Supplementary Online Content

Blomquist JL, Muñoz A, Carroll M, Handa VL. Association of delivery mode with pelvic floor disorders after childbirth. *JAMA*. doi:10.1001/jama.2018.18315

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods

This section expands on the statistical methods used for the derivation of lognormal models, estimates of cumulative incidences and time ratios; as well as those for semiparametric methods to estimate and test significance of hazard ratios.

The left censored data provided by the participants with the event present at entry to the study (i.e., prevalent) permitted the estimation of the cumulative incidence in the first five years from first delivery, as some indeed had the event during that interval. Specifically, if F denotes the cumulative incidence function, f denotes it's rate of increase (i.e., density function), and t denotes the time since first delivery, the information provided by the participants with PFDs at entry into the study (left censored) at t years from first delivery was F(t); those with incident disorders (uncensored) between visits v_i and v_{i+1} at t_i and t_{i+1} years from first delivery were treated as having the event at the midpoint (i.e., at $(t_i + t_{i+1})/2$) and contributed with $f((t_i + t_{i+1})/2)$; and those who remained disorder-free at the last study visit (right censored) contributed to the likelihood function with 1-F(t). The concatenation of the information provided by the full data and the use of a parametric survival model (e.g., lognormal) and maximum likelihood methods[1] yielded estimates of the cumulative incidence spanning from first delivery.

The times to PFDs were modeled as a lognormal variate with location β and scale σ whereby $F(t) = \Phi((\log(t) - \beta)/\sigma)$ with Φ representing the cumulative distribution function of a standard normal variate so that the p^{th} percentile of the times to PDF is the antilog of $\beta+\sigma Z_p$ with Z_p being the p^{th} percentile of a standard normal distribution (e.g., exp(β) is the median). [1] Conventional lognormal models (i.e., allowing delivery modes to modify the location parameters but with a common scale) were used to estimate and to contrast the cumulative incidences for each PFD over time, as well as the corresponding hazards (= f(t)/(1-F(t))) for each disorder. Using the estimates from these lognormal models, the antilogs of the differences of the location parameters between delivery groups directly quantify time ratios[1] (i.e. the extent by which a delivery group either contracts or expands the time to event relative to the reference group) as shown in supplementary eTable 1. Denoting the maximum likelihood estimate of the location parameter of the i^{th} delivery mode group by $\hat{\beta}_i$ (i= 0,1,2 for spontaneous vaginal, cesarean and operative vaginal delivery groups, respectively) and the estimate for the common scale by $\hat{\sigma}$, the estimate of the ratio of the times to PDF among the cesarean delivery group to those among the spontaneous delivery group is $\exp(\hat{\beta}_1 - \hat{\beta}_0)$ and similarly, the time ratios of operative delivery group to spontaneous delivery group is $\exp(\hat{\beta}_2 - \hat{\beta}_0)$. Furthermore, the estimate of the cumulative incidence for the i^{th} delivery mode at a fixed time, say 5 years, was $\Phi((\log(5) - \hat{\beta}_i)/\hat{\sigma})$. Using the covariance matrix of the maximum likelihood estimators and the delta method, we calculated 95% confidence intervals for the cumulative incidence estimates.

To estimate and test for the statistical significance of hazard ratios (reported in Table 2) using the prospective data collected after 5 years from first delivery, the information for the outcome of a participant was summarized by three variables: 1) w= years after first delivery when participant enrolled in the study minus 5 years; 2) t= years after first delivery when event occurred or when participant was last seen event-free minus 5 years; and 3) an indicator of the event status at time t. We used standard methods for semiparametric regression models appropriately incorporating late entries (i.e., w) and including both fixed covariates (e.g., race) and time-varying covariates (e.g., BMI). To further determine the putative additional information provided by genital hiatus among women with the same delivery mode, we used stratified methods whereby the hazard of a PDF at time t for the i^{th} delivery mode and according to genital hiatus was modeled as $h_{0i}(t)\exp(\theta_1(if\ GH = 3) + \theta_2(if\ GH \geq 3.5))$ with $h_{0i}(t)$ being the hazard for those with the i^{th} delivery mode and GH≤2.5. The delivery mode stratified hazard ratios were $\exp(\theta_1)$ for GH=3, relative to GH≤2.5 and $\exp(\theta_2)$ for GH≥3.5, relative to GH≤2.5.

eReferences:

1. Cox C, Chu H, Schneider MF, et al. Parametric survival analysis and taxonomy of hazard functions for the generalized gamma distribution. Stat Med. 2007;26(23):4352-71

eTable: Descriptive statistics and lognormal models for time to pelvic floor disorders with years from first delivery as time scale.

	Stress Urinary Incontinence	Overactive Bladder	Anal Incontinence	Pelvic Organ Prolapse
Types of times observed				
Left censored (prevalent)				
N	168	98	167	36
median (range), years from first delivery	6.2 (5.1 – 12.0)	6.3 (5.1 -12.0)	6.2 (5.1 – 12.0)	6.6 (5.2-10.6)
Uncensored (incident)				
N	138	117	168	153
median (range), years from first delivery	9.6 (5.7 – 17.3)	9.4 (5.8 – 17.8)	8.8 (5.8 – 17.1)	9.8 (5.8 – 16.5)
Right censored (event-free)				
N	1222	1313	1193	1339
median (range), years from first delivery	10.8 (5.0 – 18.7)	11.0 (5.0 – 18.7)	10.8 (5.0 – 18.7)	10.5 (5.0 – 18.7)
Lognormal models				
Location				
Cesarean only ($\hat{\beta}_1$)	3.969	4.016	3.530	3.596
Spontaneous vaginal ($\hat{\beta}_0$)	3.255	3.678	3.348	3.062
Operative vaginal ($\hat{\beta}_2$)	3.111	3.295	3.102	2.794
Scale ($\hat{\sigma}$)	1.348	1.243	1.265	0.675
Estimates from lognormal models				
Cumulative Incidence (%) at 5 years				
Cesarean only	4.0 (2.8- 5.2)	2.6 (1.7-3.6)	6.5 (4.9-8.0)	0.2 (0.1-0.3)
Spontaneous vaginal	11.1 (8.7-13.5)	4.8 (3.3-6.3)	8.5 (6.4-10.5)	1.6 (0.9-2.3)
Operative vaginal	13.3 (9.0-17.5)	8.7 (5.4-12.1)	11.9 (8.0-15.8)	4.0 (2.0-5.9)
Cumulative Incidence (%) at 15 years				
Cesarean only	17.5 (14.5-20.5)	14.6 (11.8-17.5)	25.8 (22.3-29.3)	9.4 (6.8-12.1)
Spontaneous vaginal	34.3 (29.9-38.6)	21.8 (17.8-25.7)	30.6 (26.4-34.9)	30.0 (25.1-34.9)
Operative vaginal	38.2 (31.0-45.5)	31.8 (24.7-38.9)	37.8 (30.6-44.9)	44.9 (37.0-52.8)
Time ratios= antilog of location differences				
Cesarean only	2.04 (1.63 – 2.56)	1.40 (1.13 – 1.73)	1.20 (0.99 – 1.45)	1.70 (1.48 – 1.95)
Spontaneous vaginal	1	1	1	1
Operative vaginal	0.87 (0.65 – 1.15)	0.68 (0.51 – 0.91)	0.78 (0.59 – 1.03)	0.76 (0.66 – 0.89)