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## Maternal, Labor, Delivery, and Perinatal Outcomes Associated with Placental Abruption: A Systematic Review

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### Abstract

**Objective**—Risk factors for placental abruption have changed, but there has not been an updated systematic review investigating outcomes.

**Methods**—We searched PubMed, EMBASE, Web of Science, SCOPUS, and CINAHL for publications from January 1, 2005 through December 31, 2016. We reviewed English-language publications reporting estimated incidence and/or risk factors for maternal, labor, delivery, and perinatal outcomes associated with abruption. We excluded case studies, conference abstracts, and studies that lacked a referent/comparison group or did not clearly characterize placental abruption.

**Results**—A total of 123 studies were included. Abruption was associated with elevated risk of cesarean delivery, postpartum hemorrhage and transfusion, preterm birth, intrauterine growth restriction or low birth weight, perinatal mortality, and cerebral palsy. Additional maternal outcomes included relaparotomy, hysterectomy, sepsis, amniotic fluid embolism, venous thromboembolism, acute kidney injury, and maternal intensive care unit admission. Additional perinatal outcomes included acidosis, encephalopathy, severe respiratory disorders, necrotizing enterocolitis, acute kidney injury, need for resuscitation, chronic lung disease, infant death, and epilepsy.

**Conclusion**—Few studies examined outcomes beyond the initial birth period, but there is evidence that both mother and child are at risk of additional adverse outcomes. There was also considerable variation in, or absence of, the reporting of abruption definitions.

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Conflict of Interest  
None.

## Keywords

delivery; labor; neonatal; perinatal; placental abruption

Placental abruption, the premature detachment of the placenta from the uterine wall, before birth and after 20 weeks of gestation, is one of the most significant determinants of maternal morbidity as well as perinatal morbidity and mortality.<sup>1–4</sup> It is estimated to occur in 0.6 to 1% of pregnancies in the United States,<sup>5</sup> but the reported incidence is lower (0.4–0.5%) in Nordic countries<sup>5</sup> and higher (3.5–3.8%) among some south Asian countries.<sup>3,6</sup> It typically presents with maternal symptoms of vaginal bleeding, abdominal pain and contractions, and/or abnormal fetal heart rate tracings.<sup>2,7,8</sup> The disorder is also characterized by chronic placental dysfunction and separation from the uterine wall, which, with progression, can lead to a corresponding decrease in the placental surface area available for oxygen exchange and nutrient supply for the fetus.<sup>9</sup> This process can lead to an elevated risk of low birth weight, prematurity, and perinatal mortality.<sup>5</sup> Severe cases of abruption can rapidly progress to significant maternal blood loss, fetal hypoxia, and fetal death and necessitate emergent cesarean delivery.<sup>5</sup>

With the recent creation of the National Institute of Health's Human Placenta project, placental functioning and dysfunction has come to the forefront of research priorities in the United States.<sup>10</sup> However, the only two extant systematic reviews that included outcomes associated with abruption were based on studies that are all over a decade old.<sup>5,11</sup> In the past 10 years, there have been changes in several key risk factors for abruption, including increasing maternal age and body mass index and increasing use of assisted fertility methods. Furthermore, considerable new evidence has emerged on maternal, labor, delivery, and perinatal outcomes associated with placental abruption since that time. Finally, changes in medical and diagnostic technology over the past decade may mean that risk estimates in systematic reviews of studies prior to 2005 no longer accurately represent the risk associated with today's cases. Therefore, the aim of this study was to provide a comprehensive, systematic review of the scientific literature examining outcomes associated with placental abruption published between January 1, 2005, and December 31, 2016.

## Data Sources

A systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement guidelines.<sup>12</sup> We searched PubMed (includes MEDLINE), Embase, Science Citation Index, SCOPUS, and CINAHL databases from January 2005 through December 2016 using the following key words: "abruption," "abruption placentae," "premature separation of the placenta," "retroplacental hemorrhage," and "retroplacental hematoma." To identify outcomes, the key words "maternal," "neonatal," "perinatal," and "fetal" were used in conjunction with the outcome terms "outcomes," "morbidity," "mortality," "hemorrhage," "intensive care unit," "transfusion," "hysterectomy," "disseminated intravascular coagulopathy," "premature rupture of membranes," "mode of delivery," "cesarean," "labor," "preterm birth," "low birth weight," "small for gestational age (SGA)," "intrauterine growth restriction (IUGR),"

“neonatal intensive care unit,” “respiratory,” “respiratory distress syndrome,” “apnea,” “anemia,” “asphyxia,” “need for transfusion,” “anomalies,” “cerebral palsy,” “death,” and “sudden infant death syndrome.”

Only English-language, peer-reviewed, original research publications were reviewed. We excluded clinical case studies, animal studies, conference abstracts, and studies that lacked a referent/comparison group. Studies in which abruption was combined with other disorders to form a composite risk factor without provision of a separate risk estimate for abruption in particular were also excluded. Studies reporting risk of congenital anomalies<sup>13</sup> associated with abruption were not formally included in this review, but are included in the references. After excluding duplicate publications and applying the aforementioned exclusion criteria, 123 articles were selected for this review. The summary tables in this review include outcome incidence among pregnancies with abruption versus those without abruption, as well as any available risk estimates, with preference given to adjusted risk estimates. Studies are organized first by type (cohort, followed by case-control), then by year of publication, and then alphabetical by first author. The term “mild” or “severe” abruption is used in the descriptive text of this review if the original authors described their results in that language, but it should be noted that there is substantial variation in how this is defined. Overall, the reported incidence of abruption in the reviewed literature ranged from 0.01 to 5.1%, but the majority of studies had an incidence ranging from 0.5 to 1.0% (Table 1–7).

## Obstetrical Morbidity

Cesarean delivery risk ranged from 2.4 to 61.8 (incidence range: 33.3–91%) and was the most frequently reported labor and delivery outcome associated with abruption (Table 1).<sup>2,8,14–24</sup> The variation in risk estimates is likely attributable to the specification of subpopulations or types of cesarean, as the lowest risk was seen in a cohort study of periviable neonates<sup>14</sup> and the highest risk was seen in non-planned cesareans among multiparous women.<sup>18</sup> A single study did not find elevated risk of cesarean associated with abruption, but it was limited to deliveries 22 to 26 weeks and the nonabruption cesarean delivery rate was unusually high at 67%.<sup>25</sup> Abruption was also associated with 3.5 to 31.1 times elevated risk of relaparotomy following cesarean,<sup>26–28</sup> as well as need for hysterectomy.<sup>15,29,30</sup> One study that did not find an association with hysterectomy may have been underpowered, as they only had two cases of abruption among the hysterectomy group, but it was unclear how many cases of abruption presented in the overall study population.<sup>31</sup> We classify cesarean delivery, relaparotomy, and hysterectomy as obstetric morbidities, but it is important to note that cesarean delivery is often necessary in the setting of placental abruption to limit further oxygen deprivation to the fetus; to reduce blood loss for the mother; and, in extreme cases, to prevent the death of the fetus, the mother, or both.<sup>2</sup> Similarly, relaparotomy and hysterectomy are often necessary and life-saving measures when they are performed. The risks of performing these interventions must be weighed against the potential benefits of reduction in maternal and fetal morbidity and mortality.

## Short-Term Maternal Morbidity and Mortality

Postpartum hemorrhage (PPH) was the most frequently reported maternal morbidity associated with abruption, but there was a lack of consensus in the literature as to whether the risk was truly elevated (Table 2). Estimates of PPH risk ranged from 1.62 to 17.9 (incidence: 0.4–50%) and five of eight studies reported a significantly elevated risk in the setting of abruption.<sup>2,20,32–34</sup> Of the three studies reporting nonsignificant associations, one did not provide a definition of hemorrhage<sup>15</sup> and the other two were examining risk of severe hemorrhage versus nonsevere hemorrhage,<sup>35,36</sup> which likely explains the conflicting findings. Variation in risk estimates in the remaining studies is likely due to specification of subpopulations (only cesarean deliveries, only emergent cesareans, etc.), as well as the different definitions for PPH (>500 mL, >1,000 mL, 500–1,500 mL, and >2,000 mL).

In what is likely a secondary consequence to PPH, abruption was also associated with elevated risk of transfusion, which varied from 2.37 to 14.6.<sup>15,20,37–40</sup> The one study which reported results separately by delivery mode found that the estimated risk of transfusion was higher among vaginal deliveries (odds ratio [OR]: 14.4) than cesarean delivery (OR: 3.1), but there was no direct comparison of modes reported.<sup>40</sup> The difference by delivery mode may be due to either a more rapid delivery or the ability to directly access the uterus for control of the bleeding. Additionally, risk of sepsis,<sup>15</sup> amniotic fluid embolism (AFE),<sup>41–44</sup> venous thromboembolism (VTE),<sup>45</sup> acute kidney injury (AKI),<sup>46</sup> intensive care unit (ICU) admission,<sup>47</sup> and maternal mortality attributed to abruption<sup>4,20,41,46</sup> have also been reported. A recent report examining outcomes associated with mild and severe abruption found elevated risk of several additional serious maternal complications, including pulmonary edema, puerperal cerebrovascular disorders, acute heart failure, acute myocardial infarction, cardiomyopathy, acute respiratory failure, and coma.<sup>44</sup> The degree of PPH associated with abruption is the likely explanation behind many of these serious maternal complications.

## Preterm Birth and Fetal or Neonatal Size

Preterm birth (<37 weeks) was one of the most frequently reported outcomes associated with abruption (Table 3). Estimated risk ranged from 1.2 to 31.7 with incidence ranging from 5.8 to 80.1%, but the majority of studies reported between 40 and 60%.<sup>1,2,8,15,17,48–63</sup> Approximately 50 to 80% of preterm births in the setting of abruption are spontaneous (preterm labor or membrane rupture), but abruption is also considered the fourth most common cause of medically indicated preterm birth.<sup>50,64</sup> Spontaneous preterm birth due to abruption is thought to be the result of bleeding from the separation of the placental which irritates the uterine lining and stimulates contractions which progress into preterm labor.<sup>65</sup> Similar to cesarean delivery, medically indicated preterm birth can be necessary in the setting of abruption to reduce the risk of maternal and perinatal morbidity and mortality.<sup>50,66</sup>

Abruption is also frequently reported as a risk factor for low birth weight, which is primarily related to the corresponding incidence of preterm birth described previously (Table 3).<sup>15,17,20,49,55,60,67,68</sup> However, abruption has also been associated with IUGR and SGA. Depending on the population specified (singletons vs. twins, preterm vs. term, intrapartum vs. antepartum abruption), IUGR/SGA was reported to occur in 2 to 40% of abruption cases

(Table 3).<sup>2,8,15,22,23,25,48,55,60,68–72</sup> The majority of studies reported an elevated risk of IUGR/SGA ranging between 1.3 and 17.4 associated with abruption. The two studies reporting null findings may have been underpowered, as each had fewer than 200 cases of abruption, compared with the other studies which included several hundred to several thousand cases.<sup>25,60</sup> The association between abruption and fetal growth is likely to be a reflection of underlying chronic placental ischemic disease, which reduces the oxygen and nutrient availability to the fetus, thereby stunting fetal growth. It is also possible that a milder, partial separation of the placental could occur earlier in gestation, thereby directly reducing supply to the fetus, while not triggering a preterm birth.

## Intrauterine Fetal Demise, Neonatal Death, and Perinatal Death

Abruption was most frequently reported as a risk factor for stillbirth (range: 3.4–51.8%),<sup>1,2,8,17,20,22,23,68,73–89</sup> neonatal death (range: 1.1–19%),<sup>1,2,17,20,25,69,73,79,90</sup> and overall perinatal mortality (range: 4–56.3%; Table 3).<sup>1,2,8,15,20,71,73,91–96</sup> Although more than half (55%) of excess perinatal deaths associated with abruption are attributed to preterm birth, the elevated risk of perinatal mortality remains significant even after adjusting for preterm delivery and growth restriction.<sup>1</sup> It is plausible that perinatal deaths that are not due to preterm birth are attributable to asphyxia in the setting of abruption (see discussion later).

While none of the studies that met inclusion criteria reported on the location of the abruption or the degree of separation, one case series of abruptions has reported that detachment 45%, central location, and concealed bleeding more frequently resulted in stillbirth and lesser detachment, marginal separation, and revealed bleeding were more often associated with neonatal asphyxia.<sup>97</sup> Overall, the results indicate that the characteristics of the abruption are likely important factors for determining likelihood of fetal survival.

## Other Short-Term Neonatal Morbidities

The majority of the studies of neonatal outcomes associated with abruption have focused on low birth weight, preterm birth, and perinatal mortality. A small number of publications have linked abruption and elevated risk of acidosis (a marker for exposure to hypoxia),<sup>2,25,98,99</sup> as well as brain-related injuries such as neonatal encephalopathy (NE)/hypoxic-ischemic encephalopathy (HIE).<sup>100–102</sup> The three studies examining risk of intraventricular and periventricular hemorrhage found no association with placental abruption (Table 4).<sup>25,103,104</sup> However, all three studies examined preterm neonates only; therefore, it remains unclear whether there is elevated risk in the setting of term birth. There were also single reports of abruption-associated elevated risk of respiratory distress syndrome (RDS),<sup>105</sup> necrotizing enterocolitis (NEC),<sup>106</sup> retinopathy of prematurity (ROP),<sup>107</sup> fetomaternal hemorrhage,<sup>108</sup> AKI,<sup>109</sup> and nosocomial infections (Table 4).<sup>110</sup> In a small number of studies, abruption was also associated with elevated need for resuscitation,<sup>2,71,111</sup> but not with risk of neonatal ICU admission.<sup>20,23</sup> These morbidities can largely be attributed to the associations between abruption and risk of preterm birth (RDS, NEC, ROP, AKI), hypoxia (acidosis, HIE), and blood loss (fetomaternal hemorrhage).

## Neonatal Long-Term Morbidity and Mortality

Finally, there were also long-term risks for the neonate associated with abruption, most of which were likely attributed to the in utero exposure to hypoxia (Table 5). The most frequently described long-term outcome among surviving neonates was elevated risk of cerebral palsy,<sup>58,112–116</sup> but there have also been reports of elevated risk of chronic lung disease,<sup>25,71</sup> infant mortality,<sup>48</sup> cognitive deficits,<sup>117</sup> and epilepsy.<sup>118</sup> It is worth noting that the association between abruption and cerebral palsy was not universal. In three reports, there was no difference in risk between neonates in pregnancies with and without abruption, but all three focused on particular subpopulations (women without chronic hypertension, spastic cerebral palsy only, and deliveries between 22 and 26 weeks).<sup>25,119,120</sup>

## Subsequent Pregnancy Morbidity

Although there is comparatively less research on the topic, placental abruption in a previous pregnancy is associated with elevated risks in subsequent pregnancies (Table 6). In particular, repeat abruption, preeclampsia, and small for gestational age are the most frequently reported risks in subsequent pregnancies.<sup>20,22,121–128</sup> These three conditions have been collectively termed “ischemic placental disease” and it has been suggested that all three have an origin based in uteroplacental ischemia and it is plausible that they are different manifestations of the same disease.<sup>121,129,130</sup> With that understanding, rather than a cause and effect, abruption in a previous pregnancy may be a marker of underlying disease which also makes preeclampsia and growth restriction more likely to occur.

A history of placental abruption has also been linked with thrombocytopenia, disseminated intravascular coagulopathy, renal impairment, and high-care admission >3 days among mothers, as well as spontaneous preterm birth <34 weeks and stillbirth among neonates, in subsequent pregnancies.<sup>51,126,131</sup> This risk is likely attributed, in part, to the tendency for abruption to reoccur, but in at least one analysis, history of severe abruption (defined as <37 weeks of gestational, with either birth weight <2,500 g or perinatal death) was associated with elevated risk of stillbirth (adjusted OR [aOR] = 2.7, 95% confidence interval [CI]: 1.8–3.9) that was *not* attributed to preeclampsia, small for gestational age, or repeat placental abruption.

## Long-Term Maternal Morbidity and Mortality

Finally, abruption has also been associated with long-term maternal renal and cardiovascular morbidity and mortality; notably, the risk of mortality is elevated for both cardiovascular and noncardiovascular causes (Table 7).<sup>132–137</sup> The elevated risk of cardiovascular-related morbidity and mortality may be a reflection of shared underlying pathophysiology that causes both the abruption and the future cardiovascular events. However, it is less clear how abruption increases risk of noncardiovascular deaths.

## Discussion

In this systematic review, we examined the labor, delivery, maternal, and neonatal outcomes associated with placental abruption in more recent publications when known risk factors

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have changed. Placental abruption was associated with significant maternal morbidity and perinatal morbidity and mortality. There is preliminary evidence that abruption may increase the risk of several poor outcomes independently of preterm birth and that there may also be long-term risks for mothers as well as surviving neonates.

There were several methodological issues in the abruption literature identified in the process of this review. After excluding selection errors and articles in which abruption was an outcome, approximately half of remaining articles were excluded from the review because they lacked a comparison group of any type. Without a referent group, it becomes impossible to determine whether the reported outcomes are occurring more or less frequently than would be observed without placental abruption. Other prominent issues were the lack of, or inconsistency in, definitions of abruption as well as the absence of type and severity information. There is evidence that the percentage of detachment and specific location of the separation are important factors for perinatal outcomes, yet that information is rarely reported. Additionally, as there is no gold standard for diagnosis, there is considerable heterogeneity in what is classified as an “abruption.” When the method of identification was reported, clinical diagnosis of abruption by examination of the placenta in the delivery room was most common, but depending on the study, use of ICD-9-CM or ICD-10 discharge codes, or additional clinical criteria, such as abdominal pain or vaginal bleeding, was sometimes specified. Other studies relied on pathological examination of the placenta which, at present, has uncertain reliability and validity.<sup>138</sup> The lack of standardization of both definitions and reporting requirements alike makes it difficult to interpret and compare risk estimates from various populations. There was also substantial variability in the estimated incidence of abruption, which likely depended on the modality used to identify cases (clinical inspection vs. ultrasound vs. pathological inspection) as well as the particular definition used. At present, little is known about differences in outcomes associated with antepartum versus intrapartum abruptions as well as the latency period for delivery in mild cases. The few studies that did report timing associated with abruption reported the gestational age at delivery, which may or may not be the same as the gestational age at the time the abruption initially occurred. Therefore, we were unable to determine how frequently mild cases of abruption spontaneously resolved or the amount of time that passed between when the abruption occurred and the onset of labor contractions. The lack of information about the specific timing of the abruption itself also makes it more difficult to identify instances of chronic versus acute abruption. Certain outcomes could be used as proxy indicators, such as IUGR for chronic abruption and fetal distress for acute abruption. However, it is entirely possible that IUGR could have resulted from underlying placental dysfunction, which culminated with an acute abruption or that a chronic abruption suddenly worsened, leading to fetal distress. It is certainly likely that chronic and acute abruptions are associated with different patterns of maternal and fetal-neonatal complications, but it remains difficult to clearly distinguish the two with the current state of the science of placental monitoring.

Beyond these issues, little is known about the effect of abruption on labor. It is possible that the hypertonic uterine activity that is frequently associated with abruption contributes to the development of labor contractions and may act in a synergistic manner, effectively shortening the duration of labor. Conversely, it could also be that the contraction pattern associated with

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abruption disrupts or interferes with labor contractions, which could then result in dysfunctional labor.

The optimal mode of delivery in the setting of abruption is also uncertain. Most countries report higher usage of cesarean delivery in the setting of abruption, but again, it is unclear whether these studies were including mild or severe cases (or both).<sup>2,8,22</sup> Case studies (not included in this review) in countries that reported low usage of cesarean in this setting (25–40%) also typically reported higher perinatal mortality (40.4–67.9%), indicating possibly low resource settings.<sup>139–142</sup> It is difficult to determine whether vaginal delivery resulted in more intrapartum fetal deaths, or whether the mother had a vaginal delivery because there was an antepartum fetal death. It may be that cesarean delivery is associated with better birth outcomes in certain circumstances, but these circumstances remain to be identified. Surprisingly, little has been published on delivery practices with abruption in the United States. In one study that met the criteria for this review, 48% of abruption cases were delivered by cesarean, but this study was based on deliveries occurring prior to 2005 and focused exclusively on perivable neonates.<sup>14</sup> Current estimates in a general, representative population remain unknown.

Finally, as a broader methodological issue, there was considerable variation in both the reporting and analysis of related conditions (preeclampsia, IUGR) when estimating risk attributed to abruption specifically. In some instances, these conditions were analyzed as covariates<sup>20,127</sup>; in others, the presence of these disorders was an exclusion criteria<sup>136</sup> or the conditions (and whether they were present or absent) were not mentioned at all.<sup>1,2,73</sup> The optimal methods for accounting for the relative contribution of these related conditions to maternal and neonatal outcomes is not established, but standardizing the reporting of the incidence and how frequently they co-occur with abruption would be advisable. Likewise, it is not clear how frequently other placental disorders (abnormal cord insertion, single umbilical artery, etc.) co-occur with abruption and how such combinations may impact the outcomes.

## Conclusion

Beyond elevated risk of low birth weight, preterm birth, and perinatal mortality, little is known about the short-term or long-term perinatal/neonatal morbidity associated with abruption. Only a handful of studies have examined other outcomes and those have yielded conflicting results. It is also unknown whether these outcomes are found only in severe cases or if mild cases of abruption are also associated with elevated risks.

Despite these limitations, it is clear that placental abruption is associated with significant maternal morbidity and perinatal morbidity and mortality. There is preliminary evidence that abruption may increase the risk of several poor outcomes independently of preterm birth and that there may also be long-term risks for surviving neonates. Our findings underscore the growing recognition for need of standardized definitions of both placental abruption and morbidities in obstetrics to improve comparison of outcomes across research studies and populations.<sup>143</sup> Future studies should include more detailed information about the abruption location, percentage of detachment, and, preferably, the timing and severity of the abruption.

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**Table 1**Obstetrical morbidity incidence and risk estimates<sup>a</sup>

Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	Cesarean	Relaparotomy	Hysterectomy
<b>Cohort</b>					

Gedikbasi et al, Turkey (2008) <sup>26</sup>	All cesarean deliveries, 2002–2006; single site	28,799 (547)	NR	1.5% vs. NR; OR: 15.3 (6.9–33.8)	NR
Tucker Edmonds et al, Multistate (2011) <sup>14</sup>	All deliveries, 23–24 wk, 1995–2005; registry	8,290 (1,197)	48.0 vs. NR; aOR: 2.4 (2.1–2.8)	NR	NR
Pariente et al, Israel (2011) <sup>15</sup>	All deliveries 1988–2008; single site	185,476 (1,365)	67.7 vs. 12.8%; OR: 14.3 (12.7–16.0)	NR	0.4 vs. 0.1%; OR: 7.9 (3.4–18.1)
Chen et al, China (2013) <sup>31</sup>	All deliveries 20 wk, 2009–2010; registry	34,014 (NR)	NR	NR	Peripartum: NR; aOR: 3.0 (0.7–13.1) NS
Boisramé et al, France (2014) <sup>2</sup>	All deliveries >24 wk, 2003–2012; single site	55,926 (247)	90.3 vs. 19.8%; NR	NR	NR
do Nascimento et al, Brazil (2014) <sup>16</sup>	All stillbirths, 2005–2008; single site	163 (2)	NR; aHR: 45.0 (3.1–654.0)	NR	NR
Morikawa et al, Japan (2014) <sup>17</sup>	Singleton deliveries 30 wk, 2005–2009; multisite	293,899 (2,649)	71.7 vs. 27.7%; NR	NR	NR
Räisänen et al, Finland (2014) <sup>18</sup>	Singleton deliveries >22 wk, >500 g, 2000–2010; registry	620,463 (NR)	Nonplanned, nulliparous: NR; aOR: 29.4 (24.2–35.7); nonplanned, multiparous: NR; aOR: 61.8 (52.9–72.2)	NR	NR
Janoudi et al, Canada (2015) <sup>19</sup>	All deliveries >20 wk, >500 g, live birth, maternal age 20, 2011–2012; single site	134,088 (805)	NR; RR: 2.31 (2.18–2.45)	NR	NR
Macheku et al, Tanzania (2015) <sup>20</sup>	All deliveries 28 wk, 2000–2010; registry	39,993 (112)	75.9 vs. 32.4%; aOR: 5.6 (3.6–8.8)	NR	NR
Spiegel et al, Israel (2015) <sup>21</sup>	All twin deliveries with vaginal delivery of first twin, 1988–2010; single site	19,066 (25)	Emergent delivery of second twin: NR; OR: 3.6 (1.5–8.9)	NR	NR
Friedman et al, United States (2016) <sup>30</sup>	All deliveries among women with low to moderate risk for peripartum hysterectomy, 1998–2011; registry	55,214,208 (573,723)	NR	NR	Peripartum: 0.3 vs. NR; aRR: 2.8 (2.5–3.2)
Gul et al, Pakistan (2016) <sup>24</sup>	All deliveries presenting with antepartum hemorrhage >28 wk, 2011–2013; single site	334 (69)	36.2 vs. 23.8%; NR	NR	NR
<b>Case-Control</b>					
Lindqvist and Happach, Sweden (2006) <sup>22</sup>	All deliveries, 1992–1999; single site	2,483 (112)	81.3 vs. 9.4%; NR	NR	NR
Tikkanen et al, Finland (2006) <sup>8</sup>	All deliveries >22 wk, >500 g, 1997–2001; single site	594 (198)	91 vs. 24%; OR: 34.7 (20.0–60.1)	NR	NR

Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	Cesarean	Relaparotomy	Hysterectomy
Bodelon et al, Washington (2009) <sup>29</sup>	All deliveries with cases defined as peripartum hysterectomy, 1987–2006; registry	4,451 (126)	NR	NR	Peripartum: NR; aOR: 3.2 (1.8–5.8)
Kessous et al, Israel (2012) <sup>27</sup>	All cesarean deliveries, 1989–2009; single site	34,469 (1284)	NA	NR; aOR: 3.5 (1.8–6.8)	NR
Levin et al, Israel (2012) <sup>28</sup>	All cesarean deliveries, 2000–2010; single site	177 (6)	NA	NR; OR: 31.1 (3.2–1531)	NR
Hasegawa et al, Japan (2014) <sup>23</sup>	Singleton deliveries >24 wk, 2005–2012; single site	738 (123)	Emergent: 33.3 vs. 5.5%; NR	NR	NR
Furukawa et al, Japan (2015) <sup>25</sup>	All deliveries 22–26 wk, admitted to perinatal center, 2000–2010; single site	101 (32)	56 vs. 67% NS; NR	NR	NR

Abbreviations: aOR, adjusted odds ratio; CD, cesarean delivery; NR, not reported; NS, not significant; OR, odds ratio.

Note: Studies are organized first by type (cohort, followed by case–control), then by year of publication, and then alphabetically by first author.

<sup>2</sup> All outcomes are reported as incidence among abruptio cases versus nonabruption cases followed by risk estimates (confidence interval). When available, preference was given to adjusted risk estimates. Information that was not reported in the original article is designated with “NR.”

Maternal morbidity and mortality incidence and risk estimates<sup>a</sup>

Table 2

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Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	PPH	Transfusion	Other morbidity	Mortality
Cohort						
Abenhaim et al, United States (2008) <sup>41</sup>	All deliveries, 1999–2003; registry	2,940,362 (14,702)	NR	NR	AFE: NR; aOR: 8.0 (4.0–15.9)	AFE: NR; aOR: 2.8 (0.6–13.6) NS
Jacobsen et al, Multicountry (2008) <sup>45</sup>	All deliveries, 1990–2003; registry	613,533 (3,481)	NR	NR	VTE: NR; aOR: 2.5 (1.4–4.6)	NR
Madan et al, New Jersey (2009) <sup>47</sup>	All deliveries, 1997–2005; registry	1,004,116 (NR)	NR	NR	ICU admission: NR; aOR: 8.9 (8.3–9.6)	NR
Spiliopoulos et al, New Jersey (2009) <sup>42</sup>	All deliveries, 1997–2005; registry	1,004,116 (NR)	NR	NR	AFE: NR; aOR: 4.0 (1.5–10.9)	NR
Fong et al, California (2010) <sup>4</sup>	All deliveries with PPH, 1991–2000; registry	138,316 (NR)	NA	NR	PPH: NR; OR: 2.4 (1.4–4.2)	NR
Kolås et al, Norway (2010) <sup>32</sup>	All cesarean deliveries >23 wk, 1998–1999; multisite	2,536 (81)	>1,000 mL: 7.4 vs. 2.7%; aOR: 5.4 (2.0–14.5)	NR	NR	NR
Pariente et al, Israel (2011) <sup>15</sup>	All deliveries, 1988–2008; single site	185,476 (1,365)	0.8 vs. 0.5%; OR: 1.5 (0.8–2.7) NS	14.9 vs. 1.2%; OR: 14.3 (12.2–16.7)	Sepsis: 0.3 vs. 0%; OR: 17.4 (6.1–49.5)	NR
Bentata et al, Morocco (2012) <sup>46</sup>	All deliveries >20 wk, admitted or transferred to ICU during pregnancy or immediately postpartum, 2008–2011; single site	137 (17)	NR	NR	AKI: NR; aOR: 6.3 (1.4–27.6)	ICU: NR; OR: 2.5 (0.7–8.9) NS
Ehrenthal et al, Delaware (2012) <sup>37</sup>	All deliveries 20 wk, 350 g, single 2000–2008; site	59,282 (35)	NR	All deliveries: 11.4 vs. 1.0%; OR: 12.4 (4.37–35.24); vaginal deliveries: NR; aOR: 10.4 (0.9–117.5) NS; Cesarean deliveries: NR; aOR: 2.37 (0.6–9.7) NS	NR	NR
Skjeldestad and Oian, Norway (2012) <sup>33</sup>	All cesarean deliveries, singleton or twins, 1999–2008; registry	80,658 (1,918)	500–1,500 mL after emergent CD: NR; aOR: 2.3 (2.1–2.6); >1,500 mL after emergent CD: NR; aOR: 4.8 (4.0–5.8)	NR	NR	NR

Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	PPH	Transfusion	Other morbidity	Mortality
Suzuki et al, Japan (2012) <sup>38</sup>	All deliveries >22 wk, 2003–2011; single site	17,405 (91)	NR	Singletons, cesarean deliveries: NR; OR: 13.5 (6.7–27.0)	NR	NR
Mehrabadi et al, Canada (2013) <sup>34</sup>	All deliveries, 2001–2009; registry	371,193 (NR)	Atonic: NR; aOR: 1.6 (1.4–1.9)	NR	NR	NR
Mhyre et al, New York (2013) <sup>39</sup>	All deliveries, 1998–2007; registry	690,742 (NR)	NR	10 units red blood cells <24 h: NR; aOR: 14.6 (11.2–19.0)	NR	NR
Boisramé et al, France (2014) <sup>2</sup>	All deliveries >24 wk, 2003–2012; single site	55,926 (247)	12.2 vs. 5.5%; NR	16.6 vs. NR; NR	0%	0%
Wikkelsø et al, Denmark (2014) <sup>40</sup>	All deliveries among women with a first and second pregnancy, 2001–2009; registry	96,545 (374)	NR	Vaginal delivery: NR; cesarean: NR; OR: 3.1 (2.0–4.8)	NR	NR
Coret et al, France (2015) <sup>35</sup>	All deliveries with PPH, 2004–2006; multisite	7,236 (20)	>2000mL: 50 vs. 18.7%; aOR: 3.1 (1.0–9.4) NS	NR	NR	NR
Ekin et al, Turkey (2015) <sup>36</sup>	All deliveries with PPH >24 hrs after delivery, 2011–2014; single site	536 (90)	Severe PPH: NR; aOR: 0.5 (0.2–1.3) NS	NR	NR	NR
Fong et al, California (2015) <sup>43</sup>	All deliveries, 2001–2007; registry	2,770,781 (NR)	NR	AFE: 0.05 vs. 0.004%; aOR: 7.6 (4.2–13.9)	NR	NR
Macheku et al, Tanzania (2015) <sup>20</sup>	All deliveries ≥ 28 wk, 2000–2010; registry	39,993 (112)	8.9 vs. 0.4%; aOR: 17.9 (8.8–36.4)	38.4 vs. 5.6%; aOR: 9.6 (6.5–14.1)	Altered liver function: 1.8 vs. 0.3%; aOR: 5.3 (1.3–21.6); Acute renal failure: 0.9 vs. 0.4%; aOR: 2.2 (0.3–15.5) NS Prolonged hospital stay: 16.1 vs. 3.5%; aOR: 3.5 (1.8–9.6)	3.6% vs. NR; aOR: 1.6 (1.5–1.8)
Ananth et al, United States (2016) <sup>44</sup>	Singleton deliveries, 2006–2012; registry	27,796,465 (268,050)	NR	Severe abruption: AFE: 0.05% vs. 0.004%; aOR: 10.6 (8.4–13.2) <sup>b</sup>	NR	NR

Abbreviations: AFE, amniotic fluid embolism; AKI, acute kidney injury; aOR, adjusted odds ratio; CD, cesarean delivery; ICU, intensive care unit; NR, not reported; NS, not significant; OR, odds ratio; PPH, postpartum hemorrhage; RR, relative risk; VTE, venous thromboembolism.

Note: Studies are organized first by type (cohort, followed by case-control), then by year of publication, and then alphabetically by first author.

<sup>a</sup> All outcomes are reported as incidence among abortion cases versus nonabortion cases followed by risk estimates (confidence interval). When available, preference was given to adjusted risk estimates. Information that was not reported in the original article is designated with "NR."

<sup>b</sup> Additional outcomes reported in this study as associated with abruptio include pulmonary edema, puerperal cerebrovascular disorders, acute heart failure, acute myocardial infarction, cardiomyopathy, acute respiratory failure, and coma.

**Table 3**Neonatal morbidity and mortality incidence and risk estimates<sup>a</sup>

Cohort	Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abortions)	GA <37 wk	IUGR/SGA	Birthweight <2,500 g	IUFD	Neonatal death	Perinatal death
Ananth et al, United States (2005) <sup>48</sup>	Twin deliveries, 22 wk and 500 g, live birth, 1989–2000; registry	1,073,743 (13,527)	80.1 vs. 51.9%; aRR: 1.5 (1.4–1.6)	11.7 vs. 9.2%; aRR: 1.3 (1.2–1.4)	NR	NR	NR	NR	NR
Levy et al, Israel (2005) <sup>49</sup>	All deliveries 1988–2002; single site	153,396 (1,152)	NR; aOR: 1.2 (1.0–1.4)	NR	NR; aOR: 1.4 (1.1–1.6)	NR	NR	NR	NR
Salihu et al, United States (2005) <sup>73</sup>	All deliveries, 1995–1998; registry	Singletons: 15,051,87 (93,968) Twins: 41,3,619 (5,051) Triplets: 22,585 (355)	NR	NR	NR	Singletons: 8.3 vs. 0.5%; aOR: 18.9 (16.9–20.8) Twins: 6.8 vs. 1.7%; aOR: 3.6 (3.6–4.9) Triplets: 10.2 vs. 2.2%; aOR: 5.7 (3.2–10.2)	Singletons: 4.2 vs. 0.3%; aOR: 11.1 (10.0–12.3) Twins: 4.2 (3.7–4.8) Triplets: 9.8 vs. 5.2%; aOR: 2.0 (1.1–3.5)	Singletons: NR; aOR: 14.3 (13.2–15.4) Twins: NR; aOR: 4.4 (3.9–4.9) Triplets: NR; aOR: 3.0 (2.0–4.6)	Singletons: NR; aOR: 14.3 (13.2–15.4) Twins: NR; aOR: 4.4 (3.9–4.9) Triplets: NR; aOR: 3.0 (2.0–4.6)
Tricconi et al, Zimbabwe (2005) <sup>67</sup>	All deliveries, 2000–2001; single site	1,768 (NR)	NR	NR	NR; aOR: 5.49 (1.28–23.52)	NR	NR	NR	NR
Ananth and Vintzileos, Missouri (2006) <sup>50</sup>	Singleton deliveries >19 wk, live birth, 1989–1997; multisite	684,711 (1,812)	<35 wk: 5.8 vs. 0.5%; aRR: 8.8 (8.3–9.3)	NR	NR	NR	NR	NR	NR
Ananth et al, United States (2006) <sup>68</sup>	Singleton deliveries 22 wk–500 g, 1995–2002; registry	30,378,902 (179,204)	NA	Preterm: 16.5 vs. 9.4%; aRR: 1.93 (1.90–1.97) Term: 22.5 vs. 9.2%; aRR: 2.95 (2.91–3.00)	Preterm: 77.5 vs. 37.7%; NR Term: 12.0 vs. 2.6%; NR Term: 3.4 vs. 0.1%; NR	Preterm: 9.8 vs. 2.0%; NR Term: 3.4 vs. 0.1%; NR	NR	NR	NR
Getahun et al, Missouri (2007) <sup>74</sup>	Singleton deliveries 21 wk,	626, 883 (NR)	NR	NR	White: 4.7 vs. NR; aHR: 10.2	NR	NR	NR	NR

Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	GA <37 wk	IUGR/SGA	Birthweight <2,500 g	IUFD	Neonatal death	Perinatal death
	1989–1997; registry	36,453 (295)	Spontaneous >34 wk; NR; aOR: 13.4 (9.4–19.2)	NR	NR	(8.1–12.9) Black; 6.8 vs. NR; aHR: 10.9 (7.4–15.9)		
Lo et al, Taiwan (2007) <sup>51</sup>	Singleton deliveries >20 wk, structurally and chromosomally normal, 1990–2003; single site	1,854,463 (24,492)	NR	NR	NR	NR	NR	NR
McDonald et al, Canada (2007) <sup>86</sup>	All deliveries, 1995–2001; registry	87,231 (668)	NR	NR	NR	NR; aOR: 11.4 (10.6–12.2)	NR	NR
De Lange et al, Australia (2008) <sup>91</sup>	All deliveries with cases defined as perinatal deaths, 2001–2005; registry	16,445 (42)	NR	NR	NR	NR	NR	NR; aOR: 6.40 (4.80–8.55)
Engel et al, Australia (2008) <sup>87</sup>	Singleton deliveries, 1995–1999; registry	1,011 (NR)	NR	NR	NR	NR; OR: 25.1 (11.44–55.25)	NR	NR
Hossain et al, Pakistan (2009) <sup>88</sup>	All vaginal deliveries, cases defined as stillbirths >28 wk, 2008; single site	309,304 (2,031)	NR	NR	NR	NR; OR: 137 (52.7–356.3)	NR	NR
Bhattacharya et al, Scotland (2010) <sup>89</sup>	All deliveries >24 wk, with first and second pregnancies recorded, 1981–2000; registry	1,105,666 (10,225)	NR; aHR: 2.73 (2.67–2.78)	NR	NR	NR; aOR: 1.96 (1.63–2.35)	NR	NR
Burton and Ananth, United States (2010) <sup>52</sup>	Twin deliveries, 20–44 wk, 1995–2004; registry	NR; aOR: 3.8 (1.5–9.5)	NR	NR	NR	NR	NR	NR
Gargano et al, Michigan (2010) <sup>53</sup>	Singleton deliveries, POUCH study, multisite	996 (31)	NR	NR	NR	NR	NR	NR
Ananth and VanderWeele, United States (2011) <sup>1</sup>	Singleton deliveries, 1995–2002; registry	26,364,462 (170,068)	48.7 vs. 8.2%; NR	NR	NR	NR; aRR: 16.91	Early neonatal: NR; aRR: 8.98 (8.58–9.37); Late neonatal:	NR; aRR: 13.76 (13.45–14.08)

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Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	GA <37 wk	IUGR/SGA	Birthweight <2,500 g	IUFD	Neonatal death	Perinatal death
Auger et al, Canada (2011) <sup>54</sup>	Singleton deliveries, 1989–2006; multisite	1,329,737 (22,278)	31.9 vs. NR; aOR: 7.9 (7.7–8.2)	NR	NR	(16.45– 17.36)	NR; aRR: 5.86 (5.44–6.28)	
Ohana et al, Israel (2011) <sup>76</sup>	All deliveries 22 wk, 500 g, 1988–2009; single site	228,239 (NR)	NR	NR	NR	NR	NR	NR
Pariente et al, Israel (2011) <sup>15</sup>	All deliveries, 1988–2008; single site	185,476 (1,365)	56 vs. 7.5%; NR	8.1 vs. 2.1%; OR: 4.2 (3.4–5.1)	54.9 vs. 7.6%; NR	NR	NR	19.4 vs. 1.1%; aOR: 2.7 (2.2–3.3)
Stringer et al, Zambia (2011) <sup>75</sup>	All deliveries 1,000 g, 2006–2009; registry	100,454 (95)	NR	NR	NR	NR; aOR: 5.21 (2.93– 9.29)	NR	NR
Crippa et al, Italy (2012) <sup>69</sup>	All deliveries <1500 g, live-born, 2004–2007; single site	240 (17)	NR	NR; OR: 0.17 (0.04– 0.69)	NR	NR	Composite neonatal death or adverse neurodevelopmental: NR; aOR: 1.6 (0.4–5.9) NS	NR
Faliz et al, New Jersey (2012) <sup>77</sup>	Singleton deliveries, 20 wk, >500 g, 1997–2005; registry	933,258 (NR)	NR	NR	NR	NR; aHR: 40.2 (36.9– 43.9)	NR	NR
Hu et al, Taiwan (2012) <sup>78</sup>	All deliveries 20 wk, >500 g, 2001–2004; registry	940,978 (NR)	NR	NR	NR	NR; aOR: 6.20 (5.35– 7.19)	NR	NR
Sarkar et al, Michigan (2012) <sup>90</sup>	All deliveries 36 wk with asphyxia and receipt of hypothermia for HIE, single site	68 (15)	NR	NR	NR	NR	Composite death or abnormal brain MRI: NR; aOR: 10.3 (1.4–76.7)	NR
Tikkainen et al, Finland (2012) <sup>55</sup>	All deliveries, 22 wk OR >500 g, 1980–2005; registry	1,582,282 (6,231)	48.6 vs. 6.3%; NR	9.4 vs. 2.3%; NR	38.4 vs. 4.5%; NR	NR	NR	NR
Anderson et al, New Zealand (2013) <sup>70</sup>	Singleton deliveries, 2006–2009; single site	26,254 (134)	NR	NR; aOR: 2.57 (1.74– 3.78)	NR	NR	NR	NR
Ogawa et al, Japan (2013) <sup>93</sup>	Singleton deliveries, 22–36 wk, <1,000 g,	1,713 (95)	NR	NR	NR	NR	38.9 vs. 20.3%; aOR: 2.5 (1.2–5.0)	

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Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	GA <37 wk	IUGR/SGA	Birthweight <2,500 g	IUFD	Neonatal death	Perinatal death
	2001–2002; registry	20,195 (26)	NR	NR	NR	NR	NR	NR
Oliveira and Costa, Brazil (2013) <sup>92</sup>	All deliveries admitted to obstetric ICU and maternal near miss, 2007–2010; single site	1,390,742 (2,634)	>28 wk: NR; aOR: 23.41 (18.87– 29.04); 28–31 wk: NR; aOR: 31.69 (29.92– 37.32); 31–36 wk: NR; aOR: 12.18 (11.04– 13.44)	NR	NR	NR	NR	NR
Räisänen et al, Finland (2013) <sup>56</sup>	Singleton deliveries 22 wk OR >500 g, 1987– 2010; registry	1,137,466 (4,336)	NR	NR	NR	NR	NR	NR
Tikkainen et al, Finland (2013) <sup>94</sup>	All deliveries 22 wk, >500 g, 1987–2005; registry	458,384 (2,606)	34–36 wk: 21.6 vs. 5.2%; aRR: 2.3 (2.0– 2.7)	NR	NR	NR	NR	NR
Bassil et al, Canada (2014) <sup>57</sup>	All deliveries, 34– 40 wk, >500 g, 2005–2012; registry	55,926 (247)	69.2 vs. 10.7%; NR	15.1 vs. 5.9%; NR	NR	12.3 vs. 0.4%; NR	6.1 vs. 0.5%; aOR: 0.9 (0.5–1.7)NS	18.4 vs. 0.9%; NR
Boisrancé et al, France (2014) <sup>2</sup>	All deliveries>24 wk, 2003–2012; single site	30 (15)	NR	40 vs. 6.7%; NR	NR	NR	NR	26.7 vs. 0%; NR
Kobayashi et al, Japan (2014) <sup>71</sup>	Singleton deliveries with suspected risk of abortion with recurrent bleeding 5–21 wk and exposed defined as chronic abruption–oligohydramnios sequence, 2005–2011; single site	293,899 (2,649)	60.1 vs. 11.0%; NR	61.6 vs. 15.8%; NR	12.4 vs. 0.4%; NR	Early neonatal death: 1.1 vs. 0.2%; NR	NR	NR
Morikawa et al, Japan (2014) <sup>17</sup>	Singleton deliveries>30 wk, 2005–2009; multisite							

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Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	GA <37 wk	IUGR/SGA	Birthweight <2,500 g	IUFD	Neonatal death	Perinatal death
Patel et al, Utah (2014) <sup>55</sup>	Singleton deliveries ≤30 wk admitted to NICU, 2010–2013; single site	342 (57)	NR	NR	NR	NR	NR	Composite death, severe IVH or NEC; NR; aOR: 1.95 (1.03–3.69)
Trønnes et al, Norway (2014) <sup>58</sup>	All deliveries 23–43 wk, 1967–2001; registry	1,764,509 (7,736)	NR; aOR: 13.5 (12.8–14.2)	NR	NR	NR	NR	NR
Vogel et al, World (2014) <sup>79</sup>	Singleton deliveries 22 wk, >500 g, 2010–2011; multisite	308,392 (1045)	NR	NR	NR	NR	NR	NR
Cetinkaya et al, Turkey (2015) <sup>66</sup>	All deliveries, 1,500 g, live-born, 2008–2012; single site	241 (NR)	NR	NR	NR	NR	NR	NR; OR: 3.4 (0.8–14.1) NS
Fallahi et al, Iran (2015) <sup>59</sup>	All deliveries >20 wk, 2012–2013; single site	1,700 (83)	NR; RR: 4.30 (2.44–7.59)	NR	NR	NR	NR	NR
Kidanto et al, Tanzania (2015) <sup>85</sup>	All deliveries, 2013; multisite	15,305 (NR)	NR	NR	NR	NR	NR	NR
Kuryka et al, New Jersey (2015) <sup>72</sup>	Singleton deliveries >21 wk among Asian Indian and non-Hispanic White women, 2008–2011; registry	192,556 (748)	NR	Asian Indian: NR; aRR: 1.63 (1.18–2.26) Non-Hispanic White: NR; aRR: 1.99 (1.73–2.30)	NR	NR	NR	NR
Macheku et al, Tanzania (2015) <sup>20</sup>	All deliveries 28 wk, 2000–2010; registry	39,993 (112)	26.8 vs. 11.2%; aOR: 0.4 (0.1–7.1) NS	NR	50 vs. 13.2%; aOR: 5.9 (3.9–8.7)	51.8 vs. 37.7%; aOR: 23.7 (15.6–35.9)	Early neonatal death: 4.5 vs. 0.8%; aOR: 4.3 (1.8–9.9)	56.3 vs. 4.4%; aOR: 17.6 (11.3–27.3)
Chidwesha et al, Zambia (2016) <sup>144</sup>	Singleton and first-born twin deliveries 28 wk,	200,557 (122)	NR	NR	41 vs. 10.5%; aOR: 5.2 (2.8–9.4)	NR	NR	NR

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Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	GA <37 wk	IUGR/SGA	Birthweight <2,500 g	IUFD	Neonatal death	Perinatal death
	1,000 g, 2006–2012; registry							
Delorme et al, France (2016) <sup>45</sup>	Singleton live births 24–34 wk, 2011; registry	3,138 (92)	NR	NR	NR	NR	NR	13 vs. NR; aOR: 1.6 (0.7–3.7) NS
Leal et al, Brazil (2016) <sup>63</sup>	All deliveries, 2011–2012; multisite	23,448 (291)	NR; aOR: 2.38 (1.27–4.47)	NR	NR	NR	NR	NR
<b>Case–Control</b>								
Aagaard-Tillery et al, Utah (2006) <sup>80</sup>	All deliveries 20 wk, non-anomalous, 1992–2002; registry	4,286 (NR)	NR	NR	NR	NR; aOR: 8.67 (4.92–15.27)	NR	NR
Lindqvist and Happach, Sweden (2006) <sup>22</sup>	All deliveries, 1992–1999; single site	2,483 (112)	NR	14.3 vs. 5%; NR	NR	4.5 vs. 0.1%; NR	NR	NR
Shaaban et al, Saudi Arabia (2006) <sup>81</sup>	Singleton deliveries, 1,500 g, 2001–2002; single site	16,562 (24)	NR	NR	NR	NR; OR: 23.4 (4.6–119.3)	NR	NR
Tikkainen et al, Finland (2006) <sup>8</sup>	All deliveries >22 wk, >500 g, 1997–2001; single site	594 (198)	59 vs. 10%; OR: 12.9 (8.3–19.8)	25 vs. 4%; OR: 7.9 (4.4–14.3)	NR	4.8 vs. 0.5%; NR	NR	9.2 vs. 1%; OR: 10.1 (3.4–30.1)
Nath et al, New Jersey (2008) <sup>60</sup>	Singleton deliveries 20 wk, 2002–NR; multisite	326 (156)	SGA: 10.3 vs. 1.8%; aOR: 17.4 (4.6–64.9) Non-SGA: 57.1 vs. 12.4%; aOR: 15.8 (8.4–29.8)	37 wk: 5.1 vs. 8.9%; aOR: 1.7 (0.6–4.3) NS <37 wk: 10.3 vs. 1.8%; aOR: 17.4 (4.6–64.9)	60.3 vs. 11.2%; aOR: 13.7 (7.4–25.2)	NR	NR	NR
Ofori et al, Quebec (2008) <sup>61</sup>	All deliveries, 1997–2003; registry	70,207 (2,080)	Singleton: 25.8 vs. 5.9%; aOR: 4.9 (4.3–5.5); Multiple: 42.9 vs. 27.9%; aOR: 2.0 (0.8–5.2) NS >28 wk: NR; aOR: 18.0 (12.9–25.0); 28–32	NR	NR	NR	NR	NR

Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	GA <37 wk	IUGR/SGA	Birthweight <2,500 g	IUFD	Neonatal death	Perinatal death
		wk: NR; aOR: 11.0 (8.9–13.7); 33–36 wk: NR; aOR: 3.4 (3.0–3.9)						
Helgadottir et al, Norway (2011) <sup>82</sup>	All deliveries wk, >500 g, 1990–2003; multisite	88,987 (491)	NR	NR	NR	NR; aOR: 22.0 (15.8–30.8)	NR	NR
Al-Kadi and Tamim, Saudi Arabia (2012) <sup>84</sup>	Singleton deliveries 24 wk, single site >500 g, 2008–2009;	375 (26)	NR	NR	NR	NR; aOR: 25.81 (5.84–114.13)	NR	NR
Brailevschi et al, Israel (2012) <sup>83</sup>	All deliveries 24 wk, >500 g, alive at start of labor, 1988–2008; single site	204,102 (1,221)	NR	NR	NR	NR; aOR: 3.24 (1.74–6.05)	NR	NR
Hasegawa et al, Japan (2014) <sup>23</sup>	Singleton deliveries >24 wk, 2005–2012; single site	738 (123)	NR	Intrapartum: 31.2 vs. 15.9%; NR; Anepartum: 28.9 vs. 15.9%; NR	NR	4.9 vs. 2.1% NS; NR	NR	NR
Joseph et al, Nova Scotia (2014) <sup>62</sup>	Singleton deliveries, 21 wk, 500 g, 1988–2003; registry	132,714 (NR)	sPTB: NR; aRR: 9.15 (7.78–10.8); Iatrogenic: NR; aRR: 12.6 (9.14–17.5)	NR	NR	NR	NR	NR
Funkawa et al, Japan (2015) <sup>25</sup>	All deliveries 22–26 wk, admitted to perinatal center, 2000–2010; single site	101 (32)	NA	2 vs. 14% NS; NR	NR	19 vs. 12% NS; NR	NR	NR

Abbreviations: aHR, adjusted hazard rate; aOR, adjusted odds ratio; aRR, adjusted relative risk; GA, gestational age; HIE, hypoxic-ischemic encephalopathy; IUFD, intruterine fetal demise; IUGR, intrauterine growth restriction; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; NICU, neonatal intensive care unit; NR, not reported; NS, not significant; OR, odds ratio; RR, relative risk; SGA, small for gestational age; sPTB, spontaneous preterm birth.

Note: Studies are organized first by type (cohort, followed by case-control), then by year of publication, and then alphabetically by first author.

<sup>a</sup> All outcomes are reported as incidence among abruption cases versus nonabruption cases followed by risk estimates (confidence interval). When available, preference was given to adjusted risk estimates. Information that was not reported in the original article is designated with "NR."

**Table 4**

## Other short-term neonatal morbidities

Cohort	Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	Prematurity-related morbidity	Hypoxia-related morbidity	Other morbidity
Luig et al, Australia (2005) <sup>106</sup>	All deliveries 24–31 wk, admitted to NICU, 1994–1999; multisite	4,649 (108)	NEC: NR; aOR: 2.09 (1.30–3.35)	NR	NR	
Andreani et al, Italy (2007) <sup>98</sup>	Singleton deliveries 24–33.6 wk, 1993–2005; single site	786 (60)	NR	Acidosis: NR; OR: 6.9 (2.9–15.8)	NR	
Gouyon et al, France (2008) <sup>105</sup>	All deliveries 37 wk, live births, 2000–2003; registry	65,000 (112)	RDS: NR; aOR: 5.0 (1.2–20.5)	NR	NR	
Távora et al, Brazil (2008) <sup>110</sup>	All deliveries, admitted to NICU, 2003; single site	948 (59)	NR	NR	Nosocomial infection: 45.8 vs. 25.5%; aOR: 2.7 (1.4–5.4)	
Dani et al, Italy (2010) <sup>103</sup>	All deliveries 28 wk, admitted to NICU, 1999–2007; single site	218 (19)	IVH: 32 vs. 30%; aRR: 0.94 (0.47–1.88) NS	NR	NR	
Strastrup and Trasande, United States (2012) <sup>108</sup>	Singleton deliveries, 1993–2008; registry	65,516,569 (55,274)	NR	NR	FMH: NR; aOR: 9.77 (7.18–13.31)	
Chen et al, China (2013) <sup>104</sup>	All deliveries 34 wk, 2005–2006; multisite	1,792 (NR)	IVH or PVL: NR; OR: 1.30 (0.25–6.87) NS	NR	NR	
Lee et al, Multistate (2013) <sup>107</sup>	All deliveries 28 wk, 2002–2004; multisite	1,199 (126)	ROP: Stage 3–5: NR; aOR: 0.6 (0.3–1.0) NS; Plus disease: NR; aOR: 0.5 (0.2–1.1) NS; Zone I: NR; aOR: 0.2 (0.1–0.8); Prethreshold/threshold: NR; aOR: 0.3 (0.1–0.7); ET-ROP treatable: NR; aOR: 0.6 (0.3–1.2) NS	NR	NR	
Akinloye et al, Canada (2014) <sup>111</sup>	All deliveries 35 wk, requiring positive pressure ventilation at birth, 1994–2013; single site	3,305 (91)	NR	NR	Prolonged PPV: NR; OR: 2.5 (1.5–4.1)	
Boisramé et al, France (2014) <sup>2</sup>	All deliveries ≥24 wk, 2003–2012; single site	55,926 (247)	NR	Acidosis: 12.4 vs. 0.6%; aOR: 14.9 (9.2–23.9)	Resuscitation: 63.4 vs. 9.1%; aOR: 4.6 (3.1–6.8)	
Kobayashi et al, Japan (2014) <sup>71</sup>	Singleton deliveries with suspected risk of abortion with recurrent bleeding 5–21 wk and exposed defined as chronic abruptio-oligohydramnios sequence, 2005–2011; single site	30 (15)	NR	NR	Mechanical ventilation: 86.7 vs. 13.3% NR; High-frequency oscillation: 46.7% vs. 6.7%; NR; Home oxygen therapy: 45.5 vs. 6.7%; NR	

Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	Prematurity-related morbidity	Hypoxia-related morbidity	Other morbidity
Nelson et al, Texas (2014) <sup>100</sup>	Singleton deliveries 36 wk, live-born, 2005–2011; single site	86,371 (171)	NR	Whole-body cooling: NR; aOR: 17.4 (6.9–43.6)	NR
Macheku et al, Tanzania (2015) <sup>20</sup>	All deliveries 28 wk, 2000– 2010; registry	39,993 (112)	NR	NR	NICU admission: 20.5% vs. 14.2%; aOR: 1.5 (0.9–2.4); NS
Zhao et al, China (2015) <sup>146</sup>	All deliveries 37 wk and Apgar 7, 2012; single site	1,199 (4)	NR	NR	Retinal hemorrhage: NR; OR: 1.03 (0.11– 9.89) NS
Sabol and Caughey, Oregon (2016) <sup>99</sup>	Singleton deliveries 37 wk, nonanomalous with 5-min Apgar 7, 1990–2009; single site	26,669 (NR)	NR	pH 7.0: 13.2 3.4%; vs. NR	NR
<b>Case–Control</b>					
Locatelli et al, Italy (2010) <sup>101</sup>	All deliveries 37 wk, live births with cases defined as neonatal encephalopathy, 1993–2003; single site	127 (5)	NR	NE: NR; OR: 17.2 (2.4–118.9)	NR
Hasegawa et al, Japan (2014) <sup>23</sup>	Singleton deliveries >24 wk, 2005–2012; single site	738 (123)	NR	NR	NICU admission: 38.2 vs. 35.1% NS; NR
Arcinie et al, Ohio (2015) <sup>109</sup>	All deliveries with cases defined as neonates with AKI and either ELW or birth weight <750 g who were admitted to NICU, 1998–2008; single site	211 (NR)	AKI: NR; OR: 2.26 (1.30–3.94)	NR	NR
Furukawa et al, Japan (2015) <sup>25</sup>	All deliveries 22–26 wk, admitted to perinatal center, 2000–2010; single site	101 (32)	IVH: 22 vs. 23% NS; NR	Acidosis: 0 vs. 4.3% NS; NR	NR
Nasiell et al, Sweden (2016) <sup>102</sup>	All deliveries with cases defined as infants receiving hypothermia for treatment of HIE, 2007–2010; multisite	141 (8)	NR	HIE: NR; OR: 20.31 (1.99– 207.53)	NR

Abbreviations: AKI, acute kidney injury; aOR, adjusted odds ratio; aRR, adjusted relative risk; CD, cesarean delivery; ELBW, extremely low birth weight; FMH, fetomaternal hemorrhage; HIE, hypoxic-ischemic encephalopathy; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; NICU, neonatal intensive care unit; NR, not reported; NS, not significant; PPV, positive pressure ventilation; OR, odds ratio; RDS, respiratory distress syndrome; ROP, retinopathy of prematurity; RR, relative risk.

Note: Studies are organized first by type (cohort, followed by case–control), then by year of publication, and then alphabetically by first author.

<sup>a</sup> All outcomes are reported as incidence among abrupton cases versus nonabruption cases followed by risk estimates (confidence interval). When available, preference was given to adjusted risk estimates. Information that was not reported in the original article is designated with “NR.”

**Table 5**Long-term infant morbidity and mortality incidence and risk estimates<sup>a</sup>

Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	Cerebral palsy	Chronic lung disease	Infant mortality	Epilepsy	Cognitive deficit
Cohort							
Ananth et al, United States (2005) <sup>48</sup>	Twin deliveries, 22 wk and 500 g, live birth, 1989–2000; registry	1,073,743 (13,527)	NR	NR	Non-SGA, term: 1.3 vs. 3.1%; aRR: 2.0 (1.0–3.9) NS; SGA only: 3.5 vs. 3.1%; aRR: 9.9 (5.4–14.5); Preterm only: 7.9 vs. 3.1%; aRR: 25.0 (22.3–28.1); SGA and preterm: 5.9 vs. 3.1%; aRR: 36.2 (28.4–44.1)	NR	NR
Whitehead et al, Canada (2006) <sup>118</sup>	All deliveries with live births, 1986–2001; registry	124,207 (1,054)	NR	NR	NR	NR; aRR: 2.3 (1.5–3.6)	NR
Hjern and Thorngren-Jerneck, Sweden (2008) <sup>112</sup>	All deliveries, neonates surviving first year, 1987–1993; registry	805,543 (3,778)	NR; OR: 10.9 (8.4–14.1)	NR	NR	NR	NR
Love et al, United Kingdom (2012) <sup>19</sup>	All deliveries among primigravidae women without hypertension, 1995–2008; registry	28,967 (172)	NR; aOR: 2.46 (0.65–9.24) NS	NR	NR	NR	NR
Kobayashi et al, Japan (2014) <sup>71</sup>	Singleton deliveries with suspected risk of abortion with recurrent bleeding 5–21 wk and exposed defined as chronic abruption–oligohydramnios sequence, 2005–2011; single site	30 (15)	NR	73.3 vs. 6.7%; NR	NR	NR	NR
Trønnes et al, Norway (2014) <sup>58</sup>	All deliveries 23–43 wk, 1967–2001; registry	1,764,509 (7,736)	NR; aOR: 8.0 (6.6–9.6)	NR	NR	NR	NR
Ananth et al, United States (2016) <sup>17</sup>	Singleton deliveries 24 wk, 1959–1966; registry	40,539 (635)	NR	NR	NR	NR	8 mo abnormal Bayley motor: 3.3 vs. 0.9%; aRR: 2.35 (1.39–3.98); 8 mo abnormal Bayley mental: 2.5 vs. 0.9%; aRR: 2.03 (1.13–3.64); 4 y IQ <70: 5.3 vs. 4.1%; aRR:

Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	Cerebral palsy	Chronic lung disease	Infant mortality	Epilepsy	Cognitive deficit
Hassegawa et al, Japan (2016) <sup>116</sup> Case–Control	Singleton deliveries 33 wk, 2,000 g, live birth, no major congenital anomalies, 2009–2011; registry	144,339 (161)	NR; aRR: 20.89 (11.82–36.9)	NR	NR	NR	1.77 (1.23–2.55); 7 y IQ <70; 3.7 vs. 3.1%; aRR: 1.59 (0.97–2.60) NS
<b>Case–Control</b>							
Stelmach et al, Estonia (2005) <sup>113</sup>	All cases with CP <16 years old, 2000; registry	421 (17)	NR; OR: 13.1 (2.99–57.7)	NR	NR	NR	NR
Thorngren-Jerneck and Herbst, Sweden (2006) <sup>114</sup>	All cases of CP 4 years old, 1984–1998; registry	1,602;303 (NR)	NR; OR: 8.58 (5.63–13.3)	NR	NR	NR	NR
Nielsen et al, Denmark (2008) <sup>120</sup>	Singleton deliveries with cases defined as spastic cerebral palsy, 1982–1990; registry	434 (45)	NR; OR: 1.1 (0.56–1.99) NS	NR	NR	NR	NR
Kulak et al, Poland (2010) <sup>115</sup>	All deliveries ≥36 wk, live birth, 1990–2005; single site	493 (34)	NR; OR: 2.41 (1.16–4.97)	NR	NR	NR	NR
Furukawa et al, Japan (2015) <sup>25</sup>	All deliveries 22–26 wk, admitted to perinatal center, 2000–2010; single site	101 (32)	28 vs. 33% NS; NR	66 vs. 43%; NR	NR	NR	NR

Abbreviations: aOR, adjusted odds ratio; aRR, adjusted relative risk; NR, not reported; NS, not significant; OR, odds ratio; SGA, small for gestational age; SIDS, sudden infant death syndrome.

Note: Studies are organized first by type (cohort, followed by case–control), then by year of publication, and then alphabetically by first author.

<sup>a</sup> All outcomes are reported as incidence among abortion cases versus nonabortion cases followed by risk estimates (confidence interval). When available, preference was given to adjusted risk estimates. Information that was not reported in the original article is designated with “NR.”

**Table 6**Subsequent pregnancy maternal and perinatal morbidity and mortality incidence and risk estimates<sup>a</sup>

Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	Preeclampsia	Repeat abruption	Other maternal morbidity	Perinatal morbidity and mortality
<b>Cohort</b>						
Ananth et al, Missouri (2007) <sup>121</sup>	Singleton delivery pairs, live births, 1989–1997; registry	154,810 pairs (2,167)	15.0 vs. 8.2%; aOR: 1.91 (1.52–2.40)	2.8 vs. 0.7%; aOR: 3.16 (2.18–4.58)	NR	SGA: 15.0 vs. 8.2%; aOR: 1.6 (1.4–1.9)
Ananth et al, Sweden (2007) <sup>122</sup>	Singleton delivery pairs, 1983–2001; registry	526,690 pairs (2,673)	NR	4.4 vs. 0.4%; aOR: 11.6 (9.5–14.1)	NR	NR
Lo et al, Taiwan (2007) <sup>51</sup>	Singleton deliveries >20 wk, structurally and chromosomally normal, 1990–2003; single site	36,453 (295)	NR	NR	NR	sPTB <34 wk; NR; aOR: 7.9 (2.4–26.0)
Rasmussen, Norway (2007) <sup>123</sup>	Delivery pairs 16 wk, 1967–2005; registry	119,518 pairs (990)	Mild: 4.5 vs. 1.8%; aOR: 2.4 (1.6–3.6); Severe: 1.8 vs. 0.6%; aOR: 2.7 (1.4–5.1); Early onset: 1.6 vs. 0.5%; aOR: 5.3 (2.7–10.4)	3.9 vs. 0.4%; aOR: 8.3 (5.1–13.5)	NR	SGA: 14.3 vs. 8.3%; aOR: 1.7 (1.4–2.2)
Rasmussen et al, Norway (2009) <sup>131</sup>	Singleton delivery pairs 16–44 wk, 1967–2005; registry	611,957 pairs (3,295)	NR	NR	NR	Stillbirth: NR; Overall: aOR: 2.8 (2.2–3.5); mild abruption: aOR: 1.4 (0.8– 2.4) NS; severe abruption: aOR: 3.4 (2.6– 4.5)
Ananth et al, Norway (2015) <sup>124</sup>	Singleton delivery pairs, 1967–2009; registry	747,566 pairs (4,218)	NR	Overall: 3.9 vs. 0.5%; NR	NR	NR
Macheku et al, Tanzania (2015) <sup>20</sup>	All deliveries 28 wk, 2000–2010; registry	39,993 (112)	NR	0.7 vs. 0.2%; aOR: 2.3 (1.8–3.4)	NR	NR
Ruitter et al, the Netherlands (2015) <sup>125</sup>	Singleton delivery pairs, 1999–2007; registry	264,424 pairs (709)	NR	5.8 vs. 0.1%; aOR: 93 (62–139)	NR	NR
<b>Case–Control</b>						
Lindqvist and Happach, Sweden (2006) <sup>22</sup>	All deliveries, 1992–1999; single site	2,483 (112)	NR	NR; OR: 25.8 (9.8– 68.3)	NR	NR
Mataseng et al, South Africa (2006) <sup>126</sup>	Deliveries >24 wk; NR; single site	108 (63)	NR	35.5 vs. 3.1%; NR	Thrombocytopenia: 26 vs. 14% NS; NR; DIC: 15.6 vs. 0%; NR; Renal impairment: 11.1	NR

Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	Preeclampsia	Repeat abortion	Other maternal morbidity	Perinatal morbidity and mortality
Tikkainen et al, Finland (2006) <sup>128</sup>	All deliveries >22 wk, >500 g, 1997–2001; single site	594 (198)	NR	NR; OR: 4.5 (1.1–18.0)	vs. 3.0% NS; NR; High-care admit >3 d: 13.0 vs. 1.5% NS; NR	NR
Parker et al, Finland (2015) <sup>127</sup>	Singleton deliveries 22 wk, 500 g, multiparous; 1996–2010; registry	32,435 (207)	NR; aOR: 1.7 (1.2–2.3) <34 wk; NR; aOR: 3.0 (1.6–5.4); 34 wk; NR; aOR: 1.5 (1.1–2.2)	NR	NR	NR

Abbreviations: aOR, adjusted odds ratio; ARR, adjusted relative risk; CP, cerebral palsy; DIC, disseminated intravascular coagulopathy; NR, not reported; NS, not significant; OR, odds ratio; SGA, small for gestational age; SIDS, sudden infant death syndrome; sPTB, spontaneous preterm birth.

Note: Studies are organized first by type (cohort, followed by case-control), then by year of publication, and then alphabetically by first author.

<sup>a</sup> All outcomes are reported as incidence among abortion cases versus nonabortion cases followed by risk estimates (confidence interval). When available, preference was given to adjusted risk estimates. Information that was not reported in the original article is designated with "NR."

**Table 7**Long-term maternal morbidity and mortality incidence and risk estimates<sup>a</sup>

Authors, location (year)	Inclusion criteria and dates; data source	Sample size (abruptions)	Morbidity	Mortality
<b>Cohort</b>				
Lykke et al, Denmark (2010) <sup>132</sup>	Women aged 15–50 y with a first singleton delivery and no history of preceding cardiovascular diagnosis, 1978–2007; registry	796,915 (7,684)	NR	Noncardiovascular: 1.4 vs. NR; aHR: 1.56 (1.29–1.89) Cardiovascular: 0.2 vs. NR; aHR: 1.23 (0.78–1.93) NS
Ray et al, Canada (2012) <sup>133</sup>	Women aged 14–50 y delivering at ≥ 20 wk who were disease free at least a year prior to delivery, 1992–2009; registry	1,130,764 (10,935)	Hospitalization for heart failure or an atrial or ventricular dysrhythmia: NR; aHR: 1.51 (0.97–2.35) NS	NR
Pariente et al, Israel (2014) <sup>134</sup>	All deliveries, 1988–1998; Registry	47,585 (653)	NR	Cardiovascular: 0.6 vs. 0.1%; aHR: 4.3 (1.1–18.6)
Arazi et al, Israel (2015) <sup>135</sup>	All deliveries without known renal disease before or during pregnancy, 1988–2012; registry	99,354 (1,807)	Renal morbidity: 0.2 vs. 0.1%; aOR: 1.8 (0.6–4.8) NS; Renal-related hospitalization: 0.2 vs. 0.1%; aHR: 1.6 (0.6–4.2) NS	NR
DeRoo et al, Norway and Sweden (2016) <sup>136</sup>	Women with singleton deliveries, 1967–2002 (Norway), 1973–2003 (Sweden); registry	2,117,797 (10,981)	NR	Noncardiovascular: Abruptio in first pregnancy: 2.5 vs. 1.9%; aHR: 1.2 (1.0–1.3); Abruptio in any pregnancy: 2.4 vs. 1.9%; aHR: 1.2 (1.1–1.3) Cardiovascular: Abruptio in first pregnancy: 0.5 vs. 0.3%; aHR: 1.8 (1.3–2.4); Abruptio in any pregnancy: 0.5 vs. 0.3%; aHR: 1.8 (1.5–2.2)
Ray et al, Canada (2016) <sup>137</sup>	Women ≥ 20 y undergoing a first percutaneous coronary intervention or artery bypass with a history of 1 deliveries, 1993–2012; registry	1,985 (48)	NR	Death after coronary artery revascularization: NR; aHR: 2.79 (1.31–5.96)

Abbreviations: aHR, adjusted hazard ratio; aOR, adjusted odds ratio; aRR, adjusted relative risk; CP, cerebral palsy; NR, not reported; NS, not significant; OR, odds ratio; SIDS, sudden infant death syndrome.

Note: Studies are organized first by type (cohort, followed by case–control), then by year of publication, and then alphabetically by first author.

<sup>a</sup>All outcomes are reported as incidence among abruption cases versus nonabruption cases followed by risk estimates (confidence interval). When available, preference was given to adjusted risk estimates. Information that was not reported in the original article is designated with “NR.”