Epidémiologie des cardiopathies congénitales

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Definition

Étude de la dynamique des phénomènes de santé dans les populations, dans le but de mettre en évidence les facteurs qui les déterminent et leur rôle, et de mettre en œuvre les mesures de correction appropriées

John Snow

Découverte de la transmission du choléra par l'eau contaminée à Londres en 1854

- Décrire, comprendre, agir

Épidémiologie descriptive vs. analytique

Descriptive

- Étudie les variations dans la fréquence des maladies
- Où?
- Quand?
- Qui?

Analytique

- Étudie le lien **causal** entre une maladie et une exposition
- Vise à quantifier cette relation

Critère de Bradford Hill

- **La force de l'association**

Est-ce que mon effet est important ≠ significatif

- **La constance de l'association**

Est-ce que mon effet est reproduit (attention à l'erreur d'échantillonage)

- **La spécificité de l'association**

Est-ce que mon exposition est associée à un effet spécifique

- **La temporalité**

Est-ce que mon exposition précède la survenue de l'évènement ? Est-ce que le délais de survenu de l'évènement est suffisant et cohérent avec l'exposition ?

- **Le gradient/ la relation dose effet**

Est-ce que lorsque l'exposition est majoré la survenu de l'évènement augmente ?

- **La plausibilité**

Est-ce que les résultats sont cohérents avec l'état de connaissance actuelle et surtout dans d'autre discipline

- **La cohérence**

Est-ce que mes résultats sont sous tendu par des preuves physiopathologique ?

- **Expérimentation**

Est-ce que je peux établir un protocole interventionnel qui va confirmer mon hypothèse ?

- **Analogie**

Y a-t-il des explications alternative aux résultats observées ?

Validité interne d'une étude

La **validité <u>interne</u>** (« qualité spécifique à l'étude ») est un indicateur de qualité qui permet au chercheur d'évaluer la fiabilité ou la certitude de ses conclusions internes.
= fiabilité de la stratégie d'analyse et des statistiques

Est-ce que la mesure d'association déterminé est correcte, y a-t-il une erreur systématique (ou biais) qui peut fausser les résultats de l'étude.

→ Accepter l'hypothèse nulle
→ Rejeter l'hypothèse nulle et accepter l'hypothèse alternative

Les biais

Un biais de sélection est une erreur non aléatoire lié aux procédures de recrutement/ de suivi des sujets de l'étude. Il y a biais de sélection lorsque la relation entre exposition et outcomes est différente chez les sujets éligibles pour l'étude et chez les sujets effectivement inclus.
Exemple : biais d'attrition lié au perdus de vus

Un biais d'information résulte d'une erreur de classement/ de mesure portant soit sur l'exposition soit sur l'outcome. On peut distinguer un biais différentiel et non différentiel
Exemple : Etude avec mesure échographique

Un biais de confusion survient lorsqu'il existe une co-variable modifiant la distribution de l'exposition et la distribution de l'outcome étudié.
Exemple : La prématurité dans l'étude du neurodéveloppement des différents groupe de CC

Validité externe

Extrapolation des résultats : Est-ce que mon échantillon est représentatif de ma population cible

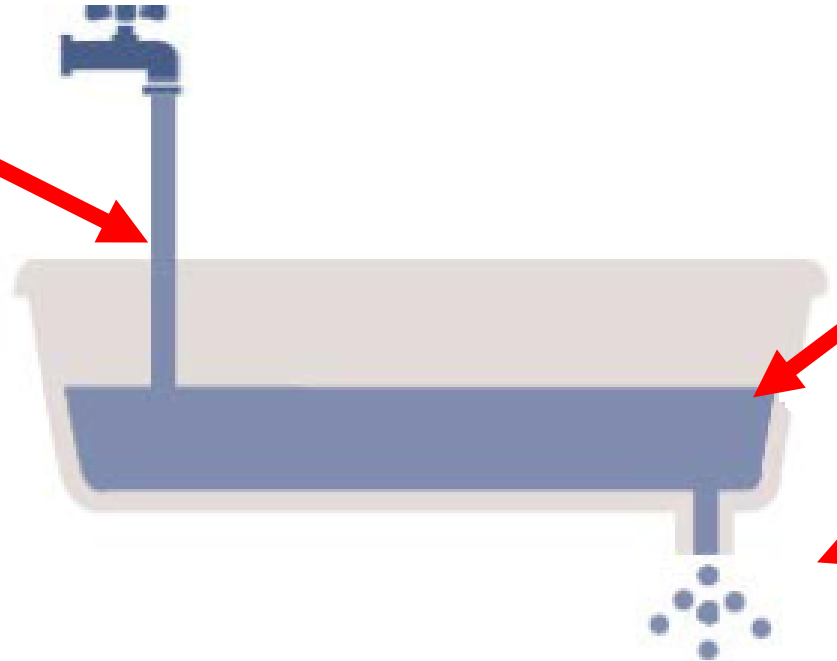
L’objectif ultime de toute étude épidémiologique

Prévalence et incidence

La **prévalence :** le nombre de cas de CC, à un instant donné ou sur une période donnée. On calcule le **taux de prévalence** en rapportant ce nombre à la population considérée. Le taux de prévalence est une proportion

L'incidence : ***nombre de nouveaux cas*** de CC dépisté au cours d'une ***période de temps*** donnée, dans une population à risque (taux) = vitesse

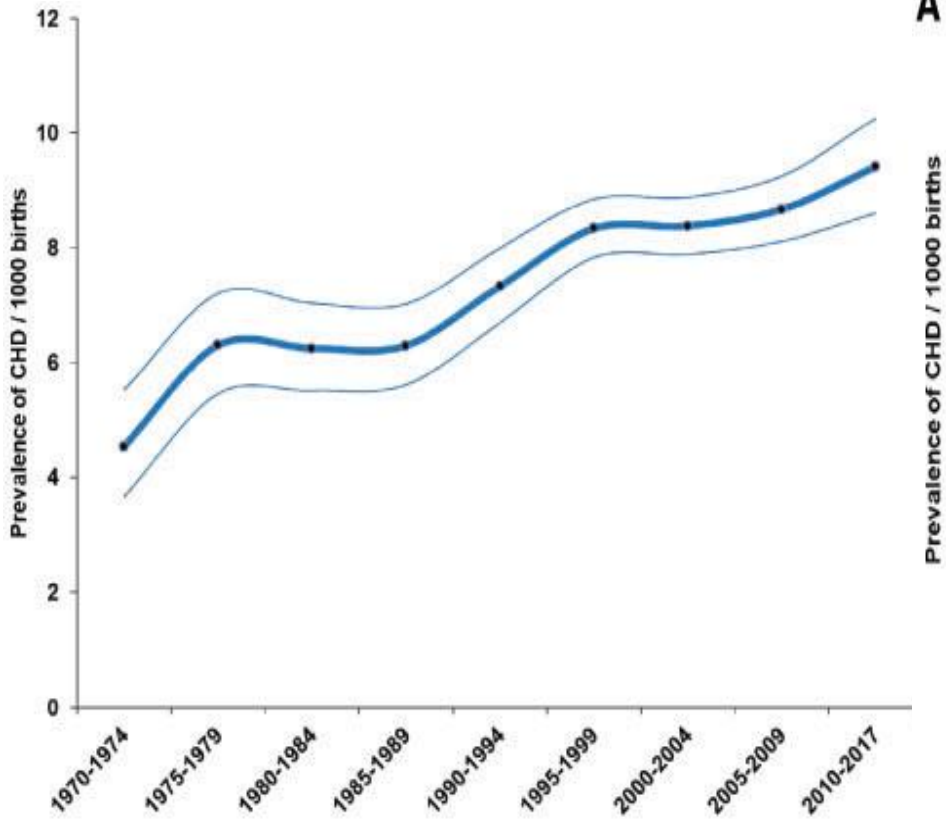
Incidence
= nouveaux cas



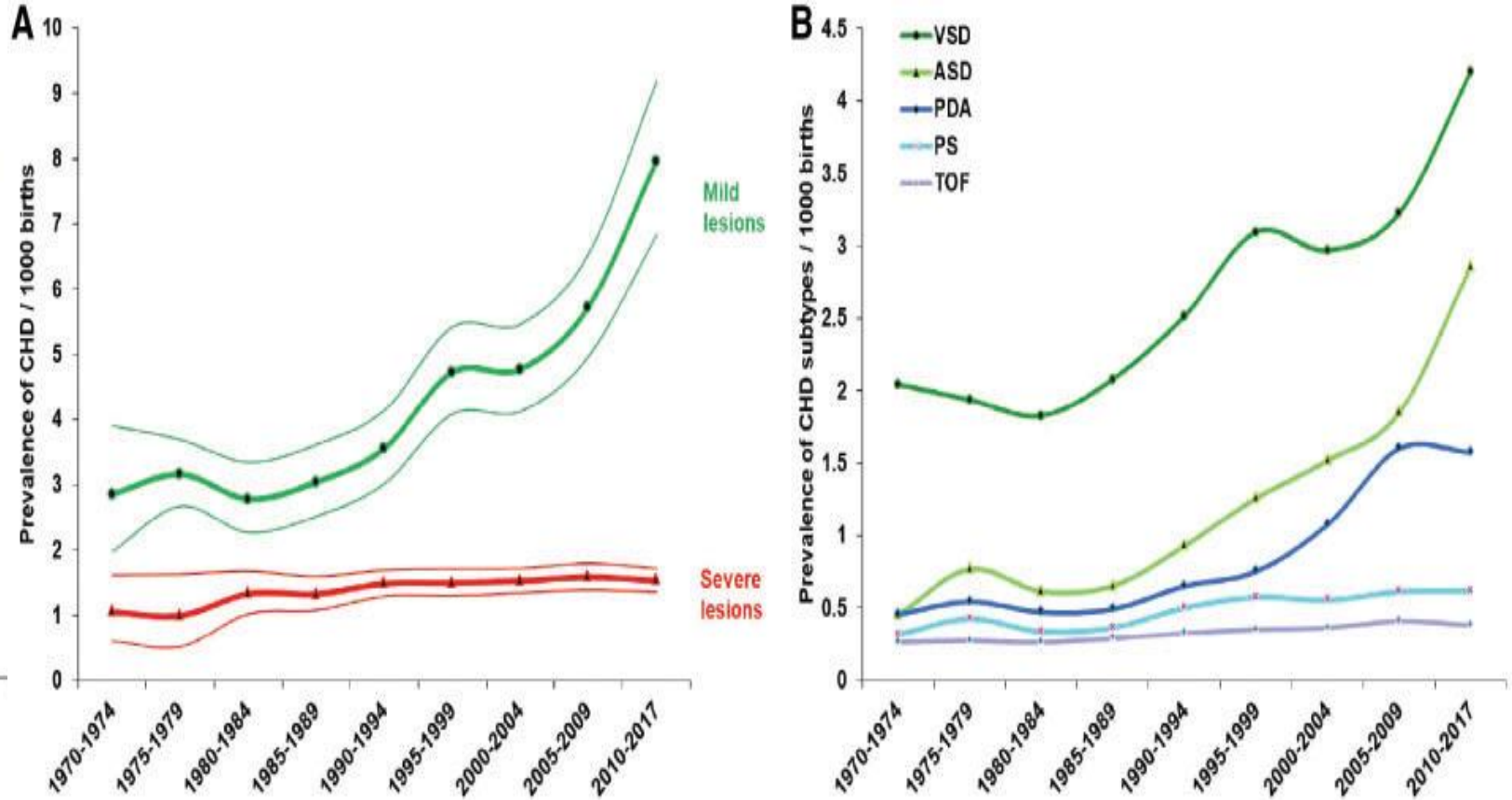
Prévalence
= cas existants

Dècès
Guérison
Sortie de la zone d'étude

Prévalence mondiale des CC



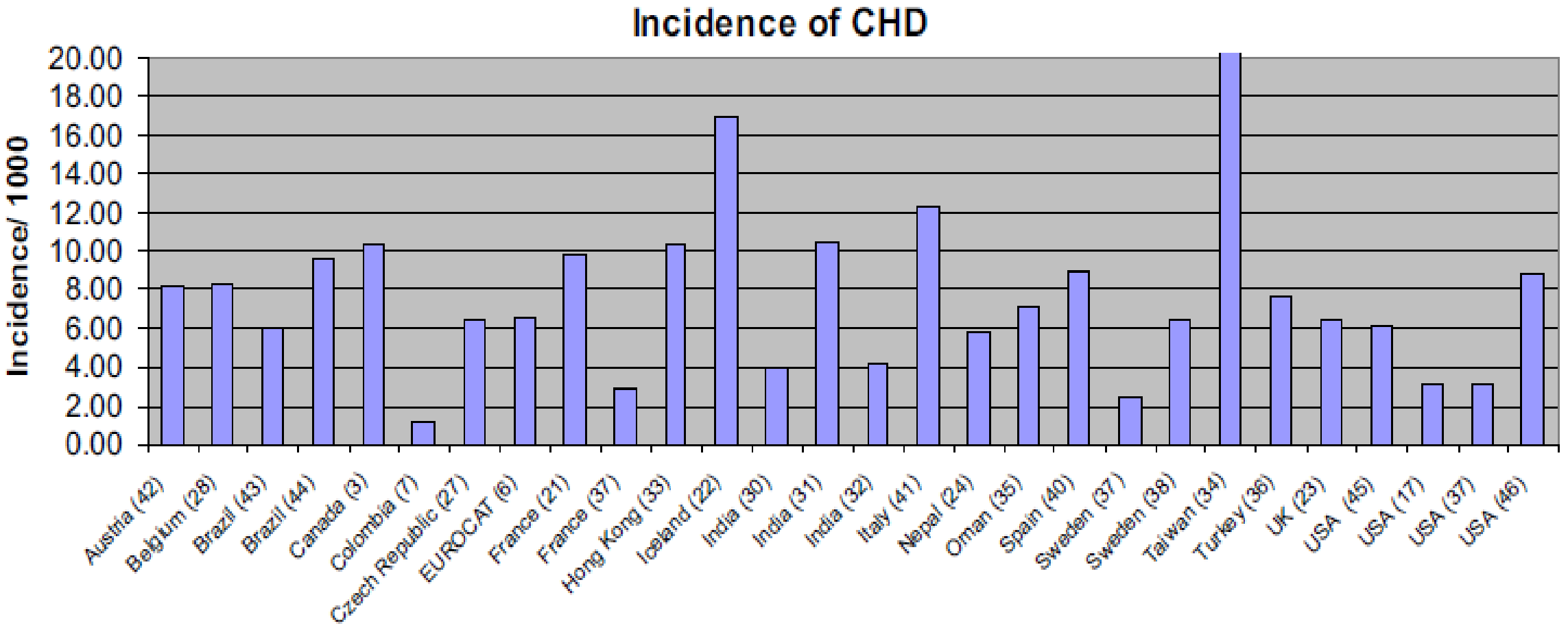
Changes in the birth prevalence of CHD 1970–2017.



The birth prevalence of CHD subtypes and their changes over time.
(A) The prevalence of mild and severe CHD lesions during 1970–2017.
(B) The birth prevalence of the five most frequent CHD subtypes during 1970–2017.

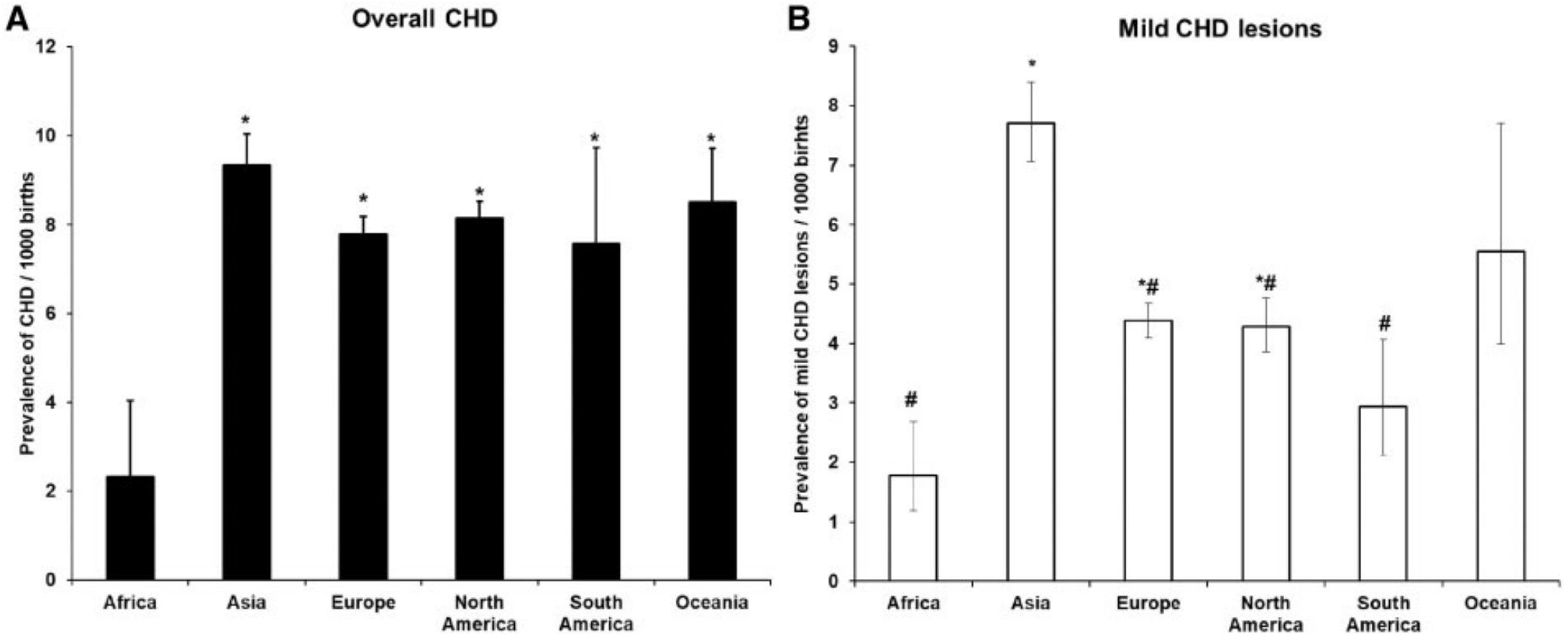
Liu Y, Chen S, Zühlke L, Black GC, Choy MK, Li N, Keavney BD. Global birth prevalence of congenital heart defects 1970-2017: updated systematic review and meta-analysis of 260 studies. Int J Epidemiol. 2019

Différence dans le monde ?



Bernier PL, Stefanescu A, Samoukovic G, Tchervenkov CI. The challenge of congenital heart disease worldwide: epidemiologic and demographic facts. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2010

Différence dans le monde ?



CHD prevalence in different geographic regions 1970–2017. (A) The prevalence of overall CHD in six geographic regions. (B) The prevalence of mild lesions in six geographic regions. The number of studies for each region was: **Africa 4** (69 304 births), Asia **74** (12 975 858 births), Europe **110** (56 272 142 births), North America 58 (59 498 436 births), **South America 9** (667 353 births) and Oceania 5 (1 275 758 births). Data for (A) and (B) are presented as Mean6SE. *, P<0.05, compared with Africa, #, P<0.05, compared with Asia.

Liu Y, Chen S, Zühlke L, Black GC, Choy MK, Li N, Keavney BD. Global birth prevalence of congenital heart defects 1970-2017: updated systematic review and meta-analysis of 260 studies. Int J Epidemiol. 2019

Prévalence mondiale des CC

CHD subtype	Prevalence of CHD subtype per thousand (95% confidence interval)	Percentage of CHD subtype, % (95% confidence interval)
Ventricular septal defect	3.071 (2.845–3.305)	35.568 (33.876–37.278)
Atrial septal defect	1.441 (1.215–1.687)	15.378 (13.492–17.363)
Patent ductus arteriosus	1.004 (0.803–1.228)	10.172 (8.519–11.954)
Pulmonary stenosis	0.546 (0.485–0.611)	6.233 (5.703–6.784)
Tetralogy of Fallot	0.356 (0.326–0.387)	4.422 (4.064–4.794)
Transposition of the great arteries	0.295 (0.269–0.322)	3.819 (3.446–4.210)
Atrioventricular septal defect	0.290 (0.265–0.316)	3.595 (3.302–3.900)
Coarctation of the aorta	0.287 (0.261–0.314)	3.570 (3.273–3.879)
Pulmonary arteriovenous aneurysm	0.272 (0.153–0.425)	2.975 (1.858–4.343)
Congenital heart block	0.268 (0.028–0.752)	3.223 (0.268–9.263)
Aortic valve insufficiency	0.251 (0.137–0.400)	2.318 (1.271–3.667)
Aortic stenosis	0.186 (0.161–0.214)	2.334 (2.016–2.674)
Hypoplastic left heart syndrome	0.178 (0.162–0.195)	2.564 (2.251–2.897)
Mitral insufficiency	0.152 (0.097–0.220)	1.348 (0.899–1.886)
Tricuspid atresia or stenosis	0.117 (0.091–0.146)	1.071 (0.905–1.250)
Double outlet right ventricle	0.106 (0.090–0.124)	1.303 (1.127–1.491)
Pulmonary atresia	0.098 (0.085–0.112)	1.308 (1.113–1.518)
Single ventricle	0.093 (0.080–0.108)	1.145 (0.975–1.330)
Dextrocardia	0.089 (0.073–0.106)	1.027 (0.825–1.250)
Total anomalous pulmonary venous return	0.083 (0.071–0.095)	1.501 (1.163–1.882)
Mitral stenosis	0.083 (0.047–0.130)	0.955 (0.564–1.446)
Truncus arteriosus	0.078 (0.067–0.089)	0.982 (0.849–1.124)
Ebstein anomaly	0.044 (0.040–0.049)	0.534 (0.467–0.606)
Coronary artery aneurysm	0.044 (0.025–0.068)	0.417 (0.287–0.571)
Interrupted aortic arch	0.041 (0.032–0.051)	0.609 (0.412–0.844)
Partial anomalous pulmonary venous return	0.039 (0.027–0.053)	0.314 (0.238–0.400)
Cor triatriatum	0.022 (0.014–0.031)	0.245 (0.125–0.405)

Prévalence en Europe et en France des CC

Table 1. Population* (No. EUROCAT Registries, Births, Percentage National Coverage) and Total Prevalence† (95% CI) of All, Nonchromosomal and Nonchromosomal SI and SII CHDs per 1000 Births by Country, 2000 to 2005

Countries*	Registries,* n	Total Births, 2000 to 2005, in Registry Regions, n	Annual National Births Covered, 2005, %	All CHD		Nonchromosomal CHD		Nonchromosomal CHD, SI and SII	
				No.	Prevalence per 1000 Births (95% CI)	No.	Prevalence per 1000 Births (95% CI)	No.	Prevalence per 1,000 Births (95% CI)
Austria	1	62 667	13	960	15.32 (14.37–16.32)	871	13.90 (12.99–14.85)	163	2.60 (2.22–3.03)
Belgium	2	182 467	27	1212	6.64 (6.27–7.03)	1058	5.80 (5.45–6.16)	343	1.88 (1.69–2.09)
Croatia‡	1	33 933	14	182	5.36 (4.61–6.20)	161	4.74 (4.04–5.54)	41	1.21 (0.87–1.64)
Denmark	1	32 003	8	291	9.09 (8.08–10.20)	265	8.28 (7.31–9.34)	65	2.03 (1.57–2.59)
France‡	3	343 715	8	2853	8.30 (8.00–8.61)	2447	7.12 (6.84–7.41)	879	2.56 (2.39–2.73)
Germany‡	2	124 952	3	1457	11.66 (11.07–12.28)	1315	10.52 (9.96–11.11)	269	2.15 (1.90–2.43)
Ireland	3	215 021	63	1423	6.62 (6.28–6.97)	1083	5.04 (4.74–5.35)	476	2.21 (2.02–2.42)
Italy‡	3	431 727	15	2944	6.82 (6.58–7.07)	2744	6.36 (6.12–6.60)	754	1.75 (1.62–1.88)
Malta	1	23 668	100	348	14.70 (13.20–16.33)	301	12.72 (11.32–14.24)	51	2.15 (1.60–2.83)
Netherlands	1	119 104	10	732	6.15 (5.71–6.61)	639	5.37 (4.96–5.80)	272	2.28 (2.02–2.57)
Norway	1	346 838	100	3538	10.20 (9.87–10.54)	3236	9.33 (9.01–9.66)	611	1.76 (1.63–1.91)
Poland	1	206 170	9	2304	11.18 (10.72–11.64)	2116	10.26 (9.83–10.71)	297	1.44 (1.28–1.61)
Spain‡	2	194 234	7	1080	5.56 (5.23–5.90)	904	4.65 (4.36–4.97)	399	2.05 (1.86–2.27)
Switzerland	1	42 874	10	576	13.43 (12.36–14.58)	512	11.94 (10.93–13.02)	105	2.45 (2.00–2.97)
Ukraine‡	1	25 835	6	201	7.78 (6.74–8.93)	180	6.97 (5.99–8.06)	46	1.78 (1.30–2.38)
UK‡	5	951 001	26	6497	6.83 (6.67–7.00)	5516	5.80 (5.65–5.96)	1974	2.08 (1.99–2.17)
Total	29	3 336 209	13	26 598	7.97 (7.88–8.07)	23 348	7.00 (6.91–7.09)	6745	2.02 (1.97–2.07)

Prévalence en France des CC 2013-2019 EuroCAT

Country/Registry	Anomaly	Years	Case with genetic conditions
Auvergne (France), Britta	All Anomalies	2013 to 2019	Including genetic anomalies

How to read the data
Export the raw data

Anomaly group	Total cases	Live births	Stillbirths	TOPFA
All Anomalies	339.76 (335.25 - 344.32)	251.78 (247.90 - 255.71)	5.46 (4.90 - 6.07)	82.52 (80.30 - 84.78)
Nervous system	40.37 (38.83 - 41.96)	15.38 (14.44 - 16.38)	0.96 (0.73 - 1.23)	24.03 (22.84 - 25.27)
– Neural Tube Defects	13.84 (12.95 - 14.79)	1.44 (1.16 - 1.77)	0.24 (0.13 - 0.39)	12.17 (11.32 - 13.05)
– – *Anencephalus and similar*	5.81 (5.23 - 6.43)	0.13 (0.05 - 0.25)	0.11 (0.04 - 0.23)	5.57 (5.01 - 6.18)
– – *Encephalocele*	1.96 (1.63 - 2.34)	0.39 (0.25 - 0.58)	0.06 (0.02 - 0.16)	1.51 (1.22 - 1.84)
– – *Spina Bifida*	6.07 (5.48 - 6.71)	0.93 (0.71 - 1.19)	0.06 (0.02 - 0.16)	5.09 (4.55 - 5.67)
– Hydrocephalus	6.62 (6.01 - 7.29)	2.75 (2.36 - 3.19)	0.16 (0.07 - 0.29)	3.72 (3.26 - 4.22)
– Severe microcephaly	4.54 (4.03 - 5.09)	3.23 (2.81 - 3.71)	0.16 (0.07 - 0.29)	1.15 (0.90 - 1.44)
– Arhinencephaly/holoprosencephaly	3.01 (2.60 - 3.47)	0.49 (0.33 - 0.69)	0.14 (0.06 - 0.27)	2.39 (2.02 - 2.80)
Eye	6.20 (5.60 - 6.84)	4.93 (4.40 - 5.50)	0.08 (0.02 - 0.18)	1.19 (0.94 - 1.49)
– Anophthalmos/micropthalmos	1.59 (1.29 - 1.93)	0.78 (0.58 - 1.03)	0.06 (0.02 - 0.16)	0.74 (0.54 - 0.98)
– – *Anophthalmos*	0.30 (0.18 - 0.47)	0.09 (0.03 - 0.21)	0.00 (0.01 - 0.06)	0.20 (0.11 - 0.35)
– Congenital cataract	1.85 (1.53 - 2.22)	1.76 (1.45 - 2.12)	0.00 (0.01 - 0.06)	0.09 (0.03 - 0.21)
– Congenital glaucoma	0.69 (0.50 - 0.93)	0.69 (0.50 - 0.93)	0.00 (0.01 - 0.06)	0.00 (0.01 - 0.06)
Ear, face and neck	2.61 (2.22 - 3.03)	2.15 (1.81 - 2.54)	0.08 (0.02 - 0.18)	0.38 (0.24 - 0.56)
– Anotia	0.41 (0.27 - 0.60)	0.31 (0.19 - 0.48)	0.00 (0.01 - 0.06)	0.09 (0.03 - 0.21)
Congenital heart defects	95.08 (92.70 - 97.50)	77.97 (75.81 - 80.17)	1.74 (1.43 - 2.10)	15.37 (14.42 - 16.36)
– Severe CHD	26.48 (25.23 - 27.77)	15.87 (14.91 - 16.88)	0.89 (0.68 - 1.16)	9.72 (8.97 - 10.51)
– Common arterial truncus	0.93 (0.71 - 1.19)	0.35 (0.22 - 0.52)	0.03 (0.00 - 0.11)	0.55 (0.38 - 0.76)
– Double outlet right ventricle	1.84 (1.52 - 2.20)	0.96 (0.73 - 1.23)	0.05 (0.01 - 0.14)	0.83 (0.62 - 1.09)
– Transposition of great vessels	3.70 (3.25 - 4.21)	2.92 (2.52 - 3.37)	0.11 (0.04 - 0.23)	0.67 (0.49 - 0.91)

https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-data/prevalence_en

Evolution DAN IMG et Mortalité

TABLE 1. Prenatal Diagnosis, Pregnancy Termination, and Perinatal and Early Neonatal Mortality for CHD*, Paris Registry of Congenital Malformations, 1983–2000

	1983–1988			1989–1994			1995–2000			p‡
	N†	%	95% CI	*N*	%	95% CI	*N*	%	95% CI	
Prenatal diagnosis										
All	409	23.0	19.0–27.4	755	31.7	28.3–35.1	805	47.3	43.8–50.8	<.001
All except VSD	297	31.0	25.8–36.6	480	47.5	43.0–52.1	567	61.4	57.2–65.4	<.001
Pregnancy termination										
All	415	9.9	7.2–13.2	755	14.7	12.3–17.4	812	15.4	13.0–18.1	.037
All except VSD	303	13.5	9.9–17.9	480	23.1	19.4–27.2	574	21.8	18.5–25.4	.010
Stillbirth										
All	374	7.0	4.6–10.0	644	4.0	2.7–5.9	687	3.2	2.0–4.8	.028
All except VSD	262	9.2	6.0–13.3	369	6.8	4.4–9.8	449	4.5	2.7–6.8	.021
First-day mortality										
All	348	2.9	1.4–5.2	618	1.1	0.5–2.3	665	1.1	0.4–2.2	.075
All except VSD	238	4.2	2.0–7.6	344	2.0	0.8–4.1	429	1.6	0.7–3.3	.132
First-week mortality										
All	348	10.1	7.1–13.7	618	4.9	3.3–6.9	665	3.3	2.1–5.0	<.001
All except VSD	238	14.7	10.5–19.9	344	8.7	6.0–12.2	429	4.9	3.1–7.4	<.001
Perinatal mortality										
All	374	16.3	12.7–20.5	644	8.7	6.6–11.1	687	6.4	4.7–8.5	<.001
All except VSD	262	22.5	17.6–28.1	369	14.9	11.4–19.0	449	9.1	6.6–12.2	<.001

VSD indicates ventricular septal defects.
* Cases with chromosomal anomalies were excluded.
† For prenatal diagnosis and pregnancy terminations, the denominators (*N*) were the total number of cases (stillbirths + live births + terminations of pregnancy) with CHD. For stillbirth and perinatal mortality, the denominator was stillbirths + live births, and for neonatal mortality, the denominator was live births.
‡ Test of significance for cusum linear annual trend.

Babak Khoshnood et al *Pediatrics* 2005

Evolution DAN IMG et Mortalité

TABLE 3. Prenatal Diagnosis, Pregnancy Termination, and Perinatal and Early Neonatal Mortality for Selected (Isolated) Congenital Heart Anomalies, Paris Registry of Congenital Malformations, 1983–2000

	1983–1988			1989–1994			1995–2000			*P*†
	N	%	95% CI*	*N*	%	95% CI*	*N*	%	95% CI*	
TGA										
Prenatal diagnosis	16	12.5	1.6–38.3	27	48.1	28.7–68.1	40	72.5	56.1–85.4	0.001
Pregnancy termination	17	0	0–19.5	27	7.4	0.9–24.3	40	0	0–8.8	0.62
First-week mortality	16	18.8	4.0–45.6	24	8.3	1.0–27.0	39	2.6	0.1–13.5	0.04
Perinatal mortality	17	23.5	6.8–49.9	25	12.0	2.5–31.2	40	5.0	0.6–16.9	0.02
HLHS										
Prenatal diagnosis	22	31.8	13.9–54.9	29	82.8	64.2–94.2	27	88.9	70.8–97.6	<0.001
Pregnancy termination	22	13.6	2.9–34.9	29	72.4	52.8–87.3	27	63.0	42.4–80.6	<0.001
First-week mortality	18	83.3	58.6–96.4	8	75.0	34.9–96.8	10	50.0	18.7–81.3	0.12
Perinatal mortality	19	84.2	60.4–96.6	8	75.0	34.9–96.8	10	50.0	18.7–81.3	0.10
Coarctation of aorta										
Prenatal diagnosis	6	0	0–45.9	21	33.3	14.6–57.0	33	42.4	25.5–60.8	0.03
Pregnancy termination	6	0	0–45.9	21	0	0–16.1	34	0	0–10.3	-
First-week mortality	6	0	0–45.9	21	0	0–16.1	34	0	0–10.3	-
Perinatal mortality	6	0	0–45.9	21	0	0–16.1	34	0	0–10.3	-
Tetralogy of Fallot										
Prenatal diagnosis	10	20.0	2.5–55.6	16	37.5	15.2–64.6	33	69.7	51.3–84.4	0.005
Pregnancy termination	10	10.0	0.3–44.5	16	12.5	1.6–38.3	34	0	0–10.3	0.07
First-week mortality	9	0	0–33.6	13	0	0–24.7	33	0	0–10.6	-
Perinatal mortality	9	0	0–33.6	14	7.1	0.2–33.9	34	2.9	0.1–15.3	0.63

Babak Khoshnood et al *Pediatrics* 2005

Prévalence EPICARD et Prénatal

Table 2 Total and live birth prevalence of congenital heart defects: the EPICARD

ACC-CHD categories	N	LB %	TOP %	SB %	Prevalence (per 10 000) Total*	95% CI	Live birth†	95% CI
1. Heterotaxy, including isomerism and mirror-imagery	37	21.6	75.7	2.7	1.2	0.8 to 1.6	0.2	0.1 to 0.5
2. Anomalies of the venous return	31	83.9	16.1	0.0	1.0	0.7 to 1.4	0.8	0.5 to 1.2
3. Anomalies of the atria and interatrial communications	182	95.6	4.4	0.0	5.7	4.9 to 6.6	5.5	4.7 to 6.4
4. Anomalies of the atrioventricular junctions and valves	213	51.2	42.7	6.1	6.7	5.8 to 7.7	3.5	2.8 to 4.2
5. Complex anomalies of atrioventricular connections	13	53.8	46.2	0.0	0.4	0.2 to 0.7	0.2	0.1 to 0.5
6. Functionally univentricular hearts	158	30.4	62.7	6.9	5.0	4.2 to 5.8	1.5	1.1 to 2.0
7. Ventricular septal defects (VSD)	1491	93.6	5.7	0.7	47.0	44.6 to 49.4	44.4	42.1 to 46.8
8. Anomalies of the ventricular outflow tracts	563	79.4	18.5	2.1	17.7	16.3 to 19.3	14.2	12.9 to 15.6
9. Anomalies of the extrapericardial arterial trunks	170	73.5	23.5	3.0	5.3	4.6 to 6.2	4.0	3.3 to 4.7
10. Congenital anomalies of the coronary arteries	9	100.0	0.0	0.0	0.3	0.1 to 0.5	0.3	0.1 to 0.5
All	2867	81.9	16.3	1.8	90.3	87.0 to 93.6	74.8	71.8 to 77.8
All, excluding cases associated with chromosomal anomalies	2471	89.2	9.8	1.0	77.8	74.8 to 80.9	68.4	67.3 to 73.2
All, excluding cases associated with chromosomal or other anomalies	2036	92.8	6.4	0.8	64.1	61.4 to 67.0	60.2	57.5 to 62.9
All, excluding cases associated with chromosomal or other anomalies and IVSD‡	930	84.2	14.0	1.8	29.3	27.4 to 31.2	24.9	23.2 to 26.7

Association établis pour un risque majoré de survenue de grossesse avec CC

Exposition maternelles et risque (établi ou éventuel) de CC

TABLE 2. Exposures Associated With Definite or Possible Risk of Offspring With CCVD*

	Defect	RR	Reference(s)
Maternal illness			
PKU	Any defects	>6	17–20
Pregestational diabetes	Any defects	3.1–18	6, 23, 33, 34
	Conotruncal defects	5.55	36
	Laterality and looping	8.3	6
	d-TGA	3.8–27.2	6, 33
	AVSD	10.6	6
	Septal defects	2.9–20.2	6, 33, 35
	HLHS	3.9	6
	Outflow tract defects	3.7–17.9	33, 35
	PDA (BTW >2500 g only)	56.9	33
Febrile illness	Any defects	1.8–2.9	6, 16, 62, 63
	Conotruncal defects	1.55	36
	Any right-sided obstructive defects	2.2–2.9	6, 15
	Tricuspid atresia	5.1–5.2	6, 15
	All left-sided obstructive defects	2.7	15
	Aortic coarctation	2.7	15
	VSD	1.8	15

Jenkins KJ et al Noninherited risk factors and congenital cardiovascular defects: current knowledge Circulation. 2007

Exposition maternelles et risque (établi ou éventuel) de CC

TABLE 2. Exposures Associated With Definite or Possible Risk of Offspring With CCVD*

	Defect	RR	Reference(s)
Influenza	Any defects	2.1	10, 63
	Conotruncal defects	1.74	36
	d-TGA	2.1	10
	All right-sided obstructive defects	2.5	10
	All left-sided obstructive defects	2.9	10
	Aortic coarctation	3.8	10
	VSD	2.0	10
	d-TGA with intact ventricular septum	2.2	6
	Tricuspid atresia	4.3	6
Maternal rubella	Any defects	†	55–57
	VSD	†	58, 59, 196
	PDA	†	58, 59, 196
	Pulmonary valve abnormalities	†	58, 59, 196
	Peripheral pulmonic stenosis	†	58, 59, 196
Epilepsy	Any defects	†	82

Jenkins KJ et al Noninherited risk factors and congenital cardiovascular defects: current knowledge Circulation. 2007

Exposition maternelles et risque (établi ou éventuel) de CC

TABLE 2. Exposures Associated With Definite or Possible Risk of Offspring With CCVD*

	Defect	RR	Reference(s)
Maternal nontherapeutic drug exposure			
Maternal vitamin A	Outflow tract defects	0.0–9.2	169, 170
	Cranial neural crest defects (cardiac and noncardiac)	0.7–4.8	168, 171, 172
	Pulmonic stenosis and other noncardiac defects	0.5	173
Maternal therapeutic drug exposure			
Anticonvulsants	Any defects	4.2	105–107
Indomethacin tocolysis	PDA	†	123, 124
NSAIDs			
Ibuprofen	Any defects	1.86	122
	d-TGA	2.5	4
	AVSD (Down syndrome)	2.4	4
	VSD	1.9	4
	Bicuspid aortic valve	4.1	4
Sulfasalazine‡	Any defects	3.4	13
Thalidomide	Any defects	†	84
Trimethoprim-sulfonamide‡	Any defects	2.1–4.8	13, 14

Jenkins KJ et al Noninherited risk factors and congenital cardiovascular defects: current knowledge Circulation. 2007

Exposition maternelles et risque (établi ou éventuel) de CC

TABLE 2. Exposures Associated With Definite or Possible Risk of Offspring With CCVD*

	Defect	RR	Reference(s)
Vitamin A congeners/retinoids	Any defects	†	85, 86
Maternal nontherapeutic drug exposure			
Marijuana	VSD	1.9	160
	Ebstein's	2.4	6
Environmental (maternal)			
Organic solvents	Conotruncal defects	2.3–3.9	150, 175
	HLHS	3.4	6
	Aortic coarctation	3.2	6, 176
	Pulmonic stenosis	5.0	6
	d-TGA with intact ventricular septum	3.4	6
	Tetralogy of Fallot	2.7	6
	TAPVR	2.0	6, 214
	AVSD, nonchromosomal	5.6	6
	Ebstein's anomaly	3.6	6, 215
	VSD		119

Jenkins KJ et al Noninherited risk factors and congenital cardiovascular defects: current knowledge Circulation. 2007

Exposition maternelles et diminution du risque de CC

TABLE 1. Maternal Multivitamin/Folic Acid Supplements and Decreased Risk of Offspring With Congenital Cardiovascular Defects

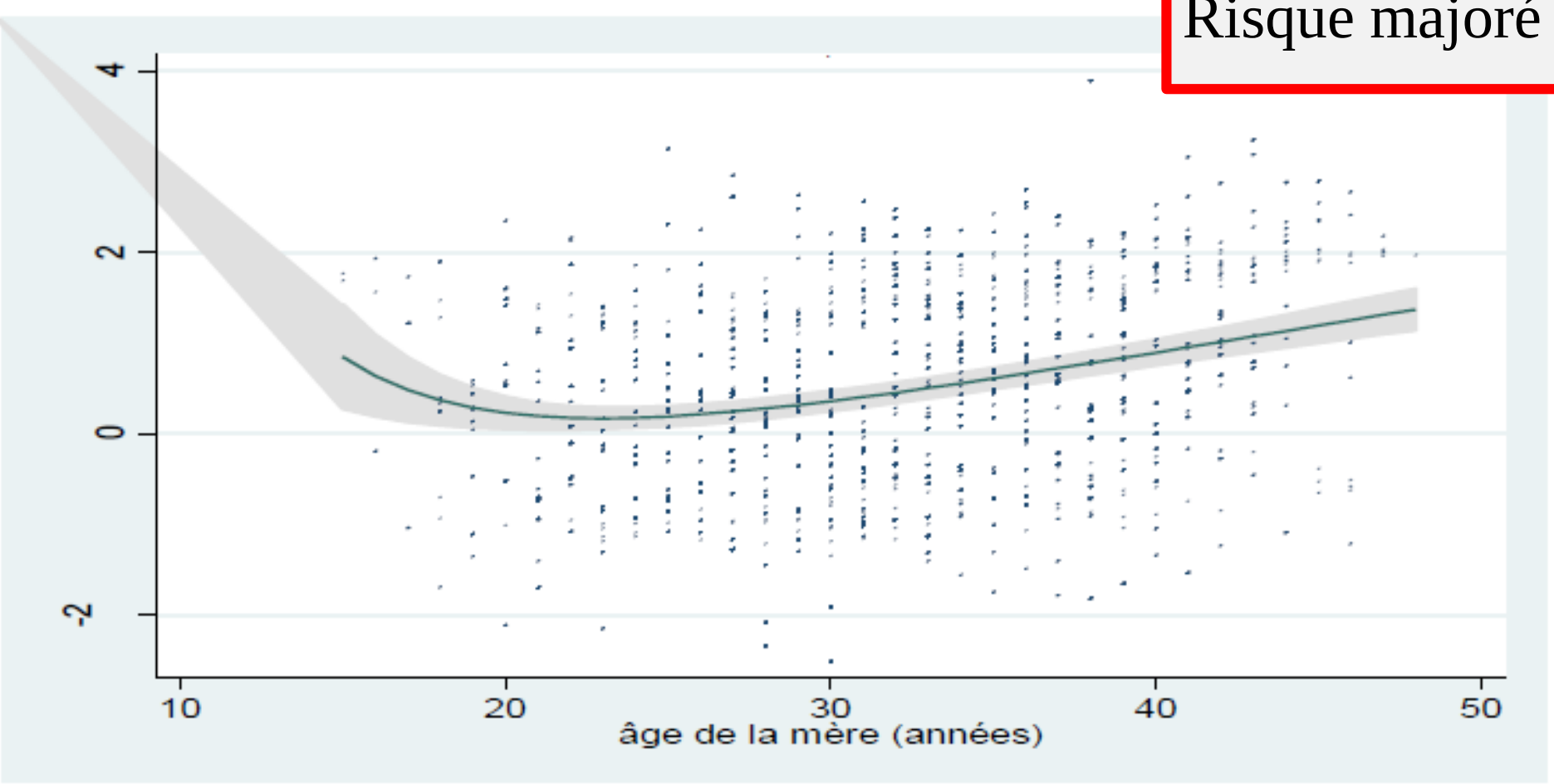
Vitamin/Supplement	Defect	OR	Reference(s)
Multivitamin supplements (including folic acid)	Any	0.5–0.8	8–10
	VSD	0.2–1.2	9, 10, 12
	Conotruncal defects	0.5–1.0	10–12
Multivitamin supplements (including folic acid) in women with febrile illness	Any	*	15
Folate antagonist only	Any	2.1	13, 14

*OR not applicable.

Jenkins KJ et al Noninherited risk factors and congenital cardiovascular defects: current knowledge Circulation. 2007

Age maternel

Risque majoré : + 4% /an



K. Tararbit et *al*. 2013

Et les pères ???

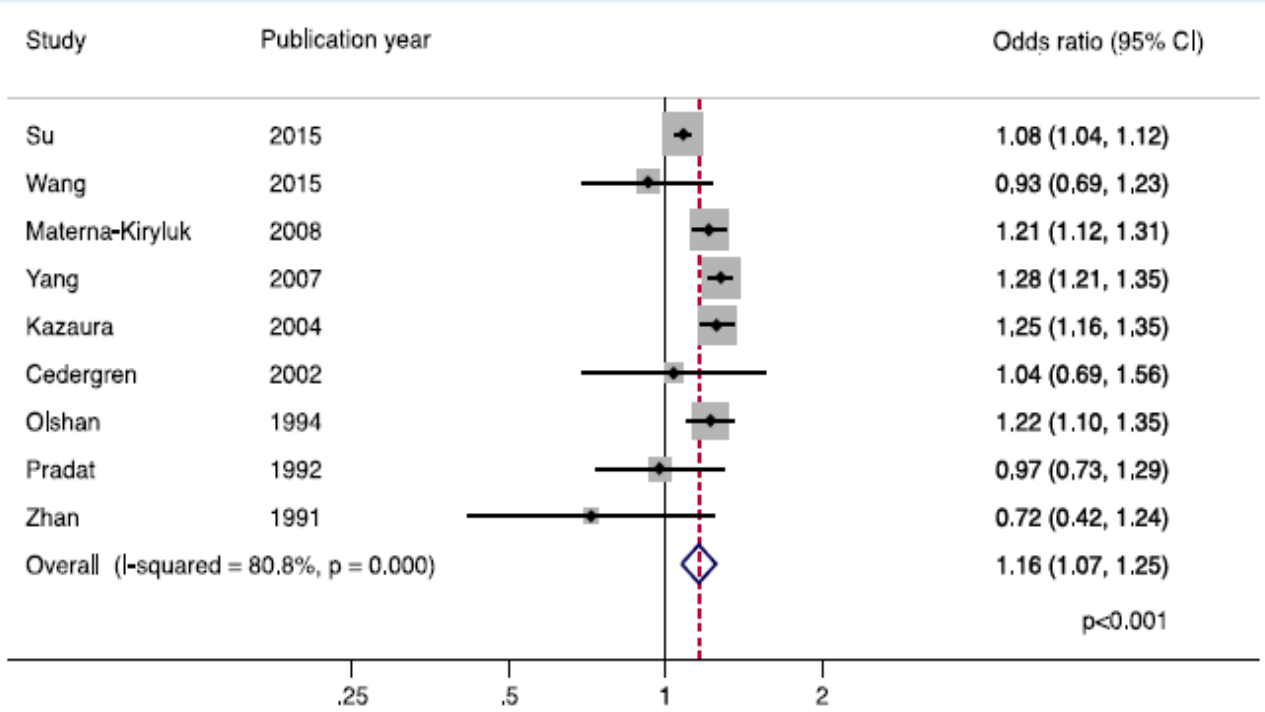


Figure 2. Association between advanced paternal age and CHD (congenital heart defects): main meta-analysis (nine studies, random-effects model).

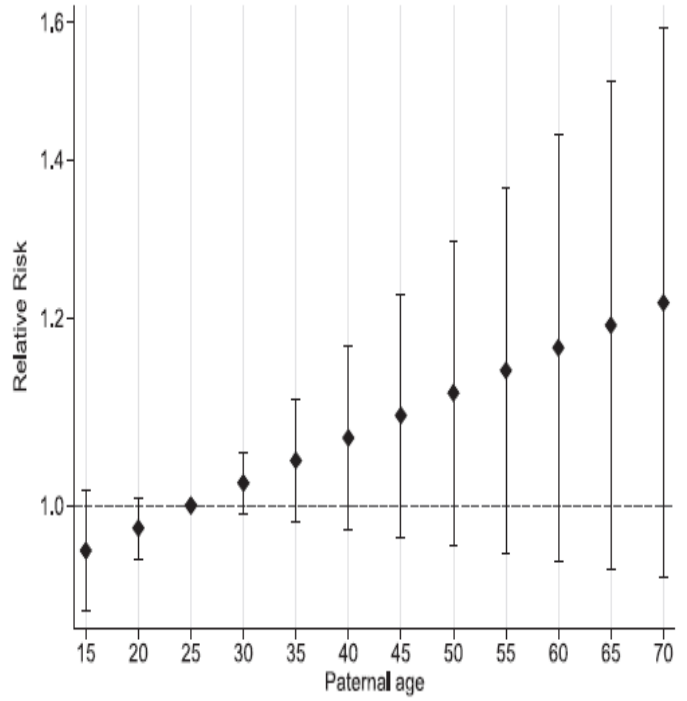


Figure 4. Dose–response meta-analysis. The measures of associations in the selected studies were ORs or RRs (relative risk) depending on the study design.

Joinau-Zoulovits F at *al* Hum Reprod. 2020 Nov

Diagnostic prénatal et variable socio économique

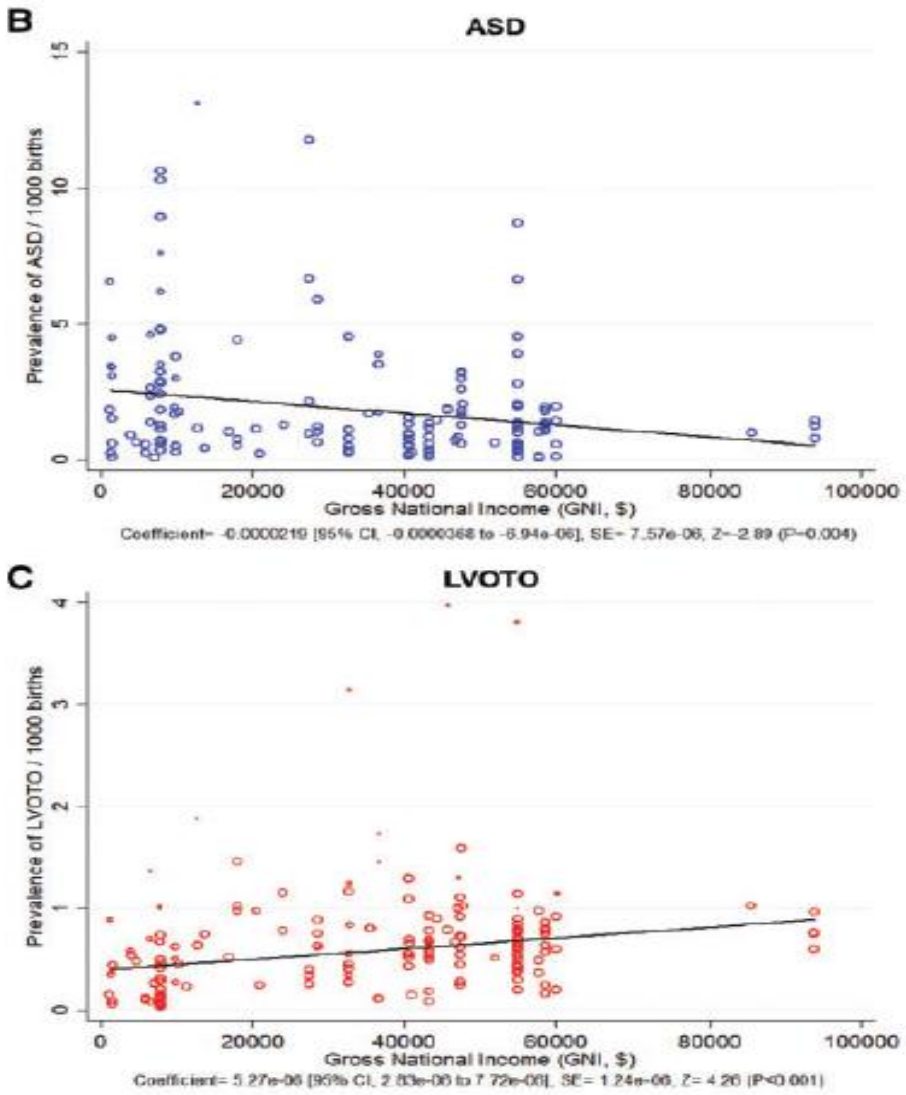
Table 3 Association between the odds of TOPFA and maternal socioeconomic and clinical factors in fetuses with isolated CHD-VSD excluded

	n	% of TOPFA	95%CI	*p*
Maternal age (years)				
≤34	184	24	18–31	0.5
35–37	43	32	18–47	
≥38	47	30	16–43	
Gravidity				
Primigravida	99	27	20–33	0.8
Multigravida	175	26	18–36	
Maternal geographic origin				
France	152	33	25–40	0.003
Africa	66	11	3–18	
Other	56	28	16–40	
Maternal occupation				
Professional	91	31	21–40	0.12
Intermediate	36	25	11–39	
Administrative/public service	51	25	13–38	
None	74	15	6–23	

OR (Afr vs Fr) = 0.1[0.02–0.4]

Tararbit K et al Clinical and socioeconomic predictors of pregnancy termination for fetuses with congenital heart defects: a population-based evaluation. Prenat Diagn. 2013

Prévalence et SES



Ethny ?
Genetic ?
Environnement ?
Measurement and publication bias ?

Liu Y, Chen S, Zühlke L, Black GC, Choy MK, Li N, Keavney BD. Global birth prevalence of congenital heart defects 1970-2017: updated systematic review and meta-analysis of 260 studies. Int J Epidemiol. 2019

Assistance médicale à la procréation

Table 3 Logistic regression analyses of the associations between assisted reproductive technologies (all methods combined) and congenital heart defects

	Cases	Crude OR[a]	95% CI	Adjusted[b] OR[a]	95% CI
All	All CHD	1.0	Ref.	1.0	Ref.
		1.3	1.1–1.6	1.3	1.0–1.6
	CHD without chromosomal abnormalities	1.0	Ref.	1.0	Ref.
		1.4	1.1–1.7	1.4	1.1–1.7
	CHD without chromosomal abnormalities and excluding VSD	1.0	Ref.	1.0	Ref.
		1.4	1.1–1.8	1.5	1.1–1.9
Singletons only	All CHD	1.0	Ref.	1.0	Ref.
		1.1	0.8–1.5	1.1	0.8–1.5
	CHD without chromosomal abnormalities	1.0	Ref.	1.0	Ref.
		1.1	0.8–1.5	1.2	0.9–1.6
	CHD without chromosomal abnormalities and excluding VSD	1.0	Ref.	1.0	Ref.
		1.1	0.8–1.5	1.2	0.8–1.6

[a]Odds ratios represent the odds of a birth (including live births, stillbirths, and pregnancy terminations) with congenital heart disease (cases) relative to the odds of a birth with one of the malformed controls (see the Methods section for details).
[b]Adjusted for maternal age, geographic origin, occupation, and year of birth.

Registre MFP
5493 cases of CHD
3847 malformed controls

K. Tararbit et *al*. EHJ 2011

This higher risk for CHD varied specifically according to the method of ART and the type of CHD **and may be** due to ART per se and/or the underlying infertility of couples.

Assistance médicale à la procréation

Table 5 Logistic regression analyses of the associations between assisted reproductive technologies (all methods combined) and subcategories of congenital heart defects

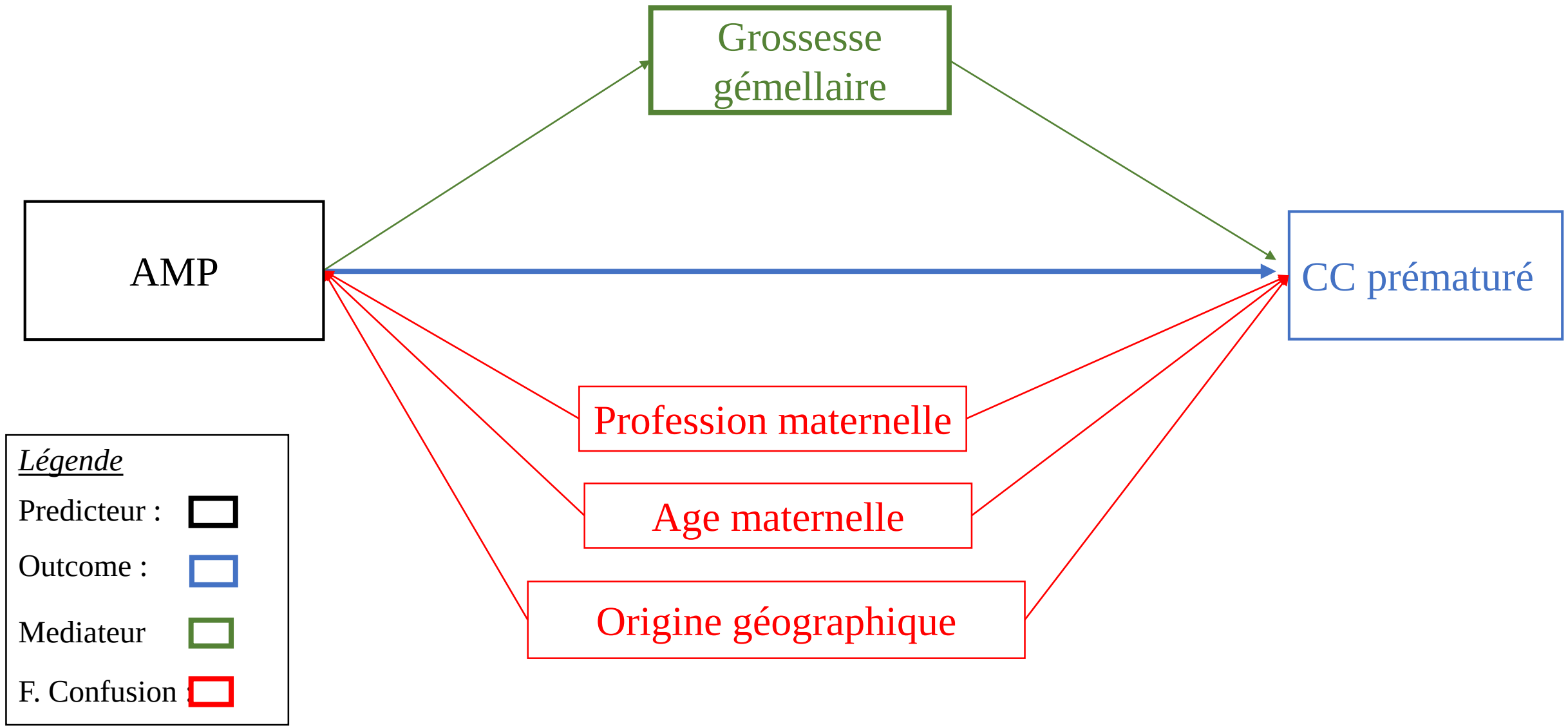
Subcategories	Crude OR[a]	95% CI	Adjusted[b] OR[a]	95% CI
Malformations of the outflow tracts and ventriculoarterial connections	1.0	Ref.	1.0	Ref.
	1.6	1.2–2.2	1.7	1.2–2.4
Malformations of the atrioventricular valves and atrioventricular connections	1.0	Ref.	1.0	Ref.
	0.7	0.4–1.2	0.6	0.4–1.2
Functionally univentricular CHD	1.0	Ref.	1.0	Ref.
	0.7	0.4–1.3	0.6	0.3–1.3
Anomalies of the great arteries	1.0	Ref.	1.0	Ref.
	1.3	0.8–2.2	1.3	0.8–2.3
Ventricular septal defects	1.0	Ref.	1.0	Ref.
	1.4	1.1–1.8	1.3	1.0–1.6
Anomalies of the atria and interatrial communications	1.0	Ref.	1.0	Ref.
	1.4	0.6–3.2	2.0	0.8–5.0
TGA, heterotaxy syndrome, and discordant atrioventricular connections	1.0	Ref.	1.0	Ref.
	1.2	0.8–2.0	1.3	0.8–2.3
Cardiac neural crest defects and double outlet right ventricle without ventricular hypoplasia	1.0	Ref.	1.0	Ref.
	1.6	1.1–2.5	1.7	1.1–2.7

[a]Odds ratios represent the odds of a birth (including live births, stillbirths, and pregnancy terminations) with congenital heart disease (cases) relative to the odds of a birth with one of the malformed controls (see the Methods section for details).
[b]Adjusted for maternal age, geographic origin, occupation, and year of birth.

Registre MFP
5493 cases of CHD
3847 malformed controls

K. Tararbit et *al*. EHJ 2011

Association entre AMP et CC Prématuré avec médiation par grossesse gémellaire



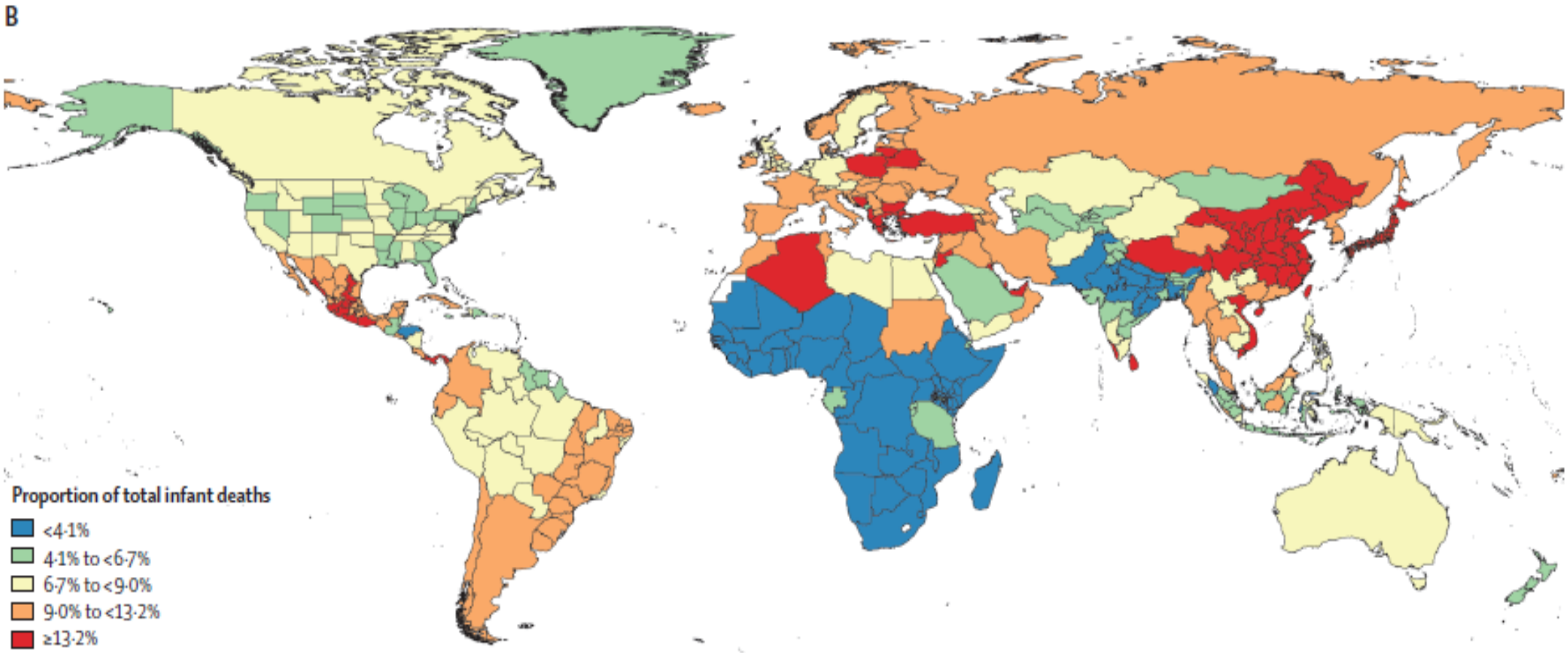
Association entre AMP et CC Prématuré avec médiation par grossesse gémellaire

Table 4 Decomposition of the total effect of infertility treatments on the risk of preterm birth into its direct and indirect (ie, mediated through multiple pregnancies) components

		Total effect				Direct effect				Indirect effect				Estimated size of the indirect effect (%)
CHD	Infertility treatments	Unadjusted OR*	95% CI	Adjusted† OR*	95% CI	Unadjusted OR*	95% CI	Adjusted† OR*	95% CI	Unadjusted OR*	95% CI	Adjusted† OR*	95% CI	
All CHDs	None	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	
	All methods combined‡	4.7	3.0 to 7.4	4.8	2.8 to 8.0	1.8	1.1 to 2.8	1.7	1.0 to 2.8	2.6	2.0 to 3.5	2.9	2.0 to 4.2	66.9
	IVF±ICSI‡	5.2	2.9 to 9.5	5.2	3.0 to 9.0	1.9	1.1 to 3.1	1.7	1.0 to 3.0	2.8	2.0 to 3.9	3.0	2.1 to 4.2	66.7
Isolated CHD	None	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	
	All methods combined‡	5.4	3.3 to 8.7	5.5	2.9 to 10.2	1.7	1.0 to 2.8	1.7	1.0 to 2.9	3.2	2.3 to 4.4	3.2	2.3 to 4.5	68.1
	IVF±ICSI‡	5.7	3.0 to 11.0	5.9	3.0 to 11.4	1.7	0.9 to 3.3	1.8	0.9 to 3.5	3.3	2.2 to 5.0	3.3	2.2 to 5.1	68.2
Isolated major CHD	None	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	
	All methods combined‡	4.6	1.7 to 11.9	3.9	1.5 to 9.9	2.2	0.8 to 6.0	1.8	0.7 to 4.5	2.1	1.3 to 3.5	2.2	1.2 to 3.9	57.7
	IVF±ICSI‡	5.6	1.7 to 18.5	4.5	1.2 to 17.4	2.3	0.7 to 8.1	1.8	0.5 to 6.4	2.5	1.3 to 4.5	2.6	1.4 to 4.6	62.7

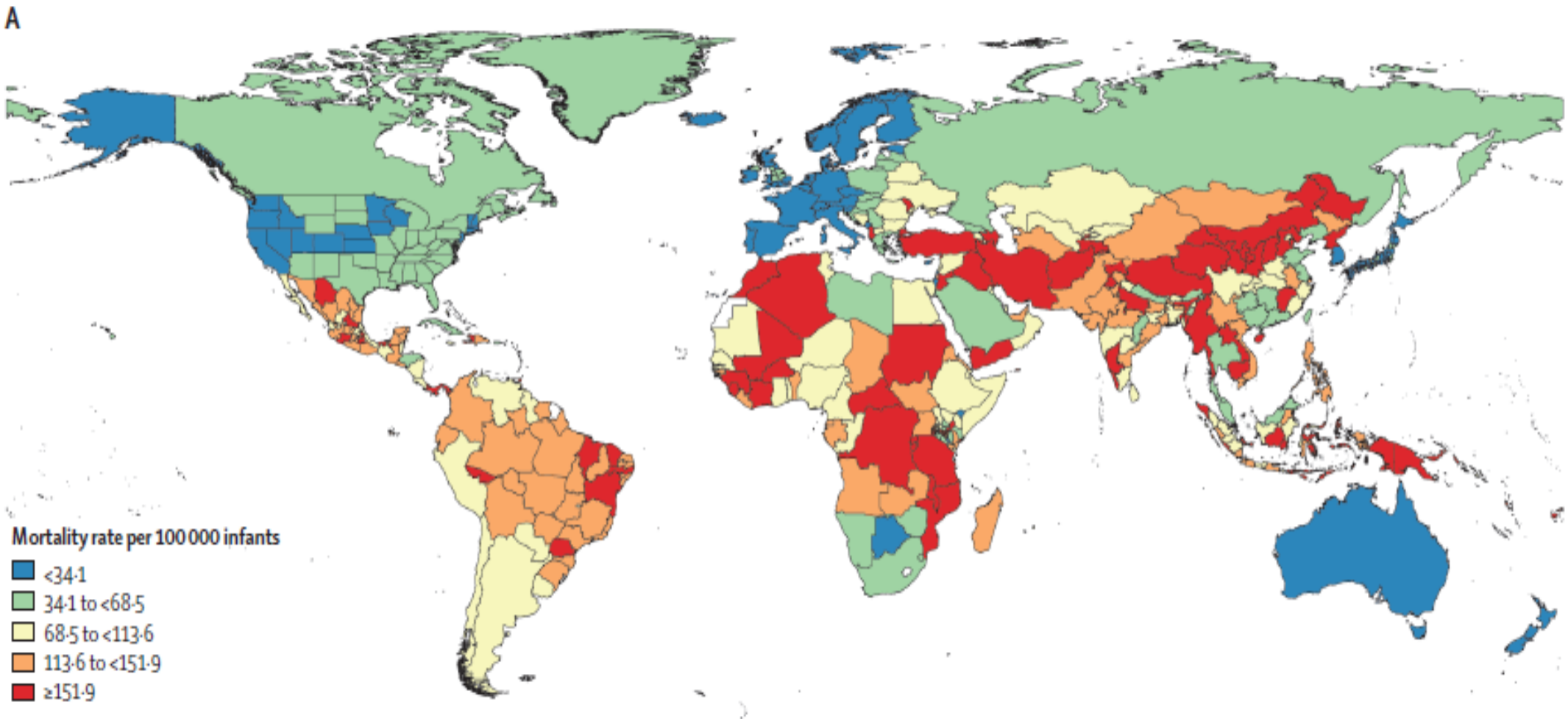
*ORs represent the odds of preterm birth in fetuses with CHD exposed to ART relative to the odds of preterm birth in fetuses with CHD unexposed to ART.
†Adjusted for maternal sociodemographic characteristics (age, geographical origin, occupation), gravidity, diabetes mellitus, vaginal bleeding, invasive prenatal testing, prenatal diagnosis of CHD, intrauterine growth restriction, medical induction of labour or caesarean delivery before labour and year of birth.
‡Including induction of ovulation.
ART, assisted reproductive technique; CHD, congenital heart defect; ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilisation; Ref, reference.

CC: proportion de mortalité infantile totale



GBD 2017 Congenital Heart Disease Collaborators. Global, regional, and national burden of congenital heart disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Child Adolesc Health. 2 Mar;4(3):185-200. doi: 10.1016/S2352-4642(19)30402-X. Epub 2020 Jan 21. Erratum in: Lancet Child Adolesc Health. 2020 Feb

CC: mortalité infantile ajusté



GBD 2017 Congenital Heart Disease Collaborators. Global, regional, and national burden of congenital heart disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Child Adolesc Health. 2 Mar;4(3):185-200. doi: 10.1016/S2352-4642(19)30402-X. Epub 2020 Jan 21. Erratum in: Lancet Child Adolesc Health. 2020 Feb

Mortalité et évolution

1990	Global	Low SDI	Low-middle SDI	Middle SDI	High-middle SDI	High SDI
Lower respiratory infections	1	1	1	1	2	7
Neonatal preterm birth	2	3	2	2	1	1
Diarrhoeal diseases	3	2	3	4	5	18
Neonatal encephalopathy due to birth asphyxia and trauma	4	4	4	3	3	4
Other neonatal disorders	5	5	5	6	6	6
Congenital heart disease	6	13	8	5	4	2
Neonatal sepsis and other neonatal infections	7	9	6	7	9	8
Tetanus	8	6	10	10	22	82
Protein-energy malnutrition	9	8	9	9	12	53
Measles	10	10	7	13	17	62
Malaria	11	7	11	35	86	115
Other congenital anomalies	12	17	13	8	7	5
Haemolytic disease and other neonatal jaundice	13	12	12	16	15	30
Syphilis	14	11	14	12	18	23
Whooping cough	15	15	17	14	14	51
Drug-susceptible tuberculosis	16	14	16	17	21	49
Neural tube defects	17	19	19	15	8	12
Other meningitis	18	16	15	19	23	19
Digestive congenital anomalies	19	23	20	18	10	10
Sudden infant death syndrome	20	20	21	22	13	3
Pulmonary aspiration and foreign body in airway	21	29	22	11	11	9
H influenzae type B meningitis	22	21	18	21	16	22
Paralytic ileus and intestinal obstruction	23	28	23	20	19	24
Other unspecified infectious diseases	24	24	25	26	25	25
Visceral leishmaniasis	25	18	43	89	96	102

GBD 2017 Congenital Heart Disease Collaborators. Global, regional, and national burden of congenital heart disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Child Adolesc Health. 2020

Mortalité et évolution

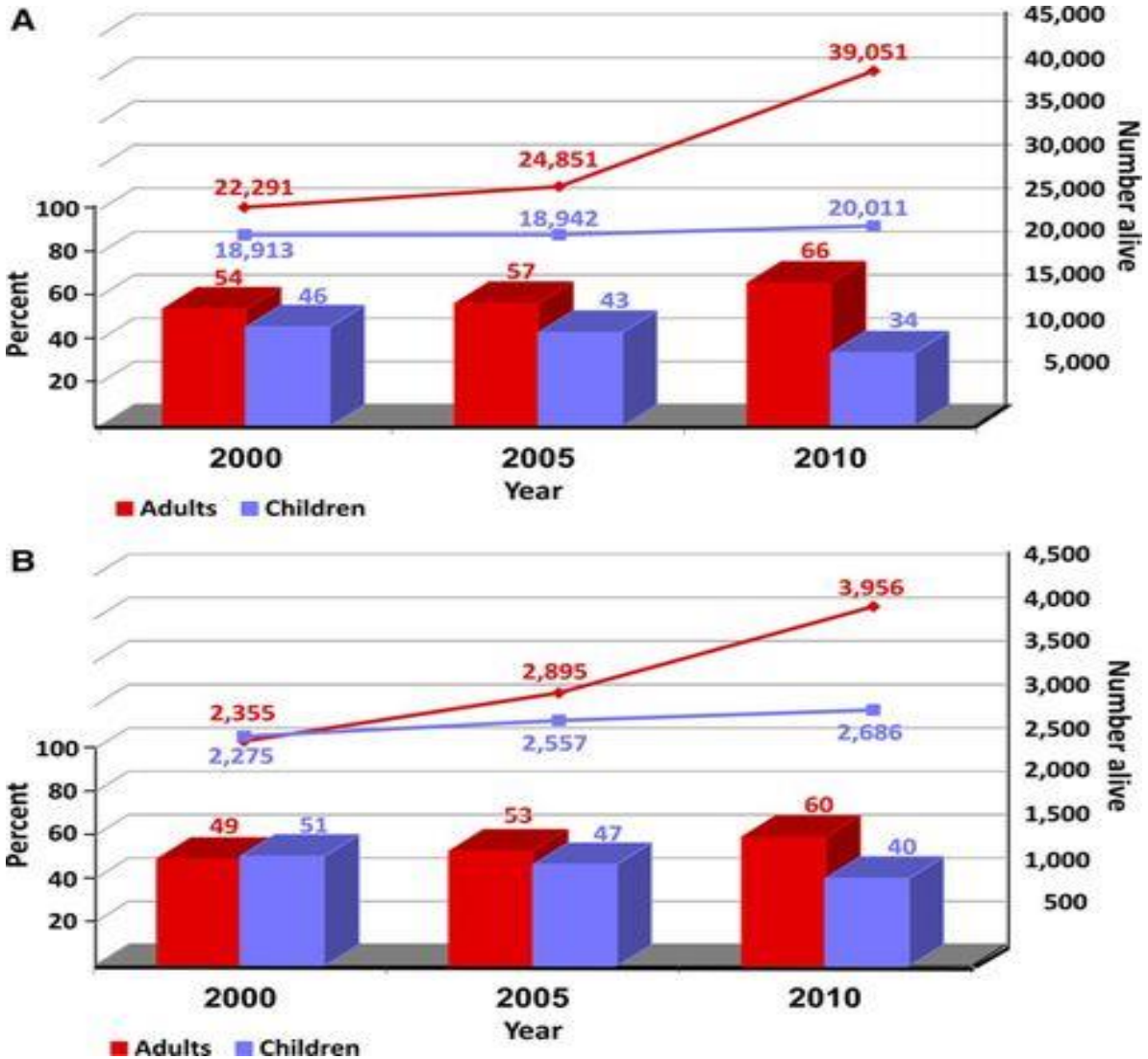
2017	Global	Low SDI	Low-middle SDI	Middle SDI	High-middle SDI	High SDI
Neonatal preterm birth	1	2	1	1	1	1
Lower respiratory infections	2	1	2	2	5	10
Neonatal encephalopathy due to birth asphyxia and trauma	3	3	3	3	3	3
Other neonatal disorders	4	5	5	5	4	2
Diarrhoeal diseases	5	4	4	7	11	15
Neonatal sepsis and other neonatal infections	6	6	6	6	7	8
Congenital heart disease	7	8	7	4	2	4
Malaria	8	7	8	30	80	117
Syphilis	9	9	10	9	10	19
Other congenital anomalies	10	11	9	8	6	6
Protein-energy malnutrition	11	10	12	12	29	60
Haemolytic disease and other neonatal jaundice	12	15	11	16	19	37
Neural tube defects	13	13	16	13	12	12
Digestive congenital anomalies	14	17	15	11	8	11
Other meningitis	15	14	13	20	30	27
Whooping cough	16	12	17	19	33	53
Sudden infant death syndrome	17	16	18	15	13	5
HIV/AIDS resulting in other diseases	18	18	14	17	22	39
Pulmonary aspiration and foreign body in airway	19	27	22	10	9	9
Drug-susceptible tuberculosis	20	19	20	23	44	78
Measles	21	20	21	22	40	86
H influenzae type B meningitis	22	23	19	25	23	30
Paralytic ileus and intestinal obstruction	23	25	23	14	17	21
Other unspecified infectious diseases	24	22	27	29	18	20
Tetanus	25	21	24	36	68	97

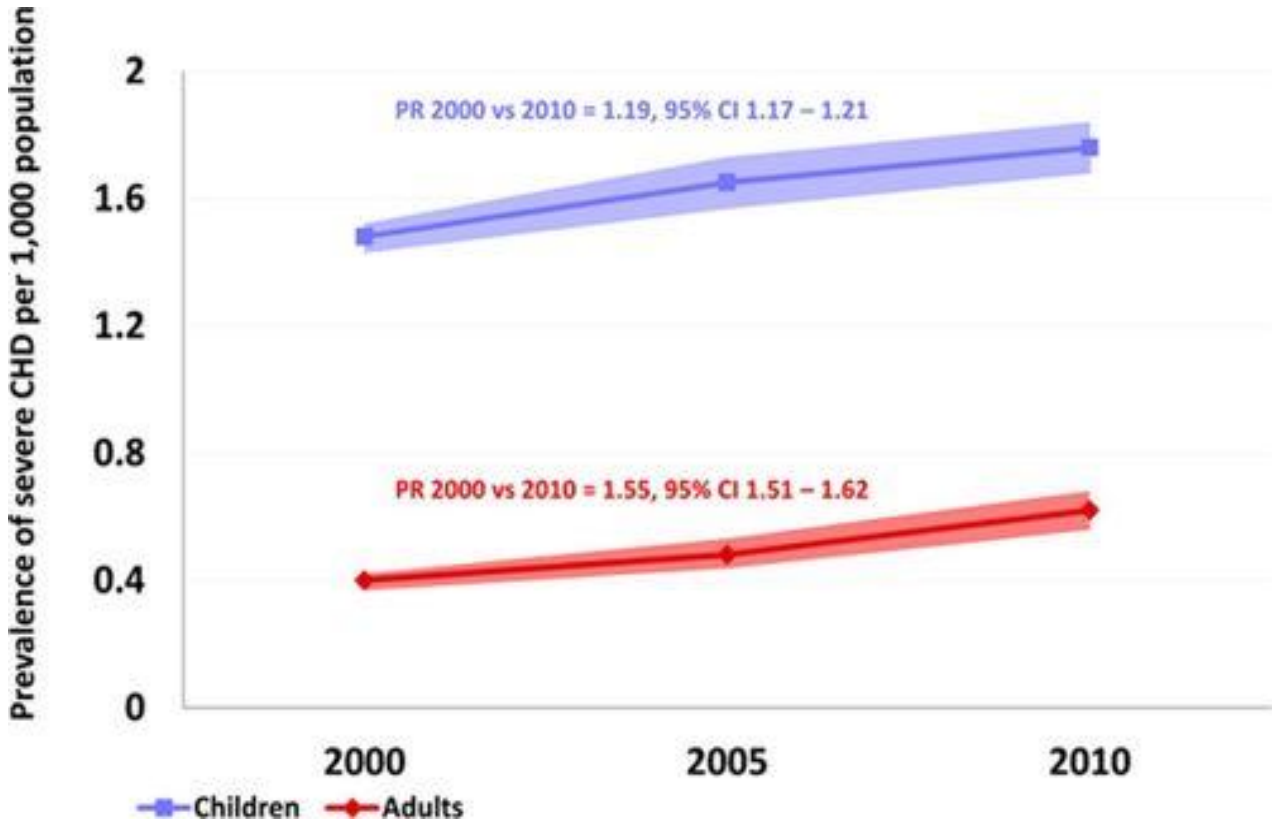
Death rate per 100 000 children

0·0 to 8·27 | >8·27 to 24·01 | >24·01 to 47·23 | >47·23 to 88·16 | >88·16 to 227·63 | >227·63 to 2214·30

GBD 2017 Congenital Heart Disease Collaborators. Global, regional, and national burden of congenital heart disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Child Adolesc Health. 2020

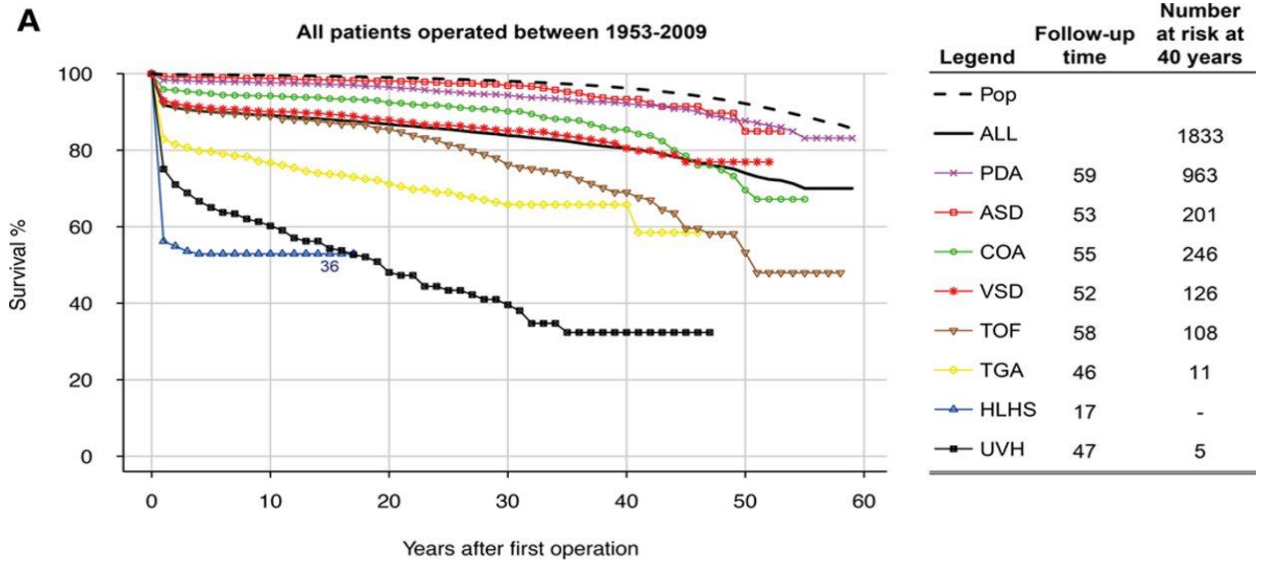
Mortalité et évolution



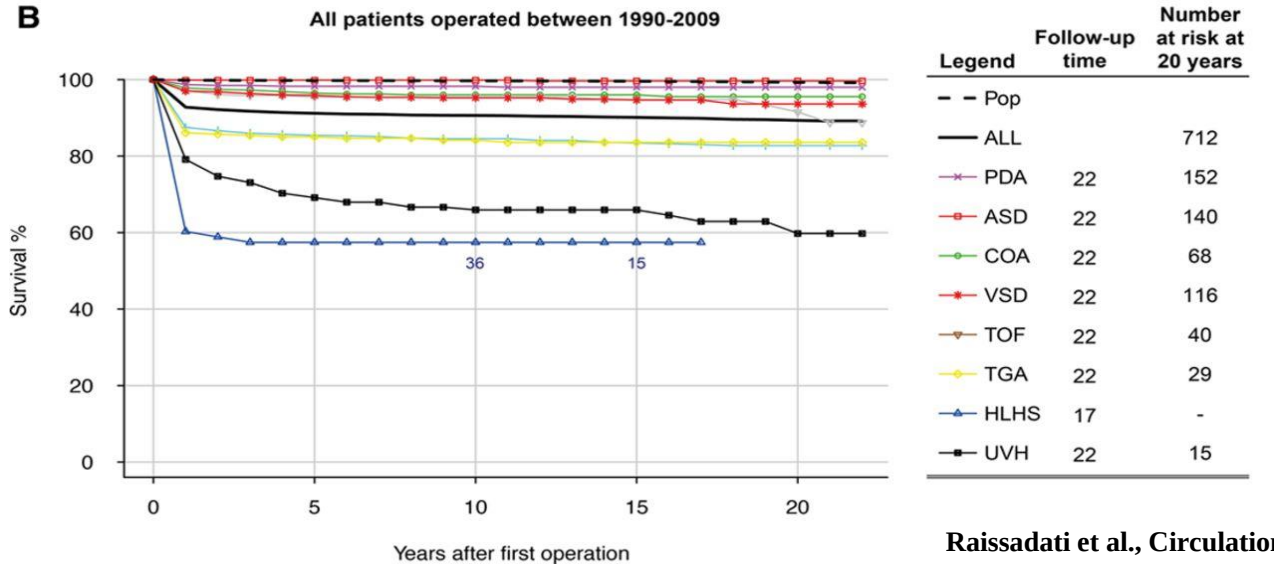


Ariane J. Marelli. Circulation. Lifetime Prevalence of Congenital Heart Disease in the General Population From 2000 to 2010,

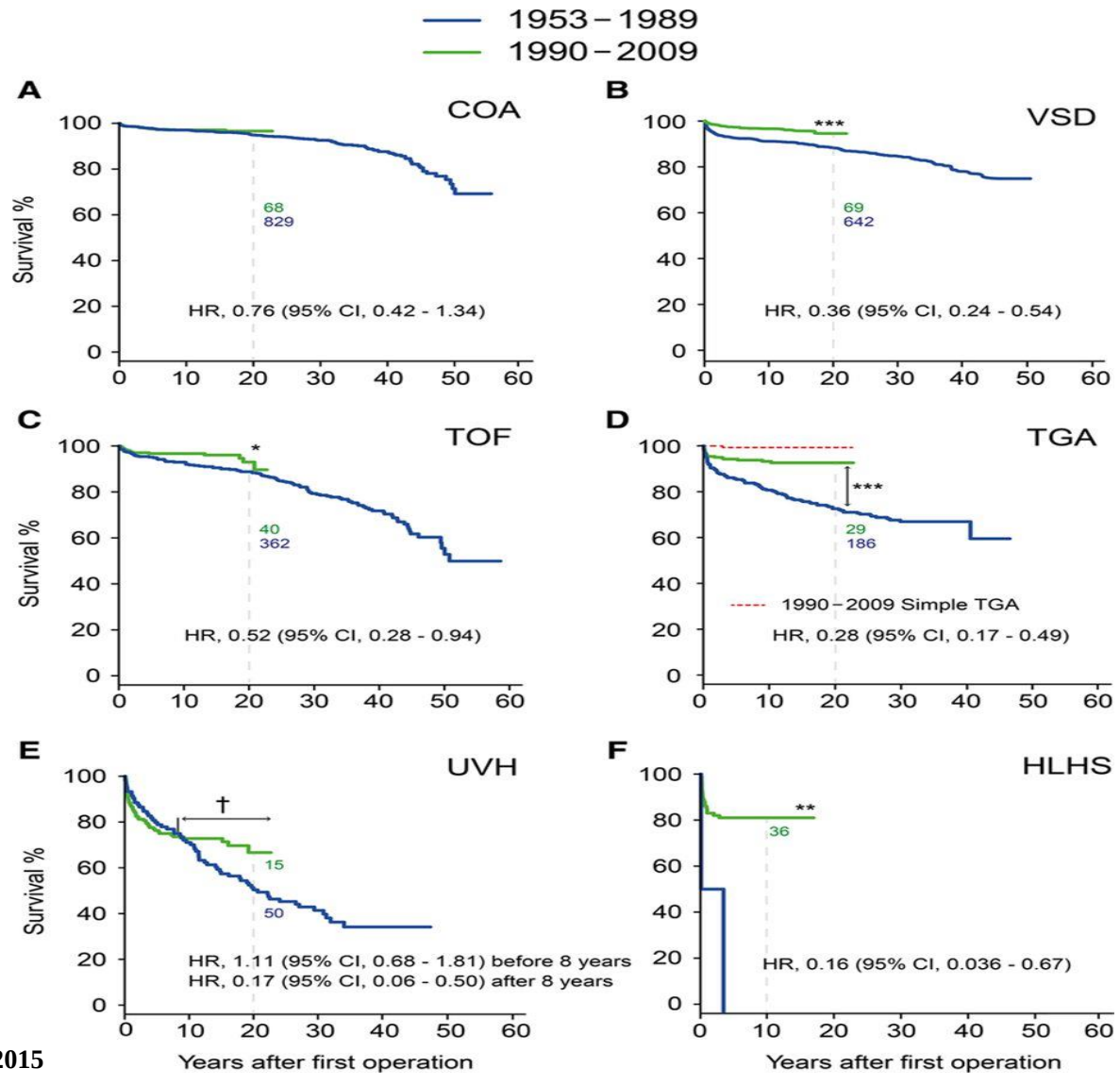
Morbidité : le nouveau challenge



Legend	Follow-up time	Number at risk at 40 years
Pop		
ALL		1833
PDA	59	963
ASD	53	201
COA	55	246
VSD	52	126
TOF	58	108
TGA	46	11
HLHS	17	-
UVH	47	5



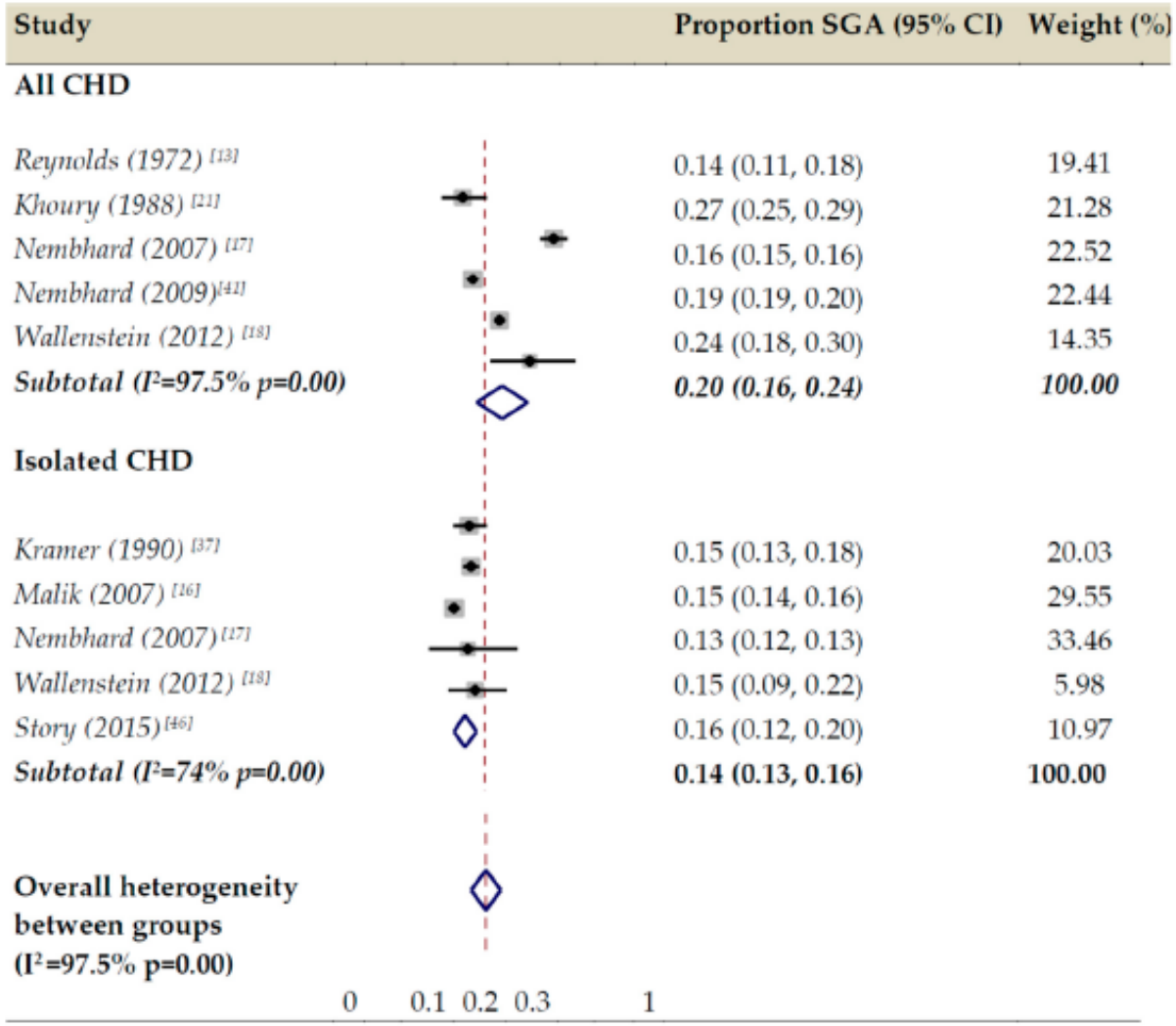
Legend	Follow-up time	Number at risk at 20 years
Pop		
ALL		712
PDA	22	152
ASD	22	140
COA	22	68
VSD	22	116
TOF	22	40
TGA	22	29
HLHS	17	-
UVH	22	15



Raissadati et al., Circulation 2015

Morbidité court moyen et long terme

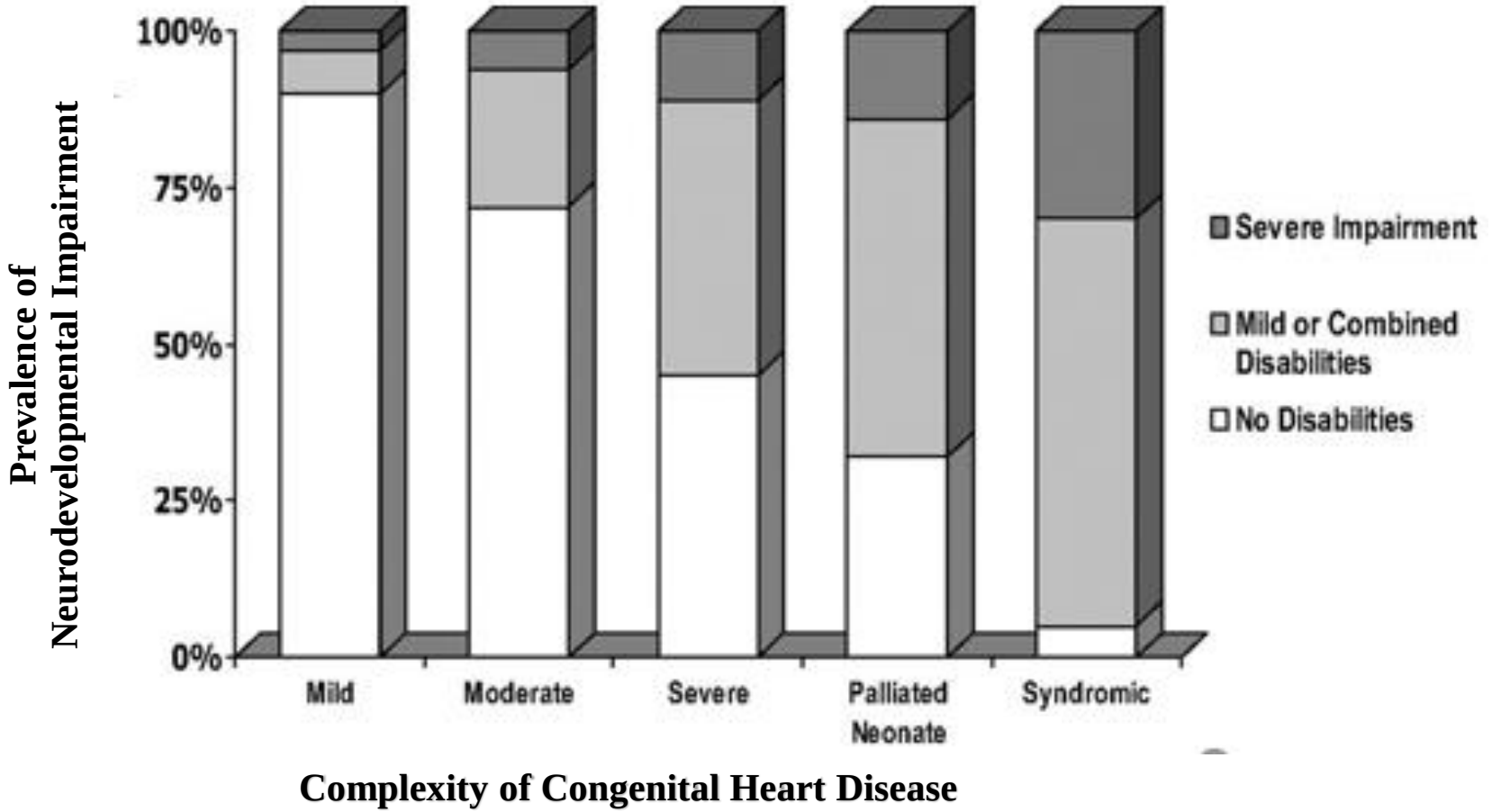
CC et PAG



Subgroup	Author	Pooled Proportion (95% CI)		% Weight
HLHS				
Total pooled result		21	(19–23)	
	Khoury (1988) [12]	23	(15–33)	7.36
	Nembhard (2009) [41]	23	(18–28)	22.81
	Williams (2010) [49]	20	(17–24)	48.79
	Swenson (2012) [47]	19	(15–24)	21.04
ToF				
Total pooled result		30	(24–37)	
	Khoury (1988) [12]	34	(25–43)	29.05
	Nembhard (2009) [41]	26	(23–30)	48.18
	Swenson (2012) [47]	36	(25–48)	22.77
TGV				
Total pooled result		17	(13–22)	
	Khoury (1988) [12]	17	(11–23)	28.79
	Nembhard (2009) [41]	20	(17–24)	41.34
	Swenson (2012) [47]	13	(8–18)	29.87
VSD				
Total pooled result		19	(18–20)	
	Khoury (1988) [12]	27	(24–31)	13.1
	Nembhard (2009) [41]	17	(16–19)	86.9
CoAo				
Total pooled result		22	(19–25)	
	Khoury (1988) [12]	28	(21–36)	19.06
	Nembhard (2009) [41]	20	(17–24)	80.94
AVSD				
Total pooled result		27	(21–32)	
	Khoury (1988) [12]	28	(20–38)	37.3
	Williams (2010) [49]	25	(18–33)	53.51
	Swenson (2012) [47]	32	(15–54)	9.19
TA				
Total pooled result		27	(21–35)	
	Williams (2010) [49]	30	(22–39)	74.84
	Swenson (2012) [47]	21	(10–37)	25.16
CAT				
Total pooled result		23	(17–30)	
	Khoury (1988) [12]	24	(11–41)	19.66
	Nembhard (2009) [41]	25	(17–34)	64.1
	Swenson (2012) [47]	18	(6–37)	16.24

Ghanchi et al Children Born with Congenital Heart Defects and Growth Restriction at Birth: A Systematic Review and Meta-Analysis

Neurodéveloppement des CC



Associé à

Troubles des apprentissage

Echecs scolaires

Problèmes de comportement

Problèmes sociaux

Transition vers l'âge adulte

Qualité de vie (enfants et adultes)

- Dolk H, Loane M, Garne E, European Surveillance of Congenital Anomalies (EUROCAT) Working Group. Congenital heart defects in Europe: prevalence and perinatal mortality, 2000 to 2005. Circulation. 1 mars 2011;123(8):841-9.
- Khoshnood B, Lelong N, Houyel L, Thieulin A-C, Jouannic J-M, Magnier S, et al. Prevalence, timing of diagnosis and mortality of newborns with congenital heart defects: a population-based study. Heart. nov 2012;98(22):1667-73
- Raissadati et al., « Progress in Late Results among Pediatric Cardiac Surgery Patients

Flow chart

EPICARD cohort

children born alive

N= 2348

Exclusion

Genetic or syndromic abnormalities reported at 8 years of age n= 467
VSD/ASD[1] not selected for follow-up after sampling at random n = 613
Death n = 70
Diagnostic error n = 2

Eligible population

N= 1196 [2]

Refusal to participate n = 176 (14.7%)
Lost to follow up n = 422 (35.3 %)

Child with 8 years follow-up

N=598 (50 %)

Postal mail follow-up n = 117 (9.8 %)
Uninterpretable tests [3] or incomplete n = 8 (0.7%)

Study population

N= 473 (39.5%)

[1]Children with ventricular septal defect or atrial septal defect with spontaneous closure
[2] Reference for all percentages
[3] Severe hearing and/or visual impairment, language barrier

Linear regression coefficient of the overall IQ

μ = 100 (15)

	IQ			
	Unadjusted	*p*	**Adjusted***	*p*
CCHD with heart failure	- 9.14	***0.006***	- 7.9	***0.008***
CCHD without heart failure	- 9.57	***0.006***	- 7.3	***0.02***
No CCHD with heart failure	- 5.8	***0.05***	- 4.31	*0.12*
Minor CHD requiring intervention	- 3.63	*0.19*	- 2.64	*0.29*
Minor CHD not requiring intervention	- 3.66	*0.097*	- 2.55	*0.19*

*Covariates of adjustment: sex of the child, prematurity, maternal origin in 4 classes, language spoken at home and level of maternal education in 5 classes

Heckman selection model used complexity variable in 3classes

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Linear regression coefficient of specific domains

μ = 10 (3)

	Learning and Memory		Comprehension of instructions(**language**)		Repetition of non-sense words(**language**)	
	Ajusted*	*p*	**Adjusted***	*p*	**Adjusted***	*p*
CCHD with heart failure	- 1.18	*0.06*	- 1.96	***0.000***	- 0.5	*0.24*
CCHD without heart failure	- 0.51	*0.42*	- 0.58	*0.24*	- 0.73	*0.12*
No CCHD with heart failure	- 1.36	***0.008***	- 1.46	***0.000***	- 1.1	***0.007***
Minor CHD requiring intervention	- 0.76	*0.11*	- 0.45	*0.19*	- 0.39	*0.27*
Minor CHD not requiring intervention	- 0.038	*0.91*	- 0.26	*0.33*	- 0.24	*0.39*

*Covariates of adjustment: sex of the child, prematurity, maternal origin in 4 classes, language spoken at home and level of maternal education in 5 classes

Heckman selection model used complexity variable in 3classes

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Qualité de vie lié à la santé

Cohen'd effect size compared QoL score of isolated CHD vs non isolated CHD

	Reported by children			Reported by parents		
	Physical score	**Psychosocial score**	**Total score**	**Physical score**	**Psychosocial score**	**Total score**
Isolated CHD vs non-isolated CHD	**- 0.33** [-0.53: -0.14]	**- 0.44** [-0.65: -0.25]	**- 0.49** [-0.69: -0.29]	**- 0.77** [- 0.93: -0.57]	**- 0.76** [-0.92: -0.55]	**- 0.84** [-1.0: -0.65]

d coefficient of 0.2 is considered as a "small effect size"
d coefficient of 0.5 is considered as a "medium effect size"
d coefficient of 0.8 is considered is considered as "large effect size"

Evaluation	Seuil
Small	0.2
Medium	0.5
Large	0.8

Derridj N *et al (submitted)*

Qualité de vie lié à la santé

Cohen’d effect size compared QoL score of each group of CHD to control

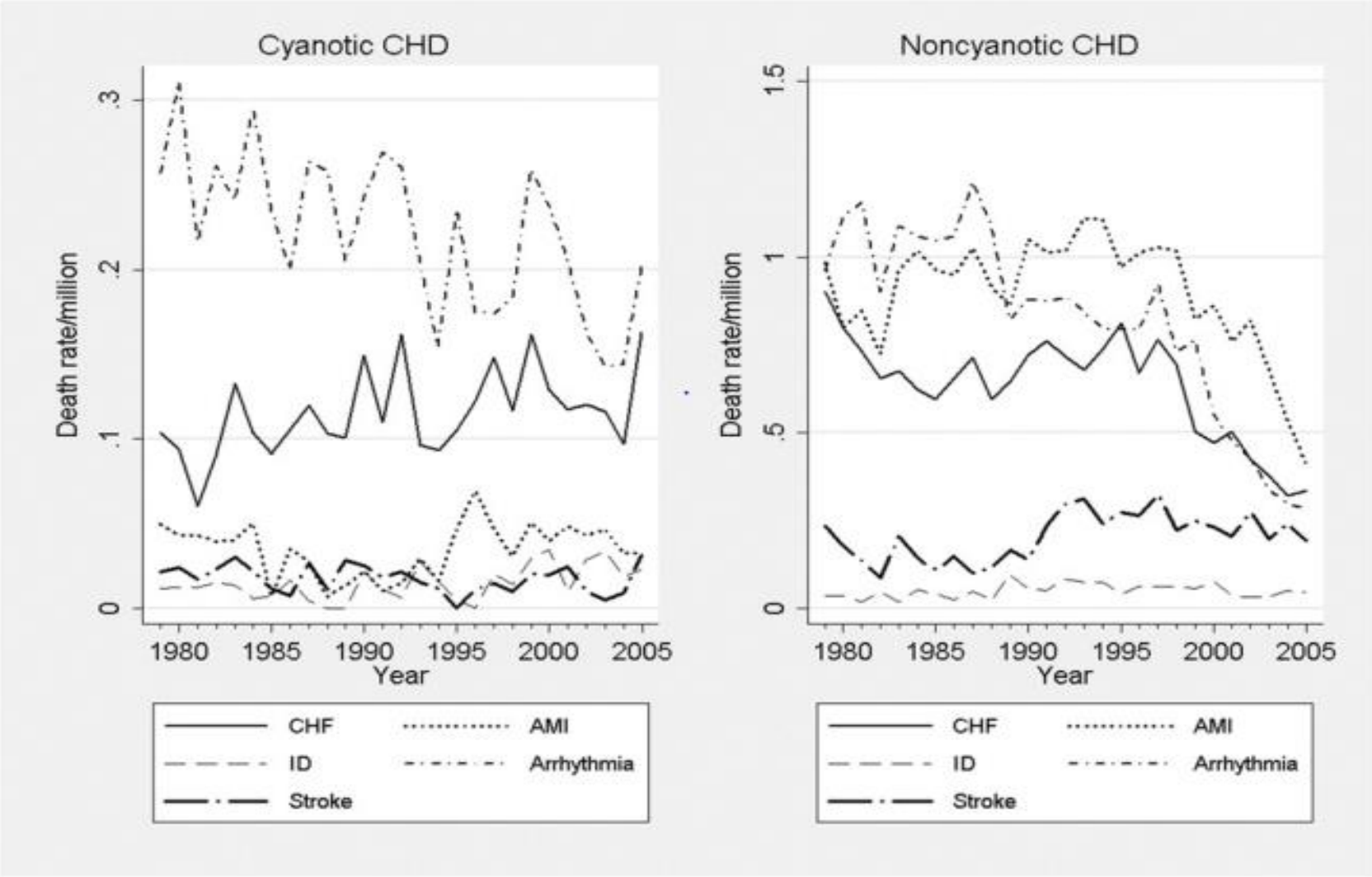
	Reported by children			Reported by parents		
	Physical score	**Psychosocial score**	**Total score**	**Physical score**	**Psychosocial score**	**Total score**
Follow-up in consultation without intervention at 8 years old	- 0.22	- 0.13	- 0.26	- 0.07	- 0.11	- 0.11
Complete repair before 3 years old	- 0.21	- 0.40	- 0.40	- 0.10	- 0.22	- 0.21
Complete repair after 3 years old	- 0.10	- 0.86	- 0.55	- 0.67	- 0.88	- 0.93
Palliative repair	- 0.30	- 0.93	-0.74	- 1.81	- 0.81	- 1.27

Cohen d effect size interpretation

Evaluation	Seuil
Small	0.2
Medium	0.5
Large	0.8

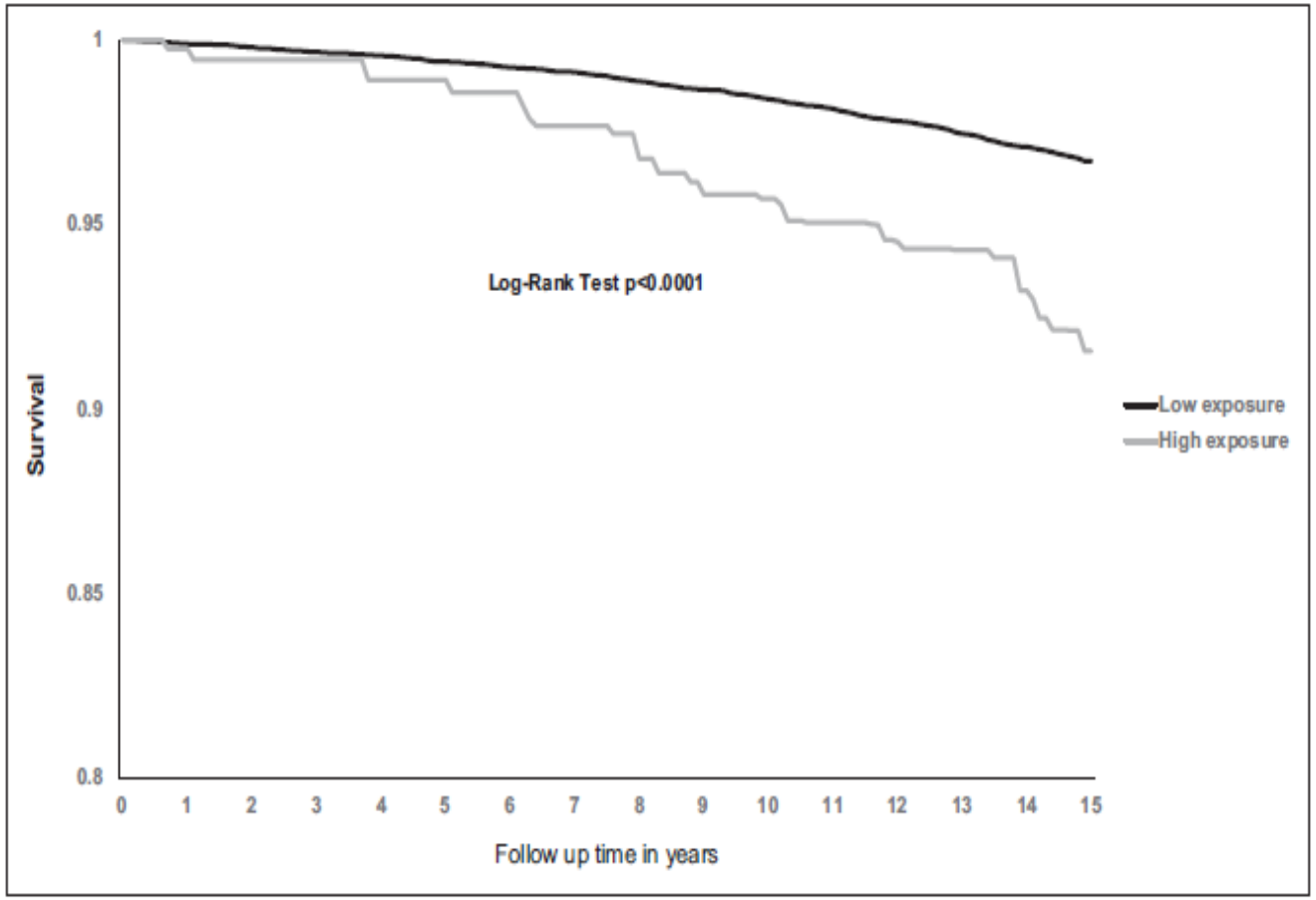
Derridj N *et al (submitted)*

Etiologie et mortalité des GUCHD

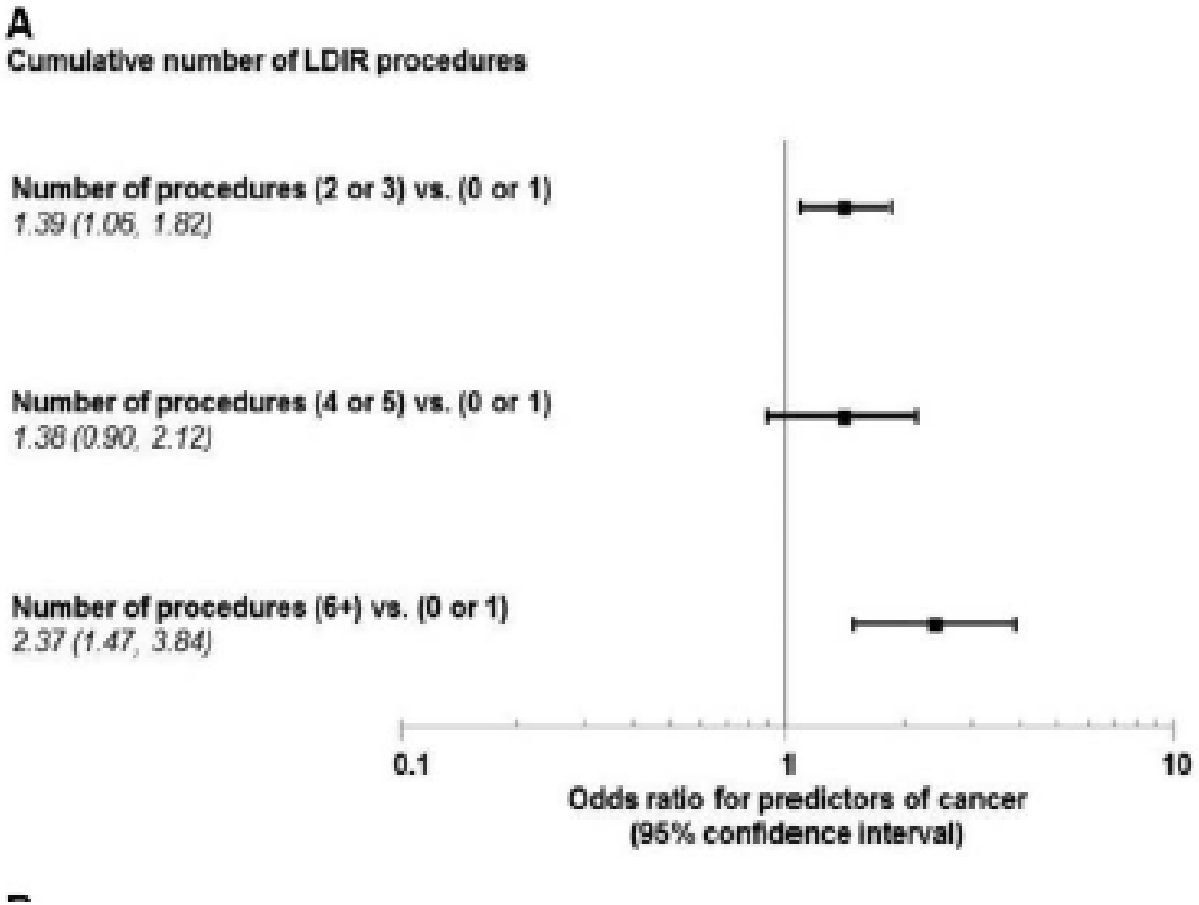


Priya Pillutla *et al* Mortality associated with adult congenital heart disease: Trends in the US population from 1979 to 2005

GUCHD et risque de Cancer

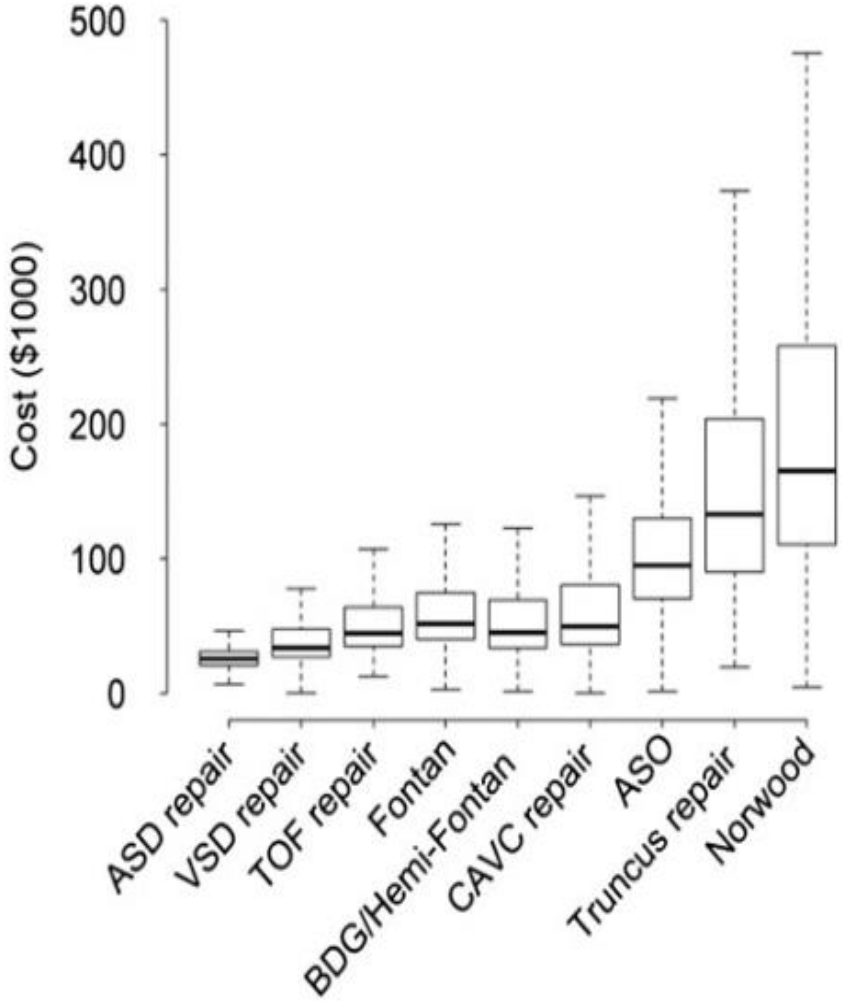


The effect of LDIR from cardiac procedures on cancer risk in ACHD in the case-control study with LDIR exposure represented with the cumulative number of procedures

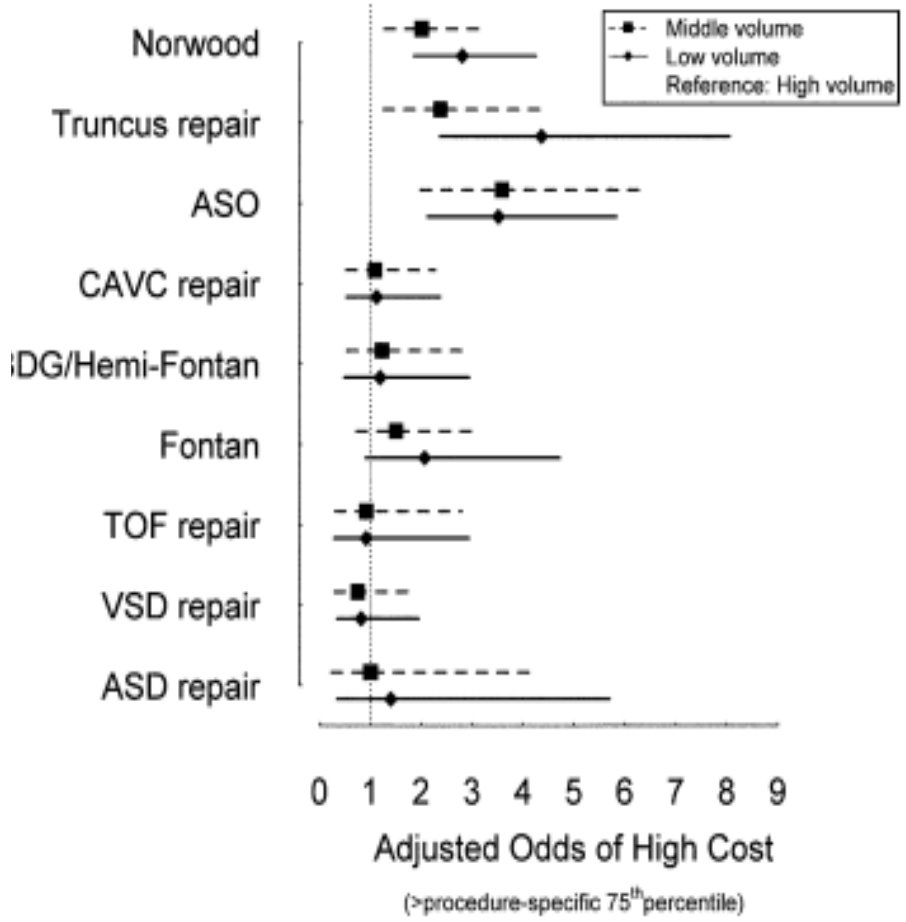


Adjusted Kaplan-Meier* curve for cancer-free survival probability for patients with high exposure from LDIR-related cardiac procedures (at least 6 procedures, dashed line) in comparison with low exposure (0 or 1 procedure, solid line).

Les coûts pour la société



Operation	Median cost/case (IQR)
ASD repair	$25,499 (20,645–30,962)
VSD repair	$33,679 (26,915–47,381)
TOF repair	$44,318 (34,743–63,808)
Fontan	$51,464 (39,976–74,640)
BDG/Hemi-Fontan	$44,893 (33,695–69,400)
CAVC repair	$49,445 (36,293–80,545)
ASO	$94,902 (70,357–129,984)
Truncus repair	$133,006 (90,189–204,006)
Norwood	$165,168 (110,446–257,980)



Sara K. Pasquali *et al* Pediatrics 2015

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