

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Reese JA, Peck JD, Deschamps DR, et al. Platelet counts during pregnancy. *N Engl J Med* 2018; 379:32-43. DOI: [10.1056/NEJMoa1802897](https://doi.org/10.1056/NEJMoa1802897)

## **PLATELET COUNTS DURING PREGNANCY**

### **SUPPLEMENTAL FIGURE AND TABLES**

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- A. Platelet counts of nonpregnant women and pregnant women stratified by race/ethnicity at each trimester and at delivery
- B. Platelet counts of nonpregnant women and pregnant women stratified by age at each trimester and at delivery
- C. Platelet counts of nonpregnant women, women with singleton pregnancies and women with twin pregnancies at each trimester and at delivery

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- A. Uncomplicated pregnancies; also for evaluating cause of thrombocytopenia in women with platelet counts <80,000
- B. Pregnancy-related complications
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- A. Data for women with pregnancy-related complications
- B. Data for women with preexisting disorders

Figure S1A.

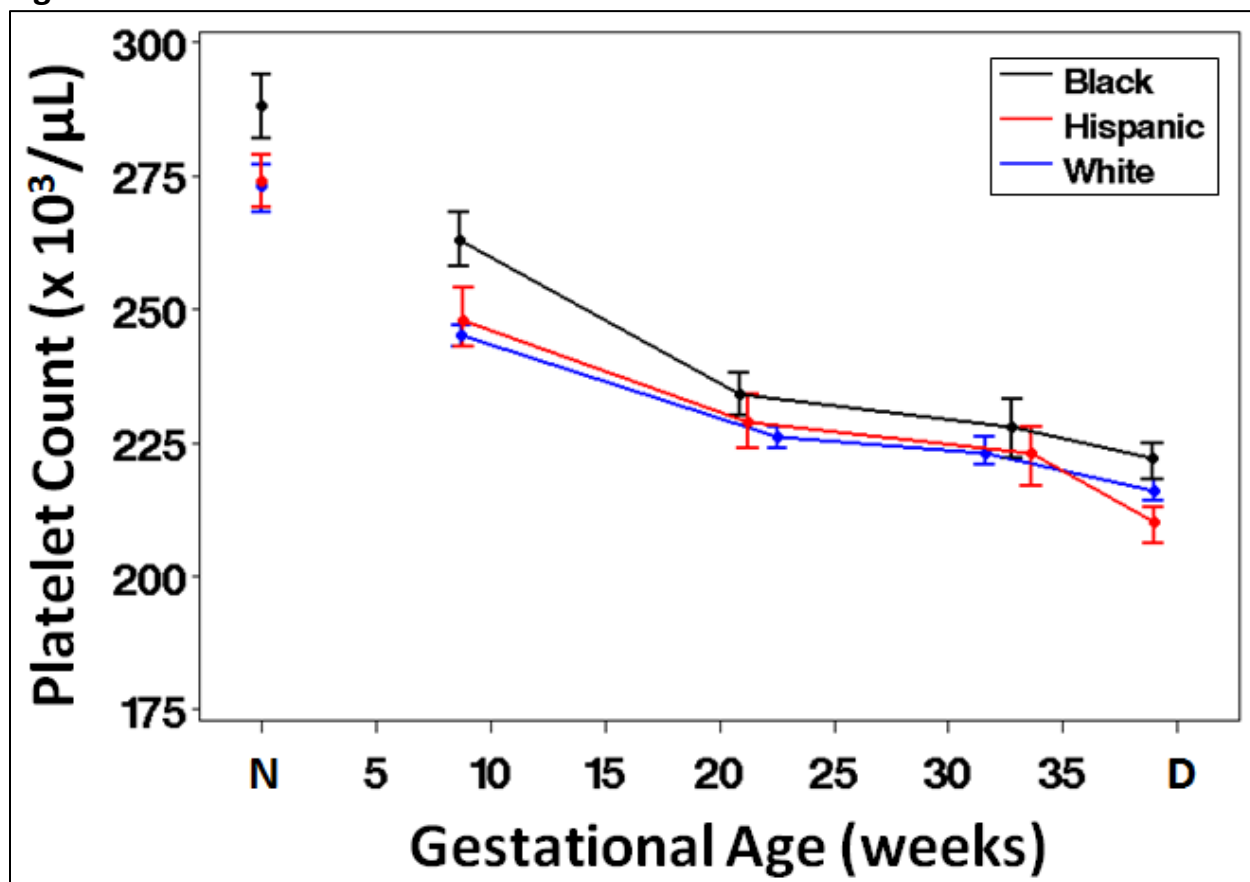


Figure S1B.

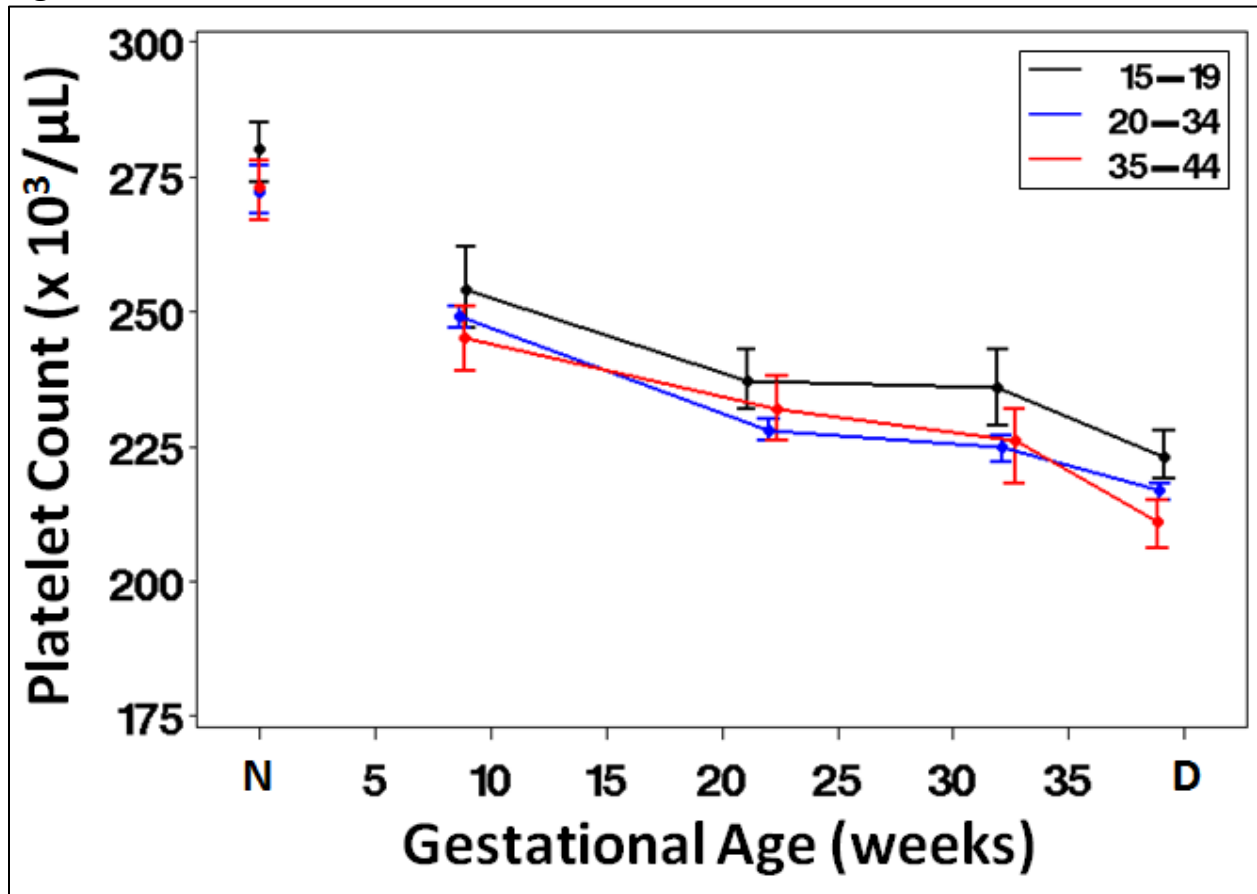
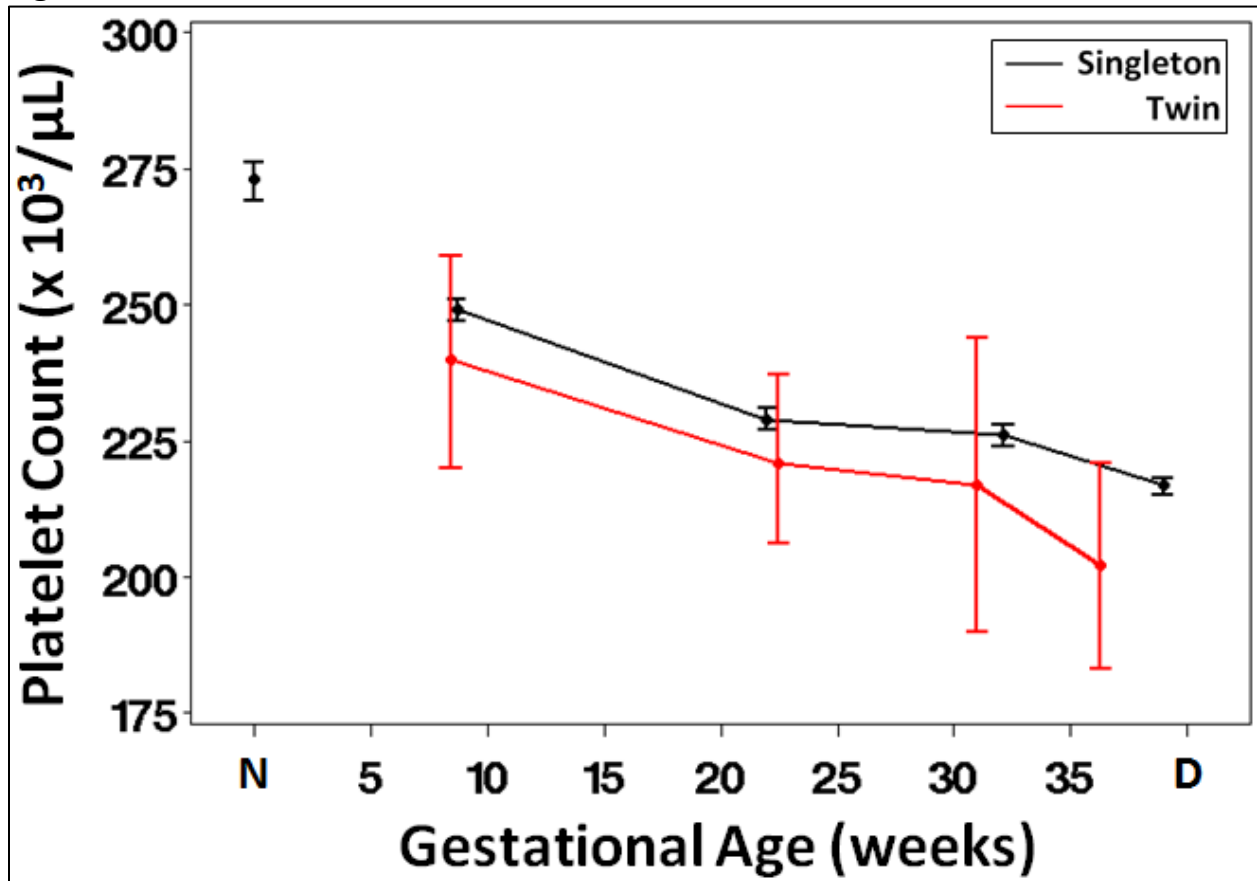


Figure S1C.



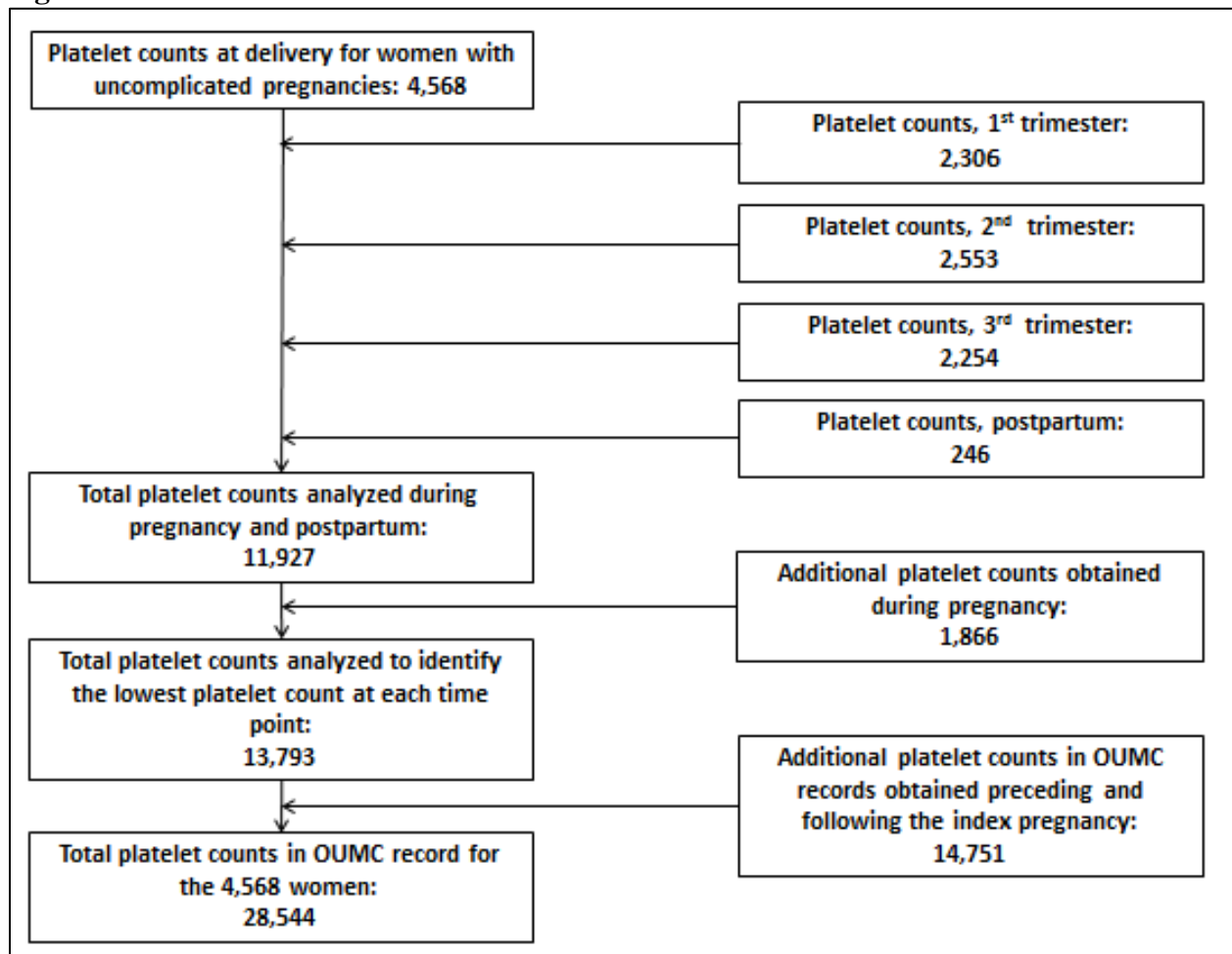
**Figure S1 legend.** Platelet counts (with 95% confidence intervals) in nonpregnant women are designated by N on the abscissa in each Figure. Platelet counts (with 95% confidence intervals) in women with uncomplicated pregnancies are presented at each trimester (with the mean gestational age when they were obtained indicated on the abscissa) and at delivery (D). Table 1 presents all platelet counts in these three Figures with mean values, range, and 95% confidence intervals.

**Figure S1A. Platelet counts of nonpregnant women and pregnant women stratified by race/ethnicity.** Platelet counts of the 8885 nonpregnant women and the 4568 women with uncomplicated pregnancies were stratified by race/ethnicity at each trimester and at delivery. At delivery, non-Hispanic black women had higher platelet counts than white and Hispanic women ( $P < 0.001$ ), similar to the nonpregnant women.

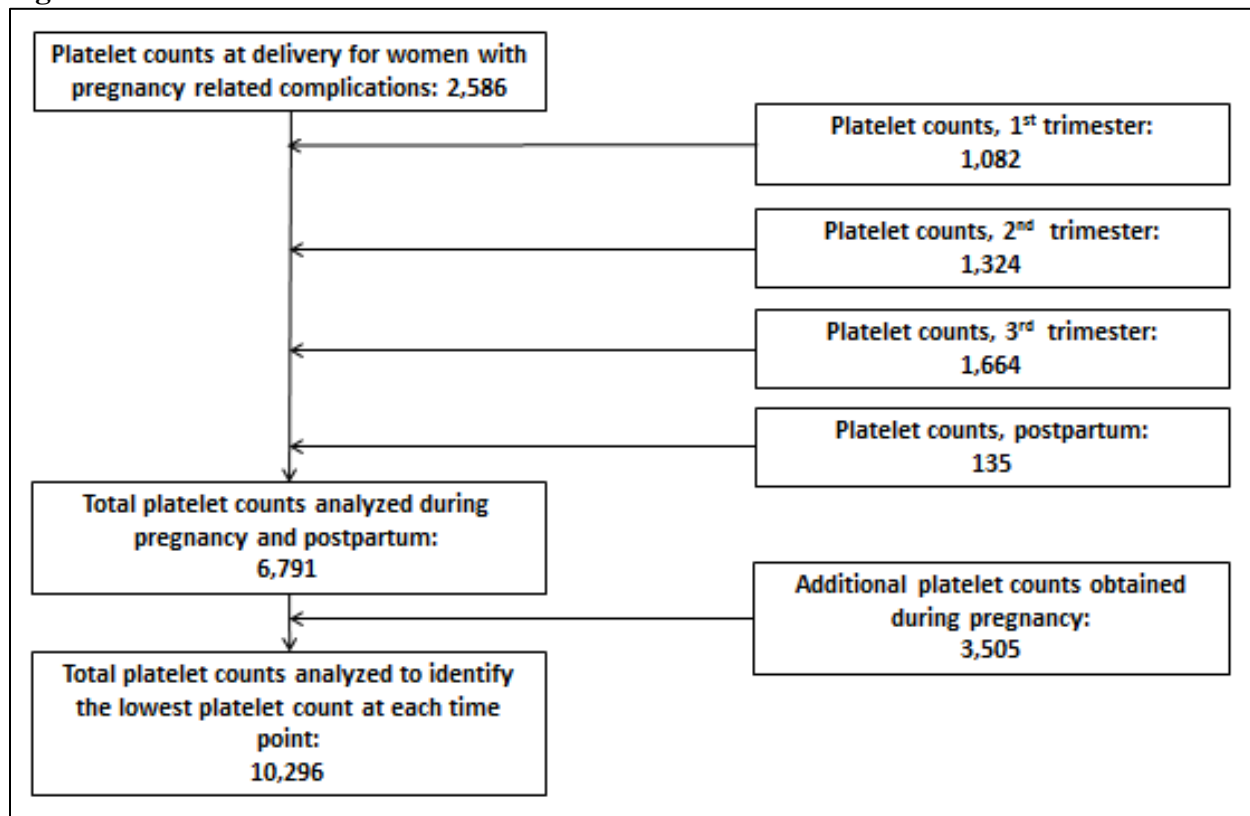
**Figure S1B. Platelet counts of nonpregnant women and pregnant women stratified by age.** Platelet counts of the 8885 nonpregnant women and the 4568 women with uncomplicated pregnancies were stratified by age at each trimester and at delivery. At delivery, younger women (ages 15-19) women had higher platelet counts than older women (ages 20-44,  $P < 0.001$ ), similar to the nonpregnant women.

**Figure S1C. Platelet counts of nonpregnant women, women with singleton pregnancies and women with twin pregnancies.** Platelet counts of the 8885 nonpregnant women, the 4568 women with uncomplicated pregnancies, and 67 women with uncomplicated twin pregnancies. Among the 328 women with a twin pregnancy, 219 were excluded because of pregnancy-related complications, 4 with missing gestational age, 12 with no platelet count at delivery, and 26 with no additional platelet count during gestation. The platelet counts of women with twin pregnancies were lower than the platelet counts of women with singleton pregnancies, but the difference was not significant at delivery ( $P = 0.0689$ ).

**Figure S2A.**

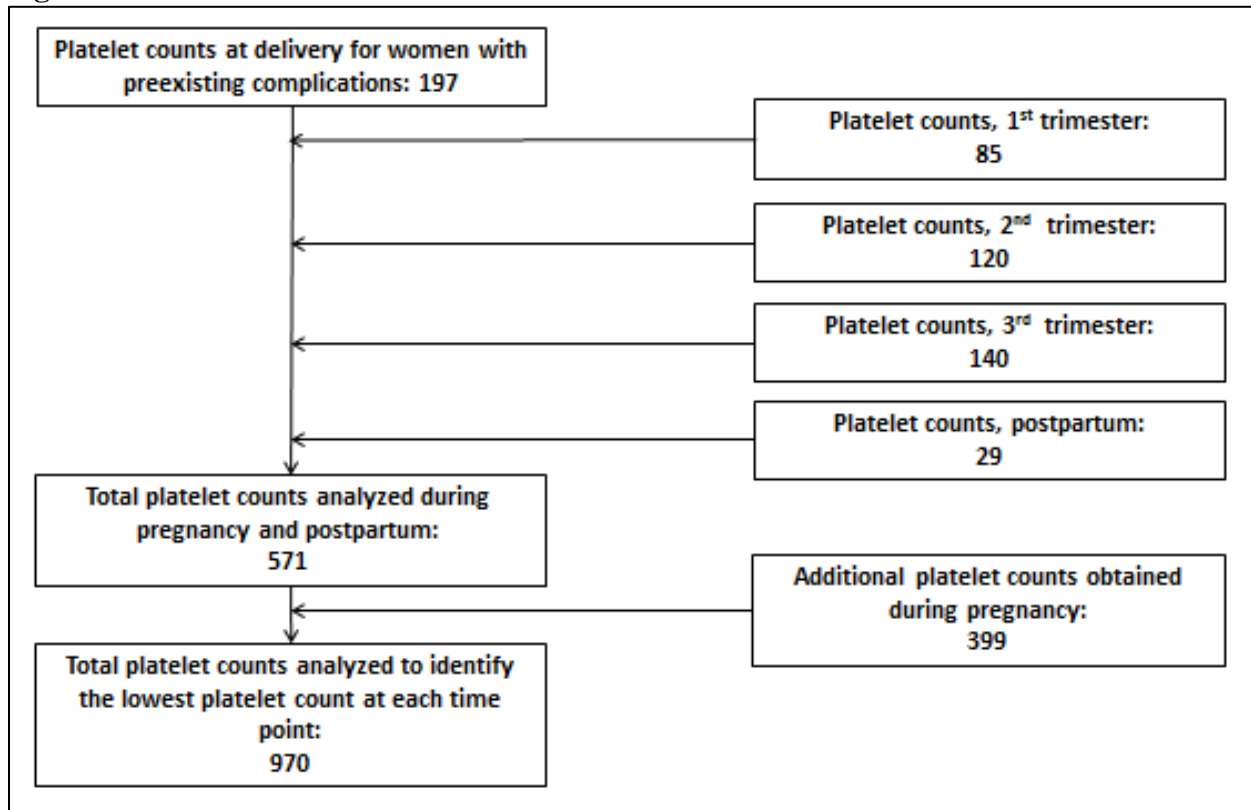


**Figure S2B.**





**Figure S2C.**



**Table S1.**

<b>Characteristics</b>	<b>Uncomplicated singleton pregnancies</b>	<b>Pregnancy-related complications</b>	<b>Preexisting disorders</b>	<b>Nonpregnant women (weighted)</b>
<b>Number of women</b>	4568	2586	197	8885
<b>Age</b>				
15-19	420 (9.2%)	213 (8.2%)	8 (4.1%)	18.5%
20-34	3,736 (81.8%)	1915 (74.1%)	151 (76.6%)	49.2%
35-44	412 (9.0%)	423 (16.4%)	35 (17.8%)	32.3%
Missing	0 (0%)	35 (1.3%)	3 (1.5%)	0%
<b>Race/ethnicity</b>				
White (non-Hispanic)	2,474 (54.2%)	1330 (51.4%)	109 (55.3%)	63.1%
Black (non-Hispanic)	829 (18.1%)	502 (19.4%)	44 (22.4%)	12.4%
Hispanic	636 (13.9%)	380 (14.7%)	16 (8.1%)	17.6%
Other	625 (13.7%)	372 (14.4%)	28 (14.2%)	6.9%
Missing	4 (0.1%)	2 (0.1%)	0 (0%)	0%
<b>Delivery</b>				
Vaginal	3,359 (73.5%)	1454 (56.2%)	117 (59.4%)	
Cesarean Section	1,207 (26.4%)	1129 (43.7%)	80 (40.6%)	
Missing	2 (0.04%)	3 (0.1%)	0 (0%)	
<b>Parity</b>				
0	1,167 (25.5%)	660 (25.5%)	36 (18.3%)	
≥1	2,800 (61.3%)	1549 (59.9%)	131 (66.5%)	
Missing	601 (13.2%)	377 (14.6%)	30 (15.2%)	
<b>Gestational age at delivery (weeks)</b>				
Median (range)	39.6 (37.2-43.2)	37.6 (1.1-42.3)	38.6 (21.7-42.0)	
Missing	0 (0%)	0 (0%)	0 (0%)	
<b>Birthweight (grams)</b>				
Median (range)	3381 (1760-5140)	3000 (8-6232)	3030 (120-4540)	
Missing	47 (1%)	130 (5%)	6 (3%)	

**Table S2.**

<b>Variable</b>	<b>First trimester</b>	<b>Delivery</b>	<b>Nonpregnant</b>
n	2306	4568	8885
Mean (95% CI)	251 (249-253)	217 (215-219)	282 (280-283)
Median	245	211	274
SD	56	58	70
$\pm 2$ SD Range	139-363	101-318	142-422
Number -2SD (%)	21 (1%)	39 (1%)	66 (1%)
Number +2SD (%)	70 (3%)	243 (5%)	292 (3%)

Analysis of the platelet count distribution curves illustrated in the text Figure

3. Symmetry of the platelet count distribution curves was assessed by comparison of the mean and median values. The median values were less than the mean values by 2.3-2.8% at the three time points. Whether the curves were skewed was assessed by calculating the number of platelet counts at both ends of the curves that were excluded by the mean  $\pm 2$  SD. All three curves were slightly and similarly skewed to higher platelet counts. Unweighted data were used for nonpregnant women, providing a different mean (and 95% CI) from the data in Table 1, which were calculated from weighted data.

**Table S3.**

Pt	Platelet counts (x 10 <sup>3</sup> /μL)						Comments (Clinical diagnosis in italics)
	Before pregnancy	During pregnancy				Postpartum (4-8 wks)	
		Trimester			Delivery		
		1	2	3			
1	0	0	0	109, 113	63	0	<i>Gestational thrombocytopenia</i> . No alternative diagnosis
2	0	0	172	0	67	160	<i>Gestational thrombocytopenia</i> . Recovery postpartum
3	76 170	0	129	62	68	0	<i>Gestational thrombocytopenia</i> . Platelet count of 76 at delivery of previous pregnancy, then 170 at 4 months postpartum
4	0	0	136	123 89	78 87	0	<i>Gestational thrombocytopenia</i> . No alternative diagnosis. Diagnosis of gestational thrombocytopenia recorded by obstetrician at delivery
5	81	164	0	65-95	171	185	<i>Gestational thrombocytopenia</i> . Platelet count of 81 preceding pregnancy attributed to trauma, spinal fracture, surgery. 3 <sup>rd</sup> trimester thrombocytopenia attributed to gestational thrombocytopenia. Gestational thrombocytopenia recurred with pregnancy one year later.
6	93-213	0	72	108	90	0	<i>ITP</i> . Mild thrombocytopenia for 18 years prior to pregnancy (mean platelet count, 134)
7	0	99	111 120	105, 72 74	72, 64 72	96	<i>ITP</i> . Persistent mild thrombocytopenia throughout pregnancy and postpartum
8	64	0	120	0	63 (194)	0	<i>Pseudothrombocytopenia</i> . Physician note at delivery: "Blood smear, normal platelets. Estimated count, 194".
9	179 176	0	222 75	142	226	0	<i>Pseudothrombocytopenia</i> . Physician note at 2 <sup>nd</sup> trimester: "platelet clumps on blood smear"
10	204-370	0	207 266	0	68 268	0	<i>Laboratory error</i> . Delivery platelet count, 68. Repeat platelet count 3 hours after delivery platelet count, 268
11	0	182	31 158 145	132	116	0	<i>Laboratory error/ Gestational thrombocytopenia</i> . Platelet count of 31 when seen for minor vaginal bleeding; evaluation normal. Repeat platelet count 2 days later, 158. Subsequent mild thrombocytopenia attributed to gestational thrombocytopenia
12	32-58	0	0	57	200	0	<i>May-Hegglin anomaly</i> (giant platelets) previously diagnosed; automated platelet counts 32-58 during previous 10 years. At delivery, the platelet count of 200 was a manual platelet count estimate

Table S3. Clinical evaluation of the 12 women who had platelet counts <80,000/ $\mu$ L during pregnancy and/or at delivery. To determine the cause of thrombocytopenia in these 12 women, their entire OUMC medical records including all of their additional platelet counts during this pregnancy and also for all years before and following this pregnancy were reviewed to determine if there was an identifiable cause for the low platelet count during this pregnancy. The preexisting ITP in Patient 6 had not been identified by our initial search of electronic medical records for the diagnosis codes for all 15,723 women. The diagnosis of ITP in Patient 7 was not considered until thrombocytopenia persisted after her pregnancy. The diagnosis of hereditary thrombocytopenia (May-Hegglin anomaly, Patient 12) was not included in our search of diagnosis codes. In the absence of another apparent cause, the thrombocytopenia was attributed to gestational thrombocytopenia (Patients 1-5).

**Table S4A. 2586 women with pregnancy-related complications**

<b>Complication</b>	<b>No. (%)</b>	<b>US prevalence (%)</b>	<b>Platelet counts &lt;80,000/<math>\mu</math>L No. (%)</b>
Hypertension, including preeclampsia	1,469 (20.0%)	10.5% <sup>1</sup>	17 (1.2%)
HELLP syndrome	25 (0.3%)	0.7% <sup>2</sup>	7 (28%)
Diabetes	668 (9.1%)	7.0% <sup>3</sup>	9 (1.3%)
Preterm birth (<37 weeks)	1,199 (16.3%)	12.0% <sup>4</sup>	16 (1.3%)
Stillbirth	110 (1.5%)	0.6% <sup>5</sup>	4 (3.6%)
Placental abruption, previa, accreta	39 (0.5%)	1.7% <sup>6-8</sup>	0
<b>No. of complications</b>	<b>3510</b>		

2586 women, 35.2% of all 7351 evaluable women, had 3510 pregnancy-related complications. 764 (30%) of these 2586 women had 2-4 complications. The frequency of these complications among all 7351 evaluable women is compared to their frequency among US pregnant women. 31 (1.2%) of the 2586 women had platelet counts <80,000/ $\mu$ L during pregnancy and/or at delivery: 10 of the 31 women had 2 complications, 6 women had 3 complications.

**Table S4B. 197 women with preexisting disorders associated with thrombocytopenia**

<b>Disorder</b>	<b>No. (%)</b>	<b>Platelet counts &lt;80,000/<math>\mu</math>L No. (%)</b>
Immune thrombocytopenia (ITP)	24 (0.3%)	13 (54.2%)
Systemic lupus erythematosus (SLE)	67 (0.9%)	4 (6.0%)
Human immunodeficiency virus (HIV)	40 (0.5%)	1 (2.5%)
Hepatitis	71 (1.0%)	1 (1.4%)
<b>No. of preexisting disorders</b>	<b>202</b>	

197 women, 2.7% of all 7351 evaluable women had preexisting disorders associated with thrombocytopenia. Five women had been diagnosed with two disorders: ITP and SLE (3), HIV and hepatitis (1), HIV and SLE (1). 93 (47%) of the 197 women also had pregnancy-related complications; 35 (38%) of these 93 women had 2-3 complications. 17 (8.6%) of the 197 women had platelet counts <80,000/ $\mu$ L during pregnancy and/or at delivery; two of these 17 women had been diagnosed with both ITP and SLE.

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