Maternal intensive care unit admission as an indicator of severe acute maternal morbidity: A population-based study

Charlotte Godeberge
Université de Paris, Centre for Epidemiology and Statistics Sorbonne Paris Cité (CRESS), Obstetrical Perinatal and Pediatric Research Team, EPOPé, INSERM, INRA, Paris; Department of Anesthesiology and Critical Care, Hôpital Cochin, Assistance Publique Hôpitaux de Paris, Paris

Catherine Deneux-Tharaux (✉ catherine.deneux-tharaux@inserm.fr)
INSERM U1153 https://orcid.org/0000-0002-6561-3321

Aurélien Séco
Université de Paris, Centre for Epidemiology and Statistics Sorbonne Paris Cité (CRESS), Obstetrical Perinatal and Pediatric Research Team, EPOPé, INSERM, INRA

Mathias Rossignol
Department of Anesthesiology and Critical Care, Hôpital Lariboisière, Assistance Publique Hôpitaux de Paris, Paris

Anne Alice Chantry
Université de Paris, Centre for Epidemiology and Statistics Sorbonne Paris Cité (CRESS), Obstetrical Perinatal and Pediatric Epidemiology Research Team, EPOPé, INRA, Paris, Baudelocque Midwife School, Assistance Publique Hôpitaux de Paris, Paris

Marie-Pierre Bonnet
Université de Paris, Centre for Epidemiology and Statistics Sorbonne Paris Cité (CRESS), Obstetrical Perinatal and Pediatric Research Team, EPOPé, INSERM, INRA, Paris, Department of Anesthesiology and Critical Care, Hôpital Armand TRousseau, Assistance Publique Hôpitaux de Paris, Paris

Research

Keywords: critical care, epidemiology, intensive care unit, obstetrics, severe acute maternal morbidity, obstetric hemorrhage

Posted Date: January 31st, 2020

DOI: https://doi.org/10.21203/rs.2.22398/v1

License: ☒ ☀ This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Version of Record: A version of this preprint was published at Anesthesia & Analgesia on May 14th, 2021. See the published version at https://doi.org/10.1213/ANE.0000000000005578.
Abstract

Background Severe acute maternal morbidity, accounting for any life-threatening complication during pregnancy or after delivery, is a major issue in maternal health. Measuring and monitoring it seems critical for assessing the quality of maternal health care. We explored the relevance of maternal ICU admission as an indicator of severe acute maternal morbidity by characterizing, among maternal ICU admissions, the profile of women with severe acute maternal morbidity and their ICU stay, according to the association with other criterion of severe acute maternal morbidity.

Methods Secondary analysis of a multiregional prospective population-based study of 2,540 women with severe acute maternal morbidity according to a multicriteria definition based on national experts’ consensus and including ICU admission.

Results 511 women were admitted to an ICU during or up to 42 days after pregnancy (2.8 per 1,000 deliveries; 20.1% of women with severe acute maternal morbidity); 15.5% had no other severe acute maternal morbidity criterion. Among women with severe acute maternal morbidity, on multivariable multinomial analysis and adjusting for cause, the odd of intensive care unit admission with another morbidity criterion was increased for migrant from outside of Europe or Africa (adjusted odds ratio = 2.1 [95% CI 1.3-3.4]), with multiple gestation (adjusted odds ratio =1.5 [1.0-2.2]), and intrapartum cesarean (adjusted odds ratio =1.5 [1.1-2.2]). The odd of intensive care unit admission with no other morbidity criterion was increased with pre-existing medical conditions (adjusted odds ratio =2.2 [1.2-4.0]) and cesarean before labor (adjusted odds ratio =3.0 [1.4-6.1]). Women admitted to an ICU with no other morbidity criterion had no interventions for organ support.

Conclusions Among women with severe acute maternal morbidity, one in five is admitted to an ICU; 15.5% of these have no other severe acute maternal morbidity criterion and their admission appears mostly indicated for continuous monitoring. The use of ICU admission alone as a single criterion morbidity is misleading to define severe acute maternal morbidity; this criterion needs to be refined to be included in the definition of severe acute maternal morbidity. These results also challenge the current organization of acute care for women with severe maternal morbidity.

Background

Maternal mortality is considered as a major marker of maternal health and of health system performance [1]. However, for every woman who died, 20 to 100 women experience a potentially life-threatening complication during pregnancy or just after, defining severe acute maternal morbidity [2]. For several years, given the rarity of maternal deaths, severe acute maternal morbidity has received increasing attention. Measuring and monitoring severe acute maternal morbidity seems critical for assessing the quality of maternal health care. Yet there is still no consensual definition of severe acute maternal morbidity that would allow for international and temporal comparisons, and its burden remains poorly documented.
Maternal admission to an intensive care unit (ICU) is commonly used as a single indicator of severe acute maternal morbidity [3–8]. However, maternal ICU admission depends on not only patient severity but also care organization and local practices [9–13]. Consequently, women admitted to the ICU could present heterogeneous levels of severity in maternal morbidity. Including maternal ICU admissions in the severe acute maternal morbidity definition could bias the estimations of the true incidence, causes and risk factors of severe acute maternal morbidity. A retrospective study from the United States [14] reported a 10-fold higher incidence of maternal ICU admission than in two other population-based studies from France [9] and from The Netherlands [12]; such a difference may reflect variations in ICU definition and in the care of women with severe acute maternal morbidity, and not just potential differential rates of severe acute maternal morbidity. Two previous studies estimated the proportion of women admitted to an ICU without receiving any intensive care-specific intervention, but both had limitations: one from Southern England conducted 20 years ago was not population-based [10], the other used data not specifically collected to explore maternal morbidity but rather routinely coded data from hospitals in Maryland between 1999 and 2008 to ascertain cases [14]. By improving our knowledge of maternal ICU admissions with no other morbidity criterion with recent prospective population-based detailed data, we could identify potential pitfalls of using maternal ICU admission as a severe acute maternal morbidity indicator.

To determine whether maternal ICU admission is a relevant indicator of severe acute maternal morbidity, we performed a population-based study characterizing, among maternal ICU admissions, the profile of women with severe acute maternal morbidity and their ICU stay, according to the association with other criterion of severe acute maternal morbidity.

**Methods**

We performed a secondary analysis of the EPIMOMS study, a prospective population-based study specifically designed to study severe acute maternal morbidity in six French regions (2012–2013) [15–17]. The EPIMOMS study was approved by the Commission Nationale de l'Informatique et des Libertés (CNIL, no. 912210). All women included were informed about the study and did not indicate their opposition to participate. According to the French legislation at that time, no written informed consent was necessary. The source population consisted of 182,309 pregnant women receiving care at 119 maternity units and 136 ICUs, that is, one fifth of pregnant women in France, with similar characteristics as the national profile obtained from the French National Perinatal Survey [18]. Women ≥ 18 years old who delivered at ≥ 22 weeks’ gestation were eligible for inclusion.

The first step of the EPIMOMS project was to develop a definition of severe acute maternal morbidity by using an extensive national-expert Delphi consensus process, with the objective to include acute maternal complications that could induce severe health changes [15]. The final EPIMOMS definition of severe acute maternal morbidity is a combination of six diagnostic criteria (major obstetric bleeding, eclampsia, severe pre-eclampsia, pulmonary embolism, cerebrovascular accident, selected psychiatric disorders), six organ dysfunction criteria (hepatic, hematologic, respiratory, cardiovascular, renal, neurologic) and two interventional criteria (ICU admission, laparotomy after delivery) occurring between 22 weeks’ gestation
and 42 days after delivery (Additional file 1: The EPIMOMS multi-criteria definition of severe maternal morbidity) [15–17]. Maternal ICU admission is one of the criteria of the EPIMOMS definition of severe acute maternal morbidity; it includes admission to an ICU or to specialty acute care units, but not admission to a post-anesthesia care unit or to an intermediate care unit [19].

During the study period, in every participating unit, a caregiver prospectively identified women with severe acute maternal morbidity according to the EPIMOMS definition. The completeness of case ascertainment was further validated by a review of delivery logbooks, birth registers, hospital discharge databases, and laboratory records. For every woman meeting criteria of severe acute maternal morbidity, the clinicians in charge identified the causal condition responsible for severe acute maternal morbidity. Detailed information on individual characteristics was collected by a manual review of medical charts.

Our study population included all women with severe acute maternal morbidity identified in the EPIMOMS study (N = 2,540), differentiated into three groups: women not admitted to an ICU, women admitted to an ICU with at least one other criterion of severe acute maternal morbidity, and women admitted to an ICU with no other criterion of severe acute maternal morbidity.

We explored the following characteristics: maternal characteristics (age, place of birth, obesity, chronic hypertension, other notable pre-existing medical conditions); pregnancy characteristics (previous pregnancies, in vitro fertilization for current pregnancy, multiple gestation); and characteristics of delivery (gestational age at delivery, mode of delivery); cause of acute maternal complication in 10 exclusive categories (seven corresponding to single causes [obstetric hemorrhage, hypertensive disorders of pregnancy, pulmonary embolism, cerebrovascular accident, sepsis, decompensation of a pre-existing medical condition, other isolated causes] and three combining several causes [obstetric hemorrhage and hypertensive disorders of pregnancy, obstetric hemorrhage and conditions other than hypertensive disorders of pregnancy, and a combination of conditions different from obstetric hemorrhage]); timing of acute complication occurrence (antepartum, intra- or postpartum, and postpartum after discharge from the delivery stay). The characteristics explored among women admitted in an ICU were ICU length of stay, some specific interventions performed during the ICU stay (non-invasive ventilation, mechanical ventilation, arterial catheter insertion, central venous catheter insertion, hemodialysis, vasopressor infusion), presence of organ dysfunction (according to the EPIMOMS definition, see Additional file 1), and maternal death.

**Statistical analysis**

The rate of maternal ICU admission was calculated with its 95% confidence interval (95% CI) in the source population and among all women with severe acute maternal morbidity.

Causes and timing of acute maternal complication, and the characteristics of women, pregnancy, and delivery were described overall and compared between the three groups of women.
We identified characteristics associated with maternal ICU admission by using univariable then multivariable multinomial logistic regression models. The dependent variable was in three categories: women not admitted to an ICU (reference category), women admitted to an ICU with at least one other criterion of severe acute maternal morbidity, and women admitted to an ICU with no other criterion of severe acute maternal morbidity. All the models were adjusted for the cause of acute maternal complication. The selection of the other variables included in the models was based on the literature and on results of the univariable analysis. Maternal age was the only continuous variable in the final model and did not show any deviation from linearity. The characteristics of delivery were taken into account only for women with intra- or postpartum severe acute maternal morbidity, since for women with antepartum severe acute maternal morbidity, the antepartum condition responsible for morbidity may have influenced both the admission to an ICU (outcome) and the mode of delivery (exposure, for example cesarean).

Among women admitted to an ICU, we compared those with at least one other criterion of severe acute maternal morbidity and those with no other criterion of severe acute maternal morbidity for ICU length of stay, occurrence of organ dysfunction, maternal death and performance of intensive care interventions.

Continuous variables are presented as mean ± standard deviation (SD) except for ICU length of stay, which is presented as median (interquartile range [IQR]). Categorical variables are summarized as number (%). Tests for comparisons were chi-square or Fisher exact tests for categorical variables and Student t or Wilcoxon rank sum tests for quantitative variables, as appropriate.

In the multivariable model, 16.5% of women had missing values for at least one variable. Characteristics of women with missing values were similar to those of women with non-missing data (Additional file 2: Comparison of women without and with missing data). We used multiple imputations with chained equations to impute missing data (three datasets). All results are presented with the imputed data. We also performed a multivariable logistic regression in complete cases. P < 0.05 was considered statistically significant; all statistical tests were two-tailed. Analyses were performed with Stata 13 (StataCorp LP, College Station, TX, USA).

Results

In the source population, 511 women were admitted to an ICU (2.8 per 1000 deliveries [95% CI 2.6–3.1]), accounting for 20.1% (18.5–21.6) of 2,540 women with severe acute maternal morbidity. Among these 511 admitted women, 79 (15.5%, 12.4–18.6) did not have another criterion of severe acute maternal morbidity (Fig. 1).

The distribution of causes of acute maternal complication differed between the 3 groups of women (Table 1). Among women not admitted to an ICU and among those admitted to an ICU with another morbidity criterion, the most frequent causes were obstetrical hemorrhage and hypertensive disorders of pregnancy. Among women admitted to an ICU with no other morbidity criterion, the two most frequent causes were hypertensive disorders and other isolated causes (mostly continuous monitoring of women
with a condition at risk of acute aggravation (44% of other isolated causes), and acute digestive or hepatic diseases (25%). Overall, there were 14 maternal deaths (7.7/100,000 deliveries), including 8 women admitted to ICU with another morbidity criterion and none among women admitted with no other morbidity criterion.
Table 1
Characteristics of the acute maternal complication overall and by maternal intensive care unit admission

| Characteristics of the acute maternal complication                                      | All women with SAMM n = 2,540 | No ICU admission n = 2,029 (79.9%) | ICU admission | P<sup>a</sup> |
|----------------------------------------------------------------------------------------|---------------------------------|------------------------------------|---------------|-------------|
|                                                                                        |                                 |                                    | With another SAMM criterion n = 432 (17.0%) | With no other SAMM criterion n = 79 (3.1%) |
| Cause<sup>b</sup>                                                                     |                                 |                                    |               |             |
| Obstetric hemorrhage                                                                 | 1,498 (59.0%)                  | 1,337 (65.9%)                     | 151 (34.9%)   | 10 (12.7%)  |
| Hypertensive disorders of pregnancy<sup>c</sup>                                         | 383 (15.1%)                    | 255 (12.6%)                       | 105 (24.3%)   | 23 (29.1%)  |
| Pulmonary embolism                                                                   | 27 (1.1%)                      | 18 (0.90)                         | 9 (2.1)       | 0 (0)       |
| Cerebrovascular accident                                                              | 28 (1.1%)                      | 10 (0.50)                         | 18 (4.2)      | 0 (0)       |
| Sepsis                                                                                | 32 (1.3%)                      | 17 (0.80)                         | 9 (2.1)       | 6 (7.6)     |
| Decompensation of a pre-existing medical condition                                  | 56 (2.2%)                      | 30 (1.5)                          | 17 (3.9)      | 9 (11.4)    |
| Other isolated causes                                                                | 281 (11.1%)                    | 228 (11.2%)                       | 28 (6.5)      | 25 (31.6)   |
| Obstetric hemorrhage and hypertensive disorder of pregnancy                          | 52 (2.1%)                      | 26 (1.3)                          | 25 (5.8)      | 1 (1.3)     |
| Obstetric hemorrhage and other condition                                              | 105 (4.1)                      | 60 (2.9)                          | 45 (10.4)     | 0 (0)       |

<sup>a</sup> test of differences between the three groups

<sup>b</sup> in exclusive categories

<sup>c</sup> pre-eclampsia, eclampsia or HELLP syndrome

Proportions are presented by column

SAMM: severe acute maternal morbidity

ICU: intensive care unit
Table 2 shows the proportion of ICU admissions among women with severe acute maternal morbidity by maternal, pregnancy and delivery characteristics (Table 2, row percentages). On multivariable analysis, after adjustment for the cause of acute maternal complication, women from regions other than Europe or Africa and with multiple gestation were more likely to be admitted to an ICU with another morbidity criterion, whereas women with pre-existing medical conditions were more likely to be admitted to an ICU with no other morbidity criterion (Table 3). Among women with intra- or postpartum severe acute maternal morbidity (n = 1936), similar associations were found (Additional file 3: Risk factors of maternal ICU admission with or with no other morbidity criterion for women with intra or postpartum SAMM). In addition, women who had a cesarean delivery during labor were more likely to be admitted to an ICU with another morbidity criterion (adjusted odds ratio (aOR) = 1.5, 95% CI = 1.1–2.2), whereas women with cesarean delivery before labor were more likely to be admitted to an ICU with no other morbidity criterion (aOR = 3.0, 95% CI = 1.4–6.1), as compared with vaginal delivery. The analysis conducted with non-missing data provided similar results (Additional file 4: Risk factors of maternal intensive care unit admission with or with no other morbidity criterion for women with intra or postpartum SAMM).
admission with and without another morbidity criterion for women with severe acute maternal morbidity, analyses in complete cases, N = 2120).
Table 2
Maternal, pregnancy and delivery characteristics among women with SAMM overall and by maternal ICU admission

| Characteristics                          | All women with SAMM N = 2,540 | No ICU admission N = 2,029 (79.9%) | ICU admission | p^a |
|------------------------------------------|-------------------------------|-----------------------------------|--------------|-----|
|                                          | n (Col %)                     | n (Row %)                         | n (Row %)   | n (Row %) |
| Maternal characteristics                 |                               |                                   |              |     |
| Age (years)^b                            | 31.3 ± 5.6                    | 31.2 ± 5.6                        | 31.6 ± 5.8   | 30.1 ± 6.0 | 0.42 |
| Maternal place of birth                  |                               |                                   |              |     |
| Europe                                   | 1,641 (72.6)                  | 1,335 (81.3)                      | 254 (15.5)   | 52 (3.2)  | < 0.01|
| North Africa                             | 234 (10.4)                    | 183 (78.2)                        | 46 (19.7)    | 5 (2.1)   |     |
| Sub-Saharan Africa                       | 245 (10.8)                    | 187 (76.3)                        | 53 (21.6)    | 5 (2.0)   |     |
| Other^c                                  | 141 (6.2)                     | 101 (71.6)                        | 37 (26.2)    | 3 (2.1)   |     |
| Obesity                                  | Yes                           | 357 (15.2)                        | 286 (80.1)   | 58 (16.3) | 0.54 |
|                                          | No                            | 1,997 (84.8)                      | 1,622 (81.2) | 323 (16.2) | 52 (2.6)|     |
| Chronic hypertension                     | Yes                           | 70 (2.8)                          | 55 (78.6)    | 12 (17.1) | 3 (4.3)| 0.69 |
|                                          | No                            | 2,434 (97.2)                      | 1,946 (80.0) | 418 (17.1) | 70 (2.9)|     |
| Other pre-existing medical condition^d    | Yes                           | 310 (12.4)                        | 231 (74.5)   | 57 (18.4) | 22 (7.1)| < 0.01|
|                                          | No                            | 2,196 (87.6)                      | 1,770 (80.6) | 374 (17.0) | 52 (2.4)|     |
| Pregnancy characteristics                |                               |                                   |              |     |
| Previous pregnancies                     |                               |                                   |              |     |
| Primiparous                              | 1,235 (49.7)                  | 987 (79.9)                        | 207 (16.8)   | 41 (3.3)  | 0.86 |
| Characteristics                          | All women with SAMM N = 2,540 | No ICU admission N = 2,029 (79.9%) | ICU admission |
|-----------------------------------------|-------------------------------|-----------------------------------|---------------|
|                                         | n (Col %)                     | n (Row %)                         | n (Row %)     | n (Row %) |
| Multiparous without prior cesarean      | 810 (32.6)                    | 650 (80.3)                        | 140 (17.2)    | 20 (2.5)  |
| Multiparous with prior cesarean         | 439 (17.7)                    | 350 (79.7)                        | 76 (17.3)     | 13 (3.0)  |
| In vitro fertilization                 |                               |                                   |               |           |
| Yes                                     | 150 (6.0)                     | 123 (82.0)                        | 27 (18.0)     | 0          |
| No                                      | 2,355 (94.0)                  | 1,878 (79.7)                      | 405 (17.2)    | 72 (3.1)  |
| Multiple gestation                      |                               |                                   |               |           |
| Yes                                     | 207 (8.3)                     | 157 (75.8)                        | 49 (23.7)     | 1 (0.5)   |
| No                                      | 2,299 (91.7)                  | 1,843 (80.2)                      | 382 (16.6)    | 74 (3.2)  |

Characteristics of delivery among women with SAMM intra- or postpartum

| Gestational age (weeks) | N = 1,936 | N = 1,588 (82.0%) | N = 285 (14.7%) | N = 63 (3.3%) |
|-------------------------|-----------|-------------------|-----------------|--------------|
| < 37                    | 344 (18.0)| 251 (73.0)        | 72 (20.9)       | 21 (6.1)     |
| ≥ 37                    | 1,564 (82.0)| 1,320 (84.4)      | 206 (13.2)      | 38 (2.4)     |

| Mode of delivery | N = 1,936 | N = 1,588 (82.0%) | N = 285 (14.7%) | N = 63 (3.3%) |
|------------------|-----------|-------------------|-----------------|--------------|
| Vaginal delivery | 1,025 (53.4)| 888 (86.6)       | 120 (11.7)      | 17 (1.7)     |
| Cesarean during labor | 399 (20.8)| 312 (78.2)       | 78 (19.6)       | 9 (14.8)     |
| Cesarean before labor | 496 (25.8)| 376 (75.8)       | 86 (17.3)       | 34 (6.9)     |

a: test of differences between the three groups

b: mean ± SD
| Characteristics | All women with SAMM N = 2,540 | No ICU admission N = 2,029 (79.9%) | ICU admission | Pa |
|-----------------|-------------------------------|----------------------------------|---------------|----|
|                 |                               |                                  | With another SAMM criterion N = 432 (17.0%) | With no other SAMM criterion N = 79 (3.1%) |
|                 | n (Col %)                     | n (Row %)                        | n (Row %)     | n (Row %)     |

\(^c\): Asia (Japan, China, South East Asia), America (North America, South America), India, Middle East

\(^d\): Other pre-existing medical condition, defined by a binary variable for the presence of at least 1 of the following: Hematologic disease or hemoglobinopathy, psychiatric illness, diabetes, history of venous thromboembolism, coronary artery disease, cardiomyopathy, congestive heart failure, epilepsy, multiple sclerosis, liver disease including infectious hepatitis, auto-immune disease, inflammatory bowel disease, nephropathy, history of hemodialysis, pulmonary disease, myasthenia gravis, neoplasia, HIV, and any other chronic medical condition

SAMM: Severe acute maternal morbidity

ICU: intensive care unit
Table 3
Risk factors of maternal intensive care unit admission with and without another morbidity criterion for women with severe acute maternal morbidity

| Characteristics                      | ICU admission | With another SAMM criterion | With no other SAMM criterion |
|--------------------------------------|---------------|------------------------------|------------------------------|
|                                      | cOR | 95% CI  | aOR | 95% CI | cOR | 95% CI  | aOR | 95% CI |
| Age (years)                          | 1.0 | 0.99–1.0 | 1.0 | 0.99–1.0 | 0.96 | 0.92–1.0 | 0.96 | 0.92–1.0 |
| Maternal place of birth              |     |          |     |        |     |          |     |        |
| Europe                               | 1.0 | 1.0–2.0  | 1.4 | 0.9–1.9 | 0.6 | 0.2–1.5  | 0.5 | 0.2–1.4 |
| North Africa                         | 1.3 | 0.9–1.9  | 1.4 | 0.9–2.0 | 0.6 | 0.2–1.5  | 0.5 | 0.2–1.4 |
| Sub-Saharan Africa                   | 1.5 | 1.0–2.0  | 1.2 | 0.9–1.7 | 0.7 | 0.2–1.9  | 0.6 | 0.2–1.8 |
| Othersb                              | 1.9 | 1.2–3.0  | 2.1 | 1.3–3.4 | 0.8 | 0.2–2.3  | 0.6 | 0.2–2.1 |
| Obesity                              | 1.0 | 0.7–1.4  | 0.9 | 0.7–1.4 | 1.2 | 0.6–2.4  | 0.9 | 0.5–1.9 |
| Pre-existing medical conditionc      | 1.2 | 0.9–1.6  | 0.9 | 0.6–1.2 | 3.0 | 1.8–5.0  | 2.2 | 1.2–4.0 |
| Multiple gestation                   | 1.5 | 1.1–2.1  | 1.5 | 1.0–2.2 | 0.2 | 0.04–1.6 | 0.3 | 0.03–1.9 |

Univariable and multivariable multinomial logistic analyses of characteristics of women admitted to an ICU with or without another severe morbidity criterion in women with severe acute maternal morbidity (N = 2540) – imputed data. The reference category is women with severe acute maternal morbidity not admitted to an ICU.

a: Multivariable multinomial logistic model including all the variables listed in the table and the cause of severe acute maternal complication (one variable with 10 exclusive categories).

b: Asia (Japan, China, South East Asia), America (North America, South America), India, Middle East

c: Other pre-existing medical condition, defined by a binary variable for the presence of at least 1 of the following: Hematologic disease or hemoglobinopathy, psychiatric illness, diabetes, history of venous thromboembolism, coronary artery disease, cardiomyopathy, congestive heart failure, epilepsy, multiple sclerosis, liver disease including infectious hepatitis, auto-immune disease, inflammatory bowel disease, nephropathy, history of hemodialysis, pulmonary disease, myasthenia gravis, neoplasia, HIV, & any other chronic medical condition

cOR: crude odds ratio
Among maternal ICU admissions, 37.6% of women received at least one intensive care intervention (Table 4). Length of ICU stay was shorter and intensive care interventions were less frequent for women admitted to an ICU with no other morbidity criterion than for those admitted with another morbidity criterion. Among women with no other acute maternal morbidity criterion, six had intensive care interventions but none for organ support: two women had mechanical ventilation after general anesthesia, four had arterial catheter insertion for continuous hemodynamic monitoring, and only one had a central venous catheter indicated for enteral feeding in the context of acute pancreatitis. None of these women had organ dysfunction.
Table 4
Specific intensive care interventions, organ dysfunctions and maternal death among women admitted to an ICU during or up to 42 days after pregnancy

| Characteristics                          | Maternal ICU admission n = 511 | With another SAMM criteria n = 432 | With no other SAMM criterion n = 79 | p\textsuperscript{a} |
|------------------------------------------|-------------------------------|-----------------------------------|------------------------------------|------------------|
| Length of stay (days\textsuperscript{b}) | 2.0 [1.0–4.0]                 | 2.0 [1.0–4.0]                     | 1.0 [0.58–2.5]                     | < 0.01           |
| <24 hours                                | 80 (15.7)                     | 58 (13.4)                         | 22 (27.8)                         | < 0.01           |
| At least one intensive care intervention | 192 (37.6)                    | 186 (43.0)                        | 6 (7.6)                           | < 0.01           |

Intensive care interventions

| Intensive care interventions          | Maternal ICU admission n = 511 | With another SAMM criteria n = 432 | With no other SAMM criterion n = 79 |
|--------------------------------------|-------------------------------|-----------------------------------|------------------------------------|
| Non-invasive ventilation             | 37 (7.7)                      | 37 (9.0)                          | 0                                  |
| Mechanical ventilation               | 116 (23.7)                    | 114 (27.8)                        | 2 (2.5)                            |
| Arterial catheter                    | 79 (16.3)                     | 75 (18.5)                         | 4 (5.1)                            |
| Central venous catheter              | 64 (13.2)                     | 63 (15.5)                         | 1 (1.3)                            |
| Hemodialysis                         | 25 (5.1)                      | 25 (6.1)                          | 0                                  |
| Use of vasopressor drugs             | 28 (5.7)                      | 28 (6.9)                          | 0                                  |
| Organ dysfunction                    | 219 (42.9)                    | 219 (50.7)                        | 0                                  |
| Maternal death                       | 8 (1.6)                       | 8 (1.9)                           | 0                                  |

\textsuperscript{a}: test of differences between women admitted to an ICU with another severe acute maternal morbidity criterion and women admitted to an ICU with no other severe acute maternal morbidity criterion

\textsuperscript{b}: median (interquartile range [IQR])

Proportions are presented in column (Col)

Discussion

Among women with severe acute maternal morbidity, one in five was admitted to an ICU; 15.5% of these had no other severe acute morbidity criterion. The profile of maternal ICU admission differed according to
an association with another morbidity criterion in terms of cause, maternal individual characteristics, and need for intensive care interventions.

Our results suggest that the use of ICU admission alone as a single criterion morbidity is misleading to define severe acute maternal morbidity, because a significant part of maternal ICU admissions do not have other serious severity criteria. According to the organization of care in each specific context, the extent of this subgroup may vary. Thus, the use of ICU admission as a single criterion of severe acute maternal morbidity may lead to overestimate the incidence of severe acute maternal morbidity, skew the comparisons of severe acute maternal morbidity between different settings, and alter the profile of women with severe acute maternal morbidity both quantitatively and qualitatively. Our results provide support to the recent recommendations from the American College of Obstetricians and Gynecologists and the Society for Maternal–Fetal Medicine on the screening of severe acute maternal morbidity, which challenged the use of maternal ICU admission as a single severe acute maternal morbidity indicator \[4\]. In these recommendations, the experts propose to include, in a list of diagnoses and complications constituting severe acute maternal morbidity, “any intensive care unit admission that includes treatment or diagnostic or therapeutic procedure” \[4\]. Indeed, the use of ICU admission in combination with at least one other marker of severity to monitor severe acute maternal morbidity would decrease the impact of care organization on the assessment of severe acute maternal morbidity rate and profile.

The original approach of this study was to explore potential differences in characteristics of women and of complications among maternal ICU admissions, according to the presence of other severe morbidity criteria more directly reflecting the acute status of the women. This analysis was possible because of the EPIMOMS study’s design and definition. Risk factors of maternal ICU admission in women with another morbidity criterion were similar to those of severe acute maternal morbidity usually described in high-resource countries, such as foreign maternal demographic origin, multiple gestation, and cesarean delivery during labor \[20, 21\]. However, admission to an ICU with no other morbidity criterion was associated with pre-existing medical conditions and cesarean delivery before labor. These women did not receive any intensive care intervention for organ support and had shorter ICU length of stay than those admitted with another morbidity criterion. Consequently, ICU admission does not appear as an appropriate marker of severe acute maternal morbidity in this sub-group. In addition, ICU admission in these women, more as a precautionary measure or limited to continuous monitoring, raises the concern of exposing these women to several stressors: noise, sleep deprivation and immobilization \[22–24\]. Anxiety and depression are frequently reported after ICU admission and could result in post-traumatic stress disorder \[25–27\]. Additionally, in the obstetric context, maternal ICU admission leads to separating the mother from her child, which could affect maternal–infant bonding \[28, 29\]. Finally, at the collective level, admission to an ICU has substantially higher costs than admission to other units \[30\]. However, obviously some pregnant or postpartum women with severe co-morbid disease without an acute morbid event need close continuous monitoring, which cannot be delivered in a maternity unit or general ward. In this context, alternatives to ICU admission, such as admission to intermediate acute care units, with enhanced nursing care able to provide some elements of ICU monitoring but in a less intensive environment, have been proposed. Intermediate care units specialized in the care of severe obstetric
patients within an obstetric setting have been set up in the last decades in some high-resource countries such as the United Kingdom, United States, or France [31]. The potential benefits of these units and the quality of care delivered remain to be evaluated.

This study has several strengths. As compared with other studies exploring severe acute maternal morbidity [3, 8, 32, 33], we used a comprehensive definition for severe acute maternal morbidity obtained by formalized national experts’ consensus [15–17]. The prospective identification of women with severe acute maternal morbidity and the review of inclusions guaranteed good exhaustiveness of the study population and minimized the risk of selection bias. This study was population-based and performed during a short time period, so the results were not affected by changes in ICU practices. As compared with epidemiologic studies on maternal ICU admission using routine hospital databases [9, 13, 14], detailed data on maternal ICU admission were available, particularly the time sequence of events. Additionally, the cause of severe maternal complication was identified by the clinicians in charge and not by algorithms of codes.

This study has some limitations. The proportion of women with missing data for at least one covariate was 16.5%. However, the profile of these women was similar to that of women without missing data, which supports the hypothesis of missing at random and allows for using multiple imputations. The number of intermediate care units may have increased in France since the 2012-2013-study period, and maternal admissions in these units may be more frequent now [36]. Indications for maternal ICU admission may differ across countries, because of specific organization systems, especially billing, and ICU bed availability [13, 37, 38]; however, the incidence of maternal ICU admissions we found was similar as that reported in other high-resource countries [8, 13, 39].

Conclusions

Maternal ICU admission represents a heterogeneous profile of women: women admitted to an ICU with no other morbidity criterion have different underlying causes, different modes of delivery and less severe outcomes than women admitted with other morbidity criteria. Consequently, maternal ICU admission alone is misleading as a single indicator of severe acute maternal morbidity; this criterion needs to be refined or expanded to be included in the definition of severe acute maternal morbidity. Finally, these results also challenge the current organization of acute care for women with severe maternal morbidity.

Abbreviations

ICU
intensive care unit
IQR
inter quartile range
SD
standard deviation
Declarations

Ethics approval and consent to participate
The EPIMOMS study was approved by the Commission Nationale de l’Informatique et des Libertés (CNIL, no. 912210). All women included were informed about the study and did not indicate their opposition to participate. According to the French legislation at that time, no written informed consent was necessary.

Consent for publication
Not applicable

Availability of data and materials
The datasets generated and/or analyzed during the current study are not publicly available due to ethical and legal restrictions. This is because the present study includes an important number of variables that, together, could be used to re-identify the participants based on a few key characteristics and then be used to have access to other personal data. Therefore, the French National Data Safety Authority (CNIL) strictly forbids making such data freely available. But they are available from the corresponding author upon reasonable request from the EPIMOMS steering committee.

Competing interests
The authors declare they have no competing interests.

Funding
The EPIMOMS study was funded by support from the National Research Agency (Agence Nationale de la Recherche (ANR), Paris France; grant no. ANR-10-BLAN-1134-01) and the Ile de France Regional Health Agency (Agence Régionale de la Santé Ile de France, Paris, France; grant no.PPS784). CG received a grant from the Club d’Anesthésie Réanimation en Obstétrique (CARO, Paris, France).

Authors’ contributions
CDT, MPB, CG had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. CDT, MPB, CG, MR and AAC conceptualized the study and wrote the manuscript. CG and AS performed the statistical analysis. CDT obtained funding and supervised the study. All authors contributed to the analysis plan and interpretation of the results and reviewed and approved the final manuscript. CDT is the guarantor.

**Acknowledgments**

The authors thank the EPIMOMS study group for the conception of the EPIMOMS study: Bruno LANGER, for the Naître en Alsace perinatal network; Corinne DUPONT and René-Charles RUDIGOZ, for the Rhône-Alpes Aurore perinatal network; Françoise VENDITTELLI, for the Auvergne perinatal network; Gaël BEUCHER, for the Basse-Normandie perinatal network; Patrick ROZENBERG, for the MYPA perinatal region, Ile de France region; Lionel CARBILLON, for the Naître dans l’Est Francilien network, Ile de France region; Elie AZRIA and Nathalie BAUNOT, for the Paris Nord perinatal network; Catherine CRENN-HEBERT and Gilles KAYEM, for the 92 Nord perinatal network, Ile de France region; Jeanne FRESSON, for the Lorraine perinatal network; Alexandre MIGNON for the Société Française d’Anesthésie Réanimation (SFAR); Sandrine TOUZET, for the Santé Publique pole, Hospices Civils de Lyon; Marie-Pierre BONNET, Marie-Hélène BOUVIER-COLLE, Anne CHANTRY, Coralie CHIESA-DUBRUILLE, Catherine DENEUX-THARAUX and Aurélien SECO, for the INSERM EPOPé Research team.

The authors thank the coordinators of the participating regional perinatal networks: Alsace, Aurore, Auvergne, Basse-Normandie, Maternité Yvelines et Paris (MYPA), Naître dans l’Est Francilien (NEF), Paris Nord, 92 Nord, Lorraine; and the following individuals: Chloé Barasinski (R.M., Ph.D., Auvergne perinatal network, Clermont-Ferrand), Sophie Bedel (R.M., Lorraine perinatal network, Nancy), Aline Cline D’Amour (R.M., National Institute for Health and Medical Research (INSERM) Unit 1153 Obstetrical, Perinatal and Pediatric Epidemiology Research Team (EPOPé), Paris), Laurent Gaucher (R.M., Aurore perinatal network, Lyon), Isabelle Lecreff (R.M., 92 Nord perinatal network, Colombes), Blandine Masson (R.M., Aurore perinatal network, Lyon), Carole Ramousset (B.S., Alsace perinatal network, Strasbourg), Mathias Rossignol (M.D., Assistance Publique Hôpitaux de Paris (APHP), Paris), Zelda Stewart (M.D., M.Sc., Caen University Hospital, Caen), Dalila Talaourar (R.M., National Institute for Health and Medical Research (INSERM) Unit 1153 Obstetrical, Perinatal and Pediatric Epidemiology Research Team (EPOPé), Paris), Yacine Toure (B.S., Lower Normandy perinatal network, Caen), Nicole Wirth (R.M., Lorraine perinatal network, Nancy) for their contribution to the implementation of the EPIMOMS study in their region; the obstetricians, midwives and anesthetists who contributed to case identification and documentation in their hospital, and the research assistants who collected the data.
References

1. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A-B, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014;2:e323-333.

2. Geller SE, Koch AR, Garland CE, MacDonald EJ, Storey F, Lawton B. A global view of severe maternal morbidity: moving beyond maternal mortality. Reprod Health. 2018;15:98.

3. Callaghan WM, Grobman WA, Kilpatrick SJ, Main EK, D'Alton M. Facility-based identification of women with severe maternal morbidity: it is time to start. Obstet Gynecol. 2014;123:978–81.

4. American College of Obstetricians and Gynecologists and the Society for Maternal–Fetal Medicine, Kilpatrick SK, Ecker JL. Severe maternal morbidity: screening and review. Am J Obstet Gynecol. 2016;215:B17-22.

5. Bouvier-Colle M-H, Mohangoo AD, Gissler M, Novak-Antolic Z, Vutuc C, Szamotulska K, et al. What about the mothers? An analysis of maternal mortality and morbidity in perinatal health surveillance systems in Europe. BJOG Int J Obstet Gynaecol. 2012;119:880–9.

6. Kilpatrick SJ, Berg C, Bernstein P, Bingham D, Delgado A, Callaghan WM, et al. Standardized severe maternal morbidity review: rationale and process. Obstet Gynecol. 2014;124:361–6.

7. Main EK, Abreo A, McNulty J, Gilbert W, McNally C, Poeltler D, et al. Measuring severe maternal morbidity: validation of potential measures. Am J Obstet Gynecol. 2016;214:643.e1-643.e10.

8. Zwart JJ, Richters JM, Ory F, de Vries JIP, Bloemenkamp KWM, van Roosmalen J. Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: a nationwide population-based study of 371,000 pregnancies. BJOG Int J Obstet Gynaecol. 2008;115:842–50.

9. 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.

10. Hazelgrove JF, Price C, Pappachan VJ, Smith GB. Multicenter study of obstetric admissions to 14 intensive care units in southern England. Crit Care Med. 2001;29:770–5.

11. Zhao Z, Han S, Yao G, Li S, Li W, Zhao Y, et al. Pregnancy-Related ICU Admissions From 2008 to 2016 in China: A First Multicenter Report. Crit Care Med. 2018;46:e1002–9.

12. Zwart JJ, Dupuis JRO, Richters A, Ory F, van Roosmalen J. Obstetric intensive care unit admission: a 2-year nationwide population-based cohort study. Intensive Care Med. 2010;36:256–63.

13. Aoyama K, Pinto R, Ray JG, Hill AD, Scales DC, Lapinsky SE, et al. Variability in intensive care unit admission among pregnant and postpartum women in Canada: a nationwide population-based observational study. Crit Care. 2019;23:381.

14. Wanderer JP, Leffert LR, Mhyre JM, Kuklina EV, Callaghan WM, Bateman BT. Epidemiology of obstetric-related ICU admissions in Maryland: 1999-2008*. Crit Care Med. 2013;41:1844–52.

15. Deneux-Tharaux C, Bouvier-Colle M-H. Severe acute maternal morbidity in France: the EPIMOMS population-based study. Am J Obstet Gynecol. 2017;216:S345–6.
16. Korb D, Goffinet F, Seco A, Chevret S, Deneux-Tharaux C, EPIMOMS Study Group. Risk of severe maternal morbidity associated with cesarean delivery and the role of maternal age: a population-based propensity score analysis. CMAJ Can Med Assoc J J Assoc Medicale Can. 2019;191:E352–60.

17. Madar H, Goffinet F, Seco A, Rozenberg P, Dupont C, Deneux-Tharaux C. Severe Acute Maternal Morbidity in Twin Compared With Singleton Pregnancies. Obstet Gynecol. 2019;133:1141–50.

18. Blondel B, Coulm B, Bonnet C, Goffinet F, Le Ray C, National Coordination Group of the National Perinatal Surveys. Trends in perinatal health in metropolitan France from 1995 to 2016: Results from the French National Perinatal Surveys. J Gynecol Obstet Hum Reprod. 2017;46:701–13.

19. Leone M, Constantin J-M, Dahyot-Fizelier C, Duracher-Gout C, Joannes-Boyau O, Langeron O, et al. French intensive care unit organisation. Anaesth Crit Care Pain Med. 2018;37:625–7.

20. Creanga AA, Bateman BT, Kuklina EV, Callaghan WM. Racial and ethnic disparities in severe maternal morbidity: a multistate analysis, 2008-2010. Am J Obstet Gynecol. 2014;210:435.e1-8.

21. Guglielminotti J, Landau R, Wong CA, Li G. Patient-, Hospital-, and Neighborhood-Level Factors Associated with Severe Maternal Morbidity During Childbirth: A Cross-Sectional Study in New York State 2013-2014. Matern Child Health J. 2019;23:82–91.

22. Kalfon P, Mimoz O, Auquier P, Loundou A, Gauzit R, Lepape A, et al. Development and validation of a questionnaire for quantitative assessment of perceived discomforts in critically ill patients. Intensive Care Med. 2010;36:1751–8.

23. Parthasarathy S, Tobin MJ. Sleep in the intensive care unit. Intensive Care Med. 2004;30:197–206.

24. Simons KS, Verweij E, Lemmens PMC, Jelfs S, Park M, Spronk PE, et al. Noise in the intensive care unit and its influence on sleep quality: a multicenter observational study in Dutch intensive care units. Crit Care. 2018;22:250.

25. Parker AM, Sricharoenchai T, Raparla S, Schneck KW, Bienvenu OJ, Needham DM. Posttraumatic stress disorder in critical illness survivors: a metaanalysis. Crit Care Med. 2015;43:1121–9.

26. McKinley S, Aitken LM, Alison JA, King M, Leslie G, Burmeister E, et al. Sleep and other factors associated with mental health and psychological distress after intensive care for critical illness. Intensive Care Med. 2012;38:627–33.

27. Righy C, Rosa RG, da Silva RTA, Kochhann R, Migliavaca CB, Robinson CC, et al. Prevalence of posttraumatic stress disorder symptoms in adult critical care survivors: a systematic review and meta-analysis. Crit Care. 2019;23:213.

28. Bystrova K, Ivanova V, Edhborg M, Matthiesen A-S, Ransjö-Arvidson A-B, Mukhamedrakhimov R, et al. Early contact versus separation: effects on mother-infant interaction one year later. Birth. 2009;36:97–109.

29. Howard K, Martin A, Berlin LJ, Brooks-Gunn J. Early mother-child separation, parenting, and child well-being in Early Head Start families. Attach Hum Dev. 2011;13:5–26.

30. McLaughlin AM, Hardt J, Canavan JB, Donnelly MB. Determining the economic cost of ICU treatment: a prospective “micro-costing” study. Intensive Care Med. 2009;35:2135–40.
31. Saravanakumar K, Davies L, Lewis M, Cooper GM. High dependency care in an obstetric setting in the UK. Anaesthesia. 2008;63:1081–6.

32. Brace V, Penney G, Hall M. Quantifying severe maternal morbidity: a Scottish population study. BJOG Int J Obstet Gynaecol. 2004;111:481–4.

33. Nair M, Kurinczuk JJ, Knight M. Establishing a National Maternal Morbidity Outcome Indicator in England: A Population-Based Study Using Routine Hospital Data. PloS One. 2016;11:e0153370.

34. Wanderer JP, Leffert LR, Mhyre JM, Kuklina EV, Callaghan WM, Bateman BT. Epidemiology of obstetric-related ICU admissions in Maryland: 1999-2008*. Crit Care Med. 2013;41:1844–52.

35. Panchal S, Arria AM, Harris AP. Intensive care utilization during hospital admission for delivery: prevalence, risk factors, and outcomes in a statewide population. Anesthesiology. 2000;92:1537–44.

36. Barry Y, Deneux-Tharaux C, Saucedo M, Goulet V, Guseva-Canu I, Regnault N, et al. Maternal admissions to intensive care units in France: Trends in rates, causes and severity from 2010 to 2014. Anaesth Crit Care Pain Med. 2019;38:363–9.

37. Wong DJN, Popham S, Wilson AM, Barneto LM, Lindsay HA, Farmer L, et al. Postoperative critical care and high-acuity care provision in the United Kingdom, Australia, and New Zealand. Br J Anaesth. 2019;122:460–9.

38. Gooch RA, Kahn JM. ICU bed supply, utilization, and health care spending: an example of demand elasticity. JAMA. 2014;311:567–8.

39. Pollock W, Rose L, Dennis C-L. Pregnant and postpartum admissions to the intensive care unit: a systematic review. Intensive Care Med. 2010;36:1465–74.

Figures
Figure 1
Study population