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By

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מרכז פדרמן לחקר הרציונליות

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Association of Catastrophic Neonatal Outcomes with Increased Rate of Subsequent Cesarean Deliveries

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Abstract

Objective: To evaluate whether full-term deliveries resulting in neonates diagnosed with hypoxic-ischemic encephalopathy are associated with a significant increase in the rate of subsequent unscheduled cesarean deliveries.

Methods: We conducted a retrospective chart review study and examined all deliveries in the department of Obstetrics and Gynecology at Hadassah University Hospital, Mt. Scopus campus, Jerusalem, Israel during 2009-2014. We reviewed all cases of hypoxic-ischemic encephalopathy in singleton, term, liveborn deliveries and identified seven such cases: three of which were attributed to obstetric mismanagement and four which were not. We measured the rate of unscheduled cesarean deliveries before and after the events and their respective hazard ratio (HR).

Results: Prior to a mismanaged delivery resulting in hypoxic-ischemic encephalopathy, the baseline rate of unscheduled cesarean deliveries was approximately 80 unscheduled cesarean deliveries for every 1,000 deliveries. In the first 4 weeks immediately after each of the three identified cases, there was a significant increase in the rate of unscheduled cesarean deliveries by an additional 48 unscheduled cesarean deliveries per 1,000 deliveries (95% CI 27−70/1,000). This increase was transient and lasted approximately 4 weeks. We estimated that each case was associated with approximately 17 additional unscheduled cesarean deliveries (95% confidence interval 8-27). There was no increase in the rate of unscheduled cesarean deliveries in cases of hypoxic-ischemic encephalopathy that were not associated with mismanagement.

Conclusion: The increase in the rate of unscheduled cesarean deliveries after a catastrophic neonatal outcome may result in short-term changes in obstetricians' risk evaluation.

Introduction

Everyday experience, as well as psychological research, shows that outcomes of our decisions shape future actions. Specifically, it has been shown that the catastrophic event of uterine rupture in specific scenarios is associated with an increase in elective cesarean deliveries[1]. One interpretation of this result is that the catastrophic event *per se* changes physicians' decision-making process. Alternatively, the change in behavior could be due to the association of the catastrophic event with the medical decisions that may have contributed to it. In the former case, the change in behavior is a form of associative learning, whereas in the latter it is a form of operant learning[2–4].

To test these hypotheses, we considered hypoxic-ischemic encephalopathy[5] in full-term neonates. Hypoxic-ischemic encephalopathy is a catastrophic neonatal condition of acute or sub-acute brain injury secondary to asphyxia, with estimated incidence of 1.5 per 1000 live births[6]. This condition can arise in labor while being associated or not being associated with obstetric mismanagement. Operant learning predicts a change in behavior only after mismanaged incidents. By contrast, associative learning suggests a change of behavior, independent of the cause of the incidents. We compared the rate of unscheduled cesarean deliveries after cases, both associated and not associated with obstetric mismanagement, to the same rate preceding them. Specifically, we considered the following two questions: (1) Is there an increase in the rate of unscheduled cesarean deliveries after mismanaged hypoxic-ischemic encephalopathy deliveries? (2) If so, does a similar change in behavior occur after incidents not associated with obstetric mismanagement?

Materials and Methods

This retrospective chart review study was approved by the Ethics Committee of the Hadassah Medical Organization (Decision 0604-14-HMO). The study population was drawn from singleton, term liveborn infants (gestational age $\geq$ 37 weeks from last menstrual period) at

Hadassah University Hospital, Mt. Scopus, Jerusalem, Israel. This tertiary care facility is one of two major hospitals serving a diverse population. We examined the records of all deliveries from February 2009 to November 2014. During this period, there were 26,320 deliveries: 19,910 (76%) of them vaginal, 3,819 (14%) elective cesarean deliveries, and 2,591 (10%) unscheduled cesarean deliveries. Elective cesarean deliveries included all cases of planned cesarean deliveries (repeat, maternal request, abnormal presentation and placentation). Unscheduled cesarean deliveries were defined as any unplanned, emergent cesarean deliveries, mainly the result of non-reassuring fetal monitoring or arrest of labor disorders. The database was obtained from the hospital's medical records department using ICD9 codes. In Israel, standard obstetric practice consists of midwives and obstetricians, where non-complicated deliveries are handled by midwives with obstetricians present in the delivery room available to intervene if complications arise. The Mt. Scopus Obstetrics' Department is comprised of 25 senior physicians, including 4 MFMs, as well as 15 residents and 31 midwives.

Cases of hypoxic-ischemic encephalopathy were identified from the Neonatal Intensive Care Unit database. Seven cases of term neonates in singleton pregnancies, occurring between June 2010 and October 2013, who developed hypoxic-ischemic encephalopathy, were included. The average interval between the incidents was 206 days (range: 8-515). A different obstetrician managed each case. Diagnosis of hypoxic-ischemic encephalopathy was based on the criteria set by The American College of Obstetricians and Gynecologists (ACOG)[7]. All cases of hypoxic–ischemic encephalopathy that met study inclusion criteria were reviewed by study staff (DHC and AS) and divided, unanimously, into two groups based on etiology: (1) three cases of hypoxic-ischemic encephalopathy developed secondary to obstetric mismanagement (fetal heart monitor changes were not identified correctly). (2) Four deliveries complicated with hypoxic-ischemic encephalopathy, not attributed to obstetric mismanagement (one case developed hypoxic-ischemic encephalopathy despite normal fetal monitoring throughout labor and delivery; two cases of fetal heart changes occurring less than 5 minutes prior to the delivery; one case of difficulty in implementing neonatal resuscitation). No obstetrician or staff members suffered any disciplinary action related to these cases. Per hospital policy, all cases were reported to the risk management department for review within 7 - 10 days and proper changes such as education regarding fetal monitoring, neonatal ACLS and proper standardization of equipment alarms were instituted to prevent reoccurrence.

Our analysis focused on the change in the probability of a laboring woman having an unscheduled cesarean delivery relative to a vaginal delivery, in temporal association with a case of hypoxic-ischemic encephalopathy. To calculate this probability, we measured the change in the rate of unscheduled cesarean deliveries after a delivery complicated with hypoxic-ischemic encephalopathy and independently compared the rate of unscheduled cesarean deliveries in the ten-week period before and six weeks after each of the seven cases (see Appendix 1).

Changes in physicians' decision-making may be attributed to external factors, unrelated to events in the hospital or in the professional environment. To control for these factors, we compared rates of unscheduled cesarean deliveries, in the corresponding time periods, with the rate of unscheduled cesarean deliveries in another branch of the hospital, Hadassah Medical Center, Ein Kerem, Jerusalem (supervised by the same administration and policies and sharing the same demographic population). This comparison did not reveal any significant change in unscheduled cesarean deliveries rate at this control hospital (see Appendixes 2 and 3).

Data analysis and figure generation were performed using custom Matlab code (version R2014b).

Results

Out of the 26,320 singleton term liveborn infants in the study period (69 months), we identified seven term neonates from singleton deliveries complicated by hypoxic-ischemic encephalopathy, three of them associated with obstetric mismanagement and the remaining four cases not associated with obstetric mismanagement, for an overall rate of 0.03%. To test the association of hypoxic-ischemic encephalopathy associated with obstetric mismanagement, with the rate of unscheduled cesarean delivery, we reviewed the deliveries in the 10-week period preceding these events and evaluated the rate of unscheduled cesarean deliveries (approximately 80 unscheduled cesarean deliveries for every 1,000 deliveries). Then, we reviewed the deliveries in the six weeks after each hypoxic-ischemic encephalopathy and computed the rate of unscheduled cesarean deliveries in blocks of two weeks (approximately 173 deliveries). We observed (Figure 1) that the probability of an unscheduled cesarean delivery significantly increased in the first four weeks after delivery of an infant with hypoxic-ischemic encephalopathy due to obstetric mismanagement, resulting in 48 excessive unscheduled cesarean deliveries per 1,000 deliveries in that period (95% confidence interval [CI] 27/1000 – 70/1000, $p < 0.001$). Considering each case of hypoxic-ischemic encephalopathy associated with obstetric mismanagement separately, we found a significant increase in the rate of unscheduled cesarean deliveries in the four weeks after each of the incidents relative to the period preceding it ($p < 0.05$).

Another way of quantifying this change in behaviour is to consider the hazard ratio (HR), the rate of change in the probability of an unscheduled cesarean delivery. The HR of unscheduled cesarean deliveries in the first 4 weeks after an obstetric mismanaged hypoxic-ischemic encephalopathy was significantly > 1 (0-2 weeks: HR = 1.72, 95% CI 1.31 – 2.21; 2-4 weeks: HR = 1.45, 95% CI 1.07 – 1.88 p) but was not significantly different from 1 after 4 weeks (4-6 weeks: HR = 1.09, 95% CI 0.77 – 1.46, Fig. 2A). To test whether the increased HR was associated with the outcome or with the presumed causative factors, we computed the HR of unscheduled cesarean deliveries after hypoxic-ischemic encephalopathy deliveries not associated with obstetrical mismanagement (Fig. 2B). We found no significant increase in the rate of unscheduled cesarean delivery after these events (0-2 weeks: HR = 0.88, 95% CI 0.67 – 1.11; 2-4 weeks: HR = 0.72, 95% CI 0.53 – 0.93; 4-6 weeks: HR = 1.02, 95% CI 0.80 – 1.27). In line with these results, a significant difference was found between the hazard ratios of unscheduled caesarean deliveries after hypoxic-ischemic encephalopathy deliveries that were and those which were not associated with obstetric mismanagement, in weeks 0-2 post the incidents ($p < 0.05$), but not in weeks 2-4 ($p < 0.1$) or 4-6 ($p > 0.1$). The association between hypoxic-ischemic encephalopathy associated with obstetric mismanagement and a higher rate of unscheduled cesarean delivery persists for approximately four weeks (Figure 1 and 2A).

To better quantify the dynamics of change in the rate of unscheduled cesarean deliveries after cases of hypoxic-ischemic encephalopathy associated with obstetric mismanagement, we utilized a method that is based on the cumulative sum of unscheduled cesarean deliveries (see Appendixes 4 and 5). Based on this analysis, each case of hypoxic-ischemic encephalopathy associated with obstetric mismanagement was associated with approximately 17 additional unscheduled cesarean deliveries (95% CI 8-27).

Discussion

Like other medical specialties, obstetric practice may result in adverse outcomes despite the best care given[1,8]. However, not all obstetric catastrophic events occurring in the delivery room are associated with change in future practice. When dividing hypoxic-ischemic encephalopathy cases by causative factor, obstetric mismanagement compared to non-obstetric mismanagement, we found a substantial and significant increase in the rate of unscheduled cesarean deliveries after obstetric mismanagement. The increased rate of unscheduled cesarean deliveries was transient and reverted to its baseline rate approximately 4 weeks after the incidents. Repeating the analysis for hypoxic-ischemic encephalopathy deliveries not associated with mismanagement did not reveal a similar increase in the rate of unscheduled cesarean deliveries.

What is the cause of the change in behavior? It is important to note that the catastrophic outcome per se, is not sufficient to change the practice, as the same fetal outcome is not associated with change in subsequent behavior if it is not related to mismanagement. Therefore, the change in behavior cannot be attributed to outcome bias[9]. Rather, it is plausible that the interaction of the outcome and the sequence of events that led to it drive the change in behavior, as in operant learning[10].

Research suggests that preventable outcomes are a key factor in eliciting counterfactuals (i.e., thoughts of how things might have been different)[11] which, in turn, may trigger more cautious behavior aimed at prevention of catastrophic events. We propose that in cases of obstetric mismanagement, physicians may feel that in order to prevent future unfortunate outcomes, they should overcompensate and choose a perceived safer modality of delivery, such as cesarean delivery, in borderline cases in which, under normal circumstances, they would have proceeded with a spontaneous vaginal or instrumental delivery. In accordance with this hypothesis, when hypoxic-ischemic encephalopathy is not associated with obstetric mismanagement it may be perceived as less preventable and hence no change in behavior is expected, as was observed in our study.

Why is the change in behavior transient? We hypothesize that the time limitedness nature of the observed association with higher rates of unscheduled cesarean deliveries may be attributed to the psychological phenomenon known as "availability heuristic" according to which, events' frequencies are evaluated "by the ease with which relevant instances come to mind"[12]. Hence, this bias predicts that more recent events would be judged as more frequent and more probable. In general, cesarean deliveries are considered as a safer mode of delivery for the neonates, hence they are utilized more frequently in high risk pregnancies, *In-Vitro* fertilization pregnancies, egg donation pregnancies, etc[13,14]. Thus, after an untoward neonatal outcome, it is understandable that physicians may opt for a cesarean delivery to minimize perceived risk. As the incident becomes more distant in time, it is perceived as less likely to reoccur, thus reverting the physicians' risk-assessment back to the baseline.

Due to the rarity of neonatal hypoxic-ischemic encephalopathy, as well as the practice structure, our analyses were performed on the obstetrics department as a whole, rather than addressing the physicians individually. However, all catastrophic events are reviewed and deliberated at daily staff meetings, for educational and training purposes, attended by all obstetricians. In this aspect, the change of behavior of the obstetricians is qualitatively different from standardly studied biases of choice that focus on how the actions of a human subject and their consequences affect subsequent actions of that subject[15–17].

Our results suggest that mismanaged deliveries complicated by neonatal catastrophic outcomes may have a significant effect on future medical decision making and may transiently influence the threshold for performing cesarean delivery. By acknowledging the interaction between event-management and undesirable outcomes, health care providers may increase physicians' awareness in order to counter-bias such effects and promote better, and more uniform medical decision-making.

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Figures

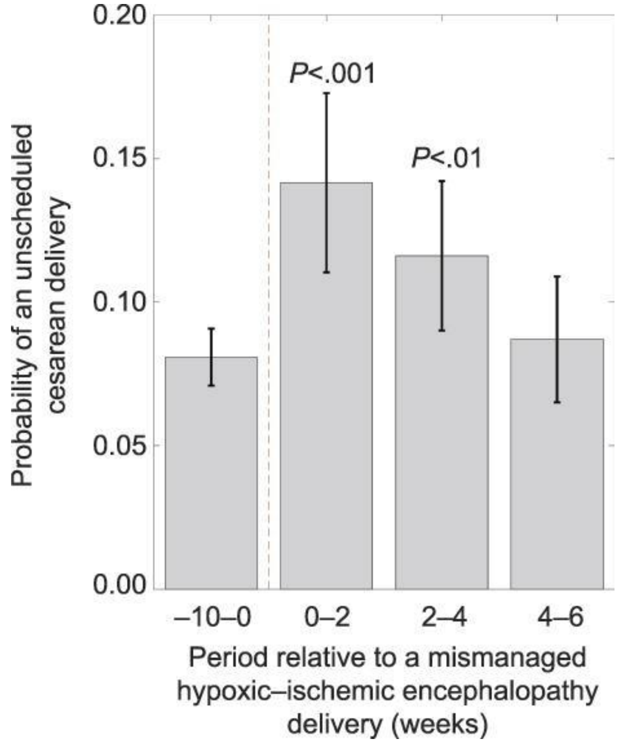


Fig. 1. The probability of unscheduled cesarean delivery. *Red dashed line* denotes the timing of hypoxic-ischemic encephalopathy events. Error bars indicate 95% confidence intervals.

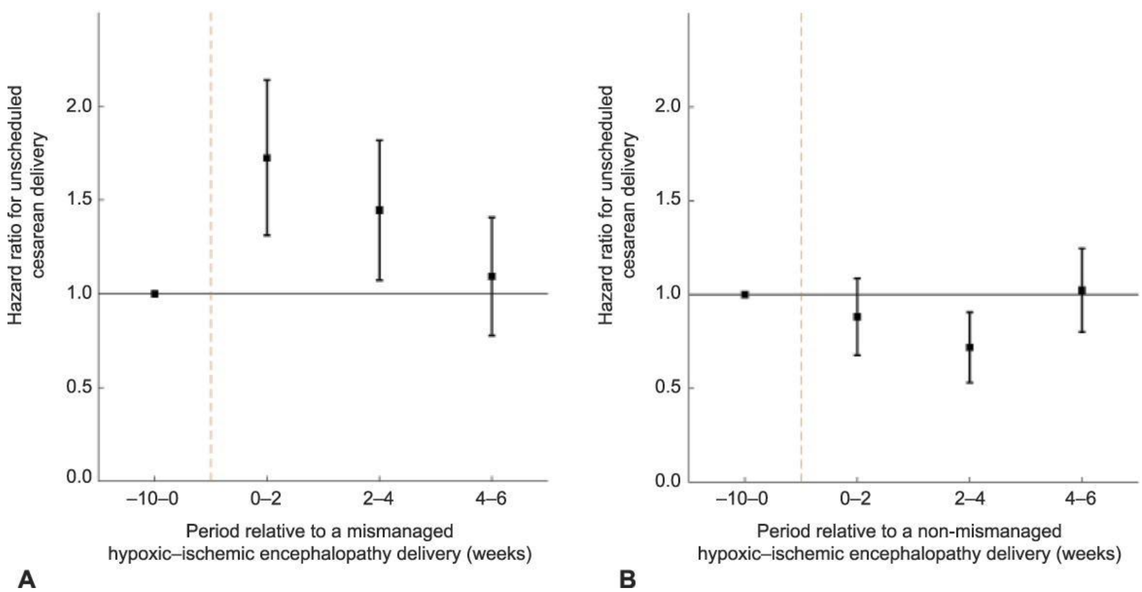


Fig. 2. Hazard ratios (HR) for unscheduled cesarean delivery A. Hazard ratios for an unscheduled cesarean delivery after cases of hypoxic-ischemic encephalopathy associated

with obstetric mismanagement. **B.** Hazard ratios for an unscheduled cesarean delivery after cases of hypoxic-ischemic encephalopathy not associated with obstetric mismanagement. *Red dashed line* denotes the timing of hypoxic-ischemic encephalopathy events. Error bars indicate 95% confidence intervals.

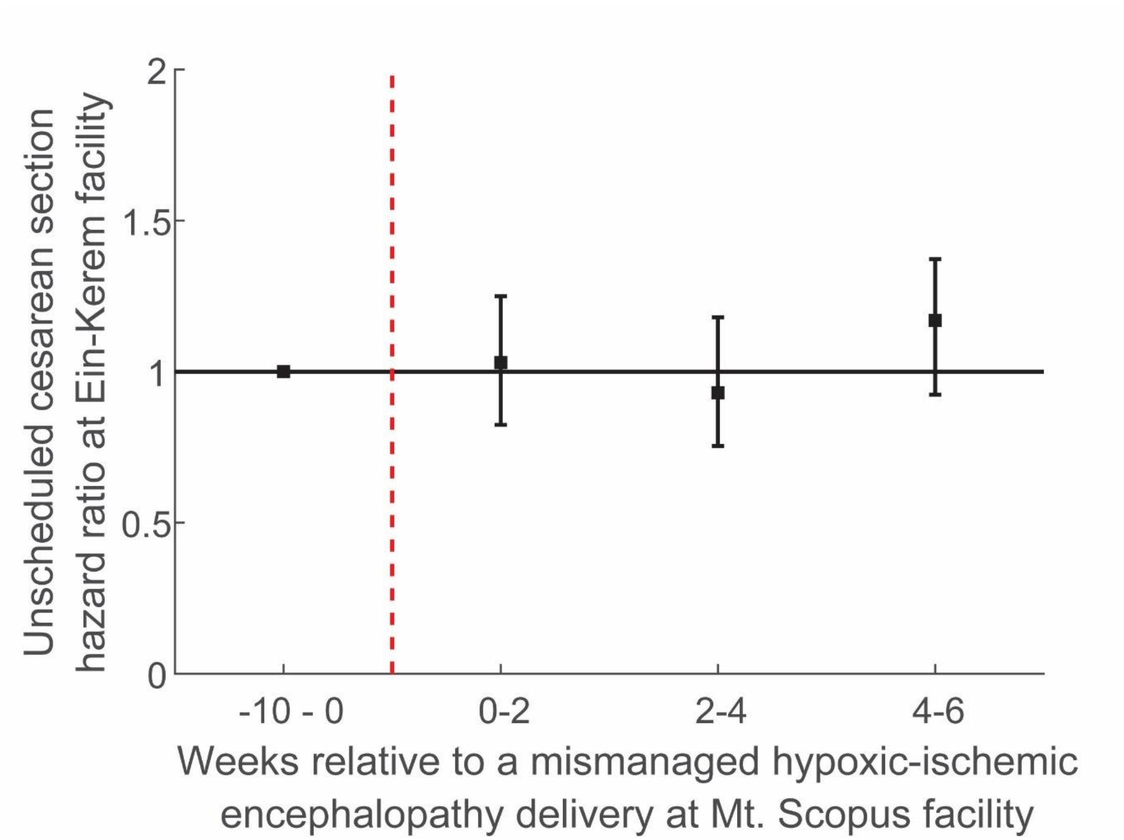
Appendix 1. Deliveries and unscheduled cesarean deliveries incidence prior to and following hypoxic-ischemic encephalopathy events, classified as either associated or not associated with obstetric mismanagement.

		Number of weeks prior to\following hypoxic-ischemic encephalopathy deliveries				
		-10 – 0 weeks	0 – 2 weeks	2 – 4 weeks	4 – 6 weeks	
Event 1	Total deliveries	888	155	161	164	mismanaged
	Unscheduled cesarean deliveries	72	17	22	12	
Event 2	Total deliveries	877	167	144	176	
	Unscheduled cesarean deliveries	66	27	12	16	
Event 3	Total deliveries	846	137	160	177	
	Unscheduled cesarean deliveries	73	21	20	17	
Event 1	Total deliveries	840	164	159	167	non-mismanaged
	Unscheduled cesarean deliveries	108	17	10	13	
Event 2	Total deliveries	865	169	168	199	
	Unscheduled cesarean deliveries	82	19	13	18	
Event 3	Total deliveries	905	181	171	179	
	Unscheduled cesarean deliveries	95	14	12	22	
Event 4	Total deliveries	879	193	169	165	
	Unscheduled cesarean deliveries	97	17	20	25	

Appendix 2. Deliveries and unscheduled cesarean deliveries incidence at Ein-Kerem facility prior to and following hypoxic-ischemic encephalopathy events at Mt. Scopus facility.

		Number of weeks before\ after events of mismanaged hypoxic-ischemic encephalopathy at **Mt. Scopus facility**				
		-10-0 weeks	0-2 weeks	2-4 weeks	4-6 weeks	
Event 1	Total deliveries	1226	243	210	261	Deliveries at **Ein-Kerem facility**
	Unscheduled cesarean deliveries	148	34	22	29	
Event 2	Total deliveries	1248	231	228	213	
	Unscheduled cesarean deliveries	148	32	27	29	
Event 3	Total deliveries	1108	256	233	260	
	Unscheduled cesarean deliveries	156	29	32	46	

Appendix 3. Hazard ratio (HR) of cesarean deliveries at a control facility is not significantly larger than 1 after mismanaged hypoxic-ischemic encephalopathy deliveries at the reported facility. *Red line* denotes events of obstetric mismanaged hypoxic-ischemic encephalopathy deliveries at the reported facility (Mt. Scopus). The HR of cesarean deliveries was assessed in following weeks at a different facility (Ein-Kerem) to control for possible environmental factors and was not found to be significantly different than 1 (0-2: HR = 1.03, 95% CI 0.82 –1.25, 2-4: HR = 0.93, 95% CI 0.76 – 1.18, 4-6: HR = 1.17, 95% CI 0.93 – 1.37).



Appendix 4. Statistical analysis.

Assessing the significance of unscheduled cesarean deliveries' rate change following hypoxic-ischemic encephalopathy delivery. To assess the significance of change in unscheduled cesarean deliveries' rate following a hypoxic-ischemic encephalopathy event (separately for obstetric mismanaged and non-mismanaged deliveries) we performed the following permutation test. First, all deliveries were sorted according to the time of delivery and indexed. Let N be the number of hypoxic-ischemic encephalopathy deliveries. Denoted by i_j, $j \in \{1 \dots N\}$, the index of hypoxic-ischemic encephalopathy incidents, we considered as surrogate-incidents all indexes of the N-tuple of deliveries i'_j that were equally spaced in the index space, such that $i'_{j+1} - i'_j = i_{j+1} - i_j \; \forall j < N$. This generated tuples of deliveries that were similarly spaced in time as the original hypoxic-ischemic encephalopathy deliveries. For each surrogate-incidents tuple, we compared the mean rate of unscheduled cesarean deliveries following the surrogate-incidents to that mean rate preceding these surrogate-incidents. Because of boundary conditions, we did not consider the small fraction of tuples in which the time of the first surrogate incident i'_1 was less than 10 weeks from the first delivery in the dataset, precluding us from estimating the baseline rate. Similarly, we did not consider the small fraction of tuples, in which we were similarly unable to compute the rate of events following the last surrogate incident, i'_N. This procedure yielded a null-hypothesis distribution of differences in the rates of unscheduled cesarean deliveries following a hypoxic-ischemic encephalopathy delivery and we computed the percentile of difference in the rates of unscheduled cesarean deliveries in view of this distribution. We note that this permutation statistical test is more conservative than a Binomial test, which yielded qualitatively similar results.

Confidence intervals for HRs and unscheduled cesarean deliveries' rate. We used bootstrapping to compute the 95% CIs of unscheduled cesarean deliveries' rates (figure 1) and HR (figure 2) in a given period of time before or after obstetric mismanaged and non-mismanaged hypoxic-ischemic encephalopathy deliveries, independently. Let N be the number of hypoxic-ischemic encephalopathy deliveries. Denoting by i_j , $j \in \{1 \dots N\}$, the index of hypoxic-ischemic encephalopathy delivery, we considered, independently for each event, the empirical number of labors n_i and the respective ratios of unscheduled cesarean deliveries p_i in the given time period. We used these empirical values as parameters for a binomial distribution from which we simulated 10^5 independent, random draws for each incident. The average over the values drawn per incident, $\frac{\sum_{j=1}^{N} x_j}{\sum_{j=1}^{N} n_j}, s.t. x_j \sim Bin(p_j, n_j)$, was used to construct a simulated distribution. The 2.5 and 97.5 percentiles of this distribution were used for estimating the CI.

Comparing HRs of obstetric mismanaged and non-mismanaged hypoxic-ischemic encephalopathy deliveries. To estimate whether the HR was significantly different following obstetric mismanaged and non-mismanaged hypoxic-ischemic encephalopathy deliveries in a given time period (e.g. 2-4 weeks) we used one-sided Wilcoxon rank sum test.

Estimating the time-scale and magnitude of increase in unscheduled cesarean deliveries following obstetric mismanaged hypoxic-ischemic encephalopathy deliveries. To estimate the time-scale and the extent of increase in unscheduled cesarean deliveries associated with obstetric mismanaged hypoxic-ischemic encephalopathy deliveries, an exponential decay model was fitted to the sequence of deliveries. The model assumes that there exists a base-rate of unscheduled cesarean deliveries *b* which, following the incidents, is increased by a constant factor and then decays exponentially back to the baseline with every subsequent delivery, such that the probability of an unscheduled cesarean delivery at the n^{th} delivery following an incident is given by:

$$b + a\frac{e^{-n/\tau}}{\tau} \text{ (Eq. 1)}$$

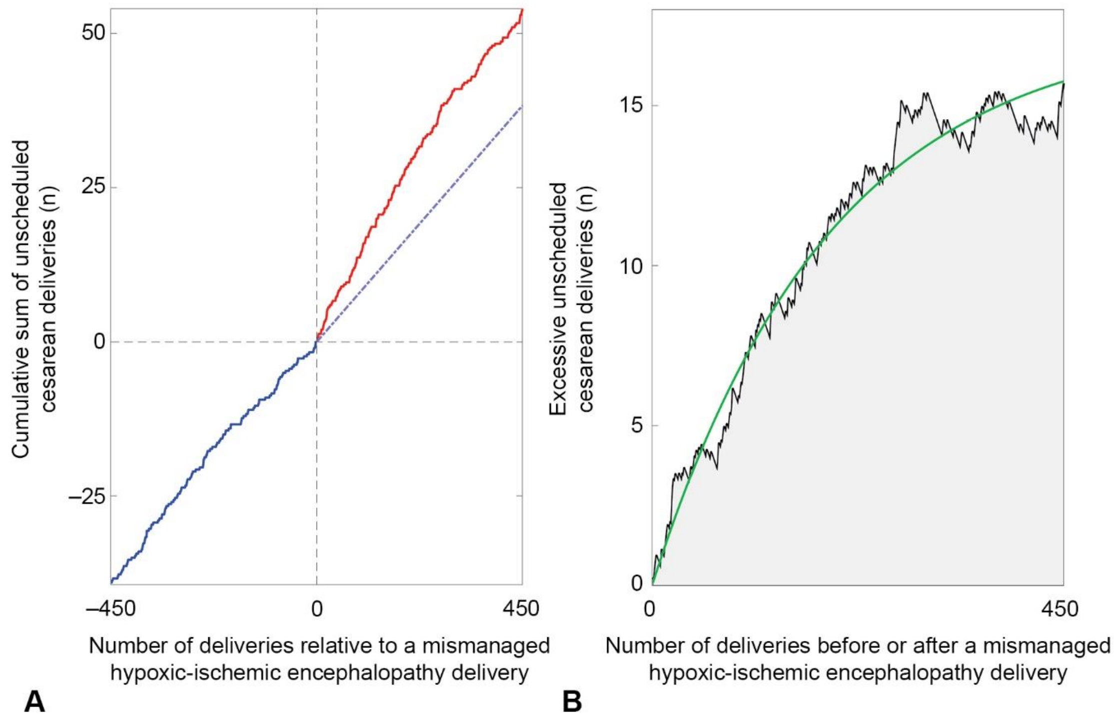
The parameter τ denotes the timescale of the change in behavior (in units of deliveries) and the parameter a denotes the total number of excessive unscheduled cesarean deliveries after a long period of time ($n \to \infty$).

The value of b was estimated by considering the average rate of unscheduled cesarean deliveries in the ten-week period prior to obstetric mismanaged hypoxic-ischemic encephalopathy deliveries (b = 0.086, 95% CI = 0.072 – 0.10); the values of a and τ were estimated using the method of maximum likelihood over all deliveries in the period of six weeks following the obstetric mismanaged hypoxic-ischemic encephalopathy deliveries. The saturation value of the function (a in Eq. 1) is 17 (95% CI 8 – 27; $p < 0.01$), indicating that each obstetric mismanaged hypoxic-ischemic encephalopathy delivery resulted in approximately additional 17 ECDs. The saturation "point" (τ in Eq. 1) was 210 (95% CI 88 – 322), which corresponds to approximately 17 days. To assess the significance of a ($a > 0$), we simulated the null hypothesis ($a = 0$) 10,000 times and used this simulation to compute the probability of obtaining a value of a that is larger than observed ($p < 0.01$). To estimate the confidence intervals for a and τ we used parametric bootstrapping: we simulated the model 10,000 times (Eq. 1) with the estimated parameters and recomputed these parameters from each of the simulations. To estimate the confidence interval for b we used the empirical values of number of deliveries (n_i) and rate of emergent cesarean deliveries (p_i) following each of the events ($i \in \{1, 2, 3\}$) as parameters for a binomial distribution from which we simulated 10^5 independent, random draws for each incident. The average over the values drawn per incident, $\frac{\sum_{i=1}^{3} x_i}{\sum_{i=1}^{3} n_i}, s.t.\, x_i \sim Bin(p_i, n_i)$, was used to construct a simulated distribution.

The 2.5 and 97.5 percentiles of this distribution were used for estimating the CI.

Appendix 5. The dynamics of change in unscheduled cesarean deliveries' rate after an obstetric mismanaged hypoxic-ischemic encephalopathy delivery.

A. **The mean cumulative sum of unscheduled cesarean deliveries**. *Blue solid line* denotes the mean cumulative sum of unscheduled cesarean deliveries prior to obstetric mismanaged hypoxic-ischemic encephalopathy deliveries; *Red line* denotes the mean cumulative sum of unscheduled cesarean deliveries after obstetric mismanaged hypoxic-ischemic encephalopathy deliveries; *Blue dashed line* denotes the *predicted* mean cumulative sum of unscheduled cesarean deliveries based on the rate of unscheduled cesarean deliveries in the 10 weeks prior to obstetric mismanaged hypoxic-ischemic encephalopathy deliveries. Zero index at the abscissa denotes the time of an obstetric mismanaged hypoxic-ischemic encephalopathy delivery. **B**. **Number of excessive caesarean deliveries**. *Black line* denotes the difference between the mean cumulative sum of unscheduled cesarean deliveries (*red line* in **A**) and the predicted mean cumulative sum of unscheduled cesarean deliveries (*dashed blue line* in **A**). *Green line* is an exponential fit to the excessive unscheduled cesarean deliveries over time (measured in units of deliveries) relative to prediction (i.e. fitted to *black line*). The saturation value of the exponential fit denotes the total excessive number of unscheduled cesarean deliveries, 17 unscheduled cesarean deliveries for each obstetric mismanaged hypoxic-ischemic encephalopathy delivery. The width of the fitted curve is indicative to the number of deliveries that were associated with an increased rate of unscheduled caesarean deliveries, following an obstetric mismanaged hypoxic-ischemic encephalopathy delivery, estimated as 210 deliveries (approximately 17 days). See Appendix 4 for details.


50
25
0
–25
Cumulative sum of unscheduled cesarean deliveries (n)
–450
0
450
Number of deliveries relative to a mismanaged hypoxic-ischemic encephalopathy delivery
A
15
10
5
0
Excessive unscheduled cesarean deliveries (n)
0
450
Number of deliveries before or after a mismanaged hypoxic-ischemic encephalopathy delivery
B