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Review

Neonatal Outcomes in the Birth Center Setting: A Systematic Review

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Introduction: This systematic review investigates the effect of the birth center setting on neonatal mortality in economically developed countries to aid women and clinicians in decision making.

Methods: We searched the Google Scholar, CINAHL, and PubMed databases using key terms *birth/birthing center* or *out of hospital* with *perinatal/neonatal outcomes*. Ancestry searches identified additional studies, and an alert was set for new publications. We included primary source studies in English, published after 1980, conducted in a developed country, and researching planned birth in centers with guidelines similar to American Association of Birth Centers standards. After initial review, we conducted a preliminary analysis, assessing which measures of neonatal health, morbidity, and mortality were included across studies.

Results: Neonatal mortality was selected as the sole summary measure as other measures were sporadically reported or inconsistently defined. Seventeen studies were included, representing at least 84,500 women admitted to a birth center in labor. There were substantial differences of study design, sampling techniques, and definitions of neonatal outcomes across studies, limiting conclusive statements of the effect of intrapartum care in a birth center. No reviewed study found a statistically increased rate of neonatal mortality in birth centers compared to low-risk women giving birth in hospitals, nor did data suggest a trend toward higher neonatal mortality in birth centers. As in all birth settings, nulliparous women, women aged greater than 35 years, and women with pregnancies of more than 42 weeks' gestation may have an increased risk of neonatal mortality.

Discussion: There are substantial flaws in the literature concerning the effect of birth center care on neonatal outcomes. More research is needed on subgroups at risk of poor outcomes in the birth center environment. To expedite research, consistent use of national and international definitions of perinatal and neonatal mortality within data registries and greater detail on adverse outcomes would be beneficial.
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Keywords: birth center, birthing center, neonatal mortality, neonatal outcomes, out-of-hospital birth, perinatal mortality, perinatal outcomes, midwifery unit

INTRODUCTION

Birth centers provide out-of-hospital maternity care to low-risk women in many economically developed countries. They are recognized by the American College of Obstetricians and Gynecologists and the American College of Nurse-Midwives as an appropriate location of birth for low-risk women with uncomplicated pregnancies.[1] The National Institute for Health and Clinical Excellence (NICE) advises low-risk women in England to consider out-of-hospital birth to improve outcomes.[2] In the United States, planned out-of-hospital birth settings include homes, birth centers accredited by the Commission for the Accreditation of Birth Centers (CABC), and nonaccredited centers. In 2014, 30% of out-of-hospital births in the United States occurred in birth centers.[3,4]

Birth centers accredited by the CABC are required to have licensed and/or certified providers and emergency equipment available, as well as formal transfer relationships with local hospitals.[5,6] Centers accredited by the CABC may be freestanding, meaning they are not attached to a hospital, or they may be a distinctly separate facility physically attached to or housed within a hospital. Clear clinical guidelines and an integrated approach to transfer improve outcomes and differentiate birth in an accredited center from other types of out-of-hospital birth.[6,7] While there is published research on outcomes of out-of-hospital birth, there are few publications synthesizing current literature on birth center safety,[8] and no systematic reviews of outcomes for infants born in accredited or similar birth centers. Since poor neonatal outcomes are rare in the developed world and births within birth centers make up only a fraction of total births in developed nations,[9] synthesis of studies increases the ability to identify trends. Our original intention was to perform a systematic review of neonatal outcomes associated with birth center care in developed countries and compare outcomes across studies and between low-risk hospital comparison groups provided within the studies. However, good, uniform measures of neonatal outcomes are not consistent across this body of literature, thereby not allowing for meaningful comparisons. As a result, our review was refined; this article systematically reviews the peer-reviewed literature on neonatal mortality related to care in birth centers that follow components of care similar to the American Association of Birth Centers (AABC) Standards for Birth Center Care,[6] and compares neonatal outcomes across studies and against within-study comparison groups.

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Quick Points

- The review encompassed 17 studies of intrapartum care in birth centers using clinical practice guidelines similar to the American Association of Birth Center Standards. The studies included more than 84,500 pregnant women between 1982 and 2011.
- No researchers using a low-risk hospital control group found a statistically significant difference in mortality between groups; 4 articles reported lower rates in the birth center, and 5 found higher rates that were not statistically significant. Three studies reporting higher mortality rates among the birth center sample noted that deaths occurred long after antepartum transfer and/or were not related to location of birth.
- Consistent with the literature on birth in all settings, newborns of women who are nulliparous, aged greater than 35 years, or with pregnancies of more than 42 weeks' gestation may have an increased risk of neonatal mortality.
- The inability to combine study data and examine outcomes by covariates known to affect perinatal mortality, such as parity and maternal and gestational age, limits the ability to make conclusive statements about which subgroups may have increased risk of poor neonatal outcomes in the birth center setting compared with the hospital setting.
- Use of national and international definitions of perinatal and neonatal mortality within data registries, as well as inclusion of details of adverse outcomes, would be beneficial in expanding research on this location of birth.

METHODS

The following inclusion and exclusion criteria were used to identify applicable research: primary source studies published after 1980 in peer-reviewed journals, English text available, conducted in a developed country as outlined by World Bank criteria, research that assessed outcomes of planned birth in a birth center with guidelines similar to AABC standards as specified by 7 specific components of care (Table 1), and reported neonatal outcome data but not focused on a single component of care such as vaginal birth after cesarean or breastfeeding. These criteria were selected because the first study of US birth center care was published in 1980 as identified in a previous literature review[8]; our team could only critically assess literature in English; peer-reviewed journals and publications have greater quality and veracity of findings; developed countries have the infrastructure needed to support rapid transport to higher-level care, moreover the inclusion of international studies expands the available literature; and the AABC standards provide concise criteria to differentiate birth center care. The Standards for Birth Centers include 7 criteria that have been key components of birth center care since the beginning of what is now AABC and differentiate adhering centers from facilities that care for moderate- and high-risk women.[6] In investigating the effect of location of intrapartum care, we wanted sources to be comprehensive and not limited to a single variable other than morbidity and mortality.

In August 2015, we searched the Google Scholar, CINAHL, and MEDLINE/PubMed databases using key terms *birth/birthing center* or *out of hospital* with *perinatal/neonatal outcomes*. This strategy resulted in 2837 citations from PubMed and CINAHL, and 23,700 from Google Scholar (Figure 1). Initial screening of the citations for inclusion and exclusion criteria using advanced search techniques within the search engine (eg, English sources, peer-reviewed journals, published after 1980) as well as searching within the references of obtained sources resulted in 333 citations whose abstracts were reviewed for congruence with inclusion and exclusion criteria. An alert was set for new publications, and the ClinicalTrials.gov website was searched for pertinent clinical trials.

Of the 333 abstracts reviewed in August 2015, 31 sources appeared to meet the criteria for inclusion, and the full-text articles were obtained for comprehensive review. Five additional studies, published later, were discovered via citation alerts and their full-text reviewed; 4 were found not to meet inclusion criteria, and one was included in analysis. Each of the 36 studies meeting initial screening criteria was assessed for inclusion and exclusion criterion and data quality by authors (J.C.P., K.D., and J.A.). In articles with tables, the calculations were checked. Any inaccuracies were rechecked by outside experts to assess if the error affected study results. Two sources had mathematical errors; of these, one study was excluded due to a calculation error in the birth center data.[10] Two studies were excluded because a significant proportion of their samples included home birth or nonaccredited birth centers that do not

Table 1. Birth Center Components Required for Study Inclusion

Home-like environment
Providers are licensed in the geographic area or certified by a national certifying organization
Regular assessment of maternal risk status with only low-risk women permitted to have intrapartum care in the birth center (the definition of low-risk changes over time)
Fetus is assessed to be term, singleton, and vertex at the time of intrapartum admission
Intermittent intrapartum monitoring only
Regional anesthesia, forceps, or vacuum assist not provided in the birth center
Synthetic oxytocin (Pitocin) used only postpartum

Adapted from the American Association of Birth Centers Standards for Birth Centers.[6]

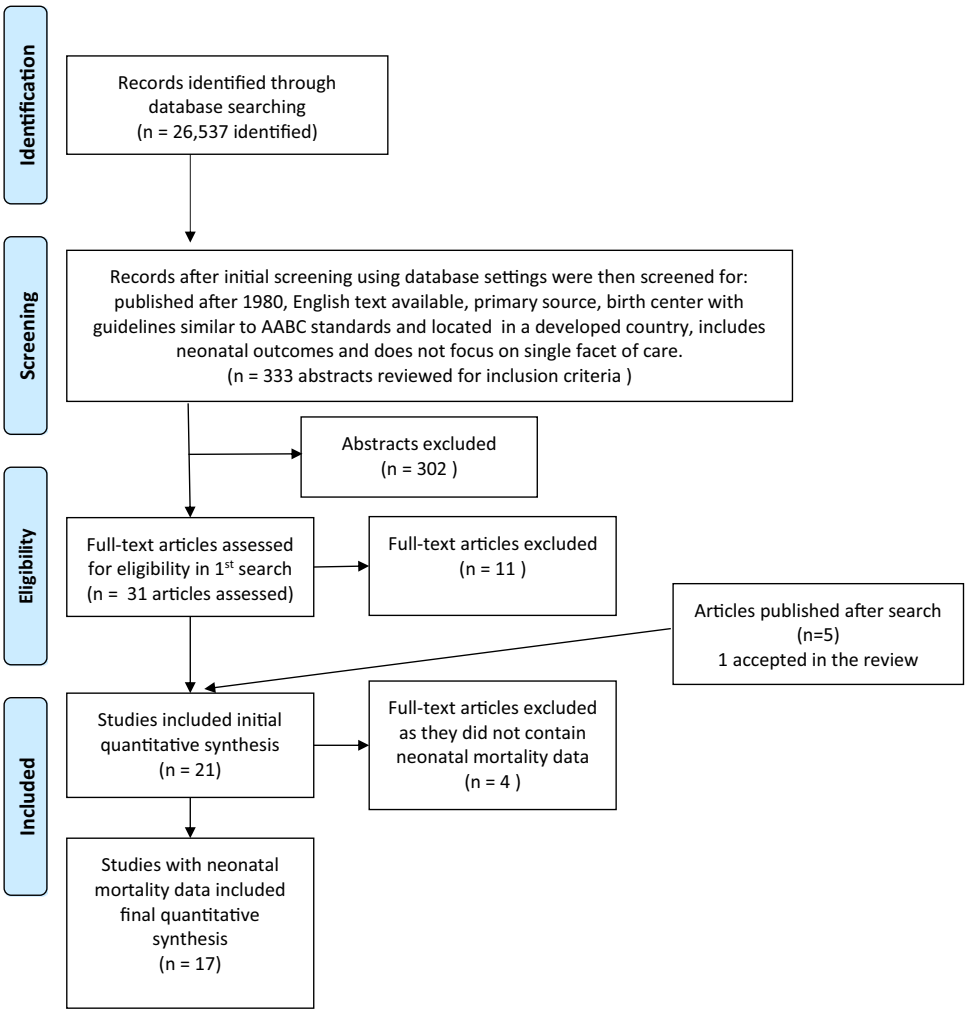

Figure 1. PRISMA flow diagram of article identification and screening

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med.* 6(7):e1000097.

consistently uphold AABC standards.[11,12] Twenty-one studies were included in the initial outcomes review assessing neonatal outcomes.

Neonatal outcomes data were entered into a table by one author and rechecked for accuracy by a second. Differences were reconciled through discussion and verification by a third author. After table completion and verification, we conducted a preliminary analysis, assessing which high-quality measures of neonatal health, morbidity, and mortality were included across studies. Neonatal mortality was chosen as the sole summary measure as other measures were sporadically reported or inconsistently defined. Studies that did not report neonatal mortality (4 articles) were removed from analysis, leaving 17 in the final review (Table 2).

PRISMA guidelines for systematic review include an assessment of study bias[29-30]; however, there are problems with bias within the birth center literature as a whole. It is ethically difficult to randomize women to birth locations, creating selection bias in all but the 3 studies that did randomize women to a birth site,[18–20] and even those randomized studies noted the women assigned to the control group may have been dissatisfied as they entered the study with a desire for birth center care.[15,18–20] Instead, most researchers examined perinatal outcomes by place of birth or women's intended place of birth, introducing selection and sampling bias and preventing blinding. While researchers may employ an intent-to-treat analysis to decrease bias, inconsistency exists across the literature on when in pregnancy to generate the sample and begin the intent-to-treat approach (at the first prenatal appointment, at the beginning of labor, upon admission to the birth center, or at the time of birth). Publication bias may also exist as researchers or journals may not publish studies with mortality rates skewed by one death in a small sample.

We acknowledged these caveats as relevant to the body of literature and did not assess them at the individual level. We included studies employing a variety of sampling strategies in order to capture all outcomes potentially related to birth center care. For example, limiting the review to studies of women admitted to the birth center in labor may have advantages for studying effects of birth location on neonatal outcomes; however, when women planning birth center care have complications and present first to a birth center, treatment delays

Table 2. Literature Review Table

Study, Setting, Design, Dates, and Sample	Definition of Mortality, Perinatal Mortality Rate With Details About Perinatal Deaths and Transfer Rates
Scupholme et al[13] 1986 Freestanding BC in Florida, United States Prospective matched cohort study Data collected 1982-1984 BC sample: 250 women who planned BC birth at onset of labor, including those transferred to the hospital after initial assessment and prior to BC admission. Comparison sample: 250 matched low-risk women in hospital	Mortality rate includes IP and neonatal deaths. No clear definition of neonatal mortality provided. IP transfers: 21% BC mortality (per 1000 births): 0 (1 death at 5 weeks due to congenital anomaly) Low-risk hospital mortality (per 1000 births): 0
Feldman & Hurst[14] 1987 Freestanding BC in New York, United States Retrospective matched cohort study Data collected 1981 BC sample: 77 women who planned BC birth at 37 weeks. Sample includes AP transfers after 37 weeks. Comparison sample: 72 matched low-risk women in hospital	Mortality rate includes fetal deaths after 37 weeks, IP and neonatal deaths. No clear definition of neonatal mortality provided. AP transfers: 8% IP transfers: 14% BC mortality (per 1000 births): 0 Low-risk hospital mortality (per 1000 births): 14 (n = 1)[a]
Scupholme & Kamons[15] 1987 Freestanding BC in Florida, United States Prospective matched cohort study Data collected 1984-1985 BC sample: 494 women admitted to BC in labor; 281 assigned to BC care; 213 self-selected BC care; 148 matched pairs	No clear definition of neonatal mortality provided IP transfers in assigned group: 24% IP transfers in self-selected group: 26% BC mortality (per 1000 births): 0 (in both groups)

(*Continued*)

Table 2. Literature Review Table

Study, Setting, Design, Dates, and Sample	Definition of Mortality, Perinatal Mortality Rate With Details About Perinatal Deaths and Transfer Rates
Rooks et al[16] 1989 84 freestanding BCs in 35 states in the United States Prospective observational study—no comparison group Data collected 1985-1987 BC sample: 11,814 women admitted to BC in labor. Denominator is 11,826 infants, which is greater than number of women due to 12 sets of unexpected twins.	Mortality rate includes IP and infant deaths. All infant deaths reported were within 7 days, but infant death data collected at 6-week PP visit. No clear definition of neonatal mortality provided. IP transfers: 12% BC mortality (per 1000 births): IP: 0.42[a] Neonatal: 0.85[a] Total: 1.27[a] BC mortality excluding congenital anomalies (per 1000 births): IP: 0.34[a] Neonatal: 0.34[a] Total: 0.68[a] Deaths not due to congenital anomaly (p. 1808): IP deaths (n = 4, n = 5 w anomalies) 1. Term pregnancy, partial placenta previa, died in BC. 2. Term pregnancy, transfer during first stage for meconium and fetal distress. Born in hospital. 3. Postterm pregnancy, placental abruption (died in BC). 4. Posterm pregnancy, low-grade fever and preeclampsia (died in BC). Neonatal deaths (n = 4, n = 10 w anomalies) 1. Term pregnancy, transfer in first stage of labor for fetal distress, born and died in hospital with pneumonia and pneumothorax. 2. Term pregnancy, prolonged rupture of membranes, born in BC with transfer for respiratory distress, pneumonia, and hyaline membrane disease. Died in hospital. 3. Postterm pregnancy, transferred in first stage of labor for thick meconium and fetal distress. Born and died in hospital. 4. Term pregnancy, uncomplicated labor. Died at home at 1 week, autopsy revealed no cause (SIDS).
Rooks et al[17] 1992 Same study as above Data collected 1985-1987	Mortality rate includes IP and infant deaths. All infant deaths reported were within 7 days, but infant death data collected at 6-week PP visit. No clear definition of time period for neonatal mortality. BC mortality by parity (per 1000 births): Para 0: 1.7^ Para 1 or 2: 1.0^ Para 3 or 4: 0^ Para 5: 5.6^ (1 of 177) BC mortality by EGA (per 1000 births): 37-42 weeks: IP: 0.20[a] Neonatal: 0.71[a] Total: 0.91[a] 37-42 weeks without anomalies: IP: 0.20[a] Neonatal: 0.30[a] Total: 0.51[a] ≥42 weeks: IP: 2.30[a] Neonatal: 1.53[a] Total: 3.83[a] ≥42 weeks without anomalies: IP: 1.53[a] Neonatal: 0.77[a] Total: 2.30[a]

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Table 2. Literature Review Table

Study, Setting, Design, Dates, and Sample	Definition of Mortality, Perinatal Mortality Rate With Details About Perinatal Deaths and Transfer Rates
MacVicar et al[18]	Data provided by study include stillbirths (undefined) and infant deaths <7days.
1993	AP transfers: 23%
Alongside BC in Leicester, United Kingdom	IP transfers: 22%
Randomized control trial with 2-to-1 randomization	Percent giving birth in BC: 46%
Data collected 1989-1991	BC mortality (per 1000 births): Stillbirths: 5.64[a] Neonatal: 2.17[a] Total: 7.81[a]
BC sample: 2304 low-risk women randomized to BC.	Low-risk hospital mortality (per 1000 births, 2-to-1 randomization): Stillbirths: 4.15[a] Neonatal: 0
Intent-to-treat sample includes AP transfers (23%) and women who declined birth center care (8%). 1553 women admitted in labor. Comparison sample: 1206 low-risk women randomized to hospital care	Deaths (pp. 319-320): Stillbirths (n = 13) Authors note majority of women with stillborn neonates had been referred to specialist care prior to IUFD. Possible avoidable factors identified in 2 deaths: 1. Reported decreased fetal movement in the week prior to birth with no electronic fetal monitoring or antenatal testing ordered; IUFD upon admission in labor. 2. Fetal tachycardia (160 bpm) via Doppler on admission, no further testing ordered, no heart tones heard after AROM with thick meconium. Neonatal (n = 5) 1. Two deaths were at <28 weeks' gestation, prior to first BC prenatal care appointment. 2. Remaining 3 deaths were to women who had been referred to specialist care during pregnancy. Deaths were due to hydrocephaly, nonimmune hydrops, and GBS sepsis.

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Table 2. Literature Review Table

Study, Setting, Design, Dates, and Sample	Definition of Mortality, Perinatal Mortality Rate With Details About Perinatal Deaths and Transfer Rates
Hundley et al[19] 1994 Alongside BC in Aberdeen, United Kingdom Randomized control trial with 2-to-1 randomization Data collected 1991-1992 BC sample: 1900 low-risk women randomized to BC. Intent-to-treat sample includes AP transfers. Comparison sample: 944 low-risk women randomized to hospital care.	Perinatal mortality undefined. Data provided by study include IUFDs, stillbirths (undefined), and infant deaths (time period undefined). AP transfer: 38% IP transfer: 16% Percent giving birth in BC: 46% BC mortality (per 1000 births): Stillbirths: 3.16[a] Stillbirths excluding congenital anomalies: 2.63[a] Neonatal death: 4.74[a] Stillbirths + Neonatal deaths: 7.89[a] Total including IUFDs: 10.53[a] Hospital mortality (per 1000 births): Stillbirth: 4.24[a] Neonatal deaths: 2.12[a] Stillbirths + Neonatal deaths: 6.36[a] Deaths (p. 1402): Stillbirths (n = 6) In all cases, FHTs were absent upon admission in labor. One was result of maternal aortic aneurysm. One was due to congenital anomaly. Neonatal (n = 9) All but 2 deaths due to congenital anomaly or preterm birth. 1. Woman transferred antenatally and had hospital birth. 2. Woman transferred during first stage for thick meconium, gave birth by emergent cesarean 18 hours after transfer.

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Table 2. Literature Review Table

Study, Setting, Design, Dates, and Sample	Definition of Mortality, Perinatal Mortality Rate With Details About Perinatal Deaths and Transfer Rates
Waldenstrom et al[20] 1997 Alongside BC in Stockholm, Sweden Randomized control trial Data collected 1989-1993 BC sample: 928 women assigned to BC care. Intent-to-treat sample includes AP transfers. 762 admitted in labor to BC. Comparison sample: 932 low-risk women randomly assigned to hospital care	Mortality rate includes fetal deaths after 22 weeks, IP deaths, infant deaths <7 days. AP transfers: 13% IP transfers: 19% (23% of those admitted in labor) Percent giving birth in BC: 63% BC mortality (per 1000 births): 8.62[a] Mortality of those admitted to BC in labor (per 1000 births): 1.31[a] Low-risk hospital mortality (per 1000 births): 2.15[a] Deaths (pp. 415-416): AP deaths (n = 7) Two due to preterm birth <28 weeks. 1. Primigravida, 37 weeks, unknown cause, suspected IUGR. 2. Nullipara, 38.4 weeks, cord accident. 3. Multigravida, 41 weeks, cord accident. 4. Nullipara, 42.2 weeks, unknown cause, postterm. 5. Possible preventable factors identified: Multigravida, 39.4 weeks, placental abruption. Called BC to report no fetal movement in 2 hours, slightly tense uterus. Advised to call back if persistently absent movement. Called 8 hours later, advised to present to BC, immediate transfer for emergent cesarean for fetal bradycardia, stillborn neonate. IP deaths (n = 1) 1. Possible preventable factors identified: Nullipara, 41.6 weeks. Admitted to BC in early labor. After 3.5 hours and at 4cm dilatation, loss of FHT. Reviewers noted that CEFM on arrival may have detected FHT abnormality. Neonatal deaths (n = 0)
David et al[21] 1999 2 Freestanding BCs in Berlin, Germany Retrospective BC record review, comparison group low-risk women in hospital care Data collected 1992-1994 BC sample: 801 women admitted to BC in labor. Comparison sample: 3271 low-risk women planning hospital birth	Mortality rate includes intrapartum deaths, infant deaths <7 days. BC mortality (per 1000 births): 0 Low-risk hospital mortality (per 1000 births): 0.14[b]

(*Continued*)

Table 2. Literature Review Table

Study, Setting, Design, Dates, and Sample	Definition of Mortality, Perinatal Mortality Rate With Details About Perinatal Deaths and Transfer Rates
Jackson et al[22] 2003 Freestanding BC in San Diego, California Prospective cohort study with concurrent comparison group Data collected 1994-1996 BC sample: 1808 women enrolled in BC care. Intent-to-treat approach includes AP transfers. Comparison sample: 1149 low-risk women in hospital care.	Unable to calculate mortality rate from data provided. Deaths below include intrauterine fetal death >20 weeks, IP deaths, neonatal deaths <28 days. AP transfers: 27.2% IP transfers: 18.5% Other transfers: 8.5% Percent giving birth in BC: 45.3% BC mortality (% of sample): IUFDs: 4%[b] Neonatal: 2%[b] Low-risk hospital mortality (% of sample): IUFDs: 4%^ Neonatal: 3%[b]
Gottvall et al[23] 2004 Alongside BC in Stockholm, Sweden Retrospective chart review. Comparison group generated from Swedish National Birth Registrar of low-risk women in hospital care Data collected 1989-2000 BC sample: 3256 women enrolled in birth center care prenatally. Sample includes AP transfers. 2200 women gave birth at birth center. Comparison sample: 180,380 low-risk women in hospital care	Mortality rate includes fetal deaths after 28 weeks, IP deaths, infant deaths <7days, data on infant deaths <28 days also provided. AP transfer: 14% IP transfer: 18% Percent giving birth at BC: 67.6% BC mortality (per 1000 births): AP: 3.38[a] IP: 0.92[a] Neonatal <7: 1.23[a] Neonatal 7-27: 0.31[a] IP and Neonatal mortality <7 days: 2.15[a] IP and Neonatal mortality <28 days: 2.46[a] Total including neonatal <7 days: 5.53[a] Total including neonatal <28 days: 5.84[a] Low-risk hospital mortality (per 1000 births): AP: 2.99[a] IP: 0.20[a] Neonatal <7 days: 1.66[a] Neonatal <28 days: 0.53[a] Total including neonatal <7 days: 4.85[a] Total including neonatal <28 days: 5.37[a] Mortality rate by parity (per 1000 births): Nulliparas (statistically significant): BC: 9.4[b] Hospital: 5.2[b] Multiparas: BC: 2.2[b] Hospital: 4.5[b] Total (BC + hospital) mortality by maternal age (per 1000 births): ≤35 years: 4.5[b] >35 years: 6.54[b] Total (BC + hospital) mortality rate by EGA (per 1000 births): 37-42 weeks: 2.35[b] ≥42 weeks: 3.32[b] Deaths (pp. 74-75) AP (n = 11) 1. Nullipara, 40 weeks, AP transfer for IUGR, cause of death IUGR. 2. Multipara, 41.2 weeks, AP transfer for HTN, transfer back to BC with normal pressures. IUFD at 41-week checkup, cause of death cord accident.

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Table 2. Literature Review Table

Study, Setting, Design, Dates, and Sample	Definition of Mortality, Perinatal Mortality Rate With Details About Perinatal Deaths and Transfer Rates
	3. Multipara, 39.5 weeks, placental abruption. Emergent cesarean 17 minutes after transfer from BC. IUFD. 4. Nullipara, 38.4 weeks, ROM, meconium, IUFD upon arrival to BC. Cause of death cord accident. 5. Multipara, 31.3 weeks, AP transfer for IUGR, cause of death lethal anomaly. 6. Nullipara, 42.2 weeks, IUFD on arrival to BC, cause of death placental insufficiency. 7. Nullipara, 34.1 weeks, AP transfer due to personal circumstances, cause of death lethal anomaly. 8. Nullipara, 40.1 weeks, IUFD at routine checkup, cause of death cord accident. 9. Nullipara, 40 weeks, IUFD at routine checkup, cause of death cord accident. 10. Nullipara, 42.0, IUFD on arrival to BC. Cause of death placental insufficiency, asphyxia. 11. Possible avoidable factors identified: Nullipara, 42.2 weeks, IUFD at routine checkup, cause of death suspected intrauterine asphyxia. Reviewers noted insufficient antenatal testing for postdates. IP (n = 3) 1. Nullipara, 41.3 weeks, only one antenatal visit at BC, IP death during labor at BC, cause of death GBS infection. 2. Possible avoidable factors identified: Nullipara, 42 weeks, IP death during labor at BC, cause of death intrauterine infection. Reviewers noted that FHT decelerations were auscultated by stethoscope with no transfer, noted that woman declined CEFM. 3. Possible avoidable factors identified: Nullipara, 41.6 weeks, IP death during labor at BC, cause of death meconium aspiration. Reviewers noted long second stage and possible need for CEFM monitoring. Neonatal (n = 4) 1. Multipara, BC birth at 42.3 weeks, meconium-stained amniotic fluid, Apgar 10 at 5 minutes, discharged at 12 hours PP, readmitted 14 hours later, death at 27 hours, cause of death meconium aspiration and persistent fetal circulation. Death occurred at home after hospital discharge. 2. Nullipara, 25.1 weeks, SROM, death at 39 minutes, cause of death prematurity and intrauterine infection. 3. Nullipara, 22.5 weeks, SROM, death at 40 minutes, cause of death prematurity. 4. Possible avoidable factors identified: Nullipara, 41.6 weeks, IP transfer for slow progress in labor at 5-6 cm cervical dilatation, infant death at 55 minutes, cause of death meconium aspiration. Reviewers noted that after transfer, woman was treated as a natural labor candidate in spite of complicated labor course.

(*Continued*)

Table 2. Literature Review Table

Study, Setting, Design, Dates, and Sample	Definition of Mortality, Perinatal Mortality Rate With Details About Perinatal Deaths and Transfer Rates
Tracy et al[24] 2007 Alongside BCs in Australia. Sample drawn from National Perinatal Data Collection System, and includes all women who gave birth in a BC. Comparison group includes low-risk women who gave birth in a hospital during that time period Data collected 1999-2002 BC sample: 21,800 women who gave birth in a BC. Comparison sample: 972,664 low-risk women gave birth in hospital. Note: Inconsistent reporting sample. When a woman transfers to a hospital in labor, some states record place of birth as birth center and some record place of birth as hospital. All women with AP transfers to hospital care are included (if still low risk) in hospital sample.	Mortality rate includes fetal deaths after 20 weeks, IP deaths, and infant deaths <28 days. Stillborn (p. 196): birth resulting from viable pregnancy where fetus has no signs of life after birth, includes IP and AP periods. Live birth (p. 196): infant with signs of life after pregnancy of at least 20 weeks' gestation and/or birth weight of at least 400 g. BC mortality rate: 1.51 per 1000 Hospital mortality rate (per 1000 births): All women: 10.03 Low-risk and term (37-41 weeks EGA) women: 1.69 Mortality rate at term (>37 weeks EGA) by parity (per 1000 births): Nulliparas: BC: 1.50[a]Low-risk hospital: 1.83[a] Multiparas: BC: 0.65[a] Low-risk hospital: 1.58[a] Deaths (p. 198): N = 33 15 induced stillbirths (n = 15); preterm <32 weeks EGA (n = 12); term deaths (n = 20) Cause of death available (n = 8) 3 unexplained AP deaths; 3 due to anomaly; 1 "hypoxic peripartum death"; 1 due to "specific perinatal conditions" 40% of infant deaths at term in BC were to women aged >35 years[b] 0 deaths among women who gave birth in BC with fetus 42-45 weeks EGA[b]
Hollowell et al[25] 2011 Birth centers throughout England Prospective national data collection in multiple freestanding and alongside birth centers, and random sample of 37 hospitals Data collected 2008-2010 Low-risk women (BCs + hospital): 47,698 Freestanding BCs: 11,282 women planned birth in freestanding BC at onset of labor. Alongside BCs: 16,710 women planned birth in Alongside BC at onset of labor. Hospital: 19,706 women planned birth in hospital at onset of labor.	Data include IP deaths and infant deaths <7 days. Stillbirth: fetal death after onset of labor IP transfers: 21.9% Freestanding BCs: 16.5% Alongside BCs: 21.2% Freestanding BC mortality rate (per 1000 births): Stillbirth: 0.35[a] Neonatal: 0.44[a] Total: 0.79[a] Alongside BC mortality rate (per 1000 births): Stillbirth: 0.06[a] Neonatal: 0.18[a] Total: 0.24[a] Low-risk hospital mortality rate (per 1000 births): Stillbirth: 0.15[a] Neonatal: 0.25[a] Total: 0.4[a]

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Table 2. Literature Review Table

Study, Setting, Design, Dates, and Sample	Definition of Mortality, Perinatal Mortality Rate With Details About Perinatal Deaths and Transfer Rates
Laws et al[26]	Mortality includes fetal deaths after 20 weeks, IP deaths, infant deaths <28 days.
2010	IP transfers: 33.9%
Alongside BCs in Australia: New South Wales, Queensland, Western Australia, Australian Capital Territory	Percent giving birth in BC: 65.6%
	BC mortality rate (per 1000 births): Stillborn: 2.25[a] Neonatal: 1.03[a] Total: 3.28[a]
Sample drawn from National Perinatal Data Collection System, and includes all women who gave birth in a BC. Comparison group of low-risk women who gave birth in a hospital during that time period.	BC mortality rate with EGA >37 weeks (per 1000 births): 1.3[b]
	Low-risk and term (37-41 weeks) in hospital (per 1000 births): 1.7[b]
	BC mortality rate with EGA >37 weeks by parity (per 1000 births):
	Nulliparas: Stillborn: 0.98[a] Neonatal: 0.54[a] Total: 1.52[a]
	Multiparas: Stillborn: 0.70[a] Neonatal: 0.44[a] Total: 1.13[a]
Data collected 2001-2005	Hospital mortality among low-risk and term women (37-41 weeks EGA) by parity (per 1000 births):
BC sample: 22,222 women planned BC birth at onset of labor (22,232 fetuses). Comparison sample: 475,791 low-risk women planned hospital birth at onset of labor.	Nulliparous: Stillborn: 1.42[a] Neonatal: 0.51[a] Total: 1.93[a]
	Multiparous: Stillborn: 1.03[a] Neonatal: 0.44[a] Total: 1.47[a]
	No difference in mortality rates when hospital births after 41 weeks EGA included in analysis.
Overgaard et al[27]	Perinatal mortality not specifically defined, but data collected until 28 days.
2011	IP transfers: 11.6%
2 Freestanding BCs, located within a hospital that had no obstetric service due to rural location. North Jutland, Denmark	BC mortality rate (per 1000 births): 1.19[a]
	Low-risk hospital mortality rate (per 1000 births): 0
Prospective cohort study with matched comparison group	Deaths (p. 6)
Data collected 2004-2008	Neonatal (n = 1):
BC sample: 839 women admitted to the BCs in labor. Comparison sample: 839 low-risk women enrolled at urban obstetric unit with low-risk pregnancies and similar demographic characteristics.	Death due to severe congenital anomaly (diaphragmatic hernia) not diagnosed on routine anatomy scan.

(*Continued*)

Table 2. Literature Review Table

Study, Setting, Design, Dates, and Sample	Definition of Mortality, Perinatal Mortality Rate With Details About Perinatal Deaths and Transfer Rates
Stapleton et al[7] 2013 79 BCs in 33 US states. Majority freestanding. Prospective data collection. No comparison group. Data collected 2007-2010 BC sample: 15,574 women who planned and were eligible for BC birth at onset of labor, including those transferred to the hospital after initial assessment and prior to BC admission. 14,881 admitted to BC in labor.	Mortality rate includes IP deaths, infant deaths. All infant deaths reported were within 7 days, but infant death data collected at 6wk PP visit. No clear definition of time period for neonatal mortality. IP transfers: 12.4% Total mortality rate (per 1000 births): IP: 0.90[a] Neonatal: 0.58[a] Total: 1.48[a] Mortality rate among women admitted in labor (per 1000 births): IP: 0.47[a] Neonatal: 0.60[a] Total: 1.08[a] Mortality rate among those admitted in labor, excluding anomalies (per 1000 births): Neonatal: 0.40[a] Total: 0.87[a] Deaths (p. 8) IP (n = 14): 7 were diagnosed on arrival to BC in labor and were not admitted 7 occurred after admission to BC in labor - 4 deaths occurred in hospital after transfer for fetal distress - 3 unexpected stillbirths in BC Neonatal (n = 9) 3 with lethal anomalies - 2 expected, families chose BC birth - 1 unexpected (with normal anatomy scan) 3 (without anomalies) born in hospital after IP transfer - 2 transferred for fetal distress - 1 transferred for failure to progress 3 (without anomalies) transferred emergently after birth - 2 with respiratory distress syndrome - 1 with hypoxic ischemic encephalopathy attributed to prenatal insult
Thorton et al[28] 2017 79 birth centers in 43 US states. Majority freestanding. Prospective data collection with low-risk comparison group who received prenatal care in the birth center Data collected 2006-2011 BC sample: 8776 low-risk women admitted to the birth centers in labor. Comparison sample: 2527 low-risk women admitted to a hospital in labor.	Newborn mortality rate includes only infants born alive (author communication). IP transfers: not stated BC neonatal mortality rate (per 1000 births): 0.34[a] Low-risk hospital neonatal mortality rate (per 1000 births): 0.40[a] Neonatal deaths (p. 8) 3 in the BC group 1 in the hospital group No detail on neonatal deaths provided.

Abbreviations: AP, antepartum; AROM, artificial rupture of membranes; BC, birth center; CEFM, continuous external fetal monitoring; EGA, estimated gestational age; FHT, fetal heart tones; GBS, group B streptococcus; HTN, hypertension; IP, intrapartum; IUFD, intrauterine fetal death; IUGR, intrauterine growth restriction; PP, postpartum; ROM, rupture of membranes; SIDS, sudden infant death syndrome.
[a] Calculated or recalculated to second decimal place by authors from data provided in manuscript.
[b] Cannot independently calculate mortality rate based on information provided.

and poor outcomes may occur that are not captured if admission to the birth center was a sample requirement.

Following completion of the table, we entered neonatal mortality rates (deaths per 1000 births) as presented within the articles or calculated mortality rates based on the ratio of how many deaths were noted (numerator) divided by the sample of women enrolled in the study (denominator). For example, a prospective study looking at women intending to give birth at a birth center might count antepartum deaths, intrapartum deaths, and neonatal deaths (the numerator) and include all women intending to give birth at the center regardless of the actual birth location (the denominator). A different study might assess intrapartum deaths (the numerator) for infants born in a birth center (the denominator). If the data presented in the study allowed for calculations with more than one numerator or denominator type, all such calculations were included in the table. An exception to this were studies with 0 deaths, which could technically be projected into multiple categories (antepartum, intrapartum, and neonatal), but in doing so would overrepresent the 0 mortality rate. Calculations for these studies were only included when numbers of women in each category were specifically stated in the paper. Data were calculated by one author (R.D.P.) and confirmed by another (K.D.).

RESULTS

Seventeen studies were included (Table 2). There are 7 studies set in the United States,[7,13–16,22,28] 2 from Australia,[24,26] 3 from the United Kingdom,[18,19,25] 2 from Sweden,[20,23] and one each from Denmark[27] and Germany.[21] Data collection for the studies occurred from 1982[13] to 2011.[7,28] The sample includes at least 84,500 women admitted to a birth center in labor.[7,13–28]

The estimated number of women in the review excludes intent-to-treat studies that did not identify the number of women admitted in labor[14,19,22] and studies where overlapping data could not be identified.[24,28] Overlapping data occur when more than one publication uses information from the same data set and time period. Essentially, the outcomes of one woman may be assessed in more than one study. There are several sources that analyze data pulled from a central registry or database and share at least a portion of their data. For example, Thornton et al[28] used the Perinatal Data Registry, targeting the years 2006 to 2011, and Stapleton et al[7] used the same database but assessed outcomes of women expected to give birth between 2007 and 2010; as a result, these 2 studies may report the same neonatal death. While reporting of the same outcome twice would be problematic in a meta-analysis where actual numbers are combined, we examined mortality rates rather than absolute numbers. While outcomes across overlapping studies were not fully independent and clustered toward the same rate, including all studies allowed for descriptive analysis with slightly different sample sets, valuable in the assessment of rare outcomes.

Overlapping data sets included a 10-year Swedish study of perinatal mortality in birth centers that incorporated data from a published earlier randomized controlled trial[20,23]; 2 manuscripts presenting identical data from the first National Birth Center Study, one providing greater detail on mortality[16,17]; 2 articles with overlapping data from the US perinatal data registry of birth center care[7,28]; and 2 Australian studies that used different analytic methods on perinatal registry data.[24,26]

Eleven studies prospectively enrolled women.[7,13,15,16,18–20,22,24,25,27] Of these, 3 randomized women to birth center or hospital care,[18–20] while another compared outcomes of women assigned to birth center care (without randomization) to women choosing birth center care.[15] Additionally, 5 prospective studies utilized a comparison group of low-risk women birthing in a hospital.[13,22,25,27,28] Two studies reviewed clinical records to retrieve data.[14,21] Three studies used information from a national data registry,[23,24,26] and 3 used a private data registry.[7,16,28] One researcher supplemented information from a data registry with mortality data from clinical records.[23]

Ten studies presented data from freestanding centers,[7,13–17,21,22,27,28] and 6 included data from birth centers located on a unique hospital floor or adjoining building, but with guidelines similar to AABC, often known as an *alongside birth center*.[18,20,23,24,26] Hollowell and colleagues presented data from freestanding and alongside centers but separated these groups.[25] Most data on alongside units are found in international studies, while most freestanding centers were located in the United States.

As outlined in Table 2, there were differences in the calculation of mortality, with some researchers including only intrapartum fetal deaths[20] or early neonatal deaths,[18,20,21,25] while others also included late neonatal deaths.[22,24,26] One study provided data on both early and late measures of neonatal mortality.[23] Even when studies used superficially similar definitions, for example perinatal mortality, the term can have different meanings. The World Health Organization (WHO) defines perinatal mortality as fetal deaths from 28 weeks' gestation forward and newborn deaths up to the seventh completed day of life while the definition used by the US Center for Health Statistics includes deaths from 20 weeks' presumed gestation up to (but not including) the seventh day of life. In some respects, these are subtle differences, especially in the study of the direct effects of birth center care. However, the discrepancies in key terminology across countries complicates health services research of this birth setting. Table 3 provides an overview of standard definitions of perinatal and neonatal mortality. Many studies did not define the neonatal ages included in neonatal mortality, but it can be assumed they used the definition appropriate for their geographic location.[7,13–17,19,27,28] Some studies included all fetal deaths at term, including those that occurred prior to labor,[14] while others included fetal deaths after approximately 20 weeks' gestation.[18–20,22–24] Studies also differed in categorizing intrauterine fetal deaths diagnosed on arrival to the birth facility; some studies include these as antepartum deaths,[7,17,20,28] and others note them simply as "stillbirths."[18,19] One study included intrauterine fetal deaths in the category of "Apgar scores less than 4."[28] Most studies listed reasons for all fetal and newborn deaths, but deaths due to congenital anomalies were not uniformly identified or included and excluded. Table 2 includes detail about the fetal and neonatal deaths as described within the studies. This information is useful in determining if location of birth was a potential causal factor in the death.

Table 3. Definitions of Perinatal and Neonatal Mortality

Term and Defining Organization	Definition
Perinatal mortality	
World Health Organization (WHO)[31]	Deaths of live born infants in the first 7 completed days of life and fetal deaths after 28 weeks' presumed gestation. Rate is expressed as number per 1000 (live and stillborn) births.
Definition I of the US National Center for Health Statistics[32]	Deaths of a live born infant at less than 28 days of age and fetal deaths with a stated or presumed gestation of >28 weeks. Rate is expressed as number per 1000 live births plus fetal deaths in that time period.
Definition II of the US National Center for Health Statistics[32]	Deaths of a liveborn infant at less than 7 days of age and fetal deaths with a stated or presumed gestation of 20 weeks or more.
Intrauterine fetal deaths	
Fetal death defined by the US National Center for Health Statistics[32]	Intrauterine death of a fetus prior to birth. Rate is expressed as the number of fetal deaths at ≥20 weeks' gestation per 1000 live births plus fetal death at ≥20 weeks.
Early fetal death defined by the US National Center for Health Statistics[32,33]	Death of fetus from 8 weeks after conception to 20 weeks' completed gestation.
Intermediate fetal death defined by the US National Center for Health Statistics[32]	Death of fetus at 20-27 weeks' completed gestation.
Late fetal death defined by US National Center for Health Statistics[32]	Death of fetus at 28 weeks' or greater completed gestation.
Stillbirth defined by the WHO[31]	Death of a fetus with a weight of at least 1000 grams and a body length of ≥35 cm occurring at ≥28 weeks. Rate is expressed as number per 1000 (live and stillborn) births.
Antepartum stillbirth defined by the WHO[31]	A late fetal death occurring prior to the onset of labor.
Intrapartum stillbirth defined by the WHO[31]	A late fetal death occurring during labor.
Neonatal mortality	
WHO[31]	Death of a liveborn infant during the first 28 completed days of life. Rate is expressed as number per 1000 live births.
US National Center for Health Statistics[34]	Death of a liveborn infant during the first 27 days of life. Rate is expressed as number per 1000 live births.
Early neonatal mortality	
WHO[31]	Death of a liveborn infant within the first 7 days of life.
US National Center for Health Statistics[32]	Death of a liveborn infant within the first 6 days (<7 days) of life.
Late neonatal mortality	
WHO[31]	Death of a liveborn infant during days 8 to 28 of life.
US National Center for Health Statistics[32]	Death of a liveborn infant during days 7 to 27 of life.

Abbreviation: WHO, World Health Organization.

Most perinatal deaths were not attributed to intended birth setting.

The denominator group for the mortality rates also varied. One set of authors reported perinatal or neonatal mortality based solely on the location of birth,[24] while 7 sets of researchers reported infant deaths by the number of women admitted to the birth center in labor, irrespective of birth locale.[7,13,15,21,22,26,28] Three studies used the number of infants born to women admitted to the birth center for intrapartum care as the denominator, as some women gave birth to more than one child during the study period, and earlier studies reported unexpected twin births.[16,17,26] In addition, one author group noted on a request for clarification that they included women who presented to the birth center but were transferred to a hospital prior to admission, while another excluded antepartum transfers from the birth center sample.[7] Other authors did not describe how outcome data of women who presented to the birth center intrapartum but were not admitted was handled in the analysis. Six researchers' samples included all women who enrolled in birth center care during pregnancy and data were analyzed with an intent-to-treat approach, keeping women who transferred antenatally in the birth center group; in several of these studies, less than half of the birth center sample gave birth in a birth center.[14,18–20,22,23]

Figure 2 displays deaths per 1000 births for various measures of fetal or neonatal mortality including the most inclusive studies that measured antepartum, intrapartum, as well

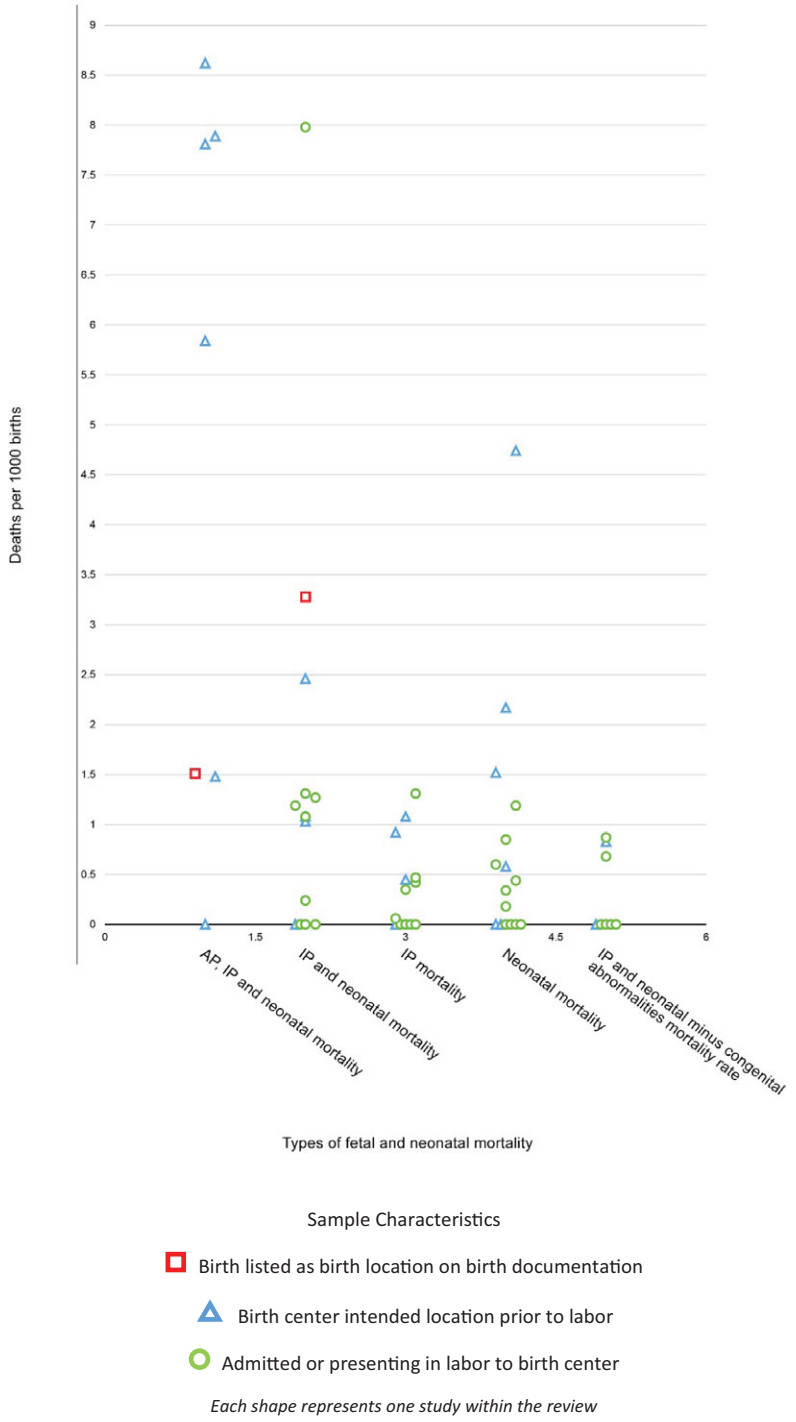

Figure 2. Fetal and Neonatal Mortality Rates by Inclusion Criteria and Study Sample

as neonatal deaths, as well as the studies that only measured infant or neonatal deaths of infants without known congenital abnormalities. This cluster graphic provides a visual depiction of mortality ratios related to the perinatal time frame included in analysis and the women sampled for the study. Neonatal mortality (neonatal deaths per 1000 births) by publication date is shown in Figure 3 to visually depict changes over time. Four of the 17 studies did not provide information that would allow calculation of a neonatal death rate.[17,22,24,26] Three studies include more than one neonatal death rate from their data based on differing sample characteristics,[7,20,25] and we include all these rates to provide a visual synopsis of all birth center mortality rates across time. Overall, perinatal mortality rates appear to be decreasing over time.

All studies with fewer than 500 births reported no intrapartum or neonatal deaths.[13–15] Thirteen studies reported at least one perinatal death in the birth center group.[7,16–20,22,23,25–28] For women admitted to a birth center in

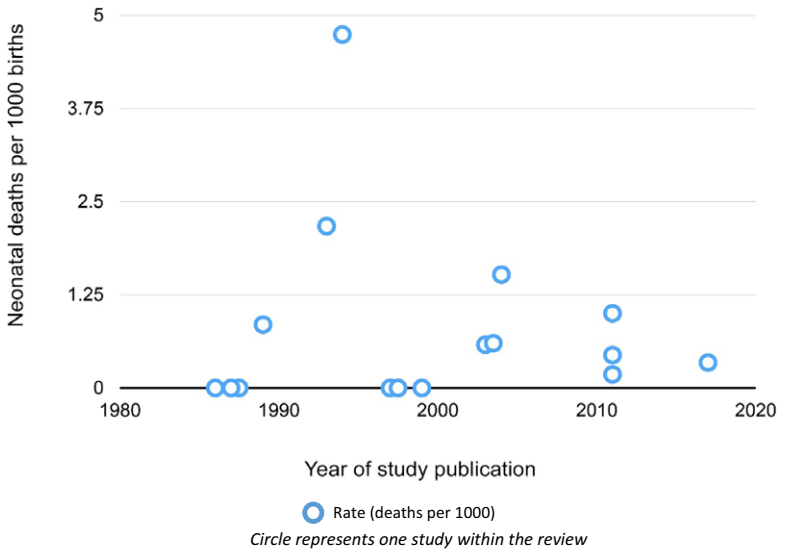

Figure 3. Neonatal Death by Date of Publication

labor, the perinatal mortality rates ranged from 0 to 1.3 deaths per 1000 births across studies.[17,20,21,26] Several of these deaths were related to congenital anomalies incompatible with life. Two studies using a sample of admitted women excluded infants with severe anomalies in subgroup analyses, resulting in modified perinatal mortality rates of 0.5[17] to 0.9[7] deaths per 1000 births.

Several studies compared rates of perinatal mortality in the birth center setting with rates among contemporary low-risk women giving birth in a nearby hospital, as mortality varies over time and geographic location.[35] No studies using a low-risk hospital control group found a statistically significant difference in mortality between groups.[18–20,22–24,26–28] When comparing mortality rates between birth center groups and low-risk hospital groups, 4 articles reported lower rates in the birth center,[22,24,26,28] and 5 found higher rates in the birth center that were not statistically significant.[18–20,23,27] In addition, 2 of the studies that reported higher perinatal mortality rates among the birth center sample noted that the reported fetal and neonatal deaths occurred weeks after antepartum transfer to specialist care and were not related to the intended location of birth,[18,19] while in a third study, the single death in the birth center group was due to congenital anomaly.[27] Hollowell and colleagues compared perinatal mortality in an alongside birth center and a freestanding birth center and found lower rates in the center physically attached to the hospital, although the overall incidence was too low to assess significance.[25]

Across the studies that provided descriptions of the circumstances surrounding perinatal deaths, most antepartum deaths were due to congenital anomalies, intrauterine fetal demise (often a cord accident), placental abruption, maternal infection, or otherwise unknown causes. When details of intrapartum deaths were provided, many occurred in the hospital after transfer from the birth center for fetal distress, prolonged labor, or placental abruption. Several intrapartum deaths were unexplained stillbirths where fetal heart tones were lost during labor or absent when women presented to the birth center in labor. Finally, the causes of neonatal death included congenital anomaly, meconium aspiration, respiratory distress syndrome, isoimmunization, and sepsis. In many studies, researchers did not discuss if being born in a higher-level facility would have affected the survival of infants born with congenital abnormalities. However, 2 studies did differentiate mortality rates between groups of infants with and without abnormalities.[7,16]

Fetal Characteristics Associated With Increased Mortality in Birth Centers

Differences in mortality by gestational age were reported. While women in preterm labor are not admitted to birth centers,[6] practice guidelines vary on postdates management. Studies included in this review found an increase in perinatal mortality past 42 0/7 weeks' gestation,[17,20,23] and Gottvall and colleagues found a similar increase in postdates (greater than 42 0/7 weeks' gestation) mortality in a combined sample of low-risk women giving birth in a hospital and a birth center.[23] Conversely, 2 analyses of data from Australia reported no increased mortality among infants born past 42 0/7 weeks' gestation.[24,26]

Maternal Characteristics Associated With Increased Mortality in Birth Centers

Researchers of 5 studies conducted further subgroup analyses to determine which women were at highest risk of perinatal mortality in the birth center setting. In all 5 studies that reported neonatal mortality by parity, an increased rate of perinatal death was seen in newborns of nulliparous women.[17,20,23,24,26] These studies include a range of 928[36] to 22,232[26] intended birth center births. While most of these studies reported relatively modest differences between the 2 groups (+/- one death per 1000 births),[17,24,26] Gottvall and colleagues reported a perinatal mortality rate of 9.4 per 1000 births among nulliparas compared to a rate of 2.2 per

1000 births among multiparas.[23] The increase in perinatal mortality among nulliparas was also seen among low-risk women giving birth in hospitals,[20,23–26] and the data are mixed on how birth setting may contribute to this increase. The 2 Australian studies using data from their National Perinatal Data System reported that low-risk nulliparas in hospitals had higher rates of perinatal mortality compared to nulliparas in birth centers.[24,26] Gottvall and colleagues, however, found the opposite.[23]

In addition, Gottvall and colleagues found an increase in perinatal mortality from 4.5 to 6.5 deaths per 1000 births among women aged 35 years and older compared to those aged younger than 35 years in a combined sample of low-risk women giving birth in a hospital and a birth center.[23] These findings were echoed by Tracy et al, who reported that among center births, 40% of infant deaths at term were experienced by women aged older than 35 years; authors did not note whether a similar trend was observed for hospital births or provide details about deaths.[24]

Neonatal Morbidity

While our focus was on neonatal mortality, most studies also presented data on morbidity experienced by neonates born to women in birth center settings. All studies that performed subgroup analysis by parity revealed that infants of nulliparous women had higher rates of almost all measures of neonatal morbidity.[17,24,26] Gottvall et al reviewed outcomes associated with more than 3000 infants whose mothers received birth center care and found a statistically higher rate of fractures and hypoglycemia among the comparison group of infants born to low-risk women giving birth in area hospitals. No other statistically significant differences in infant morbidity were noted, including brachial plexus injury, seizures, hypoxia or asphyxia, intracranial hemorrhage, infection, and immunization or hyperbilirubinemia.

In the Birthplace study, researchers grouped neonatal morbidity and mortality into one primary outcome that included intrapartum stillbirth, early neonatal death (within 7 days), neonatal encephalopathy, meconium aspiration syndrome, brachial plexus injury, and fractured humerus or clavicle.[23,25] Nulliparous women giving birth in a birth center (n = 28,443) had a slightly higher incidence of this composite newborn outcome when compared to those giving birth in a hospital, while multiparous women in birth centers (n = 35,289) had a slightly lower incidence of this outcome when compared to low-risk women giving birth in hospitals. However, because a wide range of conditions are combined in this composite outcome, it is unclear whether the morbidity and mortality differences between infants born in- and out-of-hospital are clinically significant. Nulliparous women giving birth in all settings had a higher rate of the composite poor outcome measure when compared to multiparous women. Thornton also created a composite measure including a range of poor neonatal outcomes and found no differences between the birth center and low-risk hospital sample but did not assess differences by parity.[28]

Fifteen studies presented Apgar scores,[13,14,16–22,24–28] and only one study found a statistical difference between groups, with the birth center group having a higher incidence of 5-minute Apgar scores less than 7.[28] Nine studies reported admission rates to neonatal intensive care units (NICUs).[14,15,19–22,24,26,27] While the majority of studies reported no significant differences between admissions of newborns born in or out of the hospital,[14,15,19–22,24,26,27] Laws and colleagues found that infants born in the hospital were significantly more likely to be admitted to the NICU.[26]

DISCUSSION

The use of data from multiple countries allows for a descriptive comparison of neonatal mortality from a large number of births and a much larger sample than would be possible in any single country or region alone. On a descriptive level, the relative consistency of perinatal outcomes across several different developed countries suggest that out-of-hospital physiologic birth in facilities caring for low-risk women that uphold AABC standards results in relatively similar outcomes.

The data in this systematic review suggest that maternal characteristics may provide more information about the risk of neonatal mortality than location of birth alone. No studies using a low-risk hospital control group found a statistically significant difference in neonatal mortality between birth center and hospital groups.[18–20,22–24,26–28] This finding supports the AABC birth center model as a safe option for low-risk women.

Infants of nulliparous women have a higher risk of perinatal mortality and morbidity than multiparous women, in the birth center and also in the hospital. In all studies that analyzed low-risk nulliparous women giving birth in hospitals and birth centers, nulliparous women in both settings experienced higher perinatal loss than did multiparas.[17,20,23,24,26] It is unclear from this systematic review whether nulliparas in a birth center have different perinatal mortality rates than low-risk nulliparas in a hospital; however, all studies that compared multiparas giving birth in a birth center to low-risk multiparas in hospitals reported lower rates of perinatal mortality among the birth center group.[23,24,26] The origin of the small increase in perinatal mortality for infants of nulliparous women giving birth in birth centers is not clear but warrants study. This increased rate of neonatal mortality may be related to risks that emerge with a first pregnancy. Similarly, low-risk multiparous women have demonstrated their ability to give birth without complications, and the differences between nulliparous and multiparous women may be a reflection of a greater ability to determine the low-risk status of a multiparous woman as she has previously been pregnant and given birth, and these prior outcome(s) are useful in predicting the likelihood of a successful, low-risk intrapartum and postpartum course with her current pregnancy. Moreover, several non-birth-center studies have found parity affects stillbirth risk as nulliparous women have consistently higher rates of infant mortality than multiparous women at all maternal ages and in all birth settings.[37–41]

Women aged older than 35 years experience more frequent perinatal losses across settings.[41] Two studies in this review found that women aged older than 35 years had higher rates of poor neonatal outcomes.[23,24] This finding is supported by other literature using national and international data including all locations of birth.[40,42,43] In contrast, a recent study

of out-of-hospital births (with a majority of home births) did not find that women aged older than 35 years have increased intrapartum or neonatal losses when compared with women aged 35 years and younger.[38] There were no studies that directly assessed whether outcomes for women of advanced maternal age are worse in birth centers compared to hospitals, nor do the reviewed studies contain enough data to determine the cause of this increase or whether fetal screening mitigates this risk.

In addition, most studies in this review reported increased neonatal mortality for infants born in birth centers past 42 weeks' gestation. This increase in mortality has been consistently identified in studies using US birth certificates that include all birth locations[44] and was found in a recent large study of US out-of-hospital births as well.[38] Given neonatal mortality is increased past 42 weeks' gestation in all settings, it is unclear if the increased mortality in this review is related to the location of birth.

The systematic review found that since 1980 there has been an overall downward trend in infant mortality associated with birth center care. This decrease is multifactorial and may be related to a greater ability of providers to determine which women and newborns need transfer from birth center care. For example, new information about specific perinatal risk factors, and the increased use of prenatal ultrasound, has refined the subset of women appropriate for intrapartum care in birth centers.[6] In addition, widespread group B streptococcus screening and treatment[45] as well as pulse oximetry screening of newborns[46] may also be contributing to this downward trend.

Relationship With Larger Health Care Trends

The birth center is an accepted location of intrapartum care and birth for low-risk women in developed countries with integrated regional maternity health care.[1,2] Encouraging women to use high-quality birth centers, as the NICE guidelines do in England, may improve some perinatal outcomes while decreasing costs.[2,47,48] The most recent cost comparison reported birth centers save approximately $1,163 per birth as compared to low-risk women giving birth in a hospital.[49] These estimates were just for the index birth and did not include savings related to fewer cesareans with subsequent pregnancies. An increase in numbers of low-risk women using birth centers for intrapartum care is likely to decrease the primary cesarean rate,[8] a goal of many perinatal organizations in the United States.[50]

Implications for Clinical Care

Birth center care has risks and benefits when compared with hospital care, and this information should be presented to woman to ensure informed decision making about location of birth. Women who begin labor in a birth center have substantially lower rates of cesarean birth and other obstetric interventions, increased rates of optimal outcomes, and high maternal satisfaction.[8] While neonatal outcomes have been a major impetus driving maternity care, maternal outcomes are equally important in assessment of location of birth.[1] A more balanced approach to risk assessment may be more valuable, such as an approach that focuses on ensuring that women receive the level of perinatal care appropriate to their individual risk status.[1]

The current literature clearly shows that perinatal mortality increases past 42 weeks' gestation in all birth settings, including birth centers. Women aged older than 35 years have an increased risk of perinatal and neonatal mortality when compared with younger women, although there are not clear data on risk in birth centers versus hospitals. Nulliparous women also have an elevated risk of poor neonatal outcomes across birth settings compared to multiparous women. The increase for nulliparous compared to multiparous women in the birth center setting is equivalent to an increased incidence of death of 1 per 1000 births in all but one of the sources[17,20,24,26]; however, Gotvall and colleagues calculated an increase of 7.2 deaths per 1000.[23] This increase in risk should be shared with women in order to help inform women's choice of birth location, but it is important to note that the current literature does not provide guidance on whether in-hospital birth will mitigate these risks. Women and families should be given the opportunity to assess all the risks and benefits of their perinatal care and to be supported in well-reasoned choices.[51–53]

Limitations

This systematic review has several limitations. The studies were examined to assess for the potential to combine the data in a meta-analysis, but substantial differences in study designs, measures, and calculations prohibited this analysis. The main differences were varying definitions of neonatal mortality and varying criteria for how women were assigned to birth center samples in the analyses conducted. In addition, studies with identical or overlapping data sets could include one death in multiple articles. These limitations make a standard meta-analysis of neonatal outcomes impossible to conduct with current published research.

On the other hand, even larger studies viewed individually are insufficient to assess the relationship between location of birth and neonatal mortality; because neonatal mortality is rare in economically developed countries, even one death can greatly affect study outcomes. Thus, a synthesis of outcomes and trends in neonatal mortality across studies provides valuable information for assessing this model of care. While combining data allows for a larger sample wherein the mortality ratios are less influenced by rare events, the operational definitions of key perinatal measures differ across studies. Even with the aggregation of data from 17 studies and at least 84,500 births in this synthesis, it is difficult to differentiate the effect of intrapartum birth center care on newborn outcomes. The inability to combine data and examine outcomes by covariates known to affect perinatal mortality, such as parity and maternal and gestational age, limits the ability to determine if these subgroups are at increased risk in the birth center versus any birth location. In the future, studies should assess outcomes in large, matched samples and ideally provide access to raw data. In the meantime, this systematic review provides data for counseling women about planned location of birth.

When perinatal mortality is assessed solely by actual location of birth, intrapartum and early neonatal mortality rates are lower for birth centers and increased for hospital

groups, in part because higher-risk women are transferred to hospital care at some point in perinatal care and their outcomes are then counted in the hospital cohorts.[24] However, research studies that use an intent-to-treat model and a sample of women planning birth center care early in their pregnancies provide little information about the effect of birth center care on neonatal outcomes because approximately 35% to 55% of these women will give birth in a hospital, often because they are transferred prior to labor.[14,18–20,22,23] Even those studies limited to women admitted to a birth center in labor report intrapartum transfer rates ranging from 12% to 26%,[7,15,16] with many of the poor outcomes in the birth center group occurring after transfer. In these studies, the higher rates of complications in women who were transferred during pregnancy may demonstrate that birth centers are able to correctly assess which women need hospital-based intrapartum care rather than poor outcomes related to birth center care. These sampling issues make definitive statements about the effect of the location of birth on perinatal outcomes difficult.

Birth centers provide care to low-risk women, and the exact definition of low-risk shifts with increasing knowledge of maternal and fetal conditions associated with poor outcomes. These definitions will continue to change as large studies and meta-analyses provide additional data on risk factors and location of birth. For example, earlier birth center studies include outcomes of pregnancies past 42 weeks' gestation, but AABC Standards now exclude women with pregnancies past 42 weeks' gestation since data demonstrate an increased risk after that gestation.[6] More research is needed to determine if other factors can be used to refine assessment of risk status.

Future Research

Further research is needed that will study the effect of intrapartum birth center care on maternal and neonatal outcomes. Clinicians and researchers should use nationally and internationally recognized definitions. Formation and use of uniform core outcomes across research studies is consistent with the Core Outcomes in Women's and Newborn Health (CROWN) initiative, supported by over 80 peer-reviewed journals.[54]

When uniform definitions are not possible, researchers can provide data access for later meta-analysis. Data should include information on parity, maternal age, and gestational age at birth. Editors of major journals and the US National Institutes of Health now require access to data sets (when ethically appropriate) to promote rigor, and this will facilitate meta-analyses.[55,56]

In addition, it would be useful for studies to include measures of the amount, or dose, of birth center care. In some of these studies, women experiencing neonatal deaths were transferred long before labor, often for indications associated with increased neonatal complications in any birth setting, making it difficult to assess the effect of birth center intrapartum care. Interprofessional, team-based models of care are recommended by national and international groups to assist women in accessing the level of maternity care that meets their medical and personal needs,[1,57] and have been employed in birth centers since their inception. However, when women receive care from a variety of providers, it can be difficult to assess the effects of one provider type or model of care. New definitions of midwifery care within interprofessional environments can assist clinicians and researchers in studying the outcomes of collaborative care.[58]

Due to inconsistencies in neonatal outcome reporting, the most well-defined measure, mortality, was used. However, this measure does not reflect the range of newborn health.[59] Ideally, future studies will contain more valuable assessments of newborn transition to extrauterine life and long-term outcomes. This information should be examined by gestational age, parity, intended birth location at labor onset, and contain transfer information as applicable. While it can be difficult to provide full data sets while protecting participants, registries aggregate data, decreasing concerns surrounding rare outcome disclosure. Definitions of measures in data registries should be consistent for aggregation and comparison. The addition of intended birth location to vital statistics data, similar to the 2012 change in Oregon,[12] would also improve assessment of birth settings. Moreover, inclusion of the name of the transferring facility would allow greater study of the role of facility accreditation on perinatal outcomes.

CONCLUSION

Differences in key definitions of adverse fetal and neonatal outcomes make a meta-analysis of the effects of birth center care difficult. These differences and the lack of detail on timing and reason for fetal and neonatal deaths prevent conclusive statements. However, this systematic review provides information about trends in neonatal mortality in birth centers. No study comparing all women giving birth in a birth center to low-risk women in hospital care found a significant difference in the perinatal mortality between settings, and data were mixed as to the overall trend. In subgroup analyses within studies, fetuses and neonates of women who are nulliparous, aged over 35 years, or have pregnancies of greater than 42 weeks' gestation have higher rates of perinatal and neonatal mortality in the birth center when compared with women without these risk factors. However, because perinatal mortality is increased for women aged older than 35 years or with a postdates pregnancy in any setting, the effect of the birth center on these outcomes is not clear. The increased neonatal mortality for infants of nulliparous women warrants further investigation with the statistical power to detect significant changes in this rare outcome. Consistent use of national and international definitions of perinatal and neonatal mortality within data registries and detail on adverse outcomes would be beneficial in expanding the knowledge of this location of birth.

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CONFLICT OF INTEREST

Jill Alliman, CNM, DNP, is employed by the American Association of Birth Centers as Project Director of the Strong Start for Mothers and Newborns Initiative, Grant #1D1CMS331135, funded by Center for Medicare and Medicaid Innovation. There are no other conflicts of interest to disclose.

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