Safety of Quadrivalent Recombinant Influenza Vaccine in Pregnant Persons and Their Infants

Authors: Hsiao A, Yee A, Izikson R, Fireman B, Hansen J, Lewis N, Gandhi-Banga S, Selmani A, Talanova O, Kabler H, Inamdar A, Klein NP
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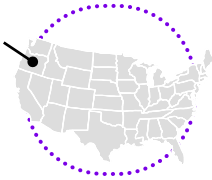
Kaiser Permanente Northern California



BACKGROUND

- Since 2004, the US ACIP has recommended that all pregnant persons receive any licensed, recommended, age-appropriate IIV or RIV during any trimester of pregnancy[1,2]
- There has been limited data regarding the safety of RIV during pregnancy[3]
- A previously reported randomized clinical trial included 382 pregnant persons vaccinated with RIV4 or SD–IIV4 during 2019–2020 or 2020–2021 influenza seasons and found that there was no increased rate of adverse outcomes among infants whose mothers received RIV4 compared with SD–IIV4[4]

OBJECTIVE

Evaluate the safety of RIV4 compared with SD–IIV4 **in a large cohort of pregnant persons and their infants**

OUTCOMES ASSESSED

Pregnancy
- Spontaneous abortion
- Preterm labor
- Stillbirth/fetal death
- Congenital/fetal anomalies (detected during pregnancy)
- Eclampsia/pre-eclampsia
- Placental abruption

Birth
- Preterm birth (<37 weeks)
- Low birthweight (<2500 grams)
- Small for gestational age

Neonatal/Infant (through 365 days)
- Infant death
- Congenital anomalies (detected after delivery)
- Failure to thrive

METHODS

Location
Northern California (209 medical clinics; 21 hospitals)

Data/System
KPNC: Integrated health care system linking medical services, laboratory tests and vaccinations

Study Design
Retrospective observational cohort study included all routinely influenza-vaccinated pregnant persons and their infants as a subset of a cluster-randomized observational study which compared the relative vaccine effectiveness of RIV4 vs. SD–IIV4 (NCT03694392)

Final Study Population
48,781 vaccinated pregnant persons and 47,394 live infants born to vaccinated pregnant persons

Seasons
2 influenza seasons:
- 2018–2019
- 2019–2020

Abbreviations: ACIP: Advisory Committee on Immunization Practices; ACOG: American College of Obstetricians and Gynecologists; IIV: inactivated influenza vaccine; KPNC: Kaiser Permanente Northern California; RIV4: quadrivalent recombinant influenza vaccine; SD–IIV4: standard dose–inactivated influenza vaccine; US: United States.

References: 1. The American College of Obstetricians and Gynecologists' Committee on Obstetric Practice. Opinion No. 741: Maternal Immunization. *Obstet Gynecol.* 2018;131(6):e214-e217. **2.** Grohskopf LA, et al. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the ACIP — United States, 2024–25 Influenza Season. *MMWR Recomm Rep.* 2024;73(5):1-25. **3.** Neels P, et al. *Vaccine.* 2017;35(18):2329-2337. **4.** Swamy G. Clinical Trial to compare safety of Recombinant Influenza Vaccine (RIV4) versus Quadrivalent Inactivated Influenza Vaccine (IIV4) in Pregnancy, CDC. 2022 https://stacks.cdc.gov/view/cdc/122379.

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RESULTS

PREGNANT PERSONS

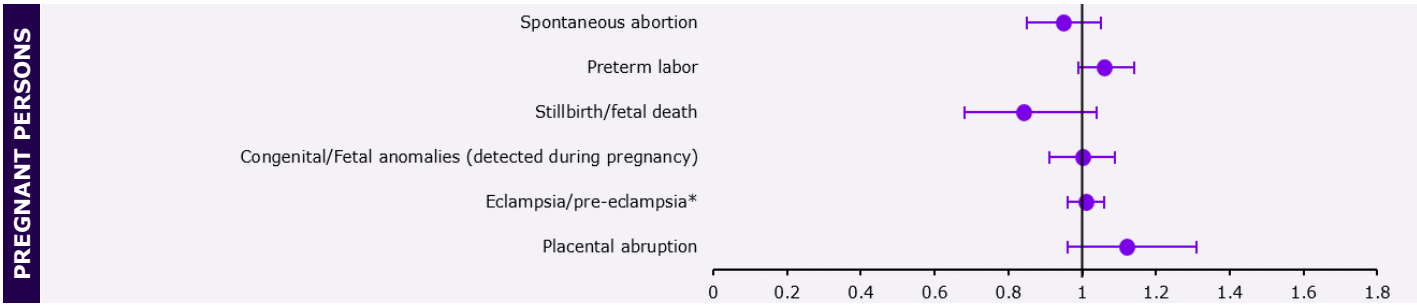
Table 1: Study population baseline characteristics

		RIV4 N=14,981 % (95% CI)	SD–IIV4 N=33,800 % (95% CI)
Maternal age*	17–24 years	10.3 (9.8, 10.8)	11.0 (10.6, 11.3)
	25–34 years	64.0 (63.2, 64.8)	63.0 (62.5, 63.5)
	35–44 years	25.4 (24.7, 26.2)	25.7 (25.2, 26.1)
	≥45 years	0.3 (0.2, 0.4)	0.3 (0.3, 0.4)
Timing of vaccine receipt	28 days prior to conception	5.0 (4.7, 5.4)	4.0 (3.8, 4.3)
	1st trimester	34.0 (33.2, 34.8)	31.9 (31.4, 32.4)
	2nd trimester	32.4 (31.6, 33.1)	33.9 (33.4, 34.4)
	3rd trimester	28.6 (27.9, 29.4)	30.1 (29.6, 30.6)
Any comorbidity†	Asthma, CHD, COPD, and/or Diabetes	13.6 (13.0, 14.1)	14.1 (13.8, 14.5)

Additionally race, ethnicity and BMI were similar between both groups
*All subjects were ≥18 years of age at the time of immunization; †Any comorbidity includes individuals with asthma, CHD, COPD, and/or diabetes diagnosed in the 3 years prior to influenza vaccination

PREGNANCY OUTCOMES

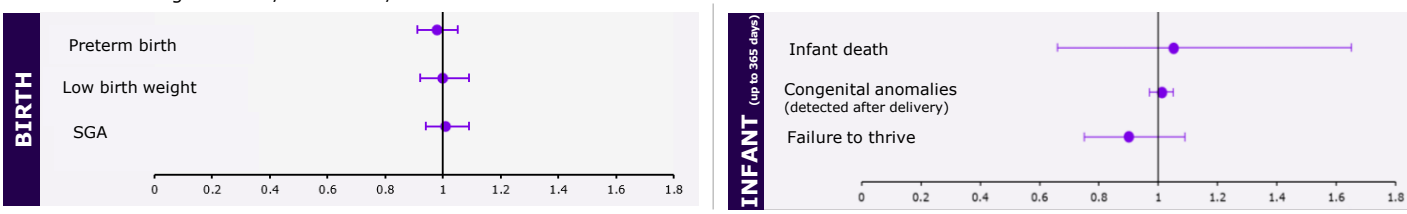
Figure 1: Forest plot of adjusted OR* for pregnancy outcomes among pregnant persons vaccinated with RIV4 vs. SD–IIV4 during the 2018/19 or 2019/20 influenza seasons



*Eclampsia was assessed in pregnant persons following vaccination during pregnancy up through 42 days after delivery
†SD–IIV4 was the reference group for all analyses. Conditional logistic regressions adjusted for maternal race, ethnicity, maternal age group, trimester of influenza vaccine receipt, chronic conditions, and BMI

BIRTH AND NEONATAL/INFANT OUTCOMES

Figure 2: Forest plot of adjusted OR* for birth and neonatal/infant outcomes among live infants born to pregnant persons vaccinated with RIV4 vs. SD–IIV4 during the 2018/19 or 2019/20 influenza seasons



*SD–IIV4 was the reference group for all analyses. Logistic regressions model was adjusted for infant sex, infant race, infant ethnicity, maternal age group, and maternal trimester of influenza vaccine receipt

STUDY STRENGTHS & LIMITATIONS

Strengths

- All pregnant persons in this observational study were a subset of a large cluster-randomized observational study of RIV4 vs. SD–IIV4 (~1.6 million adults)
  - The methodology applied helped to minimize bias
- KPNC's capture of EMR data among pregnant persons and their infants is comprehensive and gives a high degree of confidence in the outcomes of interest and minimizes confounding
- The findings may be generalizable to other pregnant persons given the influenza vaccination rates among KPNC pregnant persons was similar to what was reported nationally by the CDC in the same years

Limitations

- Imbalances in the quantity of RIV4 vs SD–IIV4 administered may have been attributed to provider preference, availability of either vaccine due to logistical constraints or other factors affecting real-world practice
- Analysis did not adjust for all factors potentially associated with high-risk pregnancies such as non-singleton pregnancies; however demographic and baseline characteristics were well balanced making it unlikely that the proportion of high-risk pregnancies would have been different between the groups

CONCLUSIONS

- Compared with receipt of SD–IIV4 during pregnancy, this large study did not identify any pregnancy, birth, or neonatal/infant safety concerns following receipt of RIV4 during pregnancy
- This study supports the safety profile of RIV4 and provides further evidence regarding the safety of influenza vaccinations administered during pregnancy

Abbreviations: BMI: body mass index; CHD: coronary heart disease; COPD: chronic obstructive pulmonary disease; CDC: Centers for Disease Control and Prevention; EMR: Electronic Medical Record; IIV: inactivated influenza vaccine; IIV–4: quadrivalent inactivated influenza vaccine; KPNC: Kaiser Permanente Northern California; OR, odds ratio; RIV4: quadrivalent recombinant influenza vaccine; rVE: relative vaccine effectiveness; SGA: small for gestational age; SD–IIV4: standard dose–inactivated influenza vaccine; US: United States.

References: 1. The American College of Obstetricians and Gynecologists' Committee on Obstetric Practice. Opinion No. 741: Maternal Immunization. *Obstet Gynecol.* 2018;131(6):e214-e217. **2.** Grohskopf LA, et al. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the ACIP — United States, 2024–25 Influenza Season. *MMWR Recomm Rep.* 2024;73(5):1-25. **3.** Neels P, et al. *Vaccine*. 2017;35(18):2329-2337. **4.** Swamy G. Clinical Trial to compare safety of Recombinant Influenza Vaccine (RIV4) versus Quadrivalent Inactivated Influenza Vaccine (IIV4) in Pregnancy, CDC. 2022 https://stacks.cdc.gov/view/cdc/122379.

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