

Tdap during pregnancy, safety and coverage data from the Vaccine Safety Datalink

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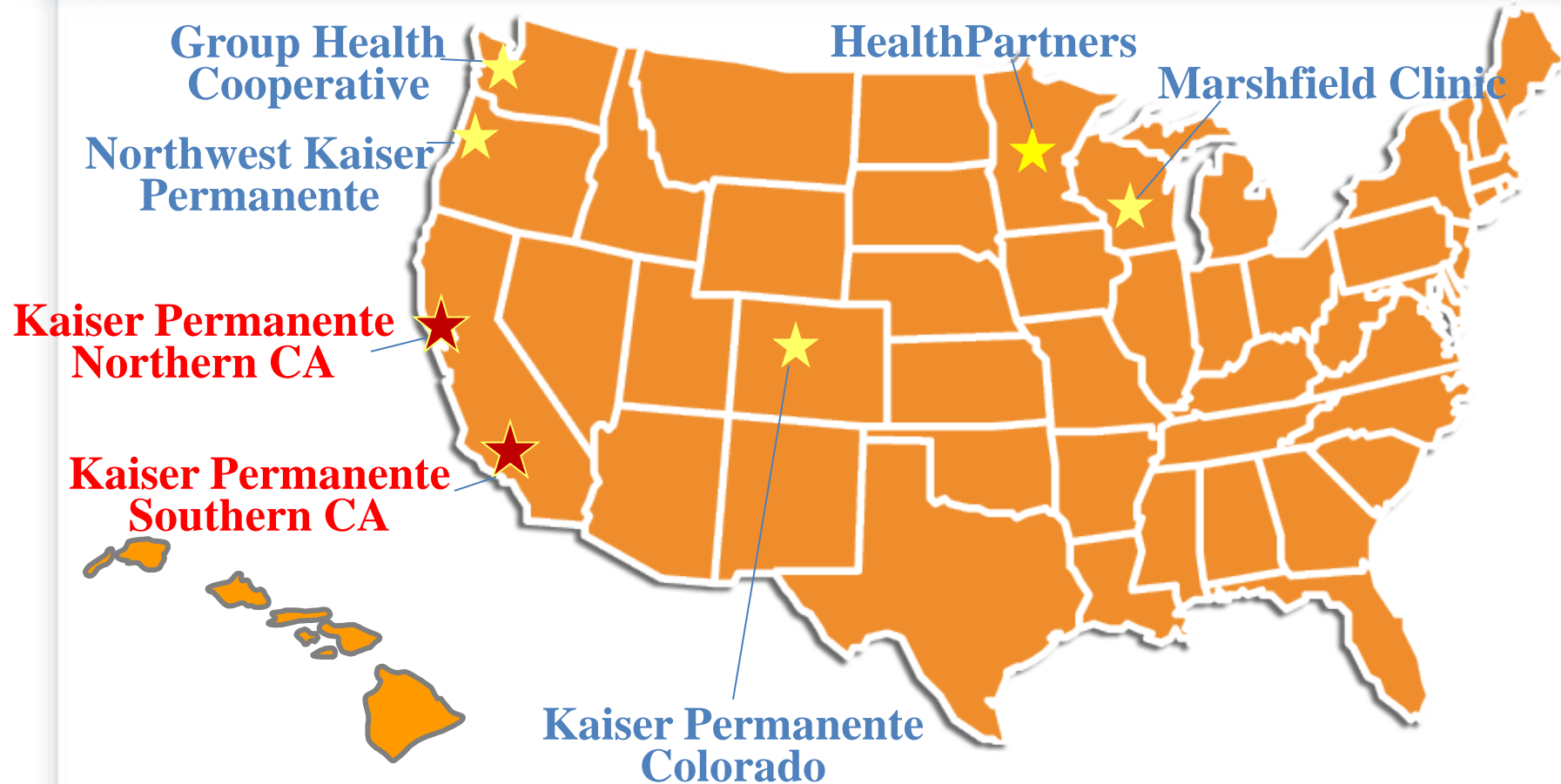


Overview of presentation

- Present updated estimates of Tdap coverage during pregnancy within 7 Vaccine Safety Datalink (VSD) sites
- Present data on Tdap safety during pregnancy



VSD sites contributing data

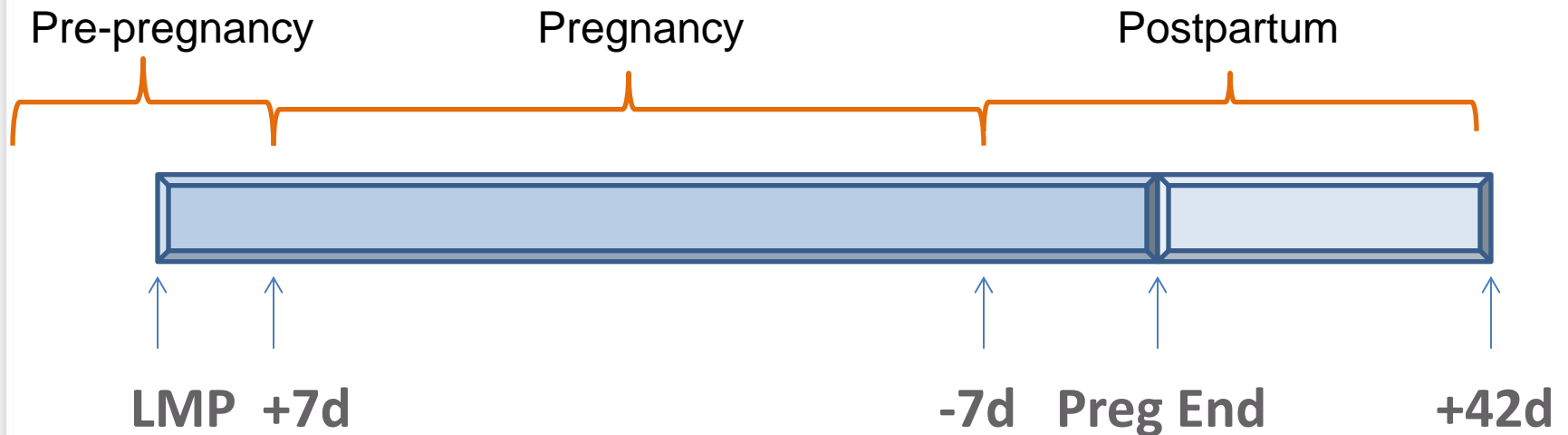


***ALL VSD sites contributed coverage data**

***Only California VSD sites contributed safety data (to date)**



Definition of Tdap timing in pregnancy



Pre-pregnancy (from 2005, up to 7 days following the last menstrual period (LMP))

Pregnancy (LMP + 8 days through 7 days before end of pregnancy)

Post-partum (6 days before end of pregnancy through 6 weeks after end of pregnancy)



Tdap coverage data

- Updated estimates for pregnancies ending between 1/1/07 – 11/15/2012
- Pregnancies identified using validated algorithm
- Receipt of Tdap from electronic health record
- Reflects
 - 2010 CA Department of Health Recommendations
 - 2011 ACIP recommendations
 - Administer Tdap to women who have not been previously vaccinated, preferably > 20 weeks gestation



Tdap coverage, all pregnancies, 7 VSD sites 2007-2012

	Pregnancies (N)	Tdap during Pregnancy (%)	Tdap Postpartum (%)
Pregnancy outcome			
Live birth	371,539	35,170 (9.5)	53,621 (14.4)
SAB, SB or TAB	146,161	1,817 (1.2)	2,289 (1.6)
Year			
2007	84,278	381 (0.5)	1,979 (2.3)
2008	84,827	554 (0.7)	5,408 (6.4)
2009	84,581	834 (1.0)	11,342 (13.4)
2010	89,888	8,292 (9.2)	16,944 (18.9)
2011	91,445	15,629 (17.1)	12,978 (14.2)
2012	82,681	11,297 (13.7)	7,259 (8.8)
Maternal age			
<18	12,488	534 (4.3)	712 (5.7)
18-24	90,069	5,449 (6.0)	7,695 (8.5)
25-34	286,516	22,259 (7.8)	33,847 (11.8)
≥35	128,627	8,745 (6.8)	13,656 (10.6)



Tdap coverage during pregnancy 2007-2012, Live Births, California

	N	Pre-pregnancy N (%)	During Pregnancy N (%)	Postpartum N (%)
Year				
2007	48,398	871(1.8)	155 (0.3)	999 (2.1)
2008	48,828	2,745 (5.6)	214 (0.4)	3,727 (7.6)
2009	48,434	5,742 (11.9)	410 (0.8)	8,703 (18.0)
2010	48,321	10,411 (21.5)	7,672 (15.9)	13,465 (27.9)
2011	49,227	17,399 (35.3)	14,765 (30.0)	9,271 (18.8)
2012	45,933	24,725 (53.8)	8,946 (19.5)	5,536 (12.1)
Maternal Age				
<18 years	5,647	2,320 (41.1)	419 (7.4)	524 (9.3)
18-24	43,903	10,356 (23.6)	4,546 (10.4)	5,492 (12.5)
25-34	171,095	34,632 (20.2)	19,615 (11.5)	25,319 (14.8)
≥35 years	68,496	14,585 (21.3)	7,582 (11.1)	10,366 (15.1)



Tdap coverage during pregnancy

2007-2012, Live Births, MN, WA, OR, CO, WI

	N	Pre-pregnancy N (%)	During Pregnancy N (%)	Postpartum N (%)
Year				
2007	13,488	701 (5.2)	108 (0.8)	859 (6.4)
2008	14,161	2,122 (15.0)	171 (1.2)	1,475 (10.4)
2009	13,965	3,705 (26.5)	192 (1.4)	2,373 (17.0)
2010	14,089	5,175 (36.7)	219 (1.6)	2,875 (20.4)
2011	14,229	6,544 (46.0)	318 (2.2)	3,052 (21.4)
2012	12,466	7,006 (56.2)	2,000 (16.1)	1,286 (10.3)
Maternal Age				
<18 years	1,238	567 (45.8)	29 (2.3)	97 (7.8)
18-24	11,976	3,674 (30.7)	473 (3.9)	1,759 (14.7)
25-34	51,356	15,712 (30.6)	1,849 (3.6)	7,486 (14.6)
≥35 years	17,780	5,300 (29.8)	657 (3.7)	2,578 (14.5)



Summary, Tdap coverage 2007-2012

- **Coverage among pregnant women**
 - In *California*
 - Tdap coverage increased substantially in 2010 and 2011 but decreased in 2012, likely because many women had received Tdap pre-pregnancy
 - In *MN, WA, OR, CO and WI*
 - Tdap coverage increased in 2012, with approximately 16% of women vaccinated in pregnancy, in response to the 2011 ACIP recommendations



Tdap safety cohort and definitions

- Observational cohort study
- Pregnancies with Live Birth outcome ***in California*** 2010-2012
- Continuous insurance enrollment
 - Minimum of 6 months before pregnancy start through 6 weeks after pregnancy end
- Exclusions
 - Multiple gestation pregnancies
 - Women with no medical care during pregnancy
 - Women who received a live virus vaccine



Safety outcomes

- **Late pregnancy complications**
 - Hypertensive disorders in pregnancy
 - Gestational hypertension, preeclampsia and eclampsia
 - Chorioamnionitis
 - Eclampsia and chorioamnionitis both required to be inpatient diagnoses
- **Birth outcomes**
 - Preterm delivery (<37 weeks)
 - SGA (<10th percentile)



Safety study - Covariates

- Propensity score created with logistic regression to estimate likelihood of receiving Tdap in pregnancy
 - Variables in propensity score: Age, race, SES, pre-existing medical conditions, and prenatal care index
- Site
- Receipt of other vaccines in pregnancy



Analyses

Outcome	Contrast	Method
Hypertensive disorders	Tdap <20 weeks versus unvaccinated	Poisson model with robust variance estimate
Chorioamnionitis	Tdap in pregnancy versus unvaccinated	Poisson model with robust variance estimate
Preterm delivery (<37 weeks)	Tdap <36 weeks versus unvaccinated	Time dependent exposure Cox model
SGA birth (<10 th percentile)	Tdap in pregnancy versus unvaccinated	Poisson model with robust variance estimate



Preliminary Results – Baseline characteristics

	Tdap during pregnancy N=26,224	Unvaccinated N=97,265
Vaccine trimester		
First	7.7%	-
Second	41.7%	-
Third	50.6%	-
Maternal Age		
<18 years	0.8%	1.4%
18-24	12.1%	13.2%
25-34	62.6%	60.8%
≥35 years	24.5%	24.6%
Race/ethnicity		
African American	7.3%	8.3%
Asian	19.0%	19.3%
Hispanic	40.7%	36.1%
White	25.0%	28.6%
Other	8.0%	7.7%



Preliminary Results – Baseline characteristics

	Tdap during pregnancy N=26,224	Unvaccinated N=97,265
Prenatal care index		
Adequate/Plus	82.8%	76.6%
Intermediate	15.6%	21.2%
Inadequate	1.6%	2.2%
Care in 1 st trimester	96.7%	96.0%
Received Tdap pre-pregnancy	4.1%	45.6%
Received another vaccine during pregnancy	53.8%	36.3%
Medical comorbidity (pre-pregnancy)	17.6%	18.7%



Preliminary Results

	Tdap in pregnancy	Unvaccinated	Adjusted Relative Risk (95% CI)
	Full cohort		
	N=26,224	N=97,265	
Chorioamnionitis	6.1%	5.5%	RR=1.19 (1.13-1.27)
Preterm <37 weeks	6.3%	7.8%	HR=0.88 (0.83-0.93)
SGA <10th percentile	8.4%	8.3%	RR=1.00 (0.96-1.06)
	Vaccinated <20 weeks		
	N=6,083	N=97,265	
Hypertensive disorders	8.2%	8.0%	RR=1.09 (0.99 -1.20)
	Vaccinated 27-36 weeks		
	N=11,351	N=97,265	
Chorioamnionitis	5.6%	5.5%	RR=1.11 (1.03-1.21)
Preterm <37 weeks	5.3%	7.8%	HR=0.83 (0.77-0.90)
SGA <10th percentile	8.6%	8.3%	RR=1.03 (0.96-1.10)



Chorioamnionitis

- Due to polymicrobial infection of the amniotic fluid, fetal membranes, placenta and/or uterus
- Diagnosed during labor in up to 8% of full term deliveries and 30-40% of preterm deliveries
- Can result in adverse consequences for mothers (infection, labor abnormalities) and for infants (preterm birth, respiratory distress, cerebral palsy)
- Risk factors
 - prolonged labor
 - use of internal monitoring
 - prolonged rupture of membranes
 - urogenital infections
 - multiple exams
 - previous diagnosis
 - substance abuse
 - obesity



Risks for Chorioamnionitis after TIV*

Outcome	Events After Vaccination: No. of Events (Rate per 1,000 Pregnancies)			Multivariable Analyses*	
	Vaccinated	Unvaccinated	P	Adjusted Hazard Rate Ratio (95% CI)	P
Vaccinated in 1st trimester	n=21,107	n=40,738			
Mild preeclampsia ^{†,‡,§}	657 (30.0)	1,249 (31.4)	.45	0.94 (0.86–1.04)	.22
Severe preeclampsia or eclampsia ^{†,‡,§}	364 (16.6)	617 (15.5)	.27	1.05 (0.92–1.19)	.51
Vaccinated at 20 weeks or greater	n=38,038	n=74,192			
Gestational hypertension ^{†,§}	1,663 (44.3)	3,046 (41.9)	.053	1.04 (0.98–1.11)	.19
Gestational diabetes [§]	1,773 (50.1)	3,925 (57.0)	< .001	0.88 (0.83–0.93)	< .001
Chorioamnionitis	1,615 (42.9)	2,861 (39.0)	.002	1.08 (1.02–1.15)	.01
Peripartum infection [†]	365 (9.3)	728 (9.8)	.84	0.98 (0.85–1.09)	.83
Venous complications [§]	21 (0.55)	63 (0.85)	.08	0.64 (0.39–1.05)	.08
Pulmonary embolus [§]	11 (0.20)	17 (0.16)	.56	1.23 (0.58–2.64)	.59
Peripartum cardiomyopathy [§]	13 (0.24)	37 (0.35)	.24	0.66 (0.35–1.24)	.20
Vaccinated in any trimester	n=74,292	n=144,597			
Mild preeclampsia ^{†,‡,§}	2,338 (18.2)	4,422 (18.2)	.73	0.97 (0.93–1.02)	.30
Severe preeclampsia or eclampsia ^{†,‡,§}	1,189 (9.2)	2,293 (9.4)	.44	0.95 (0.88–1.02)	.14
Proteinuria [†]	400 (5.3)	832 (5.8)	.09	0.88 (0.78–1.00)	.04
Urinary tract infection	1,905 (25.5)	3,655 (26.0)	.57	1.0 (0.94–1.05)	.91

CI, confidence interval.

Women vaccinated in the first trimester and their unexposed matches had a mean follow-up of 6.3 months; for women vaccinated at 20 wk or greater and their unexposed matches, mean follow-up was 2.4 months; for women vaccinated in any trimester and their unexposed matches, mean follow-up was 4.1 months.

* All outcomes adjusted for receipt of medical care in the first trimester, hospitalization before vaccination or index date, and poverty; additional adjustments were outcome-specific.

[†] Also adjusted for diabetes and gestational diabetes.

[‡] Also adjusted for proteinuria.

[§] Also adjusted for obesity.

*Inactivated Influenza Vaccine During Pregnancy and Risks for Adverse Obstetric Events.

Kharbanda, Elyse; Olshen MD, MPH; Vazquez-Benitez, Gabriela; Lipkind, Heather; MD, MPH; Naleway, Allison; Lee, Grace; MD, MPH; Nordin, James; MD, MPH
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Summary, Tdap Safety in Pregnancy

- Receipt of Tdap during pregnancy was **not associated** with increased risks for adverse birth outcomes
- Chorioamnionitis findings merit further investigation
 - After adjustments, maternal age and comorbidities did not contribute to observed risk
 - Data available do not allow for evaluation of many important chorioamnionitis risk factors
 - Magnitude of potential risk is small
 - Risk largely attributable to differences in rates of chorioamnionitis in 2012 (data not shown)
 - No associated increased risk for preterm birth



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