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Research Article

Continuously Tracking Growth of Preterm Infants from Birth to Two Years of Age

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Abstract

The objective of this study is to provide gender-specific premature infant growth curves that can be incorporated with the 2006 World Health Organization growth standards to continously track weight, head circumference, and length from 22 weeks of gestion through 2 years of age. Gender-specific percentiles of birth weight, head circumference, and length for premature infants admitted to the Vanderbilt neonatal intensive care unit were used to define intrauterine growth curves from 22 to 36 weeks in terms of best-fit functions and LMS coefficients. Multiple regression and analysis of variance was used to compare the 10th, 50th, and 90th percentiles from the Vanderbilt neonatal intensive care unit with the published values for premature infants from eight studies in the United States, Australia, Italy, Israel, Turkey, Sweden, and the United Kingdom. The intrauterine growth curves were combined with the WHO growth curves and growth trajectories based on birth percentiles were generated with Z-scores. Multiple regression and analysis of variance was also used to compare the male and female 50th percentiles for birth weight from the nine studies. The 50th percentiles for birth weight, head circumference, and length from the Vanderbilt neonatal intensive care unit are statistically identical with the intrauterine values from the United States, Israel and Turkey. Five studies showed male and female 50th percentiles for birth weight differing in the 5.6% to 6.7% range. Values from a premature infant from 32w3d to 12 months and birth percentile growth trajectories were plotted on the combined intrauterine and World Health Organization growth curves. The intrauterine curves can be used to describe infants from different countries. The combined intrauterine and World Health Organization growth curves depict the growth continium of the prematurely born infant from a gestational age of 22 weeks to 2 years of age.

Keywords: Head circumference for age; Length for age; Premature growth curves; Weight for age

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Abbreviations

BW : Birth Weight
GA : Gestational Age
HC : Head Circumference
LEN : Length
LMP : Last Menstrual Period
LMS : Three age specific cubic spline curves the L curve (Box-Cox power to remove skewness), the M curve (Median), and the S curve (coefficient of variation)
NICU : Neonatal Intensive Care Unit
SD : Standard Deviation
U : Mean
WHO : World Health Organization

Introduction

Growth monitoring is a standard component of community pediatric services throughout the world [1]. Intrauterine growth charts are used to monitor the growth of premature infants in the Neonatal Intensive Care Unit (NICU). After discharge from the NICU, it is an accepted practice to plot the growth of a prematurely born infant on a term infant growth chart after determining a correction factor for the infant's age. The correction factor commonly used, which if based on a table from reference [2], is the difference between a 40 week gestation and the gestational age of the infant [3]. For term infants from ages 0 to 2 years, the Centers for Disease Control and Prevention (USA) and the Scientific Advisory Committee on Nutrition (UK) recommend using the 2006 World Health Organization (WHO) growth standards [4]. Growth of a term infant is evaluated beginning from its birth percentiles. Premature infants are often undernourished at discharge from the NICU [5] and the percentiles at a gestational age of 40 weeks may not reflect the infant's birth percentiles. Since there are over 12 million babies born prematurely each year [6], growth charts to continuously track growth of prematurely born infants from birth to two years of age are needed.

While there have been many published growth charts for premature infants, none of these has been embraced as a universal standard. One of the greatest problems in constructing intrauterine growth curves is the determination of gestational age [7]. Most intrauterine growth curves were developed prior to the routine use of ultrasound scanning. For these studies, gestational age was estimated solely by the mother's reported Last Menstrual Period (LMP), which may be biased due to erroneous recall by the mother or early bleeding in the pregnancy [8]. Since the 1980s, prenatal ultrasounds are often utilized to provide more precise estimates of gestational age. Nine studies from the United States, Australia, Italy, Israel, Turkey, Sweden and the United Kingdom with gender-specific percentiles for birth weight, head circumference, and length were compared. If some of these studies are statistically identical, we propose that the values can be used as a standard. The objective of this study is to provide gender-specific premature infant growth curves that can be incorporated with the 2006 WHO growth standards to continously track weight, head circumference, and length from 22 weeks of gestion through 2 years of age.

Materials and Methods

When comparing percentiles from different studies, it is essential to know how gestational age was determined and exclusion criteria. The details for the nine studies that were compared are as follows.

Percentiles from Thomas (USA)

The gender-specific 50th percentiles for birth weight from Thomas et al., [9] are based on infants from 85 Pediatrix medical group hospitals in the United States (1996-1998). Gestational age, in completed weeks, was assigned by a neonatologist based on obstetrical history, prenatal ultrasounds, and the postnatal physical examination [10]. No infants were excluded.

Percentiles from Dobbins (Australia)

The gender-specific percentiles for birth weight from Dobbins et al., [11] are based on data of singleton live births from the national perinatal data collection of the Australian Institute of Health and Welfare (1998-2007). Gestational age, in completed weeks, was based on the LMP or the best available clinical estimate (including early pregnancy ultrasound examination). Extreme outliers, defined as values greater than 2 times the interquartile range (25th to 75th percentiles) below the first quartile and above the third quartile for each GA [12], were excluded. For normally distributed data, this is equivalent to +/-3.37 standard devolutions.

Percentiles from Bertino (Italy)

The gender-specific percentiles for birth weight, head circumference, and length from Bertino et al., [13] are from 34 NICUs in Italy (2005-2007). Gestational age, in completed weeks plus days, was based on the LMP and ultrasound assessment within the first trimester. When the difference between the gestational age derived from the LMP and the ultrasound assessment was greater than one week (3% of the infants), the ultrasound assessment was used. Infants with fetal hydrops and major congenital anomalies diagnosed at birth were excluded. Since the gestational ages were in terms of completed weeks plus days, half a week was subtracted from the reported gestational ages.

Percentiles from Davidson (Israel)

The gender-specific percentiles for birth weight, head circumference, and length from Davidson et al., [8] are based on singleton live births from the neonatal registry of the Rabin Medical Center in Petah Tikva, Israel (1991-2005). From 1991 to 1997, gestational age, in completed weeks, was based on the LMP. From 1998 to 2005, early fetal ultrasound (crown-rump length) was used to correct the gestational age computation when the discrepancy between the recorded LMP and the fetal ultrasound was greater than 1 week. Infants outside +/- 5 standard deviations were excluded. Since the number of infants was not stratified by gender, half were assigned to each gender.

Percentiles from Kurtoglu (Turkey)

The gender-specific percentiles for birth weight, head circumference, and length from Kurtoglu et al., [14] are from the medical records of infants born in 2009 at 11 hospitals in Kayseri, Turkey. Gestational ages were recorded by the obstetricians or trained nurses in labor wards. Infants outside +/- 2 standard deviations were excluded. Since the number of infants was not stratified by gender, half were assigned to each gender.

Percentiles from Niklasson (Sweden)

The gender-specific percentiles for birth weight, head circumference, and length from Niklasson and Albertsson-Wikland [15] are based on infants from the Swedish national birth registry (1990-1999). In Sweden, gestational age is based on ultrasound estimation [16]. Stillborns, multiple births, caesarean deliveries, and values outside +/- 6 standard deviations were excluded. The 10th, 50th and 90th percentiles for birth weight, head circumference, and length were generated from the published means (U) and Standard Deviations (SD). The 10th percentile is equal to U-1.282×SD, the 50th percentile is equal to U, and the 90th percentile is equal to U+1.282×SD. Since the number of infants was not stratified by gender, half were assigned to each gender.

Percentiles from Cole (UK)

The gender-specific percentiles for birth weight, head circumference, and length from Cole et al., [17] are from five UK studies (1983-1993). The method for determining gestational age and exclusion criteria were not specified. Since the number of infants was not stratified by gender, half were assigned to each gender.

Percentiles from Olsen (USA)

The gender-specific percentiles for birth weight, head circumference, and length from Olsen et al., [18] are based on infants from 248 Pediatrix medical group hospitals in the United States (1998-2006). Gestational age, in completed weeks, was estimated by neonatologists using obstetric history, obstetric examinations, prenatal ultrasounds, and postnatal physical examinations [10]. Infants from multiple births; with missing weight, head circumference, length, or gender values; with congenital anomalies; that died before discharge; or extreme outliers were excluded. Extreme outliers were defined as values greater than 2 times the interquartile range (25th to 75th percentiles) below the first quartile and above the third quartile for each GA [12]. For normally distributed data, this is equivalent to +/-3.37 standard devolutions.

Vanderbilt NICU percentiles (USA)

With the approval of the Vanderbilt Institutional Review Board, birth measurements of infants admitted within the first 24 hours after birth to the Vanderbilt NICU for the years 1985 through 1997 were retrieved from a longitudinal database maintained by the neonatology division. There were 6,787 live born infants with gestational ages below 37 weeks (including 1,234 infants of less than 29 weeks of gestation). This subset is 89% singleton, 55% male, 76% Caucasian, 18% African American, and 6% other races. Birth weight was recorded for all of the infants. Head circumference was recorded for 90% of the group and length was recorded for 89%. Birth weight, head circumference, and length were measured by the admitting nurse while gestational age, gender, and race were assigned by the admitting neonatologist. Birth weight was measured in grams with an electronic scale. Head circumference and length were measured in centimeters with a paper tape. Race was based on the mother's race. Gestational age, in completed weeks, was based on obstetrical history, prenatal ultrasounds, and the postnatal physical examination [10]. No infants were excluded. The data were exported into Excel (Microsoft Office) (Redmond, Washington). After sorting by gender, the mean, standard deviation, and 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles for birth weight, head circumference, and length at each gestational age were determined.

To summarize and smooth the data, several mathematical models were evaluated: exponential [y = a exp (b x)], power [y = a x^b], linear [y = a x + b], quadratic [y = a x^2 + b x + c], and cubic [y = a x^3 + b x^2 + c x + d]. An exponential function analysis fits a linear function to semi-logarithmic data (logarithm Y axis) and a power function analysis fits a linear function to full-logarithmic data (logarithm X and Y axes). The mathematical models were evaluated with SAS statistical software (Cary, NC) to determine the best model based on the Akaike's information criterion [19] and the Bayesian information criterion [20].

The exponential function, which describes uninhibited growth with a constant growth velocity, was the best model for birth weight. The percentiles for birth weight (in grams) were described with the following function:

$$BW(GA) = A \times \exp(B \times 0.007 \times GA) \quad (1)$$

where variable GA is gestational age in weeks, constant A has units of grams, and constant B is the growth velocity for weight in units of g/kg/day. Power functions best described head circumference and length. When the power functions for the 50th percentile of HC and LEN were compared to the linear functions with zero intercept, the largest difference between the two models was 1 mm. The simpler linear model with zero intercept was selected to describe HC and LEN and the percentiles (in cm) were described by the following functions:

$$HC(GA) = C \times GA \quad (2)$$

$$LEN(GA) = D \times GA \quad (3)$$

where variable GA is gestational age in weeks, constant C is the growth velocity for head circumference in cm/week, and constant D is the growth velocity for length in cm/week. Using these models, best-fit equations for the 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles for birth weight, head circumference, and length were generated with PSI-Plot (Poly Software Incorporated, Pearl River, NY).

The LMS method is used to construct growth charts [21]. It estimates the percentiles in terms of three age specific cubic spline curves: the L curve (Box-Cox power to remove skewness), the M curve (Median), and the S curve (coefficient of variation). The gender-specific LMS coefficients for birth weight, head circumference, and length were determined with LMS chartmaker light version 2.54 (http://www.healthforallchildren.com/?product=lmschartmaker-light). The degrees of freedom for the fitted LMS spline curves were, respectively, 2, 6 and 4 for weight and 0, 4 and 3 for length and head circumference.

Longitudinal data from a premature infant

Weight, head circumference, and length values from a preterm infant born in 2009 were obtained from Vanderbilt University Medical Center's synthetic derivative, which is a database containing clinical information from Vanderbilt's electronic medical record that has been stripped of personal identifiers. There are 33 values while in the NICU starting at 32 weeks and 8 values from follow-up exams to 11 months old.

Combined intrauterine and WHO growth curves

The intrauterine values for gestational ages from 22 to 36 weeks were generated with equations 1-3. The values for gestation-adjusted ages from 1 to 24 months were generated with the LMS coefficients from the 2006 WHO growth standards [4]. The age 0 values, which represent gestational ages from 37 to 42 weeks, were not used. While Roche [3] suggested using a correction factor for the preterm infant's age of 40 weeks, there was better coupling between the intrauterine and term infants charts when 39 weeks was used. The gestation-adjusted age (in weeks) is equal to the infant's gestational age minus 39 weeks. The values between a gestational age of 36 weeks and a gestation-adjusted age of 1 month were linear functions connecting the 36 week intrauterine values with the 1 month term infant values. Bertino et al., [22] observed linear growth over this time period.

Birth percentile growth trajectories

Growth trajectories based on birth percentiles were generated with Z-scores. The Z-scores for weight, head circumference, and length of premature infants at birth were determined using the 10th, 50th and 90th percentiles of equations 1-3 [23]. The intrauterine growth trajectories from birth to 36 weeks were generated using these Z-scores. The term infant growth values from 1 to 24 months were generated using the birth Z-scores and the LMS values from the 2006 WHO growth charts. The values between 36 weeks and 1 month were linear functions connecting the 36 week intrauterine values with the 1 month 2006 WHO values.

Comparing premature percentiles

Multiple regression and analysis of variance [24] was used to compare the male and female percentiles for birth weight, head circumference, and length from the Vanderbilt NICU with the published values for premature infants from Thomas [9], Dobbins [11], Davidson [8], Bertino [13], Kurtoglu [14], Niklasson [15], Cole [17], and Olsen [18]. Multiple regression and analysis of variance was also used to compare the male and female 50th percentiles for birth weight from the nine studies. Multiple regression and analysis of variance determines best-fit linear equations for the individual datasets and evaluates if the slopes and intercepts of the equations are statistically equivalent (with a p-value of 0.05). If the slopes and intercepts are statistically equivalent, the datasets are identical and the best-fit equations can be used to describe both datasets. If the intercepts are statistically different and the slopes are statistically equivalent, then the best-fit equations are parallel. Since the best-fit equations for birth weight are exponential, the logarithms of the weight percentiles (which are linear) were compared. When the logarithms of weight are parallel, the weight curves have the same growth rate (constant B from equation1) and differ by a ratio of the two constant A's from equation 1.

Results

Data from Vanderbilt NICU

The Vanderbilt NICU data are expressed in terms of observed percentiles, LMS coefficients, and best-fit equations. Tables 1 and 2 contain the number of infants, means, standard deviations, and the 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles for birth weight, head circumference, and length by gestational age for the male and female infants. Table 3 contains the male and female constants for the best-fit equations of the 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles for birth weight, head circumference, and length. Table 4 contains the male and female LMS coefficients for birth weight, head circumference, and length. Figures 1 and 2 show graphical comparisons between the LMS percentiles and the best-fit functions

GA (wks)	N	mean	SD	Percentiles						
				5th	10th	25th	50th	75th	90th	95th
Weight (g)										
22	6	568	50				556			
23	22	610	81			551	600	654		
24	83	676	95	505	561	619	680	732	790	810
25	85	736	116	531	590	670	756	820	848	870
26	120	833	122	630	688	765	842	903	991	1041
27	146	968	181	655	740	861	970	1067	1199	1260
28	180	1047	203	719	769	910	1040	1177	1301	1389
29	197	1219	249	828	944	1041	1230	1369	1472	1636
30	237	1389	278	939	1056	1220	1390	1557	1712	1781
31	276	1605	315	1068	1205	1432	1608	1792	1977	2116
32	457	1748	320	1197	1348	1550	1743	1950	2124	2273
33	463	1949	381	1331	1510	1735	1950	2126	2394	2563
34	505	2186	447	1502	1661	1889	2170	2455	2699	2911
35	455	2464	484	1676	1843	2150	2459	2750	3070	3292
36	482	2689	469	1956	2100	2400	2685	2979	3269	3469
Total:	3714									
HC (cm)										
22	4	21.3					21.3			
23	13	21.2	1.6			20.0	21.0	22.0		
24	63	22.3	1.7	20.0	20.5	22.0	22.0	23.0	23.0	24.0
25	78	22.9	1.3	21.0	21.0	22.0	23.0	23.7	24.0	25.0
26	112	24.2	1.6	22.0	23.0	23.0	24.0	25.0	26.0	26.7
27	133	25.3	1.7	22.5	23.0	24.0	25.0	26.0	27.0	28.0
28	163	25.9	1.7	23.0	24.0	25.0	26.0	27.0	28.0	28.0
29	188	27.0	1.6	24.5	25.0	26.0	27.0	28.0	29.0	30.0
30	216	28.1	1.9	25.4	26.0	27.0	28.0	29.0	30.0	31.0
31	259	29.1	1.8	26.0	27.0	28.0	29.0	30.0	31.0	32.0
32	418	29.9	1.7	27.0	28.0	29.0	30.0	31.0	32.0	32.0
33	419	30.6	1.8	28.0	28.7	29.9	31.0	31.9	33.0	33.0
34	442	31.6	1.8	29.0	29.5	30.0	32.0	33.0	34.0	34.5
35	409	32.6	1.9	30.0	30.5	31.5	33.0	33.7	35.0	35.0
36	420	33.4	2.0	30.0	31.0	32.0	33.5	34.5	35.0	36.0
Total:	3337									
LEN (cm)										
22	4	30.8					30.8			
23	13	30.6	2.3			30.0	31.0	31.0		
24	61	32.4	2.6	28.0	29.0	31.0	32.0	33.5	35.5	37.0
25	76	33.2	2.0	30.0	31.0	32.0	33.0	34.0	36.0	36.0
26	105	34.5	1.8	31.0	32.0	33.0	35.0	36.0	36.0	37.0
27	131	35.8	2.6	31.0	32.0	34.0	36.0	38.0	39.0	39.3
28	158	36.9	2.1	33.0	34.0	35.5	37.0	38.0	39.0	40.0
29	186	38.5	2.6	34.0	35.0	37.0	38.5	40.0	42.0	42.0
30	213	40.1	2.4	36.3	37.0	38.5	40.0	42.0	43.0	44.0
31	261	41.7	2.9	37.0	38.0	40.0	42.0	43.5	45.0	46.0
32	414	42.9	2.9	38.0	40.0	41.0	43.0	45.0	46.0	47.0
33	411	44.0	2.7	39.0	41.0	42.5	44.0	46.0	47.0	48.0
34	444	45.4	3.1	40.0	42.0	43.9	46.0	47.0	49.0	50.0

35	404	46.9	3.2	41.2	43.0	45.0	47.0	49.0	50.0	51.0
36	409	48.0	2.8	43.0	44.0	46.0	48.0	50.0	51.5	52.0
Total:	3290									

Table 1: Number of infants (N), means, Standard Deviations (SD), and the 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles for birth weight, head circumference, and length by Gestational Age (GA) for male premature infants from the Vanderbilt NICU.

GA (wks)	N	mean	SD	Percentiles						
				5th	10th	25th	50th	75th	90th	95th
Weight (g)										
22	7	521	103				454			
23	24	589	69			538	592	642		
24	68	642	91	504	540	579	643	697	761	796
25	87	701	105	520	561	635	705	770	842	859
26	102	805	154	622	651	705	780	876	1006	1097
27	139	918	218	625	668	778	905	1025	1194	1291
28	165	1007	188	667	738	904	1020	1130	1230	1270
29	210	1191	244	797	870	1050	1219	1320	1471	1566
30	234	1365	341	991	1040	1150	1360	1497	1659	1741
31	263	1493	342	959	1084	1272	1492	1695	1863	2020
32	410	1673	338	1185	1304	1471	1655	1851	2049	2191
33	364	1880	368	1335	1450	1639	1880	2092	2331	2521
34	388	2077	412	1450	1579	1834	2041	2278	2536	2768
35	302	2274	479	1505	1720	1960	2227	2557	2862	3152
36	310	2588	561	1791	1915	2218	2551	2906	3301	3555
Total:	3073									
HC (cm)										
22	3	20.7					20.0			
23	16	22.4	2.3			21.4	22.0	22.6		
24	58	22.0	1.1	20.0	21.0	21.0	22.0	23.0	23.0	23.2
25	74	23.1	2.2	21.0	21.0	22.0	23.0	23.5	25.0	27.1
26	98	23.7	1.6	21.9	22.0	23.0	23.5	24.5	25.5	26.0
27	126	24.7	1.6	22.4	23.0	23.6	24.5	25.5	27.0	27.4
28	156	25.6	1.6	23.0	23.5	25.0	25.8	27.0	28.0	28.0
29	200	26.7	1.6	24.0	24.5	25.7	27.0	27.5	29.0	29.0
30	217	27.8	2.2	25.0	26.0	27.0	28.0	29.0	30.0	30.1
31	252	28.5	1.9	25.6	26.0	27.0	29.0	30.0	31.0	31.0
32	369	29.2	1.7	26.5	27.0	28.0	29.0	30.0	31.0	32.0
33	330	30.2	2.0	27.0	28.0	29.0	30.1	31.0	32.5	33.0
34	347	31.1	2.1	28.0	29.0	30.0	31.0	32.0	33.0	34.0
35	264	31.8	2.1	28.6	30.0	31.0	32.0	33.0	34.0	35.0
36	262	32.8	2.2	29.5	30.0	31.5	33.0	34.0	35.0	36.0
Total:	2772									
LEN (cm)										
22	3	28.3					28.0			
23	15	31.6	2.0			30.3	31.0	32.0		
24	54	32.0	2.8		29.7	30.5	32.0	33.0	34.4	35.2
25	72	32.9	2.9	28.8	29.1	31.0	33.0	34.0	36.0	36.2
26	92	33.8	2.4	30.0	31.0	32.0	34.0	35.0	36.5	38.0
27	125	35.3	2.5	32.0	32.5	34.0	35.0	36.5	38.3	39.0
28	153	36.6	2.2	33.0	33.1	35.5	37.0	38.0	39.0	40.0
29	194	38.3	3.0	32.8	34.7	37.0	38.0	40.0	42.0	42.4

30	210	39.9	2.5	36.0	37.0	38.0	40.0	41.0	43.0	44.0
31	247	41.0	2.9	36.0	37.0	39.0	41.0	43.0	44.7	45.4
32	373	42.1	2.8	38.0	39.0	40.5	42.0	44.0	45.5	46.0
33	326	43.7	2.9	39.0	40.0	42.0	44.0	46.0	47.0	48.0
34	342	44.8	2.9	40.0	41.0	43.0	45.0	47.0	48.5	49.0
35	264	45.8	3.3	41.0	42.0	43.5	46.0	48.0	50.0	51.0
36	260	47.4	3.0	42.0	43.5	45.5	47.8	49.0	51.0	52.0
Total:	2730									

Table 2: Number of infants (N), means, Standard Deviations (SD), and the 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles for birth weight, head circumference, and length by Gestational Age (GA) for female premature infants from the Vanderbilt NICU.

Percentile	**A** (g)	**B** (g/kg/day)	**C** (cm/week)	**D** (cm/week)
Female constants				
5th	34.32	15.64	0.8259	1.1715
10th	34.32	16.03	0.8484	1.2043
25th	38.02	16.2	0.8834	1.2629
50th	36.53	16.98	0.9192	1.3213
75th	40.87	16.98	0.9499	1.3720
90th	43.71	17.18	0.9838	1.4250
95th	41.90	17.69	1.0037	1.4513
Male constants				
5th	31.07	16.29	0.8423	1.1835
10th	35.15	16.21	0.8651	1.2264
25th	38.41	16.43	0.8948	1.2819
50th	40.56	16.75	0.9333	1.3381
75th	41.49	17.12	0.9636	1.3885
90th	41.86	17.52	0.9927	1.4332
95th	40.54	17.95	1.0129	1.4592

Table 3: Constants for the intrauterine growth equations at each percentile for birth weight (A&B), head circumference (C) and length (D).

	Weight for Age Curve				**HC for Age Curve**				**Length for Age Curve**		
	L Curve	**M Curve**	**S Curve**		**L Curve**	**M Curve**	**S Curve**		**L Curve**	**M Curve**	**S Curve**
GA	**Value**	**Value**	**Value**		**Value**	**Value**	**Value**		**Value**	**Value**	**Value**
Female Curves											
22	0.36140	518.91	0.12525		1	20.577	0.07864		1	29.385	0.08283
23	0.34310	576.51	0.13963		1	21.383	0.07675		1	30.561	0.08077
24	0.32477	635.57	0.15468		1	22.194	0.07488		1	31.736	0.07870
25	0.30638	704.16	0.17041		1	23.023	0.07307		1	32.923	0.07662
26	0.28792	791.20	0.18583		1	23.882	0.07134		1	34.150	0.07459
27	0.26937	895.43	0.19877		1	24.780	0.06981		1	35.443	0.07277
28	0.25063	1,017.57	0.20741		1	25.709	0.06860		1	36.801	0.07126
29	0.23167	1,161.39	0.21229		1	26.650	0.06774		1	38.199	0.07009
30	0.21279	1,316.41	0.21377		1	27.570	0.06705		1	39.590	0.06913
31	0.19437	1,477.30	0.21198		1	28.448	0.06632		1	40.937	0.06840
32	0.17595	1,651.39	0.20793		1	29.302	0.06571		1	42.245	0.06783
33	0.15709	1,841.61	0.20432		1	30.163	0.06545		1	43.530	0.06737
34	0.13778	2,045.89	0.20322		1	31.026	0.06543		1	44.784	0.06696
35	0.11825	2,264.15	0.20505		1	31.889	0.06555		1	46.024	0.06655
36	0.09862	2,493.75	0.20834		1	32.755	0.06575		1	47.271	0.06603
22	1.01841	552.61	0.11408		1	20.359	0.07056		1	29.676	0.06818
23	0.98168	610.25	0.12786		1	21.299	0.06939		1	30.874	0.06743

24	0.94495	672.11	0.14142		1	22.243	0.06822		1	32.075	0.06669
25	0.90818	743.93	0.15461		1	23.194	0.06705		1	33.288	0.06597
26	0.87141	834.71	0.16724		1	24.158	0.06594		1	34.532	0.06541
27	0.83474	944.47	0.17888		1	25.124	0.06488		1	35.823	0.06510
28	0.79831	1068.73	0.18814		1	26.087	0.06383		1	37.169	0.06499
29	0.76229	1215.90	0.19427		1	27.050	0.06281		1	38.573	0.06509
30	0.72701	1382.37	0.19724		1	28.006	0.06179		1	40.006	0.06532
31	0.69270	1560.66	0.19786		1	28.940	0.06075		1	41.425	0.06555
32	0.65926	1747.09	0.19732		1	29.846	0.05976		1	42.797	0.06561
33	0.62657	1951.93	0.19675		1	30.737	0.05895		1	44.129	0.06547
34	0.59478	2178.83	0.19530		1	31.634	0.05833		1	45.452	0.06516
35	0.56386	2419.80	0.19155		1	32.534	0.05791		1	46.764	0.06454
36	0.53343	2663.74	0.18579		1	33.429	0.05760		1	48.060	0.06366

Table 4: LMS coefficients for the premature infants from the Vanderbilt NICU.

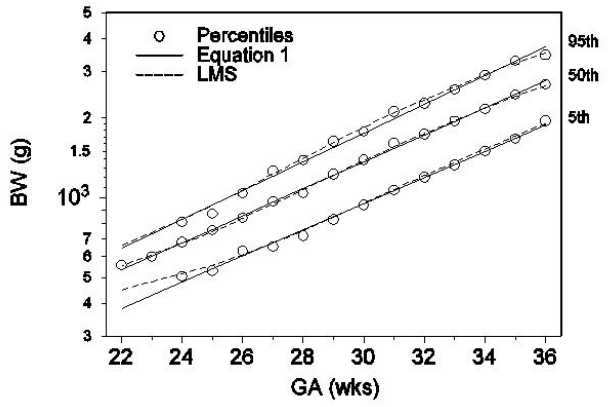

Figure 1: Comparison between the 5th, 50th and 95th percentiles for male birth weight from the Vanderbilt NICU using equation 1 and the LMS method.

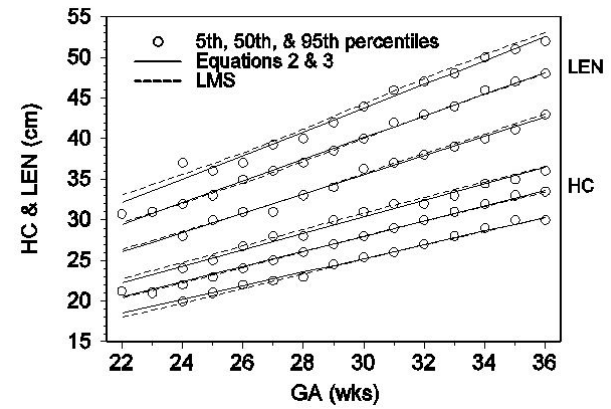

Figure 2: Comparison between the 5th, 50th and 95th percentiles for male head circumference and length from the Vanderbilt NICU using equations 2 & 3 and the LMS method.

for the 5th, 50th and 95th percentiles for birth weight, head circumference, and length. The LMS percentiles and the best-fit function percentiles for birth weight, head circumference, and length are superimposable with the best-fit functions being better defined for gestational ages less than 26 weeks.

Comparing premature percentiles from studies

Table 5, shows the results of comparing the male and female 10th, 50th and 90th percentiles from the Vanderbilt NICU and the 10th, 50th and 90th percentiles for premature infants reported by Thomas [9], Dobbins [11], Davidson [8], Bertino [13], Kurtoglu [14], Niklasson [15], Cole [17], and Olsen [18] with multiple regression and analysis of variance. Figures 3 and 4 show graphical comparisons between the 10th, 50th and 90th percentiles for weight from the combined intrauterine-WHO curves and the percentiles from Thomas [9], Dobbins [11], Davidson [8], Bertino [13], Kurtoglu [14], Niklasson [15], Cole [17] and Olsen [18].

Table 6, shows the results of comparing the male and female 50th percentiles for birth weight of premature infants from the Vanderbilt NICU, Thomas [9], Dobbins [11], Bertino [13], Davidson [8], Kurtoglu [14], Niklasson [15], Cole [17], and Olsen [18] with multiple regression and analysis of variance.

Table 7, shows the results of comparing the male and female 10th, 50th, and 90th percentiles for head circumference from the Vanderbilt NICU and the 10th, 50th, and 90th percentiles for premature infants reported by Davidson [8], Bertino [13], Kurtoglu [14], Niklasson [15], Cole [17], and Olsen [18] with multiple regression and analysis of variance. Figures 5 and 6 show graphical comparisons between the 10th, 50th, and 90th percentiles for head circumference from the combined intrauterine-WHO curves and the percentiles from Davidson [8], Bertino [13], Kurtoglu [14], Niklasson [15], Cole [17], and Olsen [18].

Table 8, shows the results of comparing the male and female 10th, 50th and 90th percentiles for length from the Vanderbilt NICU and the 10th, 50th and 90th percentiles for premature infants reported by Davidson [8], Bertino [13], Kurtoglu [14], Niklasson [15], Cole [17] and Olsen [18] with multiple regression and analysis of variance. Figures 7 and 8 show graphical comparisons between the 10th, 50th and 90th percentiles for length from the combined intrauterine-WHO curves and the percentiles from Davidson [8], Bertino [13], Kurtoglu [14], Niklasson [15], Cole [17] and Olsen [18].

Example for tracking growth of a premature infant

The scales for the growth curves are different when an infant is in the NICU and after discharge from the NICU. While in the NICU, values for weight, head circumference, and length are plotted with

Study	years	N total	N GA ≤ 36	10th	50th	90th
Vanderbilt F	1985-1997	3,073	3,073			
Thomas F	1996-1998	13,514	?		identical	
Dobbins F	1998-2007	1,228,368	67,147	different	different	identical
Bertino F	2005-2007	11,604	1,262	different	identical	identical
Davidson F	1991-2005	40,198	2,686	different	identical	different
Kurtoglu F	2009	2,375	2,375	different	identical	different
Niklasson F	1990-1999	404,156	?	parallel (11.1%)	parallel (21.6%)	different
Cole F	1983-1993	4,722	1,284	different	parallel (9.3%)	parallel (9.3%)
Olsen F	1998-2006	55,445	31,905	different	parallel (4.2%)	identical
Vanderbilt M	1985-1997	3,714	3,714			
Thomas M	1996-1998	13,514	?		identical	
Dobbins M	1998-2007	1,300,273	80,391	different	different	parallel (4.6%)
Bertino M	2005-2007	12,296	1,419	different	different	identical
Davidson M	1991-2005	40,198	2,686	parallel (3.1%)	identical	parallel (3.5%)
Kurtoglu M	2009	2,375	2,375	different	identical	different
Niklasson M	1990-1999	404,156	?	parallel (20.3%)	parallel (11.2%)	parallel (9.6%)
Cole M	1983-1993	4,722	1,284	parallel (4.9%)	parallel (4.4%)	different
Olsen M	1998-2006	73,995	40,420	parallel (5.4%)	parallel (3.9%)	parallel (3.9%)

Table 5: Comparisons between the 10th, 50th and 90th percentiles for birth weight of premature infants from other studies and those from the Vanderbilt NICU. When the studies are statistically parallel, the percent difference between the study and the Vanderbilt NICU are given in parentheses.

Study	Years	50th
Vanderbilt	1985-1997	parallel (5.9%)
Thomas	1996-1998	parallel (6.3%)
Dobbins	1998-2007	different
Bertino	2005-2007	parallel (14.3%)
Davidson	1991-2005	parallel (6.7%)
Kurtoglu	2009	parallel (2.7%)
Niklasson	1990-1999	identical
Cole	1983-1993	parallel (5.8%)
Olsen	1998-2006	parallel (5.6%)

Table 6: Comparisons between male and female 50th percentiles for birth weight of premature infants from the nine studies. When the percentiles are statistically parallel, the percent difference between the male and female percentiles are given in parentheses.

respect to the infant's gestational age, expressed in weeks. Figure 9 and 10 show the 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles of female growth curves for gestational ages from 22 to 40 weeks, values for a female premature infant, and growth trajectories of the birth values.

After discharge from the NICU, values for weight, head circumference, and length are plotted with respect to the infant's gestation-adjusted age, expressed in months. Figures 11 and 12 show the 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles of the female growth curves for gestation-adjusted ages from -4 to 24 months, values for the female premature infant, and growth trajectories of the birth values. At birth, the infant was in the 15th percentile for weight, the 15th percentile for head circumference, and the 37th percentile for length. There are 33 values while in the NICU and values at eight follow-up exams.

Discussion

The Vanderbilt gender-specific 50th percentiles for weight are identical with the gender-specific percentiles for weight from Thomas [9] (USA), Davidson [8] (Israel), and Kurtoglu [14] (Turkey). Equation 1 can be used to describe the weight of the premature infants in all these studies. The differences in the 10th and 90th percentiles could be due to different exclusion criteria. For example, Kurtoglu's 10th and 90th percentiles for birth weight may have been underestimated because values less than the 3rd percentile or greater than the 97th percentile (+/- 2 standard deviations), which represented 12.4% of the original data, were excluded before the percentiles were determined.

The 50th percentiles for weight from Niklasson [15] (Sweden), Cole [17] (UK), and Olsen [18] (USA) are parallel to the percentiles from Vanderbilt, Thomas [9] (USA), Davidson [8] (Israel), and Kurtoglu [14] (Turkey). This means these infants have the same growth velocity with systematically higher birth weights, systematic errors in estimating gestational age, and/or different exclusion criteria. Niklasson's 50th percentiles for females were 21% greater and males were 11% greater than the percentiles from Vanderbilt, Thomas [9] (USA), Davidson [8] (Israel), and Kurtoglu [14] (Turkey). Cole's 50th percentiles for females were 9% greater and males 4% greater than the percentiles from Vanderbilt, Thomas [9] (USA), Davidson [8] (Israel), and Kurtoglu [14] (Turkey). Olsen's 50th percentiles for males and females were 4% greater than the percentiles from Vanderbilt, Thomas [9] (USA), Davidson [8] (Israel) and Kurtoglu [14] (Turkey).

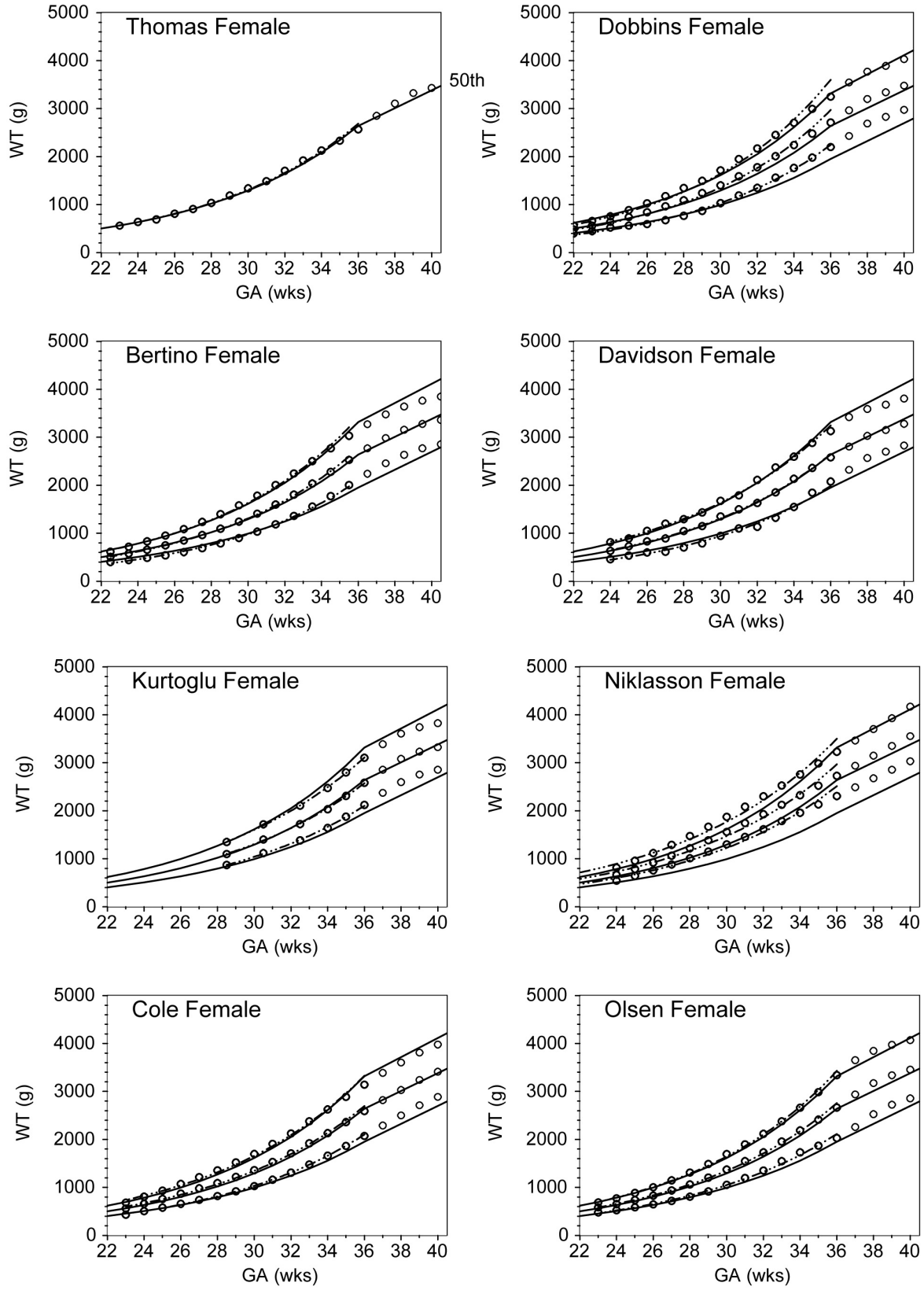

Figure 3: Graphical comparisons between the 10th, 50th and 90th percentiles from the female combined intrauterine-WHO weight growth curves (solid lines) and the percentiles from Thomas [9], Dobbins [11], Bertino [13], Davidson [8], Kurtoglu [14], Niklasson [15], Cole [17] and Olsen [18] (circles). The dot-dot-dash lines in each panel indicate the best-fit exponential functions for the studies (GA ≤ 36 weeks).

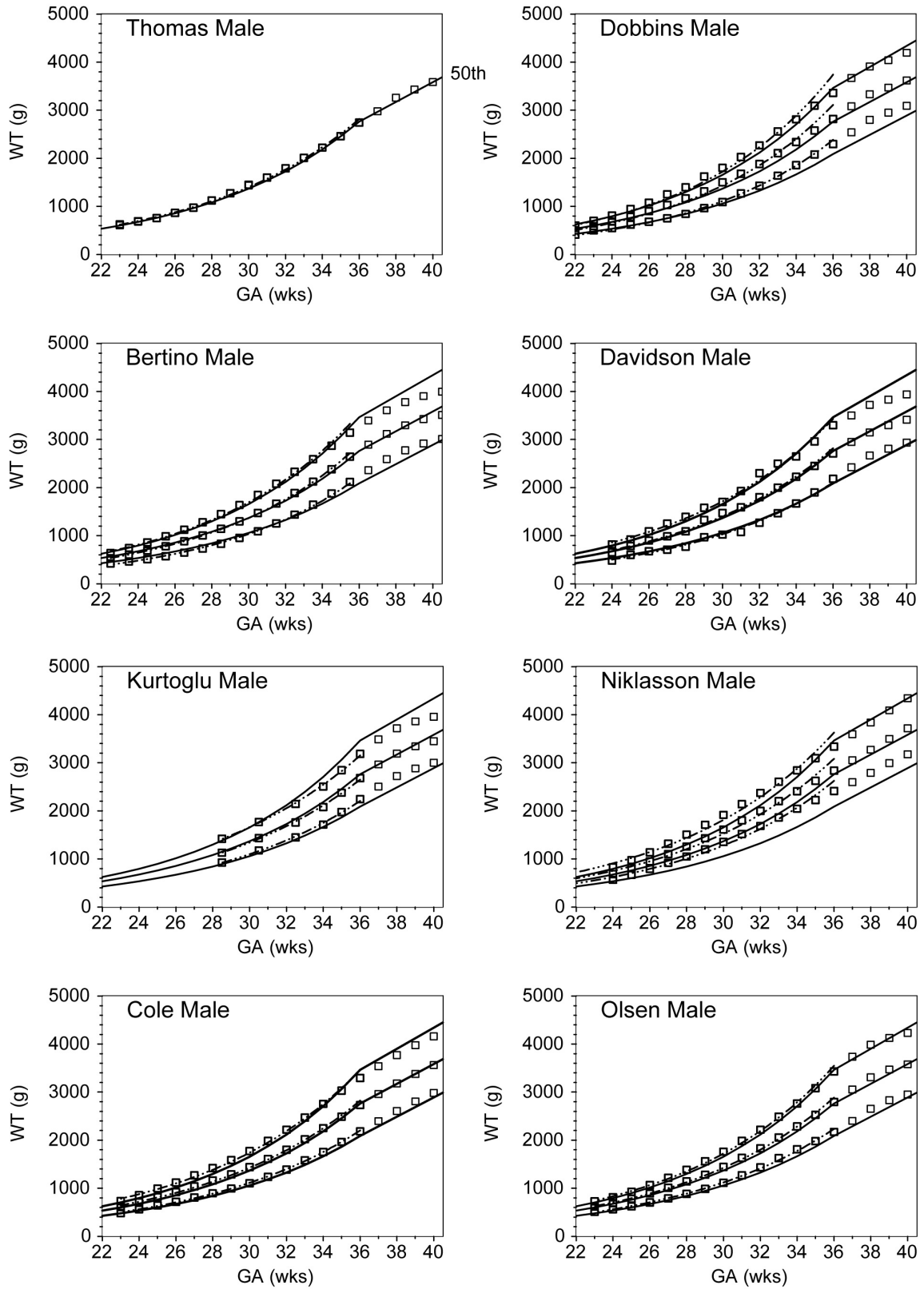

Figure 4: Graphical comparisons between the 10th, 50th and 90th percentiles from the male combined intrauterine-WHO weight growth curves (solid lines) and the percentiles from Thomas [9], Dobbins [11], Bertino [13], Davidson [8], Kurtoglu [14], Niklasson [15], Cole [17] and Olsen [18] (boxes). The dot-dot-dash lines in each panel indicate the best-fit exponential functions for the studies (GA ≤ 36 weeks).

Study	Years	N total	N GA ≤ 36	10th	50th	90th
Vanderbilt F	1985-1997	2,772	2,772			
Bertino F	2005-2007	11,604	1,262	identical	different	different
Davidson F	1991-2005	31,998	1,775	identical	different	different
Kurtoglu F	2009	2,375	2,375	different	identical	identical
Niklasson F	1990-1999	387,700	?	different	different	different
Cole F	1983-1993	921	574	different	identical	identical
Olsen F	1998-2006	55,445	31,905	identical	identical	identical
Vanderbilt M	1985-1997	3,337	3,337			
Bertino M	2005-2007	12,296	1,419	identical	identical	different
Davidson M	1991-2005	31,998	1,775	identical	identical	identical
Kurtoglu M	2009	2,375	2,375	different	different	identical
Niklasson M	1990-1999	387,700	?	different	different	identical
Cole M	1983-1993	921	574	different	different	different
Olsen M	1998-2006	73,995	40,420	identical	identical	identical

Table 7: Comparisons between the 10th, 50th and 90th percentiles for head circumference of premature infants from other studies and those from the Vanderbilt NICU.

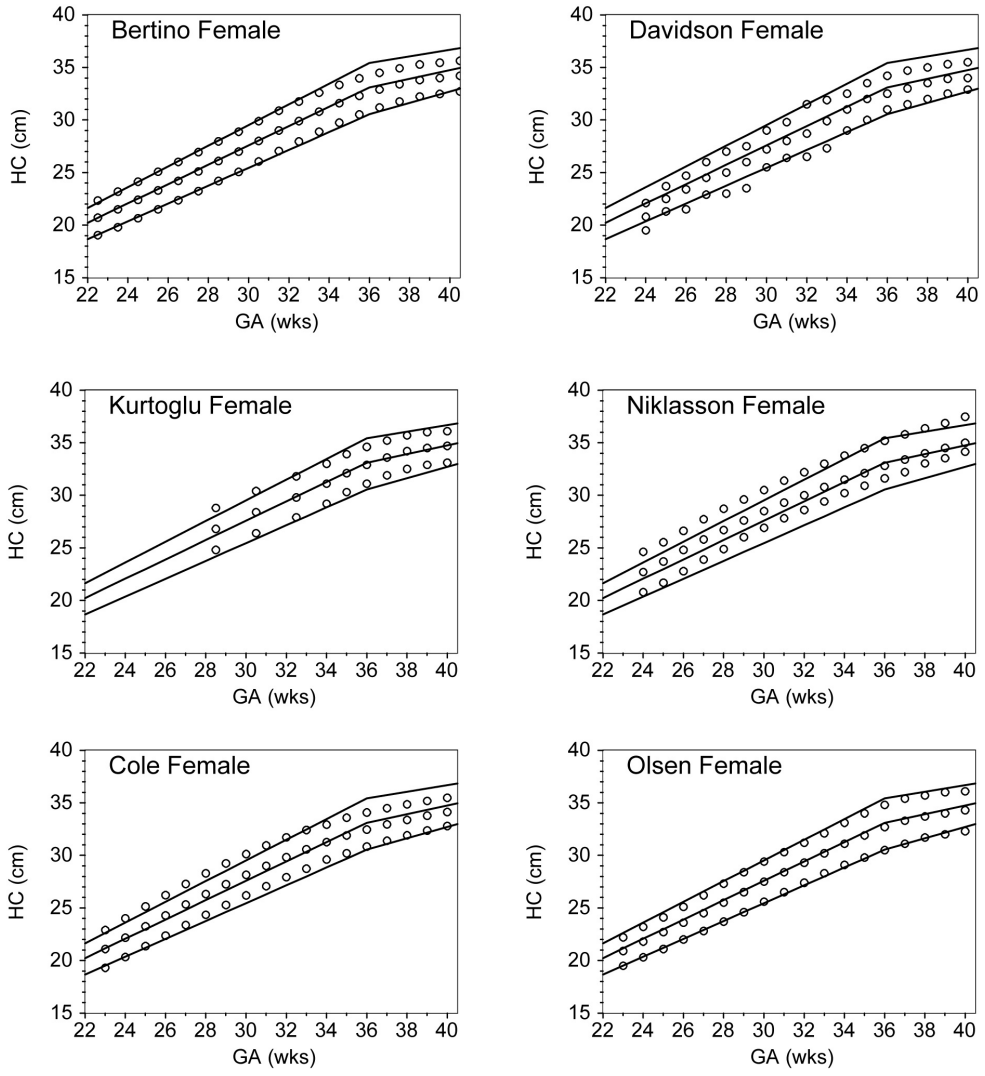

Figure 5: Graphical comparisons between the 10th, 50th, and 90th percentiles from the female combined intrauterine-WHO head circumference growth curves (solid lines) and the 10th, 50th, and 90th percentiles from Bertino [13], Davidson [8], Kurtoglu [14], Niklasson [15], Cole [17] and Olsen [18] (circles).

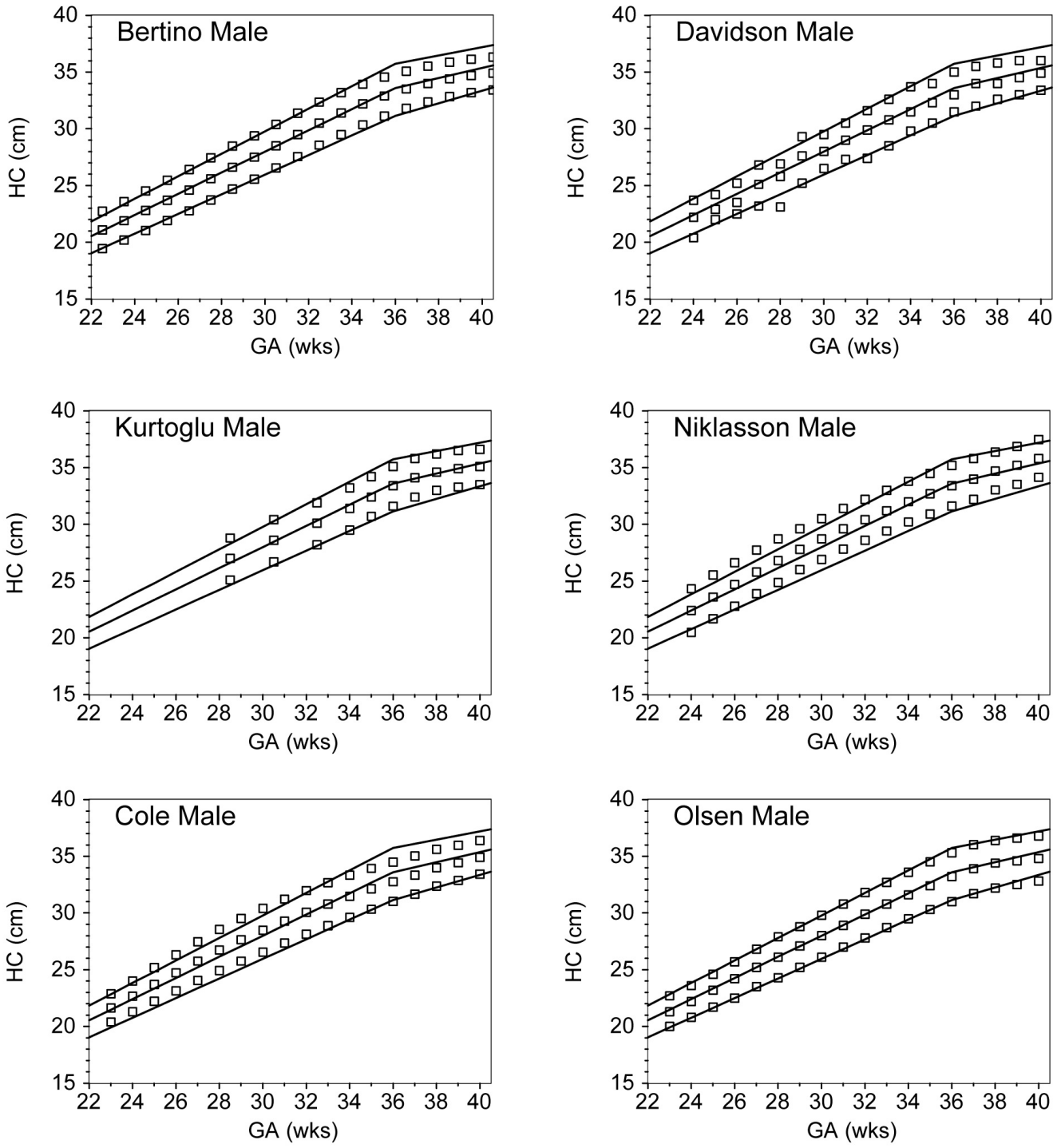

Figure 6: Graphical comparisons between the 10th, 50th, and 90th percentiles from the male combined intrauterine-WHO head circumference growth curves (solid lines) and the 10th, 50th, and 90th percentiles from Bertino [13], Davidson [8], Kurtoglu [14], Niklasson [15], Cole [17] and Olsen [18] (boxes).

Study	Years	N total	N GA ≤ 36	10th	50th	90th
Vanderbilt F	1985-1997	2,730	2,730			
Bertino F	2005-2007	11,604	1,262	identical	identical	identical
Davidson F	1991-2005	31,629	1,445	identical	identical	identical
Kurtoglu F	2009	2,375	2,375	identical	identical	different
Niklasson F	1990-1999	400,821	?	different	different	identical
Cole F	1983-1993	493	145	identical	different	different
Olsen F	1998-2006	55,445	31,905	identical	identical	identical
Vanderbilt M	1985-1997	3,290	3,290			
Bertino M	2005-2007	12,296	1,419	identical	identical	identical
Davidson M	1991-2005	31,629	1,445	identical	identical	identical
Kurtoglu M	2009	2,375	2,375	identical	different	identical
Niklasson M	1990-1999	400,821	?	different	different	identical
Cole M	1983-1993	493	145	identical	different	different
Olsen M	1998-2006	73,995	40,420	identical	identical	identical

Table 8: Comparisons between the 10th, 50th and 90th percentiles for length of premature infants from other studies and those from the Vanderbilt NICU.

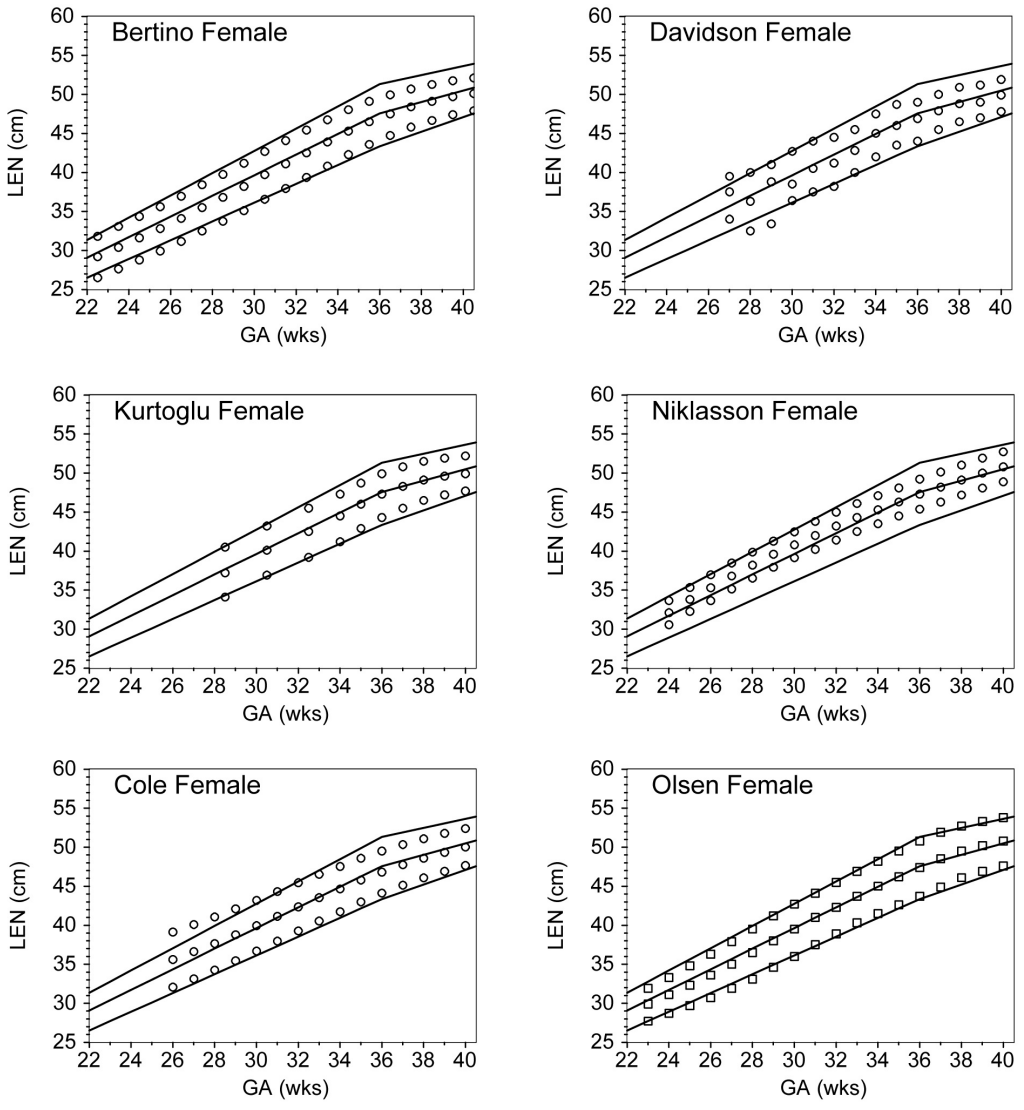

Figure 7: Graphical comparisons between the 10th, 50th, and 90th percentiles from the female combined intrauterine-WHO length growth curves (solid lines) and the 10th, 50th and 90th percentiles from Bertino [13], Davidson [8], Kurtoglu [14], Niklasson [15], Cole [17] and Olsen [18] (circles).

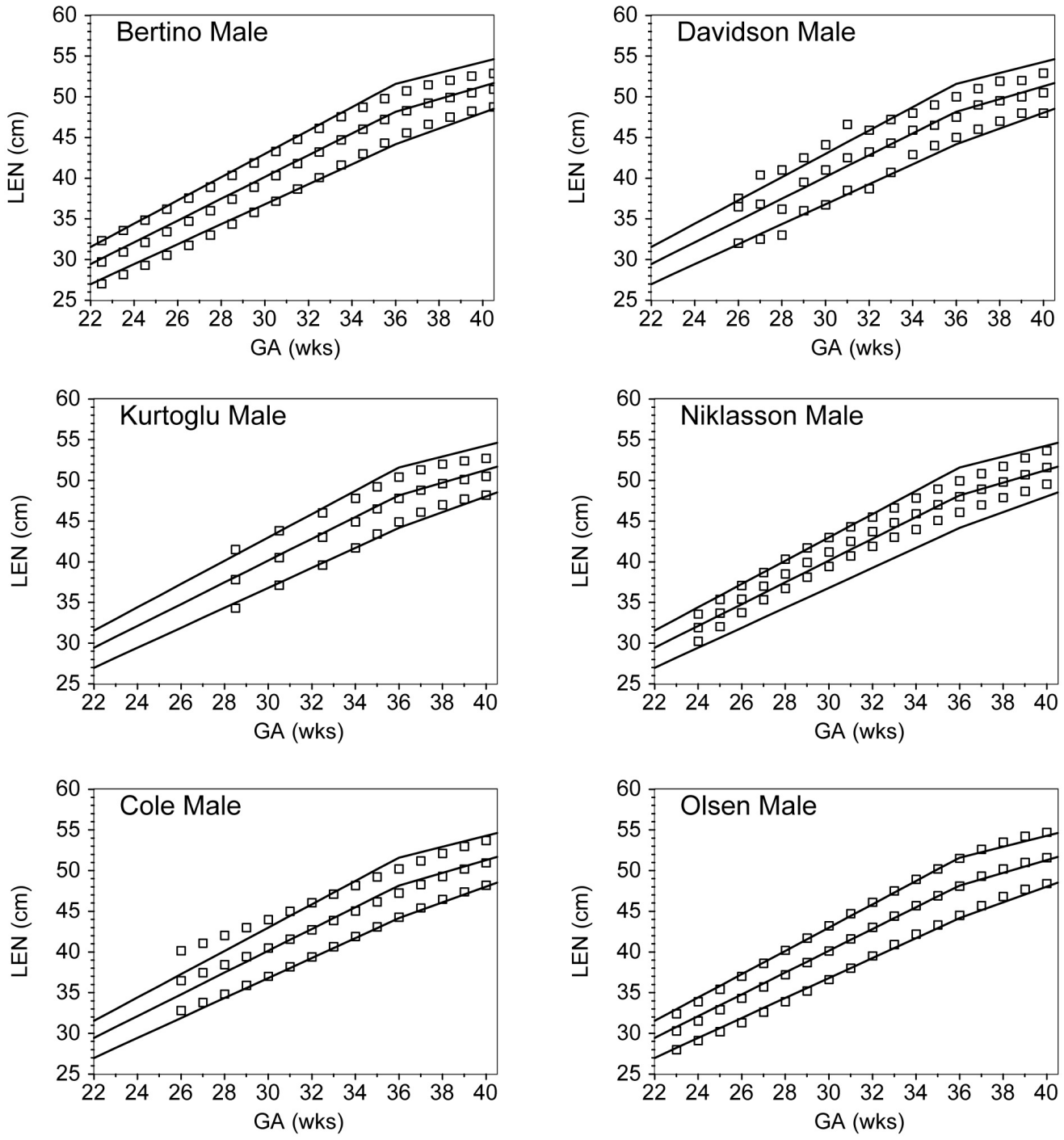

Figure 8: Graphical comparisons between the 10th, 50th, and 90th percentiles from the male combined intrauterine-WHO length growth curves (solid lines) and the 10th, 50th and 90th percentiles from Bertino [13], Davidson [8], Kurtoglu [14], Niklasson [15], Cole [17] and Olsen [18] (boxes).

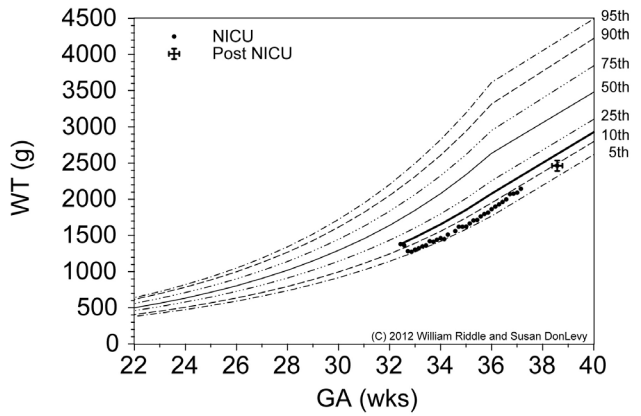

Figure 9: 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles of female combined intrauterine-WHO growth curves, values for a female infant with a birth weight of 1380 g, and growth trajectory for the 15th percentile. Estimated gestational age was 32w3d.

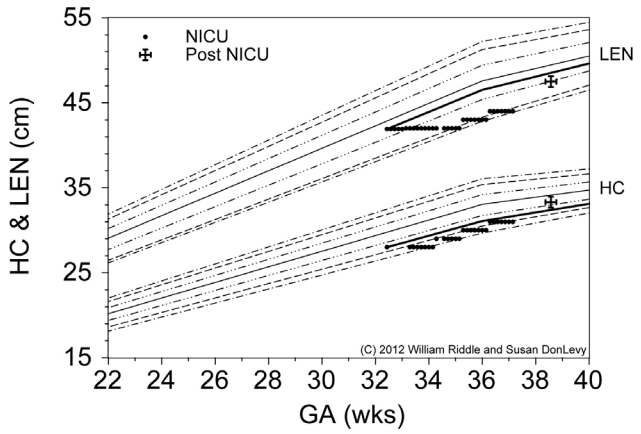

Figure 10: 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles of female combined intrauterine-WHO growth curves, values for a female infant, growth trajectory for the 15th percentile for head circumference, and growth trajectory for the 37th percentile for length. Estimated gestational age was 32w3d.

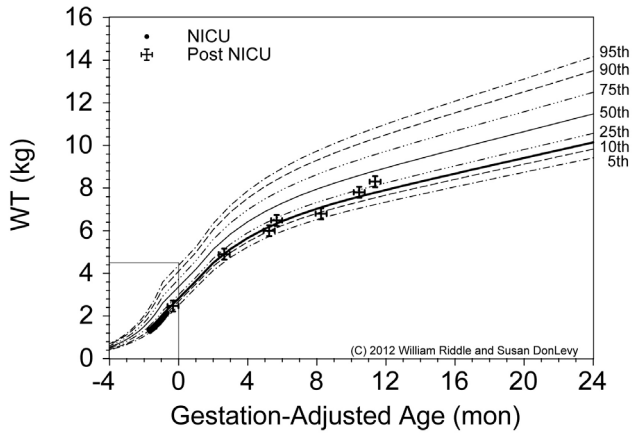

Figure 11: 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles of female combined intrauterine-WHO growth curves, values for a female infant with a birth weight of 1380g, and growth trajectory for the 15th percentile. Estimated gestational age was 32w3d.

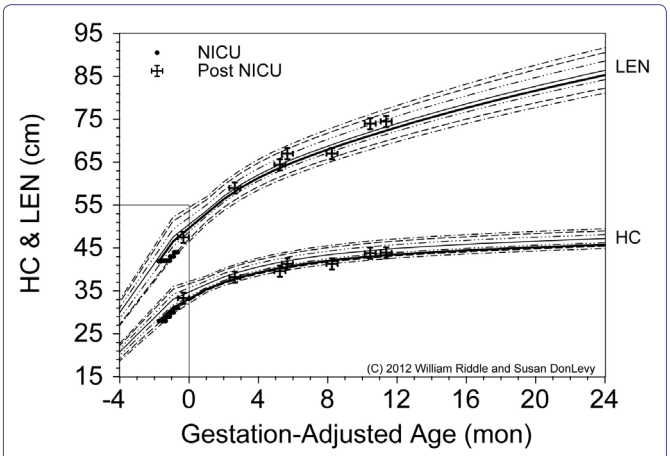

Figure 12: 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles of female combined intrauterine-WHO growth curves, values for a female infant, growth trajectory for the 15th percentile for head circumference, and growth trajectory for the 37th percentile for length. Estimated gestational age was 32w3d.

The differences between the 50th percentiles for birth weight of males and females from the nine studies showed five studies, Vanderbilt, Thomas, Davidson, Cole and Olsen, in the 5.6% to 6.7% range. Kurtoglu had 2.7% difference and Bertino had 14.3% difference. Niklasson had statistically identical male and female growth curves. This could be due to estimating gestational age solely on ultrasound estimation.

The Vanderbilt male and female 10th, 50th and 90th percentiles for head circumference are identical with percentiles from Olsen [18] (USA). This means that equation 2 can be used to describe the head circumference of the premature infants in both of these studies. Differences from the other studies could be explained by different exclusion criteria, by small numbers, and/or by different methods for determining gestational age.

The Vanderbilt male and female 10th, 50th and 90th percentiles for length are identical with the percentiles from Bertino [13] (Italy), Davidson [8] (Israel) and Olsen [18] (USA). This means that equation 3 can be used to describe the length of the premature infants in all these studies. Differences from the other studies could be explained by different exclusion criteria, by small numbers, and/or by different methods for determining gestational age.

In summary, the intrauterine curves (equations 1, 2, and 3) can be used to describe premature infants from different countries. Growth trajectories for weight, head circumference, and length based on birth percentiles provide insights for the growth for each infant. The combined intrauterine and WHO growth curves depict the growth continium of the prematurely born infant from a gestational age of 22 weeks to 2 years of age. These gender-specific curves are suitable for individualized spreadsheets and electronic medical record applications.

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