REVIEW OF INFLUENZA VACCINE SAFETY
IN PREGNANT WOMEN
(and their infants)

First WHO Integrated Meeting on Development and Clinical Trials of Influenza Vaccines that Induce Broadly Protective and Long-lasting Immune Responses
Hong Kong Baptist University, Hong Kong SAR, China

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Influenza Disease During Pregnancy

Influenza infection in pregnant women:

- Increased severity during 3\textsuperscript{rd} trimester
- Increased severity with pre-existing conditions
- Increased severity with new influenza strain
- Impacts the fetus
### TABLE 1

Relative risk of hospitalization, intensive care unit admission, death, or any severe outcome in pregnant women due to 2009 H1N1 influenza

<table>
<thead>
<tr>
<th>Paper</th>
<th>Risk of hospitalization</th>
<th>Risk of ICU admission</th>
<th>Risk of death</th>
<th>Risk of severe disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>New South Wales Public Health Network(^1)</td>
<td>RR, 5.8(^a)</td>
<td>RR, 10.2(^a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANZIC(^2)</td>
<td>RR, 7.4(^a)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Campbell et al(^2,3)</td>
<td>RR, 0.7 (0.4–1.2)(^a)</td>
<td>RR, 1.1 (0.3–4.1)(^a)</td>
<td>RR, 0.7 (0.4–1.3)</td>
<td></td>
</tr>
<tr>
<td>Creanga et al(^13)</td>
<td>RR, 7.2(^a)</td>
<td></td>
<td></td>
<td>RR, 4.3(^a)</td>
</tr>
<tr>
<td>Fuhrman et al(^62)</td>
<td>aOR, 0.3 (0.04–3.0)</td>
<td>aOR, 0.5 (0.2–0.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gérardin et al(^46)</td>
<td>RR, 0.4 (0–2.6)(^a)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hanslik et al(^23)</td>
<td>OR, 5.2 (4.0–6.9)</td>
<td>OR, 1.4 (0.3–4.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jamieson et al(^3)</td>
<td>RR, 4.3 (2.3–7.8)(^b)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kelly et al(^28)</td>
<td>RR, 5.2 (4.6–5.8)(^b)</td>
<td>RR, 6.5 (4.8–8.8)(^b)</td>
<td>RR, 1.4 (0.4–4.5)(^b)</td>
<td></td>
</tr>
<tr>
<td>Koegelemenberg et al(^20)</td>
<td>OR, 1.13 (0.14–8.88)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oliveira et al(^31)</td>
<td>OR, 1.07 (0.82–1.41)(^a)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang et al(^53)</td>
<td>OR, 0.8 (0.2–3.5)</td>
<td>OR, 0.4 (0.2–3.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zarychanski et al(^106)</td>
<td>OR, 3.64 (0.86–15.4)(^a,c)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Compared to nonpregnant women of reproductive age; \(^b\) Compared to general population; \(^c\) This number reports increased odds that pregnant women would require ICU admission over that they would require only outpatient treatment.

## Risk Factors for Severe Outcomes following 2009 Influenza A (H1N1) Infection: A Global Pooled Analysis

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>RR Hospitalization</th>
<th>RR Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>1.0 (0.8–1.1)</td>
<td>0.8 (0.7–1.0)</td>
</tr>
<tr>
<td>Respiratory Disease</td>
<td>3.3 (2.0–5.8)</td>
<td>7.8 (4.9–26.6)</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.8 (1.2–2.6)</td>
<td>1.7 (1.5–2.1)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.9 (0.5–1.7)</td>
<td>4.0 (3.1–6.9)</td>
</tr>
<tr>
<td>Cardiac Disease</td>
<td>2.0 (1.5–2.2)</td>
<td>9.2 (5.4–10.7)</td>
</tr>
<tr>
<td>Renal Disease</td>
<td>4.4 (4.2–4.5)</td>
<td>22.7 (21.0–25.4)</td>
</tr>
<tr>
<td>Liver Disease</td>
<td>3.57 (3.2–15.7)</td>
<td>17.4 (11.6–28.0)</td>
</tr>
<tr>
<td>Neurological Disease</td>
<td>1.1 (0.9–1.3)</td>
<td>13.1 (8.4–32.4)</td>
</tr>
<tr>
<td>Immune Compromised</td>
<td>24.3 (16.1–32.6)</td>
<td>27.7 (14.0–66.5)</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td><strong>6.8 (4.5–12.3)</strong></td>
<td><strong>1.9 (0.0–2.6)</strong></td>
</tr>
</tbody>
</table>

Relative Risk differed by country from 3.5 in Germany to 25.3 in France, and may reflect clinical practice variations and health care utilization.

*Van Kerkhove, Mounts PLoS Med 2011*
## Fetal Risk of Maternal Influenza (Surveillance Studies)

<table>
<thead>
<tr>
<th>Study</th>
<th>Site</th>
<th>Case</th>
<th>Control</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>McNeill AJOG 2011</td>
<td>Canada 1990-2002</td>
<td>Maternal influenza season respiratory hospitalization</td>
<td>No hospitalization (132,099)</td>
<td>Newborns of hospitalized cases were 90gm smaller, 40% more likely to be small for gestational age</td>
</tr>
<tr>
<td>Mendez-Figueroa AJOG 2011</td>
<td>USA 2009-10</td>
<td>Maternal ILI with lab confirmed pandemic H1N1 (15)</td>
<td>Maternal ILI with lab test negative (25)</td>
<td>Newborns exposed to influenza were 285gm smaller</td>
</tr>
<tr>
<td>Pierce BMJ 2011</td>
<td>UK 2009-2010</td>
<td>Pregnant women with Lab-confirmed hospitalization for pandemic H1N1 (256)</td>
<td>Historical comparison of pregnant women from 2005-2006 (1220)</td>
<td>Newborns exposed to influenza were 255 g smaller. Higher perinatal mortality and premature birth in exposed.</td>
</tr>
</tbody>
</table>
There were 117,347 eligible pregnancies in Norway from 2009 through 2010. Fetal mortality was 4.9 deaths per 1000 births. During the pandemic, 54% of pregnant women in their second or third trimester were vaccinated. Vaccination during pregnancy substantially reduced the risk of an influenza diagnosis (adjusted hazard ratio, 0.30; 95% confidence interval [CI], 0.25 to 0.34). Among pregnant women with a clinical diagnosis of influenza, the risk of fetal death was increased (adjusted hazard ratio, 1.91; 95% CI, 1.07 to 3.41). The risk of fetal death was reduced with vaccination during pregnancy, although this reduction was not significant (adjusted hazard ratio, 0.88; 95% CI, 0.66 to 1.17).
Influenza Vaccine and Pregnant Women*

- High burden of influenza illness among pregnant women.
- Excellent immunogenicity and safety profile of TIV.
- Effectiveness in infants born to vaccinated mothers.
- No good alternatives for neonates, young infants.
- Main barriers: logistics and costs.

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Influenza Vaccine in Pregnant Women

- Used for > 50 years
- Excellent safety profile
- Immunogenic in pregnant women
- No clinical effectiveness studies with lab-confirmed outcomes in pregnant women
- Studies mostly small and focused on safety, immunogenicity
- One published randomized, prospective, controlled effectiveness study in Bangladesh (influenza vaccine vs. pneumococcal polysaccharide vaccine)

Southwest Washington Health District, WA, USA
TIV Clinical Effectiveness in Immunized Pregnant Women

Zaman 2008: TIV in Bangladesh (blinded, prospective, randomized)
  • 25-45% clinical effectiveness against nonspecific criteria

Sheffield 2011: TIV given to pregnant women 2003-2004 (non-randomized)
  • 2889 women received TIV; 1998 matched controls
  • Decrease flu+ disease in women: 99% efficacy

Observational studies using administrative databases with mixed findings:
  • Black 2004: no benefit to mother or child
SAFETY OF INFLUENZA VACCINES DURING PREGNANCY

Safety of flu vaccines assessed using:*  
- Prospective clinical trials**  
- Retrospective and database studies  
- Post-marketing passive reporting systems  
- VAERS or VSD in the US  
- Yellow Card System in the UK  
- Other vaccine safety systems using databases that link vaccination history and medical outcomes  
- Post-marketing Pregnancy Registries

** Limitations:  
1. Under reporting  
2. In addition to number of events, calculation of a rate or attributable risk (using # persons vaccinated as denominator) is necessary to evaluate relationship or causality;  
3. Confounders  
4. Insufficient power

* Ortiz et al, Vaccine 2011; Blancard-Rohner, Siegrist Vaccine 2011; Munoz 2012  
** Zaman NEJM 2009; Englund JID 1993
Collaborative Perinatal Project, 1959-1965, USA\textsuperscript{1-2}

- >50,000 immunized pregnant women and their offspring were followed for up to 7 years to evaluate factors for CP, CNS damage
- 2,291 doses TIV administered, of which 650 given in first 4 mo
- No significant increase in adverse outcomes in mothers or infants (stillbirths, malformations, malignancies, neurocognitive disability, hearing loss, cancer). Excluded miscarriages, twins/triplets.

Asian Influenza Outbreak study, 1962-63 \textsuperscript{3}

- 225 pregnant (19 first term)/44 non-pregnant vaccinated vs. 104 pregnant/25 non-pregnant placebo were evaluated
- 2 injections of “polyvalent vaccine” containing 200 U A2 antigen
- Expected local/systemic reactogenicity, no fetal anomalies or miscarriage associated – 1st trimester vaccination

1976 – 1989 USA

- Over 300 pregnant women received influenza vaccine in 4 studies (A/New Jersey/8/76\textsuperscript{1-3} or TIV\textsuperscript{4}, “whole virus”)
- Vaccinations in first to third trimester
  - Pre-conception (13); 1\textsuperscript{st} trimester (46); 2\textsuperscript{nd} trimester (80); 3\textsuperscript{rd} trimester (122)
  - 2\textsuperscript{nd} or 3\textsuperscript{rd} trimester (56)
- Control groups: Non-vaccinated pregnant women, influenza vaccinated non-pregnant women, pregnant women vaccinated TT
- Follow up varied from immediate reactogenicity to 8 wks postpartum
- No significant adverse reactions, including fever, local or systemic reactions (mild fever, headache, flu-like symptoms reported)
- No fetal, perinatal or infant complications associated with the administration of influenza vaccine

Influenza Vaccine Safety in Retrospective/Database Studies

Houston, TX - USA

- 1998-2003: 252 pregnant women who received TIV within 6 months of delivery matched with 826 unvaccinated pregnant women¹
  - No SAE within 42 days of vaccination
  - No difference in pregnancy outcomes (C/S, premature birth) or infant medical conditions from birth to 6 months of age

- 2004-2005: 1,006 pregnant women vaccinated with TIV (all trimesters – mean GA 23.6 wk) matched with 1,495 unvaccinated pregnant women²
  - No SAE within 42 days of vaccination
  - No difference in maternal hospitalization for reasons other than delivery, C/S, prematurity, infant medical conditions to 6 mo of age

CDC VAERS\textsuperscript{1} from 1990 to 2009: Estimated 11.8 million vaccinated pregnant women

- 148 reports after TIV and 27 reports after LAIV
- No AEs in 30 (20.3\%) TIV and 16 (59.3\%) LAIV
- Gestational age at vaccination: TIV – 1\textsuperscript{st} (28), 2\textsuperscript{nd} (41) 3\textsuperscript{rd} (22); LAIV – 1\textsuperscript{st} (10), 2\textsuperscript{nd} (3), 3\textsuperscript{rd} (3)
- SAE: 20 (13.5\%) TIV* and 1 (4\%) LAIV**
- No maternal deaths
- Most common pregnancy specific AE was spontaneous abortion: 17 (11.5\%) TIV; 3 (11\%) LAIV [overall rate 1.9 cases/million vs. 5.5 bkg]
- No new, unusual, or unexpected pattern of adverse pregnancy events or fetal outcomes
- No increased risk of adverse pregnancy outcomes when compared to background rates

\textsuperscript{1} Moro et al. Am J Obstet Gynecol 2010; 203:1.e1-e7
* One anaphylactic reaction; ** Miscarriage at 16 weeks after receipt of LAIV at 12 weeks in a 26 year old woman
Prospective Cohort Study – UK 2009-10*

- ASO3-adjuvanted split virion H1N1 2009 vaccine, 1 dose
- Cohort of 267 pregnant women, mean age 31 yrs, mostly healthy (83%), in all trimesters (42 in 1st, 115 in 2nd, 110 in 3rd); 45% < 24 wk gestation, 55%> 24 wk – No control group
- Results: No increase in risk of adverse pregnancy outcomes including spontaneous abortion, congenital anomalies, preterm delivery, LBW or maternal complications
- Clear definitions of pregnancy outcomes, congenital anomalies and birth defects, Medically Attended AE, SAE, AE of Special Interest, and use of background rates for analysis
- Safety follow up 31 days and 6 months post vaccine for mothers, 6 months of life for babies.

Recent Publications on Influenza Vaccine Safety During Pregnancy: 2009-2012

AJOG Supplement, 2012:

- Munoz FM. Safety of influenza vaccines in pregnant women.
- Khromava A et al. Manufacturers’ post-marketing safety surveillance of influenza vaccine exposure in pregnancy
- Kharbanda EO et al. Assessing the safety of influenza immunization during pregnancy: the Vaccine Safety Datalink
- Heikkinen T et al. Safety of MF-59-adjuvanted A/H1N1 influenza vaccine in pregnancy: a comparative cohort study

Recent Reviews

Safety of Adjuvanted Influenza H1N1 vaccines in Pregnant Women, 2010-2012

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Study Group</th>
<th>Control Group</th>
<th>F/Up Period</th>
<th>Maternal Outcomes</th>
<th>Infant Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsai et al Vaccine 2010</td>
<td>Novartis trial database of MF59 adjuvanted Flu vaccines (N=23,300) and unadjuvanted (N=40,285)</td>
<td>43 pregnancies after MF59 and 60 pregnancies after nonadj flu vx; majority vx in 1st trimester</td>
<td>None</td>
<td>Delivery</td>
<td>No signals of risk but small numbers; similar rates after nonadj. &amp; MF59 adj vx</td>
<td>Not reported</td>
</tr>
<tr>
<td>Tavares et al Vaccine 2011</td>
<td>Cohort study of 267 women in all trimesters</td>
<td>267 women given ASO3-adj 2009 H1N1 vaccine</td>
<td>None</td>
<td>6 mos. Post Delivery</td>
<td>No adverse effects on pregnancy</td>
<td>No impact on fetus, infant</td>
</tr>
<tr>
<td>Gisslser et al ESPID 2012</td>
<td>Retrospective database review</td>
<td>76,043 newborn; 12,510 spon. abortions</td>
<td>No maternal vx</td>
<td>Delivery</td>
<td>Pandemrix vaccine did not affect course of pregnancy</td>
<td>Protective effect on newborns regardless of smoking hx</td>
</tr>
<tr>
<td>Mackenzie et al Br J Clin Pharm 2012</td>
<td>Safety surveillance feasibility study in Scotland</td>
<td>3754 vaccinated people, with 117 pregnant women</td>
<td>312 who declined vaccine</td>
<td>Delivery</td>
<td>No significant safety issues ; 4 miscarriages overall</td>
<td>No significant risk6 possible congenital abnormalities</td>
</tr>
<tr>
<td>Oppermann et al Vaccine 2012</td>
<td>F/up of German pregnant women given ASO3 or nonadj. flu vx</td>
<td>323 pregnant women any trimester</td>
<td>1329 controls</td>
<td>Delivery</td>
<td>No attributable risk vs. controls</td>
<td>No attributable risk vs. controls</td>
</tr>
</tbody>
</table>
Safety information for influenza vaccines continues to be reassuring.

Significant morbidity due to vaccine-preventable diseases among women and infants could be prevented by immunization of pregnant women.

Despite lack of apparent safety issues, precautions and contraindications limiting vaccine benefits to women are often included in product labeling.

Further action by GACVS (Dec 2012):
- Continue to monitor and report adverse events in pregnant women following the use of influenza vaccine
- Review relevant evidence
- Include methodological points for planning and analysis of clinical trials and post-marketing studies
- GACVS meeting to discuss maternal immunization
EFFECTIVENESS BY WHO GRADE: TABLE 1B*

Is TIV vs. no intervention or non-influenza vx in pregnant women effective to prevent influenza infection and severe outcomes of infection in pregnant women?

• Zaman 2008:
  ▪ Effectiveness against respiratory illness with fever was 36%, implying a significant reduction achieved by influenza vaccination of pregnant women.

• Englund 1993:
  ▪ No information on vaccine efficacy in pregnant women and the impact on laboratory-confirmed influenza (Note: not studied).

• Hulka 1964:
  ▪ No significant difference in effectiveness of influenza vaccine vs. other vaccine against MAARI.

• Excluded: Decades of immunogenicity studies, observational studies, effectiveness studies in non-pregnant adults, outcomes including newborn influenza or birthweight.

*http://www.who.int/immunization/position_papers/influenza_grad_maternal_outcomes.pdf
Maternal Immunization with Influenza Vaccine Protects Mothers and Babies Against Influenza*

- Prospective randomized but relatively small study (total = 340 women)
- Women immunized during 3rd trimester and followed with infants for 2 years
- Control vaccine = Pneumo PS
- Flu detection: insensitive test

<table>
<thead>
<tr>
<th>Variable</th>
<th>Episodes</th>
<th>Clinical Effectiveness (95% CI)</th>
<th>Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza Vaccine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Person-months</td>
<td>1076</td>
<td>1089</td>
<td></td>
</tr>
<tr>
<td>Respiratory illness with fever</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any fever</td>
<td>77</td>
<td>50</td>
<td>35.8 (3.7 to 57.2)</td>
</tr>
<tr>
<td>Temperature &gt;38°C</td>
<td>33</td>
<td>19</td>
<td>43.1 (-9.0 to 70.3)</td>
</tr>
<tr>
<td>Diarrheal disease</td>
<td>60</td>
<td>49</td>
<td>19.3 (-24.6 to 47.8)</td>
</tr>
<tr>
<td>Clinic visit</td>
<td>25</td>
<td>19</td>
<td>24.9 (-43.9 to 60.8)</td>
</tr>
</tbody>
</table>

Figure 2. Cumulative Cases of Laboratory-Proven Influenza in Infants Whose Mothers Received Influenza Vaccine, as Compared with Control Subjects. Testing for influenza antigen was performed from December 2004 to November 2005.

*Zaman et al, NEJM 2008;359
Lower, more conservative estimates of expected maternal and neonatal deaths obtained based on person-time observations during different risk periods, particularly at an interim safety evaluation soon after a large number of deliveries.

Median incidence of SAMM in 16 reports was 40.7 (IQR: 10.6–73.3) per 1,000 total births, and the most common causes were hemorrhage (34%), dystocia (22%), and severe hypertensive disorders of pregnancy (22%).

Proportions of liveborn infants who were LBW (median 13.3%, IQR: 9.9–16.4) or premature (median 15.4%, IQR: 10.6–19.1) were similar across geographic region, study design, and institutional setting.

The median incidence of MCM per 1,000 live births was 14.4 (IQR: 5.5–17.6).

Source: Orenstein LAV et al. PLoS ONE 7(10): e46638
## Maternal Influenza Immunization and Infant Outcomes

<table>
<thead>
<tr>
<th>Author</th>
<th>Site/ Dates</th>
<th>Design</th>
<th># VX</th>
<th># Control</th>
<th>Infant Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zaman 2008</td>
<td>Bangladesh 2004-5</td>
<td>RC Vx Trial</td>
<td>172</td>
<td>168</td>
<td>↓ 36% ILI ↓ 69% lab + flu</td>
</tr>
<tr>
<td>Poehling 2011</td>
<td>TN, OH, NY USA 2002-9</td>
<td>Case Control</td>
<td>151</td>
<td>1359</td>
<td>↓ 45-48% hospitalization</td>
</tr>
<tr>
<td>Eick 2011</td>
<td>Apache/ Najavo USA 2002-5</td>
<td>Prospective observational cohort</td>
<td>573</td>
<td>587</td>
<td>↓ 41% lab + flu</td>
</tr>
<tr>
<td>Benowitz 2010</td>
<td>CN/ USA 2000-9</td>
<td>Case-control</td>
<td>91</td>
<td>156</td>
<td>↓ 91.5% hospitalized flu+</td>
</tr>
</tbody>
</table>

*J. Englund. Presentation to SAGE. April 2012.*
Increased birth weight in babies born to TIV-immunized mothers support results of Bangladesh study

<table>
<thead>
<tr>
<th>Author</th>
<th>Site</th>
<th>Trial Design</th>
<th>Interventions</th>
<th>Control</th>
<th>Birth-weight</th>
<th>Outcomes: % SGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steinhoff 2011</td>
<td>Bangladesh</td>
<td>Random, controlled</td>
<td>Flu vx N = 172</td>
<td>Pneumo PS Vx N=168</td>
<td>↑200 g</td>
<td>↓34%</td>
</tr>
<tr>
<td>McNeil 2011</td>
<td>Nova Scotia, Canada</td>
<td>Retrospective</td>
<td>TIV given N = 208</td>
<td>No TIV N = 132,099</td>
<td>↑90g</td>
<td>↓40%</td>
</tr>
<tr>
<td>Omer 2011</td>
<td>Georgia, USA</td>
<td>Retrospective cohort analysis</td>
<td>TIV N = 578</td>
<td>No vx N =3748</td>
<td>--</td>
<td>↓70%</td>
</tr>
</tbody>
</table>
SAFETY OF INFLUENZA VACCINE DURING PREGNANCY

Must Consider:

- Risks inherent in pregnancy
- Risk of influenza in the pregnant woman:
  - Risk of influenza in the fetus
- Risks of vaccine to the woman
- Risks of vaccine to the fetus/infant

NOTE: May be difficult to dissociate the above risks
SAFETY OF INFLUENZA VACCINE DURING PREGNANCY

- Risks inherent in pregnancy: LOW-MODERATE
- Risk of influenza in the pregnant woman: MODERATE
- Risk of influenza in the fetus: VERY LOW

- Risks of vaccine to the woman: VERY LOW
- Risks of vaccine to the fetus/infant: VERY LOW

NOTE: May be difficult to dissociate the above risks
Pregnant women represent the most important risk group for receipt of inactivated seasonal influenza vaccine.

The priority accord to pregnant women was based on “compelling evidence of substantial risk of severe disease in this group and evidence that seasonal influenza vaccine is safe and effective in preventing disease in pregnant women as well as their young infants, in whom disease burden is also high.”

No recommendation for timing of influenza vaccine during pregnancy.

Revision of WHO Position Paper and Grade Tables published in Nov. 2012.
This recommendation is based on evidence of:

- **High risk of severe disease**
- **Safety** of seasonal influenza vaccine throughout pregnancy in women and fetus/infants
- **Effectiveness** of preventing influenza in the women as well as in their young infants, in whom the disease burden is also high.

Clinical Studies of Maternal Influenza Immunization Underway

- Ongoing clinical studies of influenza in pregnant women may help answer questions regarding effectiveness, safety, and benefits in outcomes.
- EXAMPLE: Prospective, randomized clinical studies of TIV in pregnant women sponsored by Gates Fndn underway in Mali, Nepal, and South Africa in 2\textsuperscript{nd} year, with thousands of pregnant women enrolled at each site.
Our research staff and:

- Justin Ortiz and Kathy Neuzil, MD - University of Washington/ PATH
- Flor Munoz, MD and WP Glezen, MD - Baylor College of Medicine
- Mark Steinhoff, MD - Cincinnati Children’s Hospital
- Jim Tielsch and Joanne Katz, Johns Hopkins School of Public Health