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Interpregnancy Interval After Pregnancy Loss and Risk of Repeat Miscarriage

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OBJECTIVE: To assess whether interpregnancy interval length after a pregnancy loss is associated with risk of repeat miscarriage.

METHODS: This analysis includes pregnant women participating in the Right From the Start (2000–2012) community-based prospective cohort study whose most recent pregnancy before enrollment ended in miscarriage. Interpregnancy interval was defined as the time between a prior miscarriage and the last menstrual period of the study pregnancy. Miscarriage was defined as pregnancy loss before 20 weeks of gestation. Cox proportional hazard models were used to estimate crude and adjusted hazard ratios and 95% CIs for the association between different interpregnancy interval lengths and miscarriage in the study pregnancy. Adjusted models included maternal age, race, parity, body mass index, and education.

RESULTS: Among the 514 study participants who reported miscarriage as their most recent pregnancy outcome, 15.7% had a repeat miscarriage in the study

pregnancy (n=81). Median maternal age was 30 years (interquartile range 27–34) and 55.6% of participants had at least one previous livebirth (n=286). When compared with women with interpregnancy intervals of 6–18 months (n=136), women with intervals of less than 3 months (n=124) had the lowest risk of repeat miscarriage (7.3% compared with 22.1%; adjusted hazard ratio 0.33, 95% CI 0.16–0.71). Neither maternal race nor parity modified the association. Attempting to conceive immediately was not associated with increased risk of miscarriage in the next pregnancy.

CONCLUSION: An interpregnancy interval after pregnancy loss of less than 3 months is associated with the lowest risk of subsequent miscarriage. This implies counseling women to delay conception to reduce risk of miscarriage may not be warranted.

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Miscarriage is the most common adverse pregnancy outcome with an estimated 17% of clinically recognized pregnancies ending in loss.¹ Most women who experience a miscarriage want to know whether they can do anything to prevent a future miscarriage from occurring, and many couples seek counsel from health care providers on how long they should wait before trying to conceive again.² No consensus for optimal spacing after a miscarriage exists. The World Health Organization is the only advisory body to put forth formal guidelines, but they note their recommendation to wait at least 6 months is limited because it is based on a single cross-sectional study that did not differentiate between induced and spontaneous abortions.^{3,4} Many physicians recommend waiting at least 3 months after a miscarriage to reduce the chance of another miscarriage.⁵ As age at first pregnancy rises in developed countries, recommendations for delaying future pregnancies need to be balanced with risk associated with increasing maternal age.⁶



The objective of this study is to evaluate the relationship between length of interpregnancy interval after a loss and risk of subsequent miscarriage in the Right From the Start community-based prospective cohort study.

MATERIALS AND METHODS

Right From the Start is a prospective cohort study that recruited women who were pregnant or planning a pregnancy from eight metropolitan areas in North Carolina, Tennessee, and Texas between 2000 and 2012.⁷ To be eligible for the study, women had to be aged 18 years or older, English- or Spanish-speaking, and not using assisted reproductive technologies to conceive. Women who were planning a pregnancy could pre-enroll and were fully enrolled at the first positive pregnancy test. Informed consent was obtained from all study participants on enrollment. The cohort was designed to enroll participants early in gestation to optimally study miscarriage. Median gestational age at enrollment for this sample was 39 days (interquartile range 34–48). All women were enrolled before 12 weeks of gestation. This study was approved by Vanderbilt University's institutional review board (070037).

Study participants completed a baseline interview at the time of enrollment and an extensive computer-assisted telephone interview at the end of the first trimester. These interviews collected information on

maternal demographics, obstetric history, lifestyle characteristics, and health behaviors around the time of conception. All participants also underwent a study ultrasonogram in the first trimester to confirm gestational dating. Maternal anthropometric measurements taken at the time of ultrasonography were used to calculate maternal body mass index (BMI, calculated as weight (kg)/[height (m)]²).

This analysis was restricted to women who were fully enrolled, consented, and pregnant. Of the 5,780 women who met these criteria, 530 reported miscarriage as their most recent pregnancy outcome. We excluded women who had induced abortions, ectopic or molar pregnancies, or pregnancies with unknown outcome, resulting in a sample population of 514 women (Fig. 1). Interpregnancy interval was defined as the time between the prior miscarriage and self-reported last menstrual period of the study pregnancy. Self-reported last menstrual period is validated in Right From the Start participants (average difference of 0.8 days between last menstrual period-based and ultrasound-based dating).⁸ We classified miscarriage in the study pregnancy as loss before 20 weeks of gestation (n=81). The comparison group included participants with a pregnancy surviving past 20 weeks of gestation (n=431 livebirths, n=2 stillbirths). Pregnancy status at 20 weeks of gestation was determined by maternal report validated by vital records.

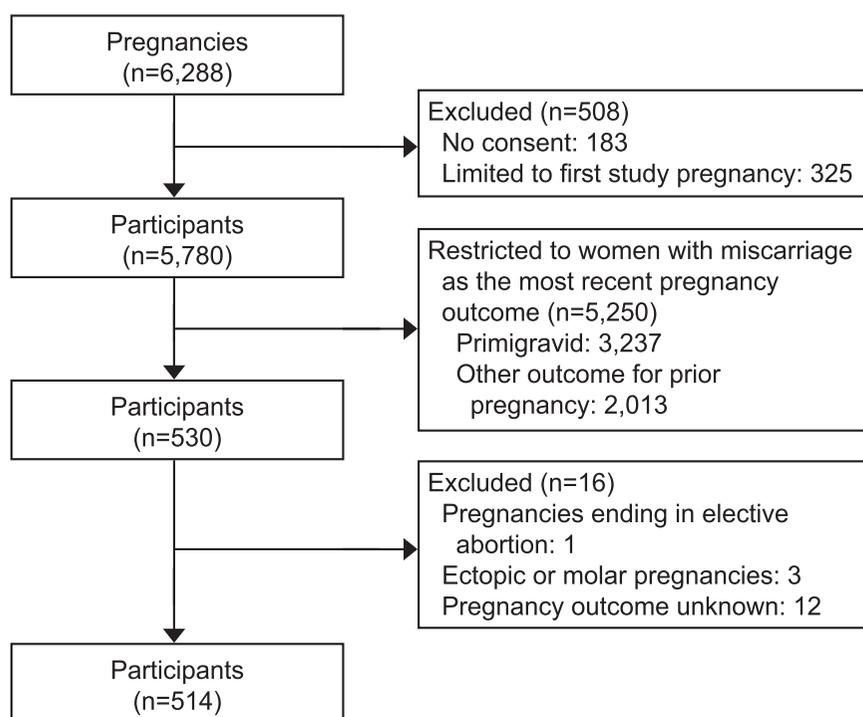


Fig. 1. Flow diagram showing inclusion and exclusion criteria for the study sample.

Sundermann. *Interpregnancy Interval After Miscarriage*. *Obstet Gynecol* 2017.



We modeled the relationship between interpregnancy interval and miscarriage risk in the study pregnancy in two ways. First, we divided interpregnancy interval into four categories to compare common recommendations (less than 3 months, 3–5.99 months, 6–17.99 months, and 18 months or greater). We also modeled interpregnancy interval as a continuous variable using restricted cubic splines to more specifically characterize the underlying relationship. We plotted the expected value of the proportion of pregnancies to end in miscarriage by interpregnancy interval length using a logistic regression model including restricted cubic spline terms for interpregnancy interval adjusted for selected covariates.

Difference in study participant characteristics by interpregnancy interval category was evaluated using Pearson's χ^2 test. We used Cox proportional hazard models to estimate the hazard ratio and 95% CI for the association between interpregnancy interval and miscarriage risk. Survival time was defined as days of gestation in the study pregnancy and accumulated to time of miscarriage or 20 weeks of gestation, whichever came first. Assumptions of proportional hazards were met. Participants missing any covariate data (maternal age, BMI, education, parity, or ethnicity) were excluded from the survival analysis ($n=3$). The interpregnancy interval of 6–17.99 months was used as the referent category because this range coincided with the World Health Organization-recommended interval. Potential confounders consisted of variables known or suspected to associate with risk of miscarriage and interpregnancy interval length. All adjusted models included the following a priori selected covariates: maternal age (years), ethnicity (non-Hispanic white, non-Hispanic black, other), BMI, parity (zero, one, two or more prior births), and education (high school or less, some college, college or more). We also present a model adjusted for number of prior miscarriages. We tested for effect modification by race and parity using the likelihood ratio test for the inclusion of interaction terms. Interaction terms were retained in the model for P values $<.20$.

Interpregnancy interval is made up of two time periods: wait time (the time after loss a couple waits before trying to conceive again) and time to pregnancy (the time a couple spends trying to conceive). At the first-trimester interview, women were asked to recall the amount of time they spent trying to conceive. We used this information and the calculated interpregnancy interval to approximate wait time. In a secondary analysis, we used logistic regression to quantify the adjusted relationship between wait time

(modeled using restricted cubic splines) and repeat miscarriage risk. The secondary analysis was limited to women who had time-to-pregnancy data ($n=471$). All analyses were completed in Stata 14.0.

RESULTS

Among the women enrolled and consented in Right From the Start, 514 reported miscarriage as their most recent pregnancy outcome before the study pregnancy. The average maternal age was 30 years (interquartile range 27–34) and 20.4% of study participants were 35 years of age or older. Nine percent of women had three or more consecutive miscarriages at the time of study enrollment and 55.6% of participants had at least one previous livebirth ($n=286$). The study population was predominantly white (76.8%) and 12.3% of participants were black.

More than half of the study participants had an interpregnancy interval less than 6 months (58.9%) and 24.3% had interpregnancy intervals of less than 3 months. Less than 15% of participants had an interpregnancy interval of greater than 18 months. Maternal age and number of previous miscarriages were not associated with interpregnancy interval length. Women with short interpregnancy intervals tended to be white, married, and college educated (Table 1). Women with long interpregnancy intervals were most likely to be obese and to come from low-income households.

The overall prevalence of repeat miscarriage in the study pregnancy was 15.7% in this sample (median gestational age 9 weeks, interquartile range 7–11 weeks). No effect modification by race or parity was detected, so we present unstratified models. When compared with women who had interpregnancy intervals between 6 and 18 months, women with interpregnancy intervals less than 3 months had the lowest risk of repeat miscarriage (7.3% compared with 22.1%; adjusted hazard ratio 0.33, 95% CI 0.16–0.71; Table 2). This trend was consistent when modeling interpregnancy interval as a continuous variable with risk of subsequent miscarriage in pregnancy being the lowest for women with short interpregnancy intervals and steadily increasing with interval length until peaking at 6 months (Fig. 2). The time a woman waited before trying to conceive again did not associate strongly with risk of miscarriage in the next pregnancy. However, miscarriage risk slightly increased with wait time up to 3 months and then plateaued (Fig. 3).

DISCUSSION

Women with an interpregnancy interval after miscarriage of less than 3 months have a significantly reduced risk of subsequent miscarriage compared with women



Table 1. Characteristics of Participants From Right From the Start With a Previous Pregnancy Ending in Miscarriage by Length of Interpregnancy Interval, 2000–2012 (N=514)

Characteristic	Interpregnancy Interval (mo)				P*
	Less Than 3 (n=125)	3–5.99 (n=178)	6–17.99 (n=137)	18 or Greater (n=74)	
Maternal age (y)					.18
19 or younger	2 (1.6)	4 (2.2)	2 (1.5)	0 (0.0)	
20–24	15 (12.0)	18 (10.1)	14 (10.2)	10 (13.5)	
25–29	40 (32.0)	48 (27.0)	32 (23.4)	26 (35.1)	
30–34	51 (40.8)	65 (36.5)	63 (46.0)	19 (25.7)	
35 or older	17 (13.6)	43 (24.1)	26 (19.0)	19 (25.7)	
Race					<.01
White, non-Hispanic	107 (85.6)	146 (82.0)	97 (70.8)	45 (60.8)	
Black, non-Hispanic	10 (8.0)	15 (8.4)	18 (13.1)	20 (27.0)	
Other	8 (6.4)	17 (9.6)	21 (15.3)	9 (12.2)	
Missing	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	
BMI (kg/m ²)					<.01
Less than 18.5	2 (1.6)	4 (2.2)	0 (0.0)	3 (4.1)	
18.5–24.9	75 (60.0)	92 (51.7)	67 (48.9)	30 (40.5)	
25–29.9	33 (26.4)	50 (28.1)	35 (25.5)	16 (21.6)	
30 or greater	14 (11.2)	31 (17.4)	35 (25.5)	25 (33.8)	
Missing	1 (0.8)	1 (0.6)	0 (0.0)	0 (0.0)	
Education					<.01
High school or less	12 (9.6)	15 (8.4)	18 (13.1)	10 (13.5)	
Some college	24 (19.2)	20 (11.2)	28 (20.4)	23 (31.1)	
College or more	89 (71.2)	143 (80.3)	91 (66.4)	41 (55.4)	
Marital status					<.01
Married or cohabiting	118 (94.4)	170 (95.5)	128 (93.4)	60 (81.1)	
Other	7 (5.6)	8 (4.5)	9 (6.6)	14 (18.9)	
Household income (\$)					.01
40,000 or less	22 (17.6)	31 (17.4)	38 (27.7)	26 (35.1)	
40,001–80,000	55 (44.0)	69 (38.8)	45 (32.9)	20 (27.0)	
Greater than 80,001	43 (34.4)	74 (41.6)	50 (36.5)	25 (33.8)	
Missing	5 (4.0)	4 (2.2)	4 (2.9)	3 (4.1)	
Parity					<.01
Nulliparous	48 (38.4)	85 (47.8)	48 (35.0)	47 (63.5)	
1 prior delivery	50 (40.0)	65 (36.5)	59 (43.1)	17 (23.0)	
2 or more prior deliveries	27 (21.6)	28 (15.7)	30 (21.9)	10 (13.5)	
Past miscarriage					.09
1	86 (68.8)	133 (74.7)	97 (70.8)	60 (81.1)	
2	24 (19.2)	32 (18.0)	23 (16.8)	13 (17.6)	
3–7	15 (12.0)	13 (7.3)	17 (12.4)	1 (1.4)	
Smoking status [†]					.05
Never or distant quit	119 (95.2)	167 (93.8)	128 (93.4)	63 (85.1)	
Current or recent quit	6 (4.8)	11 (6.2)	9 (6.6)	11 (14.9)	
Pregnancy intention					<.01
Intended	107 (85.6)	154 (86.5)	117 (85.4)	47 (63.5)	
Not intended	10 (8.0)	19 (10.7)	13 (9.5)	17 (23.0)	
Missing	8 (6.4)	5 (2.8)	7 (5.1)	10 (13.5)	

BMI, body mass index.

Data are n (%) unless otherwise specified.

* P values derived from χ^2 test (if any cell has less than five observations, Fisher exact test is used).

[†] Quitting within the 4 months before the end of first trimester interview is considered a recent quit. Quitting before that time is considered a distant quit.

with intervals between 6 and 18 months. We did not observe effect modification by race or parity. Attempting to conceive immediately after miscarriage was not associated with increased risk of miscarriage in the next pregnancy.

These findings are not consistent with recommendations to delay conception by at least 6 months, but align with recent studies.^{9–17} In a Scottish health database study, women who conceived within 6 months of a miscarriage were at lower risk for



Table 2. Association Between Interpregnancy Interval Length and Risk of Miscarriage in a Subsequent Pregnancy (n=511)*

Interpregnancy Interval (mo)	n	Miscarriage	Crude HR	95% CI	Adjusted HR [†]	95% CI	Adjusted HR [‡]	95% CI
Less than 3 mo	124	9	0.31	0.15–0.65	0.33	0.16–0.71	0.34	0.15–0.72
3–5.99 mo	177	31	0.79	0.48–1.30	0.77	0.46–1.29	0.79	0.47–1.33
6–17.99 mo	136	30	1.00	Referent	1.00	Referent	1.00	Referent
18 mo or greater	74	10	0.59	0.29–1.20	0.53	0.25–1.12	0.56	0.26–1.19

HR, hazard ratio.

* Three participants missing covariate data excluded.

[†] Adjusted for maternal age, body mass index, education, parity, and ethnicity.

[‡] Adjusted for maternal age, body mass index, education, parity, ethnicity, and number of prior miscarriages.

a subsequent miscarriage than women with an interval of 6–12 months (adjusted odds ratio [OR] 0.66, 95% CI 0.57–0.77).¹³ Similarly, a study in Egyptian women whose first pregnancy ended in miscarriage showed women with an interpregnancy interval longer than 12 months had twice the risk of miscarriage than those with an interval less than 6 months.¹⁷ A study of the Demographic Surveillance System in Bangladesh reported interpregnancy intervals of less than 3 months after loss were associated with the highest probability of a livebirth in the next pregnancy.¹⁴

A secondary analysis of the Effects of Aspirin in Gestation and Reproduction trial demonstrated women with an interpregnancy interval of less than 3 months after a miscarriage were not at increased risk of periimplantation or clinically confirmed loss when compared with women with longer intervals (adjusted risk ratios 0.95, 95% CI 0.51–1.80 and 0.75, 95% CI

0.51–1.10, respectively).¹⁵ Furthermore, the proportion of pregnancies to end in a livebirth were similar between groups. In our study, women with intervals less than 3 months had twice the odds of a livebirth than women with longer intervals (adjusted OR 2.05, 95% CI 1.03–4.08). Couples from the Effects of Aspirin in Gestation and Reproduction trial who waited less than 3 months before trying to conceive were more likely to have a pregnancy ending in a livebirth than couples who waited longer.¹⁶ In our cohort, a nonsignificantly higher proportion of livebirths occurred among couples who waited less than 3 months before attempting to conceive compared with those who waited longer (85.8% compared with 79.9%, $\chi^2 P=.10$).

A short interpregnancy interval after a loss may be associated with a reduced risk of repeat miscarriage for several reasons. The first trimester of pregnancy

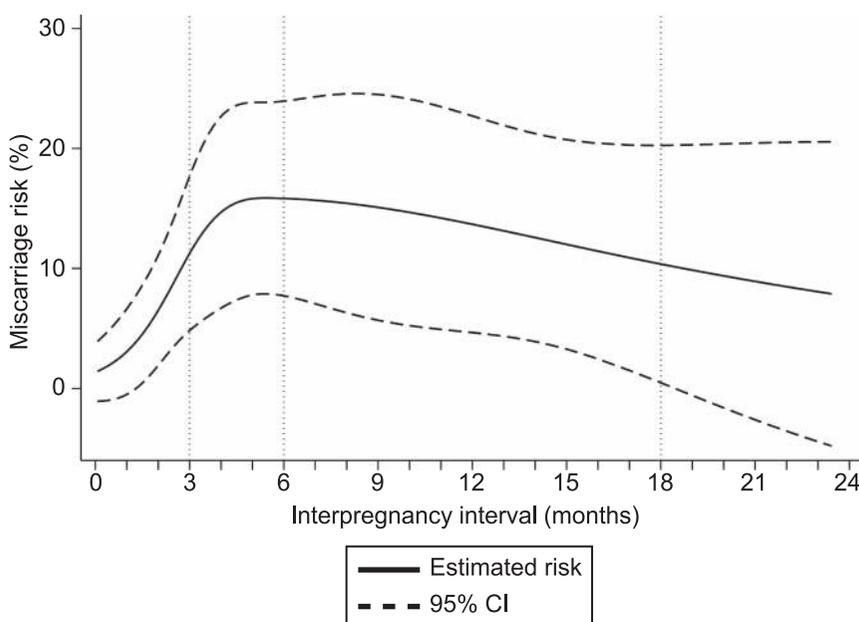


Fig. 2. Predicted probability of repeat miscarriage and 95% CIs by interpregnancy interval length after a loss (n=511). Vertical lines represent boundaries used for interpregnancy interval groups in the categorical analysis.

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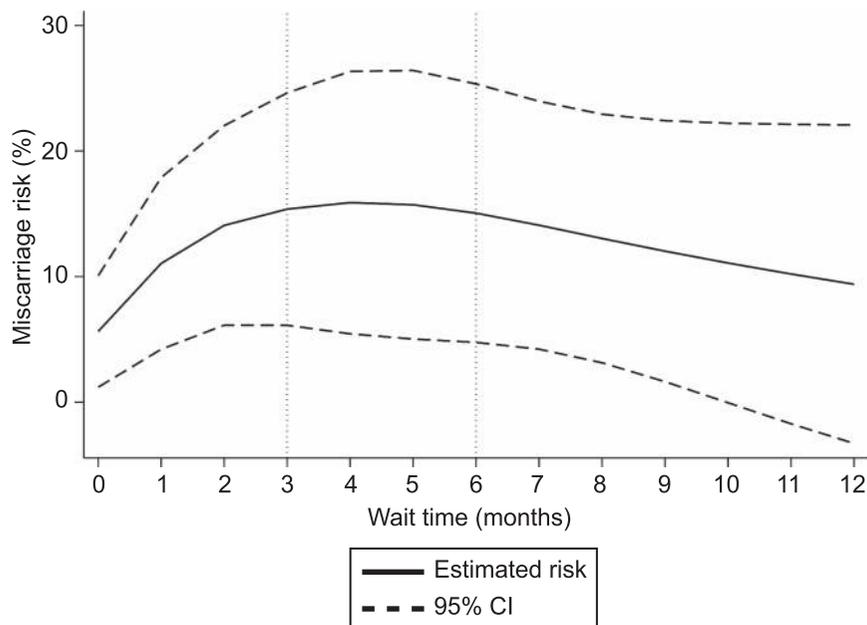


Fig. 3. Predicted probability of repeat miscarriage and 95% CIs by the length of time a couple waited after a loss before trying to conceive again (n=471). Vertical lines represent boundaries used for interpregnancy interval groups in the categorical analysis.

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involves many physiologic changes. A time may exist after miscarriage before a woman's body returns to its prepregnancy state when it is "primed" for pregnancy. Although physiologic priming is used to explain the increase in adverse pregnancy outcomes associated with long interpregnancy intervals after a livebirth,^{18,19} there is an absence of studies evaluating such changes postmiscarriage. Conception before the body's return to baseline may promote the next pregnancy's success. Also, a short time to pregnancy is associated with a favorable outcome independent of when a couple tries to conceive.^{16,20} Study participants with short interpregnancy intervals are necessarily those who achieved pregnancy quickly. The women who conceived within 3 months after loss had high fecundity and were less likely to be obese than women with longer intervals. Therefore, increased representation of women with high reproductive fitness may drive the low risk seen in this group. Our evaluation of wait time focuses on the time under a couple's control, not time to pregnancy. The decreased risk associated with a short wait time was less drastic than that with a short interpregnancy interval.

Right From the Start is well suited to study this association between interpregnancy interval after miscarriage and subsequent miscarriage risk. Many prior studies determine eligibility and measure interpregnancy interval using health care records or surveillance data. This method is vulnerable to exposure and outcome misclassification because it requires women to engage the health care system for every miscarriage

to be valid. Furthermore, this study enrolled women across three states very early in gestation, allowing us to precisely assess interpregnancy interval and research outcome in a varied population. Additionally, we collected information on how long a couple waited before trying to conceive and were thus able to characterize how both interpregnancy interval and wait time associate with miscarriage risk. We were limited by our inability to account for the role of emotional preparedness. Miscarriage can be emotionally devastating and this analysis does not measure the potential effect of emotional preparedness on the relationship between interpregnancy interval and pregnancy success.²¹

In summary, a short interpregnancy interval after a loss is not associated with increased risk of miscarriage in the next pregnancy. This implies counseling women to delay conception to prevent a repeat miscarriage is not warranted.

REFERENCES

1. Ventura SJ, Curtin SC, Abma JC, Henshaw SK. Estimated pregnancy rates and rates of pregnancy outcomes for the United States, 1900–2008. *National vital statistics reports*; vol. 60, no 7. Hyattsville (MD): National Center for Health Statistics; 2012.
2. Bardos J, Hercz D, Friedenthal J, Missmer SA, Williams Z. A national survey on public perceptions of miscarriage. *Obstet Gynecol* 2015;125:1313–20.
3. Conde-Agudelo A, Belizán JM, Breman R, Brockman SC, Rosas-Bermudez A. Effect of the interpregnancy interval after an abortion on maternal and perinatal health in Latin America. *Int J Gynaecol Obstet* 2005;89(suppl 1):S34–40.



4. World Health Organization. Report of a WHO technical consultation on birth spacing. Geneva (Switzerland): World Health Organization; 2005. p. 13–15.
5. Hurd WW. Waiting to conceive after an early pregnancy loss. *Obstet Gynecol* 2016;127:197–8.
6. Nybo Andersen AM, Wohlfahrt J, Christens P, Olsen J, Melbye M. Maternal age and fetal loss: population based register linkage study. *BMJ* 2000;320:1708–12.
7. Promislow JH, Makarushka CM, Gorman JR, Howards PP, Savitz DA, Hartmann KE. Recruitment for a community-based study of early pregnancy: the Right From the Start study. *Paediatr Perinat Epidemiol* 2004;18:143–52.
8. Hoffman CS, Messer LC, Mendola P, Savitz DA, Herring AH, Hartmann KE. Comparison of gestational age at birth based on last menstrual period and ultrasound during the first trimester. *Paediatr Perinat Epidemiol* 2008;22:587–96.
9. Vlaanderen W, Fabriek LM, van Tuyl van Serooskerken C. Abortion risk and pregnancy interval. *Acta Obstet Gynecol Scand* 1988;67:139–40.
10. Rud B, Klünder K. The course of pregnancy following spontaneous abortion. *Acta Obstet Gynecol Scand* 1985;64:277–8.
11. Wyss P, Biedermann K, Huch A. Relevance of the miscarriage new pregnancy interval. *J Perinat Med* 1994;22:235–41.
12. Bentolila Y, Ratzon R, Shoham-Vardi I, Serjienko R, Mazor M, Bashiri A. Effect of interpregnancy interval on outcomes of pregnancy after recurrent pregnancy loss. *J Matern Fetal Neonatal Med* 2013;26:1459–64.
13. Love ER, Bhattacharya S, Smith NC, Bhattacharya S. Effect of interpregnancy interval on outcomes of pregnancy after miscarriage: retrospective analysis of hospital episode statistics in Scotland. *BMJ* 2010;341:c3967.
14. DaVanzo J, Hale L, Rahman M. How long after a miscarriage should women wait before becoming pregnant again? Multivariate analysis of cohort data from Matlab, Bangladesh. *BMJ Open* 2012 Aug 20.
15. Wong LF, Schliep KC, Silver RM, Mumford SL, Perkins NJ, Ye A, et al. The effect of a very short interpregnancy interval and pregnancy outcomes following a previous pregnancy loss. *Am J Obstet Gynecol* 2015;212:375.e1–11.
16. Schliep KC, Mitchell EM, Mumford SL, Radin RG, Zarek SM, Sjaarda L, et al. Trying to conceive after an early pregnancy loss an assessment on how long couples should wait. *Obstet Gynecol* 2016;127:204–12.
17. El Behery MM, Siam S, Seksaka MA, Ibrahim ZM. Reproductive performance in the next pregnancy for nulliparous women with history of first trimester spontaneous abortion. *Arch Gynecol Obstet* 2013;288:939–44.
18. Zhu BP, Rolfs RT, Nangle BE, Horan JM. Effect of the interval between pregnancies on perinatal outcomes. *N Engl J Med* 1999;340:589–94.
19. Zhu BP, Le T. Effect of interpregnancy interval on infant low birth weight: a retrospective cohort study using the Michigan Maternally Linked Birth Database. *Matern Child Health J* 2003;7:169–78.
20. Wise LA, Mikkelsen EM, Sorensen HT, Rothman KJ, Hahn KA, Riis AH, et al. Prospective study of time to pregnancy and adverse birth outcomes. *Fertil Steril* 2015; 103:1065–73.e2.
21. Cumming GP, Klein S, Bolsover D, Lee AJ, Alexander DA, Maclean M, et al. The emotional burden of miscarriage for women and their partners: trajectories of anxiety and depression over 13 months. *BJOG* 2007;114: 1138–45.

