

Supplementary files

Figure. Gestational age at A/H1N1 pandemic vaccine administration by date of vaccination (n= 6246).

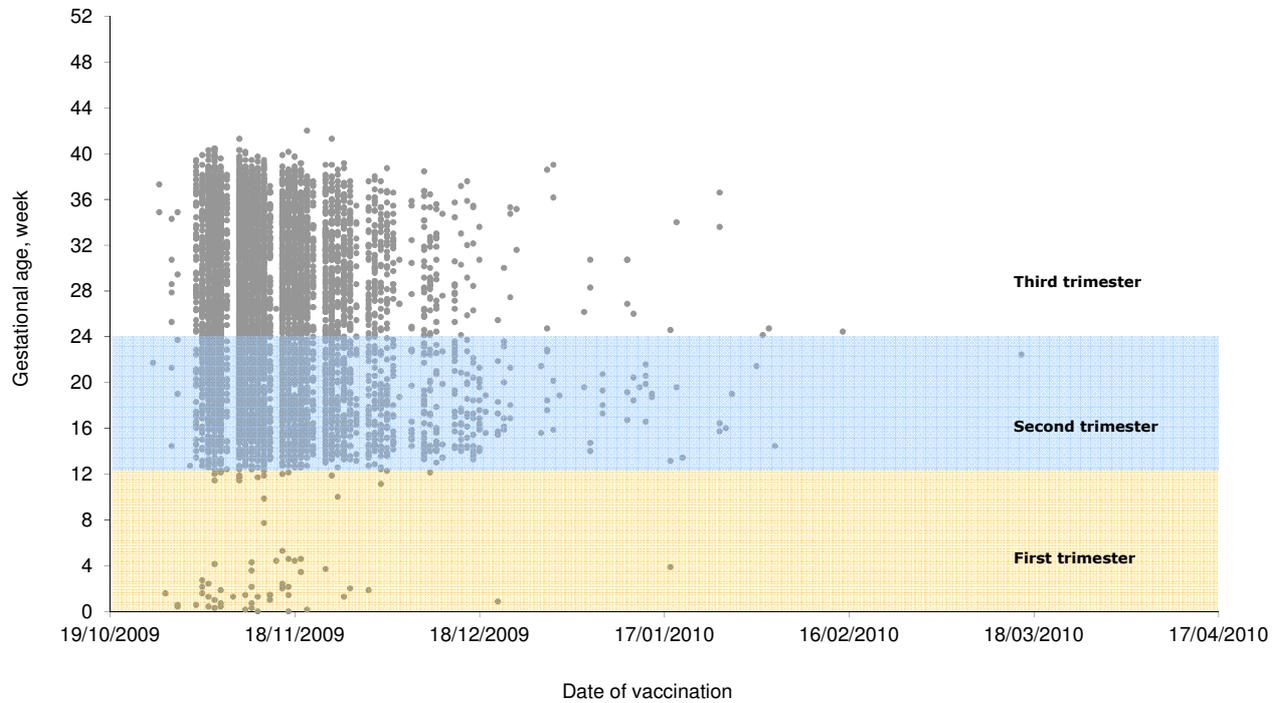


Table A. Descriptions of exclusions for congenital viral infections and chromosomal anomalies

Disease	ICD-9 codes	Excluded cases (n)
Congenital viral infections	7710; 7711; 7712	60
Down syndrome	7580	64
Patau syndrome	7581	3
Edward syndrome	7582	4
Other autosomic anomalies	7585	3
Turner syndrome	7586	4
Klinefelter syndrome	7587	6
Other chromosomal anomalies	7589	11
Autosomic translocation	7584	3

Table B. Outcome definition and source of information. Hospital Discharge (HD); Drug Prescription (DP); Birth Registry (BR)

Outcome	Definition	Source
Pre-eclampsia/Eclampsia	ICD9: 642.x; ATC: C02-03; C07-09 (without hospitalization or drug use prior the pregnancy onset + 4 gestational weeks)	HD or DP
Gestational diabetes	ICD9: 648.8, 648.03; ATC: A10 (without hospitalization or drug use prior the pregnancy onset + 4 gestational weeks)	HD or DP
In-hospital maternal death	Dead in hospital during labour or delivery (Yes/No)	HD
Admission to ICU	Transfer of mother to ICU (Yes/No)	HD
Type of delivery	Spontaneous delivery vs other modes of delivery (i.e. caesarean, forceps, vacuum, other mode)	BR
Stillbirth	Yes/No	BR
In-hospital neonatal death	In hospital neonatal death within 7 days from delivery (Yes/No)	HD
Perinatal death	Stillbirth or in hospital neonatal death	BR or HD
Small for gestational age (SGA)	live newborns with birth weight below the 10th percentile for their gestational age within the cohort of live births only. Birth weight (in grams) was retrieved from BR.	BR
Admission to neonatal ICU	Transfer of newborn to neonatal ICU (Yes/No)	HD
Occurrence of neonatal reanimation	Yes/No	BR
Composite outcome	Very low 5-minute Apgar score (≤ 3) or Acute respiratory distress syndrome (ICD9: 769) or Asphyxia (ICD9: 768.x) or Intraventricular hemorrhage (ICD9: 772.1) or Acute necrotizing enterocolitis (ICD9: 777.5)	BR or HD
Congenital Malformations (including subgroups)	ICD-9 codes reported in the EUROCAT guidelines	BR or HD

Table C. Definition of confounders and source of information.

Outcome	Definition	Source [^]	Confounding categories ^{^^}
Demographics, socio-economic status, and pregnancy history			
Hospital size	Quartile distribution of deliveries occurred in the hospitals of the Lombardy Region	BR	D
Age	Age at delivery	BR	D
Nationality	Nationality of the mother: Italian or non-Italian	BR	D
Study degree	The highest between mother and father among three categories (i.e. University; High school; Elementary school)	BR	SES
Mother occupational status	Mother occupational status, i.e. Employed; Unemployed; Housewife; Student	BR	SES
Civil Status	Mother's civil status: single; married; separate; not declared.	BR	SES
Father occupational status	Father occupational status: Employed; Unemployed; Other	BR	SES
Consanguinity between parents	Relationships by a common ancestor: 0 = no, 1= yes (relations from IV to VI degrees)	BR	SES
Low income allowance	Allowance codes = E01, E02, E04, E05	CI	SES
Previous conceptions	Yes/No	BR	PH
Previous delivery(ies)	Number of previous delivery(ies)	BR	PH
Live birth (from previous delivery)	Number of previous live birth(s)	BR	PH
Stillbirth (from previous delivery)	Number of previous stillbirth(s)	BR	PH
Spontaneous abortion	Number of previous spontaneous abortion(s)	BR	PH
Voluntary abortion	Number of previous voluntary abortion(s)	BR	PH
Caesarean delivery	Number of previous caesarean delivery(ies)	BR	PH

[^] Source of data: Hospital Discharge (HD); Drug Prescription (DP); Birth Registry (BR); Clinical Investigation (CI).

^{^^} Confounding categories: Demographics (D); Socio-economic status (SES); Pregnancy history (PH); Comorbidity and Medication (C&M); Health care utilization (HC).

Table C cont.

Outcome	Definition	Source [^]	Confounding categories ^{^^}
Comorbidities, Medications, Risk Factors, and Health Care Utilization present before the pregnancy onset. Medication history was retrieved up to 6 months before the pregnancy onset; Hospitalization and disease allowance data were retrieved up to 1 year before the pregnancy onset.			
Pulmonary diseases	ICD9:490-496 or ATC=R03 or Allowance codes=007, 024	HD or DP or CI	C&M
Cardiovascular disease	ICD9:390-459 or ATC=C01-03;C07-10;B01A or Allowance codes=021, 025, 031, A02, A31, D31	HD or DP or CI	C&M
Haematological disease	ICD9:280-289	HD	C&M
Diabetes	ICD9:250 or ATC=A10 or Allowance codes =012, 013	HD or DP or CI	C&M
Neurological and psychiatric diseases	ICD9:290-319; 330-359 or ATC=N04, N05, N06DA, N06DX or Allowance codes =005, 011, 014, 017, 029, 038, 044, 046	HD or DP or CI	C&M
Inflammatory bowel disease/Intestinal anti-inflammatory agents	ICD9:555-558 or ATC=A07E	HD or DP	C&M
Immunosuppressive drugs	ATC=L04A	DP	C&M
Antidepressants	ATC=N06A	DP	C&M
Antiepileptics	ATC=N03A	DP	C&M
Drugs for GERD	ATC=A02B	DP	C&M
Contraceptive drugs	ATC=G03A	DP	C&M
Drugs for human fertilization	ATC=G03G; G03D; H01AA; H01CC; L02AE	DP	C&M
NSAIDs	ATC=M01A; N02B	DP	C&M
Antibacterial for systemic use	J01	DP	C&M
Thyroid diseases	H03AA or Allowance codes=027, 035	DP or CI	C&M
Folic acid (before the pregnancy onset)	ATC=B03BB	DP	C&M
Folic acid (during first trimester of pregnancy)	ATC=B03BB	DP	C&M
Iron supplementation	ATC=B03AA, B03AB, B03AC, B03AE	DP	C&M
Autoimmune disease	Allowance codes=003, 006, 009, 028, 030, 034, 036, 037, 047, 054, 056	CI	C&M
Immunodeficiency conditions	Allowance codes=020, 048, 050, 052	CI	C&M
Rare diseases	Allowance codes=RAx, RBx, RCx, RDx, RFx, RGx, RIx, RJx, RLx, RMx, RNx	CI	C&M
Use of medically assisted reproduction (MPA) techniques	Yes/No	BR	C&M
Type of MPA	Drugs; Intrauterine Insemination; Gamete transfer; In vitro fertilization; Sperm injection; Other	BR	C&M
Hospital admissions	Number of hospitalizations	HD	HC
Overall drug use	Number of different substances used	DP	HC

[^] Source of data: Hospital Discharge (HD); Drug Prescription (DP); Birth Registry (BR); Clinical Investigation (CI).

^{^^} Confounding categories: Demographics (D); Socio-economic status (SES); Pregnancy history (PH); Comorbidity and Medication (C&M); Health care utilization (HC).

Table D. Research in context (aOR: adjusted Odds Ratio; aHR: adjusted Hazard Ratio; aRR: adjusted Relative Risk; 95% Confidence Intervals are reported in brackets)

	Country	Vaccine type	Total cohort	N. of vaccinated women	Gestational Diabetes	Pre-eclampsia/Eclampsia	Small for gestational age (SGA)	Congenital malformations (CMs)	Neonatal death	Stillbirth/Foetal death
Trotta 2013	I	MF59 adjuvanted	ca. 27 000	6131	aOR 1.26 (1.04-1.53)	aOR 1.19 (1.02-1.39)	aOR 0.95 (0.86-1.04)	aOR 1.14 (0.99-1.31)	aOR 1.04 (0.39-2.78)	aOR 1.13 (0.65-1.95)
Heikkinen¹ 2012	NL	MF59 adjuvanted	4508	2 295	aOR 0.48 (0.29-0.80)	aOR 1.12 (0.81-1.55)		aOR 1.33 (0.88-2.00)	aOR 1.81 (0.16-20.23)	aOR 1.44 (0.23-8.90)
Pasternak² 2012	DK	AS03 adjuvanted	ca. 14 000	ca. 7000	-	-	aOR 0.97 (0.87-1.09)	aOR 1.21^ (0.60-2.45)	aOR 1.14 (0.94-1.38)	
Pasternak³ 2012	DK	AS03 adjuvanted	ca. 50 000	ca. 7000	-	-				aOR 0.44 (0.20-0.94)
Rubinstein⁴ 2013	RA	MF59 adjuvanted	ca. 30 000	7293	-	-			aOR 0.68^^ (0.42-1.06)	
Fell⁵ 2012	CDN	not reported	ca. 55 000	23 340			aRR 0.81 (0.72-0.92)			aRR 0.66 (0.47-0.91)
Ludvigsson⁶ 2013	S	AS03 adjuvanted	ca. 21 000	13 297			aOR 0.97 (0.90-1.05)			
Haberg⁷ 2013	N	AS03 adjuvanted + non adjuvanted	ca. 117 000	ca. 50 000						aHR 0.88 (0.66-1.17)
Richards⁸ 2013	USA	not reported	ca. 3300	1125			aOR 1.26 (0.94-1.69)			
Oppermann⁹ 2012	D	AS03 adjuvanted + non adjuvanted	ca. 1600	323				aOR 0.92 (0.58-1.46)		
Conlin¹⁰ 2013	USA	not reported^^^	ca. 18 000	10 376		aHR 1.10 (0.97-1.26)		aOR 1.08 (0.87-1.35)		
Kallen¹¹ 2012	S	AS03 adjuvanted	ca 150 000	18 612	aOR 0.94 (0.81-1.09)	aOR 0.99 (0.92-1.07)	aOR 1.04 (0.92-1.17)	aOR 1.01 (0.83-1.23)		aOR 0.77 (0.57-1.03)

^only on I trimester; 330 exposed

^^perinatal mortality

^^^H1N1 vaccine vs seasonal vaccine

References Table D

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