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The association of placenta previa with history of cesarean delivery and abortion: A metaanalysis

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Abstract

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Objective: Our purpose was to determine the incidence of placenta previa based on the available epidemiologic evidence and to quantify the risk of placenta previa based on the presence and number of cesarean deliveries and a history of spontaneous and induced abortion.

Study Design: We reviewed studies on placenta previa published between 1950 and 1996 on the basis of a comprehensive literature search with use of MEDLINE and by identifying studies cited in the references of published reports. Studies were chosen for inclusion in the metaanalysis if the incidence of placenta previa and its cross-classification with either prior cesarean delivery or abortions (both spontaneous and induced) or both were available. We also extracted details about the study design (case-control or cohort study) and place where they were conducted (United States or other countries). Published case reports dealing with placenta previa and studies relating to abruptio placentae were excluded from this review. We also restricted the search to studies published in English. No attempts were made to locate any unpublished studies. Data from studies identified during the literature search were reviewed and abstracted by a single author. In case of discrepancies or when the information presented in a study was unclear, abstraction by a (blinded) second reviewer was sought to resolve the discrepancy.

Results: Data on the incidence of placenta previa and its associations with previous cesarean delivery and abortions were abstracted. Subgroup analyses were performed to identify potential sources of heterogeneity by study design and place where they were conducted. Statistical methods used for the metaanalysis included the fixed-effects logistic regression model, whereas potential sources of heterogeneity among studies were evaluated by fitting random-effects

models. The tabulation of 36 studies identified a total of 3.7 million pregnant women, of whom 13,992 patients were diagnosed with placenta previa. The reported incidence of placenta previa ranged between 0.28% and 2.0%, or approximately 1 in 200 deliveries. Women with at least one prior cesarean delivery were 2.6 (95% confidence interval 2.3 to 3.0) times at greater risk for development of placenta previa in a subsequent pregnancy. The results varied by study design, with case-control studies showing a stronger relative risk (relative risk 3.8, 95% confidence interval 2.3 to 6.4) than cohort studies did (relative risk 2.4, 95% confidence interval 2.1 to 2.8). Four studies, encompassing 170,640 pregnant women, provided data on the number of previous cesarean deliveries. These studies showed a dose-response pattern for the risk of previa on the basis of the number of prior cesarean deliveries. Relative risks were 4.5 (95% confidence interval 3.6 to 5.5) for one, 7.4 (95% confidence interval 7.1 to 7.7) for two, 6.5 (95% confidence interval 3.6 to 11.6) for three, and 44.9 (95% confidence interval 13.5 to 149.5) for four or more prior cesarean deliveries. Women with a history of spontaneous or induced abortion had a relative risk of placenta previa of 1.6 (95% confidence interval 1.0 to 2.6) and 1.7 (95% confidence interval 1.0 to 2.9), respectively. Substantial heterogeneity in the results of the metaanalysis was noted among studies.

Conclusion: There is a strong association between having a previous cesarean delivery, spontaneous or induced abortion, and the subsequent development of placenta previa. The risk increases with number of prior cesarean deliveries. Pregnant women with a history of cesarean delivery or abortion must be regarded as high risk for placenta previa and must be monitored carefully. This study provides yet another reason for reducing the rate of primary cesarean delivery and for advocating vaginal birth for women with prior cesarean delivery.

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Key words: [Cesarean delivery](#), [induced abortion](#), [metaanalysis](#), [placenta previa](#), [spontaneous abortion](#)

Although placenta previa is relatively uncommon (incidence of 3 to 9 per 1000 pregnancies), it is regarded as one of the leading causes of uterine bleeding during the latter stages in gestation¹ and has been recognized as an important determinant of maternal morbidity and adverse perinatal outcomes. Pregnancies complicated by placenta previa have resulted in excessively high rates of preterm delivery, low birth weight, stillbirths, and neonatal and perinatal deaths. Risk factors associated with placenta previa include advanced maternal age, multiparity, cigarette smoking and “crack” or cocaine use, history of placenta previa, cesarean delivery, spontaneous and induced abortions, and prior gynecologic surgeries. Nonetheless, the etiology of placenta previa largely remains obscure and speculative. In spite of the advent of ultrasonography to diagnose this disorder and the ability to assess fetal lung maturity to appropriately time delivery, efforts to improve perinatal outcomes in cases of placenta previa continue to pose a challenge.

It appears that the rate of cesarean delivery has been increasing steadily over the past two decades. Some studies have observed an increased frequency of placenta previa among women with a prior history of cesarean delivery or abortions, suggesting an association with surgical procedures that disrupt the uterine cavity. Nonetheless, the extent to which a history of cesarean delivery or spontaneous and induced abortion predisposes women to the development of placenta previa is unclear from earlier studies.

We performed a systematic review and metaanalysis of all published studies on placenta previa to determine its incidence and to quantify the risk of placenta previa on the basis of the presence and number of cesarean deliveries and a history of spontaneous and induced abortions. In addition, the systematic review of all studies enabled us to also identify sources of heterogeneity among studies.

Literature review.

We reviewed all studies published between 1950 and 1996 on placenta previa. Studies chosen for the review were selected on the basis of a comprehensive literature search with use of MEDLINE and by identifying studies cited in the bibliography of published reports. Key words that were used in the MEDLINE search included “placenta pr(a)evia,” “placental disorders,” “anteartum h(a)emorrhage,” and “anteartum bleeding.” In addition, the key words “c(a)esarean delivery,” “c(a)esarean section,” “uterine surgery,” “spontaneous abortion,” “induced abortion,” and “elective abortion” were also used in conjunction with the search leading to studies on placenta previa. Published case reports dealing with placenta previa and studies relating to abruptio placentae were excluded from this review. We also restricted the search to studies published in English. No attempts were made to locate any unpublished studies or studies in abstract form. Multiple articles resulting from the same data source (e.g., Collaborative Perinatal Project²⁻⁵) were only included once in the metaanalysis. However, if two studies came from the same data source but spanned nonoverlapping time periods of data accrual, they were both included in the metaanalysis.

Data extraction.

We identified a total of 41 published studies^{2,6-45} on the basis of our inclusion criteria relating to placenta previa. From these studies, information on the incidence of placenta previa or its association with history of cesarean delivery and abortions were available from 36 studies.^{2,6-40} These studies were reviewed critically by the first author (C.V.A.), and information on the total number of pregnancies and the number of pregnancies complicated by placenta previa and data on placenta previa cross-classified by prior cesarean delivery and spontaneous and induced abortions were abstracted. Data on the type of study design (i.e., cohort or case-control studies) and the country where the study was carried out were also ascertained. Studies^{20,41-43} that did not provide sufficient information to carry out a metaanalysis or those that did not provide data for the comparison group (e.g., number of pregnancies without placenta previa among women with prior cesarean delivery) were excluded from our metaanalysis, although these studies were still included in an analysis of incidence of previa, when data were available. In case of discrepancies or when the information presented in a study was unclear, abstraction by a (blinded) second reviewer (J.C.S.) was sought to resolve the discrepancy.

Statistical methods for metaanalysis.

The incidence (risk) of placenta previa from cohort studies was obtained by dividing the number of cases of placenta previa by the total number of pregnancies. This information was abstracted from case-control studies, if reported. We calculated odds ratios and their SEs as the effect measure on the basis of the data abstracted from each study. Data that were abstracted from each study were arranged in 2×2 tables, and 0.5 was added to cells that contained no observations to improve the precision of the effect measure.⁴⁶ Pooled estimates of odds ratios were obtained by weighting each study by the inverse variance of the effect measure on a logarithmic scale. This approach to pooling the results assumes that the study populations being compared are similar and hence corresponds to a fixed-effects analysis. The validity of pooling the odds ratios was tested (test for heterogeneity) on the basis of a χ^2 test.⁴⁷ A violation of this test implies that the studies being grouped differ from one another. In the presence of significant heterogeneity in the effect measure among studies being compared, we then performed a random-effects analysis that was based on the method described by DerSimonian and Laird.⁴⁸ The random-effects analysis accounts for the interstudy variations. Our goal of performing this metaanalysis was to identify sources of heterogeneity among studies.

To examine for the presence of any trends in the incidence of placenta previa over time, we used the locally weighted scatterplot smoother procedure.⁴⁹ This procedure is a nonparametric scatterplot smoother that down-weights observations that are distant from its neighbors and,

conversely, assigns larger weights to observations that are closer to each other. For metaanalysis relating to the number of prior cesarean deliveries, we computed an estimate of log odds ratio with their SEs on the basis of methods described by Greenland and Longnecker.⁵⁰ This method adjusts for the correlation that results from use of a single reference category (i.e., no prior cesarean delivery) while evaluating the risk of placenta previa by number of prior cesarean deliveries.

To assess the public health implications of history of cesarean delivery and abortions on placenta previa, we also computed the population attributable risk.⁵¹ The population attributable risk can be interpreted as the proportion of the adverse outcome (i.e., placenta previa) that could be attributed to cesarean delivery or spontaneous and induced abortions. All statistical analyses were performed on the SAS system version 6.11 (SAS Institute, Cary, N.C.) operating on the UNIX system.

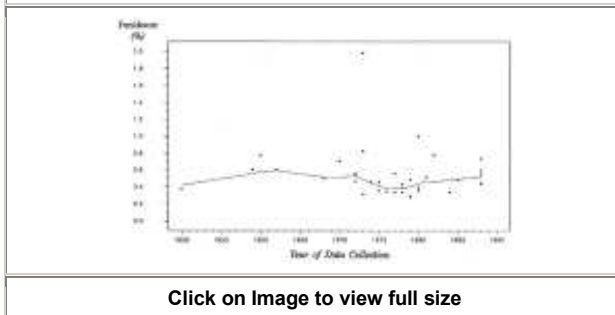
Results

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Incidence of placenta previa.

Data abstracted from 36 studies^{2,6-40} resulted in a total of 3.7 million pregnant women, of whom 13,992 were identified with placenta previa. The reported incidence of placenta previa ranged between 0.28% to 1.96%, or approximately 1 in 200 pregnancies. The incidence of placenta previa was the same for both cohort and case-control studies. An examination for trends over time in the incidence of placenta previa revealed that the incidence of this disorder was almost similar until the mid-1980s (1966 to 1974: incidence was 0.36%; 1975 to 1984, 0.37%), but the incidence was 0.48% among studies conducted between 1985 and 1995 (Fig. 1).

Fig. 1. Trends in incidence of placenta previa (*smoothed line* was generated based on locally weighted scatterplot smoother procedure, a nonparametric regression smoothing procedure).

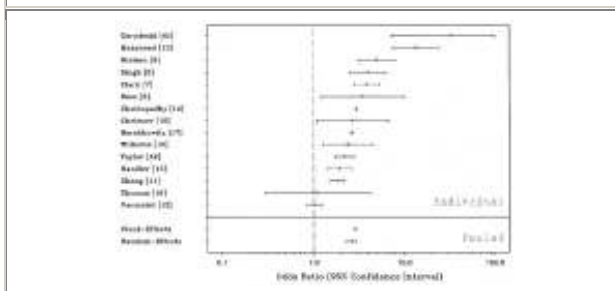


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Association with prior cesarean delivery.

Associations between history of cesarean delivery and placenta previa were evaluated in 15 published studies^{6-18,44,45} (Fig. 2).

Fig. 2. Association of placenta previa with history of cesarean delivery: Odds ratios with 95% confidence intervals (reference numbers in brackets).



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Pooling of data from all these studies resulted in an odds ratio of 2.6 (95% confidence interval 2.3 to 3.0), although the test for homogeneity of the pooled odds ratios was violated ($\chi^2 = 222.8$, 14 degrees of freedom, $p < 0.0001$) (Table I).

Table I. Association between prior cesarean delivery and placenta previa: A metaanalysis based on fixed- and random-effects models

Comparison	No. of studies	Fixed-effects OR and 95% CI	χ^2 *significance	Random-effects OR and 95% CI
Overall ^{6-18,41,42}	15	2.9 (2.8-3.0)	222.8 ($p < 0.0001$)	2.6 (2.3-3.0)
U.S. studies ^{7,10,11,15,16,18,42}	7	2.2 (1.9-2.5)	17.8 ($p < 0.0001$)	2.3 (1.7-2.8)
Other countries ^{6,8,9,12-15,17,41}	8	2.9 (2.8-3.0)	184.6 ($p < 0.0001$)	2.4 (2.0-2.9)
Cohort studies ^{6,7,9,11,12,16,17}	8	2.9 (2.8-3.0)	174.4 ($p < 0.0001$)	2.4 (2.1-2.8)
Case-control studies ^{8,10,13,15,18,41,42}	7	2.6 (2.2-3.1)	46.9 ($p < 0.0001$)	3.8 (2.3-6.4)

OR, Odds ratio; CI, confidence interval.

*Degrees of freedom for χ^2 test are number of studies minus one.

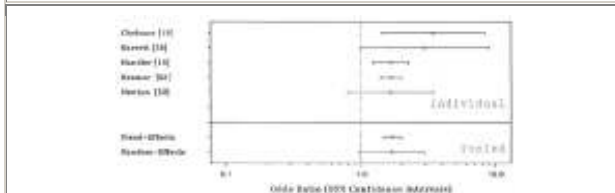
Hence stratification of the studies on the basis of their study designs resulted in a pooled odds ratio of 2.4 (95% confidence interval 2.1 to 2.8) for cohort^{6,7,10-12,16,17} and 3.8 (95% confidence interval 2.3 to 6.4) for case-control studies.^{8,10,13,15,18,41,42} Tests for homogeneity of odds ratios for both comparisons were violated. Associations between prior cesarean delivery and placenta previa were almost the same both for studies based in the United States^{6-9,11-14,17,41} and elsewhere.^{7, 10, 11, 15, 16, 42}

We further analyzed the association between placenta previa in relation to the number of prior cesarean deliveries. Data available from four studies^{7,12,14,17} encompassing a total of 170,640 pregnant women showed a dose-response pattern in the risk of previa with increasing number of prior cesarean deliveries. Odds ratios were 4.5 (95% confidence interval 3.6 to 5.5) for one and 7.4 (95% confidence interval 7.1 to 7.7) for two prior cesarean deliveries (based on all four studies), 6.5 (95% confidence interval 3.6 to 11.6) for three prior cesarean deliveries (based on two studies^{7,17}), and 44.9 (95% confidence interval 13.5 to 149.5) for four or more prior cesarean deliveries (based on one study⁷). There was an exponential increase in the risk of placenta previa with number of prior cesarean deliveries.

Association with prior abortions.

We identified five studies^{15,18,28,52,53} that evaluated the association between prior spontaneous abortion and the subsequent development of placenta previa (Fig. 3).

Fig. 3. Association of placenta previa with history of spontaneous abortion: Odds ratios with 95% confidence intervals (reference numbers in brackets).



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The random-effects pooled analysis indicated that the risk of placenta previa was 1.7 (95% confidence interval 1.0 to 2.9) for women with at least one prior spontaneous abortion (Table II).

Table II. Association between prior spontaneous and induced abortions and placenta previa: A metaanalysis based on fixed- and random-effects models

Comparison	No. of studies	Fixed-effects OR and 95% CI	χ^2 p value	Random-effects OR and 95% CI
Spontaneous abortion†				
Overall ^{15,18,28,52,53}	5	1.7 (1.5-2.0)	3.4 (0.4933)	1.7 (1.0-2.9)
Cohort studies ²⁸	1	3.0 (1.5-2.0)	—	—
Case-control studies ^{15,18,52,53}	4	1.7 (1.5-2.0)	2.5 (0.4753)	1.7 (1.5-2.0)
Induced abortion†				
Overall ^{9,15,28,42,52,54}	6	1.5 (1.3-1.7)	43.7 ($p < 0.0001$)	1.6 (1.0-2.6)
Cohort studies ²⁸	1	6.7 (2.7-16.8)	—	—
Case-control studies ^{9,15,42,52,54}	5	1.5 (1.3-1.7)	33.3 ($p < 0.0001$)	1.3 (0.7-2.3)

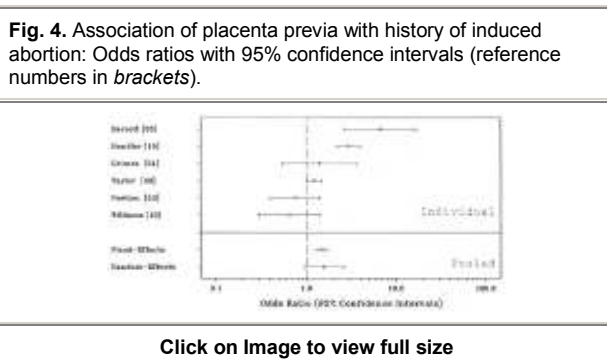
OR, Odds ratio; CI, confidence interval.

*Degrees of freedom for χ^2 test is number of studies minus one.

†All studies were based in the United States.

All five studies were cohort studies. The test for homogeneity of odds ratios was not violated ($p = 0.4933$). The association between prior spontaneous abortion and the subsequent development of placenta previa was the same when stratified on study design.

Six studies^{10,15,28,42,52,54} reported the association between placenta previa and history of induced abortions (Fig. 4), all of whom were based in the United States.



Five of the six studies were case-control studies. Although the test for homogeneity of the pooled odds ratio was violated ($\chi^2 = 43.7$, 5 degrees of freedom, $p < 0.0001$), a history of spontaneous abortion was associated with a 70% (95% confidence interval 1.0 to 2.9) increase in the risk of subsequent development of placenta previa. Restricting the analysis to the five case-control studies^{10,15,42,52,54} resulted in a decreased odds ratio (odds ratio 1.3, 95% confidence interval 0.7 to 2.3) for placenta previa, whereas the odds ratio from the single cohort study²⁸ was 6.7 (95% confidence interval 2.7 to 16.8). Additionally, with use of data from the vital records, Zhang and Savitz reported that the risk of placenta previa was 1.6 (95% confidence interval 1.3 to 1.8) for women with one abortion (either spontaneous or induced), 2.3 (95% confidence interval 1.8 to 3.0) for those with two, and 3.7 (95% confidence interval 2.7 to 5.2) for those with three or more abortions.

Comment

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Placenta previa has been reported to occur in approximately 0.3% to 0.8% of pregnancies.¹ A variation in this incidence has been attributed to methods of diagnosis, definitions used, and diverse nature of patient populations being studied. Although the overall incidence of placenta previa has been remarkably stable for almost three decades, the incidence of this disorder was almost similar until the mid-1980s (1966 to 1974: incidence was 0.36%; 1975 to 1984, 0.37%), but the incidence was 0.48% among studies conducted between 1985 and 1995 (see Fig. 1).

The increased incidence of placenta previa in the last decade may be the result of increasing cesarean delivery rates during this period or the more widespread use of ultrasonography for detecting placenta previa.

Several studies, based on ultrasonography findings, have shown that the incidence of placenta previa is about 3% to 5% in a normal obstetric population during midtrimester.⁵⁵ However, this frequency falls dramatically to almost 0.3% to 0.7% among term pregnancies as a result of the so-called placental "migration." Almost four decades ago Bender⁵⁶ first observed an increased frequency of placenta previa among women with uterine scarring (because of cesarean delivery or abortions) in prior pregnancies. Recently, few studies have explored this association and have unequivocally observed increased risks of placenta previa among women with a history of cesarean delivery. An association between placenta previa and prior cesarean delivery is biologically plausible. Damage to the endometrial and myometrial uterine lining (during cesarean delivery) can predispose to a low implantation of the placenta in the uterus. This metaanalysis quantifies the risk on the basis of the number of previous cesarean deliveries, implying a dose-response effect of multiple uterine procedures. Likewise, curettage of the uterus during a spontaneous or induced abortion may significantly damage the endometrium and uterine cavity so as to increase the risk for placenta previa. Unfortunately, we were unable to evaluate the association between curettage and subsequent development of placenta previa because of insufficient information from published studies.

The strength of this metaanalysis is the sheer size of the study. Although some of the associations observed in this study violated the homogeneity assumptions because of pooling of several studies, interstudy heterogeneity was adequately addressed through the fit of models on the basis of random-effects analysis. Nonetheless, a few methodologic limitations in this study must also be noted. First, the risk of placenta previa increases both because of aging effects of the uterus and repeated pregnancies.³⁹ Hence an association between prior uterine scarring from cesarean delivery or abortion and placenta previa may have been confounded, in part, because of repeated pregnancies. Unfortunately, insufficient data from published studies precluded us from adequately controlling for parity effect. Another potential limitation of the metaanalysis is publication bias. We may have missed identifying published studies during our literature search. In spite of our best efforts to identify studies, we may have missed some that may have reported data on placenta previa and prior cesarean delivery or abortions as a secondary analysis. Nevertheless, to account for this bias on our findings, we report the results from random-effects regression models, which assume that studies included in our metaanalysis is a (random) sample from a larger population of similar studies. In addition, we generated a "funnel-plot" (by plotting the log odds ratio against their corresponding SEs, graph not shown) to examine for indications of publication bias for history of cesarean delivery and abortions. The plots did not indicate the presence of any publication bias.

Another shortcoming of this metaanalysis is that we were unable to evaluate the risk of placenta previa in relation to uterine rupture, complications occurring with an abortion, curettage for postpartum hemorrhage or retained products of conception, postpartum complications such as endometritis, multiple gestations, and other potential risk factors for this disorder. These data were not universally available from each of the individual studies. Future prospective studies should evaluate these factors to better understand the etiology of placenta previa.

Public health implications.

The rates of primary cesarean delivery have been steadily increasing in the past decade. Although this increase has probably improved fetal and neonatal morbidities and other adverse reproductive outcomes as well, the public health implications for the rise in cesarean delivery rates have been poorly addressed.

Given that the rate of cesarean delivery is 20% in the general population and if one is interested in reducing this rate by 50% (i.e., from 20% to 10%), the population-attributable risk⁵¹ for prior cesarean delivery on the subsequent risk of placenta previa is 14%. This implies that by reducing the primary and repeat cesarean delivery rates by half the risk for placenta previa could be reduced by 14%. Similarly, assuming that the rates of spontaneous and induced

abortions are 20% and 5%, respectively, and if these rates are reduced by 50%, then 6.5% and 1.5% of placenta previa cases could potentially be averted. This suggests that a reduction in uterine instrumentation rates for the management of both spontaneous and induced abortions could further reduce the risk of placenta previa. The public health ramifications of these findings needs careful assessment in future prospective studies.

In conclusion, our (meta)analysis clearly demonstrates an elevated risk for placenta previa among women with prior cesarean delivery or abortions. Moreover, this risk increases dramatically with increasing number of prior cesarean deliveries. Pregnant women with a history of cesarean delivery or abortion must be regarded as being at increased risk for the subsequent development of placenta previa. This study provides yet another reason for reducing the primary cesarean delivery rate and for advocating vaginal birth for women with prior cesarean delivery.

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Vaginal birth after cesarean section: Trial of labor or repeat cesarean section? A decision analysis

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David D. Mankuta, MD, MHA^{a*}, Moshe M. Leshno, MD, PhD^b, Moshe M. Menasche, MD^a, Mayer M. Brezis, MD, MPH^c

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The effect of placenta previa on neonatal mortality: A population-based study in the United States, 1989 through 1997

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Cande V. Ananth, PhD, MPH^a, John C. Smulian, MD, MPH^b, Anthony M. Vintzileos, MD^b

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Placenta previa: Neonatal death after live births in the United States

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Hamisu M. Salihu, MD, PhD^a, Qing Li, MD^a, Dwight J. Rouse, MD^b, Greg R. Alexander, MPH, ScD^a

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Karrie Francois, MD, James M. Johnson, MD, Cathleen Harris, MD, MPH

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