Healthcare utilisation, induced labour and caesarean section in the

pregnancy after stillbirth: a prospective study

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Running title: Care and delivery in the pregnancy after stillbirth

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### 8 Abstract

- 9 **Objective:** To investigate healthcare utilisation, induced labour and caesarean section
- 10 (CS) in the pregnancy after stillbirth and assess anxiety and dread of childbirth as
- 11 mediators for these outcomes.
- 12 **Design:** Population-based pregnancy cohort study.
- 13 **Setting:** The Norwegian Mother and Child Cohort Study.
- Sample: 901 pregnant women; 174 pregnant after stillbirth, 362 pregnant after live
- birth and 365 previously nulliparous.
- 16 **Methods:** Data from questionnaires answered in the second and third trimesters of
- pregnancy and information from the Medical Birth Registry of Norway.
- 18 Main outcome measures: Self-reported assessment of antenatal care, register-based
- assessment of onset and mode of delivery.
- 20 **Results:** Women with a previous stillbirth had more frequent antenatal visits (mean
- 21 10.0; 95% confidence interval [CI] 9.4 10.7) compared with women with a previous
- live birth (6.0; 5.8 6.2) and previously nulliparous women (6.3; 6.1 6.6). Induced
- labour and CS, elective and emergency, were also more prevalent in the stillbirth group.
- 24 The adjusted odds ratio for elective CS was 2.5 (95% CI 1.3 5.0) compared with
- women with previous live birth and 3.7 (1.8 7.6) compared with previously
- 26 nulliparous women. Anxiety was a minor mediator for the association between stillbirth
- and frequency of antenatal visits, while dread of childbirth was not a significant
- 28 mediator for elective CS.
- 29 **Conclusions:** Women pregnant after stillbirth were more ample users of healthcare
- 30 services and had more often induced labour and CS. The higher frequency of antenatal
- 31 visits and elective CS could not be accounted for by anxiety or dread of childbirth.

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| 38 | Tweetable abstract: Women pregnant after stillbirth are ample users of healthcare    |

services and interventions during childbirth.

### Introduction

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Most couples embark on another pregnancy after a stillbirth, as many as 50% within a year (1). In pregnancies subsequent to a miscarriage or stillbirth, many women sense a threat of an additional loss (2) and increased generalised and pregnancy specific anxiety (2-7). Attempts to cope may involve asking more questions, requesting additional tests and telephoning healthcare professionals between visits (4). In Norway, antenatal care is free of charge and mainly carried out by midwifes and general practitioners. Until gestational week 32 it routinely includes five appointments including one second trimester ultrasound scan (8). Additional care and referrals to the specialist services is provided when needed, but national guidelines on antenatal care for women with previous stillbirths are non-existent. It remains uncertain whether anxiety accounts for higher healthcare utilisation in women pregnant after stillbirth and if the type of support given is helpful. In a recent international survey on care for parents in pregnancies subsequent to stillbirth, the majority was provided with additional visits and ultrasound scans (9). Care addressing psychosocial needs was less frequently reported. In another study including 36 women pregnant after pregnancy loss, increased healthcare utilisation was associated with maternal intrusion symptoms and state anxiety (5). The rate of caesarean section (CS) in Norway has increased from 4% in 1975 to 17% in 2012 (10). Worldwide, the increasing rate of CS and interventions during childbirth is of concern (11, 12) and cannot be fully explained by maternal medical factors or obstetrical complications (13). Some research indicate that the increased rate of CS is

65 partly a result of maternal requests, in turn related to fear of childbirth (11, 14). Previous 66 studies have demonstrated that previous miscarriages and a variety of delivery 67 experiences are associated with fear of childbirth (15, 16). 68 69 A retrospective Australian study on 316 subsequent deliveries after unexplained 70 stillbirth reported increased rates of preterm birth, induced labour, forceps delivery and 71 CS, both elective and emergency (17). Studies from Finland and Scotland reported 72 similar findings (18, 19). Whether anxiety, fear or dread of childbirth partially accounts 73 for more frequent use of interventions in pregnancies subsequent to stillbirth, however, 74 remains unknown. 75 76 The objectives of this study were to investigate healthcare utilisation, induced labour 77 and caesarean section in the pregnancy after stillbirth and to assess anxiety and dread 78 of childbirth as possible mediators for the frequency of antenatal visits and elective 79 CS. 80

### Methods

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This paper is based on data from the Norwegian Mother and Child Cohort Study (MoBa) and the Medical Birth Registry of Norway (MBRN). MoBa is a populationbased pregnancy cohort study conducted by the Norwegian Institute of Public Health (20) that recruited participants from all over Norway from 1999 to 2008. The participation rate was 41% and the cohort includes more than 95 000 women (21). The current substudy is based on version VIII of the quality-assured data files released on 14<sup>th</sup> of February 2014. The participants answered extensive questionnaires regarding demographic factors, reproductive history and maternal health during pregnancy. Data from the MoBa study were linked with data from MBRN (22). This substudy included women who were pregnant after a stillbirth and two reference groups; 1) women with at least one live birth and no previous stillbirth and 2) nulliparous women. Only women with singleton or twin pregnancies, and with the MoBa pregnancy resulting in a live birth were included. Women not responding to the first MoBa questionnaire, with missing MBRN data or participating more than once were excluded. Results of previous pregnancies were identified using data from the MoBa questionnaires and the MBRN. We defined stillbirth defined according to the World Health Organizations International Statistical Classification of Diseases 10<sup>th</sup> revision, ie, fetal death  $\ge$ 22 completed gestational weeks or birthweight >500 grams (23). Aside from the selection criteria, the reference women were randomly selected from the entire MoBa cohort. We identified 197 women in the MoBa cohort who had experienced stillbirth in their previous pregnancy (stillbirth group). The reference groups included 394 women with a live birth in their previous pregnancy (live birth group) and 394 nulliparous women (nulliparous group). We used data from

105 questionnaires completed at approximately 17 gestational weeks (Q1) and 106 approximately 30 gestational weeks (Q2) and data from the MBRN. 107 At the second assessment (30 gestational weeks) 174 women with a previous stillbirth, 108 362 with a previous live birth and 365 nulliparous women completed the questionnaire. 109 110 **Outcome variables** 111 Information about healthcare utilisation was collected at gestational week 30 (Q2). The 112 women were asked how many and where they had their antenatal visits, categorised as 113 family healthcare centre, physicians office or hospital outpatient clinic, unscheduled 114 contacts, number of ultrasound scans (transabdominal/transvaginal) and whether or not 115 they had been admitted to hospital during the pregnancy. 116 117 Outome variables regarding onset of labour and mode of delivery were obtained from 118 the MBRN. Onset of labour was classified as spontaneous, induced or CS. Mode of 119 delivery was classified as vaginal birth; spontaneous or instrumental (vaccum-assisted 120 or forceps-assisted) or CS; elective or emergency. Elective CS included those planned 121 >8 hours before the delivery, while emergency CS included all other CS. 122 123 **Covariates** 124 Sociodemographic, health-related and obstetrical factors that could plausibly influence 125 the association between previous stillbirth and the outcomes were identified based on 126 the literature and pre-analytical assumptions. Maternal age at the time of delivery was 127 retrieved from the MBRN. The following sociodemographic variables were obtained 128 from Q1: marital status, categorised as married/cohabiting or living alone; pre-

pregnancy daily smoking; pre-pregnancy body mass index >30 kg/m<sup>2</sup> and higher

education (>12 years of school). High parity was defined as two or more previous live births or stillbirths and verified with information from the MBRN. Previous miscarriage(s) was categorised as "yes" or "no". Pre-pregnancy comorbidity was defined as having at least one of the following previous medical problems reported in the MBRN: Asthma, hypertension, recurrent urinary tract infections, kidney disease, rheumatoid arthritis, heart disease, epilepsy, pre-pregnancy diabetes mellitus, and/or thyroid disease. For women with a previous stillbirth and women with a previous live birth, MBRN-data regarding the previous pregnancy were retrieved and included information on hypertensive disorders, instrumental vaginal delivery and CS (all pregnancies).

MBRN-data regarding the MoBa pregnancy were obtained for all three groups and included bleeding in pregnancy; hypertensive disorders, diabetes (all types), small for gestational age (birthweight <10<sup>th</sup> percentile according to gestational age and gender), macrosomia (birthweight >4.5 kg), preterm birth (delivery before week 37 gestational weeks) and delivery after 41 gestational weeks. Complications of labour such as dystocia, feto-pelvic disproportion, abnormal labour and augumention of labour were recorded in the MBRN as the variable dystocia. The inter-pregnancy interval was defined as the number of months between the previous delivery (stillbirth or live birth) and the next conception (estimated by ultrasound measurements).

#### **Potential mediators**

Anxiety was measured using a short version of the Hopkins Symptom Checklist (SCL). The SCL-25 is widely used as a screening tool for anxiety and depression and shows a high concordance with clinical assessments (24). We used a four-items subscale (SCL-4a) that correlates 0.90 with the original anxiety subscale of the SCL-25 (25). In the third trimester of pregnancy (Q2) the women were asked if they had been bothered by any of the following during the previous two weeks: 1) "feeling fearful," 2) "nervousness or shakiness inside," 3) "feeling tense or keyed up" and 4) "suddenly scared for no reason". Items are scored on a Likert scale ranging from one (not at all bothered) to four (very much bothered). We defined a mean score ≥2.0 on SCL-4a as presence of anxiety (25, 26). Cronbach's alpha of internal consistency was 0.79.

The variable "dread of childbirth" was derived from the MoBa questionnaire at gestational week 30 (Q2). Women responded to the statement "I am really dreading giving birth" with one of six response alternatives: 1) agree completely, 2) agree, 3) agree somewhat, 4) disagree somewhat, 5) disagree and 6) disagree completely. The variable was dichotomised, defining responses 1-2 as dread of childbirth. Since the item has not been tested for its validity in reflecting fear of childbirth, we named it "dread of childbirth" reflecting the wording in the questionnaire.

A variable can be considered a mediator if it accounts for the relationship between the predictor and the outcome (27). Thus, when a mediator is present, the association between the predictor and the outcome variable is reduced, either to zero (full mediaton) or not to zero (partial mediaton).

#### Statistical analyses

Categorical variables were reported as proportions and compared between groups using chi-square tests. Continuous variables were reported as means with confidence interval (CI) or standard deviation (SD) and compared between groups using independent samples t-test. To reduce potential sample distortion caused by missing values, the Estimation-Maximation procedure in SPSS was used to impute missing values on SCL-4a if at least 50% of items were present. This resulted in 0.4% missing on the SCL4a. The proportion of missing values were <5% on all other variables. Bivariate and multivariate linear regression models were used to estimate beta coefficients (B) and adjusted beta coefficients (aB) for the frequency of antenatal visits among women with a previous stillbirth compared with the two reference groups. Logistic regression models were used to estimate odds ratios (ORs) and adjusted odds ratios (aORs) for induced labour and CS among women with a previous stillbirth compared with the two reference groups. Covariates that were unevenly distributed between the groups (p <0.1) and associated with the outcome variable in a bivariate model (p <0.1) were included in the multivariate analyses. Age was included as a covariate in every multivariate model. Testing for mediators was restricted to regression models comparing women with a previous stillbirth to women with a previous live birth. Anxiety (SCL-4a) was considered a potential mediator for the association between stillbirth and frequency of antenatal visits and for the association between stillbirth and elective CS. Dread of childbirth was considered a potential mediator for the association between stillbirth and elective CS. The potential mediators were included in the multivariate regression models if they were significantly associated with the predictor and the outcome variable. Mediation analyses were conducted by using the procedure described by

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Baron and Kenny (27). Since the mediator variables (anxiety and dread of childbirth) and one of the outcome variables (elective CS) were dichotomous, the regression coefficients were standardized to make them comparable before testing the significance of the mediating effect using the Sobel test (28, 29). If the potential mediators remained significant in the multivariate regression models, they were also tested for interaction with previous stillbirth.

All data were analysed using the Statistical Package for Social Science version 23.0 (SPSS Inc., Chicago, IL, United States). Two-sided p-values <0.05 were regarded as statistically significant.

### **Results**

The mean gestational age at the time of stillbirth was 33.5 weeks (95% CI 32.5 - 34.6, range 20.4 - 42.6). Table 1 displays characteristics and covariates categorised by group. Women with a previous stillbirth and women with a previous live birth did not differ according to age, but were significantly older than the previously nulliparous women. A high BMI was more prevalent in the stillbirth group compared with both reference groups, whilst higher education was less prevalent. In addition, more women in the stillbirth group had two or more previous births compared with the live birth group, while the proportion with previous CS did not differ. In the stillbirth group the average inter-pregnancy interval was shorter compared with the live birth group. Anxiety and dread of childbirth was more prevalent in the stillbirth group (22.5% and 30.2%) compared with both reference groups (4.4% / 5.5% and 21.7% / 16.9%, respectively).

#### **Healthcare utilisation**

Table 2 displays healthcare utilisation in pregnancy and mode of delivery categorised by group. The great majority (91.3%) of women with a previous stillbirth had antenatal visits at the hospital outpatient clinic. Women with a previous stillbirth had significantly more antenatal visits (mean 10.0) compared with women with a previous live birth (mean 6.0, p <0.001) and previously nulliparous women (mean 6.3, p <0.001). Women with a previous stillbirth had performed more ultrasound scans, had more frequently unscheduled contacts with midwife (but not physician) and were more often admitted to the hospital compared with both reference groups (Table 2).

In the multivariate linear regression models, previous stillbirth was significantly associated with more antenatal visits in the subsequent pregnancy compared with both reference groups (Table 3).

| Anxiety was bivariately associated with frequency of antenatal visits (B 2.6, 95% CI 1.7-3.6, p <0.001). When included in the multivariate model, the association between anxiety and frequency of antenatal visits remained significant (aB 1.0, 95% CI 0.1-1.8). As did the association between previous stillbirth and frequency of antenatal visits (aB reduced from 3.9 to 3.7, 95% CI 3.1-4.2). The mediating effect of anxiety accounted for 7.1% of the total effect of stillbirth on frequency of antenatal care visits (Sobel Z = |
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| 101 7.170 of the total effect of stillollar on frequency of antenatal care visits (500012 =   |
| 2.078, $p = 0.037$ ). Figure 1 displays a model illustrating the mediation design.  |
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| There was a significant interaction between anxiety and previous stillbirth (aB 2.2, p =  |
| 0.020). Among women with a previous stillbirth, anxiety was associated with more  |
| frequent antenatal visits (aB 1.7, 95% CI 0.3-3.2, p = 0.021), but not among women  |
| with a previous live birth (aB -0.4, 95% CI -1.6-0.7, $p = 0.472$ ).  |
| Induced labour and mode of delivery   |
| Induced labour and CS, both elective and emergency, were more prevalent among   |
| women with a previous stillbirth compared with both reference groups (Table 2). In  |
| the multivariate logistic regression models, previous stillbirth was significantly  |
| associated with higher frequencies of induced labour (aOR 9.5 and 4.3), CS (all) (aOR   |
| 4.8 and 2.5) and elective CS (aOR 2.5 and 3.7) compared with both reference groups  |
| (Table 3).  |
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| Anxiety and dread of childbirth as potential mediators for elective caesarean   |
| section in the pregnancy after stillbirth   |
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Anxiety was not bivariately associated with elective CS (OR 1.5, 95% CI 0.6-3.7), but dread of childbirth was (OR 3.3, 95% CI 1.8-6.3). When included in the multivariate model, the association between dread of childbirth and elective CS remained significant (aOR 3.1, 95% CI 1.6-5.9). The association between previous stillbirth and elective CS also remained significant (aOR reduced from 2.5 to 2.1, 95% CI 1.1-4.3). The mediating effect of dread of childbirth accounted for 11.0% of the total effect of stillbirth on elective CS, but was not significant (Sobel Z = 1.704, p = 0.088). There was no interaction between dread of childbirth and previous stillbirth (p = 0.340).

### Discussion

#### Main findings

In this study, we found that women with a previous stillbirth had higher healthcare utilisation and more frequently induced labour or CS in the subsequent pregnancy compared with women with previous live births and previously nulliparous women. Anxiety was identified as a minor mediator for the relationship between previous stillbirth and frequency of antenatal visits, and was associated with slightly more antenatal visits among women with a previous stillbirth, but not among women with a previous live birth. Dread of childbirth was not a significant mediator for the association between previous stillbirth and elective CS in the subsequent pregnancy.

### **Strenghts and limitations**

Healthcare utilisation in pregnancy has been investigated in smaller studies including women with early pregnancy loss and neonatal loss, but with few stillbirths (5). To our knowledge, this is the first study that has exlusively assessed healthcare utilisation in the pregnancy following stillbirth compared with other pregnant women. So far, there have been few large-scale studies on mode of delivery in pregnancies following stillbirth (17, 18), particularly stillbirths of all causes (19). Thus, this study adds to a limited body of evidence. We are also the first to assess anxiety and dread of childbirth as possible mediators for increased healthcare utilisation and elective CS in this group. The data is derived from a large national cohort and our sample size is larger than most previous studies in this field. The prospective design minimised reporting bias, and applying two reference groups to further explore the impact of stillbirth is also a strength.

However, the study has a number of limitations. The participation rate of 40.6% is a weakness, but as expected for population-based studies (30). A study investigating selection bias in the MoBa study found that there was an under-representation of participants with a number of exposure variables, including previous stillbirths (31), but that self-selection was not a problem in studies of exposure-outcome associations. We therefore argue that our main findings with some caution can be generalised to other women pregnant after stillbirth.

Unfortunately, we did not have information on the causes of stillbirth, the level of fear and anxiety among caregivers or the indications for conduction of elective CS. This information could provide opportunities for meaningful stratifications of the outcomes. Another limitation to this study is the lack of validated instruments for measuring healthcare utilisation and fear or dread of childbirth. Since we did not have access to medical records, we cannot exclude the risk of recall bias when measuring health care utilisation. The estimates of anxiety in our study relied on self-reporting using a prevalidated screening tool and such questionnaires are not diagnostic. Optimally, we would also have included an instrument measuring pregnancy specific anxiety. Further, anxiety and healthcare utilisation after 30 gestational weeks was not measured. We cannot rule out that potentially increased anxiety closer to term could be a stronger mediator for health care utilisation or mode of delivery in pregnancies following stillbirth. Regarding the mediation analyses, definite conclusions about the causal relationship between anxiety and frequency of antenatal visits cannot be drawn since the variables were obtained simultaneously.

### Interpretation

Higher healthcare utilisation in the pregnancy after stillbirth is consistent with previous findings from Hutti et al. in a smaller study on women pregnant after miscarriage, stillbirth or neonatal death (5). The higher frequency of induced labour and CS in our study is consistent with findings in previous studies (17, 19), but with somewhat higher odds ratios in our study, particularly for induced labour. Reasons for this may be that our study includes women with stillbirths regardless of cause and regardless of parity for the parous women. Further, when estimating aORs for induced labour, deliveries starting with CS were excluded. Differing practices in obstetrical management between countries could also be an explanatory factor.

General anxiety was a statistically significant mediator for the association between previous stillbirth and frequency of antenatal visits, but the effect was minor. This may indicate that women with a previous stillbirth are offered more antenatal visits than other women, but this is mainly regardless of general anxiety. Alternatively, pregnancy specific anxiety could be a stronger mediator for this relationship.

Fear of childbirth has previously been demonstrated to be associated with maternal requests for CS (11, 12). While dread of childbirth was associated with elective CS in our study, it did not account for the higher frequency in women with a previous stillbirth. However, as the p-value of the mediation effect was just above the significance level, larger studies are needed to conclude as to what degree feelings of anxiety, fear or dread related to the ongoing pregnancy are mediators for labour and delivery interventions in this group. Several mechanisms are likely to explain the associations between previous stillbirth and increased healthcare utilisation, induced

labour and CS in the subsequent pregnancy, particularily the higher rate of complications (19, 32) and increased risk of recurrent stillbirth (33-35). These factors depend partly on the aetiology of the previous stillbirth (35). Thus, anxiety and dread of childbirth could potentially be mediators for elective caesarean section in pregnancies with particularly high recurrence risks. Anxiety among obstetricians may also lead to more frequent antenatal visits and affect decisions regarding induction of labour or CS. According to a postal survey regarding obstetrical management in the pregnancy after unexplained stillbirth, Robson et al. found that the tendency for early delivery, and in particular by CS, may be due in part to altered management strategies, and not solely as a consequence of complications in the pregnancy (36). Studies consistently report that the risk of stillbirth in ongoing pregnancies increases gradually from 36 gestational weeks and particularily post term (37-42), and obstetricians may decide on an early delivery for preventive reasons, even though the cost-benefit effect is uncertain (43, 44).

## Conclusion

Women pregnant after stillbirth were more ample users of healthcare services, and induced labour and caesaren section were more prevalent in this group compared with other multi- and nulliparous women. Anxiety was a minor mediator for the association between previous stillbirth and frequency of antenatal visits in the the subsequent pregnancy. Dread of childbirth was not a significant mediator for the relationhip between previous stillbirth and elective caesarean section, but larger studies are needed to conclude on this issue. Future research should include information on cause of the prior stillbirth, indications for CS in the subsequent pregnancy and caregivers levels of fear and anxiety. The quality of care provided in pregnancies following stillbirth should also be evaluated.

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| 375 |  |  |  |  |  |  |
| 376 | Contribution to authorship   |  |  |  |  |  |
| 377 | IKG, ØE, PMS, EMJ, LBH and IR participated in the conception and design of this                |  |  |  |  |  |
| 378 | substudy. IKG conducted the analyses and drafted the article. LS and ØE participated           |  |  |  |  |  |
| 379 | in the statistical analyses. All authors contributed to interpretation of the data, critically |  |  |  |  |  |
| 380 | revised the article for important intellectual content and approved the final manuscript.      |  |  |  |  |  |
| 381 |  |  |  |  |  |  |
| 382 | Details of ethics approval   |  |  |  |  |  |
| 383 | Informed written consent was obtained for all participants upon recruitment. MoBa has          |  |  |  |  |  |
| 384 | obtained a license from the Norwegian Data Protection Authority. This substudy was             |  |  |  |  |  |
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