

Clinical and socioeconomic predictors of pregnancy termination for fetuses with congenital heart defects: a population-based evaluation.

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1 **Title**

2 Clinical and socioeconomic predictors of pregnancy termination for fetuses with congenital heart
3 defects: A population-based evaluation.

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21

22 **Bulleted statement.**

23 Most of the literature on TOPFA for congenital heart defects includes single-center hospital-based
24 studies. Moreover, few studies have evaluated both socioeconomic and clinical factors that could
25 be associated with the risk of TOPFA for congenital heart defects.

26 Using population-based data, we found that, in addition to severity of congenital heart defects,
27 early prenatal diagnosis and maternal characteristics are highly associated with the probability of
28 TOPFA for isolated congenital heart defects.

29

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42

43 **ABSTRACT**

44 **Objectives.** 1) Evaluate the probability and timing of termination of pregnancy for fetal anomaly
45 (TOPFA) for all congenital heart defects (CHD) and categories of CHD; 2) assess clinical and
46 socioeconomic predictors of TOPFA for isolated CHD excluding ventricular septal defects (VSD).

47 **Methods.** Using population-based data from the Paris Registry of Congenital malformations, we
48 assessed the probability of TOPFA and gestational age at TOPFA. We used logistic regression to
49 estimate the adjusted effects of maternal characteristics, clinical factors (CHD type, fetal growth
50 restriction, nuchal translucency measurement, and gestational age at prenatal diagnosis) on the
51 odds of TOPFA.

52 **Results.** The proportion of TOPFA for prenatally diagnosed CHD was 46% for all CHD
53 combined, 82% for CHD associated with chromosomal anomalies and 27% for isolated CHD-
54 VSD excluded. Isolated CHD-VSD excluded diagnosed before 22 weeks of gestational age had a
55 3.2-fold higher odds of TOPFA (Adjusted-OR 3.2, 95%CI 1.4–7.1). Maternal occupation was not
56 associated with the odds of TOPFA. Women of African origin had a ten-fold lower odds of TOPFA
57 than women of French origin (Adjusted-OR 0.1, 95% CI 0.02–0.4).

58 **Conclusion.** In addition to severity of CHD, early prenatal diagnosis and maternal characteristics
59 were highly associated with the probability of TOPFA for CHD.

60 **Keywords.** Termination of pregnancy for fetal anomaly, prenatal diagnosis, congenital heart
61 defects, epidemiology, risk factors.

62 **INTRODUCTION**

63 Congenital heart defects (CHD) are the most frequent congenital anomalies.¹ Progress in fetal
64 ultrasonography has conducted to an increase in the overall proportion of congenital
65 malformations, and in particular CHD, that are prenatally diagnosed. The most severe cases of
66 CHD can be accurately diagnosed during fetal life.²⁻⁴ Ultrasonography screening for CHD at 13/14
67 weeks of gestation has shown to have good performances and has been proposed to be routinely
68 performed in low-risk population.⁵ In case of positive screening, a more detailed scan must be
69 performed by a pediatric cardiologist in the beginning of the second trimester.⁶ In high risk
70 population, a specialized scan should be offered in first trimester.⁷ The overall effect of prenatal
71 diagnosis on the outcome of fetuses with CHD is difficult to evaluate due to higher severity of
72 cases that are prenatally diagnosed.⁸ Nevertheless, the beneficial effect of prenatal diagnosis on
73 morbidity and mortality has been shown for certain CHD such as transposition of great arteries or
74 coarctation of the aorta.^{2,9,10}

75 For the most severe CHD, termination of pregnancy for fetal anomaly (TOPFA) following prenatal
76 diagnosis may be an option to discuss with parents.^{6,11,12} Previous studies have shown that timing
77 and accuracy of prenatal diagnosis, existence of associated anomalies, available treatment options
78 and prognosis are factors associated with decision-making regarding TOPFA in case of CHD.^{6,12,13}
79 However, most studies have examined TOPFA for CHD with single-center hospital-based
80 data^{11,13,14} and few population-based studies exist regarding TOPFA for CHD.^{2,3,15} Moreover, few
81 studies have evaluated both socioeconomic and clinical factors that could be associated with the
82 risk of TOPFA for CHD.

83 Using population-based data from the Paris Registry for Congenital Malformations, we 1)
84 examined the proportion of TOPFA and gestational age at TOPFA for all CHD and categories of
85 CHD and 2) assessed the role of socioeconomic and clinical factors associated with TOPFA and

86 gestational age at TOPFA for cases of "isolated" CHD excluding ventricular septal defects (i.e.,
87 "major" CHD with no other associated anomalies).

88 MATERIAL AND METHODS

89 Data

90 We used data from the Paris Registry for Congenital Malformations which registers all cases of
91 birth defects and chromosomal anomalies among live-borns, still-borns (≥ 22 weeks of gestation),
92 and TOPFA at any gestational age. The Registry covers the population of women who live in
93 Greater Paris area (Paris and its surrounding suburb) and deliver or have a pregnancy termination
94 in a Parisian maternity unit. The annual number of deliveries in our population is about 38 000.
95 The Paris Registry is a member of the European Network of Registries of Congenital
96 Malformations (EUROCAT)^{16,17} and of the International Clearinghouse for Birth Defects
97 Surveillance and Research.^{18,19}

98 The Registry follows the EUROCAT methodology and quality of data is routinely monitored by
99 both EUROCAT and the National Committee of Registries in France. The review of procedures
100 regarding confidentiality of data is overseen by both the National Committee of Registries and the
101 National Committee of Informatics and Freedom. Data are based on medical records and are
102 collected from several sources including maternity units, neonatology wards, and cytogenetic and
103 pathology services.

104 Our study population comprised women who lived and delivered or had a pregnancy termination
105 in Paris during the period 2001-2007.

106 Methods

107 We conducted an observational study to i) describe the proportion of TOPFA after prenatal
108 diagnosis and gestational age at TOPFA and ii) assess predictors associated with the risk (odds) of
109 TOPFA and gestational age at TOPFA.

110 Proportions of TOPFA and gestational age at TOPFA were estimated for the following categories:

111 i) all CHD combined, ii) all isolated CHD, iii) isolated CHD-ventricular septal defects (VSD)

112 excluded; the latter category was constituted in order to represent major isolated CHD that often
113 requires intervention , iv) CHD associated with chromosomal anomalies and v) CHD associated
114 with malformations of other systems.

115 Predictors of the odds of TOPFA were assessed for isolated CHD-VSD excluded. Variables
116 considered as predictors were maternal characteristics (age, occupation, geographic origin and
117 gravidity), clinical characteristics (nuchal translucency, intra-uterine growth retardation (IUGR),
118 gestational age at prenatal diagnosis, gestational age at TOPFA, and category of CHD) and year of
119 TOPFA. Maternal age was coded in three categories (≤ 34 , 35-37, ≥ 38) based on the higher risk of
120 chromosomal anomalies in women aged 35 or more and the fact that at the time of our study
121 reimbursed amniocentesis or chorionic villus sampling was available to all women over 38 years
122 of age in our study population. Maternal occupation comprised the following categories:
123 professional, intermediate, administrative/public service, and none. Maternal geographic origin
124 was coded as: French, African and other countries. Gravidity was coded in two categories:
125 primigravida and multigravida. Nuchal translucency measured at first trimester scan was
126 categorized as: normal, abnormal and not done (i.e. women who had not their 1st trimester scan).
127 IUGR was as noted in medical records and coded in two categories (no/yes). Gestational age at
128 prenatal diagnosis was dichotomized in gestational age ≤ 22 and >22 weeks, as 22 weeks is the
129 recommended term for 2nd trimester scan in France. Gestational age at TOPFA was analyzed as a
130 continuous variable. Isolated cases of CHD were classified into 4 subcategories by a pediatric
131 cardiologist (T.B.) based on the diagnosis recorded in the Registry database: i) functionally
132 univentricular CHD, ii) so-called conotruncal CHD, iii) complex CHD (at least two cardiac defects
133 combined excluding VSD) and iv) other CHD.

134

135 **Statistical analyses**

136 Data were analyzed using standard descriptive statistics (mean, standard deviation (SD), and
137 frequency). Chi-square test, or Fisher's exact test when appropriate, and ANOVA test were used
138 for univariate analyses of the differences between groups. The associations between clinical and
139 socioeconomic factors and the odds of TOPFA were assessed using logistic regression models.
140 Observations with missing values were excluded from the multivariate analyses. The statistical
141 significance level was set at $\alpha = 0.05$. All analyses were done with Stata 10 software (Statacorp,
142 TX, USA).

143

144 **RESULTS**

145 During the study period, 1465 cases of CHD were registered, among which 66% (n=968) were
146 isolated CHD, 16% (n=230) were CHD associated with chromosomal anomalies and 18% (n=267)
147 with anomalies of other systems (including genetic syndromes). VSD accounted for half of the
148 cases of isolated CHD (51%, n = 495).

149 Gestational age at prenatal diagnosis was missing for 0.4% of fetuses. There were no missing data
150 for the outcome of the pregnancy (live-birth, still-birth, TOPFA). Maternal occupation and nuchal
151 translucency were missing for 8% of cases. For the other variables, data were missing for less than
152 1% of fetuses.

153 Table 1 summarizes the proportions of prenatal diagnosis and TOPFA for all CHD, and
154 subcategories of CHD. Overall, 48% (703/1465) of cases were prenatally diagnosed and TOPFA
155 occurred for 22% of all cases of CHD (325/1465). Prenatal diagnosis was made for 35% of all
156 isolated CHD (339/968), 58% of isolated CHD - VSD excluded (274/473) and 79% of CHD
157 associated with chromosomal anomalies (182/230).

158 Among prenatally diagnosed CHD (n=703), TOPFA was performed in 46% (325/703) of cases.

159 The highest proportion of TOPFA was observed for CHD associated with chromosomal anomalies

160 (82%, 148/182). CHD associated with chromosomal anomalies accounted for 45% of cases of
161 TOPFA (148/325). Proportion of TOPFA for isolated CHD - VSD excluded was 27% (74/274).
162 Among those 74 cases of TOPFA for isolated CHD - VSD excluded, hypoplastic left heart
163 syndrome accounted for half (51%, n=38).

164 Overall, the mean gestational age at prenatal diagnosis was 20.4 weeks (SD 0.26) for the study
165 population (Table 2). Mean gestational age at prenatal diagnosis was lowest for cases associated
166 with chromosomal anomalies (19.1, SD 0.38) and highest for isolated CHD - VSD excluded (21.9,
167 SD 0.39). The mean gestational age at TOPFA was 23.2 weeks (SD 0.29) for the study population
168 (Table 2). The average gestational age at TOPFA was lowest for CHD associated with
169 chromosomal anomalies (21.7, SD 0.45) and highest for isolated CHD - VSD excluded (24.8, SD
170 0.46). The mean duration between prenatal diagnosis and TOPFA was 2.8 weeks and was similar
171 for all subcategories of CHD. More than half (57%) of TOPFA for CHD associated with
172 chromosomal anomalies were performed before 22 weeks of gestation vs. 17% for isolated CHD -
173 VSD excluded. We did not find a significant time trend in the gestational age at TOPFA over the
174 study period.

175 Table 3 summarizes the univariate analyses of the association of TOPFA for isolated CHD - VSD
176 excluded with maternal characteristics and clinical factors. TOPFA was significantly less frequent
177 for mothers of African origin (11% vs. 33% for mother of French origin and 28% for women of
178 other origin, $p=0.003$). TOPFA was significantly more frequent for CHD diagnosed before 22
179 weeks of gestation (42% vs. 17% for CHD diagnosed after 22 weeks, $p<0.001$), for functionally
180 univentricular CHD and complex CHD (60% and 34 % respectively vs. 21% for conotruncal CHD
181 and 11% for other CHD, $p<0.001$). No statistically significant associations were observed for the
182 other factors, although TOPFA tended to be more frequent in case of IUGR (50% vs. 26%,
183 $p=0.09$).

184 Table 4 summarizes the multivariate analyses of the association of TOPFA for isolated CHD -
185 VSD excluded with maternal characteristics and clinical factors. CHD diagnosed before 22 weeks
186 of gestational age had a 3.2- fold higher odds of TOPFA than those diagnosed later (adjusted OR
187 3.2, 95%CI 1.4 – 7.1). IUGR (adjusted OR 6.6, 95%CI 0.9 – 51.0), single ventricle (adjusted OR
188 21.3, 95%CI 7.7 – 59.0) and complex CHD (adjusted OR 5.8, 95%CI 1.7 – 17.4) were also
189 associated with higher odds of TOPFA but confidence intervals were fairly wide. Maternal
190 occupation was not associated with the odds of TOPFA. However women of African origin had a
191 10-fold lower odds of TOPFA than women of French origin (adjusted OR 0.1, 95% CI 0.02 – 0.4).
192 There was no significant timr trend in the odds of TOPFA during the study period.

193 Table 5 summarizes the results of the univariate analyses of predictors of mean gestational age at
194 TOPFA. Sample sizes were relatively small and no statistically significant associations were
195 observed. In particular maternal characteristics were not significantly associated with gestational
196 age at TOPFA whereas an increased nuchal translucency measurement tended to be associated with
197 a lower gestational age at TOPFA although the association was not statistically significant
198 (p=0.13).

199

200 **DISCUSSION**

201 Using population-based data from the Paris Registry for Congenital Malformations, we found that
202 the overall rate of termination of pregnancy for fetal anomaly (TOPFA) for cases with congenital
203 heart defects (CHD) prenatally diagnosed was 46%. The highest probability of TOPFA was
204 observed for CHD associated with chromosomal anomalies (82%). A prenatal diagnosis before 22
205 weeks of gestation was associated with a 3.2-higher odds of TOPFA for isolated CHD - VSD
206 excluded. Maternal occupation was not independently associated with the probability of TOPFA.
207 However, mothers of African origin had a 10 fold-lower odds of TOPFA than women of French
208 origin.

209 It is difficult to know the extent to which our results may be generaliseable to other countries.
210 France represents a particular context for prenatal diagnosis and TOPFA as it pursues an active and
211 highly codified policy of prenatal diagnosis. In contrast to many European countries, TOPFA is
212 authorized in France regardless of gestational age for incurable fetal diseases or life-threatening
213 maternal conditions.²⁰ Proportions of prenatal diagnosis and TOPFA, in particular for CHD, tend
214 to be higher in France as compared to those observed in other countries^{1,15,16} even though
215 differences in the post-natal diagnosis and the period of registration of cases in the postnatal period
216 across countries complicate the interpretation of observed differences in the proportion of prenatal
217 diagnosis for CHD in different countries.

218 We observed a lower proportion of TOPFA for isolated CHD as compared to CHD associated with
219 chromosomal anomalies or anomalies of other systems, which is consistent with the data from the
220 European surveillance of congenital anomalies (Eurocat) network of registries of congenital
221 anomalies.^{4,21} We also observed that the risk of TOPFA was significantly higher for functionally
222 univentricular CHD, which is due to the fact that the outcomes for functionally univentricular
223 CHD remain poor.^{22,23}

224 Socioeconomic factors are known to be associated with the likelihood of TOPFA for chromosomal
225 anomalies, in particular Down syndrome.²⁴⁻²⁷ This association has been little studied in the specific
226 case of CHD.²⁷ In a hospital-based study, Zyblewski *et al.*¹³ did not find an association between
227 socioeconomic factors and TOPFA. We found that maternal geographic origin, but not occupation,
228 was strongly associated with the risk of TOPFA for isolated CHD. Access to information about
229 prenatal diagnosis and TOPFA and parental decision making for chromosomal anomalies have
230 been shown to be influenced by preferences and cultural factors^{26,28}, although the barriers to
231 effective access to full information may also include language barrier since interpreters are often
232 not available. The same association between TOPFA and cultural factors may exist for isolated
233 CHD. We did not observe an association between maternal age and the probability of TOPFA for
234 isolated CHD, suggesting that the overall higher rates of TOPFA for CHD in older women were
235 due to the higher proportions of associated chromosomal anomalies. Prenatal diagnosis and
236 TOPFA occurred earlier in case of CHD associated with chromosomal anomalies.^{28,29} This may
237 have been in part due to an increased nuchal translucency measured in the first trimester which is
238 more likely to occur for both chromosomal anomalies and certain CHD. It is also possible that
239 even in the absence of an increased nuchal translucency, cytogenetic studies conducted after
240 prenatal diagnosis of a CHD diagnosed earlier in pregnancy were more likely to reveal an
241 associated chromosomal anomaly.

242 The average interval between prenatal diagnosis and TOPFA was similar (two weeks) for both
243 isolated CHD and CHD associated with chromosomal anomalies and was consistent with other
244 studies.^{4,29} This interval corresponds to the time necessary for a multidisciplinary discussion and
245 for parents to make their decision.

246 The proportion of TOPFA in fetuses with CHD has been shown to be higher when prenatal
247 diagnosis occurs earlier.^{4,5,12} We also found that isolated CHD - VSD excluded diagnosed before

248 22 weeks had a 3.2-fold higher odds of TOPFA in comparison to those diagnosed later. TOPFA
249 may indeed be more easily accepted by families at an earlier gestational age.⁴In addition, CHD
250 diagnosed earlier may have been on average more severe (associated with poorer prognosis) and
251 hence be more likely to be a candidate for TOPFA. Even though we partially took into account
252 severity of CHD in our analyses, a residual effect of severity as one explanation for the association
253 between earlier timing of prenatal diagnosis and probability of TOPFA cannot be excluded.

254 For isolated CHD - VSD excluded, gestational age at TOPFA tended to be lower in case of
255 abnormal nuchal translucency. Indeed, a more detailed examination of fetal heart is usually
256 performed after an abnormal nuchal translucency measurement on first trimester ultrasonography
257 and may therefore conduct to the earlier diagnosis of a CHD.^{30,31}

258 Our study has certain limitations. Due to small sample sizes, confidence intervals were fairly wide
259 indicating the limited precision of our estimates. We did not adjust for paternal characteristics due
260 to a high frequency of missing data. Nevertheless, paternal characteristics are strongly correlated
261 with maternal characteristics and are therefore, at least partially, taken into account by maternal
262 adjustment. Data were complete for pregnancy outcome and there were few missing data for the
263 factors included in the analyses. Bias in our estimates due to missing data is therefore unlikely.
264 However, residual bias or residual confusion due to missing data or confounding factors not taken
265 into account in this study cannot be excluded. The strengths of our study are a large sample size
266 and population-based data.

267 We explored specific associations that may exist between the risks of TOPFA and different
268 categories of CHD defined a priori based on anatomic and/or clinical criteria and classified by a
269 pediatric cardiologist. A caveat that needs to be considered is that our criteria for defining these
270 categories can be arguable. Moreover, alternative and more detailed groupings exist^{32,33}, which
271 may provide additional information for estimating the probability of TOPFA for CHD. However,

272 our results suggest that specific associations exist between the categories of CHD as defined in our
273 study and the probability of TOPFA without necessarily implying that the categories investigated
274 in our study are the most appropriate ones to use in this setting.

275 Diagnostic bias may have occurred as not all fetuses with a prenatally diagnosed CHD resulting in
276 TOPFA had a fetal pathology examination. Therefore, in these cases ascertainment of CHD was
277 based only on prenatal findings. Nevertheless, these cases represented a minority of the overall
278 study population.

279

280 **CONCLUSION.**

281 In conclusion, TOPFA occurred for 27% of isolated CHD - VSD excluded that were prenatally
282 diagnosed, 82% of CHD associated with chromosomal anomalies and 53% of CHD associated
283 with anomalies of other systems. Prenatal diagnosis of isolated CHD - VSD excluded before 22
284 weeks of gestation was associated with a 3.2-fold higher odds of TOPFA. Women of African
285 origin had a 10-fold lower odds of TOPFA than women of French origin. The categories of CHD
286 reflecting its severity were also significantly associated with the risk of TOPFA for isolated CHD -
287 VSD excluded. Gestational age at TOPFA tended to be earlier in fetuses with an abnormal nuchal
288 translucency. Timing of TOFPA was explained essentially by timing of prenatal diagnosis and the
289 time interval between prenatal diagnosis and TOPFA appeared to be essentially constant for all the
290 clinical and socioeconomic categories included in our study.

291 **Ethics approval.**

292 No ethics approval was necessary for this study.

293 **Contribution to authorship.**

294 B. K. conceived the study. T.T.T.B. conducted the main statistical analyses. K.T., N. L. and A-C. T.

295 assisted with statistical analysis. K.T. wrote the first draft of the manuscript with T.T.T.B. and B.K.

296 F.G. contributed to the conceptualization of ideas and made suggestions about the required

297 analyses. All of the authors contributed to the interpretation of findings and revisions of the article.

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Table 1. Prenatal diagnosis and termination of pregnancy for fetal anomaly (TOPFA) for fetuses with congenital heart defects (CHD).

	n	Prenatal diagnosis		Proportion of TOPFA among cases with a prenatal diagnosis	
		%	95% CI	%	95% CI
All CHD	1465	48	46 - 51	46	42 - 50
All Isolated CHD	968	35	32 - 38	16	12 - 19
Isolated CHD-VSD excluded	473	58	54 - 63	27	22 - 32
functionally univentricular CHD	68	93	86 - 99	60	48 - 72
conotruncal defect	53	72	59 - 84	21	8 - 34
complex CHD	48	85	75 - 95	34	19 - 49
other CHD	304	44	38 - 50	11	5 - 16
CHD associated with chromosomal anomalies	230	79	74 - 84	82	77 - 88
CHD associated with anomalies of other systems*	267	73	67 - 78	53	46 - 60

* including genetic syndromes

Table 2. Gestational age at prenatal diagnosis and at termination of pregnancy in fetuses with congenital heart defects.

	All CHD	Isolated CHD – VSD excluded	CHD associated with chromosomal anomalies	CHD associated with anomalies of other systems	p
Gestational age at prenatal diagnosis (weeks)					
mean (SD*)	20.4 (0.26)	21.9 (0.39)	19.1 (0.38)	21 (0.51)	< 0.001
median (IQR [§])	21 (17 - 23)	22 (21 - 23)	18 (16 - 22.5)	22 (18 - 23)	< 0.001
Gestational age at termination of pregnancy (weeks)					
mean (SD*)	23.2 (0.29)	24.8 (0.46)	21.7 (0.45)	24.1 (0.55)	< 0.001
median (IQR [§])	23 (19 - 26)	25 (23 - 26)	21.5 (18 - 25)	24 (20 - 28)	< 0.001
≤ 22	40%	17%	57%	34%	
23 - 25	30%	45%	22%	30%	< 0.001
≥ 26	30%	38%	21%	36%	
Time interval between prenatal diagnosis and termination of pregnancy (weeks)					
mean (SD*)	2.8 (0.14)	2.8 (0.26)	2.6 (0.21)	3.1 (0.3)	0.4
median (IQR [§])	2 (1 - 3)	2 (1 - 4)	2 (1 - 3)	2 (1 - 4)	0.6

*SD : standard deviation

§ IQR : interquartile range (25th percentile – 75th percentile)

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				
≤ 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	
Intra-uterine growth retardation				
no	265	26	21 - 31	0.09
yes	10	50	17 - 82	
Nuchal translucency measurement				
normal	206	28	22 - 34	0.27
abnormal	17	35	12 - 59	
not measured	31	16	3 - 29	
Gestational age at prenatal diagnosis (weeks)				
> 22	167	17	11 - 23	<0.001
≤ 22	108	42	32 - 51	
Category of CHD				
other	133	11	5 - 16	<0.001
functionally univentricular CHD	63	60	48 - 72	
conotruncal CHD	38	21	8 - 34	
complex CHD	41	34	19 - 49	

Table 4. Logistic regression analyses of the association between the odds of TOPFA and maternal socioeconomic and clinical factors in fetuses with prenatally diagnosed isolated CHD-VSD excluded.

	Unadjusted OR	95% CI	Adjusted OR	95% CI
Maternal age				
≤ 34	1.0	ref.	1.0	ref.
35 - 37	1.5	0.7 - 3.1	1.0	0.3 - 3.2
≥ 38	1.3	0.6 - 2.7	1.5	0.5 - 4.0
Maternal geographic origin				
France	1.0	ref.	1.0	ref.
Africa	0.2	0.1 - 0.6	0.1	0.02 - 0.4
Other	0.8	0.4 - 1.6	0.8	0.3 - 2.3
Maternal occupation				
professional	1.0	ref.	1.0	ref.
intermediate	0.7	0.3 - 1.8	0.7	0.2 - 2.2
administrative / public service	0.8	0.3 - 1.7	1.2	0.4 - 3.6
none	0.4	0.2 - 0.8	0.5	0.1 - 1.6
Intra-uterine growth retardation				
no	1.0	ref.	1.0	ref.
yes	2.8	0.8 - 10.1	6.6	0.9 - 51.0
Nuchal translucency measurement				
normal	1.0	ref.	1.0	ref.
abnormal	1.3	0.5 - 3.9	1.5	0.3 - 6.2
not measured	0.5	0.2 - 1.3	1.2	0.2 - 5.0
Gestational age at prenatal diagnosis				
> 22	1.0	ref.	1.0	ref.
≤ 22	3.4	1.9 - 5.9	3.2	1.4 - 7.1
Category of CHD				
other	1.0	ref.	1.0	ref.
functionally univentricular CHD	12.9	6.1 - 27.3	21.3	7.7 - 59.0
conotruncal CHD	2.3	0.9 - 5.9	2.1	0.7 - 6.6
complex CHD	4.4	1.9 - 10.3	5.7	1.8 - 17.4

Table 5. Association between gestational age at TOPFA and maternal socioeconomic and clinical factors in fetuses with isolated CHD-VSD excluded.

	n	mean gestational age	SD	p
Maternal age				
≤ 34	45	24.7	0.5	0.9
35 - 37	14	24.5	1.2	
≥ 38	14	25.6	1.3	
Gravidity				
Primigravida	27	24.0	0.5	0.2
Multigravida	46	25.3	0.7	
Maternal geographic origin				
France	50	24.8	0.6	0.8
Africa	7	24.0	1.7	
Other	16	25.1	0.9	
Maternal occupation				
professional	28	24.3	0.8	0.4
intermediate	9	27.1	1.6	
administrative / public service	13	25.1	1.1	
none	11	24.8	0.9	
Intra-uterine growth retardation				
no	69	24.8	0.5	0.7
yes	5	24.2	1.6	
Nuchal translucency measurement				
normal	58	25.3	0.5	0.13
abnormal	6	22.0	1.1	
not measured	5	24.8	2.0	
Type of CHD				
other	14	24.2	1.3	0.13
functionally univentricular CHD	38	25.2	0.6	
conotruncal CHD	8	26.9	1.3	
complex CHD	14	23.1	1.1	

383

384