Labor Outcomes With Increasing Number of Prior Vaginal Births After Cesarean Delivery

*Brian M. Mercer, MD, Sharon Gilbert, MS, MBA, Mark B. Landon, MD, Catherine Y. Spong, MD, Kenneth J. Leveno, MD, Dwight J. Rouse, MD, MSPH, Michael W. Varner, MD, Atef H. Moawad, MD, Hyagriv N. Simhan, MD, Margaret Harper, MD, Ronald J. Wapner, MD, Yoram Sorokin, MD, Menachem Miodovnik, MD, Marshall Carpenter, MD, Alan Peaceman, MD, Mary J. O'Sullivan, MD, Baha M. Sibai, MD, Oded Langer, MD, John M. Thorp, MD, and Susan M. Ramin, MD, for the National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network**

OBJECTIVE: To estimate the success rates and risks of an attempted vaginal birth after cesarean delivery (VBAC) according to the number of prior successful VBACs.

METHODS: From a prospective multicenter registry collected at 19 clinical centers from 1999 to 2002, we selected women with one or more prior low transverse cesarean deliveries who attempted a VBAC in the current pregnancy. Outcomes were compared according to the number of prior VBAC attempts subsequent to the last cesarean delivery.

RESULTS: Among 13,532 women meeting eligibility criteria, VBAC success increased with increasing number of prior VBACs: 63.3%, 87.6%, 90.9%, 90.6%, and 91.6% for those with 0, 1, 2, 3, and 4 or more prior VBACs, respectively ($P<.001$). The rate of uterine rupture decreased after the first successful VBAC and did not increase thereafter: 0.87%, 0.45%, 0.38%, 0.54%, 0.52% ($P=.03$). The risk of uterine dehiscence and other peripartum complications also declined statistically after the first successful VBAC. No increase in neonatal morbidities was seen with increasing VBAC number thereafter.

CONCLUSION: Women with prior successful VBAC attempts are at low risk for maternal and neonatal complications during subsequent VBAC attempts. An increasing number of prior VBACs is associated with a greater probability of VBAC success, as well as a lower risk of uterine rupture and perinatal complications in the current pregnancy.

(Obstet Gynecol 2008;111:285–91)

LEVEL OF EVIDENCE: II

After declining to a rate of 20.7% in 1996,[1] the frequency of cesarean delivery in the United States has progressively increased over the past decade to 30.2% in 2005, with the majority of these (71%) being the first "primary" cesarean.[2] Because of this trend, an increasing number of women are faced with the important decision of whether or not to

**For other members of the National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network, see the Appendix online at www.greenjournal.org/cgi/content/full/111/2/285/DC1.*

From the Departments of Obstetrics and Gynecology at Case Western Reserve University-MetroHealth Medical Center, Cleveland, Ohio; The Ohio State University, Columbus, Ohio; University of Texas Southwestern Medical Center, Dallas, Texas; University of Alabama at Birmingham, Birmingham, Alabama; University of Utah, Salt Lake City, Utah; University of Chicago, Chicago, Illinois; University of Pittsburgh, Pittsburgh, Pennsylvania; Wake Forest University, Winston-Salem, North Carolina; Thomas Jefferson University, Philadelphia, Pennsylvania; Wayne State University, Detroit, Michigan; University of Cincinnati, Cincinnati, Ohio; Columbia University, New York, New York; Brown University, Providence, Rhode Island; Northwestern University, Chicago, Illinois; University of Miami, Miami, Florida; University of Tennessee, Memphis, Tennessee; University of Texas at San Antonio, San Antonio, Texas; University of North Carolina, Chapel Hill, North Carolina; University of Texas at Houston, Houston, Texas; George Washington University Biostatistics Center, Washington, DC, and the National Institute of Child Health and Human Development, Bethesda, Maryland.

Supported by grants from the National Institute of Child Health and Human Development (HD21410, HD21414, HD27860, HD27861, HD27869, HD27905, HD27915, HD27917, HD34116, HD34122, HD34136, HD34208, HD34210, HD40500, HD40485, HD40544, HD40545, HD40560, HD40512, and HD36801).

The authors thank Francee Johnson, BSN, and Julia Gold, RN, for participating in protocol development and coordination between clinical research centers and Elizabeth Thom, PhD, for protocol/data management and statistical analysis.

Presented at the annual meeting of the Society for Gynecologic Investigation, March 22–25, 2006, Toronto, Ontario, Canada.

Corresponding author: Brian M. Mercer, MD, Department of Obstetrics and Gynecology, G240, MetroHealth Medical Center, 2500 MetroHealth Drive, Cleveland, OH 44109-1989.

Financial Disclosure

The authors have no potential conflicts of interest to disclose.

ISSN: 0029-7844/08

attempt a vaginal birth after cesarean delivery (VBAC). The American College of Obstetricians and Gynecologists (ACOG) has recently reaffirmed that VBAC is an appropriate alternative to elective repeat cesarean delivery after a single transverse lower segment cesarean delivery.[3]

In general, the likelihood of VBAC success is approximately 72%.[4] Attempted VBAC is associated with a 0.4–0.7% risk of uterine rupture, a risk which is increased with a prior classic or vertical uterine incision, labor induction, and possibly cervical ripening with prostaglandins.[4–6] Alternatively, repeated cesarean deliveries are associated with increased risks of placenta accreta, trauma to internal organs, transfusion, hysterectomy, and perioperative complications,[7–9] and cesarean delivery is not without risks of fetal injury.[10]

Considerable effort has been applied to determine factors that alter the likelihood of a successful trial of labor after cesarean delivery and also the maternal and fetal risks associated with attempted VBAC compared with repeat cesarean delivery. In a prospective multi-center observational cohort study of 17,898 women with prior cesarean deliveries attempting a VBAC, we have found an overall VBAC success rate of 73.4% and uterine rupture rate of 0.7% for women with a prior low transverse uterine incision.[6] Factors associated with VBAC success included any prior vaginal delivery (odds ratio [OR] 3.9, 95% confidence interval [CI] 3.6–4.3), and the occurrence of one or more prior successful VBAC attempts (OR 2.7, 95% CI 2.2–3.4).[11,12] Among women with a single prior cesarean delivery, vaginal delivery before or after the prior cesarean was the strongest predictor of VBAC success after controlling for other factors. Although this study and others have found prior vaginal birth to be associated with increased VBAC success, the impact of prior vaginal delivery on the risk of uterine rupture has been more controversial.[13–17] Several studies have suggested that prior VBAC does not alter the risk of uterine rupture and may be associated with increased uterine dehiscence.[13–15] Alternatively, in an analysis of women with one or more prior cesarean deliveries, we have found prior VBAC to be associated with a lower uterine rupture risk.[18]

The relationships between the number of prior VBACs and the probability of successful VBAC attempt or uterine rupture in the current pregnancy remain to be clearly elucidated. It is also unknown if successive labors will place an additive strain on the uterine scar, increasing the risk of uterine rupture when VBAC is attempted. The purpose of this analysis is to evaluate the impact of increasing number of prior VBACs on the likelihood of VBAC success and uterine rupture in subsequent pregnancies.

MATERIALS AND METHODS

This is a secondary analysis of a 4-year observational study conducted at 19 academic medical centers of the National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network (NICHD-MFMU Network) between 1999 and 2002. Details of the study design have been reported previously.[6] Briefly, trained and certified research nurses at each center prospectively identified women who were admitted for delivery and who had a history of cesarean delivery. The medical charts of these women were reviewed for demographic and clinical characteristics, medical and obstetric history, and pregnancy outcomes, including labor characteristics, delivery outcomes, and postpartum complications. Neonatal outcomes, including gestational age at delivery, birth weight, and major morbidities, were collected through hospital discharge or 120 days. Incomplete and equivocal details were resolved through caregiver and patient interview before discharge. Abstracted data were transmitted weekly to the data coordinating center and were edited for missing, out of range, and inconsistent values. Study approval was obtained from the institutional review board at each institution and the George Washington University Biostatistics Center.

For this analysis, we included only women with singleton pregnancies who had previously undergone at least one cesarean delivery by a low transverse uterine incision and who attempted a VBAC and delivered an infant of at least 20 weeks gestation or 500 g in the current pregnancy. Demographic characteristics and clinical outcomes were compared according to the number of prior VBACs subsequent to the last cesarean delivery.

Evaluated pregnancy outcomes included VBAC success, uterine rupture (through and through disruption or tear of the uterine muscle and visceral peritoneum or a uterine muscle separation with extension to adjacent structures), uterine rupture after labor induction, uterine dehiscence (disruption of the uterine muscle with intact serosa), surgical complications (broad ligament hematoma, cystotomy, or bowel or ureteral injury), thromboembolism (deep venous thrombosis or pulmonary embolus), transfusion, endometritis (clinical diagnosis of puerperal uterine infection in the absence of findings suggesting another source), maternal death, umbilical cord arterial pH 7.00 or less, neonatal intensive care unit admission,

Table 1. Demographic and Clinical Characteristics According to Number of Prior Successful Vaginal Birth After Cesarean Delivery Attempts

Characteristics	Number of Prior VBACs			P*
	0 (n=9,012)	1 (n=2,900)	2 or More (n=1,620)	
Age (y)	28.0±5.9	29.2±5.5	30.6±5.3	<.001†
Race				<.001
African American	33.4	39.0	46.8	
White	39.9	40.1	38.0	
Hispanic	21.2	17.6	11.5	
Other	5.5	3.2	3.8	
Insurance				<.001
Private	46.7	43.8	40.7	
Government	42.9	48.1	53.2	
Self-pay	10.3	8.1	6.0	
More than high school education‡	40.9	36.2	31.7	<.001
Pregravid body mass index (kg/m^2)	26.5±6.4	26.6±6.5	26.6±6.2	.28†
Body mass index at delivery (kg/m^2)	32.1±6.8	32.0±6.7	32.2±6.4	.45†
More than one prior cesarean delivery	4.1	4.5	7.7	<.001
Vaginal delivery before prior cesarean delivery	17.7	18.2	19.6	.10
Spontaneous labor	71.5	71.7	70.5	.52
Delivery gestation (wk)	38.8±2.8	38.7±2.7	38.6±2.6	<.001†
Preterm birth	12.9	12.8	15.5	.02
Birth weight (g)	3,263±680	3,258±679	3,237±670	.02†

VBACs, vaginal births after cesarean delivery.
Data are presented as mean±standard deviation or %.
* *P* values are from Mantel-Haenszel test for trend unless otherwise noted.
† *P* value is from Jonckheere-Terpstra test for trend.
‡ N=6,239, 1,975, and 1,082 for high school education.

neonatal hypoxic ischemic encephalopathy, and infant death. All uterine ruptures, maternal deaths, and stillbirths underwent secondary review by local study investigators and final central review to assure accuracy.

Statistical analysis was conducted with SAS 8.2 (SAS Institute, Cary, NC) and StatXact 5 (Cytel Software, Cambridge, MA). To test for trend and to calculate *P* values among women with increasing number of prior VBACs, the Mantel-Haenszel test was used for categorical variables and the Jonckheere-Terpstra test was used for continuous outcomes.[19–20] For one sample binomial interval estimation, the Blyth-Still-Casella interval was used.[21] A two-tailed nominal $P<.05$ was considered significant. No adjustment was made for multiple comparisons.

RESULTS

During the study period, there were 378,063 births, of which 45,988 had a singleton gestation and a history of cesarean delivery. Of those women with a prior cesarean delivery, 13,532 women (29.4%) had a low transverse uterine incision and attempted a VBAC, with an overall success rate of 71.8%. Among those eligible for this analysis, the number of women with 0, 1, 2, 3, and 4 or more prior VBACs were 9,012, 2,900, 1,058, 371, and 191, representing 66.6%, 21.4%, 7.8%, 2.7%, and 1.4% of the cohort, respectively. Outcomes for those with two or more prior VBACs did not change substantially with increasing number, so these women were grouped in one category. Demographic and clinical characteristics for this cohort are presented in Table 1. Maternal age and the frequencies of African-American race and government-assisted health insurance increased with increasing number of prior VBACs. Those with two or more prior VBACs were most likely to have had more than one prior cesarean delivery. Maternal body mass index, the fraction of women with a vaginal delivery before the prior cesarean, and the number of women with spontaneous labor in the current pregnancy did not differ between groups. Delivery gestation and neonatal birth weight declined statistically, but not in a clinically meaningful manner, with increasing number of prior VBACs.

The frequency of VBAC success rose with increasing number of prior VBACs, increasing from 63.3% (95% CI 62.3–64.3%) with no prior VBAC to 87.6% (95% CI 86.4–88.8%) and 90.9% (95% CI 89.5–92.3%) for those with one or two or more prior VBACs, respectively ($P<.001$, Table 2). The frequency of uterine rupture declined from 0.87% (95% CI 0.68–1.07%) with

Table 2. Pregnancy and Neonatal Outcomes According to Number of Prior Successful Vaginal Birth After Cesarean Delivery Attempts

Outcomes	Number of Prior VBACs			*P**
	0 (n=9,012)	1 (n=2,900)	2 or More (n=1,620)	
VBAC success	63.3	87.6	90.9	<.001
Uterine rupture	0.87	0.45	0.43	.01
Uterine rupture if induced	1.37	0.37	0.63	.03
Uterine dehiscence	0.94	0.24	0.25	<.001
Hysterectomy	0.23	0.17	0.06	.15
Surgical complications†	0.45	0.17	0.12	.008
Thromboembolism‡	0.09	0	0	.07
Transfusion	1.89	1.24	0.99	.002
Endometritis	3.68	1.17	1.30	<.001
Maternal death	0.02	0	0	.71
5-minute Apgar score=5 or less	2.50	2.11	1.86	.07
Cord arterial pH 7.00 or less§	2.34	1.63	1.62	.17
Neonatal intensive care unit admission	15.1	12.9	14.6	.08
Hypoxic ischemic encephalopathy	0.17	0.07	0	.05
Infant death	0.64	0.59	0.44	.35

VBAC, vaginal birth after cesarean delivery.
Data are expressed as %.
* *P* value from Mantel-Haenszel test for trend.
† Broad ligament hematoma, cystotomy, or bowel or ureteral injury.
‡ Deep venous thrombosis or pulmonary embolus.
§ N=3,249, 857, and 432 for umbilical cord arterial pH.

no prior VBACs to 0.45% (95% CI 0.24–0.76%) and 0.43% (95% CI 0.20–0.85%) for those with one or two or more prior VBACs, respectively (*P*=.01). The diagnosis of uterine dehiscence was also inversely related to the number of prior VBACs: 0.94% (95% CI 0.75–1.16%) compared with 0.24% (95% CI 0.11–0.48%) and 0.25% (95% CI 0.08–0.61%) for those with 0, 1, or 2 or more prior VBACs, respectively (*P*<.001). As is demonstrated in Figures 1 and 2, the likelihood of VBAC success appeared to reach a plateau for those with two prior VBACs and did not increase substantially thereafter (*P*<.001), whereas the risk of uterine rupture declined after one successful VBAC and did not change substantially with additional prior VBACs (*P*=.03). Further analysis of 12,908 women with only one prior cesarean delivery revealed similar results for pregnancy

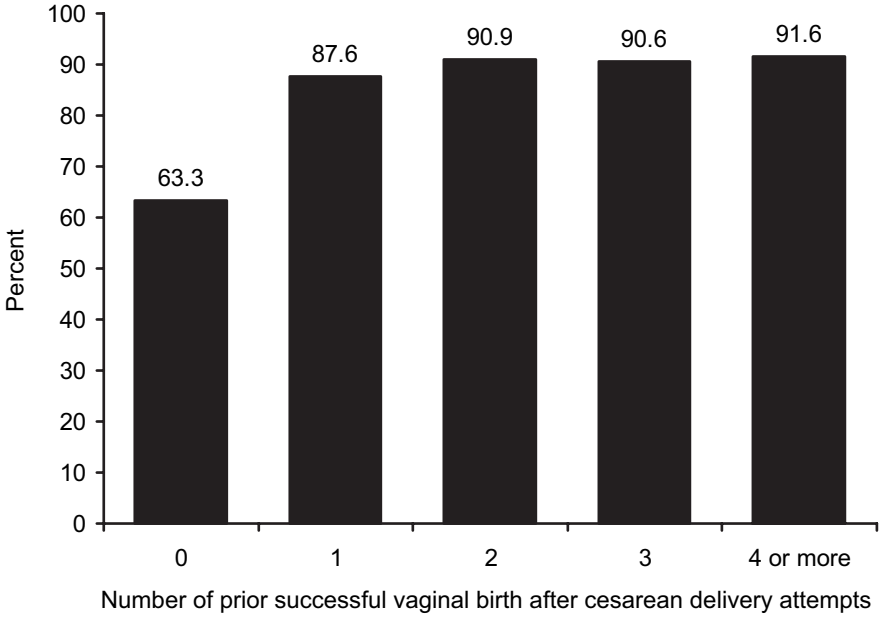

Fig. 1. Likelihood of successful vaginal birth after cesarean delivery (VBAC) according to the number of prior successful VBAC attempts (*P*<.001 for Mantel-Haenszel test of trend).

Mercer. Labor Outcome With Repeated Trials of Labor. Obstet Gynecol 2008.

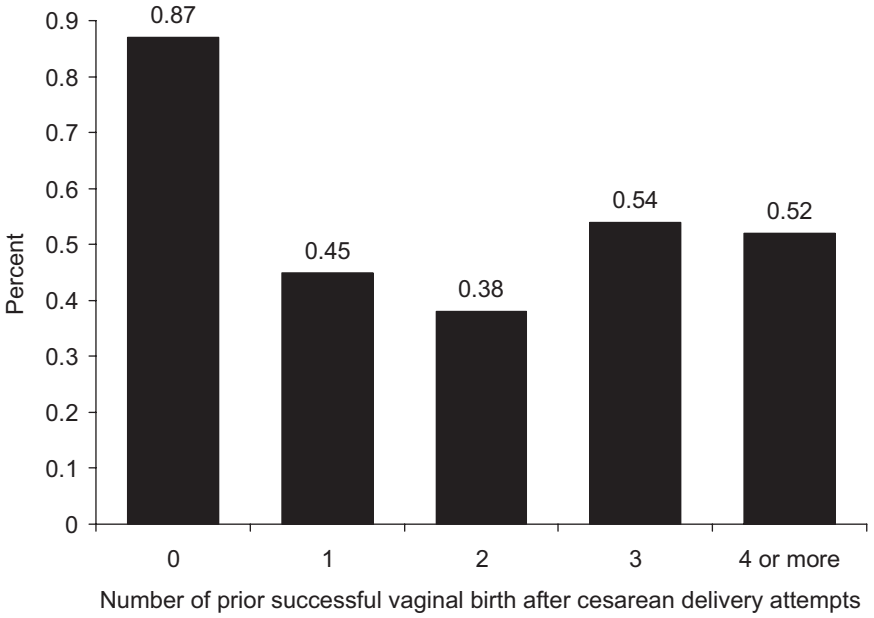

Fig. 2. Likelihood of uterine rupture during attempted vaginal birth after cesarean delivery (VBAC) according to the number of prior successful VBAC attempts (P=.03 for Mantel-Haenszel test of trend).
Mercer. Labor Outcome With Repeated Trials of Labor. Obstet Gynecol 2008.

and neonatal outcomes presented in Table 2 (data not shown).

Other maternal morbidities and peripartum complications were less common with increasing number of prior VBACs, likely related to the decreased need for cesarean delivery in the current pregnancy in this cohort. There were no evident increases in neonatal morbidities or mortality with increasing number of prior VBACs. We found trends toward reductions in the frequency of low 5-minute Apgar scores and hypoxic ischemic encephalopathy, but statistical significance was not reached.

DISCUSSION

In this analysis, we confirm earlier reports of improved VBAC success with a previous vaginal delivery, including the occurrence of a prior successful VBAC attempt.[11–16] In addition, we demonstrate a progressive improvement in the likelihood of VBAC success with increasing number of prior VBACs, with an apparent plateau at a 91% success rate after two prior VBACs. The benefits, risks, and factors affecting the outcomes of attempted VBAC have been well established.[4–7,11–16] Although considerable attention has been given to the potential risks and benefits of an attempted VBAC compared with an initial repeat cesarean, there is little information regarding the downstream effects of these decisions on future pregnancies. In a prior publication from this prospectively collected data set, we have demonstrated the risks of repeated cesarean deliveries, including increased risks of placenta accreta, trauma to maternal internal organs, need for hysterectomy and transfusion, and perioperative complications including infectious morbidities.[8] Regarding VBAC attempts, we have found that 73.4% of women attempting a VBAC will be successful and 0.7% will have a uterine rupture.[6]

Whether the risk of uterine rupture is affected by the occurrence of a prior vaginal delivery has not been clear. In separate retrospective studies of 2,204 and 1,216 pregnancies, no differences in the risk of uterine rupture were seen between those with and those without a prior vaginal delivery.[14,15] Alternatively, in a third retrospective analysis of 3,783 pregnancies, Zelop et al[17] found a lower risk of uterine rupture during a VBAC attempt for those with a prior vaginal delivery than for those without (0.2% compared with 1.1%, P=.01). In a previous analysis of women with one or more prior cesarean deliveries, a history of any prior VBAC was associated with a lower risk of uterine rupture (OR 0.52, 95% CI 0.34–0.82). However, we did not evaluate whether this association was dependent upon the number of prior VBACs.[18] In the current analysis, we found women with one or more prior VBACs to have approximately half the risk of uterine rupture when compared with those attempting their first VBAC (0.4–0.5% compared with 0.9%, P=.01). Further, contrary to prior reports of an increased risk of uterine dehiscence with a prior VBAC,[14] in this analysis we found the risk of uterine dehiscence to decline with increasing number of VBAC attempts (0.25% compared with 0.9%, P<.001) Thus, our data

do not support the notion that successive labors place additive or multiplicative strain on the uterine scar.

A major strength of this study is its size. This cohort of over 13,000 women who attempted VBAC offers insights into outcomes for the overall cohort and also for those with 0, 1, and more than two prior VBACs. Our findings were consistent between the overall cohort and a subanalysis restricted to women with only one prior cesarean delivery. Nevertheless, although the sample size was large, several of the outcomes of interest were uncommon, and the corresponding power to adequately compare outcomes between individual subgroups was limited. Regardless, this prospectively collected data set regarding the benefits and risks of repeated VBAC provides useful estimates of outcomes to practitioners and patients. It is plausible that the evaluation of outcomes in mostly large urban tertiary care hospitals in this study could bias our results toward more favorable outcomes due to increased availability of resources. However, because VBAC should not be attempted in institutions without resources and staffing available for patient monitoring and emergent cesarean delivery, we believe that this, in fact, is not a valid concern and that our findings are generalizable to institutions where VBAC is attempted. Alternatively, the tendency toward more complex patient mix in tertiary care institutions would predispose this population to more complications. Despite this, the vast majority of women attempting a VBAC did not suffer significant complications, regardless of number of prior attempts.

For those who are planning repeated pregnancies after a cesarean delivery, the decision to undergo a repeat cesarean or to attempt a VBAC has downstream consequences. The present analysis demonstrates that, due to the increased probability of VBAC success and decreased probability of uterine rupture with subsequent VBACs, the frequencies of both peripartum and perioperative complications decrease as the number of prior VBACs increases. Those who have had one or more VBACs can be reassured that the likelihood of vaginal delivery is increased and that the likelihood of complications is decreased with respect to the first attempt. This is in contrast to the increasing risks associated with multiple repeat cesarean deliveries.

We believe that the findings of this prospective analysis of a large cohort of pregnancies will provide important information for counseling women who are considering their options regarding VBAC. Our results are particularly important for those considering repeated pregnancies after an initial cesarean delivery. Although women planning large families should consider the risks associated with repeated cesarean deliveries, they should be reassured by the increasing success rates and decreasing risks associated with VBAC attempts in successive pregnancies.

REFERENCES

1. Menacker F. Trends in cesarean rates for first births and repeat cesarean rates for low risk women: United States, 1990–2003. Natl Vital Stat Rep 2005;54:1–8.
2. Hamilton BE, Martin JA, Ventura SJ. Births: preliminary data for 2005. Natl Vital Stat Rep 2006;55:1–18.
3. Vaginal birth after previous cesarean delivery. ACOG Practice Bulletin No. 54. The American College of Obstetricians and Gynecologists. Obstet Gynecol 2004;203–12.
4. Mozurkewich EL, Hutton EK. Elective repeat cesarean delivery versus trial of labor: a meta-analysis of the literature from 1989 to 1999. Am J Obstet Gynecol 2000;183:1187–97.
5. Lydon-Rochelle M, Holt VL, Easterling TR, Martin DP. Risk of uterine rupture during labor among women with a prior cesarean delivery. N Engl J Med 2001;345:3–8.
6. Landon MB, Hauth JC, Leveno KJ, Spong CY, Leindecker S, Varner MW, et al; National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. N Engl J Med 2004;16: 351:2581–9.
7. Burrows LJ, Meyn LA, Weber AM. Maternal morbidity associated with vaginal versus cesarean delivery. Obstet Gynecol 2004;103:907–12.
8. Silver RM, Landon MB, Rouse DJ, Leveno KJ, Spong CY, Thom EA, et al; National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Maternal morbidity associated with multiple repeat cesarean deliveries. Obstet Gynecol 2006;107:1226–32.
9. Nisenblat V, Barak S, Griness OB, Degani S, Ohel G, Gonen R. Maternal complications associated with multiple cesarean deliveries. Obstet Gynecol 2006;108:21–6.
10. Alexander JM, Leveno KJ, Hauth J, Landon MB, Thom E, Spong CY, et al; National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Fetal injury associated with cesarean delivery. Obstet Gynecol 2006;108:885–90.
11. Landon MB, Leindecker S, Spong CY, Hauth JC, Bloom S, Varner MW, et al; National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. The MFMU Cesarean Registry: factors affecting the success of trial of labor after previous cesarean delivery. Am J Obstet Gynecol 2005;193:1016–23.
12. Grobman WA, Lai Y, Landon MB, Spong CY, Leveno KJ, Rouse DJ, et al; National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units Network (MFMU). Development of a nomogram for prediction of vaginal birth after cesarean delivery. Obstet Gynecol 2007; 109:806–12.
13. Elkousy MA, Sammel M, Stevens E, Peipert JF, Macones G. The effect of birth weight on vaginal birth after cesarean delivery success rates. Am J Obstet Gynecol 2003;188:824–30.
14. Hendler I, Bujold E. Effect of prior vaginal delivery or prior vaginal birth after cesarean delivery on obstetric outcomes in women undergoing trial of labor. Obstet Gynecol 2004;104: 273–7.

15. Gyamfi C, Juhasz G, Gyamfi P, Stone JL. Increased success of trial of labor after previous vaginal birth after cesarean. Obstet Gynecol 2004;104:715–9.

16. Caughey AB, Shipp TD, Repke JT, Zelop C, Cohen A, Lieherman E. Trial of labor after cesarean delivery: the effect of previous vaginal delivery. Am J Obstet Gynecol 1998;179: 938–41.

17. Zelop CM, Shipp TD, Repke JT, Cohen A, Lieberman E. Effect of previous vaginal delivery on the risk of uterine rupture during a subsequent trial of labor. Am J Obstet Gynecol 2000;183:1184–6.

18. Landon MB, Spong CY, Thom E, Hauth JC, Bloom SL, Varner MW, et al. Risk of uterine rupture with a trial of labor in women with multiple and single prior cesarean delivery. Obstet Gynecol 2006;108:12–20.

19. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst 1959;22:719–48.

20. Hollander M, Wolfe DA. Nonparametric statistical methods. New York (NY): John Wiley and Sons; 1973. p. 120–3.

21. Casella G. Refining binomial confidence intervals. Can J Stat 1986;14:113–29.