# National Institute for Health and Care Excellence

### Draft for consultation

# **Antenatal** care

[W] Maternal sleep position during pregnancy

NICE guideline < number>

Evidence reviews underpinning recommendations 1.3.19 to 1.3.20

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Draft for consultation

These evidence reviews were developed by the National Guideline Alliance which is a part of the Royal College of Obstetricians and Gynaecologists



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# Maternal sleep position during pregnancy

## **3 Review question**

- 4 Is there an association between sleep position on going to sleep and stillbirth or having a
- 5 small for gestational age baby?

#### 6 Introduction

- 7 It is possible that sleep position may affect the likelihood of stillbirth or having a small for
- 8 gestational age (SGA) baby. If there is an effect of sleep position, it is important for women to
- 9 be made aware of this association so that they can try and modify their sleeping position
- 10 accordingly. It is also important to clarify which sleeping positions are not associated with
- worse outcomes to reduce unnecessary sleep pattern restriction, worry and anxiety for
- women. The aim of this review is to determine what the associations are between maternal
- 13 sleeping positions and stillbirth or SGA.

#### 14 Summary of the protocol

- 15 Please see Table 1 for a summary of the Population, Intervention, Comparison, Outcomes,
- 16 Timing and Setting (PICOTS) characteristics of this review.

#### 17 Table 1: Summary of the protocol (PRO table)

Table 1. Sullillary of the pro-	tocol (I No table)	
Population	All pregnant women	
Index (prognostic factors)	<ul> <li>Maternal sleep position on going to sleep after 24<sup>+0</sup> weeks gestation:         <ul> <li>Other¹</li> <li>Prone (in other words on tummy)</li> <li>Side                 <ul> <li>Eft lateral</li> <li>Right lateral</li> <li>Variable</li> <li>Sitting/propped</li> <li>Supine (in other words on back)</li> </ul> </li> </ul> </li> </ul>	
Comparator	Not applicable	
Outcomes	<ul> <li>Outcomes for the baby</li> <li>Stillbirth (fetal death after 24<sup>+0</sup> weeks but before delivery)</li> <li>Small for gestational age (SGA)</li> </ul>	
Timing	Any time after pregnancy	
Setting	Sleep position and outcomes to be assessed in any relevant location.	

- Notes: 1, This factor is intended to capture any sleep position not described by the other listed sleep positions.
- 19 Abbreviations: SGA: small for gestational age.
- 20 For further details see the review protocol in appendix A.

#### 21 Methods and process

- 22 This evidence review was developed using the methods and process described in
- 23 Developing NICE guidelines: the manual 2014. Methods specific to this review guestion are
- 24 described in the review protocol in appendix A.

- In the first iteration of this evidence review, only primary evidence was identified and fully
- 26 extracted. Between the first iteration and the update of this evidence review, two individual
- 27 patient data (IPD) meta-analyses were published and identified. This report includes both the
- 28 IPD meta-analysed outcomes and the original primary study outcomes, which were not meta-
- analysed at a study level.
- 30 Declarations of interest were recorded according to NICE's conflicts of interest policy.

#### 31 Clinical evidence

#### 32 Included studies

- 33 One systematic review and meta-analysis of individual patient data (IPD) (Cronin 2019)
- including data from 5 case control studies (Gordon 2015, Heazell 2018, McCowan 2017,
- O'Brien 2019, Stacey 2011) reporting on the association between sleep position and stillbirth
- 36 was included in this report.
- 37 One of the included primary studies was a phase 1 investigation whose aim was to identify
- 38 modifiable risk factors for late-pregnancy stillbirth (Gordon 2015), whilst the remaining 4
- 39 studies were phase 2 investigations that examined whether specific going-to-sleep positions
- 40 were associated with stillbirth. One study defined late stillbirth as fetal death after and
- 41 including 32 weeks gestation (Gordon 2015), whilst the remaining 4 studies defined it as fetal
- death after and including 28 weeks gestation. One study was retrospective (O'Brien 2019),
- 43 whilst the remaining studies were prospective. Four of the studies were multicentre studies,
- 44 two of which were conducted in New Zealand (McCowan 2017, Stacey 2011), one in
- 45 Australia (Gordon 2015), and one in the UK (Heazell 2018), whilst one study was an
- international online-based study (O'Brien 2019). All the studies used left lateral going-to-
- 47 sleep position as the control arm to compare against the odds of stillbirth with other sleeping
- 48 positions. Data on going-to-sleep position was reported relative to the participants'
- 49 recollection of their going-to-sleep position on the last month (Gordon 2015), last night
- 50 (Heazell 2018, Stacey 2011), and last night and last week (McCowan 2017, O'Brien 2019).
- One of the studies (McCowan 2017) only reported data according to whether late stillbirth
- 52 occurred pre-term (between 28 and 36 weeks gestation) or term (greater and including 37
- weeks gestation), whilst the remaining four studies reported data for still birth regardless of
- 54 term status.
- 55 Linked to the analysis reported in Cronin 2019, a secondary analysis (Anderson 2019) used
- 56 IPD from 4 of the included studies (Heazell 2018, Stacey 2011, McCowan 2017, Gordon
- 57 2015) and explored the association between the position in which pregnant women went to
- 58 sleep and infant birth weight.
- 59 The included studies are summarised in Table 2 and Table 3. See also the literature search
- strategy in appendix B and the study selection flow chart in appendix C.

#### 61 Excluded studies

- 62 Studies not included in this review and reasons for their exclusions are provided in appendix
- 63 K.

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#### Summary of clinical studies included in the evidence review

A summary of the studies that were included in this review is presented in Table 2 and Table 3.

Table 2: Characteristics of included studies for the association between maternal sleep position and stillbirth

Study ID Study design Country Size of cohort	Cases Number of participants	Controls Number of participants	Sleep positions assessed	Confounding factors adjusted for
Cronin 2019  SR with MA IPD  IPD from 4 case control studies: Gordon 2015; Heazell 2017; McCowan 2017; Stacey 2011 1 nested case control: O'Brien 2019	Women with singleton pregnancies who had stillbirth at ≥28 weeks gestation N=851	Women with singleton pregnancies at ≥28 weeks gestation N=2257	Going-to-sleep position (last available position, within 2 weeks of estimated fetal death in cases) and stillbirth:  • Left lateral (reference)  • Supine  • Right  • Prone  • Variable  • Propped up  • Don't remember	<ul> <li>Maternal age</li> <li>Earliest pregnancy BMI</li> <li>Ethnicity</li> <li>Parity</li> <li>Education level</li> <li>Marital status</li> <li>Pre-existing hypertension or diabetes</li> <li>Smoking</li> <li>Recreational drug use</li> <li>Fetal movements</li> <li>Infant birthweight by customised centiles</li> <li>Three confounders going-to-sleep duration, frequency of overnight toilet use, and day-time napping) analysed in sensitivity models</li> </ul>
Gordon 2015	Women with singleton pregnancies who had	Women at 32 weeks of gestation with singleton pregnancies matched for	Going-to-sleep position in last month and stillbirth:	Age     BMI

Study ID Study design Country Size of cohort	Cases Number of participants	Controls Number of participants	Sleep positions assessed	Confounding factors adjusted for
Prospective population-based case-control study  Australia  N=295	stillbirth at ≥32 weeks gestation N=103	booking hospital and gestation who were recruited at the same period as cases N=192	<ul> <li>Left lateral (reference)</li> <li>Other<sup>1</sup></li> <li>Right lateral</li> <li>Supine</li> </ul>	<ul> <li>Level of education</li> <li>Not in paid work</li> <li>Parity</li> <li>Sleep apnoea symptoms</li> <li>Smoking during pregnancy</li> </ul>
Heazell 2017  Prospective population-based case-control study  UK  N=1024	Women with singleton pregnancies who had a stillbirth ≥28 weeks gestation with no known congenital anomaly N=291	Women with an ongoing pregnancy at the time of interview with no congenital anomaly N=733	Going-to-sleep position on last night and stillbirth:  • Left lateral (reference)  • Prone  • Propped  • Right lateral  • Supine  • Variable-lateral	<ul> <li>Age</li> <li>BMI</li> <li>Ethnicity</li> <li>Level of education</li> <li>Other sleep related variables that were significant in univariable analysis (including sleep duration on last night, number of times visited toilet on last night, and number of maternal daytime naps in last 4 weeks)</li> <li>Parity</li> <li>Small-for-gestational age</li> <li>Smoking during pregnancy</li> </ul>
McCowan 2017  Prospective population-based case-control study	Women with singleton pregnancies who had a stillbirth at ≥28 weeks gestation N=164	Women with singleton pregnancies with ongoing pregnancies in the participating health region N=569	Going-to-sleep position on last night and pre-term stillbirth (28-36 weeks gestation):  • Left lateral (reference)  • Propped  • Other - Restless <sup>2</sup>	<ul><li>Age</li><li>BMI</li><li>Ethnicity</li><li>Deprivation index</li></ul>

Study ID Study design Country Size of cohort	Cases Number of participants	Controls Number of participants	Sleep positions assessed	Confounding factors adjusted for
New Zealand N=733			<ul> <li>Right lateral</li> <li>Supine Going-to-sleep position on last week and pre-term stillbirth (28- 36 weeks gestation):</li> <li>Left lateral (reference)</li> <li>Prone</li> <li>Propped</li> <li>Right lateral</li> <li>Supine</li> <li>Variable-lateral</li> <li>Going-to-sleep position on last night and term stillbirth (≥37 weeks gestation):</li> <li>Left lateral</li> <li>Other - Restless²</li> <li>Right lateral</li> <li>Propped</li> <li>Supine</li> <li>Going-to-sleep position on last week and term stillbirths (≥37 weeks gestation):</li> <li>Left lateral (reference)</li> <li>Propped</li> <li>Right lateral</li> <li>Right lateral (reference)</li> <li>Propped</li> <li>Right lateral</li> </ul>	<ul> <li>Other sleep related variables significant in univariable analysis (hours of night time sleep on the last night, getting up to toilet during the last night, sleep during the daytime in the last week)</li> <li>Parity</li> <li>Small-for-gestational age status</li> <li>Smoking during pregnancy</li> </ul>

Study ID Study design Country Size of cohort	Cases Number of participants	Controls Number of participants	Sleep positions assessed	Confounding factors adjusted for
			<ul><li>Supine</li><li>Variable-lateral</li></ul>	
O'Brien 2019 <sup>3</sup> Nested case- control study in uncontrolled cohort of known size  Anonymous international online survey  N=633	Women with a singleton stillbirth baby of ≥28 weeks gestation in month before completing the survey N=153	Women who were either pregnant with ≥28 weeks gestation or had a live birth in week before completing the survey N=480	Gong-to-sleep position on last night and stillbirth:  • Left lateral (reference)  • Propped  • Right lateral  • Supine  • Variable-lateral  Going-to-sleep position on last month and stillbirth:  • Left lateral (reference)  • Propped  • Right lateral  • Supine  • Variable-lateral	<ul> <li>Age</li> <li>BMI</li> <li>Country of residence</li> <li>Ethnicity</li> <li>Level of education</li> <li>Parity</li> <li>Smoking during pregnancy</li> </ul>
Stacey 2011  Prospective population-based case-control study  New Zealand  N=465	Women with singleton pregnancies who had a stillbirth at ≥28 weeks gestation N=155	Women selected from the pregnancy registration list of the district health board, matched for gestation to cases N=310	Going-to-sleep position on last night and stillbirth:  • Left lateral (Reference)  • Other <sup>4</sup> • Right lateral  • Supine	<ul> <li>Age</li> <li>BMI</li> <li>Ethnicity</li> <li>Parity</li> <li>Smoking during pregnancy</li> <li>Socioeconomic status</li> </ul>

Notes: <sup>1</sup> The category of 'Other' going-to-sleep position reported in this study included any going-to-sleep position other than left lateral, right lateral or supine. This categorisation was not the same as intended in the protocol and this position was therefore not included in the narrative analysis; <sup>2</sup> Restless going-to-sleep position refers to women with frequently changing positions when going to sleep and could not remember the position just before falling asleep; <sup>3</sup> Women were recruited using an online survey system, 'Study of Trends and Risk Factors for Stillbirth', developed by an international consortium of clinicians and academics together with the Star Legacy Foundation and other stillbirth and parental support groups; <sup>4</sup> The category of 'Other' going-to-sleep position reported in this study included prone, sitting, sleeping on both lateral sides, and unsure or don't remember going-to-sleep position. This categorisation was not the same as intended in the protocol and this position was therefore not included in the narrative analysis. Abbreviations: N: total number of participants in the study or case or control; BMI: body mass index; CI: confidence interval; QUIPS, Quality in Prognostic Studies checklist; SGA: small for gestational age.

Table 3: Characteristics of included studies for the association between maternal sleep position and small for gestational age

Study ID Study design Country Size of cohort	Cases Number of participants	Controls Number of participants	Sleep position assessed	Confounding factors adjusted for
Anderson 2019  Subgroup analysis of IPD MA  IPD from 4 case control studies: Gordon 2015; Heazell 2017; McCowan 2017; Stacey 2011	Women with singleton pregnancies who had stillbirth at ≥28 weeks gestation (supine) N=57	Women with singleton pregnancies at ≥28 weeks gestation (nonsupine) N=1703	Going-to-sleep position over last week/2 weeks/month (whichever was longest and available from primary study) and SGA:  • Left lateral (Reference)  • Other (not specified)  • Right lateral  • Supine	<ul> <li>Study site</li> <li>Maternal age</li> <li>Height</li> <li>Weight</li> <li>Parity</li> <li>Ethnicity</li> <li>Preexisting diabetes</li> <li>Preexisting hypertension</li> <li>Antepartum haemorrhage</li> <li>Gestational hypertensive disorder</li> <li>Gestational diabetes</li> <li>Cigarette smoking</li> <li>Recreational drug use</li> </ul>

Abbreviations: IPD MA: individual patient data meta-analysis; N: total number of participants in the study or case or control; BMI: body mass index; CI: confidence interval; SGA: small for gestational age; vs: versus

See the full evidence tables in appendix D.

# Quality assessment of studies included in the evidence review

See the evidence profiles in appendix F.

#### 1 Economic evidence

#### 2 Included studies

- 3 A systematic review of the economic literature was conducted but no economic studies were
- 4 identified which were applicable to this review question.
- 5 A single economic search was undertaken for all topics included in the scope of this
- 6 guideline. See supplementary material 2 for details.

#### 7 Excluded studies

- 8 Economic studies not included in this review are listed, and reasons for their exclusion are
- 9 provided in appendix K.

#### 10 Summary of studies included in the economic evidence review

11 No economic studies were identified which were applicable to this review question.

#### 12 Economic model

- No economic modelling was undertaken for this review because the committee agreed that
- 14 other topics were higher priorities for economic evaluation.

#### 15 Clinical evidence statements

#### 16 Individual patient data meta-analysis results

- Association between going-to-sleep position (last available position, within last 2 weeks) and stillbirth in comparison to left lateral going-to-sleep position
- High quality evidence from an IPD meta-analysis of 5 case control studies (N=3108) found
   an important association between supine going-to-sleep position and stillbirth: aOR 2.63
   (95% CI 1.72 to 4.04).
- Low quality evidence from an IPD meta-analysis of 5 case control studies (N=3108) found
   no important association between right sided going-to-sleep position and stillbirth: aOR
   1.04 (95% CI 0.83 to 1.31).
- Very low quality evidence from an IPD meta-analysis of 5 case control studies (N=3108) found no important association between prone going-to-sleep position and stillbirth: aOR 0.63 (95% CI 0.12 to 3.25).
- Very low quality evidence from an IPD meta-analysis of 5 case control studies (N=3108)
   found no important association between variable side going-to-sleep position and stillbirth:
   aOR 0.97 (95% CI 0.70 to 1.35).
- Very low quality evidence from an IPD meta-analysis of 5 case control studies (N=3108)
   found no important association between propped up going-to-sleep position and stillbirth:
   aOR 1.30 (95% CI 0.68 to 2.49).
- Moderate quality evidence from an IPD meta-analysis of 5 case control studies (N=3108) found an important association between not remembering going-to-sleep position and stillbirth: aOR 2.26 (95% CI 1.48 to 3.46).

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- Association between going-to-sleep position (last available position, within last 2 weeks) and small for gestational age in comparison to left lateral going-to-sleep position
- High quality evidence from an IPD meta-analysis of 4 case control studies (N=1760) found
   an important association between supine going-to-sleep position and babies being born
   small for gestational age: aOR 3.23 (95% CI 1.37 to 7.59).
- Very low quality evidence from an IPD meta-analysis of 4 case control studies (N=1760)
   found no important association between right sided going-to-sleep position and babies
   being born small for gestational age: aOR 1.05 (95% CI 0.58 to 1.90).
- Very low quality evidence from an IPD meta-analysis of 4 case control studies (N=1760)
   found no important association between other going-to-sleep position and babies being born small for gestational age: aOR 1.14 (95% CI 0.62 to 2.09).

#### 50 Primary study results

- Association between going-to-sleep position on last night and stillbirth in comparison to left lateral going-to-sleep position on last night
  - Very low quality evidence from 1 phase 2 prospective population-based case-control study (N=1024) examined whether there was an association between prone going-tosleep position on last night and stillbirth compared to left lateral going-to-sleep position on last night. However, no association was found in this study: aOR 1.01 (95%CI 0.13 to 7.81)
    - Very low quality evidence from 3 phase 2 case-control studies (N=2122) 2 non-nested prospective population-based studies and 1 retrospective nested study in an online cohort of known size examined whether there was an association between right-lateral going-to-sleep position on last night and stillbirth compared to left lateral going-to-sleep position on last night. However, none of the 3 studies found any such association: aOR 0.67 (95%CI 0.44 to 1.02); aOR 1.11 (95%CI 0.70 to 1.77); aOR 1.74 (95%CI 0.98 to 3.01)
    - Very low quality evidence from 2 phase 2 case-control studies 1 non-nested prospective population-based study and 1 retrospective nested study in an online cohort of known size (N=1657) examined whether there was an association between sitting/propped going-to-sleep position on last night and stillbirth compared to left lateral going-to-sleep position on last night. However, none of the studies found any such association: aOR 0.44 (95%CI 0.13 to 1.49); aOR 0.71(95%CI 0.22 to 2.30).
  - Very low quality evidence from 3 phase 2 case-control studies (N=2122) 2 non-nested prospective population-based studies and 1 retrospective nested study in an online cohort of known size examined whether there was an association between supine going-to-sleep position on last night and stillbirth compared to left lateral going-to-sleep position on last night. Two studies found that supine going-to-sleep position was associated with an increase in stillbirth compared to left lateral going-to-sleep position (aOR 2.31 [95%CI 1.04 to 5.11]; aOR 2.54 [95%CI 1.04 to 6.18]) whereas no association was found in another study: aOR 1.05 (95%CI 0.32 to 3.50). However this latter study, which was powered to detect an association between supine going-to-sleep position and stillbirth assuming a 20% exposure frequency, reported an exposure frequency of only 2.3%.
  - Very low quality evidence from 2 phase 2 case-control studies 1 non-nested prospective population-based study and 1 retrospective nested study in an online cohort of known size (N=1657) - examined whether there was an association between variable-lateral going-to-sleep position on last night and stillbirth compared to left lateral going-to-sleep

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position on last night. However, none of the studies found any such association: aOR 0.93 (95%CI 0.51 to 1.69); aOR 0.75 (95%CI 0.34 to 1.64).

# Association between going-to-sleep position on last month of pregnancy and late stillbirth in comparison to left lateral going-to-sleep position

- Very low quality evidence from 2 phase 2 case-control studies (N=928) 1 non-nested prospective population-based study and 1 retrospective nested study in an online cohort of known size examined whether there was an association between right-lateral going-to-sleep position on last month and stillbirth compared to left lateral going-to-sleep position on last month. However, none of the studies found any such association: aOR 1.1 (95%CI 0.43 to 2.6); aOR 1.14 (95%CI 0.70 to 1.85).
- Very low quality evidence from 1 phase 2 case control study a retrospective nested study in an online cohort of known size (N=633) examined whether there was an association between sitting/propped going-to-sleep position on last month and stillbirth compared to left lateral going-to-sleep position on last month. However, no association was found in this study: aOR 1.20 (95%CI 0.39 to 3.68).
- 101 Very low quality evidence from 2 case-control studies in (N=928) - 1 phase 1 non-nested prospective population-based study and 1 phase 2 retrospective nested study in an 102 103 online cohort of known size - examined whether there was an association between 104 supine going-to-sleep position on last month and stillbirth compared to left lateral goingto-sleep position on last month. One study found that supine going-to-sleep position was 105 106 associated with an increase in stillbirth compared to left lateral going-to-sleep position: 107 aOR 6.26 (95%CI 1.2 to 34.00) whereas no association was found in another study: aOR 108 0.37 (95%CI 0.04 to 3.12).
- Very low quality evidence from 1 phase 2 retrospective nested case control study in an online cohort of known size (N=633) examined whether there was an association between variable-lateral going-to-sleep position on last month and stillbirth compared to left lateral going-to-sleep position on last month. However, no association was found in this study: aOR 0.87 (95%CI 0.48 to 1.55).
- Association between going-to-sleep position on last night or last week of pregnancy and pre-term stillbirth (28 to 36 weeks gestation) in comparison to left lateral going-tosleep position on last night or last week

#### 117 Going-to-sleep position on last night

- Very low quality evidence from 1 phase 2 non-nested prospective population-based case-control study (N=733) examined whether there was an association between restless going-to-sleep position on last night and preterm stillbirth compared to left lateral going-to-sleep position on last night. However, no association was found in this study: aOR 3.50 (95%CI 0.61 to 19.97).
- Very low quality evidence from 1 phase 2 non-nested prospective population-based case-control study (N=733) examined whether there was an association between right-lateral going-to-sleep position on last night and preterm stillbirth compared to left lateral going-to-sleep position on last night. However, no association was found in this study: aOR 0.96 (95%CI 0.48 to 1.94).
- Very low quality evidence from 1 phase 2 non-nested prospective population-based case-control study (N=733) examined whether there was an association between sitting/propped going-to-sleep position on last night and preterm stillbirth compared to left lateral going-to-sleep position on last night. However, no association was found in this study: aOR 4.37 (95%CI 0.11 to 178.86).
- Very low quality evidence from 1 phase 2 non-nested prospective population-based casecontrol study (N=733) examined whether there was an association between supine

going-to-sleep position on last night and preterm stillbirth compared to left lateral goingto-sleep position on last night. However, no association was found in this study: aOR 2.25 (95%CI 0.65 to 7.84).

#### Going-to-sleep position on last week

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- Very low quality evidence from 1 phase 2 non-nested prospective population-based case-control study (N=733) examined whether there was an association between prone going-to-sleep position on last week and preterm stillbirth compared to left lateral going-to-sleep position on last week. However, no association was found in this study: aOR 10.71 (95%CI 0.43 to 268.28).
- Very low quality evidence from 1 phase 2 non-nested prospective population-based case-control study (N=733) examined whether there was an association between right-lateral going-to-sleep position on last week and preterm stillbirth compared to left lateral going-to-sleep position on last week. However, no association was found in this study: aOR 0.73 (95%CI 0.34 to 1.54).
- Very low quality evidence from 1 phase 2 non-nested prospective population-based case-control study (N=733) examined whether there was an association between sitting/propped going-to-sleep position on last week and preterm stillbirth compared to left lateral going-to-sleep position on last week. However, no association was found in this study: aOR 4.01 (95%CI 0.08 to 210.43).
- Very low quality evidence from 1 phase 2 non-nested prospective population-based case-control study (N=733) examined whether there was an association between supine going-to-sleep position on last week and preterm stillbirth compared to left lateral going-to-sleep position on last week. However, no association was found in this study: aOR 2.25 (95%CI 0.65 to 7.84).
- Very low quality evidence from 1 phase 2 non-nested prospective population-based case-control study (N=733) examined whether there was an association between variable-lateral going-to-sleep position on last week and preterm stillbirth compared to left lateral going-to-sleep position on last week. However, no association was found in this study: aOR 0.63 (95%CI 0.18 to 2.19).
- Association between going-to-sleep position on last night or last week of pregnancy
   and term stillbirth (≥37 weeks gestation) in comparison to left going-to-sleep position
   on last night or last week

#### 167 Going-to-sleep position on last night

- Very low quality evidence from 1 prospective phase 2 non-nested prospective population-based case-control study (N=733) examined whether there was an association between restless going-to-sleep position on last night and term stillbirth compared to left lateral going-to-sleep position on last night. However, no association was found in this study: aOR 2.0 (95%CI 0.64, 6.21).
- Very low quality evidence from 1 phase 2 non-nested prospective population-based case-control study (N=733) examined whether there was an association between right-lateral going-to-sleep position on last night and term stillbirth compared to left lateral going-to-sleep position on last night. However, no association was found in this study: aOR 0.98 (95%CI 0.48 to 1.99).
- Very low quality evidence from 1 phase 2 non-nested prospective population-based case-control study (N=733) examined whether there was an association between sitting/propped going-to-sleep position on last night and term stillbirth compared to left lateral going-to-sleep position on last night. However, no association was found in this study: aOR 1.02 (95%CI 0.17 to 5.97).

183 Low quality evidence from 1 phase 2 non-nested prospective population-based case-184 control study (N=733) examined whether there was an association between supine 185 going-to-sleep position on last night and term stillbirth compared to left lateral going-to-186 sleep position on last night. The study found that supine going-to-sleep position was 187 associated with an increase in stillbirth compared to left lateral going-to-sleep position: 188 aOR 10.26 (95%CI 3.01 to 35.04).

#### 189 Going-to-sleep position on last week

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- Very low quality evidence from 1 phase 2 non-nested prospective population-based casecontrol study (N=733) examined whether there was an association between right-lateral going-to-sleep position on last week and term stillbirth compared to left lateral going-tosleep position on last week. However, no association was found in this study: aOR 0.95 (95%CI 0.48 to 1.89).
- 195 Very low quality evidence from 1 phase 2 non-nested prospective population-based case-196 control study (N=733) examined whether there was an association between sitting/propped going-to-sleep position on last week and term stillbirth compared to left 198 lateral going-to-sleep position on last week. However, no association was found in this 199 study: aOR 2.64 (95%CI 0.47 to 14.81).
- Low quality evidence from 1 phase 2 non-nested prospective population-based case-200 201 control study (N=733) examined whether there was an association between supine 202 going-to-sleep position on last week and term stillbirth compared to left lateral going-to-203 sleep position on last week. The study found that supine going-to-sleep position was 204 associated with an increase in stillbirth compared to left lateral going-to-sleep position: 205 aOR 12.73 (95%CI 2.92 to 55.46).
- 206 Very low quality evidence from 1 phase 2 non-nested prospective population-based case-207 control study (N=733) examined whether there was an association between variable-208 lateral going-to-sleep position on last week and term stillbirth compared to left lateral going-to-sleep position on last week. However, no association was found in this study: 209 210 aOR 1.11 (95%CI 0.49 to 3.01).

#### The committee's discussion of the evidence 211

#### 212 Interpreting the evidence

#### 213 The quality of the evidence

- 214 The quality of each primary study was appraised using the QUIPS checklist. The main
- 215 reasons for downgrading the quality of studies were recall bias due to the time delay
- 216 between recruitment and interview, and selection bias due to limited participation from all the
- 217 eligible women. The overall quality of evidence for each outcome was assessed using a
- 218 modified GRADE framework for prognostic reviews and ranged from very low to low.
- 219 Although a phase 3 prospective cohort study is the best study design to establish the causal
- 220 relationship between a prognostic factor and an outcome, the frequency of stillbirth is low
- 221 and such a study is therefore not practically feasible to conduct. Therefore, no restrictions
- 222
- were initially placed on the appropriate types of study considered for this review with phase 1
- 223 and 2 studies initially rated as providing a moderate and high quality of evidence,
- 224 respectively. The main reasons for downgrading the overall evidence for all sleep positions
- 225 was risk of bias associated with each of the contributing studies (recall bias, selection bias),
- 226 inconsistency (variation in effect estimates across studies), indirectness (sample not clearly
- 227 representative of target population), imprecision (effect estimate has wide 95% confidence
- 228 intervals) and publication bias (due to the small number of early phase studies reporting
- 229 outcomes).

- 230 The IPD meta-analysis quality was appraised using the ROBIS checklist and both IPD meta-
- analyses were at low risk of bias. The individual outcomes within the IPD meta-analyses
- ranged in quality rating from high (for example supine sleeping position and its association
- with stillbirth) to very low. The IPD meta-analyses outcomes were typically downgraded due
- to imprecision in their estimates and publication bias (due to the small number of early phase
- 235 primary studies reporting outcomes).

#### Benefits and harms

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- Overall, the evidence suggests that there may be an increased risk of stillbirth after 28+0
- 238 weeks and babies being born small for gestational age (SGA) associated with going to sleep
- on one's back (in other words in the supine position) compared to going to sleep on one's
- left-hand side in both the primary studies and the IPD meta-analysis. The best estimate,
- from the IPD meta-analysis was that sleeping in a supine position approximately doubled the
- odds of stillbirth and trebled the odds of babies being born SGA.
- 243 While the quality of the evidence from the primary studies ranged depending on the timing
- and precise outcomes considered, the quality of the evidence from the IPD, particularly for
- the evidence around supine sleeping position, was relatively high. The evidence still may not
- be considered to be definitive evidence of causality between going to sleep position and
- 247 stillbirth or SGA as the IPD meta-analysis does not overcome issues with the study design of
- the primary studies. However the committee agreed it was of sufficient quality to advise
- 249 women to try to avoid going to sleep on their back after 28 weeks and inform women of the
- 250 likely link with stillbirth, alongside a caveat that the evidence is uncertain. The committee
- 251 chose to specifically highlight stillbirth as this is a more concerning outcome than babies
- being born SGA and they agreed that including SGA in the recommendations made the
- 253 advice less clear.
- 254 The evidence also suggests that the risk of going to sleep in any other position is the same
- as that of going to sleep on one's left side (that is, there is not an increased likelihood of
- 256 stillbirth associated with any other going-to-sleep position). The committee agreed that, as
- there has been some concern that there is such an association, it was important to highlight
- 258 that the evidence does not support the view that there is an increased likelihood of stillbirth
- associated with going to sleep on one's right side irrespective of the time of reporting
- compared to going to sleep on one's left side. However the evidence for other sleep positions
- was generally an absence of definitive association (with serious imprecision) as opposed to
- definitive evidence of no association, therefore the committee did not include this information
- 263 in the recommendations.
- The committee discussed that the studies looked at the association between going to sleep
- 265 position and outcomes because due to the nature of the observational studies relying on
- women's recall, it would not be possible to study the association between the woman's
- sleeping position and outcomes. However, the going to sleep position should be considered
- a proxy for sleeping position. Sleeping position is perhaps best controlled by controlling the
- going to sleep position. In addition, pillows or other props could be used to aid that the
- 270 position stays when sleeping. This review did not assess the effectiveness of any
- interventions to modify sleeping position but in the committee agreed, based on their
- 272 knowledge and experience, to recommend advising women to consider using for example
- 273 pillows so that they can maintain their position when sleeping.
- The committee noted that there may be a psychological impact of informing pregnant women
- of the potential link between sleeping on one's back and stillbirth or SGA and did not want to
- 276 cause undue anxiety. The committee also noted the relatively low incidence of stillbirth (1 in
- every 244 births in the UK according to 2018 Office for National Statistics [ONS] data).

278 279	However on balance they agreed that the evidence was strong enough that women should be advised about the risk.
280	Cost effectiveness and resource use
281	No economic studies were identified which were applicable to this review question.
282 283 284 285 286 287	Professional time advising women on healthy behaviours is already current practice. Therefore, the recommendations to advise women on sleeping position, and the possible link between sleep position and adverse outcomes is unlikely to require any increase in clinician time. In turn, advising women against sleeping on their backs after 28 weeks of pregnancy may reduce adverse outcomes such as stillbirth and small for gestational age reducing future healthcare costs.
288 289	

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# Appendices

# 2 Appendix A – Review protocols

- 3 Review protocol for review question: Is there an association between sleep position on going to sleep and still birth or
- 4 having a small for gestational age baby?

#### 5 Table 4: Review protocol

Field (based on PRISMA-P)	Content
Review question	Is there an association between sleep position on going to sleep and still birth or having a small for gestational age baby?
Type of review question	Prognostic factors review
Objective of the review	The aim of this review is to evaluate whether specific sleep positions are associated with still birth or having a small for gestational age baby after 24 <sup>+0</sup> weeks gestation.
Eligibility criteria – population	All pregnant women
Eligibility criteria – Risk factors (s)	Maternal sleep position on going to sleep after 24 <sup>+0</sup> weeks gestation:     Other     Prone (i.e. tummy)     Side     Left lateral     Right lateral     Variable     Sitting/propped     Supine (i.e. on back)  Notes: The position 'other' is intended to capture any other sleep position that is not listed. SGA is defined as having a birth weight below the 10th centile. Some studies will report this as Low Birth Weight (LBW) adjusted for Gestational Age (GA) rather than as SGA. For participants in the case group, sleep position reported may be usual sleep position or sleep position on the night before stillbirth.
Eligibility criteria – Confounding factors	Analysis used by studies must adjust for confounding factors using logistic regression to conduct multivariable analysis.
Outcomes and prioritisation	<ul> <li>Model performance</li> <li>Discrimination         <ul> <li>Concordance (C) statistic</li> </ul> </li> <li>Note: the C statistic is also known as 'area under the receiver operating characteristics curve' (AUC).</li> </ul>

Field (based on PRISMA-P)	Content
	Outcomes  Still birth (i.e. fetal death after 24 <sup>+0</sup> weeks but before delivery)  Small for gestational age (SGA)  Note: SGA is defined as having a birth weight below the 10th centile. Some studies will report this as Low Birth Weight (LBW) adjusted for Gestational Age (GA) rather than as SGA.
Eligibility criteria – study design	<ul> <li>Systematic reviews of prognostic studies</li> <li>Prognostic observational studies         <ul> <li>Prospective cohort studies</li> <li>Retrospective cohort studies</li> <li>Nested case-control studies within a cohort of known size</li> </ul> </li> <li>The following types of study design will be considered only if no studies of the above types are identified:         <ul> <li>Non-nested case-control studies</li> </ul> </li> </ul>
Other inclusion exclusion criteria	EXCLUDE: POPULATION:  Multiple pregnancy Pregnancy with congenital anomalies Women who had stillborn or live-born babies with congenital abnormalities  STUDY DESIGN: Cross-over studies Cross-sectional studies Non-comparative studies Randomised and quasi-randomised controlled trials  LANGUAGE: Non-English  PUBLICATION STATUS: Conference abstract  INCLUDE COUNTRY: No restriction
Proposed sensitivity/sub-group analysis, or meta-regression	If the studies are sufficiently similar to merit meta-analysis, subgroup analysis according to World Bank status of country (High-income countries; Low and middle-income countries) in which they were conducted in will be performed (see https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-worldbank-country-and-lending-groups for classification of countries).  Statistical heterogeneity will be assessed by visually examining the forest plots and by calculating the I² inconsistency statistic (with an I² value≥50% indicating serious heterogeneity, and ≥80% indicating very serious heterogeneity).

Field (based on PRISMA-P)	Content
Selection process – duplicate screening/selection/analysis	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies above 10% of the dual weeded resources will be resolved through discussion between the first and second reviewers or by reference to a third person. All data extraction will quality assured by a senior reviewer.  Draft excluded studies and evidence tables will be circulated to the Topic Group for their comments. Resolution of disputes will be by discussion between the senior reviewer, Topic Advisor and Chair.
Data management (software)	NGA STAR software will be used to generate bibliographies/citations, and to conduct study sifting and data extraction. Pairwise meta-analyses, if possible, will be performed using Cochrane Review Manager (RevMan5). For details please see Supplement 1: methods.
Information sources – databases and dates	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA, Embase Limits:  Date limit: none  Apply standard animal/non-English language exclusion Limit to prognostic studies in first instance but download all results.
Identify if an update	This is a new area in the guideline.
Author contacts	Developer: National Guideline Alliance.
Highlight if amendment to previous protocol	For details please see section 4.5 of <u>Developing NICE guidelines: the manual.</u>
Search strategy – for one database	For details please see appendix B.
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables).
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (economic evidence tables).
Methods for assessing bias at outcome/study level	<ul> <li>Quality assessment of individual studies will be performed using the following checklists:</li> <li>ROBIS for systematic reviews of prognostic studies</li> <li>QUIPS for prognostic studies</li> </ul>
	For details please see section 6.2 of <u>Developing NICE guidelines: the manual. The risk of bias for the evidence for each prognostic factor (i.e. sleep position) will be evaluated using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox': <a href="http://www.gradeworkinggroup.org/">http://www.gradeworkinggroup.org/</a>. For further details as to how GRADE will be adapted, see the following article:</u>
	<ul> <li>Huguet, A., Hayden, J. A., Stinson, J., McGrath, P. J., Chambers, C. T., Tougas, M. E., &amp; Wozney, L. (2013). Judging the quality of evidence in reviews of prognostic factor research: adapting the GRADE framework. Systematic reviews, 2(1), 71.</li> </ul>
Criteria for quantitative synthesis (where suitable)	Meta-analyses will be conducted for this review only if the same confounders are accounted for in the analyses, the same analytical methods are adapted, and the populations assessed are suitably similar. In all other cases, the results will be reported separately.
Methods for analysis – combining studies and exploring (in)consistency	The adjusted Risk Ratio or Odds Ratio and 95% confidence intervals will be plotted in RevMan if appropriate, although the results for each relative measure will be presented separately. Good model performance regarding discrimination will be defined as a C statistic >0.75 as suggested in Debray 2017:  • Debray, T. P., Damen, J. A., Snell, K. I., Ensor, J., Hooft, L., Reitsma, J. B., & Moons, K. G. (2017). A guide to systematic review and meta-analysis of prediction model performance. Bmj, 356, i6460.

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Field (based on PRISMA-P)	Content
	If a meta-analysis is conducted, inconsistency will be assessed by visual examination of the forest plots and the l² statistic (with l²≥50% indicating serious heterogeneity and l²≥80% indicating very serious heterogeneity.
Meta-bias assessment – publication bias, selective reporting bias	For details please see Supplement 1: methods and section 6.2 of <u>Developing NICE guidelines: the manual</u> . If sufficient relevant RCT evidence is available, publication bias will be explored using RevMan software to examine funnel plots. Trial registries will be examined to identify missing evidence: Clinical trials.gov, NIHR Clinical Trials Gateway.
Assessment of confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of <u>Developing NICE guidelines: the manual.</u>
Rationale/context – Current management	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and chaired by Kate Harding in line with section 3 of <a href="Developing NICE guidelines: the manual">Developing NICE guidelines: the manual</a> . Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see Supplement 1: methods.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England.
PROSPERO registration number	This protocol is not registered with PROSPERO.

AUC: area under the curve, CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; LBW: Low Birth Weight; NGA: National Guideline Alliance; NHS: National health service; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; SGA: small for gestational age

## **Appendix B – Literature search strategies**

Literature search strategies for review question: Is there an association between sleep position on going to sleep and stillbirth or having a small for gestational age baby?

Database(s): Medline & Embase (Multifile)

Last searched on Embase Classic+Embase 1947 to 2020 September 08, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to September 08, 2020

Date of last search: 9th September 2020

Multifile database codes: emczd = Embase Classic+Embase; ppez= MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily

of Print, In-Process & Other Non-Indexed Citations and Daily
Searches
Pregnancy/ use ppez
Pregnant Women/ use ppez
pregnancy/ use emczd
pregnant woman/ use emczd
pregnan\$.tw,kw.
1 or 2 or 3 or 4 or 5
Sleep/ use ppez
sleep/ use emczd
sleep pattern/ use emczd
Sleep Apnea Syndromes/ use ppez
sleep disordered breathing/ use emczd
(sleep\$ adj5 position\$).tw,kw.
(sleep\$ adj3 (pattern\$ or practice\$ or duration or quality or quantity or deprivation\$ or disruption\$ or disturb\$)).tw,kw.
(sleep\$ adj (apnea\$ or apnoea\$)).tw,kw.
(pillow\$ and sleep\$).tw,kw.
7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
maternal sleep/ use emczd
(matern\$ adj sleep\$).tw,kw.
6 and 16
17 or 18 or 19
(controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or drug therapy.fs. or (groups or
placebo or randomi#ed or randomly or trial).ab.
crossover procedure/ or double blind procedure/ or randomized controlled trial/ or single blind procedure/ or (assign* or allocat* or crossover* or cross over* or ((doubl* or singl*) adj blind*) or factorial* or placebo* or random* or volunteer*).ti,ab.
meta-analysis/
meta-analysis as topic/
systematic review/
meta-analysis/
(meta analy* or metanaly* or metaanaly*).ti,ab.
((systematic or evidence) adj2 (review* or overview*)).ti,ab.
((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
(search strategy or search criteria or systematic search or study selection or data extraction).ab.
(search* adj4 literature).ab.
(medline or pubmed or cochrane or embase or psychlit or psychinfo or psycinfo or cinahl or science citation
index or bids or cancerlit).ab.
cochrane.jw.
((pool* or combined) adj2 (data or trials or studies or results)).ab.
letter/
editorial/
news/
exp historical article/
Anecdotes as Topic/
comment/
case report/
(letter or comment*).ti.

#	Searches
44	36 or 37 or 38 or 39 or 40 or 41 or 42 or 43
45	randomized controlled trial/ or random*.ti,ab.
46	44 not 45
47	animals/ not humans/
48	exp Animals, Laboratory/
49	exp Animal Experimentation/
50	exp Models, Animal/
51	exp Rodentia/
52	(rat or rats or mouse or mice).ti.
53	46 or 47 or 48 or 49 or 50 or 51 or 52
54	letter.pt. or letter/
55	note.pt.
56	editorial.pt.
57	case report/ or case study/
58	(letter or comment*).ti.
59	54 or 55 or 56 or 57 or 58
60	randomized controlled trial/ or random*.ti,ab.
61	59 not 60
62	animal/ not human/
63	nonhuman/
64	exp Animal Experiment/
65	exp Experimental Animal/
66	animal model/
67	exp Rodent/
68	(rat or rats or mouse or mice).ti.
69	61 or 62 or 63 or 64 or 65 or 66 or 67 or 68
70	53 use ppez
71	69 use emczd
72	70 or 71
73	21 use ppez
74	22 use emczd
75	73 or 74
76	(or/23-24,27,29-34) use ppez
77	(or/25-28,30-35) use emczd
78	76 or 77
79	20 and 72
80	20 not 79
81	limit 80 to english language
82	75 or 78
83	81 and 82
84	predict.ti.
85	(validat* or rule*).ti,ab.
86	(predict* and (outcome* or risk* or model*)).ti,ab.
	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or
87	identif* or prognos*)).ti,ab.
88	Logistic models/ use ppez
89	Statistical model/ use emczd
90	decision*.ti,ab.
91	88 or 89
92	90 and 91
93	(decision* and (model* or clinical*)).ti,ab.
94	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
95	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
96	ROC curve/ use ppez
97	Receiver operating characteristic/ use emczd
98	84 or 85 or 86 or 87 or 92 or 93 or 94 or 95 or 96 or 97
99	81 and 98
100	83 or 99

#### **Database(s): Cochrane Library**

Last searched on **Cochrane Database of Systematic Reviews**, Issue 9 of 12, September 2020, **Cochrane Central Register of Controlled Trials**, Issue 9 of 12, September 2020 Date of last search: 9<sup>th</sup> September 2020

#	Searches
#1	MeSH descriptor: [Pregnancy] this term only
#2	MeSH descriptor: [Pregnant Women] this term only
#3	(pregnan*):ti,ab,kw
#4	#1 or #2 or #3
#5	MeSH descriptor: [Sleep] this term only
#6	MeSH descriptor: [Sleep Apnea Syndromes] this term only
#7	((sleep* NEAR/5 position*)):ti,ab,kw
#8	((sleep* NEAR/3 (pattern* or practice* or duration or quality or quantity or deprivation* or disruption* or disturb*))):ti,ab,kw
#9	((sleep* NEXT (apnea* or apnoea*))):ti,ab,kw
#10	((pillow* and sleep*)):ti,ab,kw
#11	#5 or #6 or #7 or #8 or #9 or #10
#12	#4 AND #11
#13	((matern* NEXT sleep*)):ti,ab,kw
#14	#12 OR #13

# Database(s): CRD: Database of Abstracts of Reviews of Effects (DARE), HTA Database Date of last search: 9<sup>th</sup> September 2020

Date of	lact deal on: 0 Coptombol 2020
#	Searches
1	MeSH DESCRIPTOR Pregnancy EXPLODE ALL TREES IN DARE,HTA
2	MeSH DESCRIPTOR Pregnant Women EXPLODE ALL TREES IN DARE, HTA
3	(pregnan*) IN DARE, HTA
4	#1 OR #2 OR #3
5	MeSH DESCRIPTOR Sleep EXPLODE ALL TREES IN DARE, HTA
6	MeSH DESCRIPTOR Sleep Apnea Syndromes EXPLODE ALL TREES IN DARE, HTA
7	(((sleep* NEAR position*))) IN DARE, HTA
8	(((sleep* NEAR (pattern* or practice* or duration or quality or quantity or deprivation* or disruption* or disturb*)))) IN DARE, HTA
9	(((sleep* NEAR (apnea* or apnoea*)))) IN DARE, HTA
10	(((pillow* and sleep*))) IN DARE, HTA
11	#5 OR #6 OR #7 OR #8 OR #9 OR #10
12	#4 AND #11
13	(((matern* NEXT sleep*))) IN DARE, HTA
14	#12 OR #13

#### Database(s): Cinahl Plus

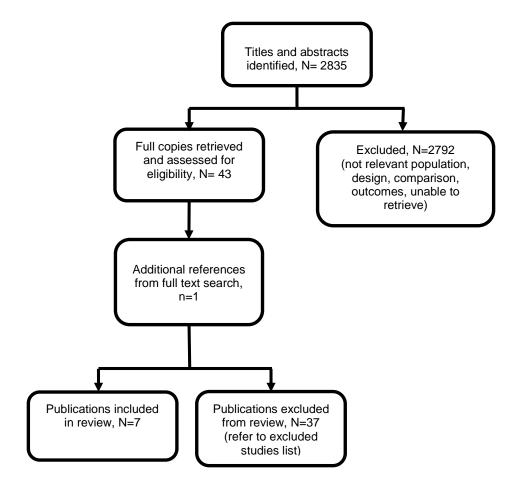
Date of last search: 9<sup>th</sup> September 2020

#	Searches
S16	S14 NOT S15 Limiters - English Language
S15	PT anecdote or PT audiovisual or PT bibliography or PT biography or PT book or PT book review or PT brief item or PT cartoon or PT commentary or PT computer program or PT editorial or PT games or PT glossary or PT historical material or PT interview or PT letter or PT listservs or PT masters thesis or PT obituary or PT pamphlet or PT pamphlet chapter or PT pictorial or PT poetry or PT proceedings or PT "questions and answers" or PT response or PT software or PT teaching materials or PT website
S14	S12 OR S13
S13	TI (matern* N1 sleep*) OR AB (matern* N1 sleep*)
S12	S4 AND S11
S11	S5 OR S6 OR S7 OR S8 OR S9 OR S10
S10	TI (pillow* and sleep*) OR AB (pillow* and sleep*)
S9	TI (sleep* N1 (apnea* or apnoea*)) OR AB (sleep* N1 (apnea* or apnoea*))
S8	TI (sleep* N3 (pattern* or practice* or duration or quality or quantity or deprivation* or disruption* or disturb*)) OR AB (sleep* N3 (pattern* or practice* or duration or quality or quantity or deprivation* or disruption* or disturb*))
S7	TI (sleep* N5 position*) OR AB (sleep* N5 position*)
S6	(MH "Sleep Apnea Syndromes")
S5	(MH "Sleep")
S4	S1 OR S2 OR S3
S3	TI pregnan* or AB pregnan*
S2	(MH "Expectant Mothers")
S1	(MH "Pregnancy")

# Appendix C - Clinical evidence study selection

Clinical evidence study selection for review question: Is there an association between sleep position on going to sleep and still birth or having a small for gestational age baby?

Figure 1: PRISMA flow chart for review question:



# **Appendix D – Clinical evidence tables**

Clinical evidence tables for review question: Is there an association between sleep position on going to sleep and still birth or having a small for gestational age baby?

Table 5: Clinical evidence tables for IPD meta-analyses

Study details	Participants	Factors	Results	Comments
Full citation  Anderson NH, Gordon A, Li M, Cronin RS, Thompson JMD, Raynes-Greenow CH, Heazel AEP, Stacey T, Culling VM, Wilson J, Askie LM, Mitchell EA. McCowan LME  Ref Id  1121708  Country/ies where the study was carried out  NA  Study type  Systematic Review  Study dates  Searches to January 2018  Consecutive recruitment  No	4 eligible case control studies. Eligible participants comprised 1,760 women  Inclusion criteria  Control participants from 4 case control studies with gestational age at birth collected in weeks and days, gestation at study interview of 28 days and 0 days or more, gestation at birth less than or equal to 42 weeks and 6 weeks and data for usual going-to-sleep position up to 4 weeks before the interview.  Exclusion criteria  A further case-control study that was included in the CRIBBS IPD was excluded from the current analysis as this online survey collected gestational age in completed weeks only. Individual participants were also excluded if they had missing variables required for calculation of birth weight centiles  Statistical method	Adjusted for study site and maternal age, height, weight, parity, ethnicity, preexisting diabetes, preexisting hypertension, antepartum hemorrhage, gestational hypertensive disorder, gestational diabetes, cigarette smoking, and recreational drug use.	Adjusted odds ratio (95% CI), vs left, INTERGROWTH-21st, <10th centile Other – 1.14 (0.62, 2.09) Right – 1.05 (0.58, 1.90) Supine - 3.23 (1.37, 7.59)  Results also available for customised growth charts where supine is no longer statistically significantly associated with <10th centile (adjusted odds ratio 1.55 (0.72 to 3.35))  Sleep position defined as usual position over the previous week/2 weeks or month (whichever was longest and available from study).	ROBIS  No concerns over relevance  Study eligibility criteria: low concern  Identification and selection of studies: low concern  Data collection and study appraisal: low concern (although not all eligible studies were included this was due to a lack of data appropriate for IPD meta-analysis and researchers made reasonable efforts to contact authors)  Synthesis and findings: low concern (no formal efforts to consider between study variation or incorporate biases in primary studies but risk of bias assessment was done and as this was an IPD meta-analysis, between study heterogeneity was less relevant).  Overall: low risk of bias

Study details	Participants	Factors	Results	Comments
Funding Funding for this research was provided by a Trans-Tasman Research Funding Grant by Cure Kids and Red Nose Australia in 2016 (grant 6601).	Birth weight and birth weight centiles were compared by maternal going-to-sleep position and adjusted for infant gestational age at birth and at time of interview, infant sex, and maternal age, height, weight, parity, ethnicity, preexisting diabetes, preexisting hypertension, antepartum hemorrhage, gestational hypertensive disorder, gestational diabetes, cigarette smoking, and recreational drug use. To account for possible study differences, multivariable analyses were also adjusted for individual studies as a covariate. For continuous outcomes (birth weight and birth weight centiles), a generalized linear model was used with predicted adjusted means obtained using least-squares means. For binary outcomes (birth weight centile <10th, <50th, and >90th) logistic regression was used, stratified by study, and aORs and 95% confidence intervals were reported.  Demographics  Age years Supine: 29.6 (5.5) years; Nonsupine: 30.3 (5.5) years  Ethnicity: White: Supine 31 (2.8%); Nonsupine 1,074 (97.2%)  Black: Supine 35 (97.2%); Nonsupine 1 (2.8%)			
	South Asian: Supine 9 (4.3%); Nonsupine 202 (95.7%)			

Study details	Participants	Factors	Results	Comments
	South East/East Asian: Supine 5 (4.6); Nonsupine 104 (95.4)  Maori: Supine 2 (1.9); Nonsupine 104 (98.1)  Pacific: Supine 9 (5.9); Nonsupine 143 (94.1)  Others: Supine 0 (0%); Nonsupine 41 (100%)  Parity: 0: 19 (2.5%) supine; 749 (97.5%) nonsupine 1: 32 (5.0%) supine; 604 (95.0%) nonsupine ≥2: 6 (1.7%); 350 (98.3%)  Education: Primary and/or secondary school: 26 (4.5%) supine; 554 (95.5%) nonsupine Trade school: 6 (2.7%) 220 (97.3%) nonsupine Tertiary (university and postgraduate): 25 (2.6%); 929 (97.4%)  Earliest pregnancy BMI (kg/m²): 24.0 (21.0, 28.7) supine; 24.6 (22.0, 29.0) nonsupine			
Full citation  Cronin RS, Li M, Thompson JMD, Gordon A, Raynes- Greenow CH, Heazell AEP, Stacey T, Culling VM, Bowring V, Anderson NH, O'Brien LM,	6 eligible case control studies; 5 provided individual level data (note the study that did not provide data, Lakshmi 2017 – did not meet the NGA protocol criteria for inclusion). Eligible	Adjusted for:  • Maternal age  • Earliest pregnancy BMI  • Ethnicity	Going to sleep position (last recorded, within 2 weeks of estimated fetal death in cases) and the odds of late stillbirth	ROBIS No concerns over relevance

Study details	Participants	Factors	Results	Comments
Mitchell EA, Askie LM, McCowan LME. An Individual Participant Data Meta-analysis of Maternal Going-to-Sleep Position, Interactions with Fetal Vulnerability, and the Risk of Late Stillbirth. The Lancet 2019; 10:49-57.  Ref Id  1242569  Country/ies where the study was carried out  NA  Study type  Systematic Review  Study dates  Searches to January 2018  Consecutive recruitment  No	participants comprised in 851 cases and 2,257 controls  Inclusion criteria  Eligible participants (stillbirth cases and pregnant controls) were extracted from the identified studies that provided maternal going-to-sleep position and late stillbirth data.  Exclusion criteria  Participant level exclusion criteria (multiple pregnancy, major congenital abnormality, gestation <28 weeks' when going-to-sleep position data during pregnancy was collected, termination of pregnancy at ≥28 weeks', and receiving a study intervention that may have affected going-to-sleep position) were applied during the analysis.  Statistical method  Potential confounders were all prespecified (maternal age, earliest pregnancy body mass index (BMI	<ul> <li>Parity</li> <li>Education level</li> <li>Marital status</li> <li>Obesity</li> <li>Pre-existing hypertension or diabetes</li> <li>Smoking</li> <li>Recreational drug use</li> <li>Fetal movements</li> <li>Infant birthweight by customised centiles</li> <li>Small for gestational age infant (&lt;10<sup>th</sup> infant birthweight customised centile)</li> <li>Term (≥37 weeks) vs preterm (&lt;37 weeks) infant</li> <li>Three confounders (going-to-sleep duration, frequency of</li> </ul>	Reference group was left-side going-to-sleep position.  Adjusted OR (95% CI)  Supine: 2.63 (1.72, 4.04) Right side: 1.04 (0.83, 1.31) Prone: 0.63 (0.12, 3.25) Variable sides: 0.97 (0.70, 1.35) Propped up: 1.30 (0.68, 2.49) Don't remember: 2.26 (1.48, 3.46)	Study eligibility criteria: low concern  Identification and selection of studies: low concern  Data collection and study appraisal: low concern (although not all eligible studies were included this was due to a lack of data appropriate for IPD meta-analysis and researchers made reasonable efforts to contact authors)  Synthesis and findings: low concern (no formal efforts to consider between study variation or incorporate biases in primary studies but risk of bias assessment was done and as this was an IPD meta-analysis, between study heterogeneity was less relevant).  Overall: low risk of bias
Funding  Funding reported as funding for the individual studies included in the review from NHMRC Career Development Fellowship #1087062; NHMRC Early Career Fellowship #1089898; Cure Kid; American Sleep	kg/m2), ethnicity, parity, education level, marital status, pre-existing hypertension or diabetes, smoking, recreational drug use, going-to-sleep position, fetal movements, and infant birthweight by customised centiles).  A one-stage approach to IPD meta-analysis was used, so that the data from all the eligible studies were included in a single model. Logistic	overnight toilet use, and day-time napping) analysed in sensitivity models		

Study details	Participants	Factors	Results	Comments
Medicine Foundation and ResMed	regression models were used for the binary outcome. A fixed study effect and study site effect were included in the model specification as strata. Univariable analysis was performed to evaluate the association between going-to-sleep position and the odds of late stillbirth. During data acquisition, one prespecified confounder, alcohol intake during pregnancy, was found to be inconsistently collected across the studies and unable to be merged, and consequently omitted from the analysis. A multivariable model was developed incorporating prespecified confounders available in all the studies.  Three confounders (going-to-sleep duration, frequency of overnight toilet use, and day-time napping) were only available in some of the studies, and were therefore analysed in sensitivity models. A sensitivity analysis was also conducted after exclusion of controls who reported their pregnancy going-to-sleep position after they had given birth. The interaction between going-to-sleep position and prespecified factors			
	indicating a vulnerable pregnancy were assessed in bi-variable regression models. Estimates of risk of late stillbirth were reported as odds ratio (OR) with 95% confidence intervals.  For missing data in each individual			
	study, no imputation was undertaken. The population attributable risk (PAR) was calculated using the unadjusted OR for the primary outcome for supine going-to-sleep position and for other			

Study details	Participants	Factors	Results	Comments
	modifiable risk factors that were significant in multivariable analysis. Statistical analyses were performed using SAS, version 9.4 (SAS Institute Inc., Cary NC USA).			
	Demographics			
	Age years <20 yrs: 38 (4.5) cases; 78 (3.5) controls 20–29 yrs: 343 (40.3) cases; 905 (40.1) controls 30-39 yrs: 425 (49.9); 1190 (52.7) controls ≥40 yrs: 45 (5.3) cases; 84 (3.7) controls			
	Ethnicity: White: 522 (61.3) cases; 1545 (68.5) controls Black: 22 (2.6) cases; 42 (1.9) controls South Asian: 90 (10.6) cases; 219 (9.7) controls South East/East Asian: 40 (4.7) cases; 111 (4.9) controls Maori: 46 (5.4) cases; 107 (4.7) controls Pacific: 91 (10.7) cases; 154 (6.8) controls Others: 40 (4.7) cases; 79 (3.5) controls			
	Parity: Nulliparous: 446 (52.4) cases; 930 (41.2) controls 1-2: 292 (34.3) cases; 1110 (49.2) controls			

Study details	Participants	Factors	Results	Comments
	3-4: 87 (10.2) cases; 176 (7.8) controls ≥5: 26 (3.1) cases; 41 (1.8) controls			
	Education: Primary: 187 (22.0) cases; 348 (15.4) controls Secondary: 161 (18.9) cases; 343 (15.2) controls University: 328 (38.5) cases; 1069 (47.4) Postgraduate: 73 (8.6) cases; 240 (10.6) controls Non-University Trade: 93 (10.9) cases; 249 (11.0) controls Earliest pregnancy BMI (kg/m²): 26.0 (22.5, 31.4) cases; 24.8 (22.0, 29.3) controls			

 Table 6: Clinical evidence tables for primary studies

Study details	Participants	Factors	Results	Comments
Full citation	Cases	Factors	Adjusted odds ratio	Limitations
Heazell, A. E. P., Li, M., Budd, J., Thompson, J. M. D., Stacey, T., Cronin, R. S., Martin, B., Roberts, D., Mitchell, E. A., McCowan, L. M. E., Association between maternal sleep practices and late stillbirth - findings from a stillbirth case-control study, BJOG: An International Journal of Obstetrics and Gynaecology, 125, 254-262, 2018	N=291  Diagnostic criteria  ReCoDe classification system.  Controls  N=733  Inclusion criteria	Sleeping practices: Maternal going-to- sleep position in the last 4 weeks and on the night prior to stillbirth for cases and night before interview for controls (left side, supine, right side, tummy, variable side, propped up, or unknown); Duration of sleep;	Late stillbirth and supine going-to-sleep position on last night Data adjusted for: Last night going-to-sleep position, maternal age group, ethnicity, parity, level of education, BMI, birthweight centile, gestation, sleep duration, duration of daytime nap, study site. Reference group was left-side going-to-sleep position.	QUIPS tool - modified version Study population: High risk of bias (multicentre (41 maternity units); >50% for cases and controls did not participate, although authors reported that women in participation and non- participant groups had similar profiles of maternal age and ethnicity; sufficient information provided on flow of participants) Study attrition: Low risk of bias (>80% seen at assessment; reasons for non- completion provided)

#### Ref Id

936669

### Country/ies where the study was carried out

UK

#### Study type

Prospective population-based case-control study

#### Study dates

April 2014 to March 2016

#### Consecutive recruitment

Nο

#### **Funding**

Funded by Action Medical Research, Cure Kids, and Sands.

- Cases: Women who had a stillbirth after 28 weeks' gestation with no known congenital anomaly;
- Controls: Women with an ongoing pregnancy at the time of interview.

#### **Exclusion criteria**

- Women with multiple pregnancies;
- Controls: Women who subsequently delivered an infant with congenital abnormality or who had a stillborn baby;
- Maternal age <16 years;
- Women unable to provide consent.

#### Statistical method

#### Power analysis

To achieve 80% power and assuming 30% non-participation, 415 cases and 830 controls were required.

#### Statistical analyses

Differences between cases and controls for categorical data were analysed using chi-squared test. Continuous variables were compared using Wilcoxon ranksum tests as the data were not normally distributed. Univariable logistic regression was conducted to evaluate the association between sleep practices and risk of late stillbirth.

the toilet during the last night: Daytime napping in the last 4 weeks. Other factors: Small for gestational age (<10th centile): Smoking during pregnancy; Obesity; Overweight. Still birth - OR (95% On last night before stillbirth for cases or night before interview for controls, women with late stillbirth more Controls: 4 (0.5) likely to report sleeping in supine position on last night before stillbirth: 2.17 (1.15 to 4.08) Women with late stillbirth had increased 1.49) likelihood of not being Variable able to recall going-to- Cases: 32 (11.0) sleep position: 3.73 (1.67 to 8.32) Women with late stillbirth more likely to report right-side going- Cases: 15 (5.2) to-sleep position: 0.91 Controls: 11 (1.5) (0.65 to 1.26) SGA - OR (95% CI) 7.01 (33.6% to 56.8%) Sleep duration previous night (hours) - number (%) < 5.49

Cases: 129 (44.3)

Right Cases: 73 (25.1) Controls: 220 (30.0) Adjusted odds ratio (aOR)=0.67 (95% CI 0.44 to 1.02) Back Cases: 19 (6.5) Controls: 24 (3.3) aOR=2.31 (95% CI 1.04 to 5.11) Tummy Cases: 3 (1.0) aOR=1.01 (95% CI 0.13 to 7.81) Propped Cases: 9 (3.1) Controls: 15 (2.0) aOR=0.44 (95% CI 0.13 to Controls: 76 (10.4) aOR=0.93 (95% CI 0.51 to 1.69) Unknown aOR=3.33 (95% CI 1.13 to 9.84) c-statistic for final multivariable model 0.827 \*Reference

previous night (before

Cases: 140 (48.1)

Controls: 383 (53.3)

Left

stillbirth/interview) - number (%)

Number of times up to Maternal going-to-sleep position Prognostic factor measurement: Moderate risk of bias (prospective data collection; definition of risk factors provided; validated measurement tool used, but potential for recall bias; adequate proportion of study sample completed data for prognostic factors; no imputation performed for missing data) Outcome measurement: Low risk of bias (validated measurement tool administered by research midwives and same for all participants; questionnaires included maternal health so blinding not possible) Confounding measurement and account: Low risk of bias (cases and controls matched and adjustments made for confounding variables) Analysis and reporting: Low risk of bias (statistical model appropriate and results reported in final multivariable model with point estimates and measures of

#### Other information

variance)

Notes: 50 cases and 119 controls reported receiving advice about sleep; obtained from the internet, health professionals, literature, and friends and family.

A multivariable logistic model was developed to incorporate ethnicity and level of education, variables associated with increased risk of stillbirth based on previous literature (age, BMI, parity, smoking, small-for-gestational-age (SGA) status), other sleep related variables significant in univariable analysis, and variables used to select cases and controls (gestation and maternity unit).

Unconditional logistic regression was used to adjust for potential confounders. night - number (%) No imputation for missing data was undertaken. The c statistic was used to assess the area under the curve.

#### **Demographics**

Maternal age (years) - median (interquartile range; IQR)

Cases: 30.2 Controls:30.5

Ethnicity - number (%)

White

Cases: 234 (80.4) Controls: 594 (81.0)

Black

Cases: 12 (4.1) Controls: 29 (4.0) South Asian

Cases: 39 (13.4) Controls: 95 (13.0)

Others

Cases: 6 (2.1) Controls: 15 (2.0) Parity - number (%)

Cases: 167 (57.4) Controls: 296 (40.4)

1 to 2

Cases: 92 (31.6)

Controls: 227 (31.0)

5.5 to 8.49

Cases: 121 (41.6) Controls: 413 (56.3)

8.5 to 9.49 Cases: 20 (6.9)

Controls: 55 (7.5)

9.5+

Cases: 19 (6.5) Controls: 36 (4.9)

Number of times up to

the toilet previous

One or less

Cases: 91 (31.3) Controls: 120 (16.4)

Two or more

Cases: 199 (68.4)

Controls: 613 (83.6) Maternal daytime

naps in previous 4 weeks - number (%)

Never

Cases: 58 (19.9) Controls: 157 (21.4)

Occasionally Cases: 49 (16.8)

Controls: 153 (20.9)

1 to 2 per week Cases: 47 (16.1)

Controls: 180 (24.6)

3 to 4 per week

Cases: 44 (15.1) Controls: 110 (15.0)

5 to 6 per week Cases: 22 (7.6) Controls: 39 (5.3)

Everyday

Cases: 71 (24.4) Controls: 93 (12.7)

Unknown Cases: 0 (0.0)

	Controls: 386 (52.7)  3+ Cases: 32 (11.0) Controls: 51 (7.0) Level of Education - number (%) Graduate Education Cases: 99 (34.0) Controls: 326 (31.84) Further Education Cases: 112 (38.5) Controls: 278 (27.15) Secondary education to 16 years Cases: 56 (19.2) Controls: 100 (9.77) No formal educational qualification Cases: 23 (7.9) Controls: 29 (2.83) Body mass index - mean (IQR) Cases: 26.91 (15.44 to 47.87) Controls: 26.02 (15.41 to 48.59) Gestational age (for cases, gestational age at diagnosis of stillbirth; for controls at time of interview) - median (IQR) Cases: 37 weeks 4 days (33 weeks 4 days to 39 weeks 5 days) Controls: 36 weeks 3 days (32 weeks 6 days to 38 weeks 5 days)	Controls: 1 (0.1)		
Full citation  Stacey, T., Thompson, J. M. D., Mitchell, E. A., Ekeroma, A. J., Zuccollo, J. M., McCowan, L. M. E., Association between maternal sleep practices and risk of late stillbirth: A case- control study, Bmj, 342 (7811) (no pagination), 2011		Factors  Sleeping practices: Maternal sleep position at the time of going to sleep and on waking (left side, right side, back, and other (front, sitting up, both sides, and unsure or don't remember)) in the last month, week,	Adjusted odds ratio  Maternal sleeping position in last night of pregnancy and risk of late stillbirth Results adjusted for age, ethnicity, overweight or obesity, parity, social deprivation level, smoking, regular sleep in daytime in last month of pregnancy; hours of night time sleep in last month of	Limitations  QUIPS tool - modified version  Study population: Moderate risk of bias (multicentre (all maternity units in Auckland region); recruitment rate 72% for cases and controls and although no significant differences in age, parity, or ethnicity between those who did and did not consent, there was potential for selection bias; sufficient information provided on flow of participants)

#### Ref Id

936670

#### Country/ies where the study was carried out

New Zealand

#### Study type

Prospective population-based case-control study

#### Study dates

July 2006 to June 2009

#### Consecutive recruitment

Nο

### **Funding**

Cure Kids, the Nurture Foundation, and the Auckland District Health Board Trust Fund.

#### Inclusion criteria

- Women who gave birth to stillborn baby at or after 28 weeks of gestation in the Auckland region:
- Controls were selected from the pregnancy registration list of the district health board, matched for gestation to cases.

#### **Exclusion criteria**

- Women whose baby died from a congenital abnormality;
- Multiple pregnancies;
- Women who had not been booked to deliver their baby within the Auckland region.

#### Statistical method

#### Power analysis

The authors reported that the study was powered to detect an odds ratio of 2 with sleep; left on waking 80% power and significance level of 5%, up with a prevalence of the risk factor of ≥20% in the control population.

Student's t-test, and the Pearson correlation coefficient was used to assess the correlation between variables.

A multivariable regression model was used to include maternal variables risk of stillbirth, based on previous

and night of pregnancy; Sleeping regularly during the daytime in the last month: Usual duration of sleep at night during the last month: Frequency of aetting up to the toilet. Changes in sleeping position on last night of pregnancy and risk of late stillbirth number (%) Left on going to sleep; left on waking up Cases: 29 (19) Controls: 95 (31) Univariable OR (95% CI): 1.00 Left on going to sleep: other on waking up Cases: 13 (8) Controls: 37 (12) Univariable OR (95% CI): 1.15 (0.54 to 2.45) Other on going to Cases: 2 (1) Controls: 11 (4)

Univariable OR (95%

Other on going to

Cases: 111 (72)

CI): 0.60 (0.13 to 2.84)

sleep; other on waking

pregnancy; number of times up to the toilet during last night of pregnancy. Left side sleeping position used as reference group, OR=1.00 Right side adjusted odds ratio (aOR)=1.74 (95% CI 0.98 to 3.01)\*\*\* Back (supine) aOR=2.54 (95% CI 1.04 to 6.18);p=0.005Other aOR=2.32 (95% CI 1.28 to

4.19)

Study attrition: Low risk of bias (>80% seen at assessment; authors reported that there was no missing data for variables included in the paper) Prognostic factor measurement: Moderate risk of bias (prospective data collection; definition of risk factors provided; validated measurement tool used, but potential for recall bias due to length of time between stillbirth and interview, 25 days on average, compared with controls who were asked about sleep practices on the previous night; adequate proportion of study sample completed data for prognostic factors; no missing data) Outcome measurement: Low risk of bias (cases selected from clinicians in participating centres and hospital birth records, with confirmation through use of New Zealand national registry; controls selected from pregnancy registration list of district health board of participating centre). The authors stated that it was not always possible to be certain as to the exact timing of fetal death, and in some cases the 'last night' was not the final night before fetal death or during which the baby died. Confounding measurement and account: Low risk of bias (cases and controls matched and adjustments made for confounding variables) Analysis and reporting: Low risk of bias (statistical model appropriate and results reported in final multivariable model with point estimates and measures of variance)

#### Other information

Auckland Stillbirth Study

## Statistical analyses

Continuous data were compared using

Controls: 167 (54) Univariable OR (95% reported to be associated with increased CI): 2.28 (1.35 to 3.52) literature (age, BMI, ethnicity, parity, smoking, and socioeconomic status). Chi-squared statistics were used to assess the significance of variables in the models, and individual level odds ratios were estimated for each category and compared to a reference category.

#### **Demographics**

Maternal age (years) - number (%)

<20

Cases: 10 (6) Controls: 24 (8) 20 to 34 Cases: 113 (73) Controls: 216 (70)

≥35

Cases: 32 (21) Controls: 70 (23) Ethnicity - number (%)

<u>Maori</u>

Cases: 19 (12) Controls: 46 (15)

Pacific Cases:

Cases: 48 (31) Controls: 67 (22) <u>European</u> Cases: 55 (35)

Cases: 55 (35) Controls: 139 (45)

<u>Other</u>

Cases: 33 (21) Controls: 58 (19) Parity - number (%)

0

Cases: 77 (50) Controls: 144 (46)

1 to 3

Cases: 62 (40) Controls: 156 (51)

≥4

Cases: 16 (10)

Regular sleep in daytime (last month of pregnancy - number

<u>(%)</u> Yes

> Cases: 78 (50) Controls: 116 (37)

No

Cases: 77 (50)
Controls: 194 (63)
Hours of nighttime
sleep (last month of
pregnancy) - number

<u>(%)</u> <6

> Cases: 30 (19) Controls: 46 (15)

6 to 8

Cases: 82 (53) Controls: 205 (66)

<u>>8</u>

Cases: 43 (28)
Controls: 59 (19)
Number of times
getting up to toilet
during night last night
of pregnancy- number

<u>(%)</u> >1

Cases: 86 (55) Controls: 207 (67)

<u>≤1</u>

Cases: 69 (45) Controls: 103 (33)

	Controls: 10 (3)  Social deprivation level - number (%)  1 to 4  Cases: 91 (59)  Controls: 218 (70)  5 (most deprived)  Cases: 64 (41)  Controls: 92 (30)  BMI at booking - number (%)  <25  Cases: 55 (35)  Controls: 156 (50)  25 to 29.9  Cases: 39 (25)  Controls: 67 (22)  ≥30  Cases: 61 (39)  Controls: 87 (28)  Smoking during pregnancy - number (%)  Cases: 46 (30)  Controls: 66 (21)			
Full citation	Cases	Factors	Adjusted odds ratio	Limitations
McCowan, L. M. E., Thompson, J. M. D., Cronin, R. S., Li, M.,	N=164	Maternal sleeping practices:	Results adjusted for gestation at interview in controls and at	QUIPS tool - modified version Study population: High risk of bias
Stacey, T., Stone, P. R.,	Diagnostic criteria	Self-reported going-to-	diagnosis of stillbirth for cases,	(multicentre (all maternity units across 7
Lawton, B. A., Ekeroma, A. J., Mitchell, E. A., Going to sleep in	PSANZ classification system	sleep position on last night (left side, right	district health board, maternal age, ethnicity, parity, social	New Zealand health regions); rate of recruitment 65.9% for cases and 62.2%
the supine position is a modifiable risk factor for late	Controls	side, restless, supine (lying on the back), on	deprivation level, earliest pregnancy BMI, marital status,	for controls, further information on flow of participants not provided; women of high
pregnancy stillbirth; Findings		the front, or propped);	smoking in pregnancy, baby	parity were underrepresented in both
from the New Zealand multicentre stillbirth case-control	N=569	Self-reported usual	birthweight centile, hours of night time sleep on the last	groups, while Indian women were over- represented and Maori women under-
study, Plos one, 12 (6) (no	Inclusion criteria	in last week (left side,	night, getting up to toilet during	represented in cases compared with
pagination), 2017	Cases: consenting women with	right side, variable side, supine (lying on	the last night, sleep during the daytime in the last week, going	eligible controls) Study attrition: Low risk of bias (>80%
Ref Id	a stillbirth at ≥28 weeks of	the back), on the front	to sleep position on last night	seen at assessment; no imputation
929927	gestation;	or propped;	and in the last week).	performed for missing data) Prognostic factor measurement: Moderate risk of bias

#### Country/ies where the study was carried out

New Zealand

#### Study type

Prospective population-based case-control study

#### Study dates

February 2012 to December 2015

#### Consecutive recruitment

No

### **Funding**

Health Research Council of New Zealand, Cure Kids, Mercia Barnes Trust, Nurture Foundation, and the University of Auckland Faculty Research Development Fund.

Controls: women with ongoing pregnancies in each participating health region.

#### **Exclusion criteria**

- Women with multiple pregnancies:
- Babies with major congenital abnormalities at any stage of the study.

#### Statistical method

#### Power analysis

To achieve 80% power and based on 70% participation, 415 cases and 830 controls were required for recruitment. Statistical analyses

Chi-squared tests were used to compare differences between categorical data. Continuous data were compared using Wilcoxon rank-sum tests. Univariable analysis was conducted to assess the association between sleep practices and risk of late stillbirth.

A multivariable model was used to incorporate ethnicity and deprivation index, variables associated with increased risk of stillbirth based on previous literature (age, BMI, parity, smoking, SGA status), other sleep variables significant in univariable analysis, and variables used to select cases and controls (gestation and District Health Boards). Unconditional logistic regression was used to adjust for potential confounders. No imputation was performed for missing

toilet during the night on the last night: on last night; Frequency of sleeping during the daytime in the last week. Going to sleep position on the last night - number (%)# Left side Cases: 78 (47.6) Controls: 328 (57.6) Adjusted OR (95% CI): 1.00 Right side Cases: 44 (26.8) Controls: 187 (32.9) Adjusted OR (95% Restless Cases: 14 (8.5) Controls: 22 (3.9) Adjusted OR (95% Supine Cases: 19 (11.6) Controls: 22 (3.9) Adjusted OR (95%

Propped Cases: 4 (2.4) Controls: 9 (1.6) Adjusted OR (95% Going to sleep position on the last week - number (%)## Left side Cases: 85 (51.8)

Getting up to go to the Going-to-sleep position on last night and pre-term stillbirth (≥28 to 36 weeks' gestation) How many hours slept Note: One pre-term case and one pre-term control had an unknown sleep position on the last night and was excluded from the multivariable model. Left side (reference group) Cases, n (%): 34 (50.0) Controls, n (%): 147 (58.3) Odds ratio: 1.00 Right side Cases: 22 (32.4) Controls: 86 (34.1) Adjusted odds ratio (aOR)=0.96 (95% CI 0.48 to 1.94) Restless Cases: 4 (5.9) Controls: 4 (1.6) CI): 0.92 (0.58 to 1.44) aOR=3.50 (95% CI 0.61 to 19.97) Back (Supine) Cases: 6 (8.8) Controls: 13 (5.2) CI): 1.98 (0.87 to 4.50) aOR=3.12 (95% CI 0.97 to 10.05) Propped Cases: 1 (1.5) Controls: 1 (0.4) CI): 3.67 (1.74 to 7.78) aOR=4.37 (95% CI 0.11 to

178.86) Going-to-sleep position on last week and pre-term stillbirth (≥28 to 36 weeks' gestation) CI): 1.11 (0.30 to 4.06) Note: One pre-term control did not recall their sleep position in last week and was excluded from the multivariable model. Left side (reference group) Cases. n (%): 38 (55.9) Controls. n (%): 137 (54.4)

(prospective data collection; definition of risk factors provided; validated measurement tool used, but potential for recall bias due to length of time between stillbirth and interview, 24 days on average; adequate proportion of study sample completed data for prognostic factors) Outcome measurement: Low risk of bias

(clear definition of outcome provided. validated measurement tool administered by research midwives, setting and measurement similar for all participants; authors state that possible in some cases 'last night' was not the night before fetal death, or the night during which the baby died.) Confounding measurement and account: Low risk of bias (cases and controls matched and adjustments made for confounding variables) Analysis and reporting: Low risk of bias (statistical model appropriate and results reported in final multivariable model with point estimates and measures of variance)

#### Other information

OR: 1.00 data (women who could not recall their Controls: 302 (53.1) going-to-sleep position on the last night Adjusted OR (95% Right side were excluded from the multivariable CI): -Cases: 19 (27.9) model). Right side Controls: 75 (29.8) Stratified analysis was carried out by Cases: 42 (25.6) aOR=0.73 (95% CI 0.34 to term (≥37 weeks') and pre-term (≥28 to Controls: 171 (30.1) 1.54) 36 weeks') gestation. The c statistic was Adjusted OR (95% Variable side calculated to assess model performance. CI): 0.82 (0.52 to 1.30) Cases: 4 (5.9) Variable side Controls: 27 (10.7) Cases: 15 (9.2) aOR=0.63 (95% CI 0.18 to **Demographics** Controls: 72 (12.7) 2.19) Adjusted OR (95% Supine Maternal age (years) - number (%) CI): 0.85 (0.44 to 1.65) Cases: 5 (7.4) Controls: 11 (4.4) Supine Cases: 9 (5.5) Cases: 15 (9.2) aOR=2.25 (95% CI 0.65 to Controls: 17 (3.0) Controls: 72 (12.7) 7.84)20 to 39 Adjusted OR (95% Propped Cases: 141 (86.0) CI): 3.46 (1.49 to 8.03) Cases: 1 (1.5) Controls: 532 (93.5) Controls: 1 (0.4) **Propped** ≥40 aOR=4.01 (95% CI 0.08 to Cases: 5 (3.1) Cases: 14 (8.5) Controls: 7 (1.2) 210.43) Controls: 20 (3.5) Adjusted OR (95% On front Ethnicity - number (%) CI): 2.10 (0.57 to 7.71) Cases: 1 (1.5) Maori On front Controls: 0 Cases: 26 (16.0) Cases: 1 (0.6) Going-to-sleep position on last Controls: 58 (10.0) night and term stillbirth (≥37 Controls: 0 Pacific weeks' gestation) Cases: 38 (23.2) Note: Four term cases had an Controls: 86 (15.1) unknown sleep position on the Indian last night and was excluded Cases: 17 (10.4) from the multivariable model. Controls: 77 (13.5) Left side Other Asian Cases, n (%): 44 (45.8) Cases: 13 (7.9) Controls, n (%): 181 (57.1) Controls: 72 (12.7) OR=1.00 European Right side Cases: 65 (39.6) Cases: 22 (22.9) Controls: 263 (46.2) Controls: 101 (31.9) <u>Other</u> aOR=0.98 (95% CI 0.48 to Cases: 5 (3.1) 1.99) Controls: 13 (2.3) Restless Parity - number (%) Cases: 10 (10.4)

Cases: 76 (46.3) Controls: 18 (5.7) Controls: 245 (43.1) aOR=2.00 (95% CI 0.64 to 1 to 3 6.21) Back (Supine) Cases: 80 (48.8) Controls: 308 (54.1) Cases: 13 (13.5) Controls: 9 (2.8) <u>≥4</u> Cases: 8 (4.9) aOR=10.26 (95% CI 3.01 to Controls: 16 (2.8) 35.04) **Propped** Cases: 3 (3.1) Controls: 8 (2.5) aOR=1.02 (95% CI 0.17 to 5.97) Going-to-sleep position on last week and term stillbirth (≥37 weeks' gestation) Note: One term case did not recall sleep position in the last week and was excluded from the multivariable model. Left side (reference group) Cases, n (%): 47 (49.0) Controls, n (%): 165 (52.1) OR=1.00 Right side Cases: 23 (24.0) Controls: 96 (30.3) aOR=0.95 (95% CI 0.48 to 1.89) Variable side Cases: 11 (11.5) Controls: 45 (14.2) aOR=1.11 (95% CI 0.49 to 3.01) Back (Supine) Cases: 10 (10.4) Controls: 5 (1.6) aOR=12.73 (95% CI 2.92 to 55.46) Propped Cases: 4 (4.2) Controls: 6 (1.9)

			aOR=2.64 (95% CI 0.47 to 14.81) c statistic for final multivariable model 0.736 Non-left versus left positions in the multivariable model resulted in non-significant increase in late stillbirth risk compared with the combined non-left positions: 1.35 (0.92 to 1.99).	
Full citation	Cases	Factors	Adjusted odds ratio	Limitations
Gordon, A., Raynes-Greenow, C., Bond, D., Morris, J., Rawlinson, W., Jeffery, H., Sleep position, fetal growth restriction, and late-pregnancy stillbirth: The sydney stillbirth study, Obstetrics and Gynecology, 125, 347-355, 2015  Ref Id  938535  Country/ies where the study was carried out  Australia  Study type  Prospective population-based case-control study  Study dates	Diagnostic criteria  PSANZ classification system  Controls  N=192  Inclusion criteria   Cases: women with singleton pregnancies who experienced stillbirth at ≥32 weeks of gestation  Controls: pregnant women at 32 weeks of gestation with singleton pregnancies who were matched for booking hospital and gestation (by estimated date of delivery) and recruited during the same	Maternal sleeping practices: Sleep position: left; right; back; other. Suspected fetal growth restriction: <10th percentile; <3rd percentile. Other factors: Maternal age; Maternal BMI; Primiparous; Not in paid work; Sleep apnoea symptoms; Smoking; Education to high school or less. SGA and stillbirth - OR (95% CI) Fetuses who were stillborn were significantly more likely to be SGA using the 10th percentile: 3.8 (1.8 to 8.2) and	Stillbirth and supine sleep position in the last month Multivariate model adjusted for maternal age group; maternal BMI; primiparous; not in paid work; sleep apnoea symptoms; smoking; suspected fetal growth restriction; education to high school or less; sleep position (left, right, back, other).  Left-side going-to-sleep position is reference group.  Left side Cases: 32 (31) Controls: 48 (25) Odds ratio=1  Right side Cases: 14 (13.6) Controls: 25 (13)  Adjusted odds ratio (aOR)=1.1 (95% CI 0.43 to 2.6)  Back Cases: 10 (9.7) Controls: 4 (2.1) aOR=6.26 (95% CI 1.2 to 34) Other	Study attrition: Low risk of bias (>80% seen at assessment; reasons for non-participation reported)

January 2006 to December 2011  Consecutive recruitment  No  Funding  Stillbirth Foundation, Australia.	period of time as women in the case group.  Exclusion criteria  Women identified as Aboriginal or Torres Strait Islander; Fetuses that had known lethal or chromosomal anomalies; Terminations of pregnancy.	less than the third percentile: 3.6 (1.2 to 10.9).  Univariate analysis  Stillbirth and suspected fetal growth restriction - OR (95% CI)  8.3 (2.3 to 30)  Stillbirth and supine sleeping over the last month - OR (95% CI)  5.0 (1.5 to 16.5)	Cases: 47 (45.6) Controls: 115 (60) aOR=0.69 (95% CI 0.36 to 1.3)	Confounding measurement and account: Low risk of bias (cases and controls matched and adjustments made for confounding variables) Analysis and reporting: Moderate risk of bias (statistical model appropriate and results reported in final multivariable model with point estimates and measures of variance; however, study underpowered to assess interactions between risk factors)  Other information
	Statistical method			
	Power analysis To achieve 80% power, based on prevalence of 10% small for gestational age (SGA) to detect an odds ratio (OR) of 25 between cases and controls, approximately 100 women were required in the case group and 200 women in the controls group.  Statistical analyses Univariate analysis was conducted using chi-squared tests for categorical data and Student's t-test for continuous variables. Conditional logistic regression was used to calculate adjusted ORs for a priori-specified risk factors and to account for matching within stratification. Risk factors identified as significant on univariate analysis, or associated with stillbirth in previous literature (even if non-significant), were included in the multivariate models. However, if previously known risk factors were present in too few patients as to make no difference to the multivariable models			

were defined as the groups likely to have the lowest risk. **Demographics** Maternal age (years) - number (%) Cases: 73 (70.9) Controls: 121 (63) 35 to 39 Cases: 22 (21.4) Controls: 53 (27.6) ≥40 Cases: 8 (9.4) Controls: 18 (7.8) BMI (kg/m²) - number (%) <25 Cases: 62 (62.6) Controls: 129 (67.9) 25 to 29.9 Cases: 22 (22.2) Controls: 44 (23.2) ≥30 Cases: 15 (15.2) Controls: 17 (8.9) Primiparous - number (%) Cases: 53 (51.5) Controls: 104 (54.2) Not in paid work - number (%) Cases: 26 (25.2) Controls: 18 (9.4) Smoker - number (%) Cases: 14 (13.6) Controls: 25 (13) Education to high school or less number (%) Cases: 43 (41.7) Controls: 49 (25.5)

Jane, Stacey, Tomasina, Heazell, Alexader E. P., Mitchell, Edwin A., Maternal Reazell, Alexader E. P., Mitchell, Edwin A., Maternal sleep practices and sultibirith- for cases and last month and last night for controls. Where the study was carried out Study special control study in uncontrolled cohort Study type  1	Full citation	Cases	Factors	Adjusted odds ratio	Limitations
position on last night before stillbirth: 2.17  Statistical method  position on last night before stillbirth: 2.17  (1.15 to 4.08)  aOR=0.75 (95% CI 0.34 to 1.64)  Participants recruited using ano online survey 'Study of Trends a	O'Brien, Louise M., Warland, Jane, Stacey, Tomasina, Heazell, Alexander E. P., Mitchell, Edwin A., Maternal sleep practices and stillbirth: Findings from an international case-control study, BirthBirth, 0  Ref Id  967090  Country/ies where the study was carried out  Various (see other information)  Study type  Nested case-control study in uncontrolled cohort  Study dates  September 2012 to August 2014  Consecutive recruitment  No  Funding	N=153  Diagnostic criteria  Not reported  Controls  N=480  Inclusion criteria   Cases: Women who had a singleton stillborn baby ≥ 28 weeks gestation within 1 month of completing the survey;  Controls: Women with an ongoing pregnancy (≥ 28 weeks gestation) or had delivered a living baby within the month before survey completion  Exclusion criteria  Women with multiple pregnancies;  Women whose fetus with known congenital abnormality;  Maternal age <18 years;  Women unable to provide	Sleeping practices:  Maternal going-to- sleep position in the month and on the night prior to stillbirth for cases and last month and last night before their pregnancy for controls (left side, supine, right side, tummy, variable side, propped up); Duration of sleep; Number of times up to the toilet during the last night; Daytime napping in the last 4 weeks. Other factors: Small for gestational age (<10th centile); Smoking during pregnancy; Obesity; Overweight. Still birth - OR (95% CI) On last night before stillbirth for cases or night before interview for controls, women with late stillbirth more likely to report	Late stillbirth and supine going-to-sleep position on last night  Maternal going-to-sleep position previous night (before stillbirth/interview) - number (%)  Left-hand going-to-sleep position used as reference group.  Left Cases: 75 (49) Controls: 193 (40.2) Odds ratio=1  Right Cases: 45 (29.4) Controls: 111 (23.1) Adjusted odds ratio (aOR)=1.11 (95% CI 0.70 to 1.77)  Back (Supine) Cases: 4 (2.6) Controls: 11 (2.3) aOR=1.11 (95% CI 0.70 to 1.77)  Tummy Cases: 0 (0) Controls: 4 (0.8)  Propped Cases: 4 (2.6) Controls: 15 (3.1) aOR=0.71 (95% CI 0.22 to 2.30)  Variable Cases: 10 (6.5)	QUIPS tool - modified version Study population: High risk of bias (international retrospective online survey so potential for self-selection bias) Study attrition: Low risk of bias (<20% missing data; prior sample size calculation which was fulfilled) Prognostic factor measurement: Moderate risk of bias (retrospective data collection; definition of risk factors provided; validated measurement tool used, but potential for recall bias; adequate proportion of study sample completed data for prognostic factors; no imputation performed for missing data) Outcome measurement: Moderate risk of bias (all outcomes self-reported via online form so potential for false reporting) Confounding measurement and account: High risk of bias (cases and controls not matched - women in case group were more likely to be non-Caucasians and nullip; but adjustments made for confounding variables) Analysis and reporting: Low risk of bias (statistical model appropriate and results reported in final multivariable model with point estimates and measures of variance)
Statistical method (1.15 to 4.08) online survey 'Study of Trends a	•	<ul><li>Maternal age &lt;18 years;</li><li>Women unable to provide</li></ul>	with late stillbirth more likely to report sleeping in supine position on last night	Variable Cases: 10 (6.5) Controls: 39 (8.1) aOR=0.75 (95% CI 0.34 to	Other information
Power analysisstillbirth had increased likelihood of not beingwhich was developed during first Stillbirth Summit in Minnear			before stillbirth: 2.17 (1.15 to 4.08) Women with late stillbirth had increased likelihood of not being		Participants recruited using anonymous online survey 'Study of Trends and Risk Factors for Stillbirth' (STARS), which was developed during first Stillbirth Summit in Minneapolis in 2011 by international consortium of

Sample size was calculated based on the anticipated exposure of supine sleep. (1.67 to 8.32) To achieve 80% power and assuming an Women with late exposure frequency of 20%, 144 cases and controls were required to detect the report right-side goingodds of stillbirth 3.0 among cases compared to controls.

#### Statistical analyses

Data were cleaned by two authors. Data 7.01 (33.6% to 56.8%) analyses were performed using SPSS using cross-tabulations, chi-squared tests and logistic regressions to find unadjusted and adjusted odds ratio with 95% confidence interval. Univariable logistic regression was conducted to evaluate the association between sleep practices and risk of late stillbirth. A multivariable logistic model was developed to incorporate maternal age, education level, smoking, body mass index, parity, country of respondant, ethnicity.

### **Demographics**

Maternal age (years) - mean±standard

deviation Cases: 31 ± 5.4 Controls:30±4.8 Ethnicity - number (%)

Caucasian

Cases: 122 (79.7)\* Controls: 430 (90.2) Non-Caucasian Cases: 31 (20.3) Controls: 47 (9.8)

Parity - median (interquartile range)

Cases: 1(0-6) Controls: 1(0-10)\*

Level of Education - number (%)

**Graduate Education** 

sleep position: 3.73 stillbirth more likely to to-sleep position: 0.91 (0.65 to 1.26) SGA - OR (95% CI) Sleep duration last

month (hours) number (%)

</=6

Cases: 15 (9.8) Controls: 47 (9.8) 6.5 to 8.5

Cases: 86 (56.2) Controls: 283 (59)

9.0+

Cases: 45(29.4) Controls: 79 (16.5)

Number of times getting up

previous month number (%)

One or less Cases: 47 (30.7) Controls: 129 (26.9)

Two or more Cases: 98(64.1) Controls: 270 (56.3)

Maternal daytime naps in previous 4 weeks - number (%)

Never

Cases: 38 (24.8) Controls: 125 (26) Occasionally

Cases: 41 (26.8) Controls: 108 (22.5) Often/almost always

Cases: 67 (43.8)

clinicians and academics, Star Legacy Foundation and other stillbirth/parental support groups. International online survey included respondents from following countries: Australia (n=21), Bahrain (n=1), Canada (n=44), Finland (n=1), Germany (n=2), Greece (n=2), India (n=2), Israel (n=1), Italy (n=1), New Zealand (n=2), Philippines (n=2), South Africa (n=2), Sweden (n=1), Switzerland (n=1), UK (n=95), USA (n=448).

Cases: 35 (22.9) Controls: 168 (35) Controls: 129 (26.9) Excessive daytime College-level Education sleepiness last month Cases: 81 (52.9) Cases: 42 (27.5) Controls: 242 (50.4) Controls: 107 (22.3) High school or lower Cases: 37 (24.2) Controls: 106 (22.1) Body mass index - median (IQR) Cases: 27 (23-32) Controls: 25 (23-31) Gestational age (for cases, gestational age at diagnosis of stillbirth; for controls at time of interview) - median (IQR) Cases: 37 weeks (34 - 39) Controls: 37 (32 - 39)

Abbreviations: aOR: adjusted odds ratio; BMI: body mass index; CI: confidence interval; IPD MA: individual patient data meta-analysis; IQR: interquartile range; N: total number of participants in the study or case or control; OR: odds ratio; SGA: small for gestational age; vs: versus;

## **Appendix E – Forest plots**

Forest plots for review question: Is there an association between sleep position on going to sleep and still birth or having a small for gestational age baby?

No meta-analyses were performed and therefore no forest plots are presented.

## **Appendix F – GRADE tables**

GRADE tables for review question: Is there an association between sleep position on going to sleep and still birth or having a small for gestational age baby? – evidence from IPD meta-analysis

Table 7: GRADE table for independent association between going-to-sleep position and stillbirth in comparison to left lateral going-to-sleep position – evidence from IPD meta-analysis

to-sleep position – evidence from	•
Phase of investigation	No restrictions were placed on phase of investigation. Given the relatively low frequency of stillbirth, a phase 3 prospective cohort study that aims to examine the role of sleep position and its effect on still birth is not feasible. Therefore no restrictions were placed on the phase of investigation.
	One IPD meta-analysis, including data from 5 case control studies <sup>a</sup> , was included and the quality of evidence was thus initially rated as high.
Results	Adjusted odds ratio (95% CI), vs left sleeping position for stillbirth:
	<b>Supine</b> : 2.63 (1.72, 4.04)
	<b>Right side</b> : 1.04 (0.83, 1.31)
	<b>Prone</b> : 0.63 (0.12, 3.25)
	Variable sides: 0.97 (0.70, 1.35)
	<b>Propped up</b> : 1.30 (0.68, 2.49)
	<b>Don't remember</b> : 2.26 (1.48, 3.46)
Study limitations	The IPD meta-analysis was rated at low risk of bias.
Inconsistency	There was no formal assessment of inconsistency within the IPD meta-analysis however the results of the IPD meta-analysis were broadly consistent with the findings of the primary studies reported in the tables below. Therefore the evidence was not downgraded for inconsistency.
Indirectness	No serious indirectness in the majority of the evidence contributing to the IPD meta-analysis.
Imprecision	Supine: no serious imprecision
	Right side: serious imprecision (confidence intervals crossed the line of no effect)
	<b>Prone:</b> very serious imprecision (confidence intervals crossed the line of no effect and subjectively were considered very wide)

	Variable sides: very serious imprecision (confidence intervals crossed the line of no effect and subjectively were considered very wide)  Propped up: very serious imprecision (confidence intervals crossed the line of no effect and subjectively were considered very wide)  Don't remember: no serious imprecision
Publication bias	The evidence was downgraded for publication bias as it came from a relatively small number of primary studies, some of which were in an early phase of investigation.
Moderate/large effect size	The evidence was upgraded if moderate (aOR > 2.5 or aOR <0.25) or large effect (aOR > 4.25 or aOR < 0.4) sizes were estimated. This applied to the supine position outcome.
Overall quality	<ul> <li>Supine: HIGH</li> <li>Right side: LOW</li> <li>Prone: VERY LOW</li> <li>Variable sides: VERY LOW</li> <li>Propped up: VERY LOW</li> <li>Don't remember: MODERATE</li> </ul>

Notes: a Cronin 2019. Abbreviations: a OR, adjusted odds ratio; CI, confidence interval.

Table 8: GRADE table for independent association between going-to-sleep position and SGA in comparison to left lateral going-to-sleep position on last night – evidence from IPD meta-analysis

delice from it b meta-analysis
No restrictions were placed on phase of investigation. Given the relatively low frequency of stillbirth, a phase 3 prospective cohort study that aims to examine the role of sleep position and its effect on still birth is not feasible. Therefore no restrictions were placed on the phase of investigation.
One IPD meta-analysis, including data from 4 case control studies <sup>a</sup> , was included and the quality of evidence was thus initially rated as high.
Adjusted odds ratio (95% CI), vs left sleeping position for SGA as defined INTERGROWTH-21st 10th centile:
Supine: 3.23 (1.37, 7.59)
Right side: 1.05 (0.58, 1.90)
Other: 1.14 (0.62, 2.09)

	Results also available for customised growth charts where supine is no longer statistically significantly associated with <10th centile (adjusted odds ratio 1.55 (0.72 to 3.35)).
Study limitations	The IPD meta-analysis was rated at low risk of bias.
Inconsistency	There was no formal assessment of inconsistency within the IPD meta-analysis however the results of the IPD meta-analysis were broadly consistent with the findings of the primary studies reported in the tables below (assuming factors leading to stillbirth and SGA are likely to be similar). Therefore the evidence was not downgraded for inconsistency.
Indirectness	No serious indirectness in the majority of the evidence contributing to the IPD meta-analysis.
Imprecision	Supine: no serious imprecision
	Right side: very serious imprecision (confidence intervals crossed 0.8 and 1.25)
	Other: very serious imprecision (confidence intervals crossed 0.8 and 1.25)
Publication bias	The evidence was downgraded for publication bias as it came from a relatively small number of primary studies, some of which were in an early phase of investigation.
Moderate/large effect size	The evidence was upgraded if moderate (aOR > 2.5 or aOR <0.25) or large effect (aOR > 4.25 or aOR < 0.4) sizes were estimated. This applied to the supine position outcome.
Overall quality	Supine: HIGH
	Right side: VERY LOW
	Other: VERY LOW

Notes: <sup>a</sup>Anderson 2019. Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

GRADE tables for review question: Is there an association between sleep position on going to sleep and still birth or having a small for gestational age baby? – evidence from primary studies

Table 9: GRADE table for independent association between going-to-sleep position on last night and stillbirth in comparison to left lateral going-to-sleep position on last night

Phase of investigation	No restrictions were placed on phase of investigation. Given the relatively low frequency of stillbirth, a phase 3 prospective cohort study that aims to examine the role of sleep position and its effect on still birth is not feasible. Therefore no restrictions were placed on the phase of investigation.
	Prone going-to-sleep position  One phase 2 prospective population-based case control study <sup>a</sup> was included in the review of prone going-to-sleep position on last night and the quality of evidence was thus initially rated as high.
	Right lateral, supine going-to-sleep position
	One phase 2 retrospective nested case-control study in a cohort of known size <sup>b</sup> and two phase 2 prospective population-based case control studies <sup>a,c</sup> were included in the review of right lateral going-to-sleep position or supine going-to-sleep position on last night and the quality of evidence was thus initially rated as high.
	Sitting/propped, variable-lateral going-to-sleep position
	One phase 2 retrospective nested case-control study in a cohort of known size <sup>b</sup> and one phase 2 prospective population-based case control study <sup>a</sup> were included in the reviews of variable-lateral or sitting/propped going-to-sleep position on last night and the quality of evidence was thus initially rated as high.
Study limitations	The three included phase 2 studies were assessed as being at overall low <sup>c</sup> , moderate <sup>a</sup> and high <sup>b</sup> risk of bias. The main sources of bias in these studies were: high <sup>a,b</sup> or moderate <sup>c</sup> risk of selection bias regarding the study population due to study attrition, and moderate risk of recall bias <sup>a,b,c</sup> for measurement of going-to-sleep position on last night given that there was a delay in all studies between birth outcome (i.e. stillbirth or live birth) and the interview in which sleep data was collected.
Inconsistency	Prone going-to-sleep position  There was only one study (N=1024) <sup>a</sup> contributing to the evidence of association between prone going-to-sleep position and stillbirth. No serious inconsistency.
	Right lateral going-to-sleep position

Although none of the studies found a statistically significant association between right lateral going-to-sleep position and stillbirth, there is some inconsistency in the results: two of the studies found positive association between pregnant women who reported right lateral going-to-sleep position on the last night and still birth compared to left lateral going-to-sleep position (aOR 1.11 [95% CI 0.70 to 1.77]<sup>b</sup>; aOR 1.74 [95% CI 0.98 to 3.01]<sup>c</sup>) whilst one of the studies found negative association between those reporting right lateral going-to-sleep position on the last night and stillbirth (aOR 0.67 [95% CI 0.44 to 1.02]<sup>a</sup>); in addition, although each of the 95% confidence intervals associated with the reported adjusted odds ratios crossed the line of no effect, there was minimal overlap in two of the studies<sup>a,c</sup>. The inconsistency in the results regarding the association between right-lateral going-to-sleep position on the last night and stillbirth was therefore considered to be serious.

### Sitting/propped going-to-sleep position

None of the studies reported a statistically significant association between sitting/propped going-to-sleep position and stillbirth and the adjusted odds ratios were similar and there was significant overlap of 95% confidence interval between the two (aOR 0.44 [95%CI 0.13 to 1.49]<sup>a</sup>; aOR 0.71 [95%CI 0.22 to 2.30]<sup>b</sup>). Thus, the inconsistency in the results regarding the association between variable going-to-sleep position on the last night and stillbirth was considered to be minimal and the evidence was not downgraded.

## Supine going-to-sleep position

Two studies<sup>a,c</sup> reported a statistically significant association between supine going-to-sleep position and stillbirth compared to left lateral going-to-sleep position whereas another study<sup>b</sup> did not find any significant association. There was inconsistency in the results: two of the studies<sup>a,c</sup> reported a statistically significant association between supine going-to-sleep position and stillbirth compared to left lateral going-to-sleep position (aOR 2.31 [95% CI 1.04 to 5.11]<sup>a</sup>; aOR 2.54 [95% CI 1.04 to 6.18]<sup>c</sup>) whereas another study<sup>b</sup> showed a positive but not a statistically significant association (aOR 1.05 [95% CI 0.32 to 3.50]<sup>a</sup>). The inconsistency in the results regarding the association between supine going-to-sleep position on the last night and stillbirth was therefore considered to be serious.

## Variable-lateral going-to-sleep position

None of the studies reported a statistically significant association between variable-lateral going-to-sleep position and stillbirth and the adjusted odds ratios were similar and there was significant overlap of 95% confidence interval between the two (aOR 0.93 [95%CI 0.51 to 1.69]<sup>a</sup>; aOR 0.75 [95%CI 0.34 to 1.64]<sup>b</sup>). Thus, the inconsistency in the results regarding the association between variable-lateral going-to-sleep position on the last night and stillbirth was considered to be minimal and the evidence was not downgraded.

#### Indirectness

Two of the included studies were multi-centre studies and included all consenting pregnant women who experienced stillbirth in high-income countries (New Zealanda and the UKc) and can therefore be

## considered to be representative of the target population. One of the included studies<sup>b</sup> was an anonymous international online survey that recruited participants through the use of web-based advertising, social media, and word of mouth. This study, unlike the other two studiesa,c, also restricted participants to those who were at least 18 years old. The evidence was therefore downgraded for serious indirectness in the population of interest. The evidence regarding indirectness in the studied prognostic factor (i.e. going-tosleep position) and outcome of interest (i.e. stillbirth) was not considered to be serious. **Imprecision** Prone going-to-sleep position One study<sup>a</sup> examined the relationship between prone going-to-sleep position and stillbirth compared to left lateral going-to-sleep position. The confidence interval around the estimated effect size was wide (0.13 to 7.81), not indicating an association between prone going-to-sleep position and stillbirth compared to left lateral going-to-sleep position. Therefore, the imprecision was considered to be very serious. Right lateral going-to-sleep position Three studies a,b,c examined the association between right lateral going-to-sleep position and stillbirth compared to left lateral going-to-sleep position. No significant effect of right lateral going-to-sleep position on the last night on stillbirth compared to left lateral going-to-sleep position was found and the 95% confidence intervals were relatively wide ([0.44 to 1.02]a, [0.70 to 1.77]b and [0.98 to 3.01])c with none of the studies indicating an association between right lateral going-to-sleep position and stillbirth compared to left lateral going-to-sleep position. The evidence was therefore downgraded for serious imprecision due to substantial uncertainty in the effect estimate of each included study. Sitting/propped going-to-sleep position Two studies<sup>a,b</sup> evaluated the association between sitting/propped going-to-sleep position and stillbirth compared to left lateral going-to-sleep position. No significant association was found in either study and the 95% confidence intervals were wide ([0.13 to 1.49]a and [0.22 to 2.30])b, not indicating an association between sitting/propped going-to-sleep position and stillbirth compared to left lateral going-to-sleep position. Therefore, the imprecision of the effect was considered to be very serious. Supine going-to-sleep position The 95% confidence intervals in all studies were wide<sup>a,b,c</sup> ([1.04 to 5.11])<sup>a</sup>, [0.32 to 3.50]<sup>b</sup> and [1.04 to 6.18])c, with 2 studies ac finding a statistically significant positive association between supine going-tosleep position and stillbirth, and one study<sup>b</sup> not finding a significant association, compared to left lateral going-to-sleep position. Thus, the results are inconclusive regarding the association and the imprecision was considered to be very serious.

Variable-lateral going-to-sleep position

	No significant association was found in either study between variable-lateral going-to-sleep position and stillbirth and the 95% confidence intervals around the effect estimates were relatively wide [(0.51 to 1.69) <sup>a</sup> and (0.34 to 1.64) <sup>b</sup> ], not indicating an association between variable-lateral going-to-sleep position and stillbirth compared to left lateral going-to-sleep position. Therefore, the imprecision was considered to be very serious.
Publication bias	Although these studies were not 'pure' cohort studies, the use of a case control design is appropriate given the low frequency of stillbirth. All three studies used multivariate analysis to adjust for potential confounders such as age, BMI, ethnicity and smoking status during pregnancy. However, since the association between any going-to-sleep position on the last night stillbirth compared to left lateral going-to-sleep position was only explored in 3 studies, the evidence was downgraded for publication bias.
Moderate/large effect size	Prone going-to-sleep position
	The estimated adjusted effect size in the study was small (aOR=1.01) <sup>a</sup> and the 95% confidence interval around the estimate crossed the line of no effect, therefore the evidence was not upgraded.
	Dight hand gains to along position
	Right-hand going-to-sleep position
	The estimated adjusted effect sizes in the three studies were all small with two studies favouring left lateral going-to-sleep position (aOR=1.11b; aOR=1.74c) compared to right-side position, and one study favouring right-side going-to-sleep position compared to left lateral position (aOR 0.67a), therefore the evidence was not upgraded.
	Sitting/propped going-to-sleep position  The odds of stillbirth for sitting/propped going-to-sleep position in two included studies were small compared to left lateral going-to-sleep position (aOR=0.44a; aOR=0.71b) and the 95% confidence intervals crossed the line of no effect, therefore the evidence was not upgraded.
	Supine going-to-sleep position
	The odds of stillbirth for supine going-to-sleep position in two studies were moderate to large (aOR=2.31a; aOR=2.54c) whereas the odds in another study was found to be small (aOR=1.05b). In the first two studiesac, the 95% confidence intervals did not cross the line of no effect, indicating the positive association between supine going-to-sleep position and stillbirth, whilst the 95% confidence interval in another studyb crossed the line of no effect. Thus, because of variability in the results, the evidence for an independent effect of supine going-to-sleep position on stillbirth was not upgraded.
	Variable-lateral going-to-sleep position
	The estimated going-to-sleep position in two included studies were small (aOR=0.93a; aOR=0.75b) and the 95% confidence intervals crossed the line of no effect, therefore the evidence was not upgraded.

Overall quality	Prone: VERY LOW
	Right-lateral: VERY LOW
	Sitting/Propped: VERY LOW
	Supine: VERY LOW
	Variable-lateral: VERY LOW

Notes: <sup>a</sup>Heazell 2018; <sup>b</sup>O'Brien 2019; <sup>c</sup>Stacey 2011. Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

Table 10: GRADE table for independent association between going-to sleep position on last month of pregnancy and late stillbirth in comparison to left lateral going-to-sleep position on last month

Companison to left lateral going-to	• •
Phase of investigation	No restrictions were placed on phase of investigation. Given the relatively low frequency of stillbirth, a phase 3 prospective cohort study that aims to examine the role of sleep position and its effect on still birth is not feasible. Therefore no restrictions were placed on the phase of investigation.
	Right-lateral going-to-sleep position, supine going-to-sleep position
	One phase 1 prospective case control study <sup>a</sup> and one phase 2 nested case-control studies in a cohort of known size <sup>b</sup> were included in the review of right lateral or supine going-to-sleep position on last month and the quality of evidence was thus initially rated as moderate.
	Variable-lateral going-to-sleep position, sitting/propped going-to-sleep position
	One phase 2 nested case-control study in a cohort of known size <sup>b</sup> was included in the review of variable-lateral or sitting/propped going-to-sleep position on last month and the quality of evidence was thus initially rated as high.
Study limitations	The included phase 1 study and phase 2 study were all assessed as being at overall low <sup>a</sup> and high <sup>b</sup> risk of bias. The main sources of bias in these studies were: high risk of selection bias due to unclear information on study population <sup>b</sup> , and incomparable baseline characteristics between cases and controls; moderate risk of recall bias <sup>a,b</sup> for measurement of going-to-sleep position on last night given that there was a delay in all studies between birth outcome (i.e. stillbirth or live birth) and the interview in which sleep data was collected.
Inconsistency	Right-lateral going-to-sleep position  None of the studies found a statistically significant association between right-lateral going-to-sleep position and stillbirth. There is minimal inconsistency in the results (aOR 1.1 [95% CI 0.43 to 2.6] <sup>a</sup> ; aOR 1.14 [95% CI 0.70 to 1.85] <sup>b</sup> ). The inconsistency in the results of these two studies was therefore not considered to be serious.

	Sitting/propped going-to-sleep position, variable-lateral going-to-sleep position  There was only one study <sup>b</sup> (N=633 <sup>b</sup> ) contributing to the evidence of association between going-to-sleep position on last month and stillbirth. No serious inconsistency.
	Supine going-to-sleep position  One study reported a statistically significant positive association between supine going-to-sleep position and stillbirth (aOR 6.26 [95%CI 1.15 to 34.00]) <sup>a</sup> whereas another study reported negative association although the result was not statistically significant (aOR 0.37 [95%CI 0.04 to 3.12]) <sup>b</sup> . Thus, the inconsistency of the results between these two studies was considered to be very serious.
Indirectness	One of the included studies was a multi-centre study and included all consenting pregnant women who experienced stillbirth in high-income countries (Australia <sup>a</sup> ) and can therefore be considered to be representative of the target population. Another study <sup>b</sup> was an anonymous international online survey that recruited participants through the use of web-based advertising, social media, and word of mouth. This study, unlike the other study <sup>a</sup> , also restricted participants to those who were at least 18 years old. The evidence was therefore downgraded for serious indirectness in the population of interest. The evidence in this study regarding indirectness in the studied prognostic factor (i.e. going-to-sleep position) and outcome of interest (i.e. stillbirth) was not considered to be serious.
Imprecision	Right-lateral going-to-sleep position  Two studies <sup>a,b</sup> examined the relationship between right-lateral going-to-sleep position and stillbirth compared to left lateral going-to-sleep position. The 95% confidence intervals around the estimated effect size crossed the line of no effect and were considered to be wide <sup>b</sup> (0.70 to 1.85) <sup>b</sup> and very wide <sup>a</sup> (0.43 to 2.6) <sup>a</sup> , not indicating an association between right-lateral going-to-sleep position and stillbirth compared to left lateral going-to-sleep position. Overall the imprecision was considered to be serious.
	Sitting/propped going-to-sleep position  The 95% confidence interval around the effect estimate in this study crossed the line of no effect and was considered to be very wide (0.39 to 3.68) <sup>b</sup> therefore, the imprecision was considered to be very serious.
	Supine going-to-sleep position  One study (N=295) <sup>a</sup> reported statistically significant positive association (aOR=6.26) <sup>a</sup> although the 95% confidence interval was considered to be very wide (1.15 to 34.00) <sup>a</sup> . However, another study (N=542) <sup>b</sup> did not find an association and the 95% confidence interval ranged from negative association (0.04) <sup>b</sup> to positive association (3.12) <sup>b</sup> . Thus, the imprecision was considered to be very serious.
	Variable-lateral going-to-sleep position

	The 95% confidence interval around the effect estimate in this study crossed the line of no effect and was considered to be wide (0.48 to 1.55) <sup>b</sup> therefore, the imprecision was considered to be serious.
Publication bias	Although these studies were not 'pure' cohort studies, the use of a case control design is appropriate given the low frequency of stillbirth. Both studies used multivariate analysis to adjust for potential confounders such as age, BMI, ethnicity and smoking status during pregnancy. However, since the association between any going-to-sleep position on the last month and late stillbirth compared to left lateral going-to-sleep position was only explored in 2 studies, the evidence was downgraded for publication bias.
Moderate/large effect size	Right-lateral going-to-sleep position  The estimated adjusted effect sizes in the two studies <sup>a,b</sup> were small (aOR=1.1 <sup>a</sup> ; aOR=1.14 <sup>b</sup> ) and therefore not upgraded.
	Sitting/propped going-to-sleep position
	The estimated adjusted effect size in the study <sup>b</sup> was small (aOR=1.20 <sup>a</sup> ) and therefore not upgraded.
	Supine going-to-sleep position
	There were significant differences in the effect estimates reported by two included studies <sup>a,b</sup> where the estimated adjusted effect size in one study was large (aOR=6.26) <sup>a</sup> and showed positive association whereas the adjusted effect estimate in another study was moderate (aOR=0.37) <sup>b</sup> and showed negative association. Given the inconsistency, the evidence was not upgraded.
	Variable-lateral going-to-sleep position
	The estimated adjusted effect size in the study was small (aOR=0.87) <sup>b</sup> and therefore not upgraded.
Overall quality	Right-lateral going-to-sleep position: VERY LOW Sitting/propped going-to-sleep position: VERY LOW Supine going-to-sleep position: VERY LOW
20 and an 2015, hO'Pring 2010, Alcharati	Variable-lateral going-to-sleep position: VERY LOW

Notes: aGordon 2015; bO'Brien 2019. Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

Table 11: GRADE table for independent association between going-to-sleep position on last night or last week of pregnancy and preterm stillbirth (28 to 36 weeks gestation) in comparison to left lateral going-to-sleep position on last night or last week

Phase of investigation	No restrictions were placed on phase of investigation. Given the relatively low frequency of stillbirth, a
	phase 3 prospective cohort study that aims to examine the role of sleep position and its effect on still birth is not feasible. Therefore no restrictions were placed on the phase of investigation.

One phase 2 prospective population-based case-control study³ was included in the review association between going-to-sleep position on last night or last week and preterm stillbirth fetal death between 28 to 36 weeks gestation). Thus, the quality of evidence was initially rate to study limitations  The included phase 2 study was assessed as being at overall moderate³ risk of bias. The nobias in this study were: moderate risk of selection bias regarding the study population due to attrition³, and moderate risk of recall bias for measurement of going-to-sleep position on last week³ given that there was a delay in all studies between birth outcome (i.e. stillbirth or live interview in which sleep data was collected.  Inconsistency  There was only one study (N=733)³ contributing to the evidence of association between going position on last night or last week and preterm stillbirth (defined as fetal death between 28 gestation). No serious inconsistency.  Indirectness  The included study was a multi-centre study and included all consenting pregnant women wexperienced stillbirth in high-income country (New Zealand³) and can therefore be consider representative of the target population. In addition, the evidence regarding indirectness in the still to the first of the target population. In addition, the evidence regarding indirectness in the still to the first of the target population.	(defined as atted as high. main sources of to study
bias in this study were: moderate risk of selection bias regarding the study population due to attritiona, and moderate risk of recall bias for measurement of going-to-sleep position on last weeka given that there was a delay in all studies between birth outcome (i.e. stillbirth or live interview in which sleep data was collected.  Inconsistency  There was only one study (N=733)a contributing to the evidence of association between going position on last night or last week and preterm stillbirth (defined as fetal death between 28 agestation). No serious inconsistency.  Indirectness  The included study was a multi-centre study and included all consenting pregnant women we experienced stillbirth in high-income country (New Zealanda) and can therefore be consider representative of the target population. In addition, the evidence regarding indirectness in the study and included regarding indirectness in the study and regarding ind	to study
position on last night or last week and preterm stillbirth (defined as fetal death between 28 a gestation). No serious inconsistency.  Indirectness  The included study was a multi-centre study and included all consenting pregnant women wexperienced stillbirth in high-income country (New Zealanda) and can therefore be consider representative of the target population. In addition, the evidence regarding indirectness in the start of the target population.	birth) and the
experienced stillbirth in high-income country (New Zealanda) and can therefore be consider representative of the target population. In addition, the evidence regarding indirectness in the second still birth in high-income country (New Zealanda) and can therefore be considered.	
prognostic factor (i.e. going-to-sleep position) and outcome of interest (i.e. preterm stillbirth considered to be serious.	red to be he studied
Imprecision Going-to-sleep position on last night	
Restless going-to-sleep position <sup>b</sup> The 95% confidence interval around the effect estimate crossed the line of no effect and we to be very wide (0.61 to 19.97) <sup>a</sup> therefore the imprecision was considered to be very seriou	
Right-lateral going-to-sleep position	
The 95% confidence interval around the effect estimate crossed the line of no effect and water to be wide (0.48 to 1.94) <sup>a</sup> therefore the imprecision was considered to be serious.	as considered
Sitting/propped going-to-sleep position  The 95% confidence interval around the effect estimate crossed the line of no effect and we to be very wide (0.11 to 178.86) <sup>a</sup> , therefore, the imprecision was considered to be very serious considered.	
Supine going-to-sleep position  The 95% confidence interval around the effect estimate crossed the line of no effect and wat to be wide (0.97 to 10.05) <sup>a</sup> , therefore, the imprecision was considered to be serious.	as considered
Going-to-sleep position on last week	

	Prone going-to-sleep position
	The 95% confidence interval around the effect estimate <sup>a</sup> crossed the line of no effect and was considered to be very wide (0.45 to 278.58) <sup>a</sup> , therefore the imprecision was considered to be very serious.
	Right-lateral going-to-sleep position
	The 95% confidence interval around the effect estimate crossed the line of no effect and was considered to be wide (0.34 to 1.54) <sup>a</sup> , therefore the imprecision was considered to be serious.
	Sitting/propped going-to-sleep position
	The 95% confidence interval around the effect estimate crossed the line of no effect and was considered to be very wide (0.08 to 210.43) <sup>a</sup> , therefore the imprecision was considered to be very serious.
	Supine going-to-sleep position
	The 95% confidence interval around the effect estimate crossed the line of no effect and was considered to be very wide (0.65 to 7.84) <sup>a</sup> , therefore the imprecision was considered to be very serious.
	Variable-lateral going-to-sleep position
	The 95% confidence interval around the effect estimate crossed the line of no effect and was considered to be very wide (0.18 to 2.19) <sup>a</sup> , therefore the imprecision was considered to be very serious.
Publication bias	Although the included study was not a 'pure' cohort study, the use of a case control design is appropriate given the low frequency of stillbirth. This study used multivariate analysis to adjust for potential confounders such as age, BMI, ethnicity and smoking status during pregnancy. However, since the association between any going-to-sleep position on the last night or last week and preterm stillbirth compared to left lateral going-to-sleep position is only explored in 1 study, the evidence was downgraded for publication bias.
Moderate/large effect size	Going-to-sleep position on last night
	Restless going-to-sleep position <sup>b</sup>
	The estimated adjusted effect size in this study was moderate (aOR=3.50) <sup>a</sup> however this was not statistically significant and was therefore not upgraded.
	Right-lateral going-to-sleep position
	The estimated adjusted effect size in this study was small (aOR=0.96) <sup>a</sup> and was therefore not upgraded.

	Sitting/propped going-to-sleep position
	The estimated adjusted effect size in this study was moderate (aOR=4.37) <sup>a</sup> however this was not statistically significant and was therefore not upgraded.
	Supine going-to-sleep position
	The estimated adjusted effect size in this study was small (aOR=2.25) <sup>a</sup> and was therefore not upgraded.
	Going-to-sleep position on last week
	Prone going-to-sleep position
	The estimated adjusted effect size in this study was large (aOR=10.71) <sup>a</sup> however this was not statistically significant and was therefore not upgraded.
	Right-lateral going-to-sleep position
	The estimated adjusted effect size in this study was small (aOR=0.73) <sup>a</sup> and was therefore not upgraded.
	Sitting/propped going-to-sleep position
	The estimated adjusted effect size in this study was moderate (aOR=4.01) <sup>a</sup> however this was not statistically significant and was therefore not upgraded.
	Supine going-to-sleep position
	The estimated adjusted effect size in this study was small (aOR=2.25) <sup>a</sup> and therefore not upgraded.
	Variable-lateral going-to-sleep position
	The estimated adjusted effect size in this study was small (aOR=0.63) <sup>a</sup> and therefore not upgraded.
Overall quality	Going-to-sleep position on last night
	Restless going-to-sleep position: VERY LOW  Right-lateral going-to-sleep position: VERY LOW
	Sitting/propped going-to-sleep position: VERY LOW
	Supine going-to-sleep position: VERY LOW
	Coing to clean position on last week
	Going-to-sleep position on last week

Prone going-to-sleep position: VERY LOW
Right-lateral going-to-sleep position: VERY LOW
Sitting/propped going-to-sleep position: VERY LOW
Supine going-to-sleep position: VERY LOW
Variable-lateral going-to-sleep position: VERY LOW

Notes: aMcCowan 2018; 'Restless' going-to-sleep position refers to women who frequently change positions when going to sleep and could not remember the position they had just before falling asleep. Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

Table 12: GRADE table for independent association between going-to-sleep position on last night or last week of pregnancy and term stillbirth (≥37 weeks gestation) in comparison to left lateral going-to-sleep position

Stillbirtii (=07 Weeks gestation) iii	comparison to left lateral going-to-sleep position
Phase of investigation	No restrictions were placed on phase of investigation. Given the relatively low frequency of stillbirth, a phase 3 prospective cohort study that aims to examine the role of sleep position and its effect on still birth is not feasible. Therefore no restrictions were placed on the phase of investigation.  One phase 2 prospective population-based case-control study <sup>a</sup> was included in the review of the association between going-to-sleep position on last night or last week and term stillbirth (defined as fetal death after 36 weeks gestation). Thus, the quality of evidence was initially rated as high.
Study limitations	The included phase 2 study was assessed as being at overall moderate risk of bias. <sup>a</sup> The main sources of bias in this study were: moderate risk of selection bias regarding the study population due to study attrition, and moderate risk of recall bias for measurement of going-to-sleep position on last night or last week given that there was a delay in all studies between birth outcome (i.e. stillbirth or live birth) and the interview in which sleep data was collected.
Inconsistency	There was only one study (N=733) <sup>a</sup> contributing to the evidence of association between going-to-sleep position on last night or last week and term stillbirth (defined as fetal death after 36 weeks gestation). No serious inconsistency.
Indirectness	The included study was a multi-centre study and included all consenting pregnant women who experienced stillbirth in a high-income country (New Zealanda) and can therefore be considered to be representative of the target population. In addition, the indirectness in the studied prognostic factor (i.e. going-to-sleep position) and outcome of interest (i.e. term stillbirth) was not considered to be serious.
Imprecision	Going-to-sleep position on last night
	Restless going-to-sleep position <sup>b</sup>
	The 95% confidence interval around the effect estimate crossed the line of no effect and was considered to be very wide (0.64 to 6.21) <sup>a</sup> therefore the imprecision was considered to be very serious.
	Right-lateral going-to-sleep position

The 95% confidence interval around the effect estimate crossed the line of no effect and was considered to be wide (0.48 to 1.99)<sup>a</sup>, therefore the imprecision was considered to be serious.

## Sitting/propped going-to-sleep position

The 95% confidence interval around the effect estimate crossed the line of no effect and was considered to be very wide (0.17 to 5.97)<sup>a</sup>, therefore the imprecision was considered to be very serious.

## Supine going-to-sleep position

The 95% confidence interval around the effect estimate did not cross the line of no effect but was considered to be wide (3.01 to 35.04)<sup>a</sup> therefore the imprecision was considered to be serious.

## Going-to-sleep position on last week

## Right-lateral going-to-sleep position

The 95% confidence interval around the effect estimate crossed the line of no effect and was considered to be wide (0.47 to 1.89)<sup>a</sup> therefore the imprecision was considered to be serious.

## Sitting/propped going-to-sleep position

The 95% confidence interval around the effect estimate crossed the line of no effect and was considered to be very wide (0.47 to 14.81)<sup>a</sup> therefore the imprecision was considered to be very serious.

## Supine going-to-sleep position

The 95% confidence interval around the effect estimate did not cross the line of no effect but was considered to be very wide (2.92 to 55.46)<sup>a</sup> therefore, the imprecision was considered to be serious.

## Variable-lateral going-to-sleep position

The 95% confidence interval around the effect estimate crossed the line of no effect and was considered to be wide (0.49 to 3.01)<sup>a</sup> therefore, the imprecision was considered to be serious.

#### **Publication bias**

The included study used multivariate analysis to adjust for potential confounders such as age, BMI, ethnicity and smoking status during pregnancy.<sup>a</sup> Although this study was a non-nested case control study, this design is appropriate given the low frequency of stillbirth. However, this is the only study to have reported results relative to time of stillbirth. The association between any going-to-sleep position on the last night or last week and term stillbirth compared to left lateral going-to-sleep position was therefore considered to not be adequately explored by the identified study and the evidence was downgraded for publication bias.

Moderate/large effect size	Going-to-sleep position on last night
	Restless going-to-sleep position <sup>b</sup>
	The estimated adjusted effect size in this study was small (aOR=2.0) <sup>a</sup> and was therefore not upgraded.
	Right-lateral going-to-sleep position
	The estimated adjusted effect size in this study was small (aOR=0.98) <sup>a</sup> and was therefore not upgraded.
	Sitting/propped going-to-sleep position
	The estimated adjusted effect size in this study was small (aOR=1.02) <sup>a</sup> and was therefore not upgraded.
	Supine going-to-sleep position
	The estimated adjusted effect size in this study was large (aOR=10.26) <sup>a</sup> . In addition, this adjusted effect estimate was statistically significant. The evidence was therefore upgraded.
	Going-to-sleep position on last week
	Right-lateral going-to-sleep position
	The estimated adjusted effect size in this study was small (aOR=0.95) <sup>a</sup> and was therefore not upgraded.
	Sitting/propped going-to-sleep position
	The estimated adjusted effect size in this study was moderate (aOR=2.64) <sup>a</sup> however this adjusted effect estimate was not statistically significant and was therefore not upgraded.
	Supine going-to-sleep position
	The estimated adjusted effect size in this study was large (aOR=12.73) <sup>a</sup> . In addition, this adjusted effect estimate was statistically significant. The evidence was therefore upgraded.
	Variable-lateral going-to-sleep position
	The estimated adjusted effect size in this study was small (aOR=1.11) <sup>a</sup> and was therefore not upgraded.
Overall quality	Going-to-sleep position on last night
	Restless going-to-sleep position: VERY LOW
	Right-lateral going-to-sleep position: VERY LOW
	Sitting/propped going-to-sleep position: VERY LOW
	Supine going-to-sleep position: LOW
	Going-to-sleep position on last week
	Right-lateral going-to-sleep position: VERY LOW
	Sitting/propped going-to-sleep position: VERY LOW
	Supine going-to-sleep position: LOW
	Variable-lateral going-to-sleep position: VERY LOW

Notes: aMcCowan 2018; b, 'Restless' going-to-sleep position refers to women who frequently change positions when going to sleep and could not remember the position they had just before falling asleep. Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

## **Appendix G – Economic evidence study selection**

Economic evidence study selection for review question: Is there an association between sleep position on going to sleep and still birth or having a small for gestational age baby?

A single economic search was undertaken for all topics included in the scope of this guideline. No economic studies were identified which were applicable to this review question. See supplementary material 2 for details.

## **Appendix H – Economic evidence tables**

Economic evidence tables for review question: Is there an association between sleep position on going to sleep and still birth or having a small for gestational age baby?

No economic evidence was identified which was applicable to this review question.

## **Appendix I – Health economic evidence profiles**

Economic evidence profiles for review question: Is there an association between sleep position on going to sleep and still birth or having a small for gestational age baby?

No evidence was identified which was applicable to this review question.

## Appendix J - Health economic analysis

Economic analysis for review question: Is there an association between sleep position on going to sleep and still birth or having a small for gestational age baby?

No economic analysis was conducted for this review question.

## Appendix K - Excluded studies

Excluded studies for review question: Is there an association between sleep position on going to sleep and still birth or having a small for gestational age baby?

## **Clinical studies**

**Table 13: Excluded studies** 

Study	Reason for exclusion
Bei, B., Neemia, D., Shen, L., Fulgoni, C., Blumfield, M. L., Drummond, S. P., Newman, L. K., Manber, R., A brief, automated cognitive behavioral program prevents sleep disturbance and insomnia in late pregnancy: A randomized controlled trial, Sleep, 41 (Supplement 1), A151, 2018	Conference abstract
Cronin, R. S., Chelimo, C., Mitchell, E. A., Okesene-Gafa, K., Thompson, J. M. D., Taylor, R. S., Hutchison, B. L., McCowan, L. M. E., Survey of maternal sleep practices in late pregnancy in a multi-ethnic sample in South Auckland, New Zealand, BMC pregnancy and childbirth, 17 (1) (no pagination), 2017	No relevant outcomes reported
Cronin, R. S., Li, M., Thompson, J. M. D., Gordon, A., Raynes-Greenow, C., Heazell, A. E. P., Stacey, T., Culling, V., Bowring, V., Askie, L., Mitchell, E. A., McCowan, L. M. E., An individual participant data meta-analysis of going-to-sleep position, interactions with fetal vulnerability and the risk of late stillbirth, Journal of Paediatrics and Child Health, 54 (Supplement 1), 3, 2018	Conference abstract
Gaudet, L., Simon, A., Pratt, M., Heslehurst, N., Hayes, L., Flynn, A., Velez, M. P., Smith, G., Skidmore, B., Hutton, B., Rybak, N., Walker, M., Predictors of adverse pregnancy outcomes in obese pregnant women a systematic review, International Journal of Gynecology and Obstetrics, 143 (Supplement 3), 600-601, 2018	Conference abstract
Heazell, A. E. P., Cronin, R. S., Li, M., Thompson, J. M. D., Gordon, A., Raynes- Greenow, C., Stacey, T., Culling, V., Bowring, V., Askie, L., Mitchell, E. A., McCowan, L. M. E., Going to sleep position and risk of late stillbirth: A systematic review and metaanalysis, Journal of Paediatrics and Child Health, 54 (Supplement 1), 24-25, 2018	Conference abstract
Heazell, A. E. P., Li, M., Thompson, J. M. D., Budd, J., Cronin, R., Mitchell, E., Stacey, T., Roberts, D., Martin, B., McCowan, L. M. E., Going to sleep supine and reduced sleep duration are risk factors for late stillbirth: Findings from the MiNESS Case-Control Study, BMC Pregnancy and Childbirth. Conference:	Conference abstract

Study	Pageon for evaluation
Study International Stillbirth Alliance Conference, 17,	Reason for exclusion
2017	
Hsu, Christine, Sleep Positions Can Predict Women's Risk of Stillbirth, Inside Childbirth Education, 9-9, 2013	Newsletter
Kempler, L., Sharpe, L., Bartlett, D., Sleep education during pregnancy for new mothers, BMC Pregnancy & Childbirth, 12, 155, 2012	Protocol
Kichler, A., Alzubaidi, M., Emery, J., Gabbard, S., Use of a positional therapy device significantly improves nocturnal gastroesophageal reflux disease symptoms in pregnant women, American Journal of Gastroenterology, 1), S703-S704, 2015	Conference abstract
Koken, G. N., Kanat-Pektas, M., Kose, S. K., Arioz, D. T., Yilmazer, M., Maternal blood pressure and dominant sleeping position may affect placental localization, Journal of Maternal- Fetal and Neonatal Medicine, 27, 1564-1567, 2014	No relevant outcomes
Lakshmi, Sujatha Thankappan et al., Risk factors for still birth: a hospital based case control study, International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 6, 970-974, 2017	Incorrect comparison (non-left vs left)
Lee,K.A., Gay,C.L., Sleep in late pregnancy predicts length of labor and type of delivery, American Journal of Obstetrics and Gynecology, 191, 2041-2046, 2004	No relevant outcomes
Li, M., McCowan, L. M. E., Thompson, J. M. D., Cronin, R. S., Anderson, N., Stacey, T., Stone, P., Lawton, B. A., Ekeroma, A. J., Mitchell, E. A., Supine going-to-sleep position is a major risk factor for term stillbirth: Findings from the New Zealand multicentre stillbirth case-control study, BMC Pregnancy and Childbirth. Conference: International Stillbirth Alliance Conference, 17, 2017	Conference abstract
Li, M., Mitchell, E. A., Cronin, R. S., Thompson, J. M. D., Gordon, A., Raynes-Greenow, C., Heazell, A. E. P., Stacey, T., Culling, V., Bowring, V., Askie, L., McCowan, L. M. E., Environmental tobacco smoke exposure is associated with increased late stillbirth: Findings from the collaborative individual participant data (IPD) sleep and stillbirth (CRIBSS) meta-analysis, Journal of Paediatrics and Child Health, 54 (Supplement 1), 31, 2018	Conference abstract
Li, M., Thompson, J. M. D., Cronin, R. S., Gordon, A., Raynes-Greenow, C., Heazell, A. E. P., Stacey, T., Culling, V., Bowring, V., Mitchell, E. A., McCowan, L. M. E., Askie, L., The Collaborative IPD of Sleep and Stillbirth (Cribss): is maternal going-to-sleep position a risk factor for late stillbirth and does maternal sleep	Protocol

Study	Reason for exclusion
position interact with fetal vulnerability? An individual participant data meta-analysis study protocol, BMJ open, 8, e020323, 2018	
Li, R., Zhang, J., Zhou, R., Liu, J., Dai, Z., Liu, D., Wang, Y., Zhang, H., Li, Y., Zeng, G., Sleep disturbances during pregnancy are associated with cesarean delivery and preterm birth, Journal of maternal-fetal & neonatal medicine, 30, 733― 738, 2017	Sleep position not examined in study
Lillis, T. A., Hamilton, N. A., Pressman, S. D., Khou, C. S., The Association of Daytime Maternal Napping and Exercise With Nighttime Sleep in First-Time Mothers Between 3 and 6 Months Postpartum, Behavioral sleep medicine, 16, 527-541, 2018	Sleep position not examined in study
McCowan, L., Contribution of maternal going-to- sleep position and fetal movements to late stillbirth, Australian and New Zealand Journal of Obstetrics and Gynaecology, 57 (Supplement 1), 19-20, 2017	Conference abstract
McCowan, Lesley M. E., Cronin, Robin S., Gordon, Adrienne, O'Brien, Louise, Heazell, Alexander E. P., Prospective Evaluation of Maternal Sleep Position Through 30 Weeks of Gestation and Adverse Pregnancy Outcomes, Obstetrics & Gynecology, 135, 218-218, 2020	Commentary
McIntyre, J. P. R., Ingham, C. M., Hutchinson, B. L., Thompson, J. M. D., McCowan, L. M., Stone, P. R., Veale, A. G., Cronin, R., Stewart, A. W., Ellyett, K. M., Mitchell, E. A., A description of sleep behaviour in healthy late pregnancy, and the accuracy of self-reports, BMC Pregnancy and Childbirth, 16 (1) (no pagination), 2016	Non-comparative study
McIntyre, J. P. R., Stone, P. R., Mitchell, E. M., Veale, A. G., How healthy women sleep in late pregnancy; A video and portable polysomnography study, Sleep and Biological Rhythms, 11, 44, 2013	Conference abstract
Morokuma, S., Shimokawa, M., Kato, K., Sanefuji, M., Shibata, E., Tsuji, M., Senju, A., Kawamoto, T., Kusuhara, K., Maternal sleep and small for gestational age infants in the Japan Environment and Children's Study: a cohort study, BMC research notes, 10, 394, 2017	Sleep position not examined in study
O'Brien, Louise M., Warland, Jane, Typical sleep positions in pregnant women, Early Human Development, 90, 315-317, 2014	Non-comparative study
Owusu, Jocelynn T., Anderson, Frank J., Coleman, Jerry, Oppong, Samuel, Seffah, Joseph D., Aikins, Alfred, O'Brien, Louise M., Association of maternal sleep practices with pre- eclampsia, low birth weight, and stillbirth among Ghanaian women, International Journal of Gynecology & Obstetrics, 121, 261-265, 2013	Cross-sectional study

Study	Reason for exclusion
Paine, S. J., Signal, T. L., Sweeney, B., Priston, M., Muller, D., Smith, A. A., Huthwaite, M., Lee, K., Gander, P. H., Ethnic differences in sleep across pregnancy: A cohort study, Sleep and Biological Rhythms, 2), 63, 2013	Conference abstract
Robertson, N., Okano, S., Kumar, S., Sleep in the supine position during pregnancy is associated with fetal cerebral redistribution, Journal of Clinical Medicine, 9, 1-12, 2020	Insufficient adjustment for confounders, insufficient detail on outcomes
Saarenpaa-Heikkila, O., Lehto, U., Kylliainen, A., Stenberg, T., Paunio, T., Paavonen, J., CHILD SLEEP-The finnish birth cohort study: The effect of maternal sleep during pregnancy on a newborn wellbeing and a mother's labor experience, Sleep Medicine, 1), e42, 2013	Conference abstract
Silver, Robert M. M. D., Hunter, Shannon M. S., Reddy, Uma M. M. D. M. P. H., Facco, Francesca M. D., Gibbins, Karen J. M. D., Grobman, William A. M. D. M. B. A., Mercer, Brian M. M. D., Haas, David M. M. D. M. S., Simhan, Hyagriv N. M. D., Parry, Samuel M. D., Wapner, Ronald J. M. D., Louis, Judette M. D., Chung, Judith M. M. D., Pien, Grace M. D., Schubert, Frank P. M. D., Saade, George R. M. D., Zee, Phyllis M. D., Redline, Susan M. D., Parker, Corette B. DrPH, Silver, Robert M., Prospective Evaluation of Maternal Sleep Position Through 30 Weeks of Gestation and Adverse Pregnancy Outcomes, Obstetrics & Gynecology, 134, 667-676, 2019	Primary outcome was a composite adverse pregnancy outcome including stillbirth, hypertensive disorders of pregnancy (mild, severe, or superimposed preeclampsia; eclampsia; or antepartum gestational hypertension), and a small-forgestational-age (SGA) newborns
Silver, Robert M., Reddy, Uma M., Gibbins, Karen J., Prospective Evaluation of Maternal Sleep Position Through 30 Weeks of Gestation and Adverse Pregnancy Outcomes, Obstetrics & Gynecology, 135, 218-219, 2020	Looked at sleep position in early pregnancy
Stacey, T., Mitchell, E. A., Sleep position and risk of late stillbirth, BMC Pregnancy and Childbirth. Conference: Stillbirth Summit, 12, 2011	Conference presentation of included study (Stacey 2011)
Stacey, T., Thomspon, J., Mitchell, E., McCowan, L., Maternal sleep practices: Possible risk factor for late stillbirth, Archives of Disease in Childhood: Fetal and Neonatal Edition, 1), Fa1, 2011	Conference abstract
Warland, J., Dorrian, J., Kember, A. J., Phillips, C., Borazjani, A., Morrison, J. L., O'Brien, L. M., Modifying maternal sleep position in late pregnancy through positional therapy: A feasibility study, Journal of clinical sleep medicine, 14, 1387-1397, 2018	No relevant outcomes
Warland, J., Dorrian, J., Morrison, J. L., O'Brien, L. M., Maternal sleep during pregnancy and poor fetal outcomes: A scoping review of the literature with meta-analysis, Sleep Medicine Reviews, 41, 197-219, 2018	Scoping review - references checked, no additional relevant studies (Lakshmi 2017 not included because it reported non-left vs left sleeping position)

Study	Reason for exclusion
Warland, J., Heazell, A. E. P., Collins, J. H., Huberty, J. L., Kliman, H. J., McGregor, J. A., Mitchell, E. A., O'Brien, L. M., Parast, M., Peesay, M., Stacey, T., Wimmer, L. J., An international internet survey of the experiences of 1,714 mothers with a late stillbirth: The STARS cohort study, BMC Pregnancy and Childbirth, 15 (1) (no pagination), 2015	Companion article to O'Brien 2017, no relevant data
Warland, J., Mitchell, E. A., A triple risk model for unexplained late stillbirth, BMC Pregnancy & ChildbirthBMC Pregnancy Childbirth, 14, 142, 2014	Description of risk model for sudden infant death syndrome
Warland, J., Mitchell, E. A., O'Brien, L. M., Novel strategies to prevent stillbirth, Seminars In Fetal & Neonatal MedicineSemin Fetal Neonatal Med, 22, 146-152, 2017	Non-systematic review of novel strategies to prevent stillbirth
Woods, J. R., Heazell, A. E. P., Stillbirth: is it preventable?, Obstetrics, Gynaecology and Reproductive Medicine, 28, 148-154, 2018	Non-systematic review of stillbirth prevention strategies

## **Economic studies**

One excluded list was created for all economic studies in this guideline. See supplementary material 2 for further information.

# **Appendix L – Research recommendations**

Research recommendations for review question: Is there an association between sleep position on going to sleep and still birth or having a small for gestational age baby?

No research recommendations were made for this review question.