

Appendix 1. EPIMOMS Study Group

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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.

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Appendix 2. EPIMOMS Multicriteria Standardized Definition of Severe Acute Maternal Morbidity, Developed Through a National Delphi Formal Expert Consensus Process, Applicable to Pregnant Women After 22 Weeks of Gestation and Until the 42nd Day After Their Delivery

ITEMS	CRITERIA (AT LEAST ONE)
Major obstetric bleeding	<ul style="list-style-type: none"> . Volume of postpartum blood loss \geq 1500 mL . Blood transfusion \geq 4 units of red blood cells . Uterine arteries embolization . Vascular ligation, compressive uterine sutures . Emergency peripartum hysterectomy
Eclampsia	Seizures in a woman either diagnosed with preeclampsia, or; if not, not attributable to another cause
HELLP syndrome	HELLP syndrome* <u>only if</u> associated with hepatic hematoma or rupture
Severe preeclampsia	Preeclampsia [†] only if it induced preterm delivery for a main maternal indication before 32 gestational weeks
Pulmonary embolism	Clinical symptoms consistent with pulmonary embolism + confirmation with imaging + treatment (imaging: computed tomography or ventilation perfusion scintigraphy or Doppler; treatment: heparin or thrombolysis or embolectomy)
Stroke	Cerebral imaging showing cerebral infarction or hemorrhage, or venous thrombosis, or subarachnoid hemorrhage

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Cerebral transient ischemic attack	Neurological deficit with symptoms [‡] completely regressive in 24 hours and normal cerebral imaging, in absence of associated migraine confirmed by neurologist
Severe psychiatric disorder	<ul style="list-style-type: none"> . Severe acute psychiatric disorder or acute decompensation of chronic disease (psychosis, major depression, bipolar disorder) diagnosed by psychiatrist . Suicide attempt
Cardiovascular dysfunction	<ul style="list-style-type: none"> . Cardiac arrest . Acute pulmonary edema with hypoxemia < 60 mmHg or SaO₂ < 90% or treated with diuretics . Shock: Systolic blood pressure < 90 mmHg during > 60 min or unresponsive to plasma expansion . Acute left ventricular dysfunction: left ventricular ejection fraction < 40% . Need for continuous IV vasopressor or inotrope drugs . Decompensation of a preexisting cardiopathy with need for specialized management . Troponinemia > 1 µg/L

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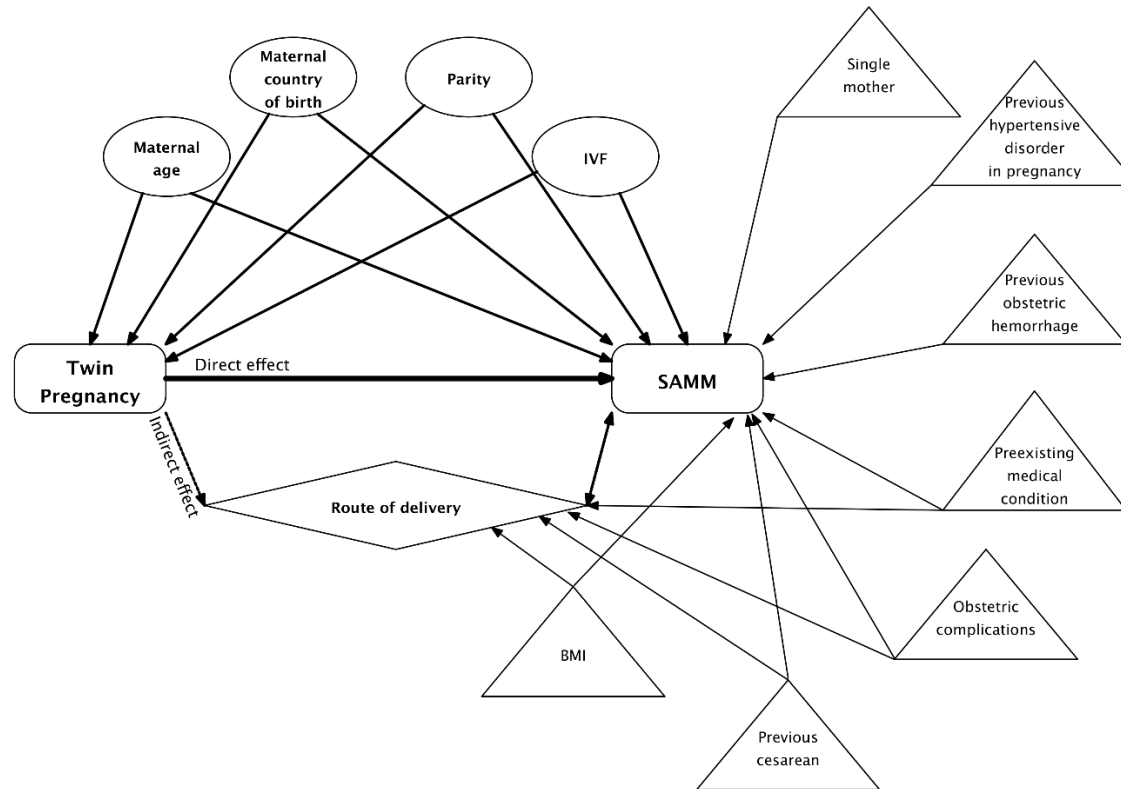
Respiratory dysfunction	. Acute hypoxemia < 60 mmHg or SaO ₂ < 90% with spontaneous ventilation . Mechanical ventilation, or noninvasive ventilation in the absence of chronic disease, not related to anesthesia	* Hemolysis, Elevated Liver enzymes > 3 times the normal level and Low Platelets < 50,000 /mm ³
Renal dysfunction	. Acute renal failure with creatininemia > 135 µmol/L . Acute oliguria < 500 mL/24h	† Defined as hypertension ≥ 140/90 mmHg and proteinuria ≥ 0.3 g/24h
Neurological dysfunction	Coma, regardless of stage and duration [§]	‡ Monocular blindness, aphasia, hemianopsia, unilateral or bilateral motor or sensory disorders
Hepatic dysfunction	. Prothrombin time < 60%, in the absence of constitutional deficiency . Direct bilirubinemia > 20 µmol/L	
Hematological dysfunction	. Thrombocytopenia < 50,000 /mm ³ in the absence of chronic disorder . Acute anemia < 7 g/dL . Disseminated intravascular coagulation: platelets < 50,000 /mm ³ or prothrombin time < 60% or fibrinogen < 2 g/L	§ Stage 1 coma = impaired consciousness with obtundation and reaction to painful stimuli only
Emergency surgery apart from childbirth procedure	. Secondary hysterectomy . Laparotomy for postdelivery complication apart from hematoma or parietal infection	
Admission to Intensive Care Unit		
Maternal death		

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Appendix 3. Directed acyclic graph illustrating causal relationships between twin pregnancy and severe acute maternal morbidity. (Circle: confounding factors; diamond: intermediate factors; triangle: variables associated with severe acute maternal morbidity but not with twin pregnancy; IVF, in vitro fertilization; BMI: body mass index). The DAG is a tool in which the exposure-outcome relationship can be depicted with confounding, exposures of interest, and mediating variables. A DAG also referred to as causal diagram, provides an indication of which variables are confounders that need to be adjusted for in an analysis and which ones do not qualify as confounders. Data from Ananth CV, Schisterman EF. Confounding, causality, and confusion: the role of intermediate variables in interpreting observational studies in obstetrics. *Am J Obstet Gynecol* 2017;217:167-175.



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Appendix 4. Characteristics of Women With Severe Acute Maternal Morbidity (Cases) (4.A) and Control Women (4.B) According to the Presence or Absence of Missing Data for the Main Analysis

4.A – Characteristics of women with severe acute maternal morbidity (SAMM cases)

Characteristics of women	SAMM cases with no missing data N = 2227	SAMM cases with ≥ 1 missing data N = 273
Main exposure		
Twin pregnancy	183 (8.2)	14 (5.1)
Maternal characteristics		
Age (y)*	31.2 (± 5.6)	31.2 (± 5.4)
Country of birth		
France	1549 (69.6)	14 (82.3)
Other Europe	68 (3.0)	0 (0.0)
North Africa	228 (10.2)	1 (5.9)

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Sub-Saharan Africa	242	(10.9)	1	(5.9)
Other	140	(6.3)	1	(5.9)
Single mother	145	(6.7)	10	(6.9)
BMI				
< 18.5	152	(7.2)	15	(6.5)
18.5-24.9	1216	(57.6)	130	(55.8)
25.0-29.9	427	(20.3)	46	(19.7)
≥ 30	315	(14.9)	42	(18.0)
Preexisting medical condition[†]	333	(15.0)	38	(14.3)
History of abdominopelvic surgery	161	(7.2)	10	(3.8)
Parity				
Nulliparous	1111	(49.9)	118	(47.4)
Parous	1116	(50.1)	131	(52.6)

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Previous cesarean delivery	400	(18.0)	37	(14.9)
Previous obstetric hemorrhage	106	(4.8)	7	(2.6)
Previous hypertensive disorder in pregnancy	124	(5.6)	13	(5.1)

Pregnancy

In vitro fertilization	136	(6.1)	10	(3.7)
Abnormal placentation	137	(6.2)	7	(2.7)
Third-trimester anemia	555	(26.5)	61	(26.9)

Delivery

Gestational age at delivery[‡] (weeks)	38.7	(35.7-40.3)	39.0	(36.7-40.4)
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Mode of delivery

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Spontaneous vaginal	713	(32.2)	105	(39.2)
Operative vaginal	294	(13.3)	40	(14.9)
Antepartum cesarean	813	(36.6)	79	(29.5)
Intrapartum cesarean	398	(17.9)	44	(16.4)

Data are n (%) unless otherwise specified

BMI: body mass index

* Mean (\pm sd)

† Chronic hypertension, diabetes, dyslipidemia, constitutional bleeding disorders, asthma, allergy, psychiatric disorders, thromboembolic disease, stroke, transient ischemic attack, coronary heart disease, severe trauma, heart disease, epilepsy, hemoglobinopathy, hepatopathy, thyroid dysfunction, systemic lupus erythematosus, autoimmune disease, inflammatory bowel disease, nephropathy, cancer, myasthenia gravis, myopathy, multiple sclerosis, respiratory disease

‡ Median (interquartile range)

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4.B – Characteristics of control women

Characteristics of women	Controls with no missing data	Controls with ≥ 1 missing data
	N = 3048	N = 602
Main exposure		
Twin pregnancy	53 (1.7)	6 (1.0)
Maternal characteristics		
Age (y)*	30.6 (± 5.2)	30.2 (± 5.4)
Country of birth		
France	2300 (75.5)	13 (86.6)
Other Europe	111 (3.7)	0 (0.0)
North Africa	315 (10.3)	1 (6.7)
Sub-Saharan Africa	172 (5.6)	1 (6.7)
Other	150 (4.9)	0 (0.0)

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Single mother	120	(4.2)	15	(3.1)
BMI				
< 18.5	216	(7.3)	45	(7.9)
18.5-24.9	1798	(61.0)	339	(59.5)
25.0-29.9	590	(20.0)	134	(23.5)
≥ 30	343	(11.7)	52	(9.1)
Preexisting medical condition†	235	(7.7)	39	(6.5)
History of abdominopelvic surgery	126	(4.1)	24	(4.0)
Parity				
Nulliparous	1283	(42.1)	234	(40.3)
Parous	1765	(57.9)	346	(59.7)
Previous cesarean delivery	379	(12.5)	62	(10.9)
Previous obstetric hemorrhage	71	(2.3)	12	(2.0)

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Previous hypertensive disorder in pregnancy	89	(2.9)	8	(1.3)
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Pregnancy

In vitro fertilization	70	(2.3)	6	(1.0)
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Abnormal placentation	20	(0.7)	5	(0.8)
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Third-trimester anemia	448	(16.1)	107	(19.1)
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Delivery

Gestational age at delivery[‡] (weeks)	39.6	(38.7-40.6)	39.6	(38.6-40.6)
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Mode of delivery

Spontaneous vaginal	2033	(66.7)	423	(70.3)
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Operative vaginal	381	(12.5)	69	(11.4)
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Antepartum cesarean	329	(10.8)	57	(9.5)
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Data are n (%) unless otherwise specified

BMI: body mass index

* Mean (\pm sd)

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‡ Median (interquartile range)

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Appendix 5. Characteristics of Severe Acute Maternal Morbidity Among Cases According to Pregnancy Type

Categories of Severe Acute Maternal Morbidity	Twin		Singleton	
	pregnancy		pregnancy	
	N = 197	(%)	N = 2,303	(%)
Timing				
Antepartum	45	(22.8)	540	(23.4)
Intra/postpartum	152	(77.2)	1763	(76.6)
Underlying causal condition*				
Obstetric hemorrhage	149	(75.6)	1492	(64.8)
Including*:				
Blood loss ≥ 1500 mL	106	(53.8)	850	(36.9)
Transfusion ≥ 4 units of red blood cells	47	(23.9)	397	(17.2)
Conservative surgery or embolization	53	(26.9)	384	(16.7)
Hysterectomy following hemorrhage	10	(5.1)	94	(4.1)
Disseminated intravascular coagulation	31	(15.7)	245	(10.6)
Acute postpartum anemia with hemoglobin < 7 g/dL in the absence of chronic anemia	59	(30.0)	749	(32.5)
Hypertensive complications [†]	37	(18.8)	451	(19.6)

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Including*:				
Severe preeclampsia	24	(12.2)	340	(14.8)
Eclampsia	4	(2.0)	47	(2.0)
Severe HELLP syndrome	16	(8.1)	158	(6.9)
Severe psychiatric disorder	3	(1.5)	92	(4.0)
Decompensation of preexisting condition	7	(3.6)	86	(3.7)
Sepsis	3	(1.5)	49	(2.1)
Pulmonary embolism	5	(2.5)	34	(1.5)
Amniotic fluid embolism	2	(1.0)	12	(0.5)
Other	23	(11.7)	224	(9.7)
<hr/>				
Severity				
Maternal near-miss [‡]	86	(43.7)	848	(36.8)
Not maternal near-miss	111	(56.3)	1455	(63.2)
Number of SAMM events:				
1	107	(54.3)	1542	(67.0)
2	54	(27.4)	497	(21.6)
≥ 3	36	(18.3)	264	(11.4)

Data are n (%)

HELLP syndrome: hemolysis, elevated liver enzymes, and low platelet count syndrome

* Non-exclusive categorization

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† Severe preeclampsia, HELLP syndrome, eclampsia, placental abruption with hypertensive disorder

‡ According to WHO definition (see Box 1) and including maternal deaths

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