Regan, A., Gissler, M., Magnus, M., Eldevik Haberg, S., Ball, S., Malacova, E., ... Pereira, G. (2019). Association between interpregnancy interval and adverse birth outcomes in women with a previous stillbirth: an international cohort study. *Lancet*, *393*(10180), 1527-1535. https://doi.org/10.1016/S0140-6736(18)32266-9

Adverse birth outcomes associated with interpregnancy interval among women with a previous stillbirth: an international cohort study

Annette K Regan, PhD;[1] Mika Gissler, PhD;[2,3] Maria C Magnus, PhD;[4,5,6] Siri E Håberg, PhD;[6] Stephen Ball, PhD;[7] Eva Malacova, PhD;[1] Natasha Nassar, PhD;[8] Helen Leonard, MBChB;[9] Gavin Pereira, PhD[1]

Author affiliations:

[1] School of Public Health, Curtin University, Perth, Western Australia, Australia

[2] National Institute for Health and Welfare, Information Services Department, Helsinki, Finland

[3] Karolinska Institute, Department of Neurobiology, Care Sciences and Society, Division of Family Medicine, Stockholm, Sweden

[4] MRC Integrative Epidemiology Unit, University of Bristol, Bristol, United Kingdom

[5] Department of Population Health Sciences, Bristol Medical School, Bristol, United Kingdom

[6] Centre for Fertility and Health (CeFH), Norwegian Institute of Public Health, Oslo, Norway

[7] School of Nursing, Midwifery and Paramedicine, Curtin University, Western Australia, Australia

[8] Menzies Centre for Health Policy, School of Public Health, University of Sydney, New South Wales, Australia

[9] Telethon Kids Institute, University of Western Australia, Subiaco, Western Australia, Australia

Corresponding Author:

Dr Annette Regan, Research Fellow

School of Public Health, Curtin University

GPO Box U1987

Perth Western Australia 6845

Email: Annette.Regan@curtin.edu.au

Phone: +61 8 9266 2168

Short title: Interpregnancy interval following stillbirth

Word count: 298 word abstract; 2,882 word manuscript text

ABSTRACT

Background: The World Health Organization recommends waiting at least two years following a live birth, and at least six months following a spontaneous or induced abortion, to reduce the risk of adverse birth outcomes in the subsequent pregnancy. There is currently no recommendation for the optimal interval following a stillbirth.

Methods: Using birth records from Finland, Norway, and Western Australia in 1980-2016, we conducted an international cohort study of interpregnancy interval after stillbirth in relation to preterm birth, small-for-gestational age, and stillbirth in the subsequent pregnancy. Odds ratios for adverse birth outcomes by interpregnancy interval by country were calculated, adjusting for age, parity, decade of delivery, and gestational length of the previous pregnancy. A fixed-effects meta-analysis was used to estimate pooled odds ratios.

Findings: A total of 14,452 births occurred after a stillbirth, and the majority (63%) of women conceived within 12 months following a stillbirth. As compared to an interpregnancy interval of 24 to 59 months, interpregnancy intervals less than 12 months were not associated with increased odds of subsequent preterm birth (pooled aOR [<6 months] 0·91, 95% CI 0.75–1.11 and pooled aOR [6–11 months], 0.91, 95% CI 0·74–1·11) or small-for-gestational age (pooled aOR [<6 months], 0·66, 95% CI, 0·51–0·85 and pooled aOR [6-11 months], 0·64, 95% CI 0·48–0·84). Similarly, there was no increase in the odds of subsequent stillbirth associated with interpregancy interval. Further, there were no differences in the association between interpregnancy interval and birth outcomes based on gestational length of the previous stillbirth.

Interpretation: Conceiving within 12 months after a stillbirth was common and was not associated with increased risk of adverse outcomes in the subsequent pregnancy.

Funding: This study received support by the National Health and Medical Research Council [GNT1099655] and Research Council of Norway [project number 262700].

RESEARCH IN CONTEXT

Evidence before this study

The interval between pregnancies has been identified as a potentially modifiable risk factor for adverse birth outcomes, with short and long intervals hypothesised to increase the risk of preterm birth, fetal growth restriction, and infant mortality. Based on existing observational studies, in 2007, the World Health Organization (WHO) recommended at least two years following a live birth and six months following an induced or spontaneous abortion before conceiving another child. However, there is currently no recommendation for the optimal interval following a stillbirth, and there is limited evidence to inform such a recommendation.

Added value of this study

To our knowledge, this is the first large-scale observational study to investigate the association between interpregnancy interval following stillbirth and subsequent birth outcomes. By pooling data from three high-income countries, we were able to establish a cohort of 14,452 births following a previous stillbirth. After adjustment for maternal age, parity decade of birth, gestational length of the previous pregnancy, educational attainment, and maternal smoking, results from this cohort consistently showed that an interpregnancy interval up to 12 months was not associated with an increase in the risk of stillbirth, preterm birth, or small-for-gestational age in the next pregnancy compared to a two year interval.

Implications of all the available evidence

Approximately 3.5 births for every 1,000 births in high-income countries are stillborn. For families experiencing a stillbirth in these countries, there is currently limited guidance available for planning future pregnancies. Results from this study suggest women who wish to become pregnant or unintentionally become pregnant quickly after a stillbirth may not be at higher risk of poor outcomes in their next pregnancy. These findings are useful for healthcare providers who engage in postpartum counselling following a stillbirth, and may be valuable for informing future recommendations for pregnancy spacing in a high-income setting.

Background

Interpregnancy interval, the length of time between pregnancies, is a potentially modifiable risk factor for adverse outcomes in infants and their mothers.[1-4] The World Health Organization (WHO) recommends waiting at least two years following a live birth and six months following a miscarriage or induced abortion, before conceiving another child.[5] There is, however, no recommendation for the optimal interpregnancy interval following a stillbirth.

Existing studies examining the interpregnancy interval following live birth[6,7] have indicated that an interpregnancy interval shorter than six months is associated with a nearly two-fold increase in the odds of preterm birth,[2] low birth weight,[7] and small-for-gestational age, as compared to longer intervals.[8] Studies evaluating optimal interpregnancy interval following pregnancy loss have mostly focused on miscarriage or induced abortion.[2,9] In contrast to results for live births, these studies have suggested a lower risk of miscarriage and preterm delivery in the next pregnancy following an interpregnancy interval <6 months.[4,10]

Since length of gestation may influence nutrient levels and health status in women,[11] it is plausible that the optimal interval following a stillbirth is somewhere between the optimal interval following miscarriage and live birth. However, few studies have investigated the interpregnancy interval following a stillbirth. One previous study included stillbirths when estimating the association between interpregnancy interval after any fetal loss and subsequent birth outcomes[12] but did not analyse stillbirths as a separate group. We assessed associations between interpregnancy interval following a previous stillbirth and the risks of preterm birth, small-for-gestational age and stillbirth in the subsequent pregnancy.

Methods

We conducted a population-based international cohort study using birth records from three high-income countries: Finland (1987 to 2016), Norway (1980 to 2015), and Australia (specifically Western Australia, 1980 to 2015). Birth records were obtained from perinatal data collections and birth registrations within each country: the Medical Birth Register of Finland,[13] the Medical Birth Registry of Norway,[14] and the Midwives Notification System in Western Australia[15] (Table S1). Validation studies have shown these data

sources have nearly complete capture of births and provide highly accurate measurements of birth outcomes.[15-17]As reporting of early fetal deaths varied across the participating countries, we restricted our study population to births ≥22 weeks gestation. We obtained information on the date of delivery, birthweight, gestational age at birth, birth status (live or stillborn), maternal age, parity, and where possible, maternal smoking, body mass index, and educational attainment (Table S2).

Assessment of interpregnancy interval

We calculated interpregnancy interval as the time between the end of pregnancy (delivery date) and the start of the next pregnancy (delivery date of next pregnancy minus gestational age at birth). All participating countries routinely use ultrasound to confirm gestational age and rely on last menstrual period (LMP) where ultrasound is not available. After 1998, when half the births would have occurred, ultrasound was used to estimate gestational age for the majority of births. We categorised interpregnancy intervals as follows: <6 months, 6–11 months, 12–23 months, 24–59 months, and >59 months. The referent category was 24–59 months, consistent with the current WHO recommendation for pregnancy spacing following a live birth of at least two years.[5] For preterm birth and small-for-gestational age, where there were sufficient data, we evaluated additional categories of interpregnancy interval (<6 months, 6-11 months, 12-17 months, 18-23 months [referent], 24-35 months, 36-59 months, and >59 months) which were similar to previous studies for live births.[2,18]

Birth outcome measures

We investigated three birth outcomes in the subsequent pregnancy: stillbirth, preterm birth, and small-for-gestational age. A stillbirth was defined as a fetal death at ≥22 weeks' gestation. Preterm birth included any birth prior to 37 completed weeks' gestation. Small-for-gestational age was defined as the birth of an infant with a birthweight in the lowest 10th percentile based on the national distributions in each country by gestational age and sex.

Exclusions

For consistency with previous studies of interpregnancy interval following live birth and miscarriage,[2,18,19] the study cohort was restricted to consecutive singleton pregnancies following a previous stillbirth with complete information. We excluded births with missing gestational age, birthweight, sex, date of birth, parity or maternal age at delivery (Figure S1).

Statistical analysis

We compared the distribution of interpregnancy interval for stillbirths to the distribution for available live births during the study time period, using a Wilcoxon rank sum test for medians. For each country, we estimated crude and adjusted odds ratios (ORs) of each birth outcome as a function of interpregnancy interval category, using logistic regression. Adjustment was made for maternal age (≤24, 25–29, 30–34, or ≥35 years), parity (one, two, or three or more previous births), decade of delivery, and gestational age of the previous pregnancy (22–27 weeks, 28–36 weeks, and ≥37 weeks). Comparable information on other covariates was not available for all countries for the entirety of the study period (Table S2). A Bonferroni correction (α/number of comparisons) was applied to logistic regression analyses to adjust for multiple comparisons.

An inverse-variance weighted fixed effects meta-analysis,[20] was used to estimate pooled effect estimates(across countries) for the associations between interpregnancy interval and preterm birth and small-for-gestational age birth. To assess heterogeneity, the I^2 statistic was calculated as 100% x (Q – df)/Q, where Q is Cochrane's heterogeneity statistic and df denotes degrees of freedom.[21] Given that the relationship between interpregnancy interval on birth outcomes may vary as a function of the length of the previous pregnancy,[22] we further evaluated the potential mediating effect of gestational length by fitting a logistic regression model using aggregate data with a random slope for country and an interaction term for previous gestational length and interpregnancy interval category, adjusting for maternal age, parity, and decade of delivery. Model fit was assessed using Akaike information criterion (or pseudo-Akaike for mixed models). Analyses were conducted using SAS (version 9.4) and STATA (version 12).

Information on educational attainment and maternal smoking was not available for all countries (Table S2). Supplementary analyses were performed investigating the potential influence of educational attainment and maternal smoking on the association between interpregnancy interval and birth outcomes, where such information was available. Since it is possible that reliance on LMP in earlier years of the cohort may have impacted the measurement of gestational age, additional analyses restricted the study sample to births occurring after 1998, when ultrasound would have mostly been used.

Ethical approval

This study was approved by the Department of Health Western Australia Human Research Ethics Committee, Curtin University Human Research Ethics Committee, and the Norwegian Regional Committees for Medical and Health Research Ethics. Each committee provided a waiver of consent for participants. For Finland, ethical approval was not required since only register data were used and no individuals were contacted.

Role of the funding source

This work was supported by the National Health and Medical Research Council [GNT1099655] and Research Council of Norway [project number 262700]. The funding sources had no role in the study design, analysis of data, interpretation of findings, writing of the manuscript, or the decision to submit for publication.

Results

A total of 14,452 singleton births were identified among mothers with a stillbirth in the previous singleton pregnancy (Figure S1): 4,170 from Finland, 6,761 from Norway, and 3,521 from Western Australia. Table S3 presents the maternal and birth characteristics of the cohort by country.

Interpregnancy interval

The median interpregnancy interval following a stillbirth was nine months (interquartile range [IQR] 4–19 months), compared to 25 months (IQR 15–42 months) following a live birth (P<0.0001). Following

stillbirth, 63·0% (n=9,109) of women conceived their next child within 12 months. Interpregnancy intervals after stillbirth were similar in the participating countries (Figure 1). Intervals <6 months were more common among women ≤24 years of age and less common among women with a lower parity (Table 1). Maternal smoking and lower education were more common among women with interpregnancy intervals >36 months (Table S4).

Birth outcomes by interpregnancy interval

There were 14,224 (98·4%) live births and 228 (1·6%) stillbirths that followed a previous stillbirth. Two-thirds (n=201) of stillbirths were preterm and one-third (n=27) were stillborn at term. Among the 14,452 births that followed a previous stillbirth, a total of 2,532 births (17·5%) were preterm and 1,284 births (8·9%) were born small-for-gestational age.

The frequency of birth outcomes by interpregnancy interval and country are provided in Table S5. Country-specific and pooled birth outcomes following stillbirth by interpregnancy interval are presented in Figures 2, 3 and 4. Pooled unadjusted analyses indicated there was no association between an interpregnancy interval <6 months (pooled OR 1·11, 95% CI, 0·68–1·79), 6–11 months (pooled OR 0·79, 95% CI 0·42–1·50), or 12–23 months (pooled OR 0·85, 95% CI 0·45–1·64) and risk of subsequent stillbirth, as compared to a 24–59 month interpregnancy interval. Adjusted analyses showed similar results (Figure 2). Similarly, there was no significant increase in the odds of preterm birth (pooled OR 0·85, 95% CI 0·70–1·03) or small-for-gestational age birth (pooled OR 0·67, 95% CI 0·52–0·86) for interpregnancy interval <6 months and compared to a 24–59 month interval. After adjustment for maternal age, parity, decade of delivery, and gestational length of the previous pregnancy (Figure 3 and Figure 4) and comparison to a 18-23 month interval (Figure S2 and Figure S3), we observed similar results.

We observed small differences in effect estimates between countries for interpregnancy intervals <59 months. With exception of estimates for stillbirth for 6–11 months (I^2=35·0%, P=0·21), and preterm birth for intervals 12–23 months (I^2=25·4%, P=0·26), the heterogeneity between estimates was <1%.

Supplemental analyses investigating the potential influence of educational attainment and maternal smoking showed adjustment for these factors did not alter study conclusions (Table S6; Table S7). Additional analyses restricted to births after 1998 were also similar (Table S7).

Assessment by gestational length of previous pregnancy

Of the 14,452 births following a stillbirth, 5,027 (34·8%) followed a term stillbirth (≥37 weeks), 5,065 (35·0%) followed a very/moderate preterm stillbirth (gestational age of 28–36 weeks), and 4,360 (30·2%) followed an extreme preterm stillbirth (gestational age of 22–27 weeks). Overall, a similar proportion of women had a <6 month interpregnancy interval following an extreme preterm (36.5%; n=1,593), very/moderate preterm (37·0%; n=1,876), and term (38·3%; n=1,924) stillbirth. A higher proportion of births following an extreme preterm or very/moderate preterm stillbirth were stillborn (2·7% [n=118] and 1·6% [n=81], respectively) or born preterm (22·8% [n=996] and 18·7% [n=949], respectively) or small-for-gestational-age (10·0% [n=435] and 10·8% [n=545], respectively) compared to births following a term stillbirth (0·6% [n=29] stillborn, 11·7% [n=587] preterm, and 6·1% [n=304] small-for-gestational age; *P*-values<0·0001). Adjusted ORs stratified by categories of gestational length of the previous stillbirth are presented in Table 2. Overall, there was no notable difference in the association between interpregnancy interval and stillbirth (*P*-value for interaction=0·60), preterm birth (*P*-value for interaction=0·69) or small-for-gestational age (*P*-value for interaction=0·18) by gestational length of the previous stillbirth. Results were similar before and after applying a Bonferroni correction.

Discussion

Compared to the current WHO recommendation of waiting two years after a live birth before conceiving again, our findings indicate that conception of another child within one year following a stillbirth was not associated with increased risk of subsequent stillbirth, preterm birth or small-for-gestational age. Short interpregnancy intervals were more common following a stillbirth as compared to a live birth. Considering

37% of women in this international cohort became pregnant within six months following a stillbirth and 63% within twelve months, these results apply to a large proportion of women conceiving after a stillbirth.

Results from investigations of interpregnancy interval following fetal loss contrast with those from studies of interpregnancy interval following live births, which have shown that intervals <6 months may be associated with increased risk of adverse outcomes in the subsequent pregnancy.[2,3] Our results, in addition to those from investigations of earlier pregnancy losses,[23] imply that risk of adverse birth outcomes is not increased with conception within six months of a fetal death. Although the mechanism linking interpregnancy interval to perinatal health is currently unclear, previous researchers have offered several hypotheses, including maternal nutritional depletion, cervical insufficiency, and breastfeeding-pregnancy overlap in closely spaced pregnancies.[11] Pregnancy and breastfeeding may deplete women of nutrients.[24] Without sufficient time to recover from a previous pregnancy, women with closely spaced pregnancies are at increased risk of entering a reproductive cycle with poor nutritional status,[25] and poor nutrition during the preconception period has been strongly linked to increased risk of fetal growth restriction and birth defects;[26] this may explain why a certain time lag is optimal before conceiving again after a live birth. Such nutritional depletion may not occur to the same extent from early pregnancy loss, and so the optimal interpregnancy interval may be different following pregnancy loss than after live births.

We found that the relationship between interpregnancy interval and adverse birth outcomes was independent of the length of gestation of the previous birth. The fact that we observed no significant influence of gestation of the previous pregnancy and no negative impact of short interpregnancy interval may imply maternal depletion was not a major factor in our study. However, this requires further study.

This was an observational study, and unmeasured confounding may have influenced our findings. Women who conceive quickly may be healthier and more fertile than women who conceive later and therefore may be less prone to adverse birth outcomes. Fertility treatment is associated with increased risks for placental complications, stillbirth, low birthweight and preterm delivery,[27,28] and reduced fertility and associated fertility treatment are more likely in women with longer interpregnancy interval. Although we included

some of the most important known confounders, we did not have information for all three countries on maternal chronic medical conditions, pregnancy intention, use of assisted reproduction technology, cause of previous stillbirth, or measures of socioeconomic status. Results from supplementary analyses suggest that the inclusion of additional confounders (i.e., education and smoking during pregnancy) did not materially change our results. Despite this, we cannot rule out the possibility of residual confounding in our results.

To address the issue of residual confounding due to between-mother differences, recent studies in the last five years have employed a maternally-matched design comparing birth outcomes among mothers with two or more live births.[2,6,18] These studies have consistently shown associations are attenuated in comparison to traditional unmatched designs. Because maternally-matched designs minimise confounding from between-mother differences, it is plausible that some of this difference is attributable to residual confounding.[18] Investigation of interpregnancy intervals within the same mother following stillbirths is impractical, since mothers included in these analyses would require at least three births, and the first two would need to be stillbirths in order to have two interpregnancy intervals following a stillbirth. Moreover, stillbirth is also used as both a predisposing factor and an outcome (e.g., stillbirth of the second child is an outcome after the first interpregnancy interval and a predisposing factor for the next birth), and therefore would not be suited to a maternally-matched design using conditional logistic regression. In general, residual confounding incorrectly inflates effect estimates, and since we observed no differences in odds ratios in this study, it is possible that residual confounding did not significantly impact our findings.There are some further limitations to consider when interpreting this study's findings. While we were able to draw from highly reliable data sources in high-income countries,[13-17] these countries have access to universal health care and free antenatal care, and the populations are primarily Caucasian, indicating these findings may not be generalisable to low or middle-income countries, to countries without access to universal health care, or to ethnic minority groups. Furthermore, information on early pregnancy losses is difficult to obtain and were not included in our study. A Danish study found that around 20% of all pregnancies intended to be

carried to term may end as miscarriages.[30] Information on miscarriages or induced abortions was not available, which may have led to overestimation of interpregnancy interval in some women and limits the application of our findings to pregnancies with a minimum gestational length of 22 weeks. Given studies have suggested that short intervals following miscarriage may be favourable,[4] exclusion of miscarriage may have also biased our estimates for longer intervals toward the null. Consistent with previous studies, our sample was restricted to singleton births. While this restriction allows comparison of our results to previous studies,[2,18] exclusion of multiple pregnancies may limit the generalisability of our findings beyond singleton pregnancies. Finally, although this is the largest study evaluating birth outcomes following a previous stillbirth by interpregnancy interval, only 228 women experienced the study outcome of a stillbirth in the subsequent pregnancy, which made some analyses assessing recurrent stillbirth impractical. Replication of our study in a larger sample of women experiencing recurrent stillbirth would be informative for evaluating the risk of interpregnancy interval. Despite this limitation, this population-based study covering a population of 1,668,816 births from three countries over a 35-year study period showed consistent results across countries, providing valuable evidence for pregnancy spacing following a stillbirth.

Our study of interpregnancy interval across three high-income countries between 1980 and 2016 demonstrates that among subsequent pregnancies with gestational length ≥22 weeks, conception within twelve months after a stillbirth was not associated with increased risk of adverse pregnancy outcomes. These observations may be used in counselling families planning future pregnancies after a stillbirth and provide reassurance to women who wish to become pregnant or unexpectedly become pregnant shortly after a stillbirth.

Declaration of interests: The authors have no potential conflicts of interest to disclose.

Authors' contribution: AKR extracted and prepared data in Australia, MCM extracted and prepared data in Norway, and MG extracted and prepared data in Finland. AKR, SB, GP, MCM, SH, and MG contributed to the study design and the development of the analytic plan. AKR performed the statistical analyses and prepared study results. AKR, GP, MCM, MG, SB, SH, EM, HL, and NN contributed to the interpretation of findings. AKR led the drafting of the manuscript, and all co-authors contributed to revising of the manuscript and approved the final version of the manuscript.

Funding source: This work was supported by funding from the National Health and Medical Research Council, including a Sidney Sax Fellowship [#1052236 to GP], Senior Research Fellowship [# 1117105 to HL], Career Development Fellowship [#APP1067066 to NN] and project grants [#1099655 to GP, NN, SJB] from the National Health and Medical Research Council. The authors have no potential conflicts of interests to disclose. M.C.M works at the MRC Integrative Epidemiology Unit at the University of Bristol which receives infrastructure funding from UK Medical Research Council (MC/UU/12013/5), and she is also supported by the following fellowship from the UK Medical Research Council (MR/M009351/1). This work was partly supported by the Research Council of Norway through its Centres of Excellence funding scheme, project number 262700. The funding bodies had no involvement in the study design, interpretation of findings, or decision to publish the results.

Acknowledgements: The authors would like to thank the Linkage and Client Services Teams at the Data Linkage Branch (Department of Health Western Australia) as well as the Data Custodian for the Midwives Notification System. The authors would also like to thank members of the Healthy Pregnancies Consumer Reference Group who provided community input and guidance in this research.

References

1 Smith GC, Pell JP, Dobbie R. Interpregnancy interval and risk of preterm birth and neonatal death: retrospective cohort study. *BMJ* 2003;**327**:313.

2 Shachar BZ, Mayo JA, Lyell DJ, et al. Interpregnancy interval after live birth or pregnancy termination and estimated risk of preterm birth: a retrospective cohort study. *BJOG* 2016;**123**:2009–17.

3 McKinney D, House M, Chen A, Muglia L, DeFranco E. The influence of interpregnancy interval on infant mortality. *Am J Obstet Gynecol* 2017;**216**:316.e1–e9.

4 Kangatharan C, Labram S, Bhattacharya S. Interpregnancy interval following miscarriage and adverse pregnancy outcomes: systematic review and meta-analysis. *Hum Reprod Update* 2017;**23**:221–31.

5 World Health Organization. Report of a WHO Technical Consultation on Birth Spacing Geneva Switzerland 13–15 June 2005. World Health Organization; 2007.

6 Hanley GE, Hutcheon JA, Kinniburgh BA, Lee L. Interpregnancy interval and adverse pregnancy outcomes: an analysis of successive pregnancies. *Obstet Gynecol* 2017;**129**:408–15.

7 Cofer FG, Fridman M, Lawton E, Korst LM, Nicholas L, Gregory KD. Interpregnancy interval and childbirth outcomes in California, 2007-2009. *Matern Child Health J* 2016;**20**:43–51.

8 Ekin A, Gezer C, Taner CE, Ozeren M, Mat E, Solmaz U. Impact of interpregnancy interval on the subsequent risk of adverse perinatal outcomes. *J Obstet Gynaecol Res* 2015;**41**:1744–51.

9 Makhlouf MA, Clifton RG, Roberts JM, et al. Adverse pregnancy outcomes among women with prior spontaneous or induced abortions. *Am J Perinatol* 2014;**31**:765–72.

10 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.

11 Conde-Agudelo A, Rosas-Bermudez A, Castano F, Norton MH. Effects of birth spacing on maternal, perinatal, infant, and child health: a systematic review of causal mechanisms. *Stud Fam Plann* 2012;**43**:93–114.

12 Wong LF, Schliep KC, Silver RM, 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.

13 Teperi J. Multi method approach to the assessment of data quality in the Finnish Medical Birth Registry. *J Epidemiol Community Health* 1993;**47**:242–7.

14 Irgens LM. The Medical Birth Registry of Norway. Epidemiological research and surveillance throughout 30 years. *Acta Obstet Gynecol Scand* 2000;**79**:435–9.

15 Downey F. Validation study of the Western Australian Midwives' Notification System: 2005 Birth Data. Perth WA: Department of Health Western Australia; 2007.

16 Gissler M, Teperi J, Hemminki E, Merilainen J. Data quality after restructuring a national medical registry. *Scand J Soc Med* 1995;**23**:75–80.

17 Moth FN, Sebastian TR, Horn J, Rich-Edwards J, Romundstad PR, Asvold BO. Validity of a selection of pregnancy complications in the Medical Birth Registry of Norway. *Acta Obstet Gynecol Scand* 2016;**95**:519–27.

18 Ball SJ, Pereira G, Jacoby P, de Klerk N, Stanley FJ. Re-evaluation of link between interpregnancy interval and adverse birth outcomes: retrospective cohort study matching two intervals per mother. *BMJ* 2014;**349**:g4333.

19 DaVanzo J, Hale L, Razzaque A, Rahman M. Effects of interpregnancy interval and outcome of the preceding pregnancy on pregnancy outcomes in Matlab, Bangladesh. *BJOG* 2007;**114**:1079–87.

20 Deeks JJ, Altman DG, Bradburn MJ. Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Davey Smith G, Altman DG, eds. Systematic Reviews in Health Care: Meta-Analysis in Context (2nd Edition). 2nd ed. London: BMJ; 2001.

21 Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**:557–60.

22 Koullali B, Kamphuis EI, Hof MH, et al. The effect of interpregnancy interval on the recurrence rate of spontaneous preterm birth: a retrospective cohort study. *Am J Perinatol* 2017;**34**:174–82.

23 Bhattacharya S, Smith N. Pregnancy following miscarriage: what is the optimum interpregnancy interval? *Womens Health* 2011;**7**:139–41.

24 Luke B. Nutrition in multiple gestations. *Clin Perinatol* 2005;**32**:403–29.

25 King JC. The risk of maternal nutritional depletion and poor outcomes increases in early or closely spaced pregnancies. *J Nutr* 2003;**133**:1732S–6S.

26 King JC. A summary of pathways or mechanisms linking preconception maternal nutrition with birth outcomes. *J Nutr* 2016;**146**:1437S–44S.

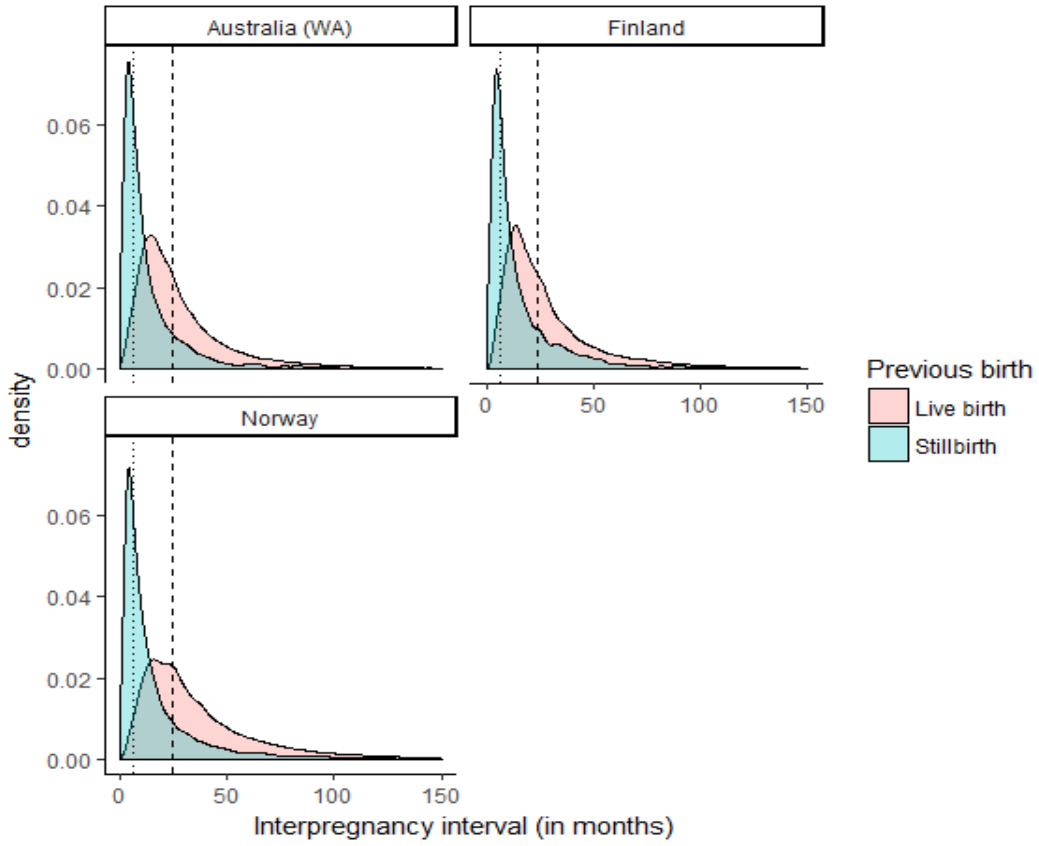
27 Marino JL, Moore VM, Willson KJ, et al. Perinatal outcomes by mode of assisted conception and sub-fertility in an Australian data linkage cohort. *PloS One* 2014;**9**:e80398.

28 Luke B, Gopal D, Cabral H, Stern JE, Diop H. Pregnancy, birth, and infant outcomes by maternal fertility status: the Massachusetts Outcomes Study of Assisted Reproductive Technology. *Am J Obstet Gynecol* 2017;**217**:327.

29 Bhattacharya S, Prescott GJ, Black M, et al. Recurrence risk of stillbirth in a second pregnancy. *BJOG* 2010;**117**:1243–7.

30 Buss L, Tolstrup J, Munk C, et al. Spontaneous abortion: a prospective cohort study of younger women from the general population in Denmark. Validation, occurrence and risk determinants. *Acta Obstet Gynecol Scand* 2006;**85**:467–75.

Figure 1. Distribution of interpregnancy interval (in months) following live birth (red, n=1,654,289) and following stillbirth (blue, n=14,452) among births in Finland, Norway and Western Australia, 1980-2016.

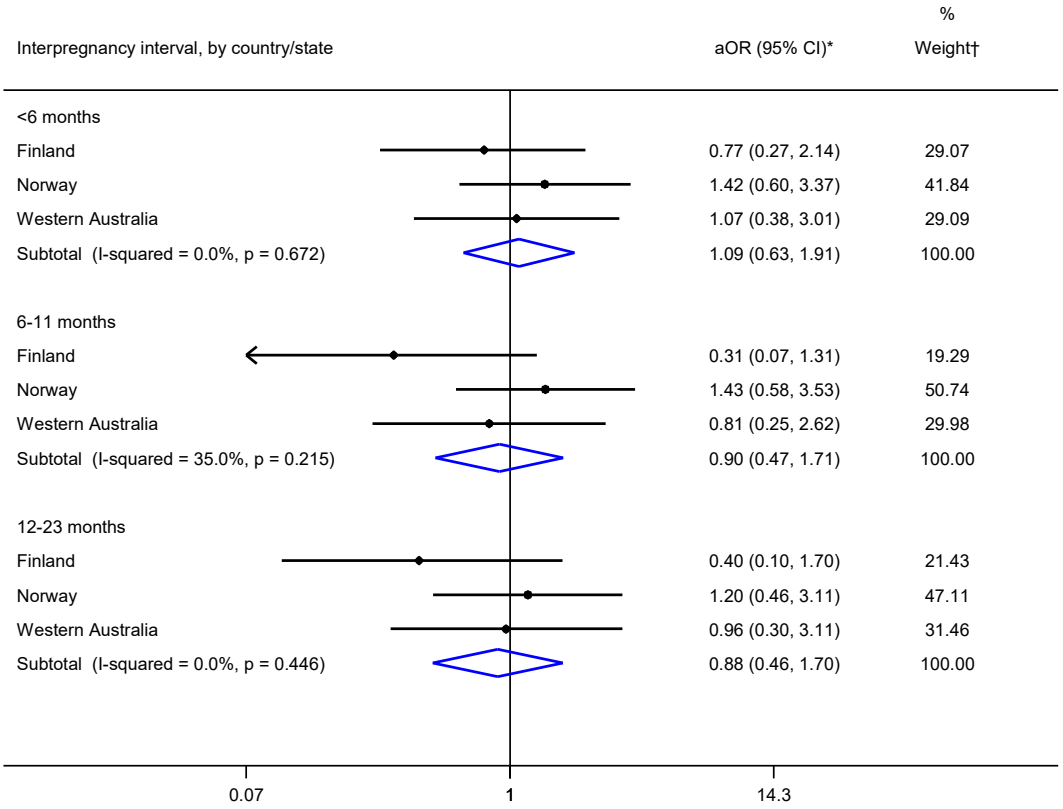


NOTE: dotted line indicates WHO recommended interpregnancy interval of ≥6 months following miscarriage or induced abortion; dashed line indicates WHO recommended interpregnancy interval of ≥2 years following live birth.

Table 1. Characteristics and birth outcomes of women with a previous stillbirth, by interpregnancy interval (n=14,452) – Finland, Norway, and Western Australia, 1980-2016.

	Interpregnancy Interval				
Characteristic	<6 months n (%)	6-11 months n (%)	12-23 months n (%)	24-59 months n (%)	>59 months n (%)
Total	5,393	3,716	2,732	1,980	631
Country/Region					
Finland	1,627 (30)	1,015 (27)	744 (27)	607 (31)	177 (28)
Norway	2,504 (46)	1,829 (49)	1,312 (48)	830 (42)	286 (45)
Western Australia	1,262 (23)	872 (23)	676 (25)	543 (27)	168 (27)
Maternal age group					
≤24 years	1,145 (21)	595 (16)	408 (15)	253 (13)	24 (4)
25-29 years	1,838 (34)	1,151 (31)	756 (28)	541 (27)	174 (27)
30-34 years	1,603 (30)	1,191 (32)	875 (32)	629 (32)	225 (36)
≥35 years	807 (15)	779 (21)	693 (25)	557 (28)	208 (33)
Parity					
Second	2,685 (50)	1,750 (47)	1,277 (47)	996 (49)	404 (64)
Third	1,593 (29)	1,161 (31)	843 (31)	587 (30)	128 (20)
Fourth or greater	1,115 (21)	805 (22)	612 (22)	427 (21)	99 (16)
Decade of delivery					
1980-89	1,380 (25)	937 (25)	686 (25)	396 (20)	59 (9)
1990-99	1,776 (33)	1,194 (32)	891 (33)	734 (37)	228 (36)
2000-10	1,436 (27)	999 (27)	762 (28)	535 (27)	237 (38)
After 2010	801 (15)	586 (16)	393 (14)	315 (16)	107 (17)

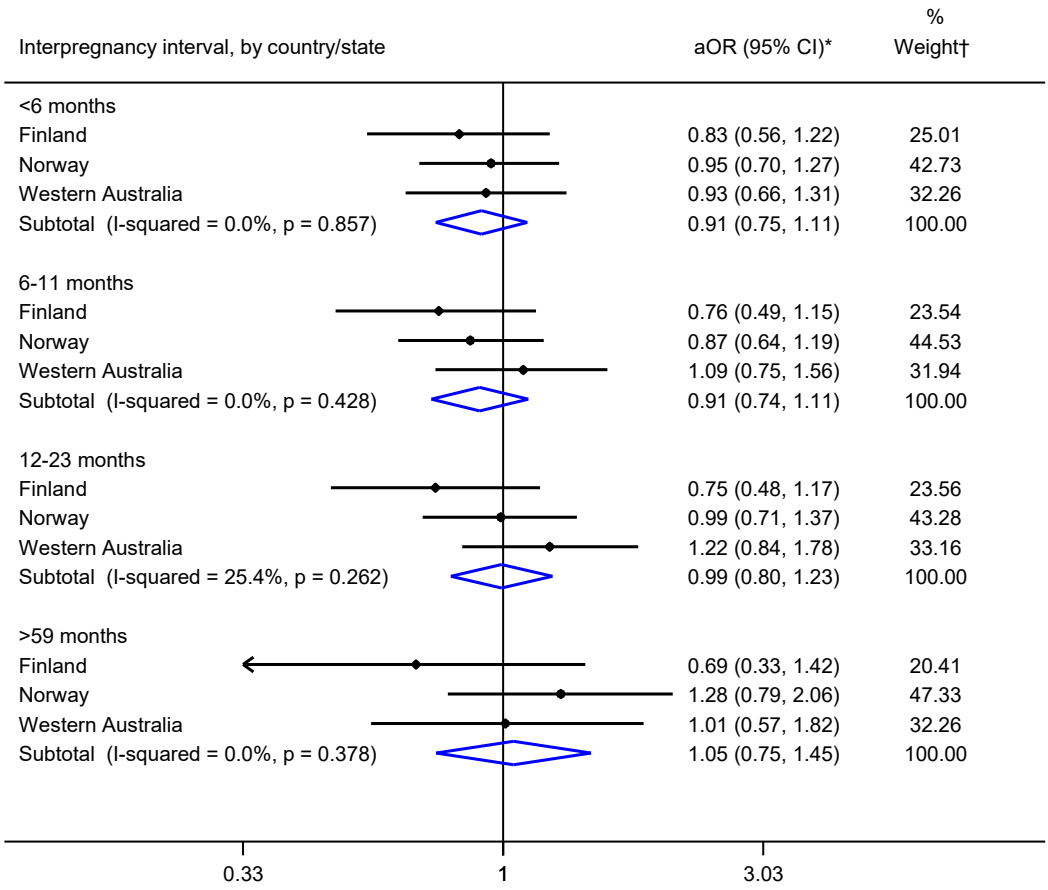
Figure 2. Adjusted odds ratios* for stillbirth associated with interpregnancy interval, as compared to a 24-59 month interpregnancy interval, by country/state (n=14,452) - Finland, Norway and Western Australia, 1980-2016.



* Odds ratios and corresponding 95% Bonferroni-corrected confidence intervals, adjusted for maternal age, parity, birth decade, and gestational length of the previous pregnancy; the reference interpregnancy interval category is 24-59 months (WHO recommendation for interval following live births).

† Weights are derived from inverse-variance

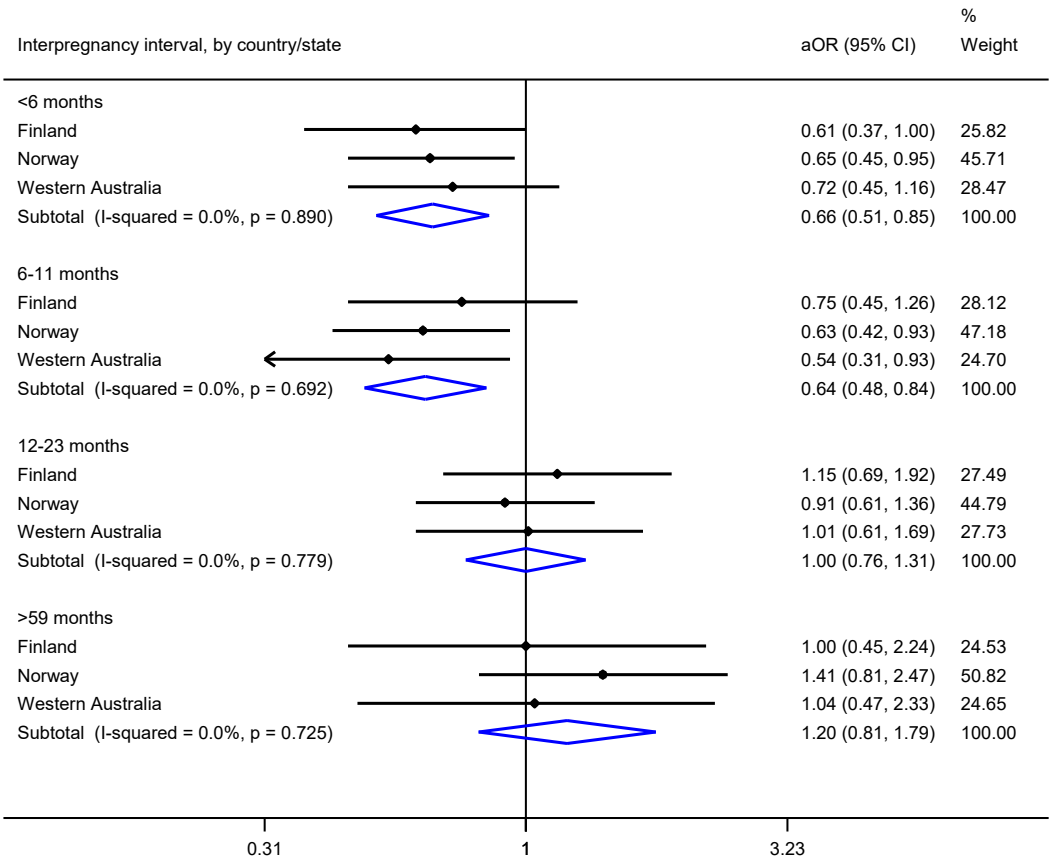
Figure 3. Adjusted odds ratios* for preterm birth associated with interpregnancy interval, as compared to a 24-59 month interpregnancy interval, by country/state (n=14,452) - Finland, Norway and Western Australia, 1980-2016.



* Odds ratios and corresponding 95% Bonferroni-corrected confidence intervals, adjusted for maternal age, parity, birth decade, and gestational length of the previous pregnancy; the reference interpregnancy interval category is 24-59 months (WHO recommendation for interval following live births).

† Weights are derived from inverse-variance

Figure 4. Adjusted odds ratios* for small-for-gestational age birth associated with interpregnancy intervals, as compared to a 24-59 month interpregnancy interval, by country/state (n=14,452) - Finland, Norway and Western Australia, 1980-2016.



* Odds ratios and corresponding 95% Bonferroni-corrected confidence intervals, adjusted for maternal age, parity, birth decade, and gestational length of the previous pregnancy; the reference interpregnancy interval category is 24-59 months (WHO recommendation for interval following live births).

† Weights are derived from inverse-variance

Table 2. Odds of preterm and small-for-gestational age births following a stillbirth by interpregnancy interval, stratified by gestational length of previous birth (n=14,452) - Finland, Norway and Western Australia, 1980-2016.

	Gestational length of previous stillbirth								
	22-27 weeks			28-32 weeks			≥37 weeks		
Birth outcome, by interpregnancy interval	Number with outcome (%)	Unadjusted OR (95% CI)*	Adjusted OR† (95% CI)*	Number with outcome (%)	Unadjusted OR (95% CI)*	Adjusted OR† (95% CI)*	Number with outcome (%)	Unadjusted OR (95% CI)*	Adjusted OR† (95% CI)*
Stillbirth									
<6 months	52 (3·3)	1·39 (0·64–3·05)	1·15 (0·60–2·22)	31 (1·7)	1·05 (0·45–2·47)	1·03 (0·52–2·01)	12 (0·6)	---§	---
6–11 months	21 (2·1)	0·91 (0·35–2·37)	0·79 (0·35–1·77)	23 (1·8)	1·20 (0·50–2·86)	1·00 (0·49–2·04)	6 (0·4)	---	---
12–23 months	24 (2·8)	1·22 (0·51–2·94)	1·08 (0·52–2·24)	11 (1·1)	0·68 (0·21–2·21)	0·52 (0·19–1·44)	<5	---	---
24–59 months	17 (2·4)	Reference	Reference	13 (1·8)	Reference	Reference	<5	---	---
Preterm birth									
<6 months	334 (21·0)	0·87 (0·65–1·19)	0·89 (0·65–1·21)	350 (18·7)	0·86 (0·64–1·15)	0·88 (0·65–1·18)	218 (11·3)	1·00 (0·66–1·53)	1·15 (0·76–1·76)
6–11 months	217 (22·1)	0·94 (0·68–1·31)	0·95 (0·68–1·33)	234 (18·3)	0·85 (0·62–1·16)	0·86 (0·63–1·18)	160 (11·0)	0·96 (0·62–1·48)	1·04 (0·67–1·61)
12–23 months	221 (26·2)	1·17 (0·85–1·62)	1·20 (0·86–1·66)	165 (17·2)	0·78 (0·55–1·10)	0·75 (0·53–1·07)	122 (13·1)	1·20 (0·77–1·88)	1·31 (0·84–2·04)
24–59 months	167 (23·6)	Reference	Reference	153 (21·0)	Reference	Reference	63 (11·6)	Reference	Reference
>59 months	57 (24·3)	1·06 (0·65–1·72)	1·07 (0·66–1·75)	47 (21·0)	1·02 (0·62–1·68)	0·97 (0·59–1·60)	24 (13·9)	1·11 (0·55–2·25)	1·13 (0·56–2·28)
Small-for-gestational age									
<6 months	142 (8·9)	0·78 (0·52–1·17)	0·79 (0·52–1·18)	175 (9·3)	0·68 (0·47–0·99)	0·62 (0·43–0·89)	100 (5·2)	0·61 (0·37–0·99)	0·55 (0·34–0·89)
6–11 months	66 (6·7)	0·56 (0·33–0·96)	0·57 (0·34–0·97)	125 (9·8)	0·71 (0·48–1·05)	0·67 (0·45–0·99)	77 (5·3)	0·62 (0·37–1·03)	0·60 (0·37–0·99)
12–23 months	113 (13·4)	1·23 (0·82–1·83)	1·25 (0·84–1·86)	113 (11·8)	0·88 (0·59–1·30)	0·84 (0·57–1·23)	72 (7·8)	0·93 (0·57–1·51)	0·92 (0·57–1·47)
24–59 months	80 (11·3)	Reference	Reference	95 (13·0)	Reference	Reference	45 (8·3)	Reference	Reference
>59 months	34 (14·5)	1·32 (0·77–2·28)	1·30 (0·75–2·24)	37 (16·5)	1·31 (0·79–2·18)	1·36 (0·81–2·27)	10 (5·8)	0·68 (0·25–1·87)	0·67 (0·24–1·90)

* A Bonferroni correction was applied to confidence intervals to correct for multiple comparisons.
† Odds ratios adjusted by maternal age, parity, and decade of delivery.
§ Insufficient data to estimate.