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REVIEW

Epidemiology of preterm birth and its clinical subtypes

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Abstract

Preterm birth (<37 weeks) complicates 12.5% of all deliveries in the USA, and remains the leading cause of perinatal mortality and morbidity, accounting for as many as 75% of perinatal deaths. Despite the recent temporal increase in preterm birth, efforts to understand the problem of prematurity have met with little success. This may be attributable to the under-appreciation of the etiologic heterogeneity of preterm birth as well as the heterogeneity in its underlying clinical presentations—spontaneous onset of labor, preterm premature rupture of membranes, and medically indicated preterm birth. In this paper, we review data regarding preterm births with particular focus on its incidence, temporal trends, and recurrence. Studies of births from the USA indicate that the recent temporal increase in the overall preterm birth rate is driven by an impressive concomitant increase in medically indicated preterm birth. However, the largest temporal decline in perinatal mortality has also occurred among medically indicated preterm births (relative to other clinical subtypes), suggesting that these obstetric interventions at preterm gestational ages are associated with a reduction in perinatal mortality. Recent data indicate that spontaneous preterm birth is not only associated with increased recurrence of spontaneous, but also medically indicated, preterm birth, and vice versa. This suggests that the clinical subtypes may share common underlying etiologies. Since medically indicated preterm birth accounts for as many as 40% of all preterm births, efforts to understand the reasons for such interventions and their impact on short- and long-term morbidity in newborns is compelling. Further research is necessary in order to understand the mechanisms and etiology of preterm birth, thus leading to the possibility of effective preventive or therapeutic strategies.

Keywords: *Preterm birth, spontaneous labour, medically indicated preterm birth, race-disparity, etiology, epidemiology, ischemic placental disease*

The prematurity problem

Preterm birth, defined by the World Health Organization as the delivery of the fetus at <37 completed weeks of gestation (or 259 days from the first day of the last menstrual period) [1], complicates over 500 000 births in the USA annually, giving a rate of 12.5% [2]. This staggering statistic translates to roughly one preterm birth every minute in the USA. Unfortunately, despite being well-studied, little progress has been made toward understanding the etiology of preterm birth [3–6], including: (i) the temporal increase in the incidence of preterm birth in the USA [7–10] and some other industrialized countries [11–13]; (ii) the sizeable and disparate etiologic heterogeneity in its clinical subtypes, namely, spontaneous and medically indicated preterm births [14–19]; and (iii) the persistent black–white disparity [4,7,15,20].

Approximately three-fourths (75–80%) of perinatal deaths occur in fetuses that are delivered at <37 weeks [21,22], and about 40% of these deaths occur in those delivered at <32 weeks [6]. Among surviving infants, preterm birth is implicated in

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approximately half of all pediatric neurodevelopmental disabilities [23–25], including cerebral palsy [26], long-term morbidity [4,6,23], and high healthcare costs [27,28].

The aims of this review are to provide an overview of the epidemiology of preterm birth focusing specifically on recent data regarding potential sources of etiologic heterogeneity of the condition, to evaluate temporal trends in preterm birth and its clinical subtypes, and to assess the extent to which preterm birth recurs in subsequent pregnancies. In addition, we discuss the potential sources of heterogeneity in the clinical subtypes of preterm birth, and finally propose directions for further research. This overview is largely confined to the problem of prematurity in the USA, although supporting data from other western societies are also presented and contrasted.

Sources of preterm birth

Despite the recognition of the etiologic heterogeneity of preterm birth, it is usually classified into subtypes based on clinical presentations: spontaneous preterm birth (spontaneous onset of labor or following preterm premature rupture of membranes (PROM)) and medically indicated preterm birth. The etiology of these underlying clinical subtypes varies considerably across populations and regions. Even within populations, variations in preterm birth clinical subtypes by patient characteristics, physician practice patterns, and more importantly, maternal race/ethnic composition, abound [14,29,30]. The stratification of preterm births based on clinical subtypes, however, remains controversial [31].

A review of studies on preterm birth subtypes among singleton and twin births are summarized in Tables I and II. Among all singleton preterm births at <37 weeks, the frequency of preterm PROM, spontaneous preterm labor, and medically indicated preterm birth as a proportion of all preterm births ranged between 8.5% and 51.2%, 27.9% and 65.4%, and 20.0% and 38.3%, respectively. Among singleton births in the USA, 69% and 31% of preterm births are the result of spontaneous and medically indicated preterm births, respectively [8].

Table I. Rates of preterm birth and its clinical subtypes among singleton gestations: summary of evidence among selected studies in the USA since 1985.

			Rate among preterm births (%)				Rate among all births (%)		
Author	Years studied	Maternal race	All (*n* (%))	PROM	Spont.	Med.	PROM	Spont.	Med.
Berkowitz [79]	1977–1978	White/black	175 (4.8)	42.3	57.7	–	2.0	2.8	–
Arias et al. [80]	1978–1979	–	355 (8.6)	34.9	29.9	35.2	3.0	2.6	3.0
Tucker et al. [81]	1982–1986	White	403 (10.4)	24.0	50.0	26.0	2.5	5.2	2.8
Tucker et al. [81]	1982–1986	Black	1042 (11.3)	29.2	45.1	25.7	3.3	5.1	2.9
Meis et al. [82]*	1983–1984	White	45 (6.1)	35.6	44.4	20.0	2.2	2.7	1.2
Meis et al. [82]*	1983–1984	Black	86 (10.8)	51.2	27.9	20.9	5.6	3.0	2.3
Main et al. [83]	1983–1984	Black	58 (15.4)	37.9	37.9	24.1	5.9	5.9	3.7
Schieve and Handler [84]	1988–1989	White	1616 (8.5)	58.2	20.1	18.6	5.0	1.7	1.6
Schieve and Handler [84]	1988–1989	Black	2482 (19.1)	20.8	67.8	11.4	4.0	12.9	2.2
Ananth et al. [8]	1989	White	246 472 (8.3)	13.3	59.0	27.7	1.1	4.9	2.3
Ananth et al. [8]	2000	White	288 675 (19.4)	8.5	53.2	38.3	0.8	5.0	3.6
Ananth et al. [8]	1989	Black	120 530 (8.5)	12.4	65.4	22.2	2.3	12.1	4.1
Ananth et al. [8]	2000	Black	97 297 (16.2)	9.3	56.1	34.6	1.5	9.1	5.6

*Includes only public clinic patients. PROM, premature rupture of membranes; Spont., spontaneous; Med., medically indicated.

Table II. Rates of preterm birth and its clinical subtypes among twin gestations: summary of evidence among selected studies in the USA since 1985.

			Rate among all births (%)				Rate among preterm births (%)		
Author	Years studied	Maternal race	All (*n*(%))	PROM	Spont.	Med.	PROM	Spont.	Med.
Gardner et al. [58]	1982–1986	White	– (52.0)	10.4	29.1	11.4	20.0	56.0	24.0
Gardner et al. [58]	1982–1986	Black	– (55.0)	11.6	29.7	13.8	21.0	54.0	25.0
Ananth et al. [7]	1989–1990	White	67 258 (46.6)	6.2	16.2	24.1	13.3	34.8	51.9
Ananth et al. [7]	1999–2000	White	104 283 (56.7)	4.8	16.6	35.2	8.6	29.3	62.1
Ananth et al. [7]	1989–1990	Black	20 443 (56.6)	7.6	21.9	26.5	13.4	38.7	47.9
Ananth et al. [7]	1999–2000	Black	24 058 (61.0)	6.2	19.5	35.3	10.2	32.0	57.8

PROM, premature rupture of membranes; Spont., spontaneous; Med., medically indicated.

Approximately half of twin pregnancies are delivered preterm (<37 weeks). Of these twin preterm births, the proportion of preterm PROM, spontaneous preterm labor, and medically indicated preterm birth ranged between 8.6% and 21.0%, 29.3% and 56.0%, and 22.0% and 62.1%, respectively. Data in the USA indicate that 44% and 56% of all preterm births among twin gestations are the result of spontaneous and medically indicated preterm births, respectively [7].

Not only are the proportions in the three clinical subtypes of preterm birth varied, but differences in patient characteristics, populations studied, high-risk composition of the patient populations, and plurality are some of the chief factors that are likely to contribute to the heterogeneity in clinical presentations leading to preterm birth.

Most of the data on underlying clinical subtypes are, nonetheless, at least 15 years old. Given the dramatic changes in patient demographic characteristics, including increases in the proportion of single mothers [32], maternal overweight and obesity [33], and increase in the burden of chronic and acute illnesses during pregnancy [34], coupled with recent increases in obstetric interventions at preterm gestations [20,35,36], the proportions of preterm birth clinical subtypes are likely to exhibit constant temporal changes [8,37]. In fact, recent studies show that approximately three-fourths (74%) of preterm births occur between 35 and 36 weeks of gestation [35,37,38]—a gestation 'window' recently termed as 'late preterm' or 'near-term' births [39].

Trends in preterm birth, its clinical subtypes, and changes in perinatal mortality

Prevention of preterm birth remains a perinatal priority in the USA and other industrialized countries [3,21,40]. Despite continued efforts to reduce the rate, local clinical and community-based preterm birth prevention programs have clearly fallen short of reducing preterm births [3,21,41]. In fact, the rate of preterm birth in the USA has been steadily increasing over the past two decades [7–10]. This temporal increase has occurred despite the increasing availability of nutrition supplementation programs, participation in adequate prenatal care, and use of tocolytic drugs to arrest contractions and impending labor at preterm gestations [4,21]. Given the current status on trends in preterm birth (discussed below), the Healthy People 2010 objectives [42] note a reduction of preterm births to 7.6%—a figure that is perhaps unachievable in light of the prevailing preterm birth trends.

We recently showed that in the USA preterm birth rates among whites with singleton live births increased from 8.3% in 1989 to 9.4% in 2000, a relative increase of 14% [8] (Table III). Over the same period, the preterm birth rate among blacks declined from 18.5% in 1989 to 16.2% in 2000, a relative decline of 15%. The increase in preterm birth among white women was largely driven by a concurrent and impressive increase in medically indicated preterm birth by 55%. On the other hand, the decrease in the overall preterm birth rate among blacks was driven by a concurrent decline in preterm PROM (37%) and preterm birth following spontaneous onset of labor (27%). This pattern occurred despite the rate of medically indicated preterm births among blacks increasing by 32% [8].

Medical interventions at preterm gestational ages are often performed in the scenario of impending serious fetal or maternal compromise. We examined changes in perinatal mortality (stillbirths at $\geq$20 weeks plus deaths within the first month) rates among singleton births between 1989 and 2000 in

Table III. Changes in rates of preterm birth clinical subtypes and perinatal mortality among singleton live births in the USA between 1989 and 2000.*

	Preterm birth rates			Perinatal mortality		
Preterm birth clinical subtypes	1989	2000	RR (95% CI)	1989	2000	RR (95% CI)
White women						
All preterm births	8.3	9.4	1.14 (1.13, 1.15)	50.6	36.2	0.71 (0.69, 0.73)
PROM	1.1	0.8	0.77 (0.76, 0.78)	60.8	42.6	0.69 (0.63, 0.74)
Spontaneous preterm	4.9	5.0	1.03 (1.02, 1.04)	41.6	29.3	0.70 (0.67, 0.73)
Medically indicated	2.3	3.6	1.55 (1.53, 1.56)	64.7	44.4	0.67 (0.64, 0.70)
Black women						
All preterm births	18.5	16.2	0.85 (0.84, 0.86)	54.1	47.4	0.87 (0.84, 0.91)
PROM	2.3	1.5	0.63 (0.62, 0.65)	74.9	70.9	0.94 (0.85, 1.05)
Spontaneous preterm	12.1	9.1	0.73 (0.70, 0.76)	47.2	41.1	0.87 (0.82, 0.91)
Medically indicated	4.1	5.6	1.32 (1.29, 1.34)	63.0	51.4	0.81 (0.75, 0.87)

Relative risks (RR) denote changes in preterm birth and perinatal mortality rates between 1989 and 2000. Perinatal mortality rates are expressed per 1000 singleton births. *The data shown in this Table are reproduced (with modification) from Ananth et al. [8] with the permission of the publisher.

the USA within categories of preterm birth clinical subtypes (Table III). Given that the largest decline in perinatal mortality occurred among medically indicated preterm births (relative to other subtypes), these data suggest a beneficial effect of medical interventions at preterm gestations insofar as mortality is concerned (Figure 1). We do, however, caution that a decline in perinatal mortality may have inadvertently led to an increase in short- and long-term morbidity in newborns [23,25].

Recurrence of preterm birth and its clinical subtypes

The observation that preterm births have a tendency to recur in subsequent pregnancies is not new. Several studies, mostly from the Scandinavian countries, have demonstrated that there is an increased recurrence of preterm birth (<37 weeks) that ranges between three- and seven-fold [43–51]. A few of these studies have also shown that not only do preterm births recur in subsequent pregnancies, but that the risk of delivering preterm occurs around the same gestation 'window' as the previous preterm birth [46,47,52]. Figure 2 shows the recurrence risks of preterm birth at <37, <35, and <32 weeks in the second pregnancy based on gestational age at delivery in the first pregnancy, in a cohort of 154 809 women with their first two consecutive singleton pregnancies resulting in live births. With advancing gestational age of the first pregnancy, the proportion of women that delivered preterm (recurrence) in the second pregnancy showed a steady decline. Nevertheless, studies on recurrence of preterm birth in the USA have been few and limited, largely mitigated by the lack of availability of appropriate maternally-linked datasets.

Despite the increased tendency of preterm birth to recur, very little is known regarding recurrence risks for spontaneous and medically indicated preterm birth, as well as recurrence risks in relation to severity of preterm birth. We recently showed that not only do preterm births tend to recur, but the recurrence risk appears greatest when the preterm birth in the first pregnancy occurred at <28 weeks with risks progressively declining with advancing gestation [52] (Table IV). In fact, when the data on preterm birth recurrence were further stratified based on its underlying clinical subtypes, the results indicated

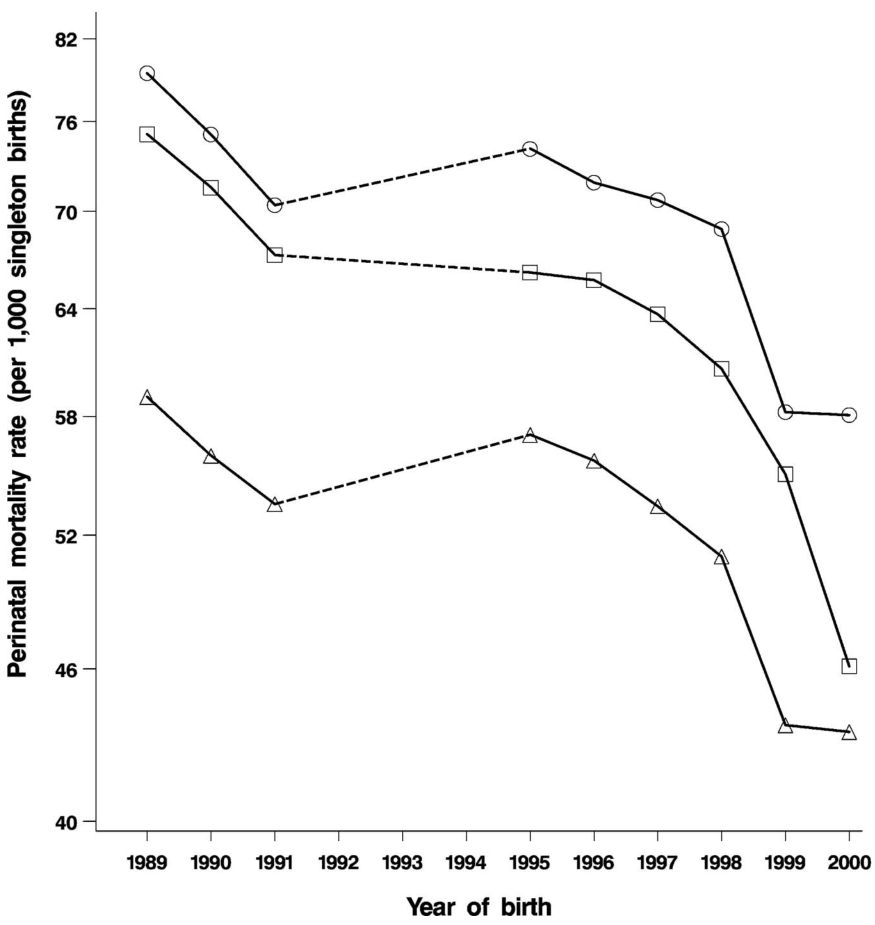

Figure 1. Changes in perinatal mortality rate between 1989 and 2000 among singleton live births in the USA. Circles denote preterm births following ruptured membranes; squares denote medically indicated preterm birth; and triangles denote spontaneous preterm birth.

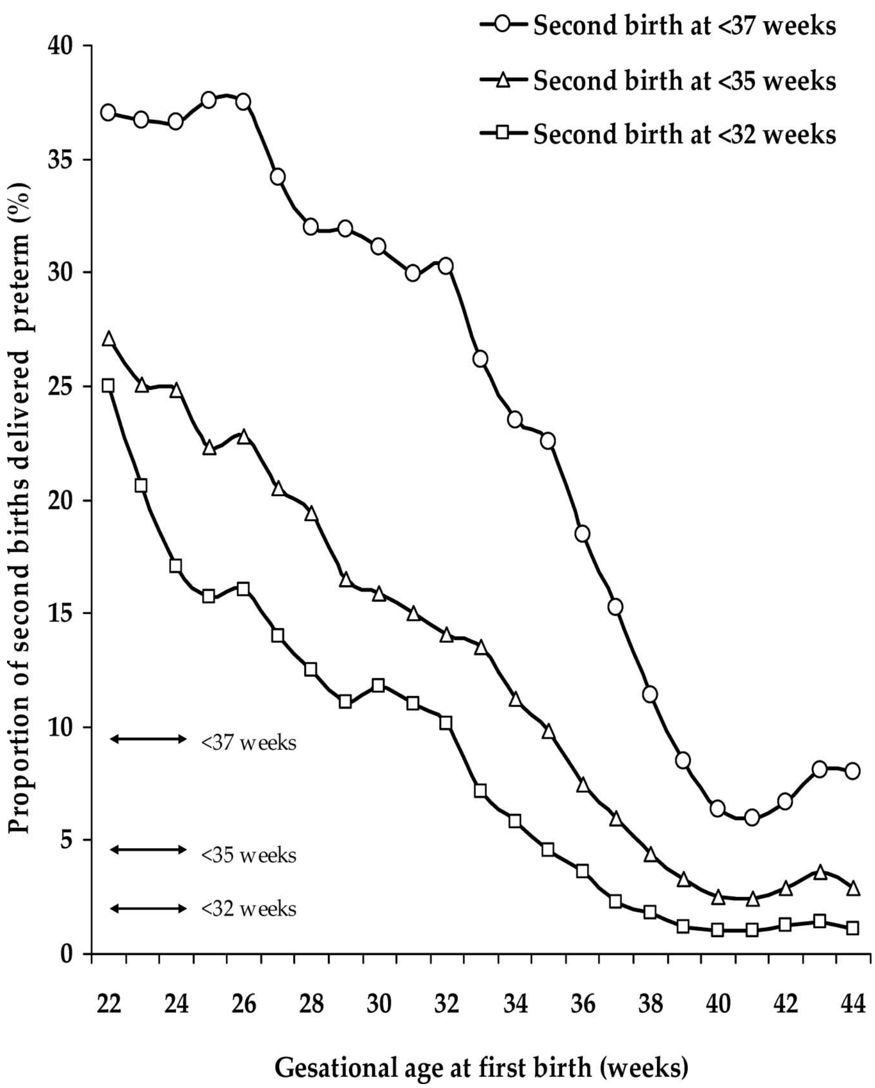

Figure 2. Preterm birth rates <37, <35, and <32 weeks in the second pregnancy based on gestational age at delivery in the first pregnancy: Missouri, 1989–1997. The horizontal arrows denote preterm birth rates (at <37, <35, and <32 weeks) in the first pregnancy. (This Figure is reproduced from Ananth et al. [52] with the permission of the publisher.)

that not only were women with a first spontaneous preterm birth likely to experience a spontaneous preterm birth, but they were also likely to deliver a medically indicated preterm birth in the second pregnancy (Table IV). This pattern was also evident in an analysis of medically indicated preterm birth. This suggests that spontaneous and medically indicated preterm births likely share overlapping etiologies, and that the two clinical subtypes are perhaps not distinct [14,18,53,54].

Heterogeneity of spontaneous and medically indicated preterm birth

There is considerable etiologic heterogeneity surrounding preterm birth clinical subtypes. The most frequent indications prompting an intervention at preterm gestational ages include preeclampsia, placental abruption, intrauterine growth restriction, and fetal distress. However, these conditions may also predispose to spontaneous onset of labor at preterm gestational ages [55–57].

Meis and colleagues [56] showed that these four conditions were present in 87% of singleton preterm births that required an iatrogenic intervention (Table V). More interestingly, 86% of twin preterm births that required a medical intervention at preterm gestational ages had one or more of these same conditions present [58]. We recently showed that preeclampsia, fetal distress, small-for-gestational age (SGA), and placental abruption were the chief conditions that were implicated in well over half of all medically indicated preterm births [59]. The four conditions are distinct in their risk factor profiles, yet they may share a common unifying etiologic mechanism—‘ischemic placental disease’ [59].

Table IV. Recurrence of preterm birth based on timing and clinical subtypes in the second pregnancy in relation to severity and clinical subtypes of previous preterm birth: Missouri, 1989–1997.*

First pregnancy	Adjusted odds ratio (95% confidence interval) for preterm birth in the second pregnancy							
	<28 weeks		28–31 weeks		32–33 weeks		34–36 weeks	
	Spont.	Med.	Spont.	Med.	Spont.	Med.	Spont.	Med.
<28 weeks								
Spont.	13.2 (8.8, 19.8)	12.6 (7.0, 22.7)	6.0 (3.9, 9.2)	6.4 (3.6, 11.3)	3.2 (1.9, 5.3)	3.4 (1.6, 7.3)	3.1 (2.4, 3.9)	2.1 (1.3, 3.4)
Med.	10.4 (5.0, 21.7)	22.7 (11.3, 46.0)	3.6 (1.4, 8.8)	19.9 (11.5, 34.3)	1.6 (0.5, 5.1)	14.1 (7.5, 26.3)	1.2 (0.7, 2.1)	14.4 (10.5, 19.8)
28–31 weeks								
Spont.	4.5 (2.8, 7.2)	5.1 (3.6, 7.2)	6.1 (3.3, 11.5)	3.0 (1.6, 5.7)	3.8 (2.7, 5.4)	2.1 (1.0, 4.4)	2.9 (2.4, 3.5)	2.1 (1.4, 3.1)
Med.	1.3 (0.3, 5.1)	14.7 (7.8, 27.6)	3.4 (1.7, 6.7)	15.3 (9.8, 24.0)	1.7 (0.7, 3.8)	12.8 (7.8, 20.9)	0.9 (0.6, 1.4)	9.6 (7.4, 12.6)
32–33 weeks								
Spont.	4.8 (3.1, 7.4)	2.3 (1.0, 5.8)	5.8 (4.2, 8.0)	2.7 (1.5, 5.0)	5.9 (4.6, 7.2)	2.6 (1.4, 4.8)	3.0 (2.5, 3.5)	1.7 (1.2, 2.4)
Med.	0.7 (0.1, 5.2)	12.5 (6.3, 24.8)	1.7 (0.6, 4.5)	8.2 (4.5, 14.7)	0.9 (0.3, 2.8)	11.9 (7.3, 19.3)	1.1 (0.7, 1.7)	10.2 (7.9, 13.1)
34–36 weeks								
Spont.	2.1 (1.6, 2.8)	1.4 (0.9, 2.4)	3.0 (2.4, 3.6)	2.1 (1.6, 2.9)	3.1 (2.6, 3.6)	1.9 (1.4, 2.6)	3.0 (2.8, 3.2)	1.0 (0.8, 1.2)
Med.	1.4 (0.7, 2.7)	4.5 (2.7, 7.6)	1.9 (1.2, 2.9)	5.3 (3.8, 7.5)	0.8 (0.4, 1.4)	6.2 (4.6, 8.5)	0.8 (0.6, 1.0)	5.8 (5.0, 6.7)

Spont., spontaneous preterm birth; Med., medically-indicated preterm birth. Odds ratios were adjusted for period of birth, maternal age, parity, maternal race/ethnicity, marital status, maternal education, smoking and alcohol use during pregnancy, and pre-pregnancy body mass index. *The data shown in this Table are reproduced from Ananth et al. [52] with the permission of the publisher.

The hierarchy of ischemic placental diseases based on the frequency of their occurrence in relation to medically indicated preterm birth at <35 weeks was examined among women that delivered singleton live births in Missouri, 1989 through 1997 [59], and the results are summarized in Table VI. Preeclampsia was the most common indication for obstetrical intervention among medically indicated preterm birth, followed by fetal distress, SGA, and placental abruption. As the number of combined conditions increases, the frequency of various combinations decreases (Table VI). This observation supports the fact that there is a 'continuum' in the clinical manifestations of ischemic placental diseases including preeclampsia, SGA, fetal distress, and placental abruption in that order of occurrence. Although ischemia can be a major cause for indicated preterm births, it can also be implicated in the etiology of approximately 20% of spontaneous preterm births [55,56,59].

Directions for future research

Data presented and reviewed here, and those of studies in other western societies and patient populations, collectively suggest that: (i) preterm birth is a heterogeneous end-point with a syndromic underpinning and pointing toward a multifactorial etiology; (ii) the origins of preterm birth, based on its underlying clinical subtypes, are complex; and (iii) the incidence, recurrence, and risk factors for preterm birth exhibit strong racial disparity. Preterm birth prevention programs have largely been a failure [4,6,40,41] and even among the few that have met with success, the impact of the intervention has only been moderate. Efforts to identify preterm birth cases and prevention programs aimed at reducing preterm birth have largely focused on spontaneous preterm birth. However, medically indicated preterm birth—a group that constitutes approximately 40% of all preterm births—has, relatively, received far less consideration.

Interventions to prevent preterm birth must be designed based on specific clinical conditions that lead to parturition at preterm gestational ages (e.g., ischemic placental disease with its clinical conditions of preeclampsia, intrauterine growth restriction, and placental abruption), rather than targeting all spontaneous preterm or medically indicated preterm births as one entity. In addition, pathways to the risk and recurrence of preterm birth must include a careful study of intrauterine and intra-amniotic infections [4,60–62], inflammation [54,63,64], and the role of thrombophilias [65,66]. The contributions of genetic thrombophilias—an understudied but emerging research focus—and the role of gene–environment interactions remain largely

Table V. Underlying clinical conditions necessitating medically indicated preterm birth.

Study authors	Plurality	Preterm birth	Conditions necessitating medically indicated preterm birth				
			Preeclampsia	IUGR or SGA	Fetal distress	Placental abruption	Other causes
Tucker et al. [81]	Singletons	<37 weeks	30%		16%		22%
Meis et al. [56]	Singletons	<37 weeks	43%		37%	7%	13%
Ananth and Vintzileos [59]	Singletons	<35 weeks	23%	19%	23%	12%	47%
Gardner et al. [58]	Twins	<37 weeks	44%	33%	9%	14%	

IUGR, intrauterine growth restriction; SGA, small-for-gestational age.

Table VI. Distribution of ischemic placental disease among medically indicated preterm birth at <35 weeks and among term/near-term births.*

Maternal–fetal conditions	Rate among term/near term births at ≥35 weeks (%)	Medically indicated preterm birth at <35 weeks	
		Rate (%)	Adjusted RR (95% CI)
Preeclampsia only	2.9	10.4	6.4 (5.9, 7.0)
Preeclampsia + SGA	0.6	5.6	16.8 (15.1, 18.7)
Preeclampsia + fetal distress	0.3	3.1	20.6 (17.8, 23.8)
Preeclampsia + SGA + fetal distress	0.1	2.6	44.5 (37.7, 52.6)
Preeclampsia + abruption	0.02	0.8	63.1 (45.8, 86.8)
Preeclampsia + SGA + abruption	0.02	0.5	38.2 (23.2, 62.9)
Preeclampsia + fetal distress + abruption	0.01	0.3	83.9 (49.9, 141.0)
Preeclampsia + SGA + fetal distress + abruption	0.01	0.2	58.6 (30.2, 113.8)
Fetal distress only	4.6	11.4	4.2 (3.8, 4.5)
Fetal distress + SGA	0.9	3.3	5.5 (4.8, 6.3)
Fetal distress + abruption	0.1	1.6	32.0 (26.1, 39.3)
Fetal distress + SGA + abruption	0.02	0.5	29.0 (20.1, 42.0)
SGA only	7.9	5.0	0.9 (0.8, 1.0)
SGA + abruption	0.1	1.4	21.5 (17.3, 26.8)
Placental abruption only	0.3	6.8	37.6 (33.8, 41.8)

CI, confidence interval; SGA, small-for-gestational age. Relative risks (RR) are adjusted for the confounding effects of period of birth, maternal age, parity, maternal race/ethnicity, marital status, maternal education, smoking and alcohol use during pregnancy, and pre-pregnancy body mass index. *The data shown in this Table are reproduced (with modification) from Ananth and Vintzileos [59] with the permission of the publisher.

understudied at the population-level and may offer new insights. With recent developments in innovative epidemiologic study designs [67,68] and data analytic methodologies [67,69], the determination of the extent to which single nucleotide polymorphisms (SNP), through high-throughput SNP arrays [69], gene expressions, and alterations in protein structure and content [70–72], are implicated in spontaneous and medically indicated preterm birth will not only complement, but vastly enhance our ongoing research pursuits in preterm birth.

Conclusions

The preterm birth rate in the USA [7–10,38] and most other industrialized countries [11–13,73], with the possible exceptions of France [74,75] and Finland [76], has been steadily increasing mainly because of increases in multiple births [11,77,78], but also among singleton births. Among singleton gestations, the increase in the overall preterm birth rate is largely driven by a concurrent temporal increase in medically indicated preterm birth. This latter increase in medically indicated preterm birth following a labor induction and/or cesarean delivery at preterm gestational ages is associated with a favorable temporal decline in perinatal mortality. Thus, the increase in preterm birth (overall in the USA), largely viewed as a 'failure' of efforts to curtail preterm birth, may actually be beneficial insofar as preventing perinatal deaths [8]. Whether such increases in obstetric interventions at preterm gestational ages do actually help avert associated short- and long-term morbidity in the newborn is open to debate, and may be a topic worthy of continued research.

Ongoing epidemiologic and clinical research on preterm birth must consider stratifying such births based on the underlying maternal and fetal indications that necessitated early delivery [79–84]. The extent to which such maternal and fetal indications are implicated in medically indicated and spontaneous births at preterm gestational ages requires careful examination. These pursuits may provide important clues toward understanding its etiology as well as developing targeted interventions to prevent the problem of prematurity.

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