaccination were 1 and 0.94, respectively. Likewise, adjusted odds ratios for infant mortality and maternal influenza or Tdap vaccination were 0.96 and 0.44. The study also showed infants hospitalized for respiratory problems had lower rates of maternal vaccination for Tdap compared to controls.

The study's findings are consistent with other studies showing vaccination during pregnancy is not linked to childhood hospitalization, development issues or chronic conditions.

# Safety of maternal influenza immunization

Safety assessments have been favourable

Systematic review	Summary
Fell et al. BJOG 2015; 122(1):17-26	<ul> <li>Systematic review of published studies up to April 2014 (n=27 studies)</li> <li>Outcomes: preterm birth; fetal death</li> <li>No evidence of any adverse effect of influenza vaccination during pregnancy on preterm birth or late fetal death</li> </ul>
McMillan et al. Vaccine 2015; 33(18):2108-17	<ul> <li>Systematic review of published studies up to March 2014 (n=19 studies)</li> <li>Outcomes: fetal death; congenital malformations</li> <li>No evidence of any adverse effect of influenza vaccination during pregnancy</li> </ul>
Bratton et al. CID 2015; 60(5):e11-9	<ul> <li>Systematic review of published studies up to November 2013 (n=7 studies)</li> <li>Outcomes: stillbirth and spontaneous abortion</li> <li>No evidence of any adverse association between influenza vaccination during pregnancy and study outcomes</li> </ul>

So, is influenza vaccine safe in pregnancy?



"Friends, Romans, countrymen, take back your ears. We have a surplus." So, is influenza vaccine safe in pregnancy?

Yes it is



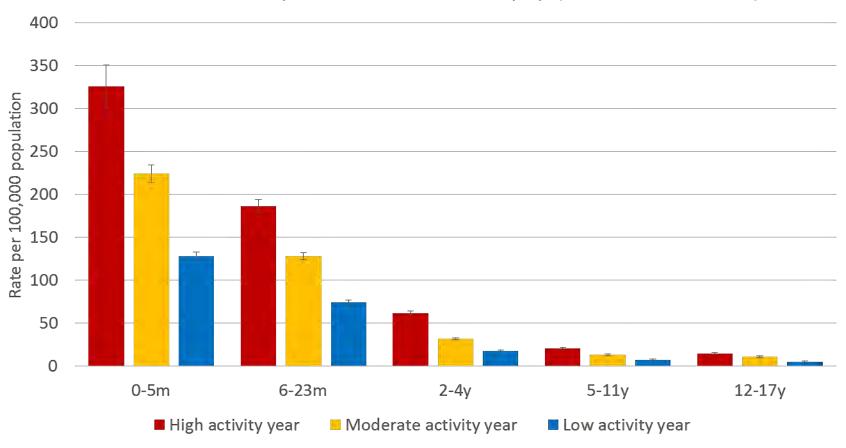
"Friends, Romans, countrymen, take back your ears. We have a surplus."

# Consequences of nonvaccination exist for both mother and newborn



# The burden of 'flu

ICD10 Coded flu hospitalisations / 100,000 pop (2002-13, excl 2009)



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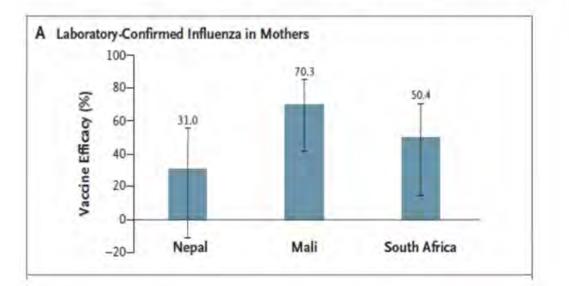
"Which kind of Flu?"

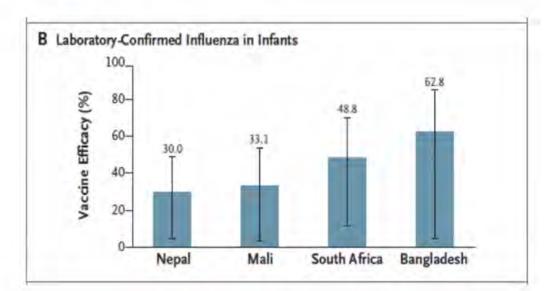


# Vaccine efficacy against influenza

- Four RCTs of influenza vaccination during pregnancy
  - Bangladesh: Zaman et al., NEJM 2008
  - South Africa: Madhi et al., NEJM 2014
  - Mali: Tapia et al., Lancet ID 2016
  - Nepal: Steinhoff et al., Lancet ID 2017

BILL& MELINDA
GATES foundation





#### ORIGINAL ARTICLE

# Influenza Vaccination of Pregnant Women and Protection of Their Infants

Shabir A. Madhi, M.D., Ph.D., Clare L. Cutland, M.D., Locadiah Kuwanda, M.Sc., Adriana Weinberg, M.D., Andrea Hugo, M.D., Stephanie Jones, M.D., Peter V. Adrian, Ph.D., Nadia van Niekerk, B.Tech., Florette Treurnicht, Ph.D., Justin R. Ortiz, M.D., Marietjie Venter, Ph.D., Avy Violari, M.D., Kathleen M. Neuzil, M.D., Eric A.F. Simões, M.D., Keith P. Klugman, M.D., Ph.D., and Marta C. Nunes, Ph.D., for the Maternal Flu Trial (Matflu) Team\*

### **Study Design**

- Double blinded RCT
- 2116 non-HIV infected pregnant women
- Immunogenicity safety and efficacy
- Mothers and newborns out to 24 weeks

## Does it work? Key findings

- Influenza vaccine was immunogenic in newborns (higher HAI titres)
- Vaccine effectiveness 50% mothers
- Vaccine effectiveness 49% infants

Clin Infect Dis. 2010 Dec 15; 51(12): 1355-1361.

doi: 10.1086/657309

PMCID: PMC3106242

PMID: 21058908

## Influenza Vaccine Given to Pregnant Women Reduces Hospitalization Due to Influenza in Their Infants

Isaac Benowitz, Daina B. Esposito, Kristina D. Gracey, Eugene D. Shapiro, 1,2,3 and Marietta Vázquez

<u>Author information</u> ► <u>Article notes</u> ► <u>Copyright and License information</u> ► <u>Disclaimer</u>

Am J Obstet Gynecol. 2011 Jun;204(6 Suppl 1):S141-8. doi: 10.1016/j.ajog.2011.02.042. Epub 2011 Feb 23.

### Impact of maternal immunization on influenza hospitalizations in infants.

Poehling KA<sup>1</sup>, Szilagyi PG, Staat MA, Snively BM, Payne DC, Bridges CB, Chu SY, Light LS, Prill MM, Finelli L, Griffin MR, Edwards KM; New Vaccine Surveillance Network.

Hum Vaccin Immunother. 2018 Mar 4;14(3):758-766. doi: 10.1080/21645515.2017.1345385. Epub 2017 Oct 18.

## Influenza vaccination during pregnancy for prevention of influenza confirmed illness in the infants: A systematic review and meta-analysis.

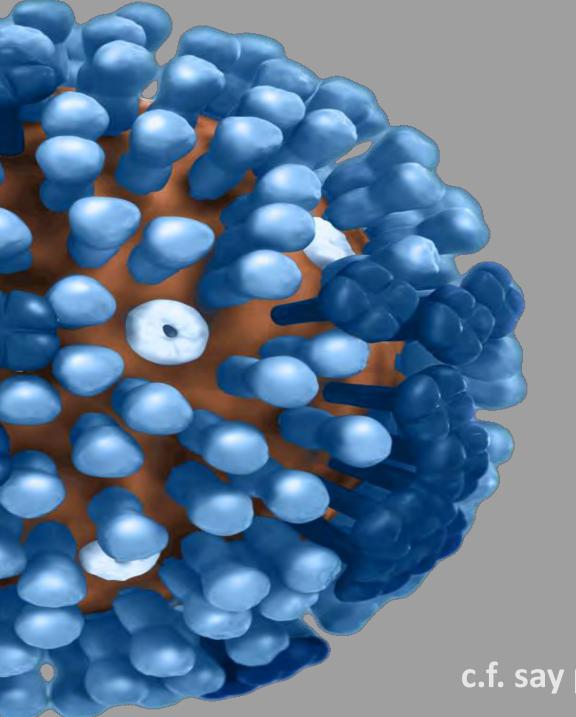
Nunes MC<sup>1,2</sup>, Madhi SA<sup>1,2,3</sup>.

Author information

### Abstract

Infants younger than 6 months of ge are at particular risk for serious illness from influenza infection. Currently available influenza vaccines are, however, not licensed for use in infants <6 months old. Influenza vaccination during pregnancy elicits robust antibody responses in the women that will protect the infants against influenza infection during the first few months of life. We aimed to determine the impact of influenza vaccination during pregnancy to prevent laboratory-confirmed influenza infection and influenza-associated hospitalisations in infants <6 months old. An electronic search identified all studies assessing the proposed outcomes in infants after administration of influenza vaccine

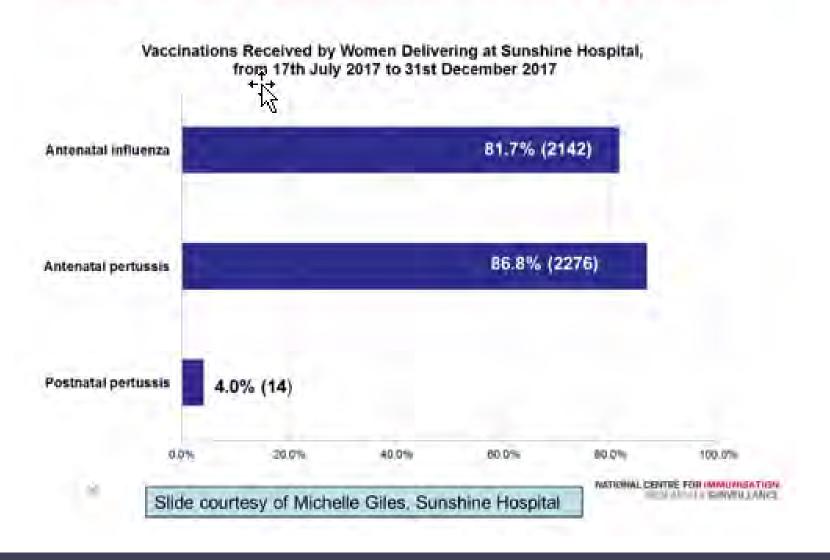
VE about 50% overall in first six months

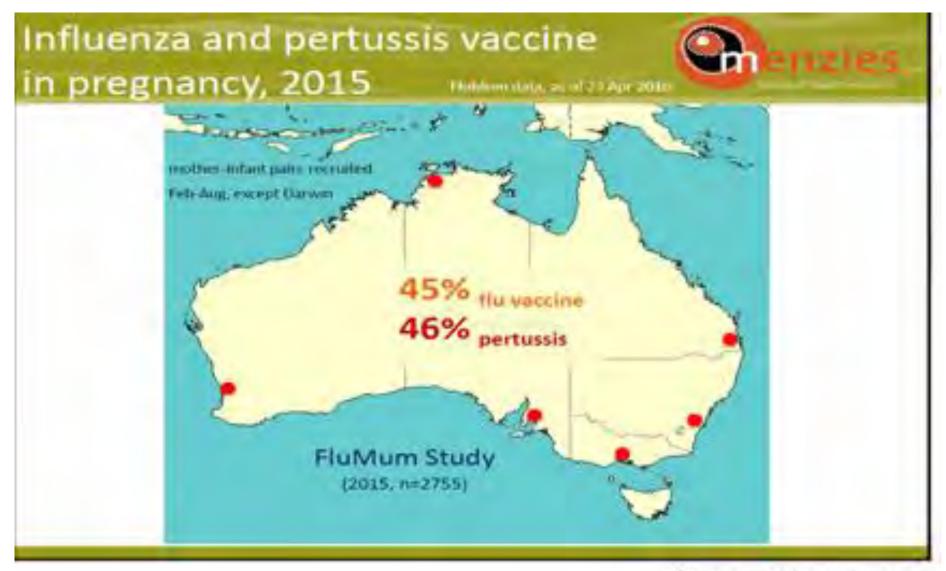


# How are we doing with this?

c.f. say pertussis?

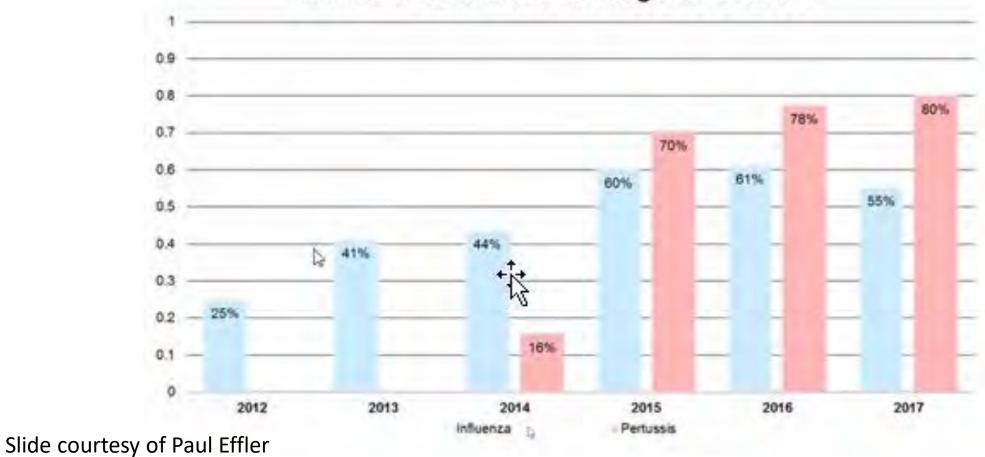
### Immunisation service in antenatal clinics = success!



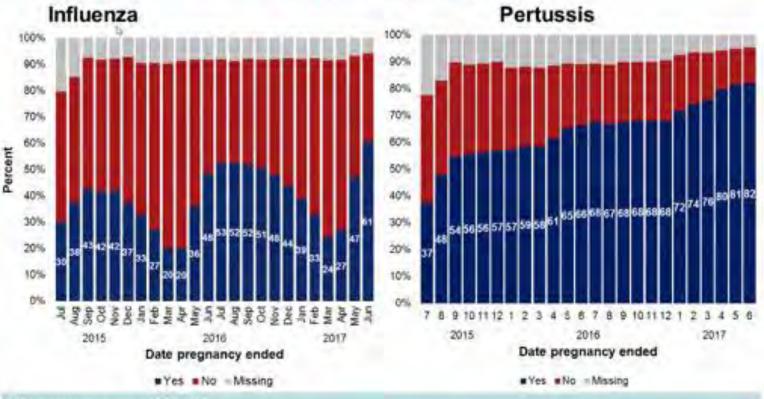


### Western Australian maternal vaccine coverage

### Antenatal vaccination coverage 2012 to 2017



### Victorian maternal vaccine coverage



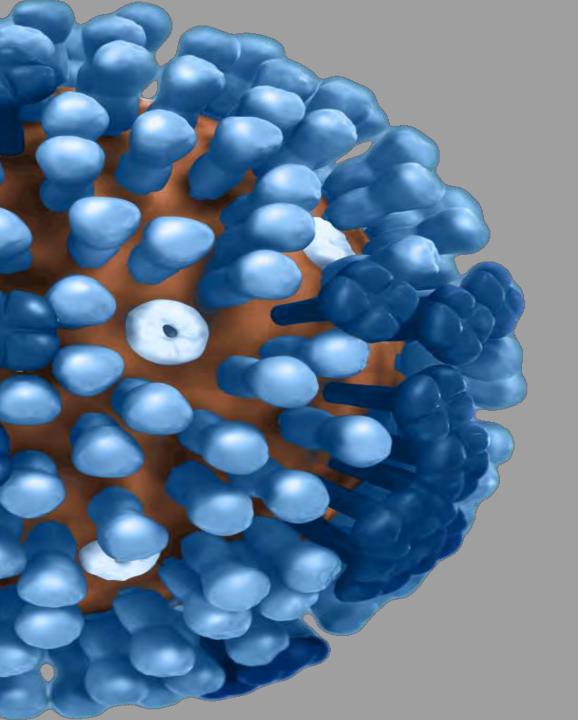
Influenza - around 40-60%

Pertussis ->80% (as at June 2017) Slide courtesy: Lucinda Franklin and Stacey Rowe

Data sourced from Clinical Council Unit, Safer Care Victoria Data compiled by Health Protection Branch NATIONAL



Health and Hum



Why don't pregnant women access influenza vaccine in pregnancy?

# Initial Pregnancy Research

- Review of Influenza vaccine uptake during the pandemic
- Higher coverage then (over 75%)
- Lots of publicity about the seriousness of the pandemic for pregnant women
- Reasons for being vaccinated were largely personal beliefs"
  - They thought the pandemic was a serious disease
  - They thought disease was worse than vaccine
- Access issues important for those not being vaccinated

# Initial Pregnancy Research

- Coverage of seasonal vaccine in same group 50%
- Reasons for being vaccinated again were largely personal beliefs
  - They thought the vaccine could not give you the flu
  - They thought vaccine was safe
- Issues important for those not being vaccinated
  - Not raised by their care provider

### Generic Research

Concerns about influenza vaccine

- Influenza is not a serious disease
- Vaccine is not safe
- Vaccine gives you GBS ...
- Vaccine gives you influenza
- Vaccine doesn't work

### Current Research

- Recruit all women birthing over a 7 month period when influenza vaccine is available
- Investigate
  - Vaccination status
  - REASONS including:
    - Vaccination status when non-pregnant
    - Attitude of provider and recommendations
    - Health belief model
    - Outcome of pregnancy including birth weight

# Highlight it with providers



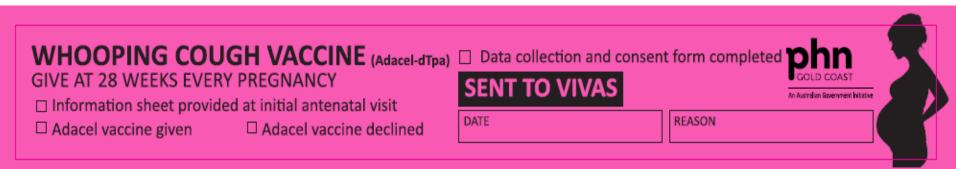




Table 2. Regression analysis of the factors influencing uptake of flu vaccination

FI J	· ·	
2	Odds ratio	P
Did you receive a flu vaccine in the	he	
year before you were pregnant?		
No	1	
Yes	5.47 (3.67-8.17)	< 0.001
D:1 1		
Did any doctor recommend you		
receive flu vaccine in pregnancy?		
No	1	
Yes	13.94 (8.79-22.11)	< 0.001
Season		
Jan-Mar	1	
Apr-Jun	1.69 (0.99 – 2.88)	0.05
Jul-Sep	5.21 (3.15-8.64)	< 0.001
Oct-Dec	2.68 (1.69-4.48)	< 0.001
Education		
Tertiary	1	
High school	1.13 (0.67-1.91)	0.65
Some tertiary	.36 (0.18 - 0.71)	0.003
Income		
80001 or more	1	
20000-40000	1.03 (0.44-2.39)	0.94
40001-80000	0.68 (0.43-1.06)	0.09
Age		
18-24 Years	1	
25-34 Year	0.91 (0.31-2.68)	0.86
35 and more	0.70 (0.23-2.14)	0.53
~		0.004

Classification is 78.9%. Hosmer and Lemeshow Test is 0.13, Nagelkerke R Square is 50.1%

< 0.001

0.02

Constant

### The Study

1028 pregnant women in 2017 85% had a pertussis vaccine 35% had an influenza vaccine

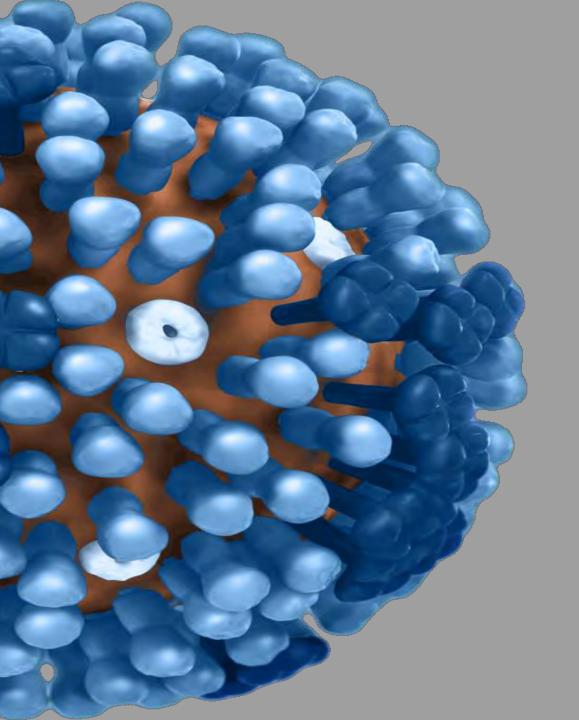
3 Major factors

Belief in vaccine (6X)

Physician (14X)

Season (5X)

Dedicated bi level marketing Extended shelf life



What now?



# Campaign to address risk benefit equation

Disease

**Bad for you** 

**Bad for unborn baby** 

**Bad for neonate** 

**Vaccine** 

Overcomes these negatives Is safe and effective

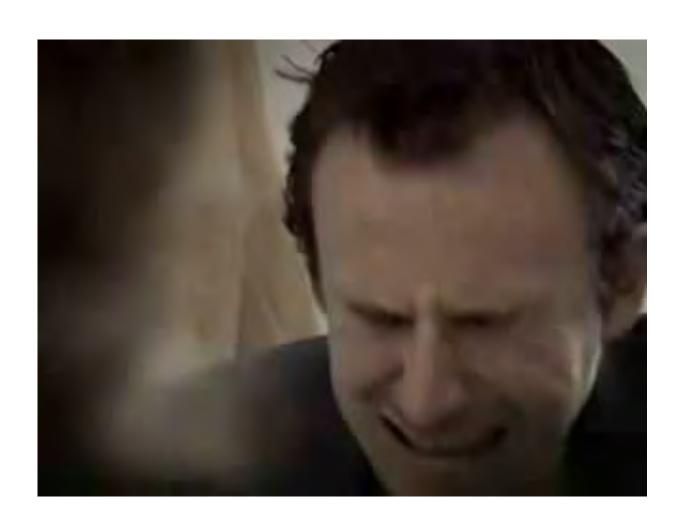
**Target** 

**Obstetric Care providers** 

# Change systems

- In our study two thirds of those receiving pertussis vaccine obtained it in hospital at antenatal clinic.
- We don't offer flu vaccine there .. Maybe we should
- Every pregnancy at any stage?? Should we fix a time and link it during some seasons
- Make sure we have flu vaccine all year
  - GSK and Seqirus extended shelf life
  - ? Store some given the shortage

# Remember the pregnancy support groups



## EducateEducateEducateEducateEducateEducateEducateEdu

# GOTYOURSHOTS?