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Research Paper

Perinatal or neonatal mortality among women who intend at the onset of labour to give birth at home compared to women of low obstetrical risk who intend to give birth in hospital: A systematic review and meta-analyses

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ABSTRACT

Background: More women are choosing to birth at home in well-resourced countries. Concerns persist that out-of-hospital birth contributes to higher perinatal and neonatal mortality. This systematic review and meta-analyses determines if risk of fetal or neonatal loss differs among low-risk women who begin labour intending to give birth at home compared to low-risk women intending to give birth in hospital.

Methods: In April 2018 we searched five databases from 1990 onward and used R to obtain pooled estimates of effect. We stratified by study design, study settings and parity. The primary outcome is any perinatal or neonatal death after the onset of labour. The study protocol is peer-reviewed, published and registered (PROSPERO No.CRD42013004046).

Findings: We identified 14 studies eligible for meta-analysis including ~500,000 intended home births. Among nulliparous women intending a home birth in settings where midwives attending home birth are well-integrated in health services, the odds ratio (OR) of perinatal or neonatal mortality compared to those intending hospital birth was 1.07 (95% Confidence Interval [CI], 0.70 to 1.65); and in less integrated settings 3.17 (95% CI, 0.73 to 13.76). Among multiparous women intending a home birth in well-integrated settings, the estimated OR compared to those intending a hospital birth was 1.08 (95% CI, 0.84 to 1.38); and in less integrated settings was 1.58 (95% CI, 0.50 to 5.03).

Interpretation: The risk of perinatal or neonatal mortality was not different when birth was intended at home or in hospital.

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Research in Context: Evidence before this study Although there is increasing acceptance for intended home birth as a choice for birthing women, controversy about its safety persists. The varying responses of obstetrical societies to intended home birth provide evidence of contrasting views. A Cochrane review of randomised controlled trials addressing this topic included one small trial and noted that in the absence of adequately sized randomised controlled trials on the topic of intended home compared to intended hospital birth, a peer reviewed protocol be published to guide a systematic review and meta-analysis including observational studies. Reviews to date have been limited by design or methodological issues and none has used a protocol published a priori.

Added value of this study Individual studies are underpowered to detect small but potentially important differences in rare outcomes. This study uses a published peer-reviewed protocol and is the largest and most comprehensive meta-analysis comparing outcomes of intended home and hospital birth. We take study design, parity and jurisdictional support for home birth into account. Our study provides much needed information to policy makers, care providers and women and families when planning for birth.

Implications of all the available evidence Women who are low risk and who intend to give birth at home do not appear to have a different risk of fetal or neonatal loss compared to a population of similarly low risk women intending to give birth in hospital.\

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1. Introduction

Birth has become the most common reason for hospital admission in well-resourced countries impacting healthcare costs [1]; however, it is unclear if hospitalisation for birth alters neonatal outcomes for women at low obstetrical risk. A small but growing number of women begin labour with the intention of giving birth at home [2] and research among this self-selected group consistently reports reduced obstetric interventions [3,4]. There is uncertainty however, whether this reduction in maternal interventions comes at the expense of neonatal wellbeing. In 2015, for example, two high-profile studies of out-of-hospital (home) birth reported contradictory findings regarding perinatal mortality and morbidity [3,4].

Acceptance of home birth as a choice for women is increasing [5], but controversy about safety persists. Quality evidence regarding outcomes associated with place of birth for low-risk pregnancies is urgently needed to inform parents, maternity care providers and policy makers. Because individual studies are underpowered to detect small but potentially important differences in rare outcomes, and randomised controlled trials are not feasible and do not contribute to these findings, a Cochrane review on this topic urged a careful systematic review and meta-analysis of cohort studies be undertaken to evaluate outcomes of intended home birth [6]. Using our peer-reviewed, published, registered protocol [7] (PROSPERO, http://www.crd.york.ac.uk, No.CRD42013004046) we undertook this systematic review and meta-analyses to determine if low-risk women who intend at the onset of labour to give birth at home are more or less likely to experience a fetal or neonatal loss compared to a cohort of similarly low-risk women who intend at the onset of labour to give birth in hospital.

2. Methods

Methods reported previously in our published protocol [7] were followed and are described briefly here.

2.1. Search Strategy and Study Selection

The search included studies from 1990 onward and was completed on April 11, 2018 using Embase, Medline, AMED, CINAHL, and the Cochrane Library. Terms either as keywords or subject headings included: home delivery, home birth, home childbirth, and homebirth. Reference lists from review articles and all included studies were crosschecked. Two reviewers independently selected studies for full review if they had comparison groups of women who were at similarly low-risk for birth complications, as defined in the study under review, and who were intending either to give birth in hospital or home; cohorts were defined by the intended location of birth rather than the actual location of birth; intention for a home birth was determined or reconfirmed at the onset of labour; parity was accounted for; and the study accounted for missing cases.

2.2. Data Collection

Two reviewers independently collected data from the included studies using a detailed data abstraction form, compared their findings and reached consensus. Missing information was requested from authors of included studies as necessary. Whenever possible, findings were reported by parity sub-groups.

Because they answer somewhat different questions, we categorised studies into one of two study designs to reflect the assembly of birth cohorts. In all cases the comparison group included women intending hospital birth and deemed to be at low obstetrical risk. Studies designed to determine the safety of home birth in actual practice, included all intended home births in a given time frame, regardless of whether they would be considered eligible for home birth according to local standards. These 'pragmatic' design studies answer the research question: "Do women who intend at the onset of labour to give birth at home experience a higher or lower incidence of fetal or neonatal loss compared to women at low obstetric risk who intend at the onset of labour to give birth in hospital?" Other studies focused on outcomes of place of birth among women who met local selection standards for home birth thus assuring that only those of low obstetrical risk were included and answer the question: "Do women who intend to give birth at home and who meet their local eligibility criteria for home birth at the onset of labour experience a higher or lower incidence of fetal or neonatal loss compared to women who would have been eligible for home birth but intend at the onset of labour to give birth in hospital?" The latter study design may have resulted in the exclusion of, for example, any twin births or breech births that may have been intended and occurred at home, but that were not supported by local standards. We termed studies of this design 'within standards.' We stratified all analyses by study design in order to address both research questions. In addition, in order not to compromise power to find small differences, we conducted sensitivity analyses for all outcomes without stratification as described in the Sensitivity Analyses section below.

We hypothesised a priori [7] that the degree of support for home birth and home birth care providers within the health care system where the study was carried out would act as an effect modifier of the relationship between intended place of birth and birth outcomes [8]. We termed this context for home birth, described in detail elsewhere, as a 'well-integrated' versus 'less well-integrated' home birth environment [9]. A well-integrated setting was described as a place where home birth practitioners: are recognised by statute within their jurisdiction; have received formal training; can provide or arrange care in hospital; have access to a well-established emergency transport system; and carry emergency equipment and supplies. Less well-integrated settings were those where one or more of these criteria are absent. Studies were categorised by an independent team of researchers [9] based on information found within the study, from the study's author via a questionnaire [9] about the context of care at the time their study was undertaken, and from secondary publications such as policies or statements regarding home birth in the country where the study took place (Table 1).

2.3. Outcome

Our primary outcome is any perinatal or neonatal death after the onset of labour. If a study reported these data both including and excluding malformed infants, to minimise categorisation bias we used data that included malformations in the primary analyses. Secondary outcomes include perinatal morality (defined as stillbirth after the onset of labour or death to 7 completed days) and neonatal mortality (defined as death between 0 and 28 days of a live born baby). Where possible, we report perinatal mortality and neonatal mortality separately; and mortality rate excluding malformed infants. Additional neonatal outcomes included neonatal resuscitation, Apgar scores of less than 7 at 1 min and less than 7 at 5 min, and admission to a neonatal intensive care unit (NICU). Definitions used by the authors for neonatal resuscitation and NICU admissions were recorded.

Because free standing birth centres cannot be considered to be a home or hospital setting, data from these out of hospital birth centres were not included. For studies that had more than one hospital comparison group, outcomes for the hospital groups were combined, provided that women in the groups being combined met eligibility criteria. If data for some or all outcomes could not be combined, we chose the comparison group most likely to minimise confounders; where the women were most like women choosing home birth, and the care providers were most like those providing care at home.

2.4. Risk of Bias

Our study eligibility criteria ensured that the observational studies included in the review had a control group, used an intention-to-treat

Table 1
Studies eligible for systematic review of perinatal and neonatal outcomes, stratified by degree of integration of home birth within the health care system and by study design.

		Type of integration into health system	
		Well-integrated	Less well-integrated
Study design	Pragmatic (includes all women who intend home birth at onset of labour)	Halfdandottir [27] Hutton [28] Hutton [3] Janssen [21] Janssen [22] van der Kooy [29] van der Kooy [19] Wiegers [24]	Blix [30] Lindgren [31]
	Within standards (includes only women who meet criteria for birth at home at ibset)	Brocklehurst [23] Davis [20] de Jonge [25] Hermus [26] Pang [18]	Hiraizumi [32] Homer [33]

approach (analysed by intended place of birth at the onset of labour), and controlled for parity. Study quality was assessed using The Newcastle Ottawa Quality Assessment Scale for Cohort Studies (NOS) [10]. Risk of publication bias across studies was assessed through inspection of inverted funnel plots for the primary outcome [11].

2.5. Synthesis of results

Meta-analyses were conducted using the 'metafor' package in R statistical software version 3.3.1. Log odds ratios (OR) and corresponding sampling variances for each study were calculated using

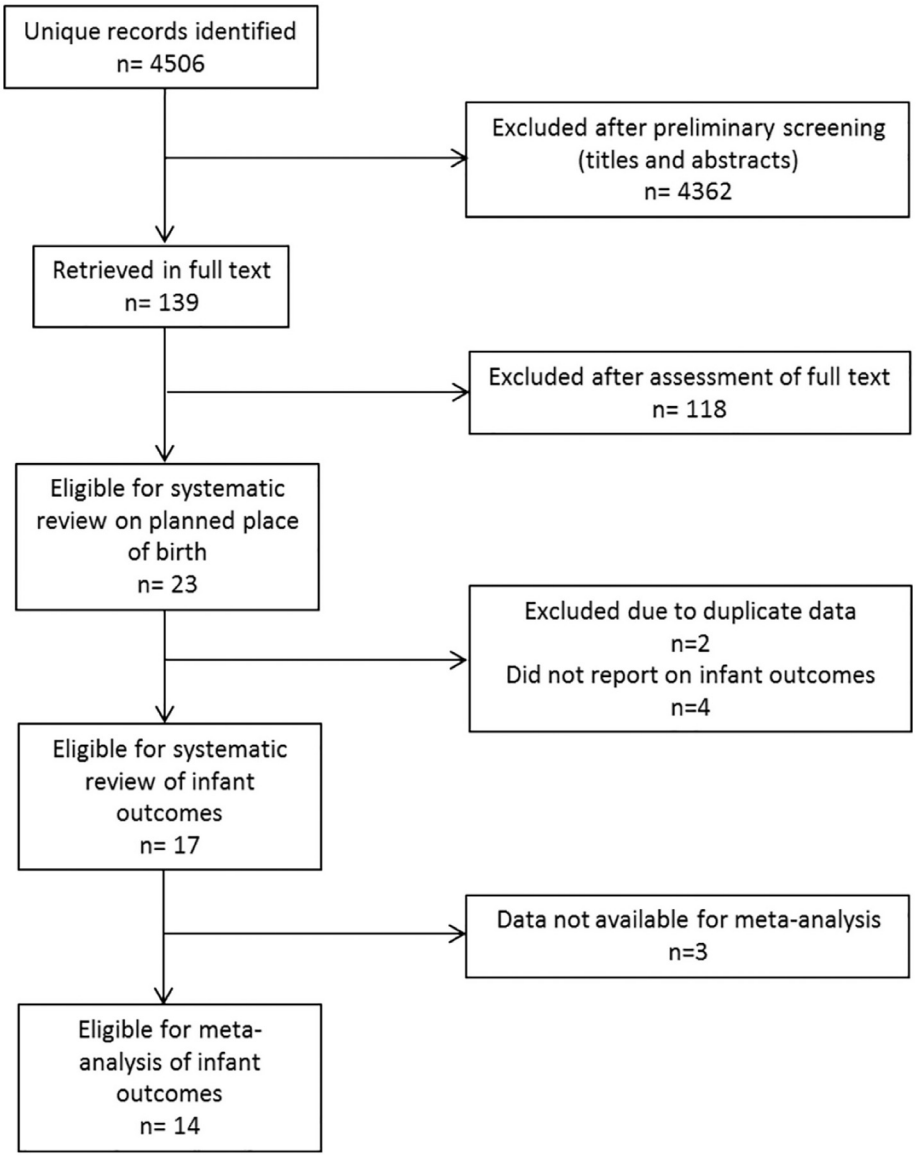


Fig. 1. Flow diagram of study selection.

Table 2
Description of included studies.

Study	Data source & time period	Method of accounting for parity	Nos quality score	Methods	Sample size	Setting and degree of integration	Outcomes reported	Author questionnaire completed
Blix E, et al. [30]	Home: Midwife's register, telephone interview, and midwife's birth protocols Hospital: Medical birth registry of Norway (MBRN) 1990–2007	Stratified	6	Pragmatic Retrospective cohort study	1631 home 16,310 hospital	Norway (Midwives less well-integrated)	**1**, **3**–**5**, **8**, 11, 12, 15–18	Yes
Birthplace in England Collaborative Group, [23]	Home: All NHS Trusts that provide home birth services OU: Random sample of 36 obstetric units within the NHS ALU: All NHS hospitals that have an alongside unit Data collection forms designed for this study 2008–2010	Stratified and adjusted	7	Within standards Prospective cohort study 4 groups: Obstetric Unit, Alongside Midwifery Unit, Free-standing birth centre, Home	16,840 home 16,710 ALU 19,706 OU 11,282 FSU Combined ALU and OU for comparison group	England (Midwives well-integrated)	**1**, **2**, **4**, **8**, **9**, 11, 12, 14–18	Yes
Bolten N, et al. [14]	DELIVER Study, recruited from 20 midwifery practices 2009–2011	Stratified	6	Within standards Prospective cohort study	2050 home 1445 hospital	Netherlands (Midwives well-integrated)	11, 12, 14, 16–18 No infant outcomes	Yes
Davis D, et al. [20]	Midwifery Maternity Provider Organisation Database 2006–2007	Adjusted	8	Within standards Retrospective cohort study	1830 home Primary unit 2877 Secondary hospital 7380 Tertiary hospital 4123 Used primary unit comparison group	New Zealand (Midwives well-integrated)	**8**, **9**, 11, 14, 16, 18	No
de Jonge A, et al. [15]	LEMMoN Study database, National Perinatal database I, National Perinatal database II, National Neonatal Register 2004–2006	Stratified	8	Within standards Prospective cohort study	92,333 home 54,419 hospital	Netherlands (Midwives well-integrated)	11 No infant outcomes	Yes
de Jonge A, et al. [25]	National Perinatal database I, National Perinatal database II, National Neonatal Register 2000–2009	Stratified	7	Within standards Retrospective cohort study	466,112 home 276,958 hospital 2000–2009	Netherlands (Midwives well-integrated)	**1**,**2**,**4**,**5**,**8**,**9**	Yes
Halfdansdottir B, et al. [27]	Icelandic electronic birth registry and original midwife and doctor records extracted by study author using a structured item list. 2005–2009	Matched and stratified	7	Pragmatic + Within standards Retrospective cohort study	307 home 921 hospital	Iceland (Midwives well-integrated)	**1**,**3**,**4**,**6**,**8**–11,14–18	Yes
Hermus M, et al. [26]	Midwifery practices using case report form developed for the study and linked with the Netherlands Perinatal Registry (Perined) 2013	Stratified	6	Within standards Prospective cohort study	1086 home 701 hospital	Netherlands (Midwives well-integrated)	**1**, **3**, **4**, **9**–12, 14–18	Yes
Hiraizumi Y, et al. [32]	Japanese Red Cross Katsushika Maternity Hospital database 2007–2011	Presumed matched, equal proportion in groups by parity	7	Within standards Retrospective cohort study	168 home 123 hospital	Japan (Midwives less well-integrated)	**8**,11–14,17,18	No
Homer C, et al. [33]	5 datasets in New South Wales. NSW Perinatal data collection NSW admitted patient data collection NSW register of congenital conditions NSW registry of births, deaths, and marriages Australian Bureau of Statistics 2000–2008	Stratified	7	Within standards Retrospective cohort study	735 home 221,284 hospital 2000–2008 (birth centre outcomes excluded)	Australia (Midwives less well-integrated)	**1**,**2**,**4**	Yes
Hutton EK, et al. [28]	Ontario Midwifery Program dataset 2003–2006	Matched, stratified	8	Pragmatic Retrospective cohort study	6692 home 6692 hospital 2003–2006	Ontario, Canada (Midwives well-integrated)	**1**–**3**,**5**,**6**,**8**–12, 14–18	Yes
Hutton EK, et al. [3]	Ontario Midwifery Program dataset 2006–2009	Matched, stratified	8	Pragmatic Retrospective cohort study	11,493 home 11,493 hospital	Ontario, Canada (Midwives well-integrated)	**1**–**6**,**8**,10–12, 14–18	Yes

(*continued*)

Table 2 (*Continued*)

Study	Data source & time period	Method of accounting for parity	Nos quality score	Methods	Sample size	Setting and degree of integration	Outcomes reported	Author questionnaire completed
Janssen P, et al. [21]	Home: Home Birth Demonstration Project Hosp: British Columbia Perinatal Database Registry 1998–1999	Matched, adjusted	6	Pragmatic Prospective and Retrospective cohort study	862 home 571 MW comparison 743 MD comparison Used MD comparison group	British Columbia, Canada (Midwives well-integrated)	**1,2,6–8,**11–18	Yes
Janssen P, et al. [22]	Home: BC Perinatal Database Registry + Rosters submitted to the College of Midwives of BC Hosp: BC Perinatal Database Registry 2000–2004	Matched, adjusted	6	Pragmatic Retrospective cohort study	2899 home 4752 MW comparison 5331 MD comparison Used MD Comparison group	British Columbia, Canada (Midwives well-integrated)	**1,2,4,6–8,** 10–18	Yes
Lindgren H, et al. [31]	Home: Home birth midwives reports, linked to Swedish Medical Birth Register Hosp: Swedish Medical Birth Register 1992–2004	Adjusted	6	Pragmatic Retrospective cohort study	897 home 11,341 hospital	Sweden (Midwives less well-integrated)	**1,2,4,**10–12, 16, 18	Yes
Miller S, et al. [16]	Midwives who chose to participate and report on their most recent nulliparous births. Not reported	Restricted to nulliparous	4	Within standards Retrospective cohort study	109 home 116 hospital	New Zealand (Midwives well-integrated)	11,12,14–18 No infant outcomes	Yes
Nove A, et al. [17]	St. Mary's Maternity Information System 1988–2000	Adjusted	8	Within standards Retrospective cohort study	5998 home 267,874 hospital	England (Midwives well-integrated)	11 No infant outcomes	Yes
Pang J, et al. [18]	Washington State birth certificate data 1989–1996	Adjusted, stratified	4	Within standards Retrospective cohort study	6133 home 10,593 hospital	Washington state, USA (Midwives well-integrated)	**1**,3,11 Data not available for meta-analysis	No
van der Kooy J, et al. [29]	Netherlands Perinatal Registry 2000–2007	Adjusted	7	Pragmatic Retrospective cohort study	402,912 home 219,105 hospital	Netherlands (Midwives well-integrated)	**1,2,4**	Yes
van der Kooy J, et al. [19]	Netherlands Perinatal Registry 2000–2007	Adjusted		Pragmatic Retrospective cohort study	402,912 home 219,105 hospital	Netherlands (Midwives well-integrated)	**1**, 18 Data not available for meta-analysis	Yes
Wiegers TA, et al. [24]	Questionnaires and the Birth Notification System 1990–1993	Stratified	6	Pragmatic Prospective and Retrospective cohort study	1140 home 696 hospital	Netherlands (Midwives well-integrated)	**1,3,4,9,**11,16–18	Yes

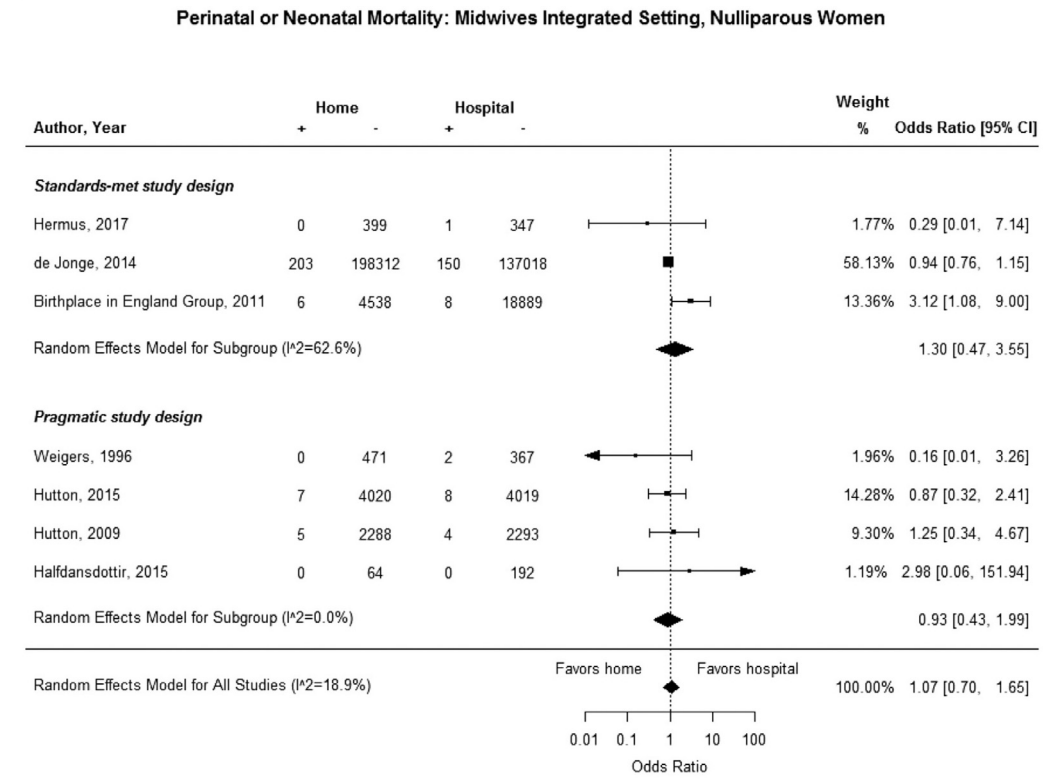
Outcomes reported by included studies are listed in the table as follows. Outcomes reported in this manuscript are bolded and underlined in the table.
1. Any perinatal or neonatal mortality.
2. Perinatal or neonatal mortality excluding malformations.
3. Perinatal or neonatal mortality including malformations.
4. Any perinatal mortality.
5. Any neonatal mortality.
6. Neonatal Resuscitation.
7. Apgar < 7 at 1 min.
8. Apgar < 7 at 5 min.
9. Admission to NICU.
10. Maternal mortality.
11. Postpartum hemorrhage
12. 3rd or 4th degree tear.
13. Maternal infection.
14. Oxytocin augmentation.
15. Epidural.
16. Episiotomy.
17. Assisted vaginal delivery.
18. Caesarean section.

count data or ORs and confidence intervals. For studies using the home birth group as the reference category, the OR was first inverted. For studies that reported risk ratios, if count data were provided and it was possible to calculate an OR, this was done. If the adjusted risk ratio was the only method by which parity was accounted for, we were unable to combine these data with ORs from other studies. In this case, risk ratios were described separately. Data were then pooled by fitting a random-effects model and forest plots were created. Pooled ORs, 95% confidence intervals and measures of consistency (I^2) were calculated for each outcome within strata (Table 1).

2.6. Sensitivity Analyses

We conducted a sensitivity analysis of our primary outcome excluding large datasets in order to determine if findings remained robust without those studies. We conducted sensitivity analyses for all outcomes without

a)



b)

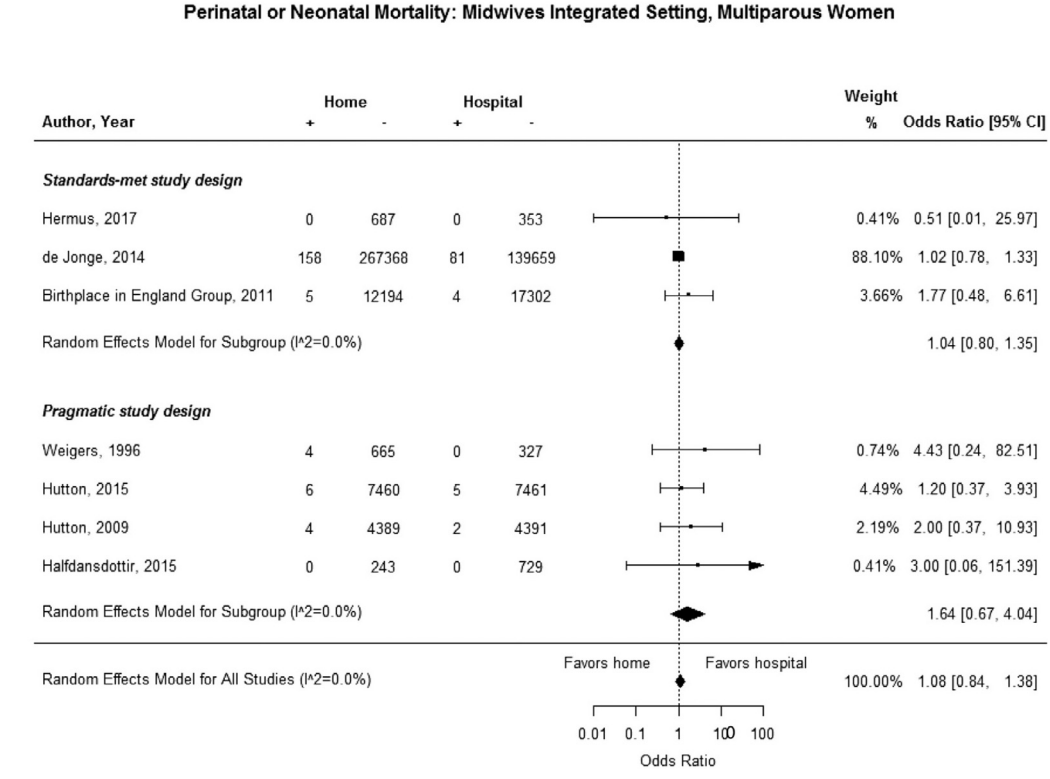
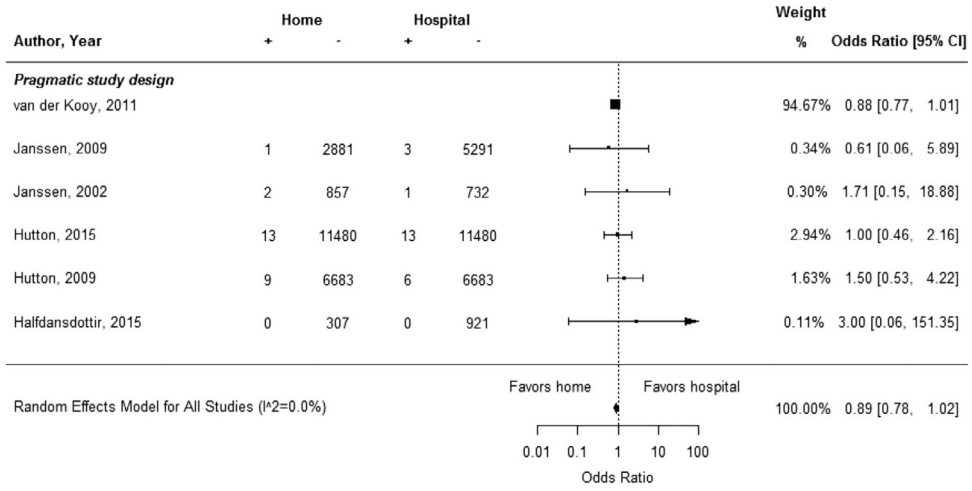


Fig. 2. Forest plots showing meta-analyses for the primary outcome of perinatal or neonatal mortality. Note that for the Birthplace in England Collaborative Group study (2011), the hospital comparison group included data from the obstetrical unit and alongside midwifery unit. For the studies by Janssen et al. (2002 and 2009), the physician-attended hospital group was used as the comparison.

c)



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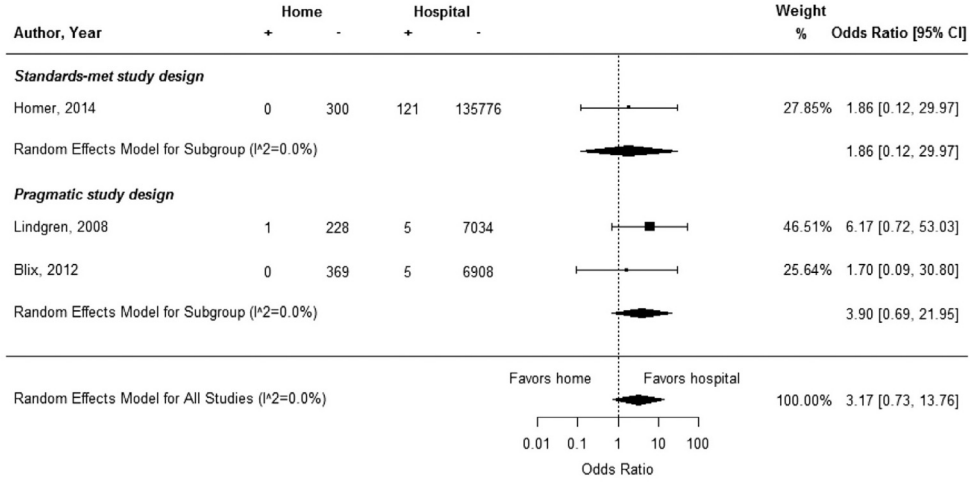

e)

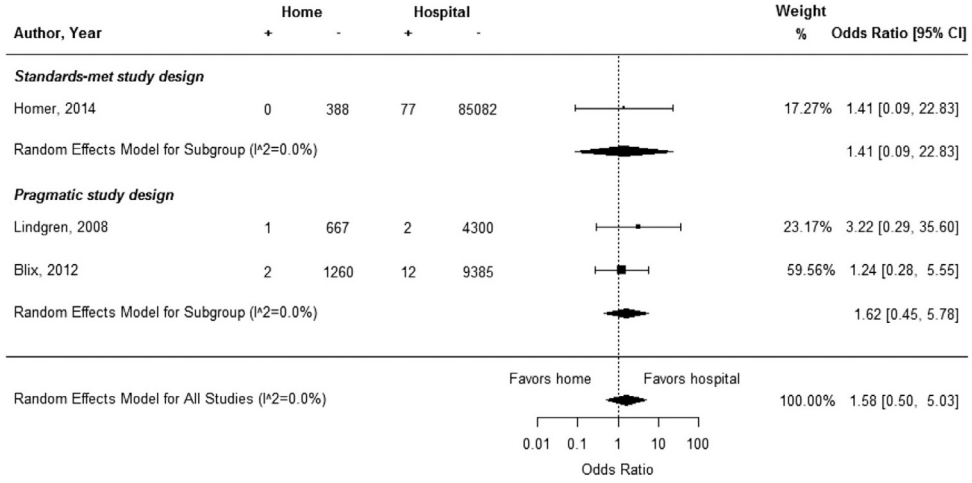

Fig. 2 Continued.

Table 3
Summary of perinatal and neonatal mortality meta-analyses findings derived from Fig. 2.

Strata	Number of studies	OR	95% CI	I^2
Primary outcome: perinatal or neonatal mortality (any)[a,b]				
Midwives well-integrated setting				
Nulliparas	7	1.07	0.70, 1.65	18.9%
Within standards	3 [23,25,26]	1.30	0.47, 3.55	62.6%
Pragmatic	4 [3,24,27,28]	0.93	0.43, 1.99	0%
Multiparas	7	1.08	0.84, 1.38	0%
Within standards	3[23,25,26]	1.04	0.80, 1.35	0%
Pragmatic	4 [3,24,27,28]	1.64	0.67, 4.04	0%
Not stratified by parity	–	–	–	–
Pragmatic	6 [3,21,22,27–29]	0.89	0.78, 1.02	0%
Midwives less well-integrated setting				
Nulliparas	3	3.17	0.73, 13.76	0%
Within standards	1 [33]	1.86	0.12, 29.97	n/a
Pragmatic	2 [30,31]	3.90	0.69, 21.95	0%
Multiparas	3	1.58	0.50, 5.03	0%
Within standards	1 [33]	1.41	0.09, 22.83	0%
Pragmatic	2 [30,31]	1.62	0.45, 5.78	0%
Outcome: perinatal or neonatal mortality (excluding malformed infants)				
Midwives well-integrated setting				
Nulliparas	4	1.17	0.70, 1.97	41.0%
Within standards	2 [23,25]	1.52	0.48, 4.85	79.1%
Pragmatic	2 [3,28]	1.00	0.45, 2.23	0%
Multiparas	4	1.08	0.83, 1.40	0.5%
Within standards	2 [23,25]	1.04	0.80, 1.35	0%
Pragmatic	2 [3,28]	1.80	0.60, 5.37	0%
Not stratified by parity	–	–	–	–
Pragmatic	4 [3,21,22,28]	1.20	0.66, 2.18	0%
Midwives less well-integrated setting				
Nulliparas	–	–	–	–
Within standards	1 [33]	1.86	0.12, 29.97	n/a
Multiparas	–	–	–	–
Within standards	1 [33]	1.41	0.09, 22.83	n/a
Outcome: perinatal or neonatal mortality (including malformed infants)[a,b]				
Midwives well-integrated setting				
Nulliparas	–	–	–	–
Pragmatic	3 [3,24,27]	0.80	0.31, 2.03	0%
Multiparas	–	–	–	–
Pragmatic	3 [3,24,27]	1.52	0.53, 4.39	0%
Not stratified by parity	–	–	–	–
Pragmatic	4 [3,27–29]	0.89	0.78, 1.01	0%
Midwives less well-integrated setting				
Nulliparas	–	–	–	–
Pragmatic	2 [30,31]	3.90	0.69, 21.95	0%
Multiparas	–	–	–	–
Pragmatic	2 [30,31]	1.62	0.45, 5.78	0%
Outcome: perinatal mortality[b]				
Midwives well-integrated setting				
Nulliparas	5	1.22	0.65, 2.27	39.1%
Within standards	2 [23,25]	1.52	0.48, 4.83	79.0%
Pragmatic	3 [3,24,27]	1.00	0.37, 2.70	0%
Multiparas	5	1.07	0.82, 1.38	0%
Within standards	2 [23,25]	1.06	0.82, 1.38	0%
Pragmatic	3 [3,24,27]	1.27	0.31, 5.27	0%
Not stratified by parity	–	–	–	–
Pragmatic	4 [3,22,27,29]	0.88	0.77, 1.01	0%
Midwives less well-integrated setting				
Nulliparas	3	3.58	0.82, 15.64	0%
Within standards	1 [33]	1.86	0.12, 29.97	n/a
Pragmatic	2 [30,31]	4.62	0.81, 26.37	0%
Multiparas	3	1.34	0.30, 5.91	0%
Within standards	1 [33]	1.41	0.09, 22.83	n/a
Pragmatic	2 [30,31]	1.31	0.23, 7.58	0%
Outcome: neonatal mortality				
Midwives well-integrated setting				
Nulliparas	2	0.96	0.71, 1.29	0%
Within standards	1 [25]	0.99	0.73, 1.34	n/a
Pragmatic	1 [3]	0.57	0.17, 1.95	n/a
Multiparas	2	1.08	0.74, 1.58	0%
Within standards	1 [25]	1.04	0.71, 1.54	n/a
Pragmatic	1 [3]	2.00	0.37, 10.92	n/a
Not stratified by parity	–	–	–	–
Pragmatic	2 [3,28]	1.07	0.50, 2.30	0%

(*continued*)

Table 3 (*Continued*)

Strata	Number of studies	OR	95% CI	I^2
Midwives less well-integrated setting				
Nulliparas	–	–	–	–
Pragmatic	1 [30]	2.08	0.11, 38.66	n/a
Multiparas	–	–	–	–
Pragmatic	1 [30]	0.68	0.09, 5.25	n/a

OR <1 favours intended home birth; >1 favours intended hospital birth.

[a] Note that Pang et al. (midwives well-integrated setting, within standards study design) reported: nulliparas RR 2.73 (95% CI, 2.06 to 7.06) and not stratified by parity RR 1.99 (95% CI, 1.06 to 3.73) [18].

[b] Note that van der Kooy et al. 2017 (midwives well-integrated setting, pragmatic study design) reported: RR 0.80 (0.71, 0.91) (not adjusted for parity) [19]. Had we included these data, the van der Kooy et al. 2011 data would have been excluded (for duplication) [29].

stratification by study design (pragmatic or within standards) to ensure that the smaller sample sizes resulting from stratification did not limit power and bias our analyses towards finding no difference.

2.7. Role of the Funding Source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

3. Results

The search, completed on April 11, 2018, provided 139 full text articles for review (Fig. 1) and resulted in 23 cohort studies that met our predefined inclusion criteria for systematic review of intended place of birth. Two of these studies [12,13] were excluded because they reported on data duplicated in other included studies and four studies because they did not include perinatal or infant outcomes [14–17]. Of 17 studies eligible for systematic review of perinatal or infant outcomes, three provided no data either published or from study authors [18–20] that could be included in a meta-analysis. Thus, the meta-analyses included 14 original cohort studies published between 1996 and 2017 that reported perinatal or neonatal outcomes for ~500,000 intended home births (Table 2). The precise number of births varies by analysis depending on the inclusion of one or the other of the large Dutch papers where there is likely considerable overlap in data. The included studies scored from 4 to 8 on the NOS. No randomised trials were found that included the outcomes of interest. A table of primary research studies excluded from this review can be found in Appendix 1.

Five included studies had more than one comparator group [20–23,33]. For the study by the Birthplace in England Collaborative Group, because all women included were low obstetrical risk, we combined outcomes of the midwifery alongside unit (an in-hospital birthing unit) and the obstetrical unit [23]. For a variety of reasons the multiple hospital comparison groups in Janssen's papers could not be combined [21,22] therefore we used the physician-attended hospital comparison group. For Davis et al., we used the primary unit comparison group [20]. For the paper by Homer et al. we included home and hospital groups and excluded the birth centre group because it may have included out of hospital birth centres.

3.1. Integration and Study Design

The 17 studies included in the systematic review (14 included in the meta-analyses) described here took place in ten settings, which are illustrated in Table 1. Thirteen studies took place in six settings where midwives attending home birth were considered to be well-integrated into the healthcare system (The Netherlands, England, Iceland, Canada, USA, New Zealand) [3,18–29]. Four studies took place in four settings where midwives attending home birth were considered to be less well-integrated into the healthcare system (Norway, Sweden, Japan, Australia) [30–33] as described elsewhere [9]. A pragmatic study design was used by ten studies [3,19,21,22,24,27–30,31], whereas seven studies included only those women who met local standards for home birth in their intended home birth cohorts [18,20,23,25,26,32,33].

3.2. Synthesis of Results

There was no difference in the primary outcome between those who intended home and those who intended hospital birth when data from 13 studies were pooled (Fig. 2 and Table 3). Among ten studies where midwives and homebirth were deemed to be well-integrated into the healthcare system, six reported results for all women (after accounting for parity through statistical adjustment or matching), and all used a pragmatic study design. The pooled OR (OR) was 0.89 (95% CI, 0.78 to 1.02). A sensitivity analyses that removed a large Dutch study (weighted 94.7% for this outcome) [29], remained non-significant for the primary outcome by intended place of birth for all women (after accounting for parity) (OR 1.16 (95% CI, 0.65 to 2.05)). Two studies reported findings as risk ratios and thus could not be included in any meta- analyses. The first, by van der Kooy et al. [19] reported outcomes similar to our pooled OR with a risk ratio (RR) of 0.80 (95% CI, 0.71 to 0.91). The second by Pang et al. used a within standards design and reported a RR of 1.99 (95% CI, 1.06 to 3.73), which favoured intended hospital birth [18].

Seven studies reported results stratified by parity in settings where midwives attending home birth were considered well-integrated into the healthcare system (three used a within standards design and four a pragmatic design). Regardless of study design and parity, no difference was found for the primary outcome between women who intended a home birth and those who intended a hospital birth. The pooled OR for nulliparous women was 1.07 (95% CI, 0.70 to 1.65) and for multiparous women 1.08 (95% CI, 0.84 to 1.38). The study by Pang et al. reported a risk ratio for nulliparous women which favoured hospital birth (RR 2.73 (95% CI, 1.06 to 7.06)) but failed to report outcomes for multiparous women [18]. Sensitivity analyses did not find statistically significant differences between intended home and hospital birth among nulliparous or multiparous women after excluding a large Dutch study (nulliparas OR 3.17 (95% CI, 0.73 to 13.76); multiparas OR 1.58 (95% CI, 0.50 to 5.03)) [25].

In settings where home birth was less well-integrated into the health care system, two studies used a pragmatic design and one a within standards design. All three studies reported results stratified by parity. The pooled ORs for all three studies did not show a statistically significant difference between intended home and intended hospital birth regardless of parity (nulliparas OR 1.25 (95% CI, 0.58 to 2.67); multiparas OR 1.62 (95% CI, 0.78 to 3.35)).

We did not find any significant differences by intended place of birth in mortality outcomes exclusive of morbidity that is for: perinatal or neonatal mortality excluding malformed infants; perinatal or neonatal mortality including malformed infants; perinatal mortality; neonatal mortality (Table 3). These findings held true regardless of parity, degree of integration of midwives providing home birth care or study design.

An Apgar score less than seven at 5 min occurred less frequently among intended home births compared to hospital births in multiparas in settings where midwives were well-integrated (OR 0.76 (95% CI, 0.60 to 0.96). This difference was not found among nulliparous women or when results were not stratified by parity. In addition, the study by Davis et al., that could not be combined due to use of risk ratios, reported no significant difference (for all women) [20]. Two studies from settings where midwives were less well-integrated into the healthcare system reported this outcome, but the findings could not be combined in meta-analyses. Neither found a significant difference (Table 4).

An Apgar score less than seven at 1 min was reported by two studies [21,22]. Both took place in settings where midwives attending home birth were well-integrated and used a pragmatic design and neither stratified by parity. A meta-analysis of these studies found a statistically significant difference in favour of intended home birth compared to intended hospital birth (OR 0.73 (95% CI 0.63 to 0.83)) (Table 4).

Need for neonatal resuscitation was reported in five studies [3,21,22,27,28], where midwives attending home birth were well-integrated and where a pragmatic study design was used. A meta-analysis found no significant difference by intended place of birth for all women. Only one study stratified by parity and reported no difference among parity groups on need for neonatal resuscitation (Table 4).

Of seven studies that reported on NICU admissions all were settings where midwives attending home birth were well-integrated, but one could not be combined in meta-analysis [20]. Among nulliparous women, no difference in NICU admissions was found by intended place of birth, regardless of study design. Studies using a within standards study design reported fewer infant admissions to NICU born to multiparous women who intended home birth (OR 0.73 (95% CI, 0.65 to 0.83)). This finding held true when these studies were meta-analysed with the pragmatic studies (OR 0.73 (95% CI, 0.65 to 0.82)). This difference was also seen when stratification for parity was removed and all women were included (OR 0.83 (95% CI, 0.69 to 0.99) (Table 4). Davis et al. reported no difference for NICU admission among all women by intended place of birth (RR 1.00 (95% CI, 0.66 to 1.50)) [20].

Table 4
Summary of infant morbidity meta-analyses findings.

Strata	Number of studies	OR	95% CI	I^2
Outcome: Apgar score < 7 at 5 min[a]				
Midwives well-integrated setting				
Nulliparas	3	1.19	0.76, 1.87	83.2%
Within standards	2 [23,25]	1.12	0.69, 1.84	91.0%
Pragmatic	1 [27]	2.07	0.56, 7.57	n/a
Multiparas	3	**0.76**	**0.60, 0.96**	44.8%
Within standards	2 [23,25]	**0.77**	**0.60, 0.99**	64.1%
Pragmatic	1 [27]	0.33	0.04, 2.62	n/a
Not stratified by parity	6	0.87	0.74, 1.03	0%
Within standards	1 [23]	0.94	0.71, 1.25	n/a
Pragmatic	5 [3,21,22,27,28]	0.84	0.69, 1.03	0%
Midwives less well-integrated setting				
Nulliparas	–	–	–	–
Pragmatic	1 [30]	0.14	0.01, 2.22	n/a
Multiparas	–	–	–	–
Pragmatic	1 [30]	0.60	0.18, 1.95	n/a
Not stratified by parity	–	–	–	–
Within standards	1 [32]	1.10	0.18, 6.68	n/a
Outcome: Apgar score < 7 at 1 min				
Midwives well-integrated setting				
Not stratified by parity	–	–	–	–
Pragmatic	2 [21,22]	**0.73**	**0.63, 0.83**	0%
Outcome: neonatal resuscitation				
Midwives well-integrated setting				
Nulliparas	–	–	–	–
Pragmatic	1 [27]	4.20	0.91, 19.30	n/a
Multiparas	–	–	–	–
Pragmatic	1 [27]	0.85	0.28, 2.62	n/a
Not stratified by parity	–	–	–	–
Pragmatic	5 [3,21,22,27,28]	1.02	0.72, 1.43	0%
Outcome: NICU admission[b]				
Midwives well-integrated setting				
Nulliparas	5	0.93	0.85, 1.02	0%
Within standards	3 [23,25,26]	0.94	0.85, 1.04	0%
Pragmatic	2 [24,27]	1.00	0.40, 2.48	77.9%
Multiparas	5	**0.73**	**0.65, 0.82**	0%
Within standards	3 [23,25,26]	**0.73**	**0.65, 0.83**	2.4%
Pragmatic	2 [24,27]	0.66	0.43, 1.03	0%
Not stratified by parity	3	**0.83**	**0.69, 0.99**	5.3%
Within standards	1 [23]	**0.73**	**0.57, 0.94**	n/a
Pragmatic	2 [27,28]	0.92	0.73, 1.17	0%

OR < 1 favours intended home birth; > 1 favours intended hospital birth.
Bolded values reflect statistical significance with $p < 0.05$

[a] Note that Davis et al. (midwives well-integrated setting, within standards study design) reported: not stratified by parity RR 0.81 (95% CI, 0.39 to 1.68) (adjusted for maternal age, parity, ethnicity and smoking) [20].

[b] Note that Davis et al. (midwives well-integrated setting, within standards study design) reported: RR 1.00 (0.66 to 1.50) (adjusted for maternal age, parity, ethnicity and smoking) [20].

3.3. Risk of Bias Across Studies

Inverted funnel plots were created to assess for reporting bias across studies for our primary outcome, one for each strata of analysis, resulting in five plots. However, plots with fewer than ten studies are difficult to interpret [11] and the largest of our plots included only seven studies (Appendix 2).

4. Discussion

This is the first systematic review and meta-analysis that has used a peer-reviewed, pre-published, registered protocol. Our results show that among low risk women who intend to give birth at home when labour starts there is no increase in perinatal and neonatal mortality or morbidity compared to similarly low risk women who intend to give birth in a hospital. There were no differences between intended home and intended hospital groups in other neonatal outcomes including NICU admission, Apgar scores, and the need for resuscitation.

In order to fully understand any effects of intended place of birth and ensure that we did not miss any mortality outcome that could be related to place of birth, we considered perinatal and neonatal mortality together as our primary outcome. Combining these outcomes increased the number of events thus increasing the power of our study to determine any clinically important differences. We recognise that regional variation may occur in definitions, or criteria to access care. However, the definition or criteria used within each reference study is likely to be consistently applied to all study participants within that study. By eliminating within study variance the likelihood of bias in our meta-analyses is minimised. Thus, for example, criteria to determine NICU admission may have varied across studies. Some may have included only NICU admissions, others may have included both NICU and special care admissions; however because within each study these approaches were used consistently for all participants we have confidence in our finding that there was no increased need for higher level care with births planned at home. In addition, with regard to perinatal mortality, the jurisdictional variation in definition that exists arises primarily from the way in which lower limits of viability are determined. Because our study included only those with low-risk pregnancies at the onset of labour, pre-term and in particular extreme preterm births are eliminated from the population under study, thus removing any concern about consistency of definition in our primary outcome.

We included only those papers that met our inclusion and exclusion criteria as defined a priori. For example, papers where cohorts for planned home birth were made early in pregnancy were excluded because changes in risk status can require a change in planned place of birth, studies with no comparison groups, or only comparison to birth centre cohorts were excluded, and so on. Other reviews have limited the scope of their review to deal with design differences or do not account for parity [34]. Because parity is such a strong

predictor of birth outcome, we included only those studies where parity was accounted for and stratified our results by parity. In terms of study design, our study takes a more inclusive approach and includes all relevant studies, dealing with design differences through stratification. In order to provide the most comprehensive understanding of the impact of choice of birthplace on perinatal outcomes, we present data both stratified and combined wherever possible to indicate where differences exist. Research design (pragmatic and within standards) did not have a significant impact on the results as findings were similar for the sub-set of women who met local criteria for choosing home birth, and for studies that included all women who intended a home birth, and thus may have included some who were non-compliant with local selection criteria. Outcomes were similar among nulliparous and multiparous women, and in settings where midwives providing home birth care were well-integrated into healthcare systems and where they were less well-integrated, although the data from integrated settings is more robust.

Select sub-groups showed results favouring home birth. The one exception to the primary outcome findings lies with the sole American study included in the review [18]. This study could not be included in the meta-analyses; however, the findings indicated a significant increase in perinatal and neonatal mortality associated with intended home birth.

As documented in our published protocol, we hypothesised a priori that the degree of support for home birth and home birth care providers within the health care system may act as an effect modifier of the relationship between intended place of birth and birth outcomes. In order to determine whether home birth and home birth providers are integrated into the health care system we collected information from each study about whether practitioners were recognised care providers within the health care system and could facilitate smooth transition from home to hospital and transfer of care to consultants when needed. Where information in the article was not explicit, we looked to secondary sources for supporting evidence, and considered information about recognition of midwifery, hospital admitting privileges for midwives or other home birth attendants, the presence of a statement regarding home birth from the jurisdiction's society/association of obstetricians and how home birth is funded. In addition, we contacted all authors of the included publications and asked them to complete a brief questionnaire, which provided information about the degree of integration of home birth within their health care system at the time that the data were collected [7]. Table 1 indicates whether authors responded to the survey with only 3 non-responders (<80% response rate). A more fulsome description of this concept is described in our earlier publication [9]. We feel confident in the process that was undertaken and the categorisations of jurisdictions on the context for midwives providing home birth care as 'integrated' versus 'less well-integrated'.

The highest quality studies came from large registries that were used in places where midwives providing home birth care were well-integrated into the health care system. Many home birth studies were ineligible for this review due to issues in study methodology such as: not including a control group of low-risk hospital births from the same region and time frame as the home births; not controlling for parity using matching, adjustment, or stratification; and excluding intended home births that transferred to hospital in labour from the home birth cohort thus potentially underestimating adverse outcomes. A table describing excluded studies provides transparency in our exclusion criteria (Appendix 1). We found that home birth studies occurring in less well-integrated settings were more often excluded perhaps due to inferior data collection practices. This may have resulted in an unavoidable bias towards excluding those studies most likely to have had untoward outcomes. In particular, having fewer quality studies from less well-integrated settings resulted in loss of power and findings that were less precise. Thus, although we found no difference in mortality outcomes for intended home versus hospital births in less well-integrated settings there was a trend towards favouring hospital birth that is, perhaps, of interest. Generalisability of our findings should, therefore, be undertaken cautiously. We challenge readers to interpret the safety of home birth within a greater societal context and consider the integration of home birth practices within health care systems.

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Contributors

All authors formulated the research objectives and designed the study methodology. GB conducted the literature search. AR and JS screened citations for eligibility and extracted data from eligible studies. JS conducted the data analyses. EKH, AR and JS prepared the initial manuscript draft. All authors edited the manuscript and approved the final version.

Declaration of Competing Interest

We declare no competing interests.

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