Los Angeles, CA 90095
yafshar@mednet.ucla.edu

O.Y. and M.R. contributed equally to this work.

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Unified standard for fetal growth: the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Fetal Growth Studies

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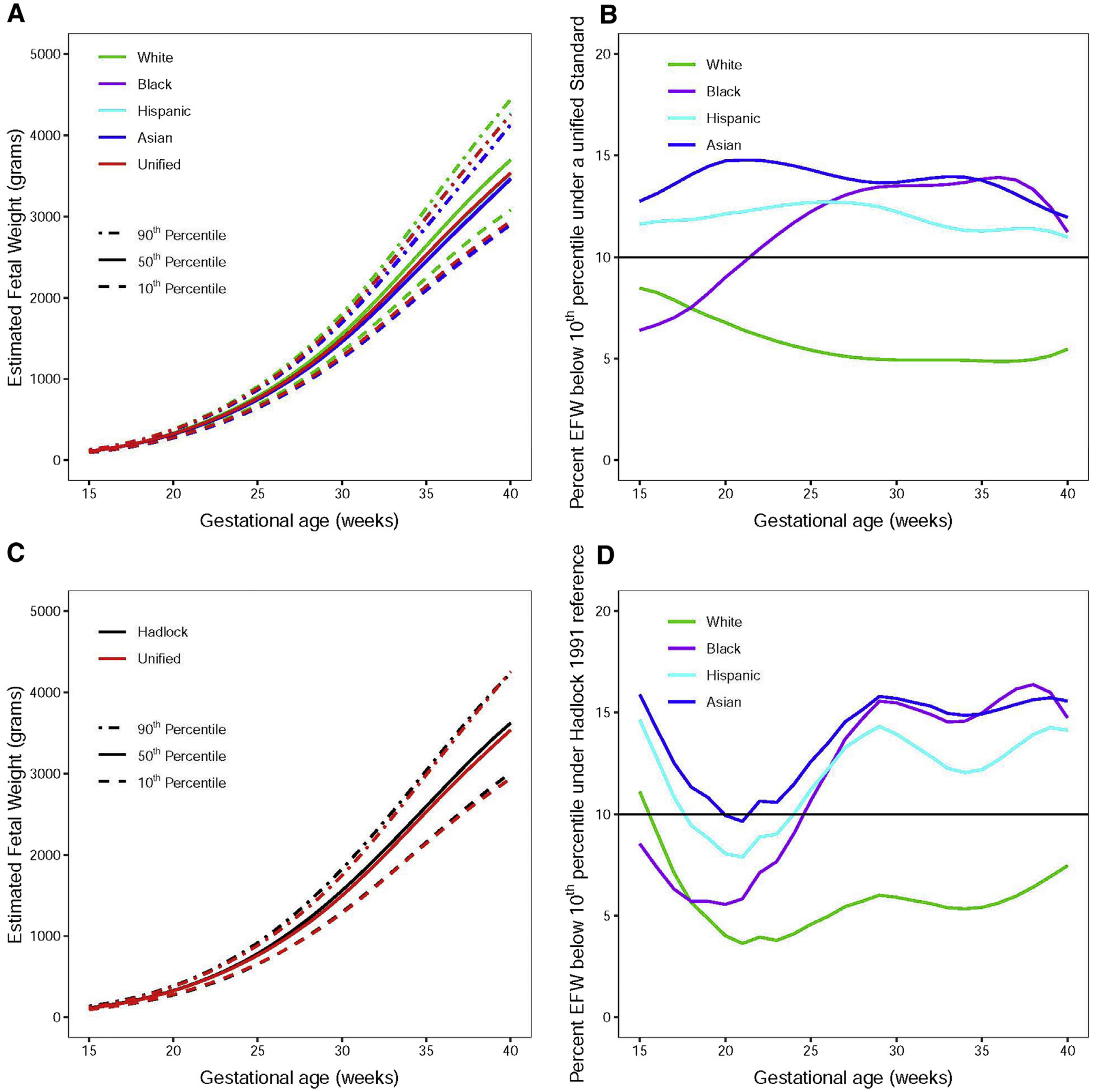
OBJECTIVE: The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Fetal Growth Studies—Singletons developed fetal growth standards in a contemporary, race and ethnicity diverse, and healthy multisite population in the United States.[1] The study revealed differences in fetal growth, represented as size-for-gestational-age, by maternally self-reported race and ethnicity, demonstrable as early as 10 to 16 weeks' gestation.[2,3] Based on these findings, fetal growth standards stratified by race and ethnicity were developed because pooling results among self-identified racial and ethnic groups may differentially classify growth at the extremes, namely small for gestational age (SGA) or large for gestational age (LGA).[4,5] For example, the study-derived standard based solely on the White racial and ethnic group classified up to 15% of fetuses born to non-White mothers as SGA (estimated fetal weight [EFW] of <fifth percentile).[2,3] Since that time, there has been recognition that inclusion of self-reported race and ethnicity in clinical algorithms may create unintended consequences for diagnosis and intervention.[6,7] In addition, if an individual does not identify as one of the specified racial and ethnic groups, then a unified standard may be more useful as a first step in the diagnostic process. We sought to create a contemporary, unified fetal growth standard, including all healthy participants in the NICHD Fetal Growth Studies—Singletons, weighted to represent the US population of pregnant women, to supplement our previous work and compare with (1) our previous racial- and ethnic-specific standards[3] and (2) the Hadlock reference[8] because the Society for Maternal-Fetal Medicine (SMFM) recommends the use of "population-based fetal growth references (such as Hadlock)."[9]

STUDY DESIGN: Analyses included the same sample used for the racial- and ethnic-specific standards,[1] composed of 1737 pregnant individuals without obesity with low-risk antenatal profiles from 12 US clinical sites (2009—2013) who delivered at ≥37 weeks' gestation.[1,2] Statistical analysis included 1732 eligible women (99.7%) with ultrasound measurements, of which 27.7%, 24.4%, 28.1%, and 19.8% self-identified as non-Hispanic White (NHW), non-Hispanic Black (NHB), Hispanic, and Asian or Pacific Islander (Asian), respectively. To approximate a nationally representative standard, the study sample was weighted back to a US population distribution of pregnant women using the natality statistics from 2011, which was the midpoint of the enrollment years (Supplement).[10] Human subjects' approval was obtained from all participating sites, and all women provided informed consent. A total of 6 research ultrasounds were performed measuring fetal biparietal diameter, head circumference (HC), abdominal circumference (AC), humerus, and femur length (FL). EFW was calculated from HC, AC and FL.[11] The individual measurements, HC-to-AC ratio, and EFW were log-transformed to stabilize variances across gestational ages and improve normal approximations for error structures. Linear mixed models with cubic splines for the fixed and random effects were used to flexibly model fetal growth trajectories.[12] Models were weighted on race and ethnicity

FIGURE
EFW in the NICHD Fetal Growth Studies



A, Distribution of EFW by a unified multiracial and ethnic group, 4 individual races and ethnicities, and gestational age (NICHD Fetal Growth Studies—Singletons). Estimated 10th, 50th, and 90th percentiles for fetal measurements by the entire cohort with race and ethnicity weighted using 2011 natality data and self-reported race and ethnicity, as estimated from linear mixed models with log-transformed outcomes and cubic splines. **B,** Percentage of fetuses with an EFW <10th percentile by racial and ethnic group, unified multiracial and ethnic group standard, and gestational age. The difference between racial- and ethnic-specific curves and the 10% referent line reflects the amount of differential classification attributed to using the unified multiracial or ethnic standard. **C,** Unified curve compared with the Hadlock reference. **D,** Percentage of fetuses with an EFW <10th percentile by racial and ethnic, group, Hadlock reference, and gestational age. The difference between racial- and ethnic-specific curves and the 10% referent line reflects the amount of differential classification attributed to using the Hadlock reference. Adapted from Hadlock.[8]

EFW, estimated fetal weight; *NICHD*, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development.

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for the unified standard and unweighted to estimate racial- and ethnic-specific EFW curves for comparison with the unified standard. Of note, 3-knot points (25th, 50th, and 75th percentiles) were chosen at gestational ages that evenly split the distributions. Percentiles were estimated on the basis of the assumed normal distribution of the random effects and error structure. Estimated curves (10th, 50th, and 90th percentiles) were determined across gestational age from the 10th to the 40th week (except for EFW, which started at 15 weeks). All analyses were implemented using the SAS software (version 9.4; SAS Institute Inc, Cary, NC) or R (version 3.1.2; R Foundation for Statistical Computing, Vienna, Austria; http://www.R-project.org). To assess the clinical relevance and impact on the classification of SGA, the unified standard was compared with the Hadlock et al[8] (1991) reference commonly used in clinical practice. The differences in fetal growth classification between the unified standard and our previously developed racial and ethnic standards and the Hadlock reference were calculated for an EFW of <10th percentile (SGA).[3] Statistical testing for comparison of the curves was not performed as each of the standards was constructed using the same dataset.

RESULTS: The racial and ethnic representations in the analytical sample after weighting were as follows: 55.0% for NHW, 12.4% for NHB, 24.5% for Hispanic, and 8.1% for Asian. The weighted mean±standard deviation age was 28.9±5.2 years, and the prepregnancy body mass index was 23.4±2.9 kg/m^2. In the weighted sample, 49.1% were nulliparous, 83.1% were married or living as married, 79.5% had education beyond high school, 56.7% had an income of ≥$75,000, 71.2% had commercial health insurance, and 75.3% were employed or full-time students. The unified and racial- and ethnic-specific EFW curves[3] are presented in the Figure, A. The 50th percentile of the unified EFW curve was lower than that of the NHW group, similar to the Hispanic group, and higher than that for the Asian and NHB groups (statistical testing not performed). For example, at 39 weeks' gestation, the 50th percentile EFWs were 3344 g for unified, 3502 g for NHW, 3330 g for Hispanic, 3263 g for Asian, and 3256 g for NHB. The unified standard classified more fetuses whose mothers identified as NHB, Hispanic, and Asian and fewer of those born to NHW mothers as being <10th percentile for EFW (Figure, B) than the racial- and ethnic-specific standards. Using the unified standard between 22 weeks' gestation and term, more than 10% of fetuses born to NHB, Hispanic, and Asian mothers were classified as <10th percentile, using cutoffs from the racial- and ethnic-specific standards. For example, at 32 weeks' gestation, a time when ultrasounds are often obtained, 5% of NHW, 14% of NHB, 12% of Hispanic, and 14% of Asian fetuses would be classified as <10th percentile based on the unified standard. Data for the unified standard percentiles (3rd, 5th, 10th, 50th, 90th, 95th, and 97th) for all measurements, HC and AC, and EFW are presented in the Table. The unified curve had a lower 50th percentile EFW than the Hadlock curve throughout gestation (Figure, C). A similar difference in classification of SGA fetuses would occur using the Hadlock reference, although the pattern differed slightly (Figure, D). Once more, at 32 weeks' gestation, 6% of NHW, 15% of NHB, 13% of Hispanic, and 15% of Asian fetuses would have been classified as <10th percentile using the Hadlock reference.

CONCLUSION: We provided a unified, multiethnic, fetal growth standard to supplement our previous work.[2,3] This unified curve for EFW falls below that for the fetuses of NHW women and above those for the fetuses of NHB, Hispanic, and Asian women. The unified multiracial and ethnic fetal standard compared with our racial- and ethnic-specific standards classified different percentages of fetuses as SGA, as expected.[5] Although a unified fetal standard might be more practical for sonographic assessment in diverse and heterogeneous populations, it will classify different percentages of fetuses as SGA and LGA among racial and ethnic groups. When applying the standard to a local population, these findings mean that it may perform differently concerning the risks of perinatal morbidity and mortality, with long-term health implications.

Numerous ultrasound-based fetal weight references are used clinically.[13] The NICHD Fetal Growth Studies addressed earlier methodologic limitations, for example, retrospective or cross-sectional designs coupled with limited and non-diverse samples without careful consideration of biases (selection, information, and residual confounding), all impacting their utility and feasibility for clinical use.[8,14–18] Of note, the following 2 other diverse, contemporary international studies with longitudinal fetal measurements have offered alternative fetal growth standards: (1) the International Fetal and Newborn Growth Consortium for the 21st Century and (2) the World Health Organization Multicentre Growth Reference Study.[19,20] Despite the 2 international studies and our including women with similar low-risk antenatal profiles, percentiles for fetal measurements and EFW varied significantly.[21] The reason for demonstrated differences in fetal growth across geographic populations is not entirely clear as the determinants of fetal growth are not fully known.[22,23] Variation in fetal growth reflects multiple maternal and paternal characteristics, including genetic factors and external factors, such as altitude, nutrition, stressors, and other environmental conditions.[24–29] Country of inhabitance, for example, is the most important factor predicting adverse infant outcomes, compared with customizing for additional maternal and fetal characteristics.[30] This observation underscores the importance of US-specific standards in clinical practice. We weighted our racial- and ethnic-specific standards to approximate their distribution in the general population using the natality data to construct a unified US standard. Ideally, we would use weights reflecting racial and ethnic distribution among women eligible to be included in the standard (low antenatal risk); however, such

TABLE

Percentiles for fetal measurements and EFW by gestational age, NICHD Fetal Growth Studies unified chart

	Biparietal diameter (mm)						
Gestational age (wk)	3rd	5th	10th	50th	90th	95th	97th
10	10.4	10.6	10.9	12.0	13.3	13.6	13.9
11	13.4	13.6	14.0	15.4	16.9	17.4	17.7
12	16.6	16.9	17.3	19.0	20.9	21.4	21.8
13	19.9	20.3	20.8	22.7	24.9	25.5	25.9
14	23.3	23.7	24.3	26.5	28.9	29.6	30.1
15	26.6	27.0	27.7	30.1	32.7	33.5	34.0
16	29.8	30.2	30.9	33.5	36.4	37.2	37.8
17	32.8	33.3	34.0	36.8	39.8	40.7	41.3
18	35.7	36.2	37.0	39.9	43.1	44.0	44.7
19	38.6	39.2	40.0	43.0	46.3	47.3	48.0
20	41.5	42.1	43.0	46.2	49.6	50.6	51.3
21	44.5	45.0	46.0	49.3	52.9	53.9	54.6
22	47.4	48.0	48.9	52.4	56.2	57.3	58.0
23	50.3	50.9	51.9	55.6	59.4	60.6	61.4
24	53.2	53.9	54.9	58.7	62.7	63.9	64.7
25	56.0	56.7	57.8	61.7	65.9	67.2	68.0
26	58.8	59.5	60.6	64.7	69.1	70.4	71.2
27	61.5	62.2	63.4	67.6	72.2	73.5	74.4
28	64.1	64.8	66.0	70.5	75.2	76.6	77.5
29	66.5	67.3	68.6	73.2	78.1	79.6	80.5
30	68.9	69.7	71.0	75.8	80.9	82.4	83.4
31	71.1	72.0	73.3	78.3	83.6	85.2	86.2
32	73.2	74.1	75.5	80.6	86.1	87.7	88.8
33	75.1	76.0	77.5	82.8	88.4	90.1	91.2
34	76.8	77.8	79.2	84.7	90.5	92.3	93.4
35	78.3	79.3	80.8	86.4	92.4	94.2	95.3
36	79.6	80.6	82.1	87.9	94.0	95.8	97.0
37	80.7	81.7	83.3	89.2	95.4	97.3	98.5
38	81.7	82.7	84.3	90.3	96.7	98.6	99.9
39	82.5	83.6	85.2	91.3	97.8	99.8	101.1
40	83.3	84.4	86.1	92.3	98.9	100.9	102.2
	Head circumference (mm)						
Gestational age (wk)	**3rd**	**5th**	**10th**	**50th**	**90th**	**95th**	**97th**
10	39.4	40.2	41.4	46.1	51.3	52.9	53.9
11	50.0	51.0	52.5	58.2	64.5	66.4	67.7
12	61.5	62.6	64.4	71.1	78.5	80.8	82.3
13	73.5	74.8	76.8	84.5	93.0	95.5	97.2
14	85.7	87.1	89.4	98.0	107.4	110.2	112.1

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(continued)

TABLE

Percentiles for fetal measurements and EFW by gestational age, NICHD Fetal Growth Studies unified chart *(continued)*

Gestational age (wk)	Head circumference (mm) 3rd	5th	10th	50th	90th	95th	97th
15	97.8	99.4	101.9	111.2	121.4	124.5	126.5
16	109.6	111.3	114.0	124.0	134.8	138.1	140.2
17	121.1	122.9	125.7	136.2	147.6	151.0	153.3
18	132.3	134.2	137.1	148.1	159.9	163.5	165.8
19	143.5	145.4	148.5	159.8	172.0	175.6	178.0
20	154.8	156.8	159.9	171.6	184.1	187.8	190.3
21	166.1	168.2	171.4	183.4	196.2	200.0	202.5
22	177.5	179.6	182.9	195.1	208.1	212.0	214.5
23	188.7	190.9	194.3	206.7	220.0	223.9	226.4
24	199.8	202.0	205.5	218.1	231.5	235.5	238.1
25	210.7	212.9	216.4	229.3	242.9	246.9	249.5
26	221.2	223.4	227.0	240.1	253.9	257.9	260.6
27	231.2	233.6	237.2	250.5	264.5	268.6	271.3
28	240.9	243.3	247.0	260.5	274.8	279.0	281.7
29	250.0	252.4	256.2	270.0	284.6	288.9	291.7
30	258.6	261.1	264.9	279.1	294.0	298.4	301.3
31	266.5	269.1	273.0	287.6	302.9	307.4	310.3
32	273.7	276.4	280.5	295.4	311.2	315.8	318.9
33	280.2	283.0	287.2	302.6	318.9	323.6	326.8
34	286.0	288.8	293.1	309.1	325.9	330.8	334.1
35	290.9	293.8	298.3	314.8	332.2	337.3	340.6
36	295.1	298.0	302.7	319.7	337.7	343.0	346.5
37	298.5	301.6	306.4	324.0	342.6	348.1	351.7
38	301.3	304.5	309.4	327.6	346.9	352.6	356.3
39	303.5	306.8	311.9	330.7	350.7	356.6	360.4
40	305.2	308.6	313.9	333.3	354.0	360.1	364.1

Gestational age (wk)	Abdominal circumference (mm) 3rd	5th	10th	50th	90th	95th	97th
10	30.9	31.5	32.4	36.1	40.1	41.3	42.1
11	39.1	39.8	41.0	45.4	50.3	51.8	52.8
12	48.2	49.1	50.5	55.8	61.6	63.3	64.5
13	58.1	59.1	60.7	66.9	73.6	75.6	77.0
14	68.5	69.7	71.5	78.5	86.1	88.4	90.0
15	79.2	80.5	82.6	90.4	98.9	101.5	103.2
16	90.1	91.5	93.8	102.4	111.8	114.6	116.4
17	101.0	102.6	105.1	114.4	124.5	127.6	129.6
18	111.8	113.5	116.2	126.2	137.1	140.4	142.6
19	122.6	124.4	127.3	138.0	149.6	153.1	155.4

Grantz. Unified standard for fetal growth. Am J Obstet Gynecol 2022.

(continued)

TABLE

Percentiles for fetal measurements and EFW by gestational age, NICHD Fetal Growth Studies unified chart *(continued)*

Gestational age (wk)	Abdominal circumference (mm) 3rd	5th	10th	50th	90th	95th	97th
20	133.3	135.2	138.3	149.7	162.0	165.7	168.1
21	143.8	145.9	149.2	161.2	174.3	178.1	180.7
22	154.2	156.4	159.9	172.6	186.3	190.4	193.1
23	164.4	166.7	170.3	183.7	198.1	202.4	205.3
24	174.3	176.7	180.5	194.6	209.8	214.3	217.3
25	184.0	186.5	190.5	205.3	221.2	226.0	229.1
26	193.4	196.1	200.3	215.8	232.6	237.6	240.9
27	202.7	205.6	210.0	226.3	244.0	249.2	252.7
28	212.0	215.0	219.6	236.9	255.4	260.9	264.6
29	221.4	224.5	229.4	247.6	267.1	273.0	276.8
30	230.8	234.1	239.3	258.5	279.2	285.4	289.4
31	240.3	243.7	249.2	269.5	291.4	298.0	302.3
32	249.6	253.3	259.1	280.5	303.7	310.6	315.2
33	258.7	262.6	268.7	291.3	315.9	323.3	328.1
34	267.4	271.5	277.9	301.9	327.8	335.6	340.8
35	275.6	279.9	286.7	311.9	339.3	347.5	353.0
36	283.2	287.7	294.8	321.4	350.3	358.9	364.7
37	290.3	295.1	302.5	330.4	360.8	370.0	376.0
38	297.1	302.1	309.9	339.1	371.1	380.8	387.1
39	303.6	308.9	317.0	347.7	381.3	391.5	398.2
40	310.1	315.5	324.1	356.3	391.6	402.3	409.3

Gestational age (wk)	Femur length (mm) 3rd	5th	10th	50th	90th	95th	97th
10	1.7	1.7	1.9	2.4	3.0	3.2	3.3
11	2.9	3.0	3.2	4.1	5.1	5.4	5.7
12	4.6	4.8	5.1	6.4	8.0	8.5	8.8
13	6.8	7.0	7.5	9.3	11.5	12.2	12.7
14	9.3	9.6	10.2	12.5	15.4	16.3	17.0
15	12.0	12.4	13.1	16.0	19.5	20.7	21.4
16	14.7	15.2	16.1	19.5	23.5	24.8	25.7
17	17.4	18.0	18.9	22.7	27.3	28.7	29.7
18	20.0	20.6	21.7	25.8	30.7	32.3	33.3
19	22.5	23.2	24.3	28.7	33.9	35.6	36.7
20	25.0	25.7	26.9	31.6	37.0	38.7	39.9
21	27.5	28.3	29.6	34.4	40.1	41.8	43.0
22	30.1	30.9	32.2	37.2	43.0	44.8	46.0
23	32.6	33.4	34.7	39.9	45.8	47.6	48.8
24	35.0	35.9	37.2	42.4	48.4	50.2	51.5

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(continued)

TABLE
Percentiles for fetal measurements and EFW by gestational age, NICHD Fetal Growth Studies unified chart *(continued)*

	Femur length (mm)						
Gestational age (wk)	3rd	5th	10th	50th	90th	95th	97th
25	37.4	38.3	39.7	44.9	50.9	52.7	54.0
26	39.7	40.6	42.0	47.3	53.3	55.1	56.3
27	42.0	42.9	44.3	49.6	55.5	57.3	58.5
28	44.2	45.1	46.5	51.8	57.7	59.4	60.6
29	46.4	47.3	48.7	54.0	59.8	61.5	62.7
30	48.6	49.5	50.9	56.1	61.9	63.6	64.8
31	50.7	51.6	53.0	58.2	63.9	65.6	66.8
32	52.7	53.6	55.0	60.2	65.9	67.7	68.8
33	54.6	55.5	56.9	62.2	67.9	69.6	70.8
34	56.4	57.3	58.7	64.0	69.9	71.6	72.8
35	58.0	58.9	60.4	65.8	71.7	73.5	74.7
36	59.4	60.3	61.8	67.4	73.5	75.4	76.6
37	60.6	61.6	63.2	68.9	75.3	77.2	78.4
38	61.6	62.6	64.3	70.3	76.9	78.9	80.2
39	62.4	63.4	65.1	71.5	78.4	80.5	81.9
40	62.9	64.0	65.8	72.4	79.7	81.9	83.4

	Humerus length (mm)						
Gestational age (wk)	3rd	5th	10th	50th	90th	95th	97th
10	1.8	1.8	2.0	2.5	3.1	3.3	3.5
11	3.1	3.2	3.4	4.3	5.3	5.7	5.9
12	4.9	5.1	5.4	6.7	8.3	8.9	9.2
13	7.2	7.4	7.9	9.7	12.0	12.7	13.2
14	9.8	10.1	10.7	13.1	16.0	16.9	17.5
15	12.5	12.9	13.6	16.5	20.0	21.1	21.9
16	15.1	15.7	16.5	19.8	23.9	25.1	26.0
17	17.6	18.2	19.2	22.9	27.3	28.7	29.7
18	20.0	20.6	21.6	25.6	30.4	31.8	32.9
19	22.2	22.9	23.9	28.2	33.1	34.7	35.7
20	24.4	25.1	26.2	30.6	35.8	37.4	38.5
21	26.6	27.4	28.5	33.1	38.4	40.0	41.1
22	28.8	29.6	30.8	35.4	40.8	42.5	43.6
23	30.9	31.7	32.9	37.7	43.1	44.8	45.9
24	33.0	33.8	35.1	39.8	45.3	47.0	48.1
25	35.0	35.8	37.1	41.9	47.3	49.0	50.1
26	37.0	37.8	39.0	43.8	49.2	50.9	52.0
27	38.8	39.6	40.9	45.7	51.0	52.6	53.7
28	40.6	41.4	42.7	47.4	52.7	54.3	55.4
29	42.3	43.1	44.4	49.1	54.3	55.9	57.0

Grantz. Unified standard for fetal growth. Am J Obstet Gynecol 2022. *(continued)*

TABLE
Percentiles for fetal measurements and EFW by gestational age, NICHD Fetal Growth Studies unified chart *(continued)*

Gestational age (wk)	Humerus length (mm) 3rd	5th	10th	50th	90th	95th	97th
30	44.0	44.8	46.1	50.7	55.9	57.5	58.5
31	45.6	46.4	47.7	52.3	57.5	59.0	60.0
32	47.1	47.9	49.2	53.9	59.0	60.5	61.6
33	48.5	49.3	50.6	55.3	60.5	62.0	63.1
34	49.9	50.7	52.0	56.8	62.0	63.5	64.6
35	51.1	51.9	53.2	58.1	63.5	65.1	66.1
36	52.2	53.0	54.4	59.4	64.9	66.6	67.7
37	53.1	54.0	55.4	60.6	66.3	68.1	69.2
38	53.9	54.8	56.2	61.7	67.6	69.4	70.6
39	54.4	55.4	56.9	62.6	68.8	70.7	71.9
40	54.6	55.6	57.2	63.2	69.8	71.8	73.1

Gestational age (wk)	Head circumference to abdominal circumference ratio 3rd	5th	10th	50th	90th	95th	97th
10	1.174	1.188	1.209	1.290	1.375	1.401	1.417
11	1.172	1.186	1.207	1.286	1.370	1.395	1.412
12	1.165	1.178	1.199	1.277	1.359	1.384	1.400
13	1.153	1.166	1.187	1.263	1.344	1.368	1.383
14	1.138	1.151	1.171	1.246	1.325	1.349	1.364
15	1.122	1.134	1.154	1.227	1.305	1.328	1.343
16	1.104	1.117	1.136	1.208	1.284	1.306	1.321
17	1.088	1.100	1.119	1.189	1.264	1.286	1.300
18	1.072	1.084	1.103	1.172	1.246	1.267	1.282
19	1.059	1.071	1.089	1.158	1.23	1.252	1.266
20	1.048	1.060	1.079	1.147	1.219	1.240	1.254
21	1.040	1.052	1.070	1.138	1.210	1.231	1.245
22	1.033	1.045	1.064	1.131	1.203	1.225	1.239
23	1.028	1.04	1.058	1.126	1.198	1.220	1.234
24	1.023	1.035	1.053	1.122	1.194	1.216	1.230
25	1.018	1.03	1.048	1.117	1.191	1.212	1.227
26	1.012	1.024	1.043	1.113	1.187	1.208	1.223
27	1.006	1.018	1.037	1.107	1.182	1.204	1.218
28	0.998	1.010	1.029	1.100	1.175	1.198	1.212
29	0.988	1.000	1.019	1.091	1.167	1.189	1.204
30	0.976	0.988	1.008	1.08	1.156	1.179	1.194
31	0.963	0.975	0.995	1.067	1.144	1.167	1.183
32	0.948	0.961	0.981	1.053	1.131	1.155	1.170
33	0.933	0.946	0.966	1.039	1.118	1.141	1.157
34	0.918	0.931	0.951	1.024	1.104	1.127	1.143

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TABLE

Percentiles for fetal measurements and EFW by gestational age, NICHD Fetal Growth Studies unified chart *(continued)*

	Head circumference to abdominal circumference ratio						
Gestational age (wk)	**3rd**	**5th**	**10th**	**50th**	**90th**	**95th**	**97th**
35	0.902	0.915	0.935	1.010	1.09	1.114	1.130
36	0.887	0.900	0.920	0.995	1.076	1.101	1.117
37	0.872	0.885	0.905	0.981	1.063	1.088	1.104
38	0.856	0.869	0.89	0.967	1.050	1.075	1.091
39	0.84	0.854	0.875	0.952	1.037	1.062	1.079
40	0.825	0.838	0.859	0.938	1.024	1.050	1.067
	EFW (g)						
Gestational age (wk)	**3rd**	**5th**	**10th**	**50th**	**90th**	**95th**	**97th**
15	90	93	96	111	128	133	137
16	114	117	121	140	161	168	172
17	142	146	152	175	202	210	216
18	177	181	189	218	251	262	269
19	218	223	233	268	310	323	331
20	265	272	283	327	378	393	404
21	319	328	341	394	456	475	487
22	380	391	407	471	544	567	582
3	449	462	481	557	644	671	690
24	526	541	564	653	756	789	810
25	612	629	656	760	881	919	945
26	706	726	757	879	1020	1064	1094
27	810	833	869	1010	1174	1225	1259
28	924	950	992	1154	1344	1403	1443
29	1048	1078	1126	1313	1532	1600	1646
30	1184	1218	1273	1488	1738	1816	1869
31	1330	1369	1431	1676	1962	2052	2112
32	1483	1528	1599	1876	2202	2304	2373
33	1643	1692	1772	2086	2455	2570	2649
34	1804	1860	1949	2301	2716	2846	2935
35	1963	2025	2124	2516	2980	3126	3225
36	2116	2185	2295	2728	3243	3406	3517
37	2264	2339	2460	2937	3506	3687	3809
38	2406	2488	2619	3142	3768	3968	4103
39	2542	2631	2774	3344	4032	4251	4400
40	2672	2769	2924	3546	4299	4540	4704

Note that week corresponds to the exact week (eg, 15 weeks=15.0 weeks). EGW was calculated from head circumference, abdominal circumference, and femur length using the Hadlock 1985 formula.[11]

EFW, estimated fetal weight; *NICHD*, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development.

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population data are not available. US professional societies do not currently recognize a national reference or standard for fetal growth. The American College of Obstetricians and Gynecologists does not specify one, whereas the SMFM recommends the use of "population-based fetal growth references (such as Hadlock)."[9,31,32] However, the Hadlock reference is cross-sectional (ie, fetal measurements taken at a single examination, and each fetus is only represented once), so it is less precise in assessing velocity.[8,33] Furthermore, the Hadlock reference was derived from a single hospital and included only White gravidas, less stringently screened for antenatal risk (eg, smokers not excluded). Moreover, it does not reflect the diversity in the US obstetrical population, as demonstrated by the differences between EFW unified and Hadlock curves and different percentages of fetuses classified as SGA compared with racial- and ethnic-specific standards. Our US-based fetal standard should apply to the current US population. However, given that we have shown differential classification at the extremes, clinical protocols may need to be adapted for use in local populations to avoid unnecessary follow-up and as a diagnostic tool for perinatal morbidity and mortality. Future studies evaluating short-term and long-term offspring health of the unified standards compared with the racial- and ethnic-specific standards are warranted. Ultimately, randomized trials are needed to establish which fetal growth standard is superior in improving outcomes. ■

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Katherine L. Grantz, MD, MS
Epidemiology Branch
Division of Population Health Research
Division of Intramural Research
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6710B Rockledge Drive
MSC 7004
Bethesda, MD 20892
katherine.grantz@nih.gov

Jagteshwar Grewal, PhD, MPH
Division of Population Health Research
Division of Intramural Research
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
Bethesda, MD

Sungduk Kim, PhD
Biostatistics Branch
Division of Cancer Epidemiology and Genetics
National Cancer Institute
Bethesda, MD

William A. Grobman, MD, MBA
Department of Obstetrics and Gynecology
Feinberg School of Medicine
Northwestern University
Chicago, IL

Roger B. Newman, MD
Department of Obstetrics and Gynecology
Medical University of South Carolina
Charleston, SC

John Owen, MD, MSPH
Division of Maternal-Fetal Medicine
Department of Obstetrics and Gynecology
University of Alabama at Birmingham
Birmingham, AL

Anthony Sciscione, DO
Department of Obstetrics and Gynecology
ChristianaCare Health System
Newark, DE

Daniel Skupski, MD
Department of Obstetrics and Gynecology
NewYork-Presbyterian Queens
Flushing, NY

Edward K. Chien, MD
Division of Maternal Fetal Medicine
Department of Obstetrics and Gynecology
Women & Infants Hospital of Rhode Island
Providence, RI
Cleveland Clinic
Cleveland, OH

Deborah A. Wing, MD
Division of Maternal-Fetal Medicine
Department of Obstetrics-Gynecology
University of California, Irvine
School of Medicine, Irvine
Orange County, CA
Fountain Valley Regional Hospital and Medical Center
Fountain Valley, CA

Ronald J. Wapner, MD
Department of Obstetrics and Gynecology
Columbia University Medical Center
New York, NY

Angela C. Ranzini, MD
Division of Maternal Fetal Medicine
Department of Obstetrics and Gynecology
Women and Infants Hospital of Rhode Island
Providence, RI
Division of Maternal and Fetal Medicine
Department of Obstetrics and Gynecology

St Peter's University Hospital
New Brunswick, NJ

Michael P. Nageotte, MD
Department of Obstetrics and Gynecology
Miller Children's Hospital/Long Beach Memorial Medical Center
Long Beach, CA

Sabrina Craigo, MD
Department of Obstetrics and Gynecology
Tufts Medical Center
Boston, MA

Stefanie N. Hinkle, PhD
Department of Biostatistics, Epidemiology and Informatics
Perelman School of Medicine
University of Pennsylvania
Philadelphia, PA

Mary E. D'Alton, MD
Department of Obstetrics and Gynecology
Columbia University Medical Center
New York, NY

Dian He, PhD
Division of Population Health Research
Division of Intramural Research
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
Bethesda, MD
The Prospective Group
Fairfax County, VA

Fasil Tekola-Ayele, PhD
Division of Population Health Research
Division of Intramural Research
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health

Mary L. Hediger, PhD
Division of Population Health Research
Division of Intramural Research
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
Bethesda, MD

Germaine M. Buck Louis, PhD, MS
Office of the Dean
College of Health and Human Services
George Mason University
Fairfax County, VA

Cuilin Zhang, PhD, MPH, MD
Division of Population Health Research
Division of Intramural Research
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
Bethesda, MD

Paul S. Albert, PhD
Biostatistics Branch
Division of Cancer Epidemiology and Genetics
National Cancer Institute
Bethesda, MD

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This study is registered on ClinicalTrials.gov.

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Transplacental transfer of SARS-CoV-2 antibodies in recovered and BNT162b2-vaccinated patients

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OBJECTIVE: Neonates have been found to be more susceptible to severe SARS-CoV-2 infection.[1] Data regarding the transfer of anti-SARS-CoV-2 antibodies to the neonate of vaccinated women is limited, including only 3 studies concerning late third-trimester vaccination.[2–4] The objective of this study was to assess the transplacental transfer of anti-SARS-CoV-2 antibodies in women vaccinated with the BNT162b2 vaccine during the second and third trimester.

STUDY DESIGN: A total of 40 parturients with singleton term pregnancies were recruited. Samples were collected from maternal and cord blood. Both maternal and neonatal samples were analyzed for anti-nucleocapsid (anti-N) and anti-spike (anti-S) antibodies. The study was approved by the local institutional review board (number 0055-21-AAA) and written informed consent was obtained from all participants.

RESULTS: Of the 40 women recruited, 28 were vaccinated with 2 doses of the BNT162b2 vaccine and 12 were COVID-19-convalescents (Supplemental Table 1). Median interval between COVID-19 diagnosis and delivery in the recovered group was 20.6 weeks (interquartile range [IQR], 17.6−36.9), whereas the median interval between second vaccine and delivery in the vaccinated group was 11.1 weeks (IQR, 9.3−15). Two women in the vaccinated group were anti-N-positive, suggesting past unknown infection (Supplemental Table 2).

Overall, maternal anti-S antibody levels were significantly higher in the vaccinated group than in the recovered group (145, IQR, 113−202 vs 41, IQR, 19−95 AU/mL, respectively; P=.008), as were neonatal anti-S antibody levels (216, IQR, 155−316 vs 64, IQR, 23−219 AU/mL, respectively; P=.026). Neonatal antibody levels were significantly higher than maternal levels in both groups (185, IQR, 85−316 vs 131, IQR, 59−198; P<.001). There was no significant difference in the neonatal to maternal anti-S ratio between the groups (Table).

There was a significant correlation between maternal and neonatal anti-S antibody levels (r=0.922, P<.001). However, there was no correlation between maternal anti-S levels and the neonatal to maternal anti-S ratio, nor between maternal anti-S levels and the interval to delivery. Moreover, the lack of correlation between maternal anti-S levels and the interval to delivery was also apparent when assessing the vaccinated and the recovered groups separately (Supplemental Table 3).

Regarding factors that may affect transplacental anti-S antibody transfer, using a linear regression model (Figure),

SUPPLEMENT

Creation of weights for race and ethnicity

We used the 2011 vital statistics file (n=3,961,220) to examine the race distributions in the United States to reweight the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Fetal Growth Study samples so that they were representative of the race and ethnic distributions in the United States among women with low-risk singleton pregnancies. The 2011 data file includes data based on both the 1989 revision of the US Standard Certificate of Live Birth (unrevised) and 2003 revision of the US Standard Certificate of Live Birth (revised). Of note, 36 states, the District of Columbia, Puerto Rico, and the Northern Marianas had implemented the revised birth certificate as of January 1, 2011. The 36 revised states and the District of Columbia (excluding Puerto Rico and the Northern Marianas) represent 83% of births to US residents. Some of the variables that were excluded were only available for the women from a state with the revised birth certificate. If the revised birth certificate data were not available, women were left in the data file.

The 2011 vital statistics file was downloaded from https://www.nber.org/data/vital-statistics-natality-data.html.

We excluded 1,508,896 women (38.1%) from the vital statistics file based on the criteria given in Supplemental Table 1. We used a maternal race variable that was based on the bridged census code. Mother's race and Hispanic origin were indicated as follows: (1) Mexican, (2) Puerto Rican, (3) Cuban, (4) Central or South American, (5) other and unknown Hispanic, (6) non-Hispanic White, (7) non-Hispanic Black, and (8) non-Hispanic other races. We grouped all Hispanic women together (1-5). Sample percentages by racial and ethnic group before and after weighting are presented in Supplemental Table 2.

The weights were applied to the 1737 pregnant individuals without obesity with low-risk antenatal profiles who delivered at 37 weeks' gestation included in the standard analysis. The racial and ethnic representations in the analytical sample after weighting were as follows: 55.0% for non-Hispanic White, 12.4% for non-Hispanic Black, 24.5% for Hispanic, and 8.1% for Asian.

SUPPLEMENTAL TABLE 1
Exclusion criteria

Criteria	Data availability	n[a]	%
Age <18 or >40 y	All birth certificates	172,637	4.36
Conception by ovulation stimulation drugs or assisted reproductive technology	Revised birth certificates only	48,437	1.22
Diabetes mellitus	Revised birth certificates only	24,896	0.63
Nonsingleton birth	All birth certificates	131,525	3.32
Prepregnancy BMI of <19.0	Revised birth certificates only	194,940	4.92
Prepregnancy BMI of ≥30.0 kg/m^2	Revised birth certificates only	712,314	17.98
Chromosomal anomalies[b]	All birth certificates	565	0.01
Previous preterm births at <37 wk among women without obesity[c]	Revised birth certificates only	56,712	1.75
Smoking before pregnancy among women without obesity	Revised birth certificates only	276,554	8.51
Chronic hypertension among women without obesity or women with missing BMI[d]	All birth certificates	25,224	0.78
Unknown race	All birth certificates	27,291	0.69

BMI, body mass index; *NICHD*, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development.

[a] n's can overlap across groups; [b] Eligibility criteria for the NICHD Fetal Growth Studies—Singletons was "no confirmed or suspected fetal congenital structural or chromosomal anomalies." For weighting, we excluded chromosomal anomalies identified on the birth certificate; [c] Previous preterm birth (<34 weeks' gestation) was an exclusion criterion for the low-risk singletons (without obesity). The birth certificate only captures previous preterm births at <37 weeks' gestation; [d] Chronic hypertension was an exclusion criterion for the low-risk singletons (without obesity). Women with obesity were only excluded if chronic hypertension or high blood pressure required ≥2 medications. Therefore, we only excluded chronic hypertension for women without obesity.

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SUPPLEMENTAL TABLE 2
Sample percentages by racial and ethnic group before and after weighting and the percentages for United States

			NICHD Fetal Growth Nonobese Cohort (N=2334)		
Race and ethnicity	2011 births	After exclusions	Original	Weight	Post-weight
Non-Hispanic White	54.21	53.40	26.31	2.0296	53.40
Non-Hispanic Black	14.71	13.60	26.18	0.5195	13.60
Hispanic	23.34	24.79	27.81	0.8914	24.79
Asian or Pacific Islander	7.06	8.21	19.71	0.4165	8.21
Unknown	0.69	—	—	—	—

Note that the Asian or Pacific Islander group included 0.5% American Indian or Alaskan Native women. They were grouped with Asians for consistency with the NICHD Fetal Growth Studies, where 0.5% of the Asian women reported being American Indian or Alaskan Native when asked a question about more detailed race and ethnicity. The weights were calculated by dividing the vital stat race proportion by the NICHD Fetal Growth Nonobese Cohort race and ethnic proportion. The weights were applied to the 1737 pregnant individuals without obesity with low-risk antenatal profiles who delivered at ≥37 weeks' gestation included in the standard analysis. The racial and ethnic representations in the analytical sample after weighting were as follows: 55.0% for non-Hispanic White, 12.4% for non-Hispanic Black, 24.5% for Hispanic, and 8.1% for Asian.

NICHD, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development.

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