

Table S1 Demographic and clinical characteristics of the study population stratified by PTB status and classification categories

Variables	All population	PTB	P value ^a	PTB categories			P value ^b
				Moderately PTB	Very PTB	Extremely PTB	
Overall	22,669,736 (100.0)	2,683,587 (100.0)		2,255,825 (100.0)	269,823 (100.0)	157,939 (100.0)	
Age (years)			<0.001				<0.001
<25	5,394,462 (23.8)	656,214 (24.5)		543,212 (24.1)	70,272 (26.0)	42,730 (27.1)	
25–34	13,097,749 (57.8)	1,448,075 (54.0)		1,222,327 (54.2)	142,180 (52.7)	83,568 (52.9)	
≥35	4,177,525 (18.4)	579,298 (21.6)		490,286 (21.7)	57,371 (21.3)	31,641 (20.0)	
Race or ethnicity							
Hispanic	5,365,989 (23.7)	643,036 (24.0)		546,734 (24.2)	61,557 (22.8)	34,745 (22.0)	<0.001
Non-Hispanic							
White	11,680,688 (51.5)	1,211,766 (45.2)		1,040,976 (46.1)	114,998 (42.6)	55,792 (35.3)	
Black	3,269,219 (14.4)	563,589 (21.0)		443,533 (19.7)	67,782 (25.1)	52,274 (33.1)	
Asian	1,418,537 (6.3)	142,052 (5.3)		122,523 (5.4)	12,567 (4.7)	6,962 (4.4)	
Others	728,635 (3.2)	96,386 (3.6)		80,794 (3.6)	10,030 (3.7)	5,562 (3.5)	
Missing	206,668 (0.9)	26,758 (1.0)		21,265 (0.9)	2,889 (1.1)	2,604 (1.6)	
MPs			<0.001				<0.001
No (single)	21,916,808 (96.7)	2,242,028 (83.5)		1,901,754 (84.3)	215,309 (79.8)	124,965 (79.1)	
Twin	732,289 (3.2)	422,097 (15.7)		342,475 (15.2)	49,336 (18.3)	30,286 (19.2)	
Triplet	19,573 (0.1)	18,446 (0.7)		11,371 (0.5)	4,723 (1.8)	2,352 (1.5)	
≥ Quadruplet	1,066 (<0.1)	1,016 (<0.1)		225 (<0.1)	4,55 (0.2)	336 (0.2)	
Education levels			<0.001				<0.001
Lower than high school	2,801,648 (12.4)	410,654 (15.3)		342,308 (15.2)	44,336 (16.4)	24,010 (15.2)	
High school	5,783,806 (25.5)	764,702 (28.5)		634,877 (28.1)	80,751 (29.9)	49,074 (31.1)	
> High school	13,769,913 (60.7)	1,463,386 (54.5)		1,244,241 (55.2)	139,870 (51.8)	79,275 (50.2)	
Missing	314,369 (1.4)	44,845 (1.7)		34,399 (1.5)	4,866 (1.8)	5,580 (3.5)	
Marital status			<0.001				<0.001
Married	12,238,999 (54.0)	1,281,488 (47.8)		1,099,623 (48.7)	118,190 (43.8)	63,675 (40.3)	
Unmarried	8,212,193 (36.2)	1,185,893 (44.2)		970,411 (43.0)	132,709 (49.2)	82,773 (52.4)	
Missing	2,218,544 (9.8)	216,206 (8.1)		185,791 (8.2)	18,924 (7.0)	11,491 (7.3)	
Pre-pregnancy BMI			<0.001				<0.001
Underweight	688,510 (3.0)	91,204 (3.4)		76,587 (3.4)	9,548 (3.5)	5,069 (3.2)	
Normal weight	9,235,434 (40.7)	981,356 (36.6)		836,489 (37.1)	95,678 (35.5)	49,189 (31.1)	
Overweight	5,920,679 (26.1)	677,010 (25.2)		573,123 (25.4)	66,547 (24.7)	37,340 (23.6)	
Obesity	6,300,997 (27.8)	846,421 (31.5)		703,447 (31.2)	86,804 (32.2)	56,170 (35.6)	
Missing	524,116 (2.3)	87,596 (3.3)		66,179 (2.9)	11,246 (4.2)	10,171 (6.4)	
Pre-pregnancy diabetes			<0.001				<0.001
Yes	219,451 (1.0)	59,837 (2.2)		49,983 (2.2)	6,551 (2.4)	3,303 (2.1)	
No	22,426,628 (98.9)	2,620,279 (97.6)		2,203,278 (97.7)	262,816 (97.4)	154,185 (97.6)	
Missing	23,657 (0.1)	3,471 (0.1)		2,564 (0.1)	456 (0.2)	451 (0.3)	
Pre-pregnancy hypertension			<0.001				<0.001
Yes	494,272 (2.2)	124,797 (4.7)		99,199 (4.4)	16,236 (6.0)	9,362 (5.9)	
No	22,151,807 (97.7)	2,555,319 (95.2)		2,154,062 (95.5)	253,131 (93.8)	148,126 (93.8)	
Missing	23,657 (0.1)	3,471 (0.1)		2,564 (0.1)	456 (0.2)	451 (0.3)	
Smoking during pregnancy			<0.001				
Yes	1,381,822 (6.1)	228,732 (8.5)		187,351 (8.3)	26,784 (9.9)	14,597 (9.2)	
No	21,182,012 (93.4)	2,436,695 (90.8)		2,054,670 (91.1)	240,761 (89.2)	141,264 (89.4)	
Missing	105,902 (0.5)	18,160 (0.7)		13,804 (0.6)	2,278 (0.8)	2,078 (1.3)	
Gestational diabetes			<0.001				<0.001
Yes	1,578,040 (7.0)	238,774 (8.9)		211,515 (9.4)	20,892 (7.7)	6,367 (4.0)	
No	21,068,039 (92.9)	2,441,342 (91.0)		2,041,746 (90.5)	248,475 (92.1)	151,121 (95.7)	
Missing	23,657 (0.1)	3,471 (0.1)		2,564 (0.1)	456 (0.2)	451 (0.3)	
Gestational hypertension			<0.001				<0.001
Yes	1,687,277 (7.4)	396,473 (14.8)		337,403 (15.0)	433,77 (16.1)	15,693 (9.9)	
No	20,958,802 (92.5)	2,283,643 (85.1)		1,915,858 (84.9)	225,990 (83.8)	141,795 (89.8)	
Missing	23,657 (0.1)	3,471 (0.1)		2,564 (0.1)	456 (0.2)	451 (0.3)	
Eclampsia			<0.001				<0.001
Yes	61,244 (0.3)	23,538 (0.9)		18,427 (0.8)	3,565 (1.3)	1,546 (1.0)	
No	22,584,835 (99.6)	2,656,578 (99.0)		2,234,834 (99.1)	265,802 (98.5)	155,942 (98.7)	
Missing	23,657 (0.1)	3,471 (0.1)		2,564 (0.1)	456 (0.2)	451 (0.3)	
History of preterm			<0.001				<0.001
Yes	792,399 (3.5)	237,373 (8.8)		191,784 (8.5)	28,007 (10.4)	17,582 (11.1)	
No	21,853,680 (96.4)	2,442,743 (91.0)		2,061,477 (91.4)	241,360 (89.5)	139,906 (88.6)	
Missing	23,657 (0.1)	3,471 (0.1)		2,564 (0.1)	456 (0.2)	451 (0.3)	
Infertility treatment			<0.001				<0.001
Yes	445,616 (2.0)	104,356 (3.9)		83,825 (3.7)	12,231 (4.5)	8,300 (5.3)	
No	22,200,463 (97.9)	2,575,760 (96.0)		2,169,436 (96.2)	257,136 (95.3)	149,188 (94.5)	
Missing	23,657 (0.1)	3,71 (0.1)		2,564 (0.1)	456 (0.2)	451 (0.3)	
Chlamydia			<0.001				<0.001
Yes	415,924 (1.8)	61,996 (2.3)		50,715 (2.2)	7,168 (2.7)	4,113 (2.6)	
No	22,189,014 (97.9)	2,606,612 (97.1)		2,193,738 (97.2)	260,753 (96.6)	152,121 (96.3)	
Missing	64,798 (0.3)	14,979 (0.6)		11,372 (0.5)	1,902 (0.7)	1,705 (1.1)	
Gonorrhea			<0.001				<0.001
Yes	71,466 (0.3)	12,940 (0.5)		2,234,182 (99.0)	1,686 (0.6)	983 (0.6)	
No	22,533,472 (99.4)	2,655,668 (99.0)		10,271 (0.5)	266,235 (98.7)	155,251 (98.3)	
Missing	64,798 (0.3)	14,979 (0.6)		11,372 (0.5)	1,902 (0.7)	1,705 (1.1)	
Syphilis			<0.001				<0.001
Yes	31,659 (0.1)	6,092 (0.2)		4,950 (0.2)	741 (0.3)	401 (0.3)	
No	22,573,279 (99.6)	2,662,516 (99.2)		2,239,503 (99.3)	267,180 (99.0)	155,833 (98.7)	
Missing	64,798 (0.3)	14,979 (0.6)		11,372 (0.5)	1,902 (0.7)	1,705 (1.1)	
Previous cesareans			<0.001				<0.001
Yes	3,506,285 (15.5)	493,406 (18.4)		421,257 (18.7)	47,957 (17.8)	24,192 (15.3)	
No	19,139,794 (84.4)	2,186,710 (81.5)		1,832,004 (81.2)	221,410 (82.1)	133,296 (84.4)	
Missing	23,657 (0.1)	3,471 (0.1)		2,564 (0.1)	456 (0.2)	451 (0.3)	
Prenatal care			<0.001				<0.001
Yes	21,719,339 (95.8)	2,480,517 (92.4)		2,108,118 (93.5)	241,309 (89.4)	131,090 (83.0)	
No	405,437 (1.8)	103,819 (3.9)		74,816 (3.3)	147,50 (5.5)	14,253 (9.0)	
Missing	544,960 (2.4)	99,251 (3.7)		72,891 (3.2)	13,764 (5.1)	12,596 (8.0)	
Mother's nativity			<0.001				<0.001
Born in the US	17,501,235 (77.2)	2,094,774 (78.1)		1,755,313 (77.8)	214,023 (79.3)	125,438 (79.4)	
Born outside the US	5,121,322 (22.6)	580,379 (21.6)		494,395 (21.9)	54,888 (20.3)	31,096 (19.7)	
Missing	47,179 (0.2)	8,434 (0.3)		6,117 (0.3)	912 (0.3)	1,405 (0.9)	

^a, difference between full-term and PTB. ^b, difference among full-term, moderately PTB, very PTB, and extremely PTB. BMI, body mass index; MPs, multiple pregnancies; PTB, preterm birth; US, United States.

Table S2 Association between MPs and PTB: a sensitivity analysis excluding female with infertility treatments

Degree of MPs	PTB, OR (95% CI)	
	Model 1	Model 2
Twin pregnancy	12.05 (11.99–12.12)	12.40 (12.35–12.49)
Triplet pregnancy	144.31 (134.13–155.28)	152.73 (141.26–165.13)
Quadruplet or more pregnancy	131.47 (92.40–187.05)	137.40 (94.57–199.64)
Any MP	12.44 (12.38–12.50)	12.83 (12.76–12.91)

Model 1: age and race or ethnicity were adjusted in this model. Model 2: model 1 + nativity, education, marital status, pre-pregnancy BMI, previous history of cesarean, previous history of PTB, pre-pregnancy diabetes, pre-pregnancy hypertension, gestational diabetes, gestational hypertension, eclampsia, smoking during pregnancy, prenatal care, and sexually transmitted diseases (chlamydia, gonorrhea, and syphilis) were adjusted. BMI, body mass index; CI, confidence interval; MPs, multiple pregnancies; OR, odds ratio; PTB, preterm birth.

Table S3 Association between MPs and PTB: a sensitivity analysis excluding pregnant individuals with pregnancy complication (gestational diabetes, gestational hypertension, and eclampsia)

Degree of MPs	PTB, OR (95% CI)	
	Model 1	Model 2
Twin pregnancy	12.37 (12.31–12.44)	12.82 (12.74–12.90)
Triplet pregnancy	160.50 (149.73–172.05)	155.87 (144.88–167.68)
Quadruplet or more pregnancy	210.48 (150.66–294.05)	183.77 (129.94–259.89)
Any MPs	12.89 (12.82–12.96)	13.33 (13.25–13.41)

Model 1: age and race or ethnicity were adjusted in this model. Model 2: model 1 + nativity, education, marital status, pre-pregnancy BMI, previous history of cesarean, previous history of PTB, pre-pregnancy diabetes, pre-pregnancy hypertension, infertility treatment, smoking during pregnancy, prenatal care, and sexually transmitted diseases (chlamydia, gonorrhea, and syphilis) were adjusted. BMI, body mass index; CI, confidence interval; MPs, multiple pregnancies; OR, odds ratio; PTB, preterm birth.

Table S4 Association between MPs and PTB: a sensitivity analysis by including pregnant women in each year from the US NVSS 2016–2021

Year	Degree of MPs	PTB, OR (95% CI)	
		Model 1	Model 2
2021	Twin pregnancy	11.87 (11.72–12.02)	11.89 (11.72–12.05)
	Triplet pregnancy	177.53 (148.37–212.41)	158.53 (131.99–190.42)
	Quadruplet or higher pregnancy	1,301.55 (182.18–9,298.50)	974.28 (135.93–6,983.28)
	Any MPs	12.33 (12.19–12.49)	12.34 (12.17–12.51)
2020	Twin pregnancy	11.37 (11.23–11.51)	11.59 (11.43–11.75)
	Triplet pregnancy	135.01 (115.37–158.20)	146.17 (122.63–174.24)
	Quadruplet or higher pregnancy	161.19 (75.35–344.85)	135.15 (62.75–291.11)
	Any MPs	11.81 (11.67–11.96)	12.03 (11.87–12.20)
2019	Twin pregnancy	11.74 (11.60–11.88)	11.83 (11.67–11.99)
	Triplet pregnancy	127.14 (110.06–146.87)	122.89 (105.39–143.30)
	Quadruplet or higher pregnancy	131.20 (66.88–257.41)	94.29 (45.65–194.76)
	Any MPs	12.21 (12.07–12.35)	12.29 (12.13–12.46)
2018	Twin pregnancy	12.34 (12.19–12.48)	12.31 (12.15–12.48)
	Triplet pregnancy	124.01 (108.47–141.78)	112.35 (97.40–129.60)
	Quadruplet or higher pregnancy	367.10 (116.77–1,154.09)	257.47 (81.01–818.25)
	Any MPs	12.85 (12.70–12.99)	12.78 (12.61–12.96)
2017	Twin pregnancy	12.04 (11.89–12.18)	12.06 (11.90–12.22)
	Triplet pregnancy	177.99 (153.10–206.94)	169.94 (144.28–200.17)
	Quadruplet or higher pregnancy	132.63 (79.91–220.14)	106.24 (63.55–177.60)
	Any MPs	12.61 (12.46–12.75)	12.59 (12.41–12.75)
2016	Twin pregnancy	12.40 (12.27–12.54)	12.55 (12.40–12.71)
	Triplet pregnancy	151.57 (132.23–173.75)	142.33 (123.76–163.69)
	Quadruplet or higher pregnancy	203.59 (111.22–372.65)	220.50 (112.76–431.20)
	Any MP	12.97 (12.82–13.12)	13.07 (12.91–13.24)

Model 1: age and race or ethnicity were adjusted in this model. Model 2: model 1 + nativity, education, marital status, pre-pregnancy BMI, previous history of cesarean, previous history of PTB, pre-pregnancy hypertension, pre-pregnancy diabetes, gestational hypertension, gestational diabetes, eclampsia, infertility treatment, smoking during pregnancy, prenatal care, and sexually transmitted diseases (chlamydia, gonorrhea, and syphilis) were adjusted. BMI, body mass index; CI, confidence interval; MPs, multiple pregnancies; NVSS, National Vital Statistics System; OR, odds ratio; PTB, preterm birth; US, United States.