

A black silhouette of a pregnant woman in profile, facing right. Her hair is styled in an updo with some strands hanging down. She is looking down at her belly.

Influenza Immunisation and Pregnancy

NSW Update

Communicable Diseases Branch

Health Protection NSW

August 2016

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

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:



Health

Influenza – risks in pregnancy & infancy

- In the US 2009 pandemic 5% of deaths were in pregnant women (1% of population)ⁱ
- In Australia the highest excess ICU admission rate was in Aboriginal people (17/100,000) and pregnant women (14/100,000)ⁱⁱ
- Increased risk of fetal death – hazard ratio 1.9ⁱⁱⁱ
- Increased risk of low birth weight & SGA^{iv}

ⁱSiston et al JAMA 2010 (303) 1517-1524

ⁱⁱ Schaffer et al BMC Public Health 2012 12:869

ⁱⁱⁱ Haberg et al NEJM 2013;368:333-40

^{iv} McNeil et al Am J Obstets Gynecol 2011: 204

Table 2 | Outcome of pregnancy for women admitted to hospital with 2009/H1N1 infection (infected cohort) and uninfected women (comparison cohort)

Outcome	No (%)		Odds ratio (95% CI)		National data, 2008	
	Infected cohort (n=256)	Comparison cohort (n=1220)	Unadjusted	Adjusted*	No (%)	Unadjusted odds ratio (95% CI)
Outcome of pregnancy:						
Live birth†	249 (95)	1226 (99)	1	1	795 004 (99)	1
Stillbirth	7 (3)	7 (1)	4.9 (1.7 to 14.2)	4.2 (1.4 to 12.4)	4 043 (1)	5.5 (2.6 to 11.7)
Loss of pregnancy before 24 weeks	5 (2)	NA	NA	NA	NA	NA
Neonatal death:						
Yes	3 (1)	2 (0)	7.4 (1.2 to 44.7)	5.6 (0.5 to 64.2)	2 557 (0)	3.8 (1.2 to 11.8)
No	246 (99)	1218 (100)	1	1	792 487 (100)	1
Perinatal death:						
Yes	10 (4)	8 (1)	6.2 (2.4 to 15.9)	5.7 (2.2 to 15.1)	6 025 (1)	5.4 (2.8 to 10.1)
No	246 (96)	1219 (99)	1	1	793 022 (99)	1
Mean (SD) birth weight (kg)	3073 (774)	3342 (614)	-270 (-356 to -183)‡	-255 (-353 to -156)‡	NA	NA
Low birth weight (<2500 g):						
Yes	50 (20)	94 (8)	2.9 (2.0 to 4.3)	3.2 (2.1 to 4.9)	57 072 (7)§	3.0 (2.2 to 4.1)
No	206 (80)	1137 (92)	1	1	713 201 (93)	1
Very low birth weight (<1500 g):						
Yes	14 (5)	22 (2)	3.2 (1.6 to 6.3)	2.9 (1.3 to 6.4)	10 955 (1)§	4.0 (2.3 to 6.9)
No	242 (95)	1209 (98)	1	1	759 318 (99)	1
Preterm (<37 weeks):						
Yes	59 (24)	89 (7)	3.9 (2.7 to 5.6)	4.0 (2.7 to 5.9)	36 283 (8)	3.6 (2.7 to 4.8)
No	192 (76)	1129 (93)	1	1	423 475 (92)	1
Very preterm (<32 weeks):						
Yes	18 (7)	18 (1)	5.2 (2.6 to 10.0)	4.9 (2.4 to 10.0)	10 932 (2)	3.2 (2.0 to 5.1)
No	233 (93)	1200 (99)	1	1	449 101 (98)	1
Delivered by caesarean section:						
Yes	100 (40)	299 (25)	2.1 (1.5 to 2.7)	2.3 (1.7 to 3.2)	139 449 (24)	2.2 (1.7 to 2.8)
No	150 (60)	921 (75)	1	1	453 951 (76)	1
Congenital anomalies:						
Yes	8 (3)	NA	NA	NA	4 308 (2)	1.9 (0.9 to 3.8)
No	243 (97)				248 644 (100)	1

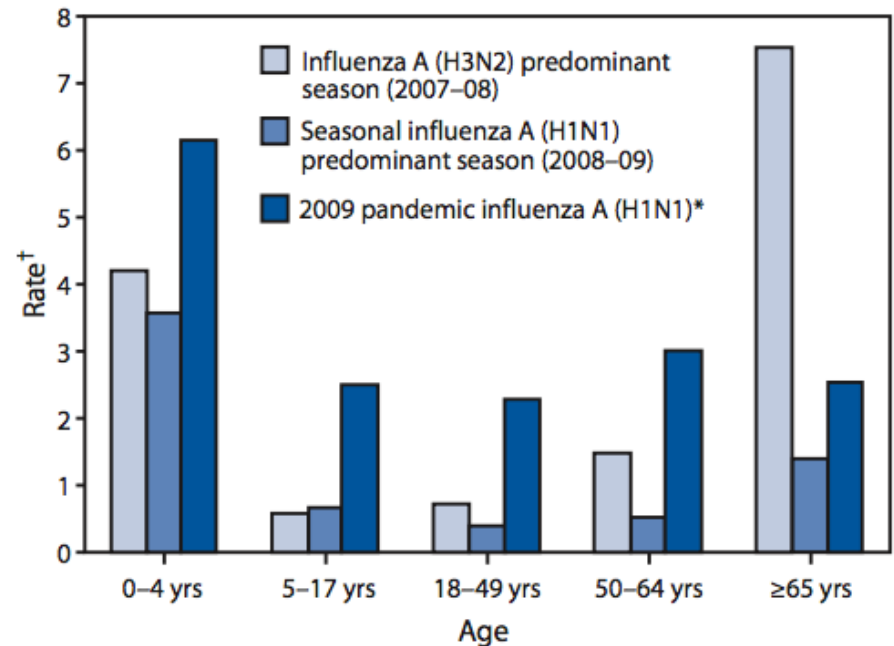
Influenza – risks in pregnancy & infancy

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

ⁱ MMWR 2010;59:1-62

ⁱⁱ MMWR 2016;65(22):567-575

FIGURE 1. Cumulative rate of hospitalizations during three influenza seasons, by age group — Emerging Infections Program, United States, 2007–2010

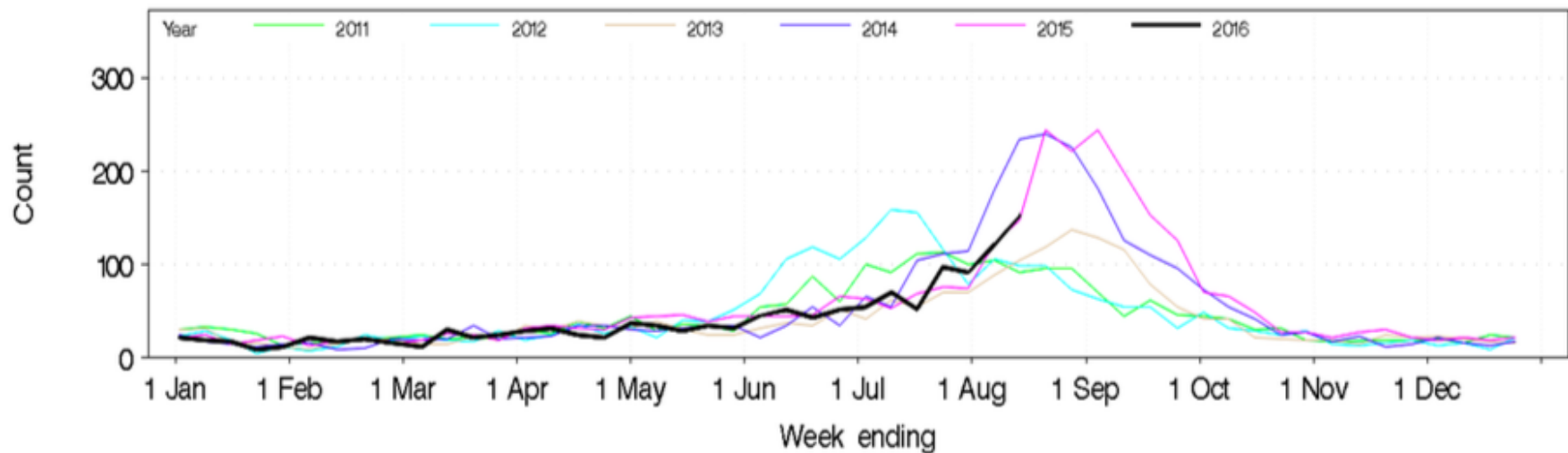


* 2009 Pandemic Influenza A(H1N1) hospitalization data from September 1, 2009–January 21, 2010.

† Per 10,000 population.

Influenza – current epidemiology

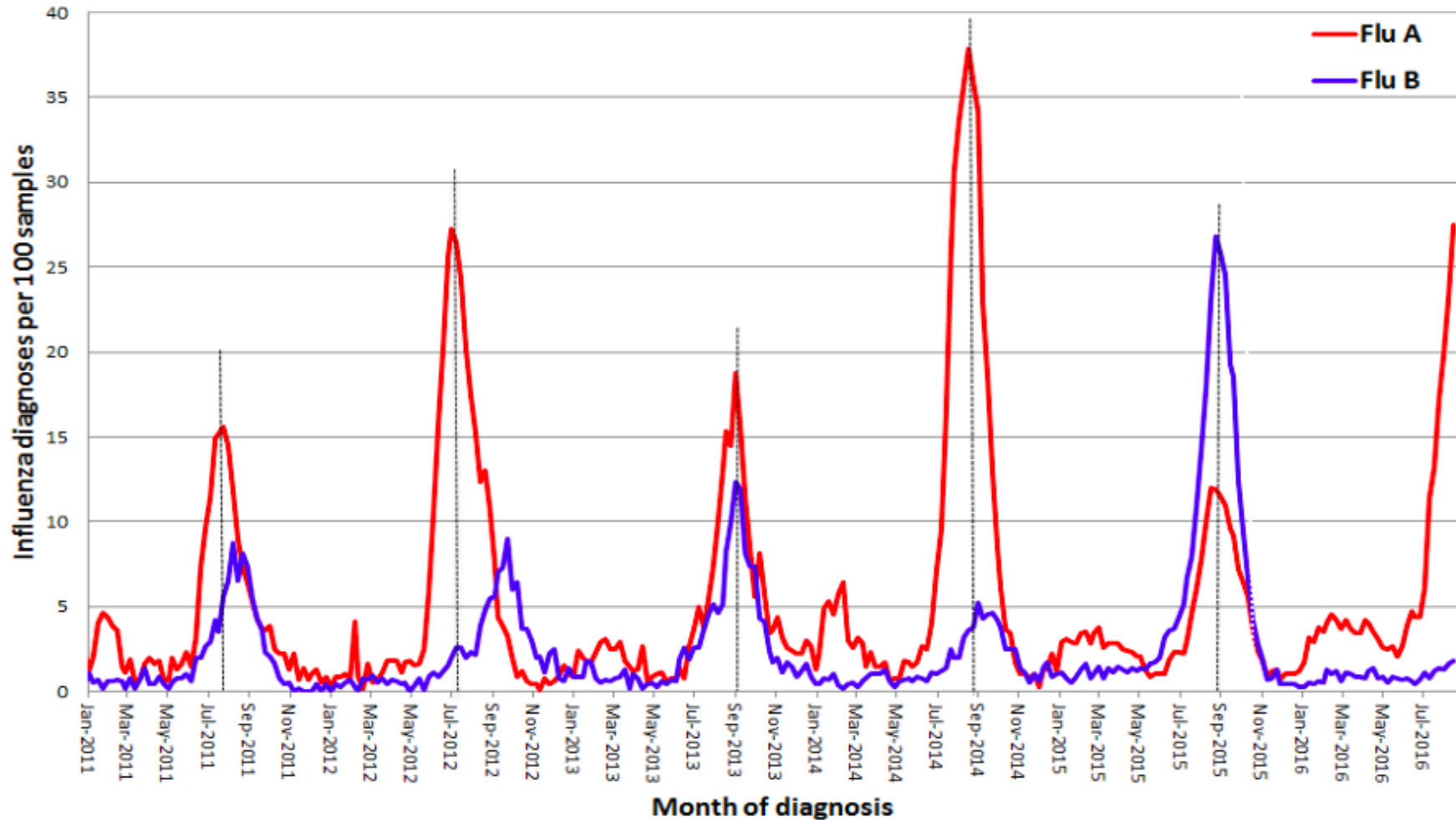
Figure 1: Total weekly counts of ED visits for influenza-like illness, all ages, from 1 January – 14 August 2016 (black line), compared with each of the 5 previous years (coloured lines).



- 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

Tamma PD, et al. Safety of influenza vaccination during pregnancy. *Am J Obstet Gynecol.* 201(6), 547–552 (2009).

Bednarczyk RA, et al. Safety of influenza immunization during pregnancy for the fetus and the neonate. *Am. J. Obstet. Gynecol. Supp.* Sept 2012

- **Contraindications:** previous anaphylaxis to flu vaccine or eggs

Influenza vaccine – evidence for efficacy

- Similar immunological response to non-pregnant women ⁱ
- 36% reduction in febrile respiratory illness in third trimester (RCT ⁱⁱ)
- 50% -70% reduction in confirmed influenza in vaccinated women (RCT ⁱⁱⁱ; population cohort ^{iv})

ⁱTamma 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

Eick Arch Ped & Adol Med 165:2 Feb 2011 (US - native American)

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

Poehling Am J Obstet Gynecol 2011: 204: S141-8 (US)

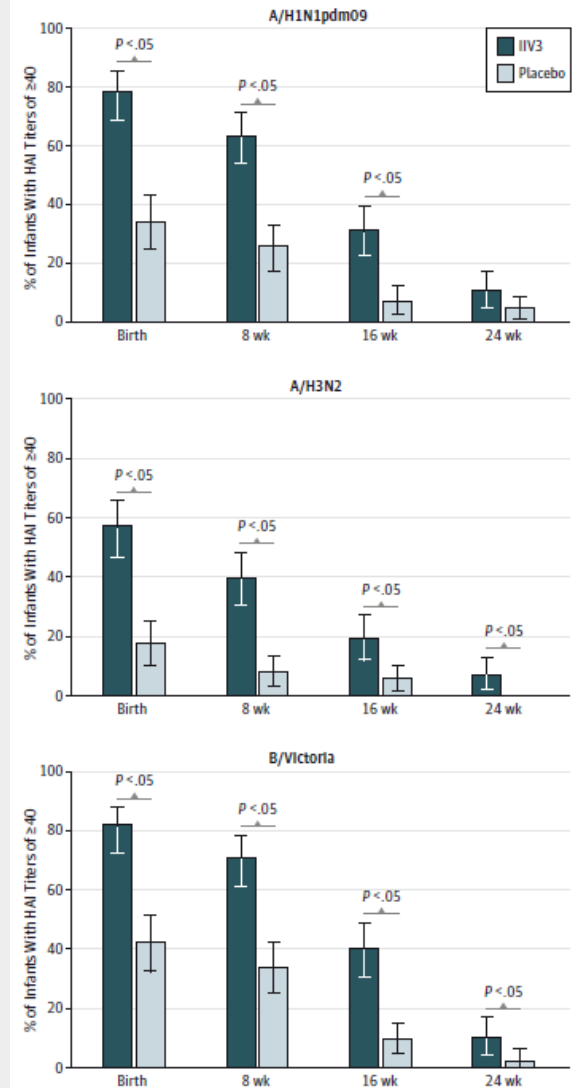
- Case control 151 infants
- 45 – 48% decrease infant influenza hospitalisation

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

Figure 2. Percentage of Infants With Hemagglutination Inhibition Titers of 1:40 or More at the Different Study Time Points



The error bars indicate 95% CIs. HAI, indicates hemagglutination inhibition; IIV3, trivalent inactivated influenza vaccine.

Influenza vaccine – evidence for efficacy

Nunes JAMA Pediatrics: July 5 2016 (South Africa)

Table 2. Incidence Rates of PCR-Confirmed Influenza Illness and Vaccine Efficacy by Age Group

PCR-Confirmed Influenza	IIV3 Group			Placebo Group			Vaccine Efficacy (95% CI)	P Value
	Infants, No.	Person-Time, mo	Incidence Rate (95% CI) ^a	Infants, No.	Person-Time, mo	Incidence Rate (95% CI) ^a		
Overall								
≤8 wk	2	2083.7	1.0 (0.2-3.8)	14	2066.4	6.8 (4.0-11.4)	85.8 (38.3-98.4)	.01
>8-16 wk	12	1818.0	6.6 (3.7-11.6)	16	1806.5	8.9 (5.4-14.5)	25.5 (-67.9 to 67.8)	.44
>16-24 wk	5	1670.5	3.0 (1.2-7.2)	7	1628.8	4.3 (2.0-9.0)	30.4 (-154.9 to 82.6)	.54
≤16 wk	14	3898.0	3.6 (2.1-6.1)	30	3847.2	7.8 (5.5-11.2)	53.9 (10.4-77.4)	.02
≤24 wk	19	5568.4	3.4 (2.2-5.3)	37	5476.1	6.8 (4.9-9.3)	49.5 (9.9-72.6)	.02
During influenza season								
≤8 wk	2	1697.8	1.2 (0.15-4.3)	14	1697.8	8.2 (4.5-13.8)	85.4 (36.5-98.4)	.01
≤16 wk	14	2538.2	5.5 (3.0-9.2)	30	2534.1	11.8 (8.0-16.9)	53.4 (9.4-77.2)	.02
≤24 wk	19	2766.1	6.9 (4.1-10.7)	36	2755.1	13.1 (9.2-18.0)	47.4 (5.9-71.5)	.02

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

^a Incidence rates calculated as number of cases per 1000 child-months, using person-time between birth and event or end of study.



First endorsed by RANZCOG: November 2011
Current: November 2013
Review due: November 2016

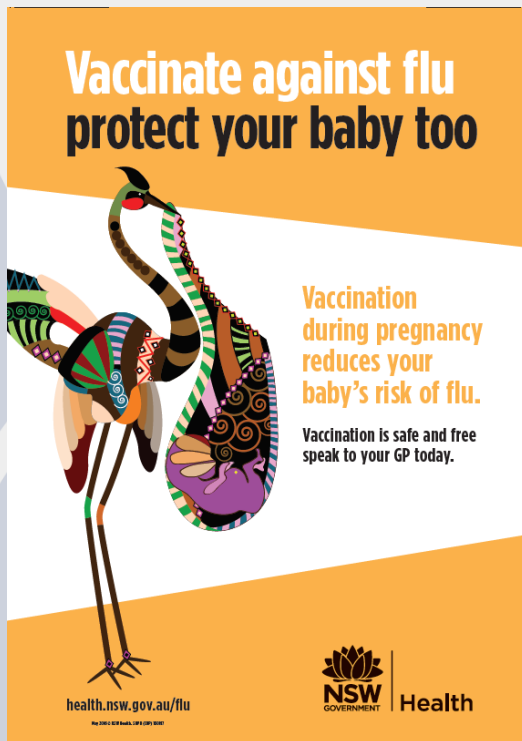
Influenza vaccination during pregnancy (and in women planning pregnancy)

2. Summary of recommendations

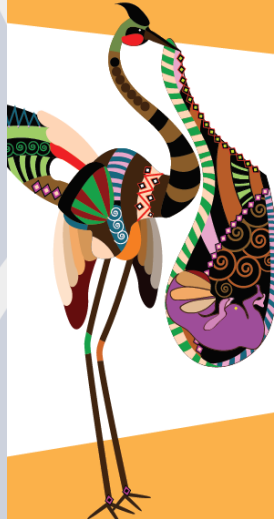
Recommendation 1	Grade and reference
<p>Influenza vaccination is recommended for all pregnant women regardless of gestation, and in women planning pregnancy.</p>	<p>Consensus-based recommendation 1</p>
Good Practice Notes	Grade
<p>Free influenza vaccine is available to all pregnant women in Australia and New Zealand.</p> <p>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.</p> <p>For more information relevant to Australia please visit: http://www.health.gov.au/internet/immunise/publishing.nsf/Content/immunise-influenza or http://www.influenza.org.nz/?t=887 for information specific to New Zealand.</p>	<p>Good Practice Note</p>
Recommendation 2	Grade
<p>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.</p>	<p>Consensus-based recommendation</p>
Recommendation 3	Grade
<p>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.</p>	<p>Consensus-based recommendation</p>

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



**Vaccinate against flu
protect your baby too**



Vaccination during pregnancy reduces your baby's risk of flu.

Vaccination is safe and free speak to your GP today.

health.nsw.gov.au/flu

NSW GOVERNMENT Health



Free flu shots for those medically at risk.

Talk to your GP.

www.health.nsw.gov.au/flu

Are you at risk of severe flu?

YOUR MEDICAL CONDITION PUTS YOU AT GREATER RISK.

- KIDNEY DISEASE
- HIV/AIDS
- DIABETES
- PREGNANT
- CANCER
- HEART DISEASE
- LIVER DISEASE
- SEVERE ASTHMA

NSW GOVERNMENT Health

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Flu vaccine uptake in pregnancy

- National Vaccination Survey 2009: 12.7% of pregnant women vaccinated
- Uptake now ~45%ⁱ
- Uptake is strongly influenced by health professional recommendation (OR: 20ⁱⁱ - 42ⁱⁱⁱ)
- 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”

FluMum Study

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

