Groupe d'Expertise et d'Information sur la Grippe

29ème Rencontres sur la Grippe et sa Prévention

Formes Cliniques De La Grippe: La Grippe Chez La Femme Enceinte

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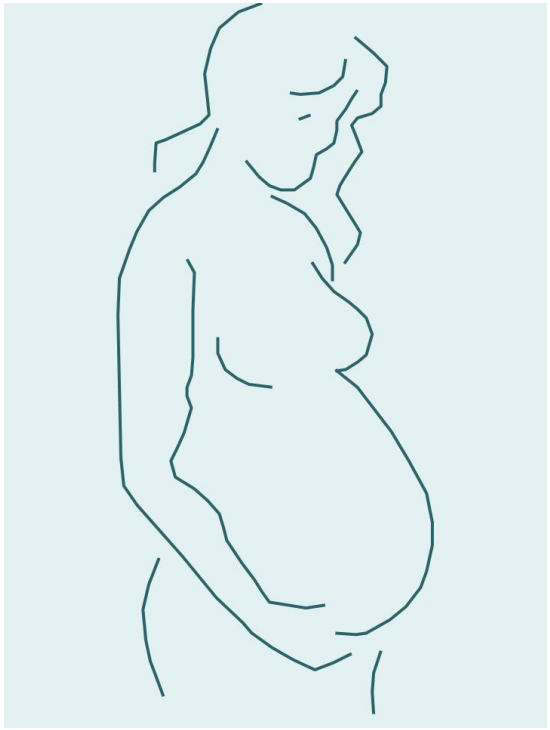
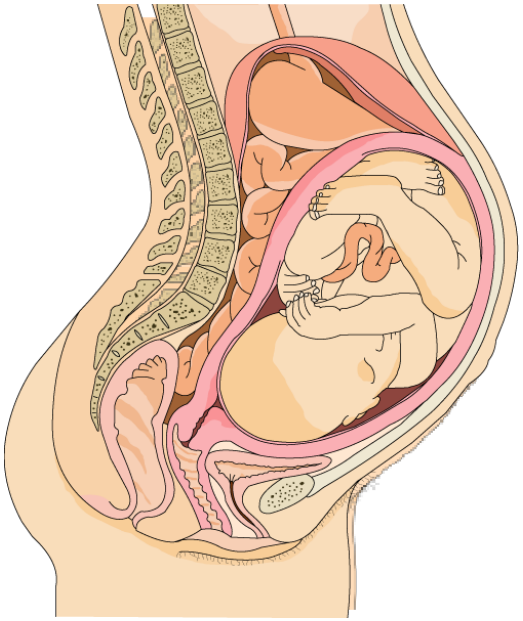
La maman



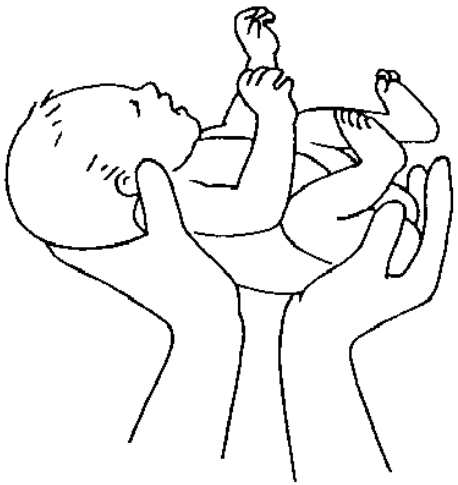
Modifications physiologiques de la grossesse:

- **cardiocirculatoire**, **pulmonaire**, rénale, digestive
- **Immunitaire**:
  - immunotolérance Th2 (: greffe semi-allogénique) = diminution de la réponse cellulaire immunitaire
  - Complexe majeur d'histocompatibilité différent = HLA-G qui diminue l'activité des cellules NK (A H1N1 exprime des antigènes HLA-G like d'où gravité potentielle)

Le fœtus



Le nouveau-né



INCIDENCE

- Peu d'études spécifiques
- Grippe ou syndrome respiratoire aigu
- 5-22% au cours de la grossesse versus 5-10% chez l'adulte

  - *Neuzil KM, Infect Dis Clin North Am 2001; Influenza vaccine: issues and opportunities*
  - *Griffiths PD, J Epidemiol Community Health 1980; A prospective study of influenza infections during pregnancy*

Pregnancy and infection, *Kourtis AP, NEJM 2014*

Table 1. Infections Associated with Increased Susceptibility or Severity among Pregnant Women, and Relevant Clinical Guidance, According to the Strength of the Evidence for an Association.

Infection	Increased Susceptibility	Increased Severity	Prevention Strategies	Management Strategies*
Stronger evidence				
Influenza	No	Yes	Influenza vaccination; antiviral prophylactic medication for selected patients	Early identification; early antiviral therapy; supportive care
Hepatitis E virus infection	No	Yes	Sanitation programs	High index of clinical suspicion; supportive care
Herpes simplex virus infection (dissemination with primary infection)	No	Yes	Protection from sexually transmitted infections during pregnancy	High index of clinical suspicion; antiviral therapy; supportive care; care of the newborn
Malaria (mainly due to *Plasmodium falciparum*)	Yes	Yes	Intermittent preventive therapy; insecticide-treated bed nets (for areas where malaria is endemic); appropriate prophylaxis (for travelers)	Early identification; appropriate antimalarial therapy; supportive care
Listeriosis	Yes	No	Dietary guidance	Early identification; appropriate antimicrobial therapy; care of the newborn
More limited evidence				
Measles	No	Yes	Vaccination	High index of clinical suspicion; supportive care
Smallpox	No	Yes	Vaccination	Very high index of clinical suspicion; supportive care
Human immunodeficiency virus type 1 infection	Yes	No	Consistent and correct condom use; protection from sexually transmitted diseases during pregnancy	Early identification; antiretroviral therapy
Varicella	No	Yes	Vaccination	Appropriate antiviral therapy; supportive care
Coccidioidomycosis	No	Yes	No proven methods of prevention	Early identification; appropriate antifungal therapy

SYMPTOMATOLOGIE CLINIQUE

TABLE 3

Self-reported symptom severity measures associated with influenza vs noninfluenza ARIs among pregnant women

Characteristics	Percentage self-reported as severe				
	Noninfluenza ARI (n = 192)		Influenza (n = 100)		*P* value
Upper respiratory symptoms					
Nasal congestion	90	(47)	42	(42)	NS
Sore throat	65	(34)	23	(23)	NS
Ear pain	17	(9)	11	(11)	NS
Lower respiratory symptoms					
Cough[a]	57	(30)	46	(46)	< .01
Wheezing	11	(6)	4	(4)	NS
Systemic symptoms					
Fatigue	66	(34)	41	(41)	NS
Myalgia	26	(14)	28	(28)	< .005
Feverishness	9	(5)	18	(18)	< .001
Chills	25	(13)	25	(25)	< .01
Headache	48	(25)	18	(18)	NS
Gastrointestinal symptoms					
Vomiting	15	(8)	5	(5)	NS
Nausea	18	(9)	5	(5)	NS

Data are counts (column percentage), unless otherwise indicated. *P* values are from Pearson χ^2, Fisher exact, or Student *t* tests.

ARI, acute respiratory illness; *NS*, not statistically significant.

[a] Ten participants reported cough as absent during their illness: in these instances, their responses were recoded as 1 (mild) because a cough was present at the time they were deemed eligible to participate in the study.

Sokolow. Influenza severity in pregnant women. Am J Obstet Gynecol 2015.

GRAVITE

- Pandémie 1918 H1N1 *(Harris JW, JAMA 1919)*
  - n= 1350
  - 50% de pneumonie avec environ 50% de décès
  - Létalité globale = 27%

	1er trimestre	2ème trimestre	3ème trimestre	9ème mois
Mortalité	7%	17%	24%	39%

- Pandémie 1918 H1N1 *(Nuzum JW, JAMA 1918)*
  - n= 86 femme enceinte hospitalisées
  - Létalité globale = 45,5%

- Pandémie 1957 H2N2 *(Freemen DW, AJOG 1959)*
  - Minnesota
  - 20% des décès maternel était du à la grippe
  - 50% des femmes en âge de procrées décédées durant cette période étaient enceintes

American Journal of Epidemiology

Vol. 148, No. 11
Printed in U.S.A.

Impact of Influenza on Acute Cardiopulmonary Hospitalizations in Pregnant Women

Neuzil KM

- Tennessee, 1974-1993
  - Etude cas-témoins: 4 369 femmes âgées de 15 à 44 ans, avec 1 événement cardio-pulmonaire aigu durant la saison grippale versus 21 845 contrôles
  - Ajusté sur les facteurs de risque d'un événement (insuffisance cardiaque, pulmonaire, …)

Pregnancy status	Prevalence (%)		OR†	95% CI†
	Cases (n = 4,369)	Controls (n = 21,845)		
Postpartum	4.4	7.7	1.0‡	
Nonpregnant	86.6	85.3	1.11	0.94–1.32
Week 1–7	0.7	1.1	1.06	0.68–1.67
Week 8–13	0.7	1.0	1.23	0.79–1.93
Week 14–20	0.9	1.2	1.44	0.97–2.15
Week 21–26	1.2	0.9	2.52	1.74–3.65
Week 27–31	1.3	0.9	2.62	1.82–3.76
Week 32–36	2.0	1.0	3.21	2.32–4.44
Week 37–42	2.2	0.9	4.67	3.42–6.39

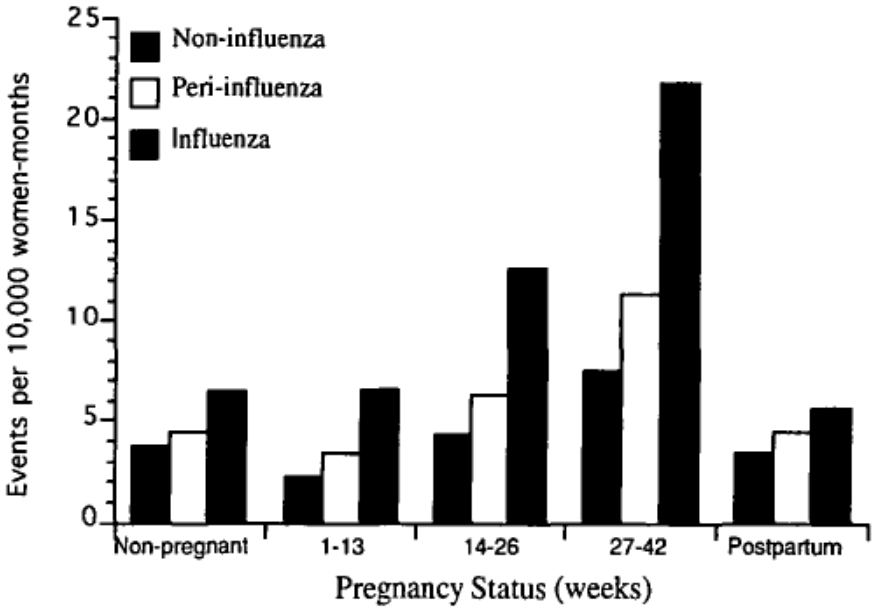
American Journal of Epidemiology
Vol. 148, No. 11
Printed in U.S.A.

Impact of Influenza on Acute Cardiopulmonary Hospitalizations in Pregnant Women

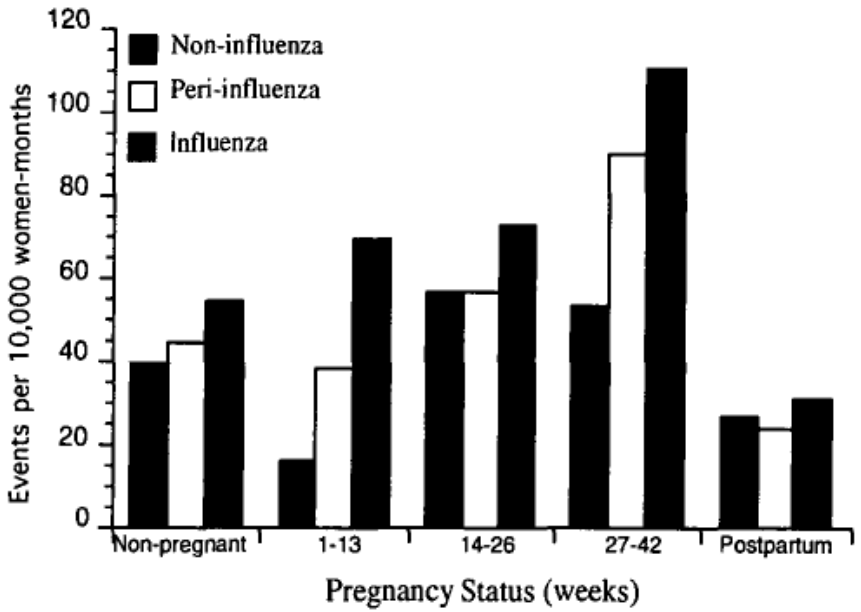
Neuzil KM

- Tennessee, 1974-1993
  - Etude rétrospective: 22 824 évènements durant 1 393 166 femmes-années
  - 3 périodes par saison grippale: « hors saison », « péri-saison », « saison »

Sans comorbidité



≥ 1 comorbidité



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Impact of Influenza on Acute Cardiopulmonary Hospitalizations in Pregnant Women

Neuzil KM

Conclusion

Pour 10 000 femmes au 3ème trimestre de grossesse

– sans autre facteur de risque que la grossesse

– et exposées à 2,5 mois de saison grippale,

25 seront hospitalisées pour une complication grave liée à la grippe

Impact of influenza exposure on rates of hospital admissions and physician visits because of respiratory illness among pregnant women

Dodds L, CMAJ 2007

- Nouvelle Ecosse, Canada, 1990-2002
- Taux d'hospitalisation et de consultation pour syndrome respiratoire aigu
  - durant la saison grippale à chaque trimestre de grossesse versus
  - La saison grippale l'année précédente
  - Et hors saison grippale

Table 1: Characteristics of study population

Characteristic	No. (%) of women *n = 134 188*
Age at delivery, yr	
< 20	10 633 (7.9)
20-29	74 406 (55.5)
30-34	35 207 (26.2)
35-49	13 942 (10.4)
Family income assistance during birth year	16 154 (12.0)
Smoking during pregnancy	38 406 (28.6)
No. of children < 5 yr of age	
0	82 044 (61.1)
1	44 948 (33.5)
≥ 2	7 196 (5.4)
Pre-existing diabetes	539 (0.4)
Respiratory disease (including asthma)	7 416 (5.5)
Asthma	6 931 (5.2)
Heart disease	1 281 (1.0)
Renal disorder	988 (0.7)
Anemia	4 051 (3.0)
Any high-risk comorbidity*	13 499 (10.1)
No. of comorbidities	
0	120 689 (89.9)
1	12 755 (9.5)
> 1	744 (0.6)

*Pre-existing diabetes, any respiratory disease, heart disease, renal disease or anemia.

Impact of influenza exposure on rates of hospital admissions and physician visits because of respiratory illness among pregnant women

Dodds L, CMAJ 2007

- 134 188 femmes enceintes
  - 510 admises à l'hôpital pour syndrome respiratoire
  - 33 775 consultent un médecin pour syndrome respiratoire
  - 6,7% des patientes avec comorbidité(s) ont reçu la vaccination anti-grippale

Table 2: Hospital admissions because of respiratory illness during the influenza season in the year before pregnancy and during pregnancy, by presence of comorbidities

Period	Women with no comorbidity			Women with ≥ 1 comorbidity		
	No. of admissions during influenza season	Rate per 10 000 woman-months	Rate ratio (95% CI)*	No. of admissions during influenza season	Rate per 10 000 woman-months	Rate ratio (95% CI)*
Year before pregnancy	49	1.4	1.0	23	5.7	1.0
Pregnancy						
First trimester	22	2.4	1.7 (1.0-2.8)	17	16.3	2.9 (1.5-5.4)
Second trimester	30	3.0	2.1 (1.3-3.3)	22	19.4	3.4 (1.9-6.0)
Third trimester	76	7.4	5.1 (3.6-7.3)	49	44.9	7.9 (5.0-12.5)

Table 3: Hospital admissions because of respiratory illness in influenza and non-influenza seasons, by trimester and presence of comorbidities

Trimester; season	Women with no comorbidity*			Women with ≥ 1 comorbidity†		
	No. of admissions	Rate per 10 000 woman-months	Rate ratio (95% CI)‡	No. of admissions	Rate per 10 000 woman-months	Rate ratio (95% CI)‡
First						
Non-influenza	24	1.4	1.0	11	5.6	1.0
Peri-influenza	12	1.3	1.0 (0.5-1.9)	13	12.4	2.2 (1.0-5.0)
Influenza	22	2.4	1.8 (1.0-3.1)	17	16.3	2.9 (1.4-6.2)
Second						
Non-influenza	26	1.6	1.0	24	13.1	1.0
Peri-influenza	24	2.6	1.6 (0.9-2.8)	13	12.7	1.0 (0.5-1.9)
Influenza	30	3.0	1.9 (1.1-3.2)	22	19.4	1.5 (0.8-2.6)
Third						
Non-influenza	53	3.1	1.0	36	18.9	1.0
Peri-influenza	49	5.4	1.8 (1.2-2.6)	9	9.3	0.5 (0.2-1.0)
Influenza	76	7.4	2.4 (1.7-3.4)	49	44.9	2.4 (1.6-3.6)

Influenza vaccine programs and pregnancy: new Canadian evidence for immunization

McNeil SA, *J Obstet Gynaecol Can. 2007*

- Risque d'hospitalisation au 3ème trimestre de grossesse durant la saison grippale versus la saison grippale l'année précédente

	Année avant	Sans comorbidité	Avec comorbidité
RR	1,0	5,1	7,9

Maternal morbidity and perinatal outcomes among pregnant women with respiratory hospitalizations during influenza season

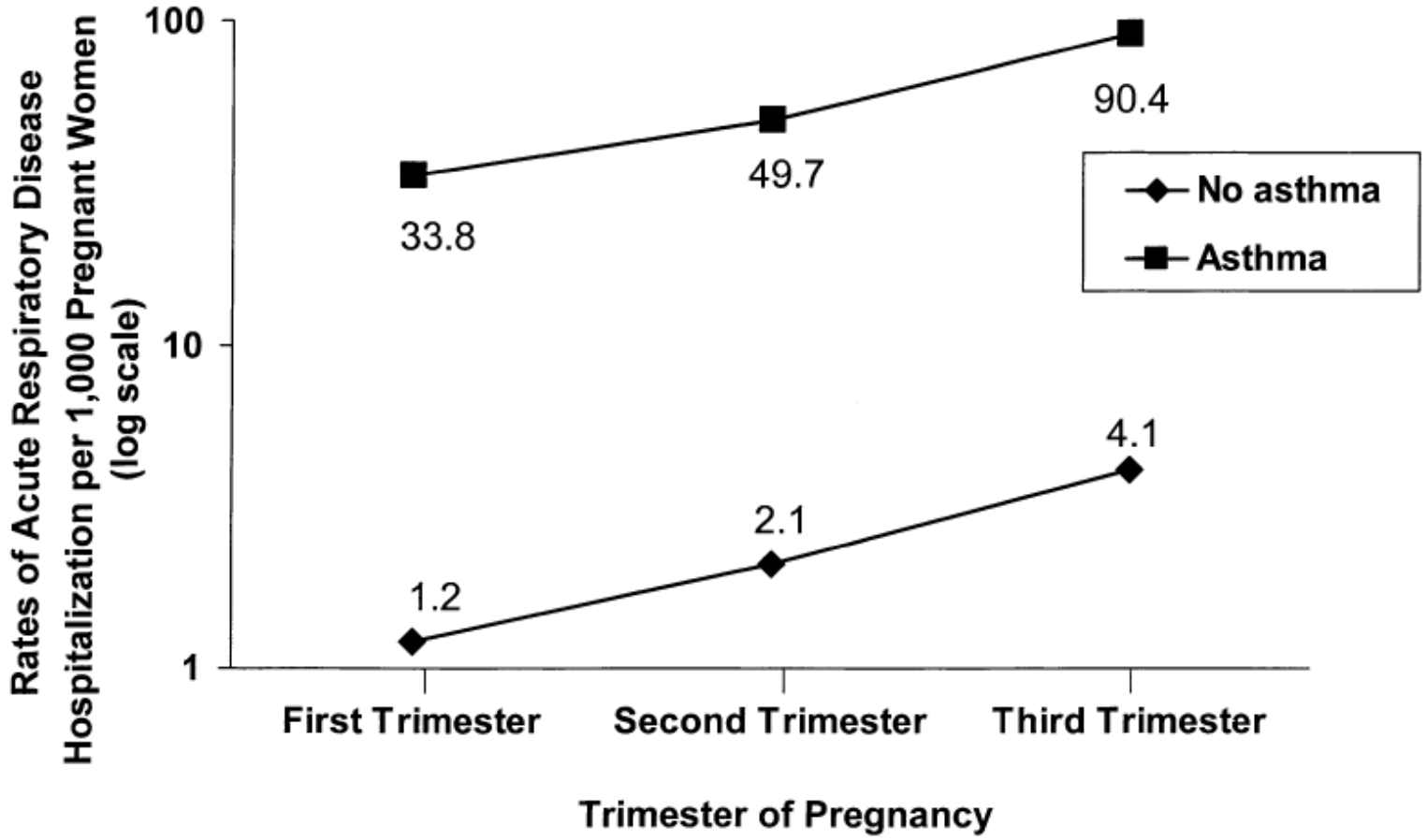
Hartert TV, AJOG 2003

- Tennessee
- Saison grippale 1985-1993
- Femmes enceintes 15-44 ans hospitalisées pour syndrome respiratoire
- Contrôle= femmes enceinte 15-44 ans appariées sur comorbidités et âge gestationnel

Characteristics of population	*Women with respiratory hospitalization during pregnancy (n = 297)*	*Source population (n = 58,640)*	*Respiratory hospitalization rate per 1000 population*	*Adjusted OR*	*95% CI*
Maternal age category					
15-24 y	195 (65.6%)	42,715 (72.8%)	4.57	1	
25-34 y	84 (28.3%)	14,319 (24.4%)	5.87	1.19	0.89-1.60
35-44 y	18 (6.1%)	1,606 (2.7%)	11.21	2.05	1.16-3.63
High-risk condition*					
Diabetes	2 (0.7%)	1,287 (2.2%)	1.55	0.22	0.05-0.89
Asthma	147 (49.5%)	2,461 (4.2%)	59.73	10.63	8.18-13.83
Other†	7 (2.4%)	700 (1.2%)	10.00	1.31	0.60-2.86
No risk	141 (47.5%)	54,192 (92.4%)	2.60	1	
Hospitalized in last 6 mo‡					
Yes	245 (82.5%)	3,248 (5.5%)	75.43	59.58	43.56-81.48
No	52 (17.5%)	55,392 (94.5%)	0.94	1	
Trimester of pregnancy§					
First	47 (15.8%)	16,939 (28.9%)	2.8	1	
Second	71 (23.9%)	17,267 (29.4%)	4.1	1.50	1.01-2.23
Third	179 (60.3%)	24,434 (41.7%)	7.3	2.81	1.98-3.99

Maternal morbidity and perinatal outcomes among pregnant women with respiratory hospitalizations during influenza season

Hartert TV, AJOG 2003



Maternal morbidity and perinatal outcomes among pregnant women with respiratory hospitalizations during influenza season

Hartert TV, AJOG 2003

Aucun retentissement sur le pronostic néonatal

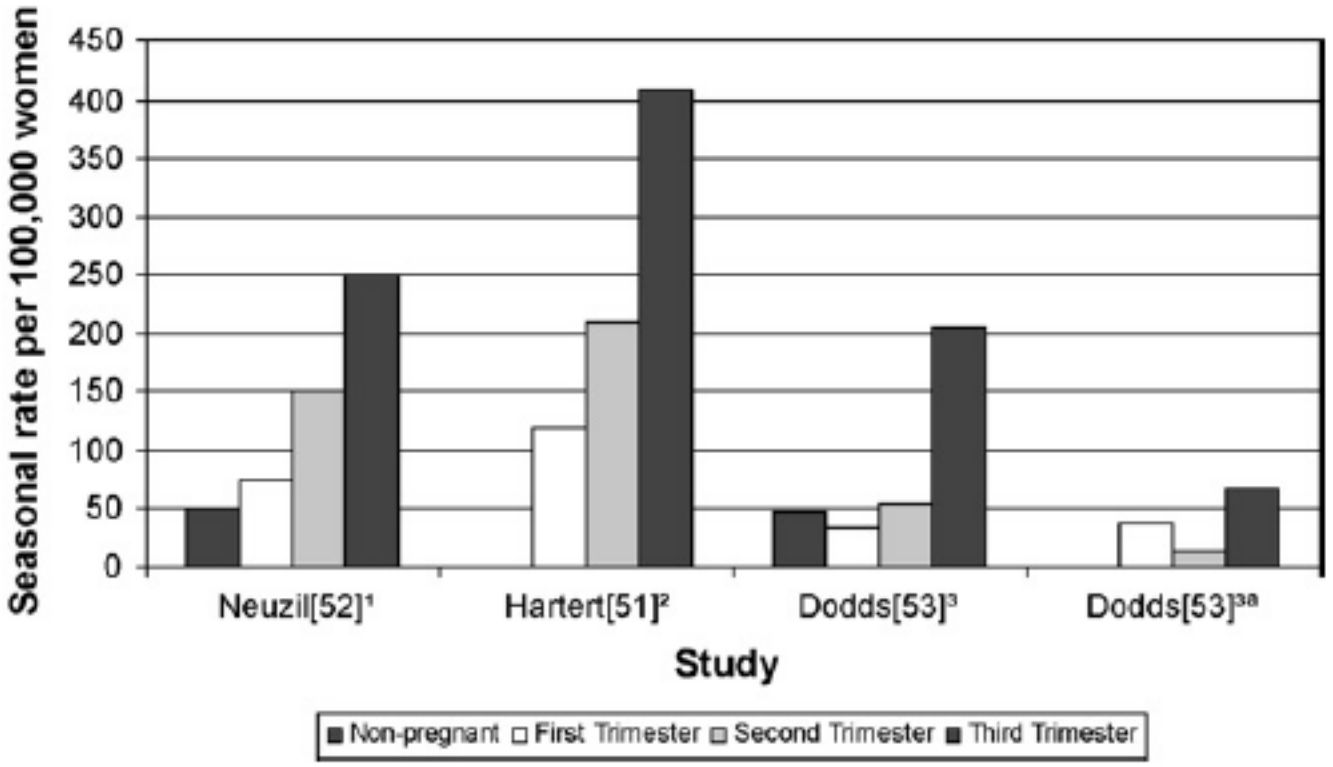
Table III. Perinatal outcomes among 293 women with singleton pregnancies requiring respiratory hospitalization during influenza season, compared with matched controls not having a respiratory hospitalization

*Perinatal outcomes**	*Pregnant women with respiratory hospitalization (n = 293)*	*Matched population-based controls (n = 587)*	*P value†*
Birth weight (g) (mean ± SD)	3,124 ± 614 g	3,223 ± 609 g	.28¶
≤1500	5 (1.7%)	9 (1.5%)	
1501-2500	26 (8.9%)	39 (6.6%)	
>2500	262 (89.4%)	539 (91.8%)	.68#
Method of delivery			
Vaginal delivery	210 (71.7%)	436 (74.3%)	
Cesarean delivery	83 (28.3%)	151 (25.7%)	.94
Delivery length of stay (median,	(N = 205)	(N = 510)	.48‖
IQ range)‡§	2 (2, 4) days	3 (2, 4) days	
Vaginal delivery			
1-3 d	142 (90.5%)	336 (88.0%)	.71
>3 d	15 (9.5%)	46 (12%)	
Cesarean delivery			
1-5 d	36 (75.0%)	109 (85.2%)	.61
>5 d	12 (25.0%)	19 (14.8%)	
Preterm labor§	(N = 241)	(N = 511)	.62
	33 (14.5%)	70 (13.7%)	
Maturity			
< 37 wk	37 (12.6%)	64 (10.9%)	.74
≥37 wk	256 (87.3%)	523 (89.1%)	
Fetal death	3	2	.34**

Is routine influenza immunization warranted in early pregnancy?

Skowronski DM, Vaccine 2009

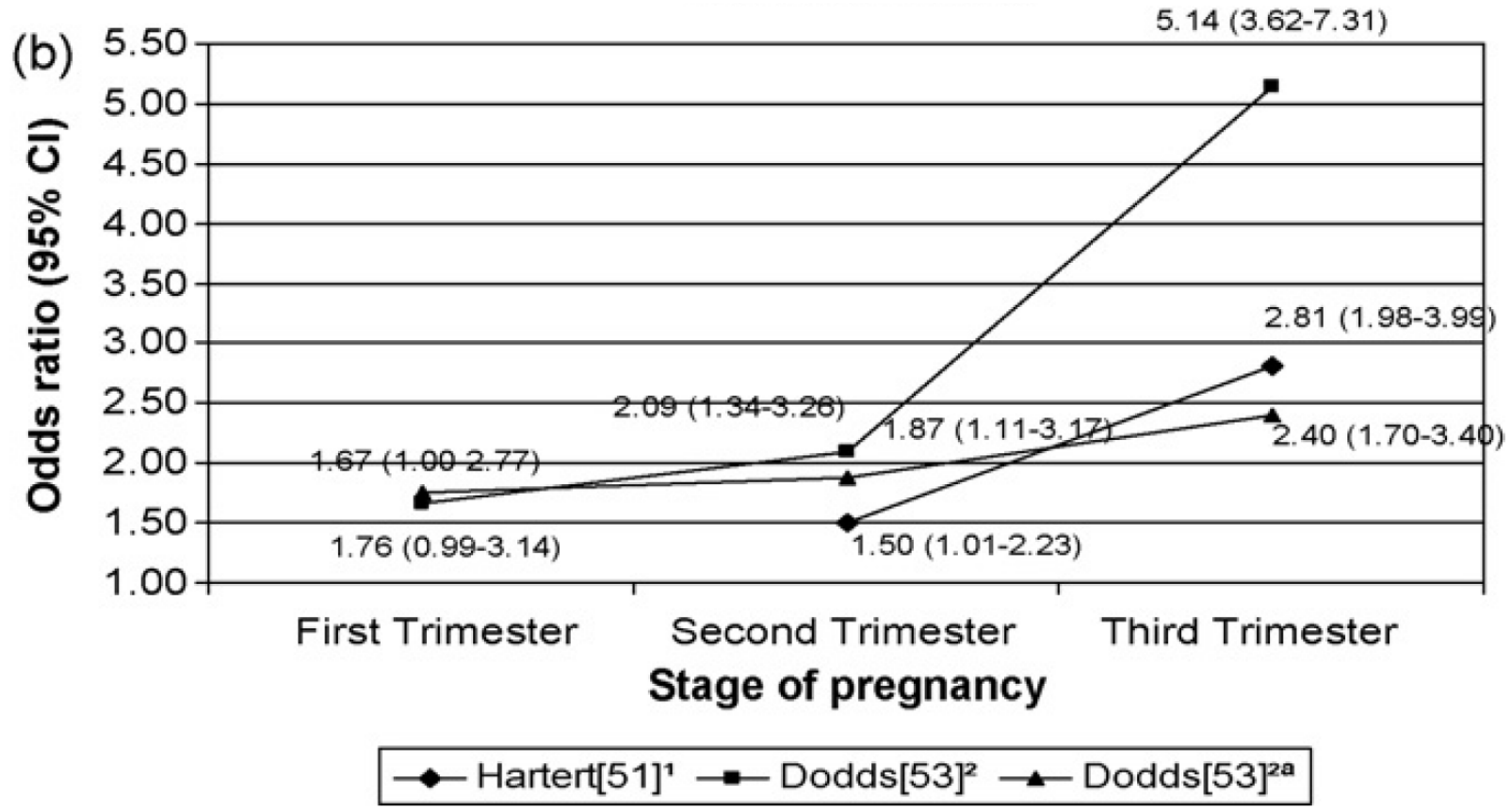
Taux d'hospitalisation attribué à la grippe chez les femmes enceintes sans comorbidité sur une saison grippale



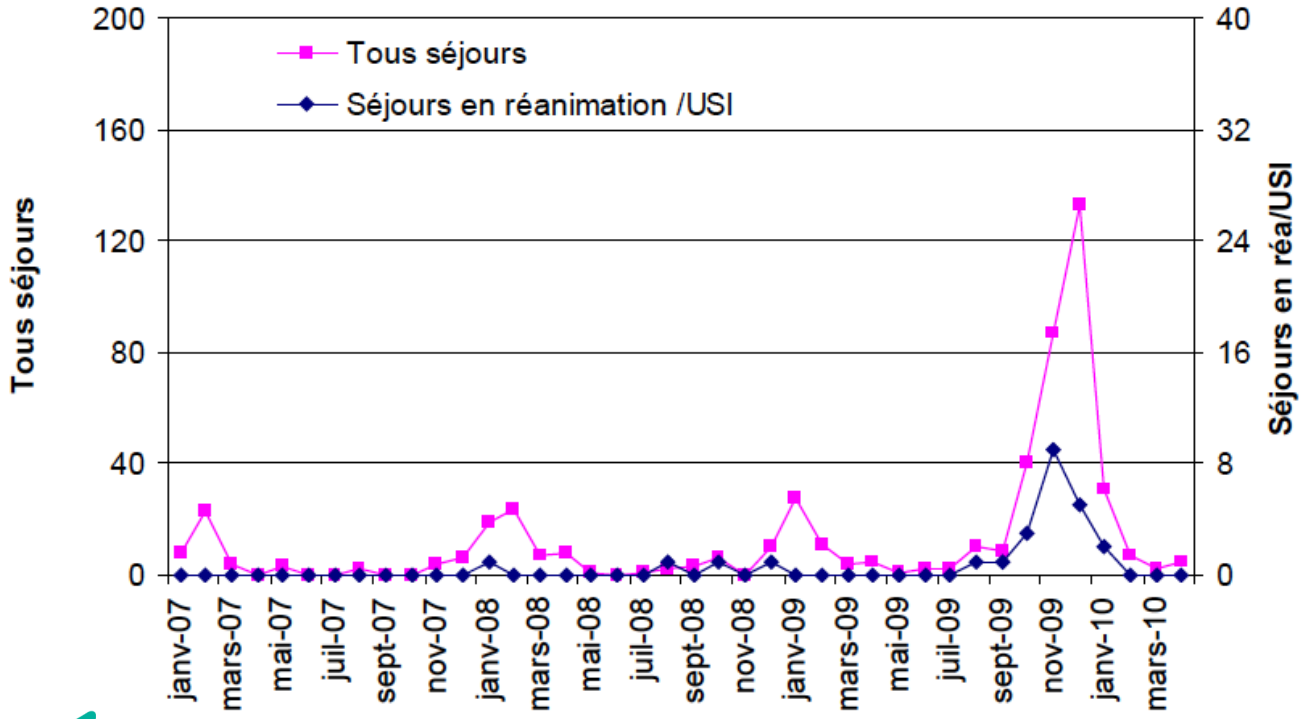
Is routine influenza immunization warranted in early pregnancy?

Skowronski DM, Vaccine 2009

Hospitalisation pour syndrome respiratoire chez les femmes enceintes sans comorbidité selon l'âge gestationnel



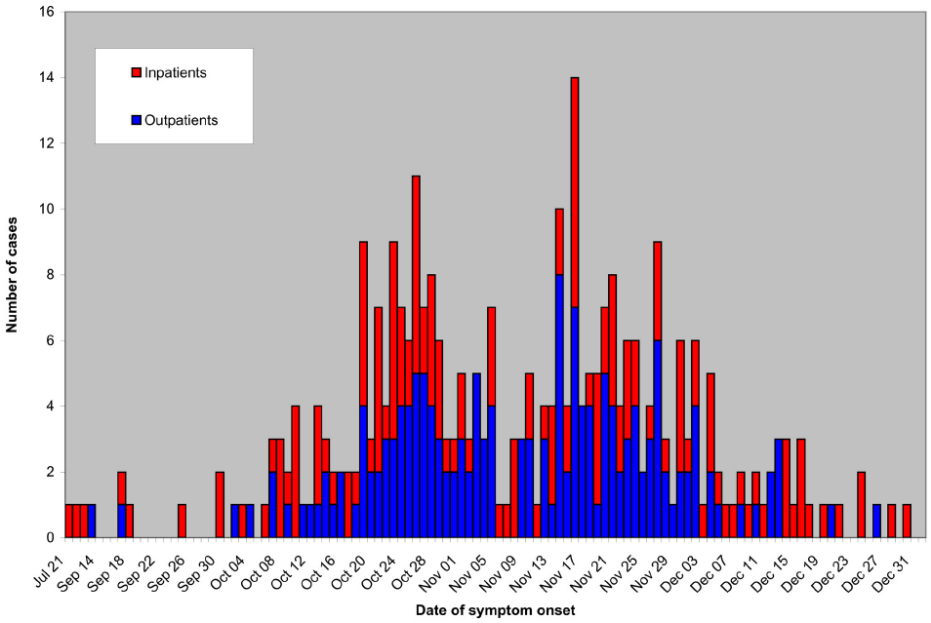
Nombre Mensuel de Séjours pour Grippe chez les Femmes Enceintes (janvier 2007-avril 2010), France



French Experience of 2009 A/H1N1v Influenza in Pregnant Women

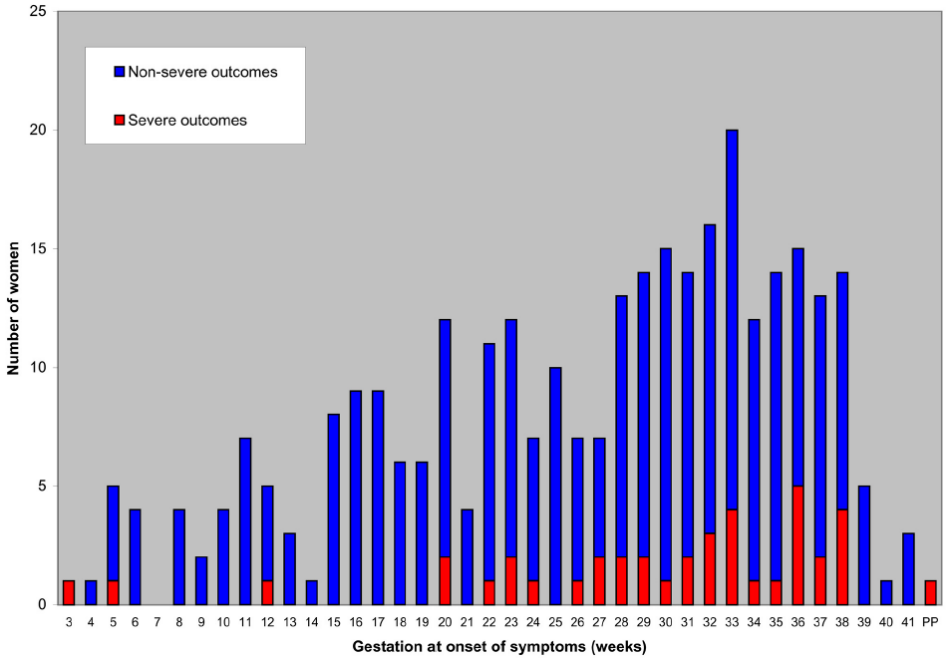
Dubar G, PlosOne 2010

- 315 patientes, grippe confirmée



Hospitalisées: 111 méd/obst + 40 réa
Ambulatoires: 164

Hospitalisées: 54% au 3ème trimestre
Réa: 70% au 3ème trimestre



French Experience of 2009 A/H1N1v Influenza in Pregnant Women

Dubar G, PlosOne 2010

Table 3. ICU-hospitalized severe patients (n = 40).

Post-partum admission to the ICU	10 (25)
Median time from symptom onset to ICU admission – days [min-max]	3 [0–17]
ICU indication(s):	
Respiratory failure †	38 (95)
Cardiac failure	9 (23)
Neurologic failure	0 (0)
Renal failure ‡	1 (3)
Decompensation of an underlying pathology ¥	3 (8)
Other *	1 (3)
Median SAPS II score on admission [min-max]	22 [6–74]
Median admission SOFA score [min-max]	2 [0–13]
Pathological admission pulmonary imaging ○	32 (80)
Documented secondary pulmonary infection¶	10 (25)
Ultimate respiratory failure:	
None	1 (3)
Moderate hypoxemia	15 (38)
Acute lung injury (200<PaO2/FiO2<300)	5 (13)
Acute respiratory distress syndrome (PaO2/FiO2<200)	19 (48)
Cardiac failure during hospitalization in the ICU ◇	17 (43)
Neurologic failure during hospitalization in the ICU ††	5 (13)
Renal failure during hospitalization in the ICU	6 (15)
Ultimate respiratory care:	
Oxygen therapy	15 (38)
Non-invasive ventilation	5 (13)
Mechanical ventilation (with or without ECMO)	20 (50)
ECMO	11 (28)
Median duration of ECMO – days [min-max]	8 [4–38]
Other treatments:	
Corticosteroids	12 (30)
Catecholamines	14 (35)
Renal replacement therapy	5 (13)
Transfusion	12 (30)
Other **	1 (3)
Median length of ventilation, days [min-max]	13 [2–55]
Median ICU length of stay, days [min-max]	10 [2–80]
Death	3 (8)

French Experience of 2009 A/H1N1v Influenza in Pregnant Women

Dubar G, PlosOne 2010

Table 5. Perinatal outcome.

	ICU patients (severe) (n = 33)	Hospitalized non-severe patients (moderate) (n = 66)	Outpatients (mild) (n = 47)	p value
A. PREGNANCY OUTCOME				
Vaginal delivery (live birth)	11 (33)	48 (73)	40 (85)	<0.001
Cesarean delivery (live birth)	20 (61)	16 (24)	5 (11)	<0.001
Intra-uterine fetal death	1 (3)	1 (2)	0 (0)	NS
term – weeks of gestation	21	29	-	
Miscarriage	1 (3)	1 (2)	1 (2)	NS
term – weeks of gestation	-	23	18	
Termination of pregnancy	0 (0)	0 (0)	1 (2)	NS
median term – weeks of gestation [range]	-	-	10	
B. NEONATAL OUTCOME*				
Median gestational age – weeks [min-max]	37 [27–41]	38 [24–41]	40 [29–42]	<0.001
< 29 weeks of gestation	2/31 (6)	1/64 (2)	0/45 (0)	
29–31 weeks of gestation	3/31 (10)	0/64 (0)	1/45 (2)	
32–36 weeks of gestation	9/31 (29)	8/64 (12)	2/45 (4)	
≥37 weeks of gestation	17/31 (55)	55/64 (86)	42/45 (93)	
Median birth weight - grams [min-max]	2780 [1215–4110]	3270 [550–4670]	3350 [1520–4380]	0.01
<1500	2/31 (6)	1/63 (2)	0 (0)	
1500–2499	12/31 (39)	6/63 (10)	1/44 (2)	
≥2500	17/31 (55)	56/63 (89)	43/44(98)	
Newborn resuscitation in the L&D unit	15/31 (48)[†,¥]	8/61 (13)	3/45 (7)	<0.001
Admission to neonatal intensive care unit	14/31 (45)	4/61 (7)	1/45 (2)	<0.001
Neonatal death (in the L&D unit or in the neonatal intensive care unit)	1/31 (3)	1/61 (2)	0/45 (0)	NS

2009 pandemic influenza A (H1N1) in pregnancy: a systematic review of the literature

Mosby LG, AJOG 2010

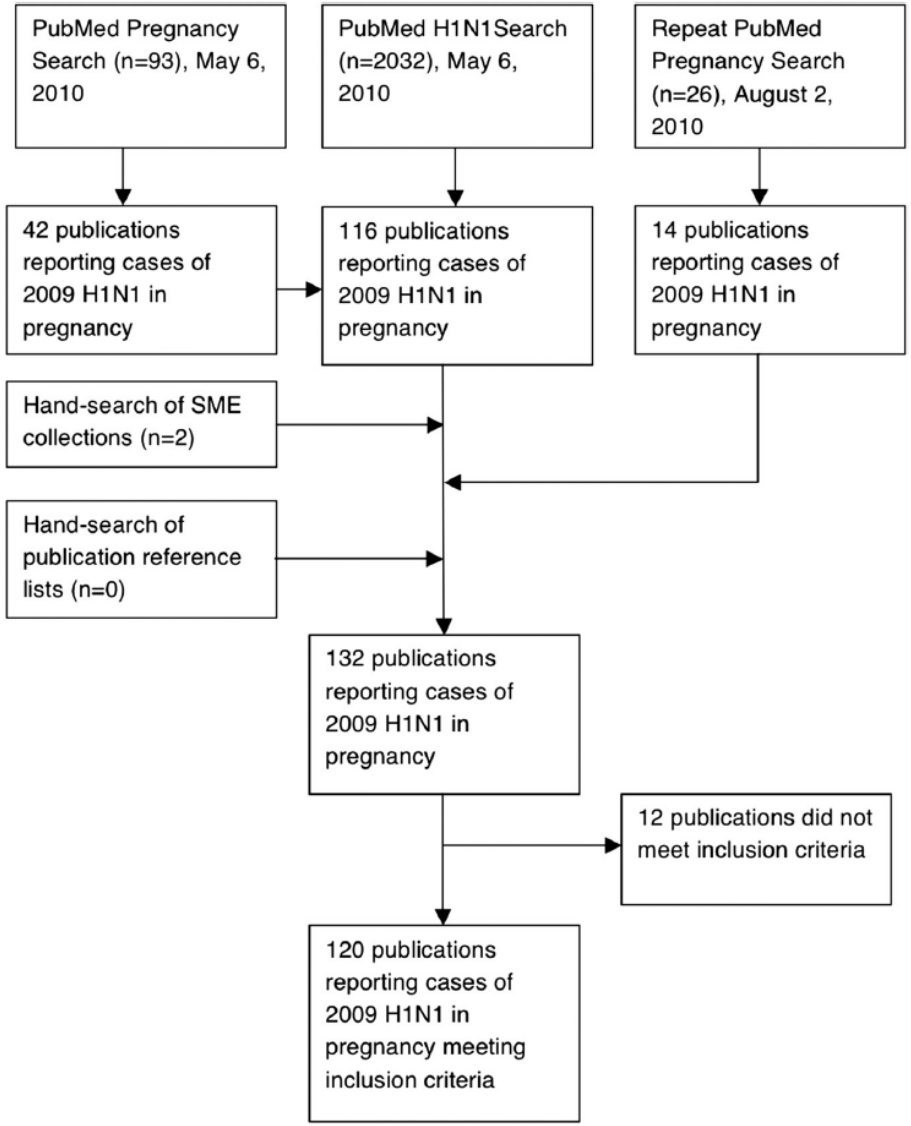


TABLE 1

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

Paper	Risk of hospitalization	Risk of ICU admission	Risk of death	Risk of severe disease
New South Wales Public Health Network[110]		RR, 5.8[a]	RR, 10.2[a]	
ANZIC[8]		RR, 7.4[a]		
Campbell et al[123]		RR, 0.7 (0.4–1.2)[a]	RR, 1.1 (0.3–4.1)[a]	RR, 0.7 (0.4–1.3)
Creanga et al[13]	RR, 7.2[a]			RR, 4.3[a]
Fuhrman et al[62]			aOR, 0.3 (0.04–3.0)	aOR, 0.5 (0.2–0.8)
Gérardin et al[46]		RR, 0.4 (0–2.6)[a]		
Hanslik et al[23]		OR, 5.2 (4.0–6.9)	OR, 1.4 (0.3–4.2)	
Jamieson et al[3]	RR, 4.3 (2.3–7.8)[b]			
Kelly et al[28]	RR, 5.2 (4.6–5.8)[b]	RR, 6.5 (4.8–8.8)[b]	RR, 1.4 (0.4–4.5)[b]	
Koegelenberg et al[29]			OR, 1.13 (0.14–8.88)	
Oliveira et al[81]			RR, 1.07 (.82–1.41)[a]	
Yang et al[53]			OR, 0.8 (0.2–3.5)	OR, 0.4 (0.2–3.4)
Zarychanski et al[106]		OR, 3.64 (0.86–15.4)[a,c]		

ANZIC, ANZIC Influenza Investigators and Australasian Maternity Outcomes Surveillance System; *aOR*, adjusted odds ratio; *ICU*, intensive care unit; *OR*, odds ratio; *RR*, relative risk.

[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.

Mosby. 2009 H1N1 and pregnancy. Am J Obstet Gynecol 2011.

TABLE 2

Number of deliveries, gestational age, mode of delivery, and neonatal outcome in pregnancies affected by 2009 H1N1 influenza

Paper	No. of deliveries[a]	Proportion of preterm deliveries	Proportion of cesarean deliveries	Fetal/neonatal survival
United States				
CDC[7]	9	5/9	At least 2/9	1 stillbirth; 1 neonatal death
Creanga et al[13]	22 while ill 22 after recovery	While ill: 3/22 (2 in women with severe disease) After recovery: 3/22	While ill: 11/22 After recovery: 7/22	2 neonatal deaths
Jamieson et al[3]	6	6/6	6 (5 in cases with maternal death)	
Louie et al[35]	35	25-28 wks: 3 >28 wks: 32 Of severe maternal illness: 11/13	Of severe maternal illness: 10/12	
Miller et al[49]	6	4/6	5/6	1 neonatal death
Siston et al[41]	169	30.2%	109/188	
Australia				
ANZIC[8]	59	36%	While ill: 14/22 After recovery: 6/23	4 stillbirths; 2 neonatal deaths; 1 postneonatal death
Hewagama et al[24]	15	40%		2 stillbirths; 1 neonatal death
France (La Reunion)				
Gérardin et al[46]	115	17/115; 5 precipitated by flu	21/114	No adverse neonatal outcome
United Kingdom				
Yates et al[54]	153	45/153		6 stillbirths
Singapore				
Lim et al[48]	42	13/42	6/42	
Israel				
Honarvar et al[47]	6	1/6	5/6	1 neonatal death due to H1N1 infection

ANZIC, ANZIC Influenza Investigators and Australasian Maternity Outcomes Surveillance System; *CDC*, Centers for Disease Control and Prevention.

[a] Number of deliveries of fetuses of potentially viable gestational age (definition varied by study).

Mosby. 2009 H1N1 and pregnancy. Am J Obstet Gynecol 2011.

2009 H1N1 Influenza A and Pregnancy Outcomes in Victoria, Australia

Hewagama S, CID 2010

6 hôpitaux
20 mai – 31 juillet 2009
Grippe confirmée

- 50% des patientes sans comorbidité
- 8/43 admises en réa
- 36% accouche durant l'hospitalisation
- Accouchement prématuré (< 37 SA): majorité de pneumonie
- 1 décès maternel
- 2 morts fœtales
- 1 décès néonatal

Table 1. Symptoms at Presentation and Reason for Hospital Admission

Variable	No. (%) of patients (n = 43)
Symptom at presentation	
Cough	43 (100)
Fever	36 (84)
Myalgia	27 (63)
Sore throat	26 (60)
Fatigue	23 (53)
Rhinorrhea	21 (49)
Dyspnea	16 (37)
Chest pain	10 (23)
Diarrhea	5 (12)
Reason for admission	
Uncomplicated influenza-like illness	25 (58)
Pneumonia	12 (28)
Respiratory failure	8 (19)
Labor	11 (26)
Obstetric complication	10 (23)
Fetal distress	2
Preeclampsia	1
FDIU	2
Hyperemesis	1
PPH	1
Preterm labor or TPL	3

Severe maternal morbidity due to respiratory disease and impact of 2009 H1N1 influenza A pandemic in Brazil: results from a national multicenter cross-sectional study

L. C. Pfitscher[1], J. G. Cecatti[1], R. C. Pacagnella[1], S. M. Haddad[1], M. A. Parpinelli[1], J. P. Souza[1,2], S. M. Quintana[2], F. G. Surita[1], M. H. Sousa[1], M. L. Costa[1*] and Brazilian Network for Surveillance of Severe Maternal Morbidity Group

BMC Infectious Diseases 2016

Mortalité virus pandémique versus virus non-pandémique ou autre cause

Table 1 Women with severe respiratory disease: cases non-tested for influenza A(H1N1)pdm09, influenza A(H1N1)pdm09 positive, influenza A(H1N1)pdm09 negative and other causes of morbidity according to severity of outcome (PLTC, MNM, MD) and their correspondent health indicators

Conditions	PLTC	MNM	MD	Total	Health indicators				
					MNMR/ 1000LB	SMOR/ 1000LB	MNM:MD ratio	Mortality index %	MMR/ 100000LB
Influenza A(H1N1)pdm09 positive	22	13	14	49	0.16	0.33	0.93:1	51.8	17.0
Influenza A(H1N1)pdm09 negative	55	18	10	83	0.22	0.34	1.80:1	35.7	12.2
Non-tested for influenza A(H1N1)pdm09	116	167	70	353[a]	2.03	2.89	2.39:1	29.5	85.2
Total Respiratory disease	193	198	94	485	2.41	3.55	2.11:1	32.2	114.4
Other causes	8452	572	46	9070	6.96	7.52	12.43:1	7.4	56.0

Intensive care unit surveillance of influenza infection in France: the 2009/10 pandemic and the three subsequent seasons

I Bonmarin [1], E Belchior [1], J Bergounioux [2], C Brun-Buisson [3], B Mégarbane [4], JL Chappert [5], B Hubert [5], Y Le Strat [1], D Lévy-Bruhl [1]

The risk factors independently associated with ARDS were as follows:

- Age between 36 and 55 years old (adjusted OR: 1.5; 95% CI: 1.2–2.0), with age over 55 years-old as reference;
- Pregnancy with no other risk factor (adjusted OR: 3.0; 95% CI: 1.3–6.9) or obesity with no other risk factor (adjusted OR: 1.8; 95% CI: 1.1–3.0) with no risk factor as reference;

Characteristics of influenza cases admitted to intensive care units by influenza season, France, influenza seasons 2009/10–2012/13

ICU cases	2009/10			2010/11			2011/12			2012/13		
	Missing data	CC	Multiple imputation (95% CI)	Missing data	CC	Multiple imputation (95% CI)	Missing data	CC	Multiple imputation (95% CI)	Missing data	CC	Multiple imputation (95% CI)
Age and sex												
Mean age (years)	0%	40.9	40.9 (39.7–42.1)	1%	44.6	44.6 (42.9–46.2)	0%	58.5	58.5 (55.8–61.3)	0%	52.7	52.7 (51.0–54.3)
Male	0%	53%	53% (50–56)	1%	58%	58% (54–61)	0%	55%	55% (49–60)	0%	54%	54% (51–58)
Risk factors	1%			2%			1%			1%		
None	–	27%	27% (24–29)	–	35%	35% (32–39)	–	18%	18% (14-23)	–	22%	22% (19-25)
Chronic disease and age≥65	–	63%	63% (60–66)	–	50%	50% (46–53)	–	80%	80% (76–85)	–	72%	72% (69–75)
Pregnancy with no other risk factor	–	3%	3% (2–4)	–	4%	4% (3–5)	–	1%	1% (0–2)	–	1%	1% (0–2)
Obesity with no associated risk factor	–	7%	7% (6–9)	–	11%	11% (9–13)	–	1%	1% (0–2)	–	5%	5% (3-6)
Pregnancy [a]	–	5%	5% (4–6)	–	4%	4% (3–5)	–	1%	1% (0–2)	–	2%	2% (0–2)
Obesity > 17 years-old [a]	–	20%	20% (17-22)	–	23%	23% (20–26)	–	16%	16% (11-20)	–	15%	15% (12–18)

TRAITEMENT

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 60 / No. 35
September 9, 2011

Maternal and Infant Outcomes Among Severely Ill Pregnant and Postpartum Women with 2009 Pandemic Influenza A (H1N1) — United States, April 2009–August 2010

- 15 avril 2009 – 10 aout 2010
- 437 femmes enceintes avec grippe sévère
  - 272 en réa
  - 75 décès
- 15 femmes en post-partum
  - 9 décès

TABLE 1. Characteristics of pregnant women with 2009 pandemic influenza A (H1N1) severe illness (i.e., ICU admission or death) — United States, April 15, 2009–August 10, 2010

Characteristic	Died (n = 75) No.	Died (n = 75) (%)	Admitted to ICU and survived (n = 272) No.	Admitted to ICU and survived (n = 272) (%)	p value
Maternal age (yrs)					
Mean age at illness onset (range)	26.9 (18–43)	—	25.9 (16–43)	—	0.17*
Unknown/Missing	1	—	13	—	
Race/Ethnicity					0.89†
White, non-Hispanic	21	(35.6)	88	(36.8)	
Black, non-Hispanic	12	(20.3)	44	(18.4)	
Hispanic	20	(33.9)	88	(36.8)	
Other race	6	(10.2)	19	(8.0)	
Missing	16		33		
Trimester at symptom onset					0.23†
First trimester (0–13 wks)	5	(6.9)	16	(6.5)	
Second trimester (14–28 wks)	22	(30.6)	103	(41.7)	
Third trimester (≥29 wks)	45	(62.5)	128	(51.8)	
Unknown/Missing	3		25		
Underlying illness/condition					0.04†
None of the following underlying conditions	25	(38.5)	129	(53.3)	
Any of the following underlying conditions	40	(61.5)	113	(46.7)	
Asthma	22		55		
Obesity	19		39		
Diabetes (gestational or pregestational)	11		16		
Other medical conditions§	19		40		
Unknown/Missing	10		30		
Antiviral medication prescribed					0.02†
No neuraminidase antiviral treatment	10	(13.9)	13	(5.2)	
Any neuraminidase antiviral treatment¶	62	(86.1)	238	(94.8)	
Unknown/Missing	3		21		
Total	**75**	**100.0**	**272**	**100.0**	
Days from symptom onset until treatment**					<0.01†
≤2	4	(7.0)	76	(40.6)	
3–4	11	(19.3)	47	(25.1)	
>4	42	(73.7)	64	(34.2)	
Unknown/Missing	8		72		
Total	**65**	**100.0**	**259**	**100.0**	

Pandemic 2009 Influenza A(H1N1) Virus Illness Among Pregnant Women in the United States

Siston AM, JAMA 2010

CDC
Avril – aout 2009

Table 2. Clinical Outcomes Among Pregnant Women With Pandemic 2009 Influenza A(H1N1) Illness Through August 21, 2009, United States[a]

Outcome	No. (%) of Pregnant Women
All Pregnant Women (n = 788)	
Hospital admission	
Yes	509 (65.9)
No	263 (34.1)
Unknown/missing	16
Maternal death	
Yes	30 (4.3)
No	662 (95.7)
Unknown/missing	96
Preterm delivery[b]	
Yes (<37 wk gestation)	51 (30.2)
No (≥37 wk gestation)	118 (69.8)
Delivery type	
Spontaneous abortion	8 (1.4)
Therapeutic abortion	4 (0.7)
Vaginal delivery	79 (13.5)
Cesarean delivery	109 (18.6)
Delivered, type unknown or estimated delivery date on or before November 6, 2009	263 (45.0)
Not yet delivered or estimated delivery date after November 6, 2009	122 (20.9)
Unknown/missing	203
Among Hospitalized Pregnant Women (n = 509)	
Hospital length of stay, d	
Median (range)	3 (1-73)
Unknown/missing	122
Admission to intensive care unit	
Yes	115 (24.7)
No	350 (75.3)
Unknown/missing	44
Mechanical ventilation	
Yes	77 (18.8)
No	332 (81.2)
Unknown/missing	100

Pandemic 2009 Influenza A(H1N1) Virus Illness Among Pregnant Women in the United States

Siston AM, JAMA 2010

Table 3. Comparison of Maternal Outcomes by Timing of Antiviral (Oseltamivir or Zanamivir) Treatment[a]

	No. (%) of Women							
	Hospital Admission[b]		ICU Admission Among Hospitalized Patients[c]		Mechanical Ventilation Among Hospitalized Patients[c]		Maternal Death[b]	
Treatment	Yes (n = 509)	No (n = 263)	Yes (n = 115)	No (n = 350)	Yes (n = 77)	No (n = 332)	Yes (n = 30)	No (n = 662)
Timing after symptom onset, d								
≤2	148 (67.6)	71 (32.4)	13 (9.4)	125 (90.6)	6 (4.6)	125 (95.4)	1 (0.5)	197 (99.5)
3-4	66 (78.6)	18 (21.4)	15 (22.7)	51 (77.3)	10 (17.2)	48 (82.8)	4 (5.0)	76 (95.0)
>4	67 (82.7)	14 (17.3)	37 (56.9)	28 (43.1)	32 (56.1)	25 (43.9)	20 (27.0)	54 (73.0)
No treatment	45 (57.7)	33 (42.3)	15 (34.9)	28 (65.1)	9 (21.4)	33 (78.6)	5 (6.9)	67 (93.1)
Treated, timing unknown[d]	73	52	17	47	10	41	0	115
Unknown treatment status[d]	110	75	18	71	10	60	0	153
Treatment Timing Comparisons								
3-4 vs ≤2 d								
Relative risk (95% CI)	1.2 (1.0-1.3)		2.4 (1.2-4.8)		3.8 (1.4-9.9)		9.9 (1.1-87.2)	
P Value	.06		.01		.008[e]		.03[e]	
>4 vs ≤2 d								
Relative risk (95% CI)	1.2 (1.1-1.4)		6.0 (3.5-10.6)		12.3 (5.4-27.7)		53.5 (7.3-391.7)	
P Value	.01		<.001		<.001		<.001	
None vs ≤2 d								
Relative risk (95% CI)	0.8 (0.7-1.0)		3.7 (1.9-7.2)		4.7 (1.8-12.4)		13.8 (1.6-115.7)	
P Value	.12		<.001		.002[e]		.006[e]	

Pandemic 2009 Influenza A(H1N1) Virus Illness Among Pregnant Women in the United States

Siston AM, JAMA 2010

Table 4. Impact of Trimester and Timing of Antiviral Treatment on Admission to an Intensive Care Unit Among Hospitalized Patients

Trimester and Treatment Timing[a]	No. (%) of Women: Intensive Care Admission (n = 61)	No. (%) of Women: No Intensive Care Admission (n = 192)	Relative Risk (95% CI)	*P* Value
Any trimester ≤2 d after symptom onset	13 (9.4)	125 (90.6)	1.0 [Referent]	
3-4 d after symptom onset, trimester				
First	1 (16.7)	5 (83.3)	1.8 (0.3-11.4)	.47[b]
Second	3 (14.3)	18 (85.7)	1.5 (0.5-4.9)	.45[b]
Third	9 (33.3)	18 (66.7)	3.5 (1.7-7.4)	.003[b]
>4 d after symptom onset, trimester				
First	3 (75.0)	1 (25.0)	8.0 (3.7-17.1)	.004[b]
Second	14 (58.3)	10 (41.7)	6.2 (3.3-11.5)	<.001[b]
Third	18 (54.5)	15 (45.5)	5.8 (3.2-10.6)	<.001

French Experience of 2009 A/H1N1v Influenza in Pregnant Women

Dubar G, PlosOne 2010

Table 4. Impact of coexisting illnesses and the timing of antiviral treatment on admission to an intensive care unit.

	Adjusted OR	95% CI	p value
Coexisting illness	5.11	2.22–11.78	<0.001
Delay of treatment <3 days after symptom onset	Reference	-	-
Delay of treatment 3–5 days after symptom onset	4.78	1.89–12.09	0.001
Delay of treatment >5 days after symptom onset	61.24	14.35–261.25	<0.001

The Journal of Infectious Diseases
MAJOR ARTICLE

Benefit of Early Initiation of Influenza Antiviral Treatment to Pregnant Women Hospitalized With Laboratory-Confirmed Influenza

Grippe confirmée
2010-2014 (FluSurv-NET, USA)

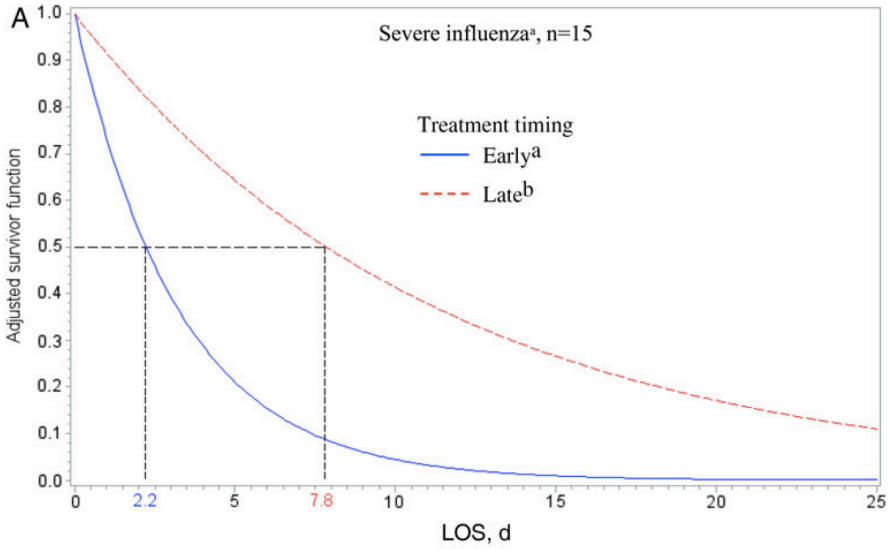
Table 1. General Characteristics of Pregnant Women Hospitalized With Laboratory-Confirmed Influenza During the 2010–2014 Influenza Seasons, Overall and by Disease Severity

Characteristic	Overall (n = 865)	Severe[a] (n = 63)	Nonsevere (n = 802)	*P* Value[b]
Age group, y				.88
15–24	315 (36)	24 (38)	291(36)	
25–34	451 (52)	31 (49)	420 (52)	
35–44	99 (11)	8 (13)	91 (11)	
Race/ethnicity[c]				.26
Non-Hispanic white	314 (42)	28 (53)	286 (41)	
Non-Hispanic black	240 (32)	15 (28)	225 (33)	
Hispanic	188 (25)	10 (19)	178 (26)	
Pregnancy trimester on admission, wks[d]				**.04**
First, ≤13	88 (11)	9 (15)	79 (10)	
Second, 14–28	266 (32)	25 (43)	241 (31)	
Third, ≥29	478 (57)	24 (41)	454 (59)	
Underlying medical condition				
Any	278 (32)	28 (44)	250 (31)	**.03**
Asthma	182 (21)	21 (33)	161 (20)	**.01**
Metabolic disease	64 (7)	7 (11)	57 (7)	.20
Cardiovascular disease (excluding hypertension)	31 (4)	5 (8)	23 (3)	.05
Immunocompromised condition	28 (3)	4 (6)	27 (3)	.30
Blood disorder/hemoglobinopathy	20 (2)	2 (3)	18 (2)	.60
Neurologic/neuromuscular disease	18 (2)	2 (3)	16 (2)	.40
Renal disease	10 (1)	1 (2)	9 (1)	.50
Chronic pulmonary disease (excluding asthma)	7 (1)	0 (0)	7 (1)	>.99
Liver disease	4 (0)	0 (0)	4 (0)	>.99
Other characteristics				
Influenza vaccination	221 (26)	9 (14)	212 (26)	**.03**
Antiviral treatment	731 (85)	53 (84)	678 (85)	.90
Influenza virus type/subtype[e]				
Influenza A virus	739 (85)	57 (91)	682 (85)	. . .
H1N1pdm09	197 (23)	27 (42)	170 (21)	**.01**[f]
H3N2	173 (20)	7 (11)	166 (21)	
Not subtyped	494 (57)	29 (46)	465 (58)	. . .
Influenza B virus	125 (15)	6 (10)	119 (15)	. . .
Time from illness onset to hospitalization, d[g]	1 (0–2)	1(1–3)	1 (0–2)	.08
Time from hospitalization to antiviral treatment, d	0 (0–1)	0 (0–1)	0 (0–1)	.90
Time from illness onset to antiviral treatment[h]				
Overall, d	2 (1–3)	2 (1–4)	2 (1–3)	.05
Early[i], proportion (%)	353/500 (71)	14/27 (52)	339/473 (72)	**.03**
Late[i], proportion (%)	147/500 (29)	13/27 (48)	134/473 (28)	

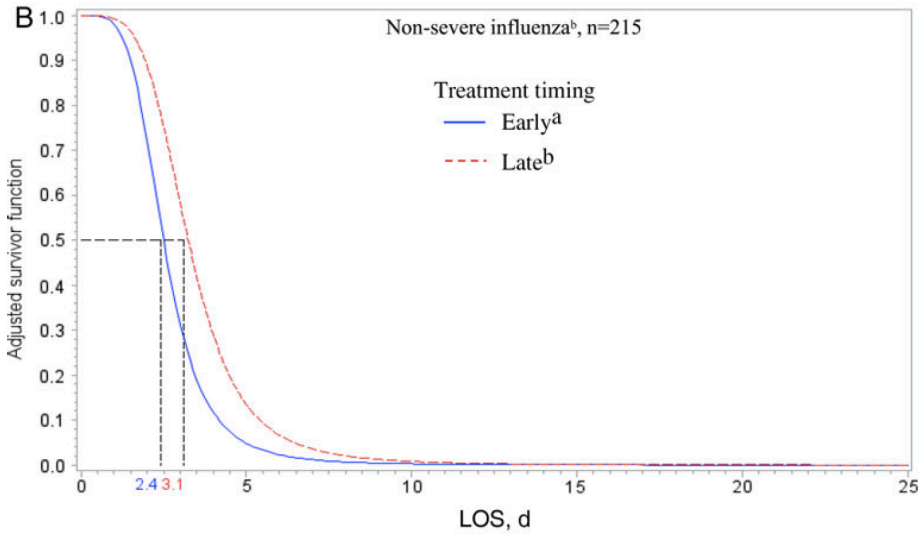
Décès: 4/865 patientes

The Journal of Infectious Diseases
MAJOR ARTICLE

Benefit of Early Initiation of Influenza Antiviral Treatment to Pregnant Women Hospitalized With Laboratory-Confirmed Influenza



Treatment Timing	Women, No.	LOS, d, Median (IQR)	*P*
Early[a]	8	2.2 (0.9–5.8)	.03
Late[b]	7	7.8 (3.0–20.6)	



Treatment Timing	Women, No.	LOS, d, Median (IQR)	*P*
Early[a]	153	2.4 (2.3–2.5)	<.01
Late[b]	62	3.1 (2.8–3.5)	

Pronostic néonatal

Perinatal outcomes after maternal 2009/H1N1 infection: national cohort study

Pierce M, BMJ 2011

- UK
- Pandémie 2009
- 256 femmes hospitalisées avec grippe confirmée
- 1220 femmes hospitalisées en contrôle

- Mortalité périnatale augmenté: 10/256 versus 9/1233

Table 2 | Outcome of pregnancy for women admitted to hospital with 2009/H1N1 infection (infected cohort) and uninfected women (comparison cohort)

Outcome	No (%)		Odds ratio (95% CI)		National data, 2008	
	Infected cohort (n=256)	Comparison cohort (n=1220)	Unadjusted	Adjusted*	No (%)	Unadjusted odds ratio (95% CI)
Outcome of pregnancy:						
Live birth†	249 (95)	1226 (99)	1	1	795 004 (99)	1
Stillbirth	7 (3)	7 (1)	4.9 (1.7 to 14.2)	4.2 (1.4 to 12.4)	4 043 (1)	5.5 (2.6 to 11.7)
Loss of pregnancy before 24 weeks	5 (2)	NA	NA	NA	NA	NA
Neonatal death:						
Yes	3 (1)	2 (0)	7.4 (1.2 to 44.7)	5.6 (0.5 to 64.2)	2 557 (0)	3.8 (1.2 to 11.8)
No	246 (99)	1218 (100)	1	1	792 487 (100)	1
Perinatal death:						
Yes	10 (4)	8 (1)	6.2 (2.4 to 15.9)	5.7 (2.2 to 15.1)	6 025 (1)	5.4 (2.8 to 10.1)
No	246 (96)	1219 (99)	1	1	793 022 (99)	1
Mean (SD) birth weight (kg)	3073 (774)	3342 (614)	−270 (−356 to −183)‡	−255 (−353 to −156)‡	NA	NA
Low birth weight (<2500 g):						
Yes	50 (20)	94 (8)	2.9 (2.0 to 4.3)	3.2 (2.1 to 4.9)	57 072 (7)§	3.0 (2.2 to 4.1)
No	206 (80)	1137 (92)	1	1	713 201 (93)	1
Very low birth weight (<1500 g):						
Yes	14 (5)	22 (2)	3.2 (1.6 to 6.3)	2.9 (1.3 to 6.4)	10 955 (1)§	4.0 (2.3 to 6.9)
No	242 (95)	1209 (98)	1	1	759 318 (99)	1
Preterm (<37 weeks):						
Yes	59 (24)	89 (7)	3.9 (2.7 to 5.6)	4.0 (2.7 to 5.9)	36 283 (8)	3.6 (2.7 to 4.8)
No	192 (76)	1129 (93)	1	1	423 475 (92)	1
Very preterm (<32 weeks):						
Yes	18 (7)	18 (1)	5.2 (2.6 to 10.0)	4.9 (2.4 to 10.0)	10 932 (2)	3.2 (2.0 to 5.1)
No	233 (93)	1200 (99)	1	1	449 101 (98)	1
Delivered by caesarean section:						
Yes	100 (40)	299 (25)	2.1 (1.5 to 2.7)	2.3 (1.7 to 3.2)	139 449 (24)	2.2 (1.7 to 2.8)
No	150 (60)	921 (75)	1	1	453 951 (76)	1
Congenital anomalies:						
Yes	8 (3)	NA	NA	NA	4 308 (2)	1.9 (0.9 to 3.8)
No	243 (97)				248 644 (100)	1

Table 4 | Characteristics of infected women, for those who delivered preterm and those who delivered at term. Values are numbers (percentages) unless stated otherwise

Characteristic	Preterm (n=59)	Not preterm (n=131)*	P value
Trimester of infection:			
First (0-11 weeks)	0 (0)	10 (8)	0.046†
Second (12-23 weeks)	8 (14)	24 (18)	
Third (≥24 weeks)	51 (86)	97 (74)	
Median (interquartile range) No of symptoms‡ at presentation	4 (3-5)	5 (3-6)	0.09§
Median (interquartile range) days before start of treatment	3 (1-7)	3 (1-6)	0.46†
Treated within 2 days of infection:			
Yes	28 (53)	69 (57)	0.61
No	25 (47)	52 (43)	
Immunised against 2009/H1N1:			
Yes	2 (4)	7 (6)	0.72§
No	54 (96)	119 (94)	
Admitted to intensive care unit:			
Yes	32 (54)	16 (12)	<0.001
No	27 (46)	115 (88)	
Pneumonia as secondary infection:			
Yes	12 (20)	5 (4)	0.001†
No	47 (80)	126 (96)	
Asthma:			
Yes	9 (15)	18 (14)	0.78
No	50 (85)	113 (86)	
Other comorbidity:			
Yes	15 (25)	23 (18)	0.21
No	44 (75)	108 (82)	
Delivered by caesarean section:			
Yes	42 (72)	39 (30)	<0.001
No	16 (28)	92 (70)	
Indication for caesarean section:			
Maternal influenza infection	22 (52)	3 (8)	<0.001†
Other	20 (48)	36 (92)	

Table 5 | Previous studies of pregnancy outcomes among women infected with 2009/H1N1

Study	Study period (2009)	Study population	No of pregnant women reported	No (%) women with outcome data	Pregnancy outcome	No (%) affected
Siston 2010[5]	14 April to 21 August	Pregnant women with 2009/H1N1 influenza, USA	788*	169 (21)	Preterm delivery	51 (30)
				200 (25)	Spontaneous abortion	8 (4)
Louie 2010[3]	23 April to 11 August	Women with confirmed 2009/H1N1 needing intensive care, California, USA	18	12 (67)	Preterm delivery	10 (83)
		Women admitted to hospital (>24 hrs) or died with confirmed 2009/H1N1, California, USA	94	37 (39)	Spontaneous abortion	2 (5)
Creanga 2010[6]	01 May to 30 June†	Women admitted to hospital with H1N1v infection, New York, USA	62	40 (65)	Preterm delivery	6 (15)
					Neonatal death	2 (5)
Hewagama 2010[22]	20 May to 31 July	Pregnant women admitted to hospital with 2009/H1N1 infection, Victoria, Australia	43	15 (35)	Preterm delivery	6 (40)
				24 (56)	Stillbirth‡/neonatal death	3 (13)
ANZIC 2010[4]	01 June to 31 August	Pregnant or recently postpartum women admitted to intensive care unit with 2009/H1N1, Australia and New Zealand	64	61 (95)	Miscarriage§	2 (3)
					Stillbirth‡	4 (7)
					Preterm delivery	22 (37)
					Low birth weight	18 (31)
Dubar 2010[23]	01 August to 31 December¶	Pregnant women admitted to hospital with confirmed 2009/H1N1, France	314	146 (46)	Stillbirth	2 (1)
					Loss of pregnancy before 24 weeks	4 (2)
					Low birth weight	22 (16)
					Preterm birth	26 (19)

Neonatal Outcomes After Antenatal Influenza Immunization During the 2009 H1N1 Influenza Pandemic: Impact on Preterm Birth, Birth Weight, and Small for Gestational Age Birth

Richard JL, CID 2013

- Géorgie, pandémie 2009
- 3 337 femmes

Table 2. Odds Ratios for Association of Maternal Influenza Immunization With Infant Outcomes, Among Infants Born During Period of 2009 Influenza A (H1N1) Virus Circulation

Outcome	H1N1 Vaccine (n = 1125) Has Outcome, No. (%)	No Vaccine (n = 1581) Has Outcome, No.	Adjusted[a] OR or Difference (95% CI)	Unadjusted OR or Difference (95% CI)
Preterm birth (27–36 wk)	86 (7.6%)	191 (12.1%)	.63 (.47–.84)[b]	.60 (.46–.79)
Birth at 27–33 wk	19 (1.7%)	52 (3.3%)	.53 (.30–.95)	.49 (.29–.83)
Birth at 34–36 wk	67 (6.0%)	139 (8.8%)	.66 (.48–.92)	.65 (.48–.87)
Low birth weight, <2500 g[c]	68 (6.4%)	132 (8.8%)	.79 (.56–1.10)	.71 (.52–.96)
Small for gestational age[c]	99 (9.3%)	123 (8.2%)	1.26 (.94–1.69)	1.15 (.87–1.52)
Birth weight, g[c], mean (95% CI)	3308.5 (3276.6–3340.4)	3245.3 (3216.5–3274.2)	45.1 (1.8–88.3)	63.2 (20.0–106.3)

Risk of fetal death after pandemic influenza virus infection or vaccination

Haberg SE, NEJM 2013

- Norvège
- 54% des femmes vaccinées

Table 2. Hazard Ratios for Fetal Death, According to Status Regarding Vaccination, Pregnancy during the Pandemic Wave, and a Clinical Diagnosis of Influenza.*

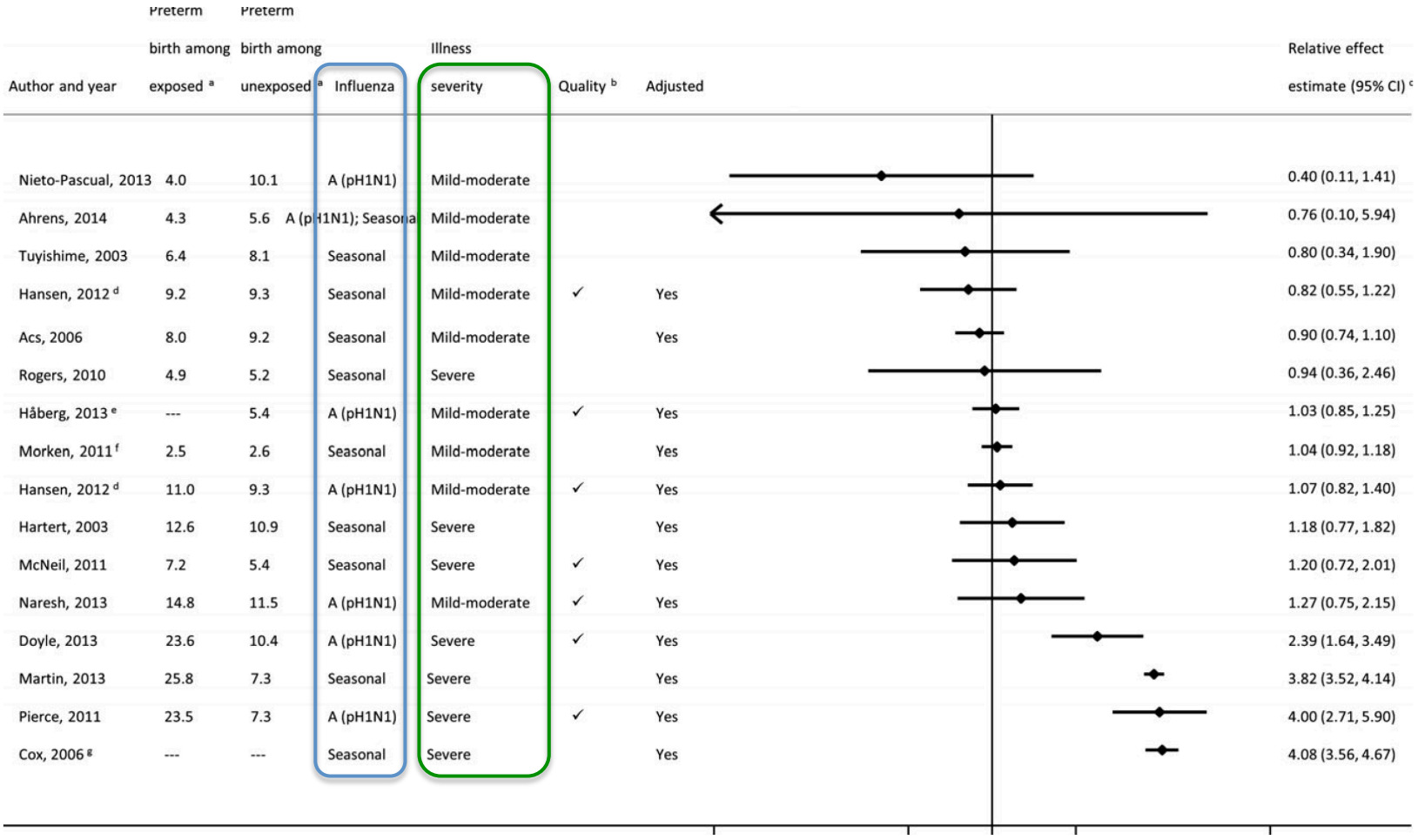
Variable	No. of Pregnancy-Days at Risk†	Hazard Ratio (95% CI)		
		Without Adjustment	With Initial Adjustment‡	With Further Adjustment§
Total no. of days	18,970,404			
Vaccinated during pregnancy				
No	15,942,252	1.00	1.00	1.00
Yes	3,028,152	0.95 (0.74–1.21)	0.84 (0.64–1.10)	0.88 (0.66–1.17)
Pregnant during the pandemic				
No	10,422,035	1.00	1.00	1.00
Yes	8,548,369	1.15 (0.96–1.37)	1.21 (1.00–1.48)	1.26 (1.02–1.55)
Without an influenza diagnosis	8,221,514	1.11 (0.93–1.33)	1.18 (0.96–1.44)	1.23 (0.99–1.52)
With an influenza diagnosis	326,855	2.00 (1.20–3.32)	2.10 (1.27–3.49)	1.91 (1.07–3.41)

Maternal influenza and birth outcomes: systematic review of comparative studies

Fell DB et al, BJOG 2016

21 études comparatives dont 12 entre 2010-2014, 5 entre 2000-2009

Accouchement prématuré



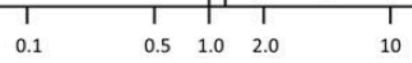
Author and year	Preterm birth among exposed [a]	Preterm birth among unexposed [a]	Influenza	Illness severity	Quality [b]	Adjusted	Relative effect estimate (95% CI) [c]
Nieto-Pascual, 2013	4.0	10.1	A (pH1N1)	Mild-moderate			0.40 (0.11, 1.41)
Ahrens, 2014	4.3	5.6	A (pH1N1); Seasonal	Mild-moderate			0.76 (0.10, 5.94)
Tuyishime, 2003	6.4	8.1	Seasonal	Mild-moderate			0.80 (0.34, 1.90)
Hansen, 2012 [d]	9.2	9.3	Seasonal	Mild-moderate	✓	Yes	0.82 (0.55, 1.22)
Acs, 2006	8.0	9.2	Seasonal	Mild-moderate		Yes	0.90 (0.74, 1.10)
Rogers, 2010	4.9	5.2	Seasonal	Severe			0.94 (0.36, 2.46)
Håberg, 2013 [e]	---	5.4	A (pH1N1)	Mild-moderate	✓	Yes	1.03 (0.85, 1.25)
Morken, 2011 [f]	2.5	2.6	Seasonal	Mild-moderate		Yes	1.04 (0.92, 1.18)
Hansen, 2012 [d]	11.0	9.3	A (pH1N1)	Mild-moderate	✓	Yes	1.07 (0.82, 1.40)
Hartert, 2003	12.6	10.9	Seasonal	Severe		Yes	1.18 (0.77, 1.82)
McNeil, 2011	7.2	5.4	Seasonal	Severe	✓	Yes	1.20 (0.72, 2.01)
Naresh, 2013	14.8	11.5	A (pH1N1)	Mild-moderate	✓	Yes	1.27 (0.75, 2.15)
Doyle, 2013	23.6	10.4	A (pH1N1)	Severe	✓	Yes	2.39 (1.64, 3.49)
Martin, 2013	25.8	7.3	Seasonal	Severe		Yes	3.82 (3.52, 4.14)
Pierce, 2011	23.5	7.3	A (pH1N1)	Severe	✓	Yes	4.00 (2.71, 5.90)
Cox, 2006 [g]	---	---	Seasonal	Severe		Yes	4.08 (3.56, 4.67)

Petit poids de naissance

Author and year	SGA among exposed [a]	SGA among unexposed [a]	Influenza	Illness severity	Quality [b]	Adjusted	Relative effect estimate (95% CI) [c]
Irving, 2000	2.8	3.9	Seasonal	Mild-moderate	✓	Yes	0.71 (0.23, 2.20)
Nieto-Pascual, 2013	14.4	14.1	A (pH1N1)	Mild-moderate			0.98 (0.47, 2.05)
Hansen, 2012 [d]	7.3	7.2	A (pH1N1)	Mild-moderate	✓	Yes	0.99 (0.77, 1.27)
Naresh, 2013	8.5	7.4	A (pH1N1)	Mild-moderate	✓	Yes	1.14 (0.59, 2.22)
Hansen, 2012 [d]	12.0	7.2	Seasonal	Mild-moderate	✓	Yes	1.59 (1.15, 2.20)
McNeil, 2011	15.3	9.7	Seasonal	Severe	✓	Yes	1.66 (1.11, 2.49)
Overall							**1.24 (0.96, 1.59)**

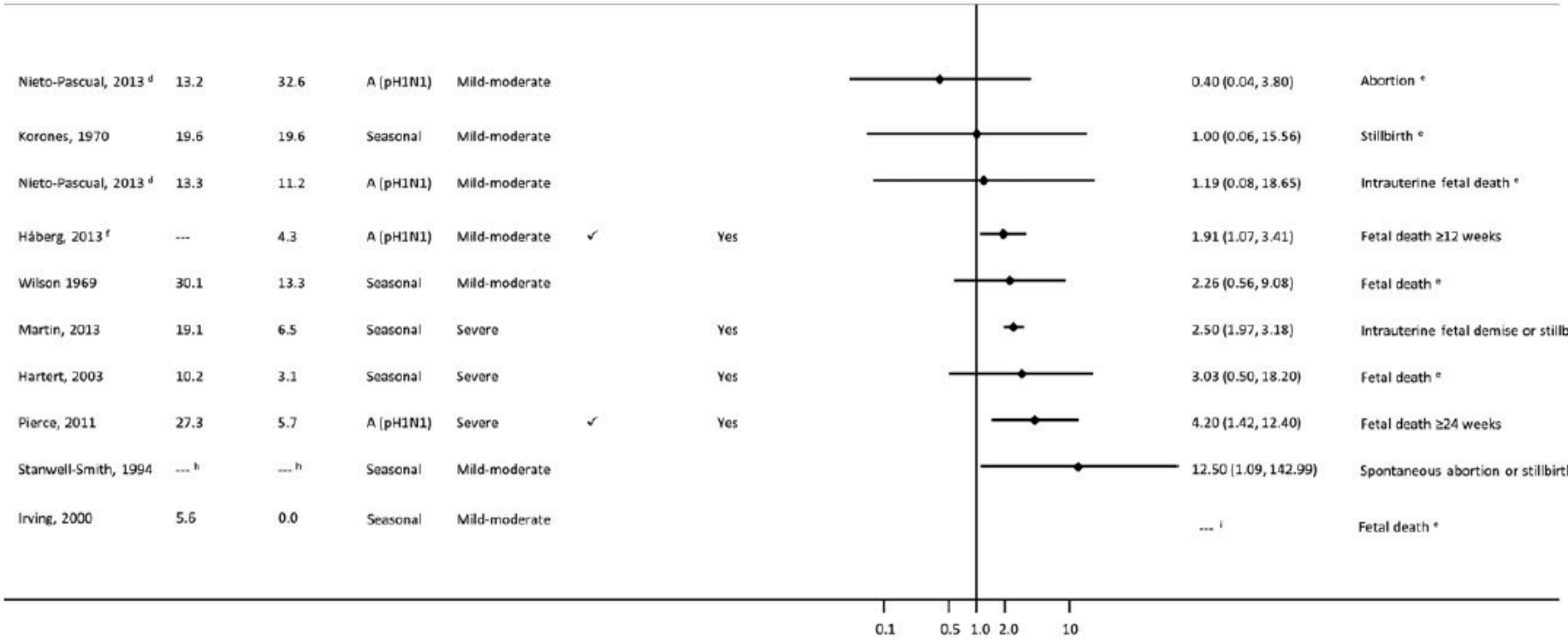
NOTE: Weights are from random effects analysis

Heterogeneity:
$\chi^2 = 8.73$, df = 5 ($P = 0.12$); $I^2 = 43\%$, 95% CI: 0 to 76



Mort fœtale

Author and year	Fetal death among exposed [a]	Fetal death among unexposed [a]	Influenza	Illness severity	Quality [b]	Adjusted	Relative effect estimate (95% CI) [c]	Definition of fetal death
Nieto-Pascual, 2013 [d]	13.2	32.6	A (pH1N1)	Mild-moderate			0.40 (0.04, 3.80)	Abortion [e]
Korones, 1970	19.6	19.6	Seasonal	Mild-moderate			1.00 (0.06, 15.56)	Stillbirth [e]
Nieto-Pascual, 2013 [d]	13.3	11.2	A (pH1N1)	Mild-moderate			1.19 (0.08, 18.65)	Intrauterine fetal death [e]
Håberg, 2013 [f]	---	4.3	A (pH1N1)	Mild-moderate	✓	Yes	1.91 (1.07, 3.41)	Fetal death ≥12 weeks
Wilson 1969	30.1	13.3	Seasonal	Mild-moderate			2.26 (0.56, 9.08)	Fetal death [e]
Martin, 2013	19.1	6.5	Seasonal	Severe		Yes	2.50 (1.97, 3.18)	Intrauterine fetal demise or stillbirth [g]
Hartert, 2003	10.2	3.1	Seasonal	Severe		Yes	3.03 (0.50, 18.20)	Fetal death [e]
Pierce, 2011	27.3	5.7	A (pH1N1)	Severe	✓	Yes	4.20 (1.42, 12.40)	Fetal death ≥24 weeks
Stanwell-Smith, 1994	--- [h]	--- [h]	Seasonal	Mild-moderate			12.50 (1.09, 142.99)	Spontaneous abortion or stillbirth [e]
Irving, 2000	5.6	0.0	Seasonal	Mild-moderate			--- [i]	Fetal death [e]



En conclusion

- La grippe chez la femme enceinte
  - Est plus grave
  - Met en jeu le pronostic de la grossesse
  - Et le pronostic du nouveau-né
- Le traitement
  - Oseltamivir
  - Le plus rapidement possible
- La vaccination
  - Protège la femme enceinte
  - Et son bébé dans les 6 premiers mois de vie