| **Evidence Table 7. Postmarketing studies: Pregnant women** | | | | | | | | | | | | | | |
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| **Author, Year, Study Design** | **Population studied** | **Vaccines included** | **Selection Bias** | **Attrition, non-response** | **Participation bias** | **Ascertainment of vaccination status** | **Ascertainment of health outcome** | **Analysis conducted** | **Adjusted for these potential confounders** | **Period data collected** | **Study funder** | **Primary results regarding vaccine** | **Any risk factor findings** | **Comment** |
| Omer,2011, Retrospective cohort[235](#_ENREF_235) | 4,168 pregnant women and their newborns enrolled in Georgia Pregnancy Risk Assessment Monitoring System (PRAMS), mean age not reported but 11.5% were <19, 12.5% were >35, and 76% were 19-35. Recruitment occurred in the flu seasons of 2004-2006. | Inactivated influenza | PRAMS is a selected segment intended to oversample black women and women who gave birth to Small for Gestational Age (SGA) babies; within PRAMS, black women are significantly less likely to get influenza vaccine | Not applicable | Yes, see selection bias | Self-report | Self-report | logistic regression | Influenza activity period (pre-influenza activity period, periods of least local/regional influenza activity, period of widespread influenza activity) maternal variables (age, multiple births, medical risk factors, labor/delivery complications, birth defects, smoking during pregnancy, hypertension, insurance coverage, maternal diabetes, use of multivitamins, alcohol use during pregnancy, black race, education, marital status) Covariates were tested for the separate multivariate models by testing which potential confounders moved the relationship between immunization and birth outcome closer to 1. | Following 2004-2005 and 2005-2006 influenza seasons | Emory University, National Foundation for Infectious Diseases | Prematurity was defined as birth < 37 weeks gestation; SGA was defined as birth weight <10th percentile for gestational age.  Infants born during the putative vaccine season to women who were vaccinated were less likely to be premature compared to infants born in the same period to unvaccinated mothers (adjusted OR 0.60, 95% CI 0.38 to 0.94) During the period of local influenza activity, this relationship increased (adjusted OR 0.44, 95% CI 0.26 to 0.73)) During the widespread influenza activity period, this relationship was greatest: adjusted OR 0.80, 95% CI 0.11. to 0.74)  Also during the widespread influenza activity period, compared with newborns of unvaccinated mothers, newborns of vaccinated mothers had 69% lower odds of being SGA (adjusted OR 0.31, 0.13 to 0.75). | NA | Maternal immunization is associated with reduced likelihood of prematurity and SGA except during the pre-influenza activity period. |
| Whitehouse et al. 2011, Prospective cohort[255](#_ENREF_255) | N=804 participants from the Western Australian Pregnancy Cohort; Location=Australia; Age=infants followed up to 20 years; | MMR | Study assessed autism scores in low and high income groups and found no differences (because those in the study tended to be more socially advantaged). Authors note, "our inclusion criterion for the gastrointestinal group – presentation to hospital, general practitioner, or clinic with gastrointestinal symptoms – may have biased this sample towards families more inclined to seek health services rather than children in actual need of assistance" | Data available for 37.6% of the 2,138 children whose whereabouts were still know (2,868 in original cohort) | Study noted that participants differed from birth cohort in that they were: more likely to have mothers who had completed secondary school at the time of pregnancy and to come from families who lived above the income ‘poverty’ threshold. | Parental report | Self-report (questionnaire) | Bivariate analyses | Primary purpose was to study association of early GI problems and ASD | Recruitment from 1989 to 1992, followed for 20 years | National Health and Medical Research Council, Raine Medical Research Foundation, University of Western Australia, the University of Western Australia Faculty of Medicine, Dentistry and Health Sciences, Tele- thon Institute for Child Health Research, and the Women’s and Infants Research Foundation | Mean autism quotient (AQ) did not differ between those who had received MMR, those who had received measles and mumps vaccine, and those who had received neither. p =0.65 | None |  |
| Xu et al. 2012, retrospective cohort[237](#_ENREF_237) | n=198 pregnant women who enrolled before 20 weeks gestation; US/Vaccine and Medication in Pregnancy Surveillance  System study | H1N1 | Self-selected population (women who contacted the system) | n/a | Participants were all pregnant women | n/r | n/r | time-independent (naive) and time-dependent covariate Cox models to account for left-truncation (due to possible enrollment later than conception) and vaccine exposure timing | vaccine exposure (1st or 2nd trimester) Previous spontaneous abortion (SAB) events (0, 1, 2, >=3) smoking maternal age asthma  Dependent variable: SAB | n/r | DHHS | Controls (n=40, no vaccine)  No. SAB: 4 SAB rate: 34%  Vaccination between LMP and date of conception(n=5) No. SAB: 1 SAB rate: 25% RR (time-independent): 1.13(0.13, 10.24) RR (time-dependent): 1.13(0.13, 10.24)  Vaccination during 1st trimester (n=119) No. SAB: 4 SAB rate: 18.6% RR (time-independent): 0.48(0.08, 2.70) RR (time-dependent): 0.79(0.19, 3.23)  Vaccination during 2nd trimester (by definition, fetal loss>20weeks is still-birth, not SAB)(n=34) No. SAB: 0  Vaccination during 1st or 2nd trimester (n=153) No. SAB: 4 SAB rate: 16.5% RR (time-independent): 0.58(0.10, 3.24) RR (time-dependent): 0.97(0.24, 3.94) | Data not shown, although none of the confounders was associated with enrollment time | Aim of this study was not to assess effect of H1N1 on SAB rate but to illustrate use of survival analysis methods to study effects of vaccines on SAB |

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| **Evidence Table 7. Postmarketing studies: Pregnant women** | | | | | | | |
| **Author- Year- Country** | **Study Design** | **McHarm Score** | **Population** | **Vaccine1** | **Timing1** | **Adverse Event1** | **OR, 95% CI, versus unvaccinated group** |
| Dodds, L. et al. 2012[234](#_ENREF_234) Canada | Cohort | NC | Sample size : 9647, Age range: <20 - >=35, Percent female: 100% | Influenza (inactived) , NR , Not reported , Adjuvant: Not Reported , Preservative: Not reported , Delivery: Not reported | Dose1: NG | Event: Small for gestational age <10th percentile : 6.6% , Syscat: 18 Event: Low birth weight : 4% , Syscat: 18 Event: Term low birth weight : 1.4% , Syscat: 18 Event: Preterm birth : 6.5% , Syscat: 18 Event: Composite outcome : 3.7% , Syscat: 18 | Composite outcome: OR 0.823 (0.636-1.067) Low birth weight: OR 0.702 (0.547-0.901)\*\* Preterm birth: OR 0.842 (0.689-1.028) Small for gestational age <10th percentile: OR 0.749 (0.614-0.914)\*\* Term low birth weight: OR 0.751 (0.488-1.154) |
| Fell D. B. et al.,2012 Canada[231](#_ENREF_231) | Cohort | 4 | Sample size: 55570, Mean age: NR, Age range: <18 - 40+, Percent female: 100% | Influenza - monovalent H1N1, NR, Adjuvant: Not Reported, Preservative: Not reported, Delivery: Not reported | Dose1: NR | Event: Preterm birth (<37w): 5.9%, Syscat: 18, Sev: 1 Event: Very preterm (<32w): 0.6%, Syscat: 18, Sev: 2 Event: Small for gestational age: <10th percentile: 8.3%, Syscat: 18, Sev: 2 Event: Small for gestational age: <3rd percentile: 2%, Syscat: 18, Sev: 3-4 Event: 5min APGAR score <7: 1.19%, Syscat: 18 Event: Fetal Death: 0.26%, Syscat: 18, Sev: 5 | 5min APGAR score <7: OR 0.925 (0.794-1.078) Fetal Death: OR 0.595 (0.439-0.806)\*\* Preterm birth (<37w): OR 0.915 (0.853-0.981)\*\* Small for gestational age: <10th percentile: OR 0.836 (0.788-0.887)\*\* Small for gestational age: <3rd percentile: OR 0.74 (0.66-0.829)\*\* Very preterm (<32w): OR 0.717 (0.584-0.879)\*\* |
| Lin T. H. et al.,2012 Taiwan[230](#_ENREF_230) | Cohort | 7 | Sample size: 396, Mean age: 32.4 (exposed), Percent female: 100% | Influenza (inactivated), AdimFlu-S®, Adimmune Corporation, Taichung, Taiwan, The vaccine evaluated in this study was produced by Adimmune Corporation (Taichung, Taiwan) using standard techniques for the production of seasonal inactivated influuenza vaccines. The vaccine is a monovalent, unadjuvanted, inactivated, split-virus vaccine. One shot (0.5ml) of AdimFlu-S®influenza A (H1N1)  vaccine contains 15 ®g of New York Medical College X-179A reassortant of the A/California/7/2009 (H1N1) like strain. Adjuvant: Adjuvant Free, Preservative: Not reported, Delivery: Intradermal | Dose1: 0 Days | Any adverse event: 35.6% Event: Infant: Hyperbilirubinemia neonatal: 2.5%, Syscat: 13 Event: Infant: Dermatitis contact: 5.4%, Syscat: 23 Event: Infant: Upper respiratory tract infection: 3.0%, Syscat: 22 Event: Infant: Seborrheic dermatitis: 4.0%, Syscat: 23 Event: Infant: Respiratory distress: 2.0%, Syscat: 22 Event: Maternal: Fever, cough, runny nose, nasal congestion, and skin itching: 2.0%, Syscat: 8 Event: Maternal: At least one adverse event: 8.6% Event: Maternal: Severe adverse event: 0% | Infant: Dermatitis contact: OR 1.882 (0.682-5.194) Infant: Hyperbilirubinemia neonatal: OR 0.083 (0.032-0.214)\*\* Infant: Respiratory distress: OR 0.66 (0.183-2.375) Infant: Seborrheic dermatitis: OR 2.042 (0.605-6.895) Infant: Upper respiratory tract infection: OR 0.742 (0.253-2.18) Maternal: At least one adverse event: OR 0.371 (0.202-0.68)\*\* |
| Nordin, J.D. et al. 2013[233](#_ENREF_233) USA | Cohort | 1 | Sample size : 223898, Mean age: 30.8, Age range: 14 - 49, Percent female: 100%, Percent pregant: Percent Pregnant: 100% | Influenza (inactived) , NR , Adjuvant: Not Reported , Preservative: Not reported , Delivery: Not reported | Dose1: NR NR | Any adverse event : 0.077% , Sev: (3 d f,u, full cohort) Event: cellulitis (3 day f/u) : 1.3% , Syscat: 23 Event: seizures (3 day f/u) : 0.1% , Syscat: 17 Event: Altererd mental status (3 day f/u) : 2% , Syscat: 19 Event: Autonomic disorders (42d f/u) : 0.1% , Syscat: 17 Event: Cranial nerve disorders (42 d) : 0% , Syscat: 17 Event: Degeneration of CNS (42 d) : 0.1% , Syscat: 17 Event: Demyelinating disease (42 d) : 0.1% , Syscat: 17 Event: Peripheral neuropathy or neuritis (42 d) : 1.6% , Syscat: 17 Event: Guillan Barre syndrome (42 d) : 0% , Syscat: 17 Event: Meningoencephalitides (42 d) : 0.4% , Syscat: 17 Event: Movement disorders (42 d) : 0% , Syscat: 17 Event: Myoneural disorders (42 d) : 0.1% , Syscat: 17 Event: Paralytic syndromes (42 d) : 0.1% , Syscat: 17 Event: Psychoses (42 d) : 0.7% , Syscat: 19 Event: Spinocerebellar disease (42 d) : 0% , Syscat: 17 Event: Myocarditis/pericarditis (42 d) : 0.1% , Syscat: 2 Event: Thrombocytopenia (42 d, full cohort)) : 10.4% , Syscat: 1 Event: Any neurologic event (42 d, first trimester exposures) : 4.1% , Syscat: 17, 19 Event: Any neurologic event ( 42d, full cohort) : 22% , Syscat: 17, 19 Event: Thrombocytopenia (42d, first trimester exposure) : 6% , Syscat: 1 Event: Any event (3d, first trimester exposure) :16% | Altererd mental status (3 day f/u): OR 1.329 (0.69-2.563) Autonomic disorders (42d f/u): OR 0.487 (0.054-4.361) Meningoencephalitides (42 d): OR 5.849 (0.608-56.235) Peripheral neuropathy or neuritis (42 d): OR 1.95 (0.876-4.34) cellulitis (3 day f/u): OR 0.928 (0.437-1.972) |
| **Evidence Table 7. Postmarketing studies: Pregnant women** | | | | | | | |
| Richards, J.L. et al. 2013[232](#_ENREF_232) US | Cohort | 2 | Sample size : 3327, Mean age: 31.2, Age range: NR, Percent female: 100% | Influenza (inactived), Influenza - monovalent H1N1 , NR , Adjuvant: Not Reported , Preservative: Not reported , Delivery: Not reported | Dose1: NR NR | Event: Pre-term birth (27-36 wk) : 7.6% , Syscat: 18 , Sev: 1,2 Event: Preterm Birth (27-33 wk) : 1.7% , Syscat: 18 , Sev: 1,2 Event: Preterm Birth (34-36 wk) : 6.0% , Syscat: 18 , Sev: 1,2 Event: Low Birth weight (<2500g) : 6.4% , Syscat: 18 , Sev: 1, 2 Event: Small for gestational age : 9.3% , Syscat: 18 , Sev: 1, 2 | Low Birth weight (<2500g): OR 0.706 (0.522-0.956)\*\* Pre-term birth (27-36 wk): OR 0.602 (0.461-0.787)\*\* Preterm Birth (27-33 wk): OR 0.505 (0.297-0.859)\*\* Preterm Birth (34-36 wk): OR 0.657 (0.486-0.889)\*\* Small for gestational age: OR 1.144 (0.868-1.508) |

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| **Evidence Table 7. Postmarketing studies: Pregnant women** | | | | | |
| **Author- Year- Country** | **Vaccine2** | **Timing2** | **Adverse Event2** | **Control group** | **Adverse Events Control** |
| Dodds, L. et al. 2012[234](#_ENREF_234) Canada |  |  |  | Nothing | Event: Small for gestational age <10th percentile : 8.6% , Syscat: 18 Event: Low birth weight : 5.6% , Syscat: 18 Event: Term low birth weight : 1.9% , Syscat: 18 Event: Preterm birth : 7.7% , Syscat: 18 Event: Composite outcome : 4.5% , Syscat: 18 |
| Fell D. B. et al.2012 Canada[231](#_ENREF_231) |  |  |  | Nothing | Event: Preterm birth (<37w): 6.41%, Syscat: 18, Sev: 1 Event: Very preterm (<32w): 0.84%, Syscat: 18, Sev: 2 Event: Small for gest age: <10th percentile: 9.77%, Syscat: 18, Sev: 2 Event: Small for gest age: <3rd percentile: 2.68%, Syscat: 18, Sev: 3-4 Event: 5min APGAR score <7: 1.28%, Syscat: 18 Event: Fetal death: 0.43%, Syscat: 18, Sev: 5 |
| Lin T. H. et al.,2012 Taiwan[230](#_ENREF_230) | : |  |  | Nothing | Any adverse event: 49% Event: Infant: Hyperbilirubinemia neonatal: 22.8%, Syscat: 13 Event: Infant: Dermatitis contact: 2.9%, Syscat: 23 Event: Infant: Upper respiratory tract infection: 3.9%, Syscat: 22 Event: Infant: Seborrheic dermatitis: 1.9%, Syscat: 23 Event: Infant: Respiratory distress: 2.9%, Syscat: 22 Event: Maternal: At least one adverse event: 20.2% Event: Maternal: Severe adverse event: 0% AE: 0% |
| Nordin, J.D. et al. 2013[233](#_ENREF_233) USA |  |  |  | Nothing | Any adverse event : 6.8% , Sev: (3 d f,u, full cohort) Event: cellulitis (3 day f/u) : 1.4% , Syscat: 23 Event: seizures (3 day f/u) : 0% , Syscat: 17 Event: Altererd mental status (3 day f/u) : 1.5% , Syscat: 19 Event: Autonomic disorders (42d f/u) : .3% , Syscat: 17 Event: Cranial nerve disorders (42 d) : 0% , Syscat: 17 Event: Degeneration of CNS (42 d) : 0% , Syscat: 17 Event: Demyelinating disease (42 d) : 22% , Syscat: 17 Event: Peripheral neuropathy or neuritis (42 d) : 1.5% , Syscat: 17 Event: Guillan Barre syndrome (42 d) : .1% , Syscat: 17 Event: Meningoencephalitides (42 d) : .2% , Syscat: 17 Event: Movement disorders (42 d) : 0% , Syscat: 17 Event: Myoneural disorders (42 d) : .1% , Syscat: 17 Event: Paralytic syndromes (42 d) : .1% , Syscat: 17 Event: Psychoses (42 d) : .4% , Syscat: 19 Event: Spinocerebellar disease (42 d) : .1% , Syscat: 17 Event: Myocarditis/pericarditis (42 d) : 0% , Syscat: 2 Event: Thrombocytopenia (42 d, full cohort)) : 11.5% Event: Any neurologic event (42 d, first trimester exposures) : 3.8% , Syscat: 17 Event: Any neurologic event ( 42d, full cohort) : 0.03% , Syscat: 17 Event: Thrombocytopenia (42d, first trimester exposure) : 20% , Syscat: 1 Event: Any event (3 d, first trimester exposure) : 31% AE: 0.02% AE: 0% AE: 0% AE: 0% AE: 0% AE: 0% AE: 0% AE: 0% |
| Richards, J.L. et al. 2013[232](#_ENREF_232) US |  |  |  | Nothing | Event: Preterm birth (27-36wk) : 12.1% , Syscat: 18 , Sev: 1, 2 Event: Preterm (27-33 wk) : 3.3% , Syscat: 18 , Sev: 1, 2 Event: Preterm (34-36wk) : 8.8% , Syscat: 18 , Sev: 1, 2 Event: Low birth weight (<2500g) : 8.8% , Syscat: 18 , Sev: 1, 2 Event: Small for gestational age : 8.2% , Syscat: 18 , Sev: 1, 2 |