



# Association between inadequate antenatal care utilisation and severe perinatal and maternal morbidity: an analysis in the PreCARE cohort

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**Objective** Because the effectiveness of antenatal care in reducing pregnancy complications is still discussed despite widespread recommendations of its use, we sought to assess the association between utilisation of recommended antenatal care and severe maternal (SMM) and perinatal morbidity (SPM).

**Design** Prospective cohort study.

**Setting** Four maternity units around Paris in 2010–2012.

**Sample** 9117 women with singleton pregnancies.

**Methods** Logistic regression models adjusted for maternal social, demographic and medical characteristics.

**Main outcome measures** Antenatal care utilisation was assessed by: (1) initiation of care after 14 weeks, (2) < 50% of recommended visits made, according to gestational age, (3) absence of the first, second or third trimester ultrasounds, (4) two modified Adequacy of Prenatal Care Utilisation indexes, combining these components. The two main outcomes were composite variables of SMM and SPM.

**Results** According to the modified Adequacy of Prenatal Care Utilisation index, 34.6% of women had inadequate antenatal care

utilisation; the incidence of severe maternal morbidity (SMM) was 2.9% and severe perinatal morbidity (SPM) 5.5%. A percentage of recommended visits below 50% (2.6% of women) was associated with SMM [adjusted odds ratio (OR) 2.40 (1.38–4.17)] and SPM [aOR 2.27 (1.43–3.59)]. Late initiation of care (17.0% of women) was not associated with SMM or SPM. Failure to undergo the recommended ultrasounds (16, 17 and 22% of women) was associated with SPM. Inadequate antenatal care utilisation according to the index was associated with SPM [aOR 1.37 (1.05–1.80)].

**Conclusion** Inadequate antenatal care utilisation is associated with SMM and SPM, to degrees that vary with the component of care and the outcome considered.

**Keywords** Adequacy of Prenatal Care Utilisation index, pregnancy complications, prenatal care, severe maternal morbidity, severe perinatal morbidity, ultrasound.

**Tweetable abstract** Inadequate antenatal care utilisation is associated with severe maternal and perinatal morbidity.

**Linked article** This article is commented on by EJ Buchmann, p. 596 in this issue. To view this mini commentary visit <https://doi.org/10.1111/1471-0528.14812>.

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## Introduction

Routine antenatal care is one of the most widely recommended measures to prevent pregnancy complications. It

has been recognised progressively by healthcare providers as effective since its development in the 1900s, despite the absence of adequate scientific evaluation.<sup>1,2</sup> Its evaluation today is not easy. In developed countries, which have already adopted antenatal care, both medical staff and women are reluctant to participate in randomised trials.<sup>3</sup>

\*The PreCARE Study Group members are in Appendix.

Observational studies report inconsistent results about its effectiveness in reducing perinatal morbidity,<sup>4–10</sup> and the association between antenatal care utilisation (ACU) and maternal morbidity has been examined even less extensively.<sup>11,12</sup> These discrepancies might reflect various methodological difficulties, including the need for a large sample size with accurate data about numerous components of antenatal care, and the large number of confounding factors that must be taken into account.

This absence of evidence has led to wide variations in national recommendations and policies throughout the world. The recommended number of antenatal visits ranges from a minimum of four for the World Health Organization<sup>13</sup> to 15 for the American Congress of Obstetrics and Gynecology.<sup>14</sup> France, like several other European countries,<sup>15</sup> recommends an intermediate number, eight.<sup>15–17</sup> Moreover, although consensus exists on the performance of some tests—such as blood pressure measurement or rhesus factor determination, recommendations differ not only concerning the numbers and timing of antenatal visits but also their content.<sup>18</sup> Several countries advise only one ultrasound, whereas France counsels three for routine antenatal surveillance. These differences highlight the need to evaluate different models of antenatal care, especially as most of the assessments in developed countries have taken place in North America.<sup>19</sup>

Conducting a secondary analysis of the French multicentre PreCARE cohort study, we aimed to assess the association between the adequacy of antenatal care utilisation and both severe maternal and perinatal morbidity in France. Initially designed to study the impact of maternal social deprivation on maternal and perinatal outcomes, this cohort makes it possible to control for many social and medical characteristics that are potential confounders in the analysis of the independent impact of antenatal care on health.

## Methods

### Study design, setting and participants

The PreCARE prospective multicentre cohort study<sup>20</sup> took place in four maternity units in university hospitals located in a geographical area characterised by a high prevalence of social deprivation in the area of northern Paris and its adjoining suburbs (France). Participants were all adult women registered to deliver or who delivered between 2010 and 2012 in these units ( $n = 10\,419$ ). Inclusion occurred at the first time during the pregnancy that the woman came in contact with the hospital. Women and newborns were followed from inclusion through to hospital discharge after delivery.

For this secondary analysis, we restricted the study population to women with singleton pregnancies who gave

birth after 21 completed weeks of gestation. We also excluded *in utero* transfers from non-participating maternity units. Women who gave birth in a non-participating hospital, who were lost to follow up or who had completely empty questionnaires were excluded (flow chart in Figure S1).

The regional review board (CPP-Ile-de-France III, No. 09.341bis, date of approval: 19 November 2009) approved the study. Each woman provided oral informed consent, in compliance with French law.

### Data collection

Participants were asked to complete two self-administered questionnaires, one at inclusion and one during the postpartum period before discharge. These questionnaires were available in four languages. A research assistant or interpreter provided assistance when needed. Some data on ACU came from the postpartum questionnaire; research assistants collected the rest from the women's medical files. Women's medical history and details of their pregnancies were collected both by research assistants and by the practitioners who performed the delivery or midwives caring for them during the postpartum hospitalisation. Data about socio-economic factors came from the self-administered questionnaires.

### Antenatal care characteristics

Several components were measured:

- late initiation of antenatal care (after 14 weeks)
- rate of completed visits on recommended visits according to gestational age at delivery, considering both scheduled outpatient and inpatient visits. Extra visits for control of maternal blood pressure or fetal heart monitoring were not taken into account in the numbers of visits.
- The absence of the ultrasounds recommended in the first (at 11–14 weeks), second (21–24 weeks) and third trimester (31–34 weeks).

We also adapted the most common index of ACU reported in the literature: the Adequacy of Prenatal Care Utilisation index (APNCU)<sup>21,22</sup> to create two modified indexes: mAPNCU-1 and mAPNCU-2, both taking French guidelines into account. In mAPNCU-1, antenatal care was considered inadequate if care did not begin until after 14 completed weeks' gestation. If care did begin before that time, the percentage of antenatal visits was used to define four categories of antenatal care: inadequate (<50% of the recommended number), intermediate (50–79%), adequate (80–109%) and adequate plus ( $\geq 110\%$ ).

The mAPNCU-2 further incorporated the recommended ultrasounds: some women with missing ultrasounds were reclassified to the inadequate category (if the first trimester ultrasound or both of the latter ultrasounds were missing)

or the intermediate category (if only the second or the third ultrasound was missing) (Figure S2).

### Outcome measures: severe maternal and perinatal morbidity

Severe maternal morbidity (SMM) was defined by at least one of the following complications: haemorrhagic shock, severe postpartum haemorrhage (second-line uterotonic treatment associated with transfusion of at least two units of packed red blood cells, and/or uterine artery ligation, and/or uterine compressive sutures, and/or embolisation and/or hysterectomy), eclampsia, placenta abruption, severe pre-eclampsia [systolic blood pressure (SBP) > 160 mm Hg, diastolic blood pressure (DBP) > 110 mm Hg, or hypertension with general signs, and one or more of the following: proteinuria >3.5 g/24 hours, serum creatinine >100  $\mu$ mol/l, diuresis <20 ml/hour, haemolysis, aspartate transaminase (ASAT) > 3N, thrombocytopenia <100 000/mm<sup>3</sup>, or before 32 weeks), severe sepsis (sepsis with organ failure), convulsions, diabetic ketoacidosis, deep venous thrombosis or pulmonary embolism, grade 3 or 4 perineal trauma, uterine rupture, intensive care unit (ICU) admission, surgical re-intervention, or maternal death.

Severe perinatal morbidity (SPM) included at least one of the following complications: very preterm birth (before 32 weeks), birthweight below the third percentile, fetal death (including medical termination of pregnancy), neonatal death (<28 days and before discharge), neonatal trauma (except collarbone fracture), brachial plexus strain, meconium aspiration syndrome, neonatal convulsions, 5-minute Apgar score <3 or umbilical cord pH <7.

### Covariates

Data were collected about socio-demographic characteristics (age, education, mother's country of birth and social deprivation), health status (number of previous pregnancies, body mass index and medical history), behaviour (tobacco consumption) and maternity unit of delivery.

A binary variable assessing the medical risk level at the beginning of pregnancy was created based on the presence or absence of high risk, in accordance with French guidelines.<sup>16</sup> It took into account history of cardiac disease, hypertension, diabetes, venous thrombosis, pulmonary embolism, Graves' disease, asthma, homozygous sickle cell anaemia, thrombocytopenia, coagulation disorder, a rare or systemic disease, nephropathy, HIV infection, late miscarriage, pre-eclampsia, growth restriction, preterm delivery, fetal death or neonatal death. We did not, however, adjust for medical risk *during* pregnancy or gestational age because we considered them to be intermediate factors in the association between ACU and severe morbidity.

As Opatowski et al.<sup>23</sup> suggested, maternal social deprivation at the beginning of pregnancy was characterised by a

quantitative index including four dimensions: (1) social isolation; (2) unstable or insecure housing conditions; (3) main household income not due to paid work (that is, income from public assistance, relatives, friends, or charitable organisations); (4) lack of standard health insurance (no healthcare insurance, healthcare insurance provided to women with an unauthorised immigration status or provided to those ineligible for standard public health insurance because unemployed or not in the labour force or assignee status). For women with missing data on these four dimensions at the beginning of pregnancy, data were imputed with data collected postpartum when available ( $n = 81$ ).

### Statistical analysis

First we compared the characteristics of the women included in the analysis with those of the women excluded for insufficient data. We then compiled descriptive statistics about the study population characteristics, their ACU and the prevalence of severe morbidity. Logistic regression models were then used to assess the associations between ACU and SMM or SPM in the study population. The variables introduced into the models were those clinically relevant or commonly found in the literature. The linearity of the association of the quantitative variables (age, body mass index and number of previous pregnancies) with ACU was tested; when the association was not linear, the variables were categorised. Maternity unit effects were handled as fixed effects. Goodness-of-fit was assessed by the Hosmer–Lemeshow test.

The missing data rates for the variables included in the multivariate model ranged from 0 to 4.8% (Table S1). To impute these data, we performed multiple imputations by chained equations (details in Table S2).

We presented the results of the imputed models as adjusted odds ratios (aOR) with their 95% confidence intervals (95% CI). The results of the complete cases analyses are available in Table S2.

All statistical tests were two-tailed and the threshold for statistical significance was set at a probability value of <0.05.

Analyses were performed with STATA<sup>®</sup> software, version 12.1 (Stata Corporation, College Station, TX, USA).

## Results

Among the 10 576 women asked to participate in the Pre-CARE study, 10 419 agreed (98.5%). Because 613 women met at least one exclusion criterion for this analysis, 559 gave birth in a non-participating maternity unit or were lost to follow up, and 64 returned blank questionnaires, our final study sample comprised 9117 women (flow chart in Figure S1). Compared with women included in the

analysis, those who delivered in other units, who were lost to follow up or who returned blank questionnaires ( $n = 623$ ) were more often underprivileged, born in sub-Saharan Africa, and primiparous; they also had more often a body mass index  $<18.5$  kg/m<sup>2</sup> and a low risk at the beginning of pregnancy (Table S3). Table 1 presents the main characteristics of the study sample.

The median number of scheduled antenatal visits was nine (interquartile range: 8–11) and nearly half the women had more than 110% of the recommended number of visits (for their duration of pregnancy). Nevertheless, 12.2% of participants had fewer than 80% of the recommended

number of visits, and 17.0% began antenatal care at 14 weeks' gestation or later. Moreover, 21.6% of the women did not have a first trimester ultrasound and about 16% missed either the second or third trimester ultrasound. Thus, 18.5% had inadequate antenatal care according to the mAPNCU-1 index, and 34.6% according to the mAPNCU-2 index, which also considered ultrasound examinations (Table 2).

SMM occurred in 259 women (2.91%). The main maternal complications were severe pre-eclampsia (0.80%), grade

**Table 1.** Characteristics of women included in the analysis. Values in  $n$  (%) unless otherwise indicated

	Subjects included in the analysis $n = 117$	
<b>Age (years)</b>		
Mean (SD)	30.8	(5.4)
<b>Social deprivation</b>		
0 criterion	6009	(66.0)
1 criterion	1659	(18.2)
2 criteria	808	(8.9)
3 or 4 criteria	633	(6.9)
<b>Education</b>		
≤Primary school,	633	(7.0)
Middle school,	1663	(18.5)
High school,	2189	(24.3)
University,	4525	(50.2)
<b>Mother's country of birth</b>		
Metropolitan France	4126	(45.6)
DOM-TOM	157	(1.7)
Europe	448	(5.0)
North Africa	2036	(22.5)
Sub-Saharan Africa	1465	(16.2)
Asia-Middle East	594	(6.6)
Others	215	(2.4)
<b>Number of previous pregnancies</b>		
0	2614	(28.7)
1	2541	(27.9)
≥2	3957	(43.4)
<b>Body mass index (kg/m<sup>2</sup>),</b>		
< 18.5	505	(5.8)
18.5–24.9	5119	(59.0)
25–29.9	1949	(22.5)
≥30	1102	(12.7)
<b>Medical risk at the beginning of pregnancy</b>		
Low	7327	(80.6)
High	1761	(19.4)
<b>Tobacco consumption</b>		
Non-smoker	7486	(82.7)
Smoker before pregnancy	760	(8.4)
Smoker during pregnancy	808	(8.9)

DOM-TOM, French overseas territories and departments.

**Table 2.** Antenatal care utilisation. Values in  $n$  (%) unless otherwise indicated

	Prevalence $n = 9117$	
<b>Initiation of care</b>		
≥14 weeks	1549	(17.0)
<14 weeks	7549	(83.0)
<b>Number of scheduled antenatal visits</b>		
Mean (SD)	9.7	(3.4)
Median (IQR)	9	(8–11)
<b>Percentage of recommended antenatal visits*</b>		
<50	233	(2.6)
50–79	870	(9.6)
80–109	3501	(38.5)
≥110	4492	(49.4)
<b>First trimester ultrasound</b>		
No	1908	(21.6)
Yes	6943	(78.4)
<b>Second trimester ultrasound</b>		
No	1502	(16.8)
Yes	7428	(83.2)
<b>Third trimester ultrasound**</b>		
No	1450	(16.2)
Yes	7521	(83.8)
<b>Antenatal care according to mAPNCU -1 index***</b>		
Inadequate	1685	(18.5)
Intermediate	584	(6.4)
Adequate	2913	(32.0)
Adequate plus	3914	(43.0)
<b>Antenatal care according to mAPNCU-2 index****</b>		
Inadequate	3044	(34.6)
Intermediate	1413	(16.1)
Adequate	1779	(20.2)
Adequate plus	2564	(29.1)

IQR, interquartile range; mAPNCU, modified Adequacy of Prenatal Care Utilisation; SD, standard deviation; weeks, weeks of gestation.

\*Percentage of recommended visits made, taking pregnancy duration into account.

\*\*For pregnancies with delivery at or after 31 weeks of gestation.

\*\*\*mAPNCU-1, which considers timing of initiation of care and percentage of recommended antenatal visits made.

\*\*\*\*mAPNCU-2, which considers initiation of care, percentage of recommended antenatal visits made, and ultrasound scans performed.

**Table 3.** Prevalence of severe maternal and perinatal morbidity

	Prevalence <i>n</i> = 9117	
	<i>n</i>	%
<b>Severe maternal morbidity or death</b>	<b>259</b>	2.91
Severe pre-eclampsia	73	0.80
Perineal trauma grade 3 or 4*	58	0.64
Severe post-partum haemorrhage	47	0.52
Maternal admission to intensive care unit	41	0.46
Surgical re-intervention	35	0.38
Deep venous thrombosis or pulmonary embolism	24	0.26
Eclampsia	15	0.16
Convulsions (excluding eclampsia)	13	0.14
Abruptio placenta	12	0.13
Uterine rupture	9	0.10
Diabetic ketoacidosis	7	0.08
Severe sepsis	7	0.08
Haemorrhagic shock	6	0.07
Maternal death	0	0.00
<b>Severe perinatal morbidity or death</b>	<b>494</b>	5.47
Birthweight <3rd percentile	269	2.96
Gestational age at birth <32 weeks	101	1.11
Fetal death	62	0.68
Umbilical cord pH <7	47	0.52
Neonatal trauma (except collarbone fracture)	43	0.48
5-minute Apgar score <3	17	0.19
Meconium aspiration syndrome	19	0.21
Early neonatal death**	13	0.14
Neonatal convulsions	6	0.07
Brachial plexus strain	2	0.02

\*Prevalence among vaginal deliveries = 0.76.

\*\*Before discharge from the maternity unit.

3 or 4 perineal trauma (0.64%), and severe postpartum haemorrhage (0.52%) (Table 3). SPM affected 494 newborns or fetuses (5.47%). The principal complications were birthweight below the third percentile (2.96%), very pre-term birth (1.11%) and fetal death (0.68%) (Table 3).

The bivariate analyses presenting the factors associated with SMM or SPM are available in Tables S4 and S5. Medical risk level at the beginning of pregnancy, social deprivation, maternal country of birth, body mass index, and number of previous pregnancies were associated with SMM. SPM was associated with all of those factors except social deprivation, as well as with maternal age, education level, and tobacco consumption.

Table 4 shows the results of the bivariate and multivariate analyses of the associations between various measures of ACU and both SMM and SPM. SMM was associated with a consultation rate of less than half the recommended visits [aOR = 2.40 (1.38–4.17)] but not with late initiation of care, absence of ultrasounds, or inadequate ACU according to either mAPNCU index. Conversely, SPM was

associated with all components of ACU (except late initiation of antenatal care). Women with fewer than either 50% or 50–79% of the recommended visits were at higher risk of SPM than were women with 80–109% of them [aOR = 2.33 (1.47–3.69) for <50% and aOR = 1.74 (1.29–2.35) for 50–79%]. Missing any ultrasound examination was associated with an increased risk of SPM [aOR = 1.32 (1.07–1.63), aOR = 1.49 (1.20–1.86), aOR = 1.31 (1.01–1.69) for first, second and third trimesters], whereas late initiation of antenatal care was not. When we considered the mAPNCU indexes, intermediate ACU according to mAPNCU-1 and inadequate ACU according to mAPNCU-2 were associated to SPM [aOR = 1.77 (1.26–2.50) and aOR = 1.38 (1.06–1.81), respectively].

We found no interaction between antenatal care utilisation and social deprivation, pre-existing medical risk level, number of previous pregnancies or mother's country of birth. There was no major difference between analyses with imputed and non-imputed data (see Table S2).

## Discussion

### Main findings

Our results show inadequate ACU, defined by an index including late initiation of care, low consultation rate, and absence of some recommended ultrasounds, among 34.6% of the study population. This inadequate utilisation was associated with severe morbidity after controlling for other characteristics of women and pregnancies. After controlling for other maternal characteristics of women and pregnancies, inadequate ACU was associated with SMM and SPM, to degrees that vary with the component of care and the outcome considered. Late initiation of care was not associated with severe morbidity. A rate below 50% of the recommended number of visits was associated with an increased risk of both SMM and SPM. Missing an ultrasound scan was associated only with SPM. When we considered the mAPNCU indexes, intermediate ACU according to mAPNCU-1 and inadequate ACU according to mAPNCU-2 were both associated to SPM.

### Strengths and limitations

The main strengths of our study are its large sample size, multicentre nature, and prospective design, which minimises recall bias, and the numerous data items collected about ACU and confounding factors.

We assessed several components of ACU and highlighted their individual associations to SMM and SPM. In addition, the use of a modified APNCU index allowed us to assess the adequacy of ACU according to French policy.

As the number of recommended antenatal visits was defined based on guidelines for low-risk pregnancies, the prevalence of ACU may be biased for women with a high-



**Table 4.** Association between antenatal care and severe maternal and perinatal morbidity

	Severe perinatal morbidity		Severe maternal morbidity	
	OR (95% CI)	aOR (95% CI)*	OR (95% CI)	aOR (95% CI)*
<b>Initiation of care</b>				
>14 weeks	1.08 (0.85–1.37)	1.05 (0.82–1.34)	1.01 (0.73–1.40)	1.07 (0.76–1.52)
≤14 weeks	1	1	1	1
<b>Percentage of antenatal visits**</b>				
<50%	<b>2.33 (1.47–3.69)</b>	<b>2.27 (1.43–3.59)</b>	<b>2.64 (1.53–4.56)</b>	<b>2.40 (1.38–4.17)</b>
50–79%	<b>1.74 (1.29–2.35)</b>	<b>1.75 (1.29–2.37)</b>	0.71 (0.42–1.20)	0.69 (0.40–1.17)
80–109%	1	1	1	1
≥110%	1.22 (0.99–1.50)	1.21 (0.98–1.49)	1.07 (0.82–1.40)	1.05 (0.80–1.38)
<b>First trimester ultrasound</b>				
No	<b>1.32 (1.07–1.63)</b>	<b>1.29 (1.04–1.62)</b>	1.08 (0.80–1.45)	1.00 (0.73–1.36)
Yes	1	1	1	1
<b>Second trimester ultrasound</b>				
No	<b>1.49 (1.20–1.86)</b>	<b>1.51 (1.20–1.89)</b>	0.96 (0.68–1.35)	0.90 (0.64–1.28)
Yes	1	1	1	1
<b>Third trimester ultrasound***</b>				
No	<b>1.31 (1.01–1.69)</b>	<b>1.30 (1.01–1.68)</b>	1.12 (0.80–1.58)	1.09 (0.78–1.53)
Yes	1	1	1	1
<b>mAPNCU-1 index****</b>				
Inadequate	1.28 (0.98–1.67)	1.25 (0.95–1.64)	1.25 (0.88–1.77)	1.29 (0.89–1.85)
Intermediate	<b>1.77 (1.26–2.50)</b>	<b>1.79 (1.26–2.54)</b>	0.64 (0.33–1.25)	0.63 (0.32–1.23)
Adequate	1	1	1	1
Adequate plus	1.14 (0.91–1.42)	1.13 (0.91–1.42)	1.13 (0.85–1.52)	1.12 (0.83–1.50)
<b>mAPNCU-2 index*****</b>				
Inadequate	<b>1.38 (1.06–1.81)</b>	<b>1.37 (1.05–1.80)</b>	1.11 (0.78–1.58)	1.11 (0.77–1.59)
Intermediate	1.24 (0.90–1.71)	1.25 (0.91–1.73)	0.75 (0.47–1.20)	0.79 (0.50–1.24)
Adequate	1	1	1	1
Adequate plus	1.07 (0.80–1.43)	1.07 (0.80–1.42)	1.19 (0.83–1.71)	1.13 (0.79–1.63)

aOR, adjusted odds ratio; CI, Confidence interval; mAPNCU, modified Adequacy of Prenatal Care Utilisation index; OR, odds ratio; weeks, weeks of gestation.

The values in bold are the statistically significant results.

\*Results of imputed models adjusted for maternal age, risk level at the beginning of pregnancy, body mass index, number of previous pregnancies, tobacco consumption, social deprivation, mother's place of birth, education level and maternity unit of delivery.

\*\*Percentage of recommended visits made, taking pregnancy duration into account.

\*\*\*For pregnancies with deliveries at or after 31 weeks of gestation.

\*\*\*\*mAPNCU-1, which considers timing of initiation of care and percentage of recommended antenatal visits made.

\*\*\*\*\*mAPNCU-2, which considers the timing of initiation of care, percentage of recommended antenatal visits made, and ultrasound scans performed.

risk pregnancy, underestimating inadequate ACU and overestimating adequate or more than adequate ACU. Yet, the difference between the number of recommended visits for low- and high-risk women was probably reduced because most of the prenatal visits added in the case of high-risk pregnancies are visits for control of maternal blood pressure or fetal heart monitoring and these visits were not included in the numbers of visits. Furthermore, in the multivariate analysis, OR were adjusted for the medical risk level at the beginning of pregnancy.

To estimate the association between ACU and severe morbidity, we used a composite variable of severe morbidity. This method enabled us to assess the impact of ACU

on SMM and SPM more globally and to take into account outcomes with a prevalence too low to allow them to be studied individually. This approach seems appropriate as we hypothesise that ACU may have an impact on each of these morbidities by providing prevention advice, explaining warning signs, screening for complications and providing care. We chose to focus on severe morbidity so that we could examine the potential impact of ACU on both the onset and the worsening of maternal and perinatal morbidity, given that most complications can only be screened for or treated but not prevented.

Despite an adjustment for major confounding factors,<sup>11,20,24–27</sup> the risk of residual confounding related to

our observational design is the main limitation of our study; some confounding factors related to psychological profile or health behaviour may remain.

The availability of the questionnaires in four different languages reduced the risks of bias and the rate of missing data. Nevertheless, the substantial number of women excluded for missing data remains a limitation of the study. Because these women were more often underprivileged and born abroad than the final sample, we hypothesise that we might have underestimated the strength of the association as they are more likely to have inadequate antenatal care<sup>20</sup> and pregnancy complications.<sup>28</sup>

Another limitation of this study is related to the high prevalence of underprivileged women and women born abroad compared with the national profile,<sup>29</sup> which limits the generalisability of our results.

### Interpretation

The assessment of ACU revealed two different trends. First, as previously reported in other developed countries,<sup>5,6,24,29,30</sup> a high percentage of women appear to have more than the recommended number of visits. Secondly, the percentage of inadequate antenatal care is higher than in similar studies. The prevalence of late initiation of care was 17.0%, versus 6.1% in Belgium.<sup>27</sup> Compared with the 2010 National Perinatal Survey,<sup>29</sup> our number of antenatal visits and our rate of first trimester ultrasounds both appear to be lower. They were, however, concordant with the results of a study conducted in the area of northern Paris.<sup>31</sup> This might be explained by the high prevalence of underprivileged and migrant women in our study sample.<sup>20</sup>

The prevalence of severe morbidity was consistent with previous studies in France,<sup>29,32–36</sup> which estimated rates of severe pre-eclampsia, severe perineal trauma, birthweight below the third percentile and very preterm birth at respectively 0.8, 0.8, 3.1 and 1.5%.

Two studies have previously reported an association between a small number of visits and perinatal morbidity: Petrou<sup>8</sup> described an association between low birthweight, admission to neonatal ICU and perinatal mortality, and Raatikainen<sup>37</sup> described an association between low birthweight, fetal and neonatal deaths. Bouvier-Colle<sup>38</sup> reported a higher risk of maternal ICU admission among women with no antenatal care. This association may reflect the importance of regular ACU to screen for and treat some pathologies, such as severe pre-eclampsia.

The timing of initiation of ACU has been studied by Ayoola,<sup>39</sup> who also found no association with neonatal ICU admission and very weak associations with preterm birth and low birthweight. Nonetheless, we must point out three limitations to consider in interpreting the absence of an association between late initiation and severe morbidity in our study. First, the threshold chosen to define late

initiation is debatable and may be too early. Secondly, information on late initiation of care was collected post-partum, and we cannot rule out the risk of non-differential misclassification. Thirdly, early interventions might have affected complications insufficiently represented in this study (fetal alcohol syndrome, congenital toxoplasmosis or rubella).

Our findings conflict with the results of a meta-analysis of randomised trials<sup>40</sup> assessing the effects of routine late pregnancy ultrasounds (after 24 weeks) that found no association between these examinations and perinatal mortality or preterm birth. Nevertheless, this meta-analysis has limitations. It considered a relatively small number of studies, half of them took place in the 1980s at an early stage of utilisation of ultrasounds in antenatal care, and the interventions and outcomes studied varied widely. Moreover, other studies found that antenatal diagnoses do affect perinatal mortality,<sup>41,42</sup> for example by improving the neonatal care of ultrasound-identified congenital malformations. Besides, our result cannot be explained by a higher rate of medical terminations among women with ultrasounds because terminations were included in SPM. Further research is needed to clarify the efficacy of routine ultrasounds in preventing SPM.

Other studies have reported an association between inadequate ACU, measured by ACU indexes, and perinatal morbidity.<sup>4–7</sup> Most of them, however, took place in North America, where nearly twice as many visits are recommended than in France. Moreover, although we did find an association between a low rate of visits and SMM, the disappearance of this association when we used the mAPNCU index highlights the importance of the measures chosen and the possible disadvantages of using indexes.

### Conclusions

Despite national policies supposed to guarantee universal access to antenatal care, a considerable proportion of women did not receive adequate antenatal care in our study. Those women are at higher risk of severely adverse maternal and perinatal outcomes, independent of their other characteristics. More attention must be paid to women at risk of inadequate ACU, and interventions to improve ACU should be assessed.

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### Disclosure of interests

None declared. Completed disclosure of interests form available to view online as supporting Information.

### Contribution to authorship

E. Azria, C. Estellat, D. Luton, J. F. Oury, T. Schmitz and L. Mandelbrot contributed to the conception of the Pre-CARE cohort and to the acquisition of data. M. Linard and E. Azria contributed to the design of the study. M. Linard, E. Azria and B. Blondel performed the analysis. M. Linard and E. Azria drafted the article. C. Estellat, B. Blondel and C. Deneux-Tharoux contributed to the interpretation of data and critically revised the article. All the authors have read and approved this version of the article.

### Details of ethics approval

The regional review board (CPP-Ile-de-France III, No. 09.341bis, date of approval 19 November 2009) approved the study. Each woman provided oral informed consent, in compliance with French law.

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## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Figure S1.** Flow diagram.

**Figure S2.** Indexes of prenatal care utilisation. Antenatal care was immediately considered inadequate if antenatal care did not begin after 14 weeks.

**Table S1.** Missing data for each variable of interest.

**Table S2.** Complete cases versus multiple imputations.

**Table S3.** Comparison of the characteristics of women included and excluded from the analysis.

**Table S4.** Bivariate analysis—factors associated with severe perinatal morbidity.

**Table S5.** Bivariate analysis – Factors associated with severe maternal morbidity. ■

## References

- Alexander GR, Kotelchuck M. Assessing the role and effectiveness of prenatal care: history, challenges, and directions for future research. *Public Health Rep* (Washington, DC 1974) 2001;116:306–16.
- Moos MK. Prenatal care: limitations and opportunities. *J Obstet Gynecol Neonatal Nurs* 2006;35:278–85.
- Dowswell T, Carroli G, Duley L, Gates S, Gülmezoglu AM, Khan-Neelofur D, et al. Alternative versus standard packages of antenatal care for low-risk pregnancy. *Cochrane Database Syst Rev* 2015;(7): CD000934. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26184394>
- Barros H, Tavares M, Rodrigues T. Role of prenatal care in preterm birth and low birthweight in Portugal. *J Public Health Med* 1996;18:321–8.
- Partridge S, Balayla J, Holcroft C, Abenheim H. Inadequate prenatal care utilization and risks of infant mortality and poor birth outcome: a retrospective analysis of 28,729,765 U.S. deliveries over 8 years. *Am J Perinatol* 2012;29:787–94.
- Heaman MI, Newburn-Cook CV, Green CG, Elliott LJ, Helewa ME. Inadequate prenatal care and its association with adverse pregnancy outcomes: a comparison of indices. *BMC Pregnancy Childbirth* 2008;8:15.
- VanderWeele TJ, Lantos JD, Siddique J, Lauderdale DS. A comparison of four prenatal care indices in birth outcome models: comparable results for predicting small-for-gestational-age outcome but different results for preterm birth or infant mortality. *J Clin Epidemiol* 2009;62:438–45.
- Petrou S, Kupek E, Vause S, Maresh M. Antenatal visits and adverse perinatal outcomes: results from a British population-based study. *Eur J Obstet Gynecol Reprod Biol* 2003;106:40–9.
- Beeckman K, Louckx F, Downe S, Putman K. The relationship between antenatal care and preterm birth: the importance of content of care. *Eur J Public Health* 2013;23:366–71.
- Fiscella K. Does prenatal care improve birth outcomes? A critical review. *Obstet Gynecol* 1995;85:468–79.
- Nair M, Knight M, Kurinczuk J. Risk factors and newborn outcomes associated with maternal deaths in the UK from 2009 to 2013: a national case-control study. *BJOG* 2016;123:1654–62.
- Maupin R, Lyman R, Fatsis J, Prystowski E, Nguyen A, Wright C, et al. Characteristics of women who deliver with no prenatal care. *J Matern Fetal Neonatal Med* 2004;16:45–50.
- World Health Organization, Department of Making Pregnancy Safer. *Standards for Maternal and Neonatal Care—Provision of Effective Antenatal Care*. Geneva: WHO, 2006.
- American Congress of Obstetricians and Gynecologists (ACOG). *Guidelines for Perinatal Care*, 7th edn. Elk Grove Village, IL: American Congress of Obstetricians and Gynecologists (ACOG), 2012.
- NICE. *Antenatal care for uncomplicated pregnancies*, 26 March 2008. Manchester: National Institute for Health and Care Excellence, 2008.
- HAS. Suiivi et orientation des femmes enceintes en fonction des situations à risque identifiées. *Rev Sage-femme* 2007;6:216–8 (in French).
- Schott S, Van Der Avoort I, Descamps P, Richmond D, Adams T, Oei G, et al. Four countries, four ways of discussing low-risk pregnancy and normal delivery. In France, Germany, the Netherlands, and the United Kingdom. *Arch Gynecol Obstet* 2014;289:451–6.



- 18 Bernloehr A, Smith P, Vydellingum V. Antenatal care in the European Union: a survey on guidelines in all 25 member states of the Community. *Eur J Obstet Gynecol Reprod Biol* 2005;122:22–32.
- 19 Buekens P, Kotelchuck M, Blondel B, Kristensen FB, Chen JH, Masuy-Stroobant G. A comparison of prenatal care use in the United States and Europe. *Am J Public Health* 1993;83:31–6.
- 20 Gonthier C, Estellat C, Deneux-Tharaux C, Blondel B, Alfaiate T, Schmitz T, et al. Association between maternal social deprivation and prenatal care utilization: the PreCARE cohort study. *BMC Pregnancy Childbirth* 2017;17:126.
- 21 Kotelchuck M. An evaluation of the kessner adequacy of prenatal care index and a proposed adequacy of prenatal care utilization index. *Am J Public Health* 1994;84:1414–20.
- 22 Alexander GR, Kotelchuck M. Quantifying the adequacy of prenatal care: a comparison of indices. *Public Health Rep* 1996;111:408–19.
- 23 Opatowski M, Blondel B, Khoshnood B, Saurel-Cubizolles M-J. New index of social deprivation during pregnancy: results from a national study in France. *BMJ Open* 2016;6:e009511.
- 24 Beeckman K, Louckx F, Putman K. Determinants of the number of antenatal visits in a metropolitan region. *BMC Public Health* 2010;10:1.
- 25 Delvaux T, Buekens P, Godin I, Boutsen M. Barriers to prenatal care in Europe. *Am J Prev Med* 2001;21:52–9.
- 26 Feijen-de Jong EI, Jansen DE, Baarveld F, van der Schans CP, Schellevis FG, Reijneveld SA. Determinants of late and/or inadequate use of prenatal healthcare in high-income countries: a systematic review. *Eur J Public Health* 2012;22:904–13.
- 27 Fobelets M, Beeckman K, Hoogewys A, Embo M, Buyl R, Putman K. Predictors of late initiation for prenatal care in a metropolitan region in Belgium. A cohort study. *Public Health* 2015;129:648–54.
- 28 Azria E, Stewart Z, Gonthier C, Estellat C, Deneux-Tharaux C. Social inequalities in maternal health. *Gynecol Obstet Fertil* 2015;43:676–82. (In French).
- 29 Blondel B, Lelong N, Kermarrec M, Goffinet F. La santé périnatale en France métropolitaine de 1995 à 2010. Résultats des enquêtes nationales périnatales. *J Gynecol Obstet Biol Reprod* 2012;41:151–66 (In French).
- 30 Backe B. Overutilization of antenatal care in Norway. *Scand J Public Health* 2001;29:129–32.
- 31 Azria E, Guittet L, Delahaye M, Koskas M, Naoura I, Luton D, et al. Improvement of first-trimester ultrasound screening in socially deprived settings through a community-based perinatal network. *Eur J Obstet Gynecol Reprod Biol* 2011;159:351–4.
- 32 Bouvier-Colle MA, Chantry AA, Saucedo M, Deneux-Tharaux C. Severe maternal morbidity: differences between women's intensive care admissions and maternal deaths in the Ile-de-France areas (2006–2009). *Bull Epidémiol Hebd* 2015;101–9.
- 33 Pommereau-Lathelize J, Maisonneuve E, Jousse M, Guilbaud L, Carbonne B, Pierre F. Severe neonatal acidosis: comparison and analysis of obstetrical practices in two French perinatal centers. *J Gynecol Obstet Biol Reprod (Paris)* 2014;43:314–21. (In French).
- 34 European Perinatal health report. The health of pregnant women and babies in Europe in 2010: Euro-Peristat project with SCPE and Eurocat, 2013.
- 35 Observatoire Régional de la Santé d'Ile de France. La santé périnatale en Ile de France. 2015. (In French).
- 36 Chantry AA, Deneux-Tharaux C, Bonnet M-P, Bouvier-Colle M-H. Pregnancy-related ICU admissions in France: trends in rate and severity, 2006–2009. *Crit Care Med* 2015;43:78–86.
- 37 Raatikainen K, Heiskanen N, Heinonen S. Under-attending free antenatal care is associated with adverse pregnancy outcomes. *BMC Public Health* 2007;7:268.
- 38 Bouvier-Colle MH, Varnoux N, Salanave B, Ancel PY, Bréart G. Case-control study of risk factors for obstetric patients' admission to intensive care units. *Eur J Obstet Gynecol Reprod Biol* 1997;74:173–7.
- 39 Ayoola AB, Nettleman MD, Stommel M. Time From pregnancy recognition to prenatal care and associated newborn outcomes. *J Obstet Gynecol Neonatal Nurs* 2010;39:550–6.
- 40 Bricker L, Medley N, Pratt JJ. Routine ultrasound in late pregnancy (after 24 weeks' gestation). *Cochrane Database Syst Rev* 2015;(6):CD001451. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26121659>
- 41 Bonnet D, Coltri A, Butera G, Fermont L, Le BJ, Kachaner J, et al. Detection of Transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. *Circulation* 1999;99:916–8.
- 42 Saari-Kemppainen A, Karjalainen O, Ylöstalo P, Heinonen OP. Fetal anomalies in a controlled one-stage ultrasound screening trial. A report from the Helsinki Ultrasound Trial. *J Perinat Med* 2009;22:279–89.

## Appendix

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