

Postpartum Maternal Mortality and Cesarean Delivery

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OBJECTIVE: A continuous rise in the rate of cesarean delivery has been reported in many countries during the past decades. This trend has prompted the emergence of a controversial debate on the risks and benefits associated with cesarean delivery. Our objective was to provide a valid estimate of the risk of postpartum maternal death directly associated with cesarean as compared with vaginal delivery.

METHODS: A population-based case-control study was designed, with subjects selected from recent nationwide surveys in France. To control for indication bias, maternal deaths due to antenatal morbidities were excluded. For the 5-year study period 1996–2000, 65 cases were included. The control group was selected from the 1998 French National Perinatal Survey and included 10,244 women. Multivariable logistic regression analysis was used to adjust for confounders.

RESULTS: After adjustment for potential confounders, the risk of postpartum death was 3.6 times higher after cesarean than after vaginal delivery (odds ratio 3.64 95% confidence interval 2.15–6.19). Both prepartum and intrapartum cesarean delivery were associated with a significantly increased risk. Cesarean delivery was associated with a significantly increased risk of maternal death from complications of anesthesia, puerperal infection, and venous thromboembolism. The risk of death from

postpartum hemorrhage did not differ significantly between vaginal and cesarean deliveries.

CONCLUSION: Cesarean delivery is associated with an increased risk of postpartum maternal death. Knowledge of the causes of death associated with this excess risk informs contemporary discussion about cesarean delivery on request and should inform preventive strategies. (*Obstet Gynecol* 2006;108:541–8)

LEVEL OF EVIDENCE: II-2

A continuous rise in the rate of cesarean delivery has been reported in many developed countries during the past decades. In France, this rate increased from 10.8 % in 1981 to 20.2 % in 2003,^{1,2} representing approximately 160,000 women having cesarean delivery each year. A concomitant increase in the prevalence of situations where cesarean delivery is indicated to prevent severe maternal or infant complications is unlikely. It seems likely that the range of indications for cesarean delivery has broadened considerably, and that more cesarean deliveries are performed with few or no medical indications. In France, the recent rise in the global cesarean rate is explained entirely by the rise in prepartum cesarean delivery.¹ Recently, some professionals have gone so far as to propose elective cesarean delivery as an acceptable first-choice method of delivery for women with normal pregnancy.³ This trend has prompted the emergence of a controversial debate on the risks and benefits associated with cesarean delivery.⁴

This study focuses on one of the potential risks of cesarean delivery: maternal mortality. Although maternal death has become rare in high-resource countries, it remains a tragic event, and excess maternal mortality risk would have a strong effect on the balance between potential harms and benefits of cesarean delivery. In addition, maternal mortality rates have shown little improvement during the past 20 years in developed countries, and factors involved

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in this stagnation need to be more completely identified. The method of delivery may constitute one potentially modifiable risk factor of maternal mortality. Finally, if an exposure is shown to be a risk factor for maternal death, it is likely to also be linked to nonlethal severe maternal morbidity, which is more prevalent but more difficult to identify.

Previous studies of the relationship between cesarean delivery and risk of maternal death have reported inconsistent results,⁵⁻¹⁵ and definitive evidence is still lacking. Most of these studies were conducted on women who delivered more than 15 years ago, and their conclusions may not be valid in application to current anesthesia and obstetric care. Moreover, previous papers have been criticized because of potential "indication bias," referring to the fact that an antenatal morbidity may be both the indication for cesarean delivery and the cause of maternal death, leading to an apparent association between cesarean delivery and maternal mortality. Finally, the timing of cesarean delivery, prepartum or intrapartum has rarely been considered.

Our objectives in this study were to provide a valid estimate of the risk of postpartum maternal death directly associated with cesarean delivery as compared with vaginal delivery, and to examine further the differential risk associated with prepartum and intrapartum cesarean delivery. A case-control study was designed, with cases and controls selected from recent nationwide surveys.

PARTICIPANTS AND METHODS

Since 1995, maternal deaths in France have been identified and characterized through a Confidential Enquiry on Maternal Deaths (Enquête Confidentielle sur les Morts Maternelles).¹⁶ This national surveillance system uses the International Classification of Diseases definition of a maternal death, which is "the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by pregnancy or its management but not from accidental or incidental causes." Deaths with any mention of pregnancy or birth or puerperium on review of the death certificate's content are selected by the national center for death statistics and reported to the Confidential Enquiry on Maternal Deaths. For each death that occurred in a current or recent context of pregnancy, a confidential enquiry is conducted by a team of assessors comprising an obstetrician and an anesthetist. Using a standardized detailed abstraction form, the assessors collect the relevant clinical information related to the woman and her

death through interviews and a review of hospital records and autopsy reports. Deaths are then anonymously reviewed by a national committee of experts, and an assessment is made regarding 1) the underlying cause of death, 2) whether the death is a maternal death (according to the ICD definition), and 3) the quality of care provided if it is a maternal death. For the 5-year study period 1996-2000, 269 maternal deaths were identified by this surveillance system. Of these, 51 occurred during pregnancy or after a pregnancy that did not result in a birth (ectopic pregnancy, abortion), and were consequently excluded, because the study focus was on the route of delivery.

To be consistent with the definition used for controls (described below), outcome of pregnancy was considered birth with a gestational age of 22 weeks or a birth weight of 500 g. Among the remaining 218 deaths, further selection was performed to exclude women with conditions before delivery likely to have influenced both their risk of dying and their probability of having a cesarean delivery (selection by indication bias). Deaths that occurred after a multiple birth were excluded. Deaths after singleton birth were then categorized in 3 groups according to the time when the morbidity responsible for the death (ie, the cause of death selected by the national expert committee) occurred: 1) deaths due to chronic conditions present before pregnancy (including diseases of the circulatory system, hematologic diseases, diseases of the respiratory system, mental disorders, disease of the digestive system, neoplasms, and chronic infections, $n=44$); 2) deaths due to obstetric conditions that developed during pregnancy but before delivery (including hypertensive disorders in pregnancy, hemorrhage due to placenta praevia or accreta and abruptio placenta, amniotic fluid embolisms, cerebral venous thrombosis, intracerebral hemorrhage, chorioamnionitis, $n=64$); and 3) deaths due to conditions that occurred during or after delivery ($n=98$). Deaths categorized in the two first groups were not included in this study, because the choice of the delivery route may have been influenced by the maternal prenatal general or obstetric morbidities. Specifically, this categorization allowed the selection and exclusion of all cases where cesarean was performed because of a maternal condition which also was responsible for the woman's death. Finally, deaths in women who were hospitalized during pregnancy were further excluded, because this characteristic was considered a marker of serious antenatal morbidity. The remaining 65 deaths were the cases included in the case-control analysis, defined as women who died within the 42 days postpartum after a pregnancy with no hospitalization



and that resulted in a singleton birth, from causes not due to conditions or complications present before delivery. Figure 1 summarizes the process of defining the cases.

Controls were selected from the 1998 French National Perinatal Survey. The French National Perinatal Surveys collect data on all births with a gestational age of 22 weeks or a birth weight of 500 g in all maternity units in France during a 1-week period, with the aim of monitoring the evolution of indicators of perinatal health and medical practice.¹⁷ Data are collected through interviews with the mother and from medical records. These surveys were conducted in 1995, 1998, and 2003. The comparison group for our case-control study was extracted from the 1998 National Perinatal Survey sample (n=13,478 women), because this year falls in the middle of the 1996-2000 time window for case inclusion. By definition, the control group should not include women who died in the 42 days postpartum. This information was not available from the survey data. However,

although we cannot exclude the fact that a few women who died in the postpartum period are included in this sample, the reported rate of maternal mortality in the country is low enough (10/100,000 live births for 1995-1999¹⁸) to consider the number of such cases negligible. The same selection criteria that were used for cases were applied. After excluding women who had multiple birth (n=236, including four women with missing information) and women who were hospitalized during pregnancy (n=2,998, including 316 women with missing information), the remaining 10,244 women constituted the final control group used in the case-control study. Ideally, and to make selection criteria completely similar for cases and controls, women with life-threatening morbidities present before delivery should have been excluded from the control group. However, these women could not be identified based on the information available for controls. We used the admission in intensive care unit (ICU) in the early postpartum period as a proxy variable for severe morbidity. A separate analysis was

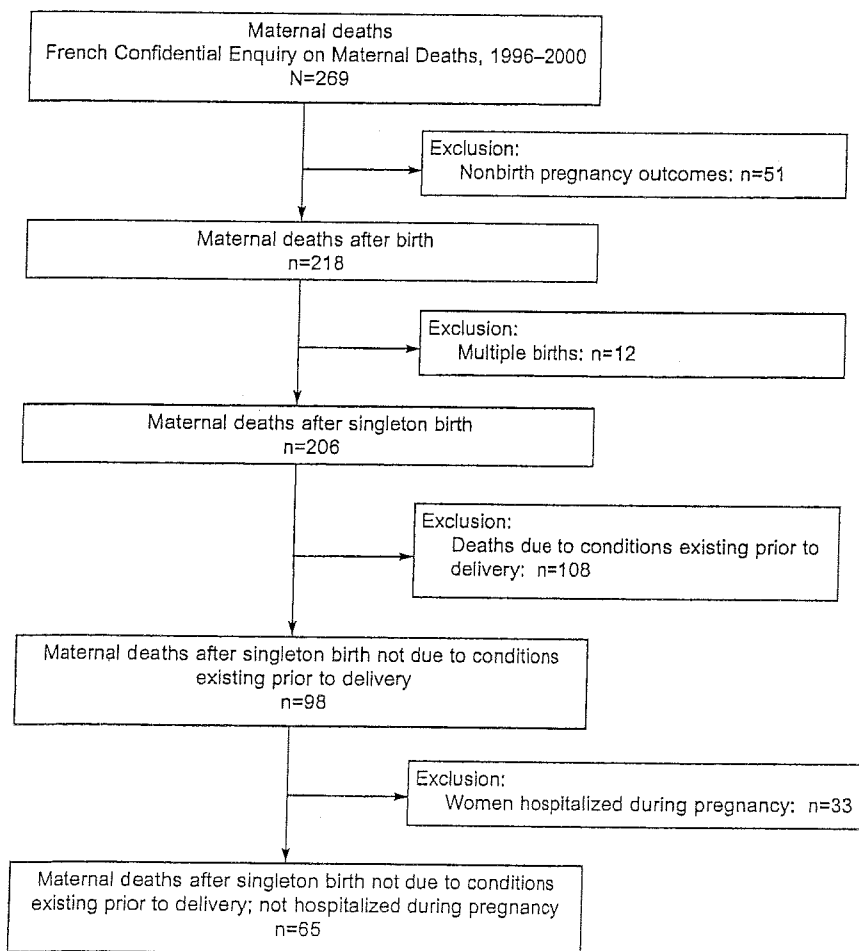


Fig. 1. Selection of cases. Deneux-Tharaux. *Maternal Mortality and Cesarean Delivery*. *Obstet Gynecol* 2006.



conducted after exclusion of controls transferred to ICU after delivery (n=37, 0.36% of controls). The French National Perinatal Surveys and the French Confidential Enquiry on Maternal Deaths have been approved by the Commission Nationale de l'Informatique et des Libertés.

The primary predictor variable of interest was the route of delivery, cesarean or vaginal. Cesarean deliveries were further classified as prepartum or intrapartum. Information on the route of delivery was available for all cases, and missing in 48 (0.5%) controls. The following variables were collected and examined as potential confounders in the association between route of delivery and maternal mortality: mother's age, nationality, parity, premature delivery, maternity unit's annual number of deliveries, maternity unit's status (in 3 categories: university public, nonuniversity public, and private).

Differences in the distribution of route of delivery between cases and controls were examined, using χ^2 and Fisher exact tests. Crude odds ratios of postpartum maternal death for cesarean delivery were calculated. Multivariable logistic regression analysis was used to adjust for relevant covariates, and adjusted odds ratios were calculated. Interactions between the route of delivery and other covariates were systematically tested. The level of statistical significance was .05. STATA software (StataCorp LP, College Station, TX) was used to conduct analyses.

RESULTS

Characteristics of cases and controls are shown in Table 1. Compared with controls, cases were significantly older, more likely to be multiparous, and to have delivered preterm.

The proportion of cesarean delivery was significantly higher among cases than among controls (41.5% compared with 14.9%, Table 2). Both prepartum and intrapartum cesarean deliveries were more frequent among cases (Table 2). Cesarean delivery was associated with a significantly increased risk for postpartum maternal death. After adjustment for potential confounders, the risk of postpartum death was 3.6 times higher after cesarean delivery than after vaginal delivery. As compared with vaginal delivery, both prepartum and intrapartum cesarean deliveries were associated with a significantly increased risk for maternal death (Table 2). The risk did not differ significantly between prepartum and intrapartum cesarean; the adjusted odds ratio (OR) of postpartum maternal death for intrapartum as compared with prepartum cesarean was 1.39 (95% confidence interval 0.62-3.15).

Table 1. Distribution of Characteristics of Women and Deliveries Among Cases and Controls

	Cases	Controls	P*
All	65 (100.0)	10,244 (100.0)	
Age (y)			
Less than 25	4 (6.2)	1,332 (13.7)	<.01
25-29	14 (21.5)	3,627 (37.3)	
30-34	18 (27.7)	3,189 (32.8)	
35-39	18 (27.7)	1,325 (13.6)	
More than 39	11 (16.9)	252 (2.6)	
Nationality			
French or other European country	55 (88.7)	9,474 (93.0)	.18
Non-European	7 (11.3)	710 (7.0)	
Parity			
0	15 (23.4)	4,300 (42.2)	<.01
1-3	40 (62.5)	5,554 (54.6)	
More than 3	9 (14.1)	323 (3.2)	
Premature delivery			
No	58 (90.6)	9,905 (97.1)	<.01
Yes (less than 37 wk)	6 (9.4)	293 (2.9)	
Size of maternity unit (annual number of deliveries)			
Less than 500	3 (5.1)	1,058 (10.3)	.32
500-1499	30 (50.8)	5,355 (52.3)	
More than 1499	26 (44.1)	3,831 (37.4)	
Status of maternity unit			
Nonuniversity public	25 (39.1)	4,830 (47.2)	.35
University public	12 (18.7)	1,426 (13.9)	
Private	27 (42.2)	3,988 (38.9)	

Data are n (%).

* For χ^2 test.

The same analysis was conducted after exclusion of preterm deliveries (gestational age of less than 37 weeks), and provided comparable results (Table 2). For term deliveries, the adjusted risk of postpartum death was 3.3 times higher after cesarean than after vaginal delivery. The risk did not differ significantly between term prepartum and intrapartum cesarean deliveries; the adjusted OR of postpartum maternal death for intrapartum as compared with prepartum cesarean was 1.89 (95% confidence interval 0.77-4.63). A separate analysis conducted after exclusion of controls transferred to ICU provided similar results (data not shown).

To better understand the association between cesarean delivery and postpartum maternal death, we examined the distribution of cause of death among cases, according to the route of delivery (Table 3). Among postpartum maternal deaths not due to conditions existing before delivery, causes of death significantly differed between vaginal and cesarean deliveries (Fisher exact test, $P=.01$).

The risk for cause-specific maternal mortality



Table 2. Crude and Adjusted Odds Ratios of Postpartum Maternal Death According to Mode of Delivery

Mode of delivery	Cases [n (%)]	Controls [n (%)]	Crude OR	95% CI	Adjusted OR	95% CI
Vaginal	38 (58.5)	8,673 (85.1)	1		1	
Cesarean	27 (41.5)	1,523 (14.9)	4.05	(2.46–6.65)	3.64*	(2.15–6.19)
Prepartum cesarean	13 (20.0)	777 (7.6)	3.82	(2.03–7.20)	3.11*	(1.58–6.10)
Intrapartum cesarean	14 (21.5)	746 (7.3)	4.28	(2.31–7.94)	4.35*	(2.23–8.45)
Term deliveries only						
Vaginal	36 (62.1)	8,424 (85.3)	1		1	
Cesarean	22 (37.9)	1,446 (14.6)	3.56	(2.09–6.07)	3.31†	(1.89–5.78)
Prepartum cesarean	9 (15.5)	737 (7.5)	2.86	(1.37–5.96)	2.42†	(1.14–5.13)
Intrapartum cesarean	13 (22.4)	709 (7.2)	4.29	(2.26–8.13)	4.58†	(2.30–9.09)

OR, odds ratio; CI, confidence interval.

* Logistic model including maternal age, nationality, parity, premature delivery.

† Logistic model including maternal age, nationality, parity.

Table 3. Distribution of Causes of Death (Postpartum Mortality Not Due to Conditions Existing Before Delivery) Among Cases, by Mode of Delivery

Cause of death	Cases		
	Vaginal	Cesarean	All
All causes	38 (100.0)	27 (100.0)	65 (100.0)
Postpartum hemorrhage	19 (50.0)	6 (22.2)	25 (38.5)
Venous thromboembolism	3 (7.9)	7 (25.9)	10 (15.4)
Amniotic fluid embolism	10 (26.3)	3 (11.1)	13 (20.0)
Puerperal infection	1 (2.6)	4 (14.8)	5 (7.7)
Complication of anesthesia	1 (2.6)	4 (14.8)	5 (7.7)
Other*	4 (10.5)	3 (11.1)	7 (10.8)

Data are n (%).

* Including after vaginal delivery: two cerebrovascular accidents, one postpartum hemolysis, elevated liver enzymes, low platelets syndrome, and one death of unknown cause; after cesarean delivery: three cardiopulmonary arrests in the immediate postpartum.

associated with cesarean delivery was further analyzed (Table 4). Cesarean delivery was associated with a significantly increased risk of postpartum maternal death from complication of anesthesia, puerperal infection, and venous thromboembolism. The

risk of death from postpartum hemorrhage did not differ significantly between vaginal and cesarean deliveries. Cause-specific mortality could not be analyzed separately for prepartum and intrapartum cesarean because the numbers of deaths were too small.

DISCUSSION

This study shows that cesarean delivery is associated with a three-fold increase in the risk of postpartum maternal death as compared with vaginal delivery, after adjustment for potential confounders. Several aspects of this study make this result of particular value. The study sample was identified from nationwide population-based data collection sources and included women who had delivered recently. Most importantly, the use of high-quality information sources led to a comprehensive characterization of maternal deaths, permitting the disentangling of antenatal mortality risk and risk associated solely with delivery route.

Previous studies on the association between the route of delivery and maternal mortality have provided heterogeneous results. In studies based on comparisons of mortality rates derived from aggre-

Table 4. Odds Ratios for Cause-Specific Maternal Mortality Associated With Cesarean Delivery

Cause of death	Cases		Controls		OR	95% CI
	Vaginal	Cesarean	Vaginal	Cesarean		
All causes	38 (58.5)	27 (41.5)	8,673 (85.1)	1,523 (14.9)	4.05	(2.46–6.65)
Postpartum hemorrhage	19 (76.0)	6 (24.0)			1.79	(0.72–4.51)
Venous thromboembolism	3 (30.0)	7 (70.0)			13.29	(3.43–51.44)
Amniotic fluid embolism	10 (76.9)	3 (23.1)			1.71	(0.47–6.21)
Puerperal infection	1 (20.0)	4 (80.0)			22.78	(2.54–203.9)
Complication of anesthesia	1 (20.0)	4 (80.0)			22.78	(2.54–203.9)
Other	4 (57.1)	3 (42.9)			–	–

Data are n (%) unless otherwise specified.



gate data, the possibilities of selecting women and of controlling for confounding factors were limited.^{8,10-15} In studies based on individual data,^{7,9} information on cause of death and medical complications was most often derived from vital statistics and administrative databases (death and birth certificates, hospital discharges). The limitations of these data for the precise assessment of maternal deaths^{19,20} as well as their imprecision in reporting maternal morbidities and pregnancy complications^{21,22} have been stressed. In the present study, maternal deaths and their causes were assessed by the national maternal mortality expert committee, based on detailed information on the circumstances of death collected from multiple sources, including medical records and autopsy reports. This precise information allowed us to conduct a careful selection of our cases, excluding all maternal deaths attributed to antenatal morbidities. In addition, the small number of deaths included in most of the previous studies led to low statistical power to detect an association between cesarean delivery and maternal death, and nonsignificant results should be interpreted cautiously.^{6,9,12} Finally, only one study included women who delivered during the last decade.⁷

The main strategy used here to control for indication bias was to exclude deaths due to morbidities present before delivery. The same analysis conducted on the sample before exclusion of these deaths, would have led to an apparently much stronger association between cesarean delivery and maternal mortality (proportion of cesarean delivery among cases was 58%, adjusted OR 5.3 95% confidence interval 3.7-7.5). The gap between this OR and the one proposed in this paper illustrates the overestimation of the cesarean delivery-related maternal mortality risk if cases where cesarean delivery is performed for a life-threatening maternal condition are not excluded.

In the present study, both prepartum and intrapartum cesarean deliveries were associated with a significantly increased risk for maternal death, and the postpartum mortality risk was not significantly different after prepartum and intrapartum cesarean. A higher risk after intrapartum cesarean delivery has generally been reported in the few previous studies that differentiated cesarean deliveries according to their timing.^{8,14,15} However, because antepartum obstetric complications were not completely taken into account in these analyses, this difference is likely to reflect the various indications of cesarean deliveries, intrapartum cesarean being more often decided in the presence of an acute complication that is potentially life-threatening for the mother. The similarly increased risk found here may indicate that this indica-

tion bias was effectively circumvented and that we were able to isolate the risk associated with cesarean delivery per se. However, in this study, the statistical power to detect a significant increased risk after intrapartum cesarean as compared with prepartum cesarean was satisfactory for a corresponding OR of 2.5 or more. A greater sample size would be needed to exclude the hypothesis of a significant association of lower strength between the time of cesarean and postpartum maternal mortality.

The increased risk of maternal mortality after cesarean delivery was not uniformly distributed among the various causes of death. Cesarean delivery was significantly associated with an increased risk of maternal deaths due to three causes that are classical peroperative or postoperative complications of any major surgery: venous thromboembolism, infection, and complications of anesthesia. Interestingly, recent studies reported that endometritis^{23,24} or rehospitalization for infectious morbidities,^{25,26} was more common in women with cesarean deliveries than in women who had spontaneous vaginal delivery. Similarly, cesarean delivery was found to be associated with an increased risk of readmission for venous thromboembolism.^{25,26} It is important to know that these results on postpartum morbidity also have an implication in terms of mortality.

Although the safety of modern anesthesia for cesarean delivery has greatly improved during the last decades, our results suggest that cesarean delivery is still associated with an increased risk of maternal death from complications of anesthesia. It must be noted that three of the four deaths due to complications of anesthesia in this study occurred after general anesthesia, whereas the fourth death occurred after spinal anesthesia. In the 1998 French Perinatal Survey, 12.9 % of cesarean deliveries were performed under general anesthesia. This suggests that general anesthesia at cesarean delivery is associated with a much greater mortality risk than regional anesthesia. As the use of general anesthesia in women undergoing cesarean delivery tends to decrease over the time (7.2 % in the 2003 French Perinatal Survey), it will be important to further monitor the anesthesia-related mortality risk at cesarean delivery.

In the present study, the risk of postpartum hemorrhage was not significantly increased after cesarean delivery. This may be considered surprising, because mean blood loss associated with cesarean delivery has been shown to be greater than after vaginal delivery.²⁷ However, this result is in agreement with previous studies examining maternal morbidity, in which the risk of postpartum hemorrhage



was not increased after cesarean compared with spontaneous vaginal delivery.^{23,24} This may reflect differential surveillance and care provided to parturient women in the immediate postpartum according to their route of delivery. Clinicians may be more concerned about blood loss in a patient who just had surgery, leading to an earlier diagnosis of increased blood loss and to more rapid interventions able to avoid severe and potentially life-threatening postpartum hemorrhage.

Persistent underidentification of maternal mortality has been reported in developed countries. A recent study found a 19% underreporting of maternal deaths in vital statistics from France.¹⁹ Cases included in the present study were selected from deaths reported to the French confidential enquiry on maternal deaths, which include not only deaths with a code for the underlying cause of death within the International Classification of Diseases obstetric chapter, but also any death with a mention of pregnancy and birth and puerperium on review of the death certificate's content. It is nevertheless likely that some maternal deaths still were missed.²⁸ However, this underidentification would introduce a bias in the present study only if postpartum deaths were differentially reported depending on the route of delivery. Since such differential underreporting has never been described, selection bias is unlikely.

To avoid bias due to medical conditions before delivery, the analysis was conducted after exclusion of women hospitalized during pregnancy, because this variable is considered a marker of serious antenatal morbidity.²⁹ Because information on conditions not leading to hospitalization was not available for controls, further adjustment on those was not possible. Some of these morbidities may have influenced both the decision of cesarean delivery and the risk of death. That is why residual confounding cannot be completely excluded. However, the presumed mildness of remaining morbidities as well as the strength of the association found here make such bias unlikely to explain the observed effect.

Although maternal mortality has become rare in high-resource regions, it is considered a sentinel event, and any factor associated with an increase in maternal mortality risk is likely to be similarly linked with many more cases of severe maternal morbidity. Although cesarean delivery is increasingly perceived as a low-risk procedure, the present study suggests that it is still associated with an increased risk of postpartum maternal death as compared with vaginal delivery, even when performed before labor. This needs to be taken into account by clinicians and

women when balancing the risks against the benefits of the different methods of delivery. In addition, knowledge of the specific causes involved in this excess maternal mortality risk should inform preventive strategies at cesarean delivery.

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