What is covered

Influenza

- Risks for pregnant women & infants
- Current epidemiology
- Vaccine efficacy & safety in pregnancy/infancy
- NSW programs & uptake
Influenza ABCs

- Respiratory viral infection – most human infection influenza A or B

- Spreads readily by respiratory droplets/fomites; incubation period 2-3 days; infectious 24 hours before onset - ~5 days

- All strains prone to drift requiring frequent revision to vaccine components

- Influenza A prone to re-assortment with avian and porcine strains leading to pandemics

- Almost all current isolates have good susceptibility to neuraminidase inhibitor antivirals (oseltamivir, zanamivir, peramivir)
Influenza – risks in pregnancy & infancy

- Immunological & physiological changes of pregnancy increase the potential severity of influenza infection
  - Suppression of cell-mediated and increased humoral immunity
  - 20-30% decrease in pulmonary functional residual capacity
  - Increased oxygen requirement

- Risk of hospitalisation from flu increases to five-fold by third trimester; further increases if woman has co-morbidities including obesity

Tamma PD et al. Expert Reviews in Respiratory Medicine, 2010: 4(9)
Influenza – risks in pregnancy & infancy

Women hospitalised with flu have:

- Longer hospital stay
- Higher odds of preterm delivery, foetal distress and caesarian section

During pandemics flu has also been associated with:

- Higher rates of spontaneous abortion
- Rapid progression to pneumonia or ARDS over 24 – 48 hours
- Venous thromboembolic events
- Renal failure

Tamma PD et al. Expert Reviews in Respiratory Medicine, 2010: 4(3)
Saleeby E Obs&Gyn 2009 114:4
Jamieson DJ Lancet 2009 374:
Influenza – risks in pregnancy & infancy

- In the US 2009 pandemic 5% of deaths were in pregnant women (1% of population)

- In Australia the highest excess ICU admission rate was in Aboriginal people (17/100,000) and pregnant women (14/100,000)

- Increased risk of fetal death – hazard ratio 1.9

- Increased risk of low birth weight & SGA

References:

1. Siston et al JAMA 2010 (303) 1517-1524
2. Schaffer et al BMC Public Health 2012 12:869
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Infected cohort (n=256)</th>
<th>Comparison cohort (n=1220)</th>
<th>Odds ratio (95% CI)</th>
<th>National data, 2008</th>
<th>Unadjusted odds ratio (95% CI)</th>
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<tbody>
<tr>
<td><strong>Outcome of pregnancy:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live birth†</td>
<td>249 (95)</td>
<td>1226 (99)</td>
<td>1</td>
<td>1</td>
<td>795 004 (99)</td>
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<td>Stillbirth</td>
<td>7 (3)</td>
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<td>4.9 (1.7 to 14.2)</td>
<td>4.2 (1.4 to 12.4)</td>
<td>4 043 (1)</td>
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<td>Loss of pregnancy before 24 weeks</td>
<td>5 (2)</td>
<td>NA</td>
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<td><strong>Neonatal death:</strong></td>
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<td></td>
<td></td>
<td></td>
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<td>Yes</td>
<td>3 (1)</td>
<td>2 (0)</td>
<td>7.4 (1.2 to 44.7)</td>
<td>5.6 (0.5 to 64.2)</td>
<td>2 557 (0)</td>
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<td>No</td>
<td>246 (99)</td>
<td>1218 (100)</td>
<td>1</td>
<td>1</td>
<td>792 487 (100)</td>
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<td><strong>Perinatal death:</strong></td>
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<td>Yes</td>
<td>10 (4)</td>
<td>8 (1)</td>
<td>6.2 (2.4 to 15.9)</td>
<td>5.7 (2.2 to 15.1)</td>
<td>6 025 (1)</td>
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<tr>
<td>No</td>
<td>246 (96)</td>
<td>1219 (99)</td>
<td>1</td>
<td>1</td>
<td>793 022 (99)</td>
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<td>Mean (SD) birth weight (kg)</td>
<td>3073 (774)</td>
<td>3342 (614)</td>
<td>-270 (-356 to -183)</td>
<td>-255 (-353 to -156)</td>
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<td>Low birth weight (&lt;2500 g):</td>
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<tr>
<td>Yes</td>
<td>50 (20)</td>
<td>94 (8)</td>
<td>2.9 (2.0 to 4.3)</td>
<td>3.2 (2.1 to 4.9)</td>
<td>57 072 (7)§</td>
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<td>No</td>
<td>206 (80)</td>
<td>1137 (92)</td>
<td>1</td>
<td>1</td>
<td>713 201 (93)</td>
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<td>Very low birth weight (&lt;1500 g):</td>
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<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>14 (5)</td>
<td>22 (2)</td>
<td>3.2 (1.6 to 6.3)</td>
<td>2.9 (1.3 to 6.4)</td>
<td>10 955 (1)§</td>
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<td>No</td>
<td>242 (95)</td>
<td>1209 (98)</td>
<td>1</td>
<td>1</td>
<td>759 318 (99)</td>
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<td>Preterm (&lt;37 weeks):</td>
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<td></td>
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<td></td>
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<td>Yes</td>
<td>59 (24)</td>
<td>89 (7)</td>
<td>3.9 (2.7 to 5.6)</td>
<td>4.0 (2.7 to 5.9)</td>
<td>36 283 (8)</td>
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<tr>
<td>No</td>
<td>192 (76)</td>
<td>1129 (93)</td>
<td>1</td>
<td>1</td>
<td>423 475 (92)</td>
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<td>Very preterm (&lt;32 weeks):</td>
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<td>Yes</td>
<td>18 (7)</td>
<td>18 (1)</td>
<td>5.2 (2.6 to 10.0)</td>
<td>4.9 (2.4 to 10.0)</td>
<td>10 932 (2)</td>
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<tr>
<td>No</td>
<td>233 (93)</td>
<td>1200 (99)</td>
<td>1</td>
<td>1</td>
<td>449 101 (98)</td>
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<td>Delivered by caesarean section:</td>
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<td></td>
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<td>Yes</td>
<td>100 (40)</td>
<td>299 (25)</td>
<td>2.1 (1.5 to 2.7)</td>
<td>2.3 (1.7 to 3.2)</td>
<td>139 449 (24)</td>
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<tr>
<td>No</td>
<td>150 (60)</td>
<td>921 (75)</td>
<td>1</td>
<td>1</td>
<td>453 951 (76)</td>
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<td>Congenital anomalies:</td>
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<td></td>
<td></td>
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<td>Yes</td>
<td>8 (3)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>4 308 (2)</td>
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<tr>
<td>No</td>
<td>243 (97)</td>
<td></td>
<td></td>
<td></td>
<td>248 644 (100)</td>
</tr>
</tbody>
</table>

REF: Pierce M et al BMJ 2011
Influenza – risks in pregnancy & infancy

- Infants in the first six months of life are highly susceptible to influenza
- Hospitalisation estimated 240-720/100,000/annum
- US paediatric mortality ~100/annum

\[\text{MMWR 2010;59:1-62} \quad \text{MMWR 2016;65(22):567-575}\]
Influenza – current epidemiology

- Influenza A(H3N2) is predominant strain
- All circulating strains well-matched to vaccine
Influenza – current epidemiology

Figure 6: Percentage of laboratory tests positive for influenza A and influenza B by week, 1 January 2010 – 14 August 2016, New South Wales.
Influenza vaccination – evidence for safety

- Only inactivated flu vaccine is used in Australia
- Studies include >10 000 pregnant women, including 700 in first trimester
- No increased risk of complications for woman or foetus


**Contraindications**: previous anaphylaxis to flu vaccine or eggs
Influenza vaccine – evidence for efficacy

● Similar immunological response to non-pregnant women

● 36% reduction in febrile respiratory illness in third trimester (RCT)

● 50% -70% reduction in confirmed influenza in vaccinated women (RCT; population cohort)

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i Tamma PD et al. Expert Reviews in Respiratory Medicine, 2010: 4(3)

ii Zaman K et al. NEJM 2008;359:1555-64

iii Madhi SA et al. NEJM 2014;371:918-31

iv Haberg et al NEJM 2013;368:333-40
Influenza vaccine – evidence for efficacy

Zaman NEJM 359:15 Oct 2009 (Bangladesh)
- RCT 340 women 3rd trimester vaccination
- 63% reduction in lab confirmed influenza in infants to 6m

Benowitz CID 51:12 Dec 2010 (urban US)
- Case control study 245 women
- 91.5% effective in preventing influenza hospitalisation of infants in first 6 months

- Prospective cohort 1160 mother-infant pairs
- 41% reduction of confirmed influenza in infants; 39% reduction in ILI hospitalisation

- Case control 151 infants
- 45 – 48% decrease infant influenza hospitalisation
Influenza vaccine – evidence for efficacy

Nunes JAMA Pediatrics: July 5 2016 (South Africa)

- Double blind, placebo controlled trial 3v flu vaccine
- >2000 participants
- Vaccinated 2nd or 3rd trimester
- Maternal immunisation efficacy highest among infants ≤ 8 weeks (85.8%)
- Efficacy decline after 8 weeks correlates with decline in maternally-derived antibody
### Table 2. Incidence Rates of PCR-Confirmed Influenza Illness and Vaccine Efficacy by Age Group

<table>
<thead>
<tr>
<th>PCR-Confirmed Influenza</th>
<th>IIV3 Group</th>
<th>Placebo Group</th>
<th>Vaccine Efficacy (95% CI)</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Infants, No.</td>
<td>Person-Time, mo</td>
<td>Incidence Rate (95% CI)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Infants, No.</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≤8 wk</td>
<td>2</td>
<td>2083.7</td>
<td>1.0 (0.2-3.8)</td>
<td>14</td>
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<tr>
<td>&gt;8-16 wk</td>
<td>12</td>
<td>1818.0</td>
<td>6.6 (3.7-11.6)</td>
<td>16</td>
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<tr>
<td>&gt;16-24 wk</td>
<td>5</td>
<td>1670.5</td>
<td>3.0 (1.2-7.2)</td>
<td>7</td>
</tr>
<tr>
<td>≤16 wk</td>
<td>14</td>
<td>3898.0</td>
<td>3.6 (2.1-6.1)</td>
<td>30</td>
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<tr>
<td>≤24 wk</td>
<td>19</td>
<td>5568.4</td>
<td>3.4 (2.2-5.3)</td>
<td>37</td>
</tr>
<tr>
<td>During influenza season</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤8 wk</td>
<td>2</td>
<td>1697.8</td>
<td>1.2 (0.15-4.3)</td>
<td>14</td>
</tr>
<tr>
<td>≤16 wk</td>
<td>14</td>
<td>2538.2</td>
<td>5.5 (3.0-9.2)</td>
<td>30</td>
</tr>
<tr>
<td>≤24 wk</td>
<td>19</td>
<td>2766.1</td>
<td>6.9 (4.1-10.7)</td>
<td>36</td>
</tr>
</tbody>
</table>

Abbreviations: IIV3, trivalent inactivated influenza vaccine; PCR, polymerase chain reaction.

<sup>a</sup> Incidence rates calculated as number of cases per 1000 child-months, using person-time between birth and event or end of study.
2. Summary of recommendations

<table>
<thead>
<tr>
<th>Recommendation 1</th>
<th>Grade and reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza vaccination is recommended for all pregnant women regardless of gestation, and in women planning pregnancy.</td>
<td>Consensus-based recommendation 1</td>
</tr>
</tbody>
</table>

**Good Practice Notes**

Free influenza vaccine is available to all pregnant women in Australia and New Zealand.

To receive the influenza vaccination, pregnant women are advised to visit their local doctor or immunisation provider. It is important to note that the vaccine is free; however a consultation fee may apply.


**Recommendation 2**

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.

**Recommendation 3**

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.
Current NSW programs for influenza vaccination

- Under the National Immunisation Program influenza vaccination is free for all pregnant women

- Quadrivalent vaccine is offered – currently available through GPs and some antenatal clinics
Flu vaccine uptake in pregnancy

- National Vaccination Survey 2009: 12.7% of pregnant women vaccinated

- Uptake now ~45% 

- Uptake is strongly influenced by health professional recommendation (OR: 20\(^{ii}\) - 42\(^{iii}\))

- Other factors: concern about foetal safety(0.5); perception of flu severity (2.2)\(^{ii}\)

\(^{i}\) FluMum study group
\(^{ii}\) Wiley K et al. MJA 198 (7) 15 April 2013
\(^{iii}\) Maher L et al. Vaccine 31(47):5557-64
Flu vaccine uptake in pregnancy

- US uptake higher ~50%

Top 6 reasons for **NOT** receiving vaccine:

- "I am concerned about safety to my baby if I get vaccinated"
- "I am concerned the vaccination would give me the flu"
- "I don’t think vaccine is effective in preventing flu"
- "I am concerned about safety risk to myself if I got vaccinated"
- "I don’t think I would get very sick if I got the flu"
- "If I get the flu I’ll get some medicine to treat it"

MMWR 60(32); 1078-82. August 19 2011
FluMum Study

- National study of effectiveness of flu vaccine in pregnancy
- Women recruited Sydney, Melbourne, Brisbane, Perth & Darwin
- Predictors of flu vaccination & vaccine effectiveness

Diagram:

- Primary Exposure: Influenza vaccine in pregnancy
- Recruited at Birth
- 6 mths
- Influenza in infancy
- Notification of lab. confirmed influenza during first 6mths of life

10,106 mother-infant pairs