National Center for Immunization & Respiratory Diseases

Vaccinating pregnant women: New data and new Healthy People goal

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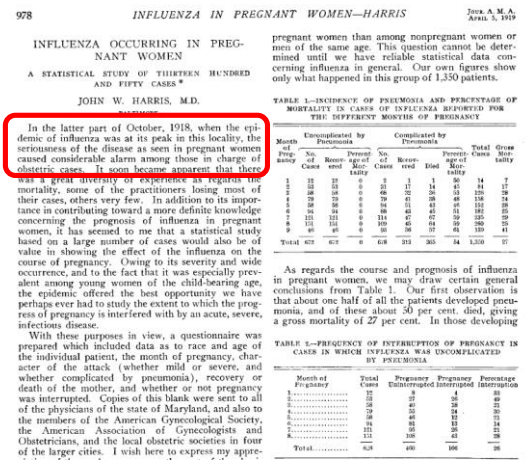
Outline

- Historical Context
- Recommendations and Healthy People 2020 Goal
- Influenza Burden and Vaccine Effectiveness in Pregnant Women
- Influenza Burden and Effectiveness of Maternal Vaccination in Infants
- Influenza Vaccine Safety
- Influenza Vaccine Cost Effectiveness
- Conclusions—What We Know Now

Early Recognition that Pregnancy Confers Increased Risk for Severe Pandemic Influenza

- Harris et al. published first case series of 1350 pregnant women with clinical influenza from the 1918 pandemic more than 10 years before isolation of the influenza virus



978 INFLUENZA IN PREGNANT WOMEN—HARRIS JOUR. A. M. A. APRIL 5, 1919

INFLUENZA OCCURRING IN PREGNANT WOMEN

A STATISTICAL STUDY OF THIRTEEN HUNDRED AND FIFTY CASES *

JOHN W. HARRIS, M.D.

In the latter part of October, 1918, when the epidemic of influenza was at its peak in this locality, the seriousness of the disease as seen in pregnant women caused considerable alarm among those in charge of obstetric cases. It soon became apparent that there was a great diversity of experience as regards the mortality, some of the practitioners losing most of their cases, others very few. In addition to its importance in contributing toward a more definite knowledge concerning the prognosis of influenza in pregnant women, it has seemed to me that a statistical study based on a large number of cases would also be of value in showing the effect of the influenza on the course of pregnancy. Owing to its severity and wide occurrence, and to the fact that it was especially prevalent among young women of the child-bearing age, the epidemic offered the best opportunity we have perhaps ever had to study the extent to which the progress of pregnancy is interfered with by an acute, severe, infectious disease.

With these purposes in view, a questionnaire was prepared which included data as to race and age of the individual patient, the month of pregnancy, character of the attack (whether mild or severe, and whether complicated by pneumonia), recovery or death of the mother, and whether or not pregnancy was interrupted. Copies of this blank were sent to all of the physicians of the state of Maryland, and also to the members of the American Gynecological Society, the American Association of Gynecologists and Obstetricians, and the local obstetric societies in four of the larger cities. I wish here to express my appre-

pregnant women than among nonpregnant women or men of the same age. This question cannot be determined until we have reliable statistical data concerning influenza in general. Our own figures show only what happened in this group of 1,350 patients.

TABLE 1.—INCIDENCE OF PNEUMONIA AND PERCENTAGE OF MORTALITY IN CASES OF INFLUENZA REPORTED FOR THE DIFFERENT MONTHS OF PREGNANCY

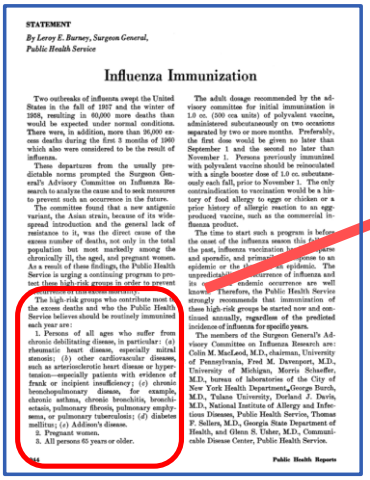
Month of Pregnancy	Uncomplicated by Pneumonia: No. of Cases	Uncomplicated by Pneumonia: Recovered	Uncomplicated by Pneumonia: Percentage of Mortality	Complicated by Pneumonia: No. of Cases	Complicated by Pneumonia: Recovered	Complicated by Pneumonia: Died	Complicated by Pneumonia: Percentage of Mortality	Total Cases	Gross Mortality
1	22	22	0	3	1	1	50	14	7
2	68	68	0	23	17	14	45	91	17
3	108	108	0	66	32	26	44.8	174	26
4	79	79	0	79	47	32	40	158	74
5	56	56	0	94	51	43	46	150	98
6	54	54	0	86	43	45	51	140	95
7	121	121	0	114	47	67	59	235	59
8	151	151	0	109	45	64	59	260	75
9	46	46	0	36	26	37	61	135	41
Total	607	607	0	610	313	365	54	1,350	57

As regards the course and prognosis of influenza in pregnant women, we may draw certain general conclusions from Table 1. Our first observation is that about one half of all the patients developed pneumonia, and of these about 50 per cent. died, giving a gross mortality of 27 per cent. In those developing

TABLE 2.—FREQUENCY OF INTERRUPTION OF PREGNANCY IN CASES IN WHICH INFLUENZA WAS UNCOMPLICATED BY PNEUMONIA

Month of Pregnancy	Total Cases	Pregnancy Uninterrupted	Pregnancy Interrupted	Percentage Interruption
1	22	8	4	33
2	53	27	26	49
3	58	40	18	31
4	79	53	24	30
5	56	43	13	23
6	54	35	19	35
7	121	93	28	23
8	151	105	43	28
9	46	36	10	21
Total	638	440	186	29

Pregnant Women Have Been a Target Group for Influenza Vaccination Since the First Recommendations



STATEMENT

By Leroy E. Burney, Surgeon General, Public Health Service

Influenza Immunization

Two outbreaks of influenza swept the United States in the fall of 1957 and the winter of 1958, resulting in 60,000 more deaths than would be expected under normal conditions. There were, in addition, more than 90,000 excess deaths during the first 3 months of 1960 which also were considered to be the result of influenza.

These departures from the usually predictable norms prompted the Surgeon General's Advisory Committee on Influenza Research to analyze the cause and to seek measures to prevent such an occurrence in the future.

The committee found that a new antigenic variant, the Asian strain, because of its widespread introduction and the general lack of resistance to it, was the direct cause of the excess number of deaths, not only in the total population but most markedly among the chronically ill, the aged, and pregnant women. As a result of these findings, the Public Health Service is urging a continuing program to protect these high-risk groups in order to prevent influenza or its consequences.

The high-risk groups who contribute most to the excess deaths and who the Public Health Service believes should be routinely immunized each year are:

1. Persons of all ages who suffer from chronic debilitating disease, in particular: (*a*) rheumatic heart disease, especially mitral stenosis; (*b*) other cardiovascular diseases, such as arteriosclerotic heart disease or hypertension—especially patients with evidence of frank or incipient insufficiency; (*c*) chronic bronchopulmonary disease, for example, chronic asthma, chronic bronchitis, bronchiectasis, pulmonary fibrosis, pulmonary emphysema, or pulmonary tuberculosis; (*d*) diabetes mellitus; (*e*) Addison's disease.
2. Pregnant women.
3. All persons 65 years or older.

The adult dosage recommended by the advisory committee for initial immunization is 1.0 cc. (500 cca units) of polyvalent vaccine, administered subcutaneously on two occasions separated by two or more months. Preferably, the first dose would be given no later than September 1 and the second no later than November 1. Persons previously immunized with polyvalent vaccine should be reinoculated with a single booster dose of 1.0 cc. subcutaneously each fall, prior to November 1. The only contraindication to vaccination would be a history of food allergy to eggs or chicken or a prior history of allergic reaction to an egg-produced vaccine, such as the commercial influenza product.

The time to start such a program is before the onset of the influenza season this fall. In the past, influenza vaccination has appeared sporadic, and primarily [illegible] to an epidemic or the threat of an epidemic. The unpredictable occurrence of influenza and its [illegible] endemic occurrence are well known. Therefore, the Public Health Service strongly recommends that immunization of these high-risk groups be started now and continued annually, regardless of the predicted incidence of influenza for specific years.

The members of the Surgeon General's Advisory Committee on Influenza Research are: Colin M. MacLeod, M.D., chairman, University of Pennsylvania, Fred M. Davenport, M.D., University of Michigan, Morris Schaeffer, M.D., bureau of laboratories of the City of New York Health Department, George Darby, M.D., Tulane University, Dorland J. Davis, M.D., National Institute of Allergy and Infectious Diseases, Public Health Service, Thomas F. Sellers, M.D., Georgia State Department of Health, and Glenn S. Usher, M.D., Communicable Disease Center, Public Health Service.

Public Health Reports

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2. Pregnant women.
3. All persons 65 years or older.

Burney LE. Public Health Rep. 1960 Oct;75(10):944

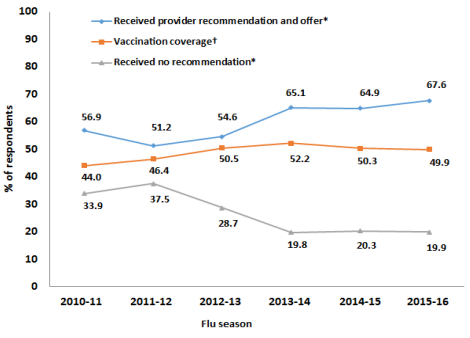
ACIP Influenza Vaccination Recommendations, 2016–17 Influenza Season

- All women who are pregnant or who might be pregnant in the upcoming influenza season should receive influenza vaccine
- Vaccine can be given during any trimester of pregnancy
- All forms of inactivated influenza vaccine (IIV) approved for use in pregnant women
  - Intramuscular and intradermal
  - Trivalent and quadrivalent

Healthy People 2020 Goal

- Increase the percentage of pregnant women who are vaccinated against seasonal influenza
  - Target: 80%
  - Baseline: 28% in 2008*

Figure 1. Trend of flu vaccination coverage before and during pregnancy and prevalence of provider recommendation / offer or no recommendation for vaccination among women pregnant anytime October through January, Internet panel survey, United States, 2010-11 through 2015-2016 flu seasons



https://www.cdc.gov/flu/fluvaxview/pregnant-coverage_1516estimates.htm

*Based on National Health Interview Survey (NHIS), CDC/NCHS

WHO SAGE Working Group on Influenza Vaccines and Immunization Position Papers

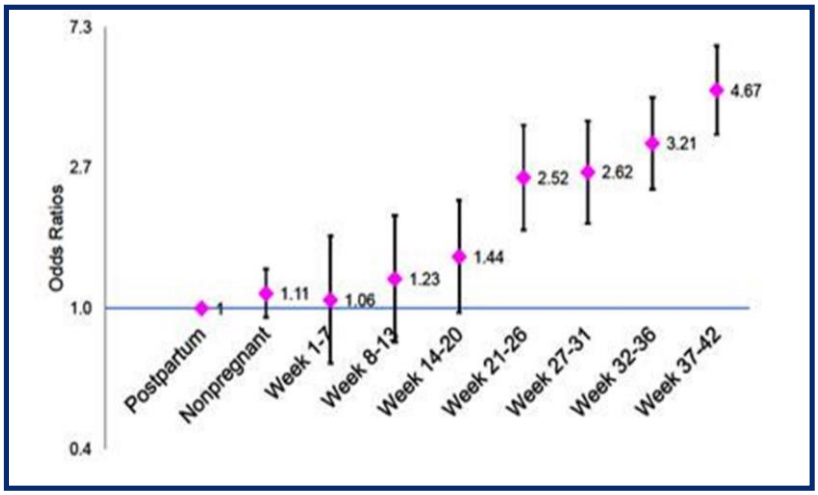
- In 2005
  - Few countries with influenza vaccination programs
  - Very limited global vaccine supply
  - Pregnant women mentioned as one of several groups that may be considered for influenza vaccination
- In 2012
  - More globally representative epidemiologic and surveillance data
  - Informed by experience and knowledge from 2009 H1N1 pandemic
  - Pregnant women identified as highest priority target group for vaccination

Influenza Burden and Vaccine Effectiveness in Pregnant Women

Impact of Seasonal Influenza on Pregnant Women

- Pregnant women have a higher risk of influenza-associated hospitalization than non-pregnant women (Neuzil, K. et al. Am J Epidemiol 1998;148:1094-102)
  - Risk comparable with adults with high risk conditions
  - Risk increased among women with other risk factors (Neuzil, K. et al. 1998; Hartert, et al., Am J Obstet Gynecol 2003;189:1705-12)
  - Risk increases by trimester
- Mortality attributed to influenza observed among pregnant women from 1998-2005 in the US, particularly in the 3rd trimester (Callaghan, Obstetric Gynecol 2010; 115: 919-23)

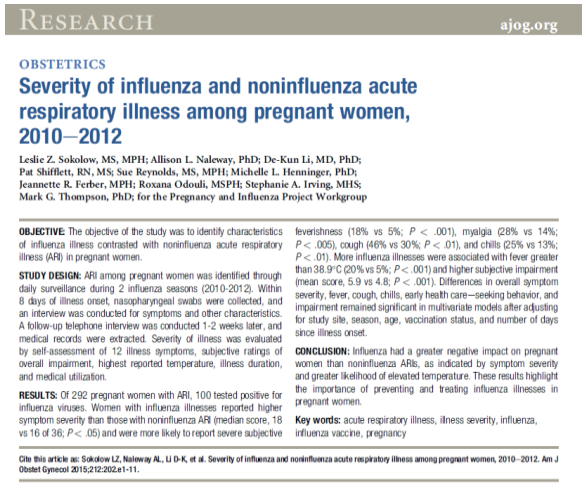
Odds of Acute Cardiopulmonary Hospitalization Increases by Trimester vs. Postpartum Period, 1974-1993



Neuzil et al., Am J Epidemiol 148:1094-102, 1998

Impact of Laboratory-Confirmed Influenza vs. Other Respiratory Illness during Pregnancy

- Case-control study of pregnant women hospitalized with respiratory illness with vs. without laboratory-confirmed influenza
- Influenza associated with higher symptom severity, more frequent fever, and higher self-perceived impairment



RESEARCH ajog.org

OBSTETRICS

Severity of influenza and noninfluenza acute respiratory illness among pregnant women, 2010–2012

Leslie Z. Sokolow, MS, MPH; Allison L. Naleway, PhD; De-Kun Li, MD, PhD; Pat Shifflett, RN, MS; Sue Reynolds, MS, MPH; Michelle L. Henninger, PhD; Jeannette R. Ferber, MPH; Roxana Odouli, MSPH; Stephanie A. Irving, MHS; Mark G. Thompson, PhD; for the Pregnancy and Influenza Project Workgroup

OBJECTIVE: The objective of the study was to identify characteristics of influenza illness contrasted with noninfluenza acute respiratory illness (ARI) in pregnant women.

STUDY DESIGN: ARI among pregnant women was identified through daily surveillance during 2 influenza seasons (2010-2012). Within 8 days of illness onset, nasopharyngeal swabs were collected, and an interview was conducted for symptoms and other characteristics. A follow-up telephone interview was conducted 1-2 weeks later, and medical records were extracted. Severity of illness was evaluated by self-assessment of 12 illness symptoms, subjective ratings of overall impairment, highest reported temperature, illness duration, and medical utilization.

RESULTS: Of 292 pregnant women with ARI, 100 tested positive for influenza viruses. Women with influenza illnesses reported higher symptom severity than those with noninfluenza ARI (median score, 18 vs 16 of 36; $P < .05$) and were more likely to report severe subjective feverishness (18% vs 5%; $P < .001$), myalgia (28% vs 14%; $P < .005$), cough (46% vs 30%; $P < .01$), and chills (25% vs 13%; $P < .01$). More influenza illnesses were associated with fever greater than 38.9°C (20% vs 5%; $P < .001$) and higher subjective impairment (mean score, 5.9 vs 4.8; $P < .001$). Differences in overall symptom severity, fever, cough, chills, early health care–seeking behavior, and impairment remained significant in multivariate models after adjusting for study site, season, age, vaccination status, and number of days since illness onset.

CONCLUSION: Influenza had a greater negative impact on pregnant women than noninfluenza ARIs, as indicated by symptom severity and greater likelihood of elevated temperature. These results highlight the importance of preventing and treating influenza illnesses in pregnant women.

Key words: acute respiratory illness, illness severity, influenza, influenza vaccine, pregnancy

Cite this article as: Sokolow LZ, Naleway AL, Li D-K, et al. Severity of influenza and noninfluenza acute respiratory illness among pregnant women, 2010–2012. Am J Obstet Gynecol 2015;212:202.e1-11.

Sokolow L. et al., Am J Obstet Gynecol 2015 Feb;212:202.e1-11

Impact of Seasonal Influenza during the First Trimester and Congenital Anomalies

- Systematic review and meta-analysis of 22 published studies
- Exposure defined as any reported influenza, influenza-like illness, fever with influenza, regardless of laboratory-confirmation

Defect	Pooled Odds Ratio
Any birth defect	2.00 (1.62-2.48)
Neural tube defect	3.33 (2.05-5.40)
Hydrocephaly	5.74 (1.10-30.00)
Congenital heart defects	1.56 (1.13-2.14)
Cleft lip	3.12 (2.20-4.42)
Limb reduction defects	2.03 (1.27-3.27)

Luteijn et al., Human Reprod 29:809-23, 2014

.

Impact of Seasonal Influenza on Adverse Pregnancy and Perinatal Outcomes

Systematic review

Maternal influenza and birth outcomes: systematic review of comparative studies

DB Fell,[a,b] DA Savitz,[c,d] MS Kramer,[a,e] BD Gessner,[f] MA Katz,[g] M Knight,[h] JM Luteijn,[i] H Marshall,[j,k,l] N Bhat,[m] MG Gravett,[n,o] B Skidmore,[p] JR Ortiz[q]

Accepted 15 April 2016. Published Online 6 June 2016.

Background Although pregnant women are considered at high risk for severe influenza disease, comparative studies of maternal influenza and birth outcomes have not been comprehensively summarized.

Objective To review comparative studies evaluating maternal influenza disease and birth outcomes.

Search strategy We searched bibliographic databases from inception to December 2014.

Selection criteria Studies of preterm birth, small-for-gestational-age (SGA) birth or fetal death, comparing women with and without clinical influenza illness or laboratory-confirmed influenza infection during pregnancy.

Data collection and analysis Two reviewers independently abstracted data and assessed study quality.

Main results Heterogeneity across 16 studies reporting preterm birth precluded meta-analysis. In a subgroup of the highest-quality studies, two reported significantly increased preterm birth (risk ratios (RR) from 2.4 to 4.0) following severe 2009 pandemic H1N1 (pH1N1) influenza illness, whereas those assessing mild-to-moderate pH1N1 or seasonal influenza found no association. Five studies of SGA birth showed no discernible patterns with respect to influenza disease severity (pooled odds ratio 1.24; 95% CI 0.96–1.59). Two fetal death studies were of sufficient quality and size to permit meaningful interpretation. Both reported an increased risk of fetal death following maternal pH1N1 disease (RR 1.9 for mild-to-moderate disease and 4.2 for severe disease).

Conclusions Comparative studies of preterm birth, SGA birth and fetal death following maternal influenza disease are limited in number and quality. An association between severe pH1N1 disease and preterm birth and fetal death was reported by several studies; however, these limited data do not permit firm conclusions on the magnitude of any association.

Keywords Fetal death, influenza, pregnancy, preterm birth, small-for-gestational-age birth, systematic review.

Tweetable abstract Comparative studies are limited in quality but suggest severe pandemic H1N1 influenza increases preterm birth.

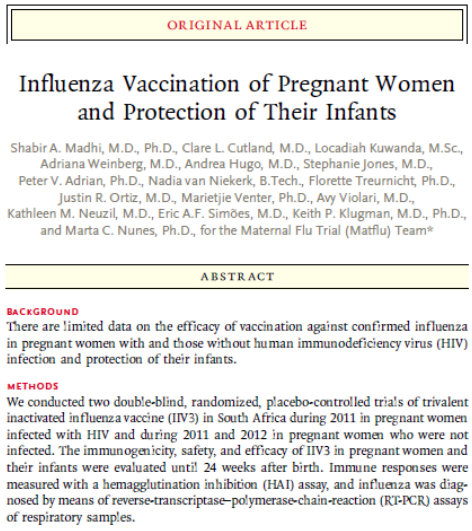
Linked article This article is commented on by JM Snowden and KF Brookfield, p. 60 in this issue. To view this mini commentary visit http://dx.doi.org/10.1111/1471-0528.14174.

Fell DB., et al. BJOG 2017 Jan;124:48-59.

- Recent review evaluated 16 published studies of preterm birth, SGA, fetal death
- Heterogeneity across studies prohibited meta-analysis for preterm birth, fetal death
- Some evidence that severe 2009 A/H1N1 pandemic influenza was associated with preterm birth and fetal death
- Insufficient data on impact of seasonal influenza on adverse perinatal outcomes

Immunogenicity of Influenza Vaccine in Pregnant Women and Antibody Transfer to Infant

- IIV induces protective levels of antibody in pregnant women (Sumaya, CV. et al. JID 1979;140:141-6)
  - both HIV-uninfected and HIV-infected (Madhi SA. et al. NEJM 2014;371:918-31)
- Vaccine-induced antibody is transferred from mother to infant (Sumaya, CV. et al. JID 1979;140:141-6; Englund JA, et al. JID 1993;168:647–56; Reuman PD, et al. Pediatr Infect Dis J 1987;6:398–403; Mahdi SA .et al. NEJM 2014;371:918-31)
  - Titers fall from 3 to 6 months of age (Tapia MD. et al. Lancet Infect Dis 2016;16: 1026–35)



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*

ABSTRACT

BACKGROUND

There are limited data on the efficacy of vaccination against confirmed influenza in pregnant women with and those without human immunodeficiency virus (HIV) infection and protection of their infants.

METHODS

We conducted two double-blind, randomized, placebo-controlled trials of trivalent inactivated influenza vaccine (IIV3) in South Africa during 2011 in pregnant women infected with HIV and during 2011 and 2012 in pregnant women who were not infected. The immunogenicity, safety, and efficacy of IIV3 in pregnant women and their infants were evaluated until 24 weeks after birth. Immune responses were measured with a hemagglutination inhibition (HAI) assay, and influenza was diagnosed by means of reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assays of respiratory samples.

Influenza VE Against Laboratory-Confirmed Influenza in Pregnant Women

- Four RCTs of IIV in pregnant women*

Setting	Years	VE	Outcome
Bangladesh	2004-05	36%	Resp illness + fever
South Africa	2011-12	50% HIV-uninfected 58% HIV-infected	RT-PCR + influenza
Mali	2011-13	77%	RT-PCR + influenza
Nepal	2011-13	Not published	RT-PCR + influenza

- Case-control study of pregnant women with ARI showed 44% reduction in RT-PCR-confirmed influenza (Thompson MG. et al. CID 2014;58:449-57)

*Zaman K. et al, NEJM 2008;359:1555-64; Madhi SA. et al. NEJM 2014;371:918-31; Tapia MD. et al. Lancet Infect Dis 2016;16: 1026–35

Influenza VE Against Adverse Pregnancy and Perinatal Outcomes

- Mixed findings from retrospective observational studies
  - Two studies reporting VE against preterm birth and differences in birthweight between infants of vaccinated vs. unvaccinated mothers (Omer SB. et al. PloS Med 2011;8:e1000441; Steinhoff M. et al. CMAJ 2012;184:645-53)
  - Three studies reporting no VE against preterm birth (Ludvigsson JF. et al. Eur J Epidemiol 2013; Pasternak B. et al. JAMA 2012;308:165-174; Nordin JD. et al. J Pediatr 2014;164)
- Studies are limited by their retrospective design and potential biases
- RCTs from South Africa and Mali did not show VE against preterm birth or differences in birth weight between treatment groups

Influenza Burden and Effectiveness of Maternal Vaccination in Infants

Rates of Hospitalization for Acute Cardiopulmonary Conditions Attributable to Influenza, U.S., 1973-1993

TABLE 1. RATES OF HOSPITALIZATION FOR ACUTE CARDIOPULMONARY CONDITIONS ATTRIBUTABLE TO INFLUENZA.

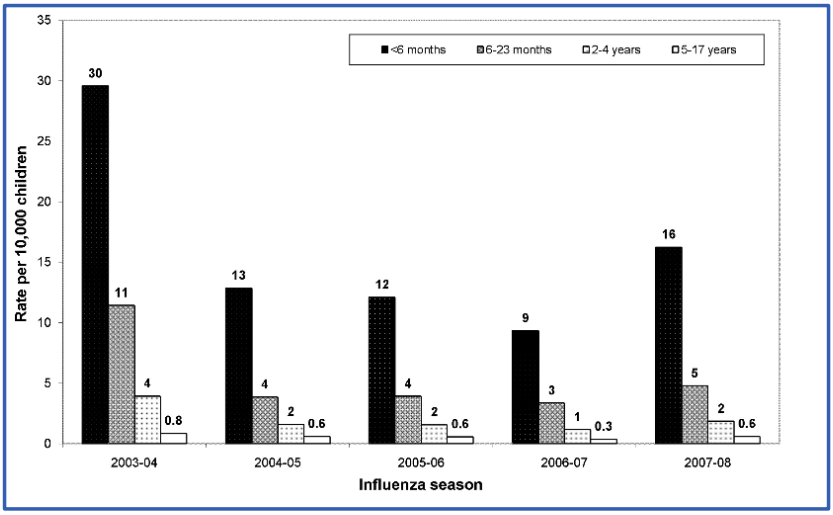
AGE	NO. OF PERSON-YEARS	NO. OF HOSPITALIZATIONS FOR ACUTE CARDIOPULMONARY CONDITIONS PER 10,000 PERSON-YEARS				NO. OF INFLUENZA-ATTRIBUTABLE HOSPITALIZATIONS PER 10,000 PERSON-YEARS*		AVERAGE EXCESS NO. OF HOSPITALIZATIONS PER 10,000 CHILDREN PER YEAR (95% CI)†
		INFLUENZA SEASON	PERI-INFLUENZA SEASON	SUMMER	TOTAL	CRUDE	STANDARDIZED‡	
<6 mo	117,205	1964	1497	608	1146	467	449	103.8 (89.0–118.6)
6 to <12 mo	82,997	1117	854	403	675	263	233	49.6 (35.3–63.8)
1 to <3 yr	324,900	464	387	233	325	77	79	18.6 (14.2–23.0)
3 to <5 yr	302,344	232	193	138	173	39	43	8.6 (4.9–12.3)
5 to <15 yr	1,207,697	120	105	86	98	15	22	4.1 (2.8–5.5)

*Values are differences in rates between the influenza season and the peri-influenza season (the base-line values).

†Values are weighted averages of annual excess hospitalizations for a population of 10,000 persons within the specified age group. The excess hospitalizations were calculated for each stratum by multiplying the stratum-specific difference in hospitalization rate by the proportion of the study year covered by the influenza season. CI denotes confidence interval.

‡The weighted average differences in rate between the influenza season and the peri-influenza season were calculated with stratum-specific person-years in all seasons as weights; strata were defined by age group, study year, race, and residence.

Variation in Incidence of Lab-Confirmed Influenza in Hospitalized Children, U.S. EIP Network, 2003-2008



Dawood, et al. J Pediatr 2010;157:808-14

Influenza VE Against Laboratory-Confirmed Influenza in Infants of Vaccinated Mothers

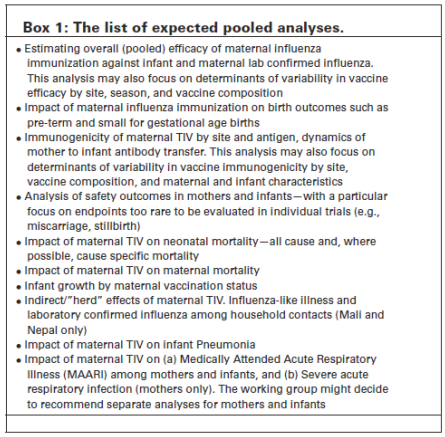
- Four RCTs of IIV all evaluating RT-PCR-confirmed influenza in infants <6 months

Setting	Years	Vaccination Timing	VE
Bangladesh	2004-05	3rd trimester	69%
South Africa	2011-12	Late 2nd/3rd trimester	49% HIV-uninfected mothers No significant VE in infants of HIV-infected mothers
Mali	2011-13	3rd trimester	68% during first 4 months 33% during first 6 months
Nepal	2011-13	2nd/3rd trimester	Not published

- Three observational studies demonstrating IIV effectiveness against hospitalization with ILI or laboratory-confirmed influenza among infants (Benowitz I. et al. CID; Eick AA. et al. Arch Pediatr Adolesc Med; Poehling K. et al. Am J Obstet Gynecol)

Pooled Analyses from Gates-Funded RCTs of IIV Efficacy Among Infants of Vaccinated Mothers

- Three RCTs in South Africa, Mali, and Nepal
- Will pool data across sites to evaluate
  - IIV impact on birth outcomes and neonatal mortality
  - IIV impact on infant pneumonia
  - Rare adverse events



Box 1: The list of expected pooled analyses.

- Estimating overall (pooled) efficacy of maternal influenza immunization against infant and maternal lab confirmed influenza. This analysis may also focus on determinants of variability in vaccine efficacy by site, season, and vaccine composition
- Impact of maternal influenza immunization on birth outcomes such as pre-term and small for gestational age births
- Immunogenicity of maternal TIV by site and antigen, dynamics of mother to infant antibody transfer. This analysis may also focus on determinants of variability in vaccine immunogenicity by site, vaccine composition, and maternal and infant characteristics
- Analysis of safety outcomes in mothers and infants—with a particular focus on endpoints too rare to be evaluated in individual trials (e.g., miscarriage, stillbirth)
- Impact of maternal TIV on neonatal mortality—all cause and, where possible, cause specific mortality
- Impact of maternal TIV on maternal mortality
- Infant growth by maternal vaccination status
- Indirect/"herd" effects of maternal TIV. Influenza-like illness and laboratory confirmed influenza among household contacts (Mali and Nepal only)
- Impact of maternal TIV on infant Pneumonia
- Impact of maternal TIV on (a) Medically Attended Acute Respiratory Illness (MAARI) among mothers and infants, and (b) Severe acute respiratory infection (mothers only). The working group might decide to recommend separate analyses for mothers and infants

Omer SB., et al. Vaccine 2015;33:3801-3812.

Influenza Vaccine Safety in Pregnant Women

Safety of Influenza Vaccination during Pregnancy

- 11 studies published between 1964 and 2008 about safety of seasonal influenza vaccination during pregnancy (Tamma et al., Am J Obstet Gynecol 201:547-52, 2009)
  - None identified maternal or fetal problems with influenza vaccination
- Several studies during and since 2009 influenza pandemic have evaluated seasonal and pH1N1 vaccines (Moro et al., 2011a; Moro et al., 2011b; Moro et al., 2013; Chambers et al., 2013; Louik et al., 2013; Nordin et al., 2014; Naleway et al, 2014)
  - None showed evidence of harm, except for two studies that showed an association with preterm birth with pH1N1-containing vaccines (<3 days decrease in gestational age) (Chambers et al., 2013; Louik et al., 2013)

Safety of Influenza Vaccination during Pregnancy

- Systematic review of 19 observational studies that evaluated fetal outcomes (fetal death, spontaneous abortion, congenital malformations) (McMillan M. et al., Vaccine 2015 Apr 27;33(18):2108-17)
  - 5 studies of seasonal influenza vaccine; 14 of A/H1N1pdm09 vaccine
  - No observed association between influenza vaccination and adverse outcomes
  - Women vaccinated in the first trimester under-represented

Influenza Vaccine Cost Effectiveness

Cost Effectiveness of IIV Use in Pregnant Women in the United States

- Decision analytic model based on hypothetical cohort of 5.2 million pregnant women during 2010-2013 seasons

Base case results for vaccination strategy among pregnant women in the United States.

	Moderate (2010–2011)	Mild (2011–2012)	Moderately severe (2012–2013)
Mother			
Averted hospitalization	3100	1181	3626
Averted outpatient visits	46,668	20,528	114,217
Infants			
Averted hospitalization	1925	704	1909
Averted outpatient visits	33,972	12,929	41,769
Total			
Direct medical cost saved (US$)	116,018,240	45,002,614	162,206,155
Indirect cost saved (US$)	4,622,804	1,724,501	5,205,207
Societal cost saved (US$)	120,641,044	46,727,115	167,411,362
Program cost (US$)	77,600,368	77,600,368	77,600,368
Net savings/costs (US$)	43,040,676	(30,873,253)	89,810,994
QALY saved	305	123	610
Cost per QALY saved	Cost-saving	250,689	Cost-saving

Cost values are given in 2013 dollars.

Xu J. et al. Vaccine 2015;34:3149-3155

Conclusions

Conclusions

- Pregnant women are at increased risk of hospitalization with influenza
  - some effect of lower threshold for admission
- Influenza vaccine is immunogenic in pregnant women
- Influenza vaccine is effective at preventing
  - laboratory-confirmed influenza among pregnant women
  - laboratory-confirmed influenza among infants of vaccinated mothers
- Influenza vaccine is safe for use in pregnant women
- Influenza vaccine is cost effective during moderate to severe influenza seasons in the United States
- Influenza vaccine *may* prevent adverse maternal and fetal outcomes
  - more data needed

Results of CDC's 2015-2016 internet panel survey of pregnant women

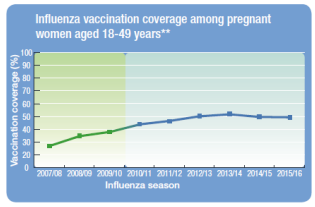
Half of pregnant women protect their babies against the flu. Time to bump it up!

With only half of pregnant moms getting their flu vaccine, too many remain unprotected

Flu shots help protect pregnant women and their babies from potentially serious illness during and after pregnancy.

During the 2015-16 flu season, an estimated 50%* of pregnant women in the U.S. protected themselves and their babies from flu by getting a flu shot. While this is a significant improvement since the years before the 2009 pandemic, about half of pregnant women, and their babies, still remain unprotected from influenza.

We can do better. All pregnant women need flu shots to protect themselves and their babies.



If you're pregnant, a flu shot:

- is safe, and can be received at any time during pregnancy
- can help protect against premature labor and delivery
- protects developing baby before birth and after birth, for the first several months, while baby is too young to get a flu shot

Pregnant women also need a whooping cough (Tdap) shot. Talk to your doctor.

Get vaccinated to protect yourself and your baby.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

www.cdc.gov/flu/protect/vaccine/pregnant.htm

NCIRDjg605 | 10/13/16

*https://www.cdc.gov/flu/fluvaxview/pregnant-coverage_1516estimates.htm **Sources: 2007-2010 BRFSS, 2010-11-2015-16 Internet Panel Survey.

Thank you

Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.