

Body mass index trajectories and adiposity rebound during the first 6 years in Korean children: based on the National Health Information Database, 2008-2015

Il Tae Hwang¹, Young-Su Ju², Hye Jin Lee¹, Young Suk Shim¹, Hwal Rim Jeong³, and Min Jae Kang^{1*}

¹ Department of Pediatrics, Hallym University College of Medicine, Chuncheon, Korea

² Department of Occupational and Environmental Medicine, National Medical Center, Seoul, Korea

³ Department of Pediatrics, Soonchunhyang University College of Medicine, Cheonan, Korea

***Corresponding author**

E-Mail: remoni80@gmail.com; mjkang@hallym.or.kr (MJK)

Abstract

Purpose

We analyzed the nationwide longitudinal data to explore body mass index (BMI) growth trajectories and the time of adiposity rebound (AR).

Methods

Personal data of 84,005 subjects born between 2008 and 2012 were obtained from infant health check-ups which were performed at 5, 11, 21, 33, 45, 57, and 69 months. BMI trajectories of each subject were made according to sex and birth weight (Bwt) and the timing of AR was defined as the lowest BMI occurred. Subjects were divided according to Bwt and AR timing as follows: very low birth weight (VLBW), $0.5 \text{ kg} \leq \text{Bwt} \leq 1.5 \text{ kg}$; low birth weight (LBW), $1.5 \text{ kg} < \text{Bwt} \leq 2.5 \text{ kg}$; non-LBW, $2.5 \text{ kg} < \text{Bwt} \leq 5.0 \text{ kg}$; early AR, before 45 months; moderate AR, at 57 months; and late AR, not until 69 months.

Main results

Median time point of minimum BMI was 45 months, and the prevalence rates of early, moderate, and late AR were 63.0%, 16.6%, and 20.4%, respectively. BMI at the age of 57 months showed a strong correlation with AR timing after controlling for Bwt ($P < 0.001$). Sugar-sweetened beverage intake at 21 months ($P = 0.02$) and no-exercise habit at 57 months ($P < 0.001$) showed correlations with early AR. When VLBW and LBW subjects were analyzed, BMI at 57 months and breastfeeding at 11 months were correlated with rapid weight gain during the first 5 months (both $P < 0.001$).

Conclusions

Based on this first longitudinal study, the majority of children showed AR before 57 months and the degree of obesity at the age of 57 months had a close correlation with early AR or early weight during infancy.

Key words: body mass index; longitudinal study; adiposity rebound; obesity

Introduction

The trajectory of an individual's body mass index (BMI) during life is quite variable. The BMI rapidly increases during the first year, then subsequently decreases and reaches a nadir around 4-8 years of age [1]. Thereafter, BMI increases again and this second rise following the last minimum BMI is referred to as the adiposity rebound (AR) [2]. The timing of AR is well-known to have a close relationship with obesity in later childhood, adolescence, and adulthood [3-7]. Although the definition of early AR varies according to studies, children who had early AR showed later obesity, insulin resistance, dyslipidemia, and hypertension [3,5,8]. Therefore, early AR is considered as a potent marker for obesity and metabolic syndrome.

The rapid postnatal weight gain showed an increased risk of early AR, obesity, and metabolic complications, especially in children born small-for-gestational age (SGA) [4,9]. Catch-up growth, which is attained by a period of supra-normal growth velocity in SGA children, is essential to gain a normal growth, but an emphasis on adequate nutritional support during early infancy is important not to gain overgrowth too rapidly. A recent study revealed that gestational age *per se* was an independent factor for the timing of AR in SGA children [10]; all together, these suggested that we should look at the BMI trajectory of SGA children more carefully.

Like secular changes in body size and tempo of growth have occurred in most countries, the timing of AR has shifted by better nutrition, hygiene, and health status [11]. This shifting of AR timing was observed not only in children with overweight and obesity, but also in children with low BMI [12]. To date, there has not been any longitudinal data available for individual's BMI in Korea. However, the National Health Information Database (NHID)

enabled us to explore sex- and birth weight- specific BMI growth trajectories of children born in the 21st century. Along with this, we also analyzed the timing of AR and related factors to early AR, especially in children born at low birth weight.

Materials and methods

Subjects and measurements

The longitudinal national cohort in NHID included the sampling unit (5% of total population) from infants and children born between January 2008 and December 2012 in South Korea. The NHID is a public database on health care utilization, health screening, socio-demographic variables, and mortality covering the whole population of South Korea and was formed by the National Health Insurance Service (NHIS) [13]. Health check-ups for infants conducted by the NHIS include mandatory examinations for growth, development assessments, dental exams, and infant care consultations reflecting health education. The infants and children may undergo seven screenings (Exams I–VII) at 4-6, 9-12, 18-24, 30-36, 42-48, 54-60, and 66-71 months of age. The median age at each exam (5, 11, 21, 33, 45, 57, and 69 months of age) was selected for analysis. The NHID covered data of 84,005 infants (based on Exam-I) and included 357,414 data points.

Data of height, weight, and BMI at each exam were retrieved. Most measurements were performed at primary health clinics. Length instead of height was used before 24 months of age and BMI was calculated as weight divided by (height or length)². As gestational age (GA) data were not available from the NHID, subjects with birth weight between 0.5 kg (which corresponds to the 3rd percentile for 23 weeks GA [14]) and 5.0 kg (which corresponds to +3.0 z-score of the male Korean standard) were included to remove outliers or errors. Height and weight at each exam was selected only when those values had increased compared to that in the previous exam, with minimum values of 25 cm (which corresponds to the 3rd percentile for 23 weeks GA [14]) and birth weight, respectively. An individual's longitudinal data were included when there were at least five valid height and weight measurements from seven

health check-ups. Therefore, 27,143 infants (based on Exam-I) with a total of 153,261 data points were analyzed in this study (Fig 1). Some questionnaires at each exam related to diet, exercise, lifestyle, and family history of metabolic syndrome were selected. The institutional Review Boards of Hallym Medical Center (IRB# KANGDONG 2018-01-001) approved this study.

Fig 1. Flow chart of the study sample size

Definition of subgroups according to birth weight, timing of AR, and rapid weight gain during early infancy

All subjects were divided into three subgroups according to birth weight as follows: very low birth weight (VLBW), $0.5 \text{ kg} \leq \text{birth weight} \leq 1.5 \text{ kg}$; low birth weight (LBW), $1.5 \text{ kg} < \text{birth weight} \leq 2.5 \text{ kg}$; and non-LBW, $2.5 \text{ kg} < \text{birth weight} \leq 5.0 \text{ kg}$. There were 100 subjects (47 males and 53 females) in the VLBW group, 1,796 (802 males and 994 females) in the LBW group, and 25,247 (12,992 males and 12,255 females) in the non-LBW group.

Seven health check-ups did not provide sufficient frequencies to identify the exact age of AR. Therefore, we determined the timing of AR at which the lowest BMI occurred as in the previous study [5]. The definition of early AR also varied according to studies [2,10]. In this study, we defined subgroups according to the timing of AR as follows: early AR, timing of AR before 45 months of age (Exam-V); moderate AR, timing of AR at 57 months of age (Exam-VI); and late AR, no AR until 69 months of age (Exam-VII). If minimum BMI was not identifiable, we considered that individual's data as missing. Therefore, the number of

subjects involved in AR timing analysis was 16,207 infants.

As rapid weight gain during early infancy is related to the development of later obesity [15], subjects were divided into two subgroups according to weight gain in the first 5 months (between birth and Exam-I). The rapid weight gain group included subjects who gained weight greater than or equal to 5.1 kg (which corresponds to the 99th percentile of the male Korean standard), while the non-rapid weight gain group included subjects who gained weight < 5.1 kg in the first 5 months.

The high BMI at age 5 years are also known as an important predictor to later obesity [11]. Therefore, we analyzed the BMI status at 57 months of age (Exam-VI) and classified as follows: underweight, BMI < 5th percentile; normal weight, 5th percentile \leq BMI < 85th percentile; overweight, 85th percentile \leq BMI < 95th percentile; and obesity, BMI \geq 95th percentile.

Data analysis

Data were presented as mean \pm standard deviation (SD). Comparisons of BMI trajectories over time between groups divided according to sex, birth weight, and AR timing were analyzed using a mixed model. Comparisons of AR timing distributions between subgroups were analyzed using the chi-square or likelihood ratio test. Comparisons of questionnaire variables related to AR among subgroups based on AR timing and rapid weight gain during early infancy were analyzed using multiple logistic regression or analysis of covariance. The odds ratio for AR timing was calculated for BMI z-score at 57 months of age (Exam-VI) by multiple logistic regressions. All statistical analyses were performed in SAS Enterprise Guide 7.1 (SAS Inc., Cary, NC). *P*-value < 0.05 was considered significant.

Results

BMI trajectories during the first 6 years

In all subjects, the mean BMI values at the ages of 5, 11, 21, 33, 45, 57, and 69 months were 17.8, 17.2, 16.3, 16.0, 15.9, 15.9, and 16.0 kg/m², respectively. There were differences in BMI values at each time point and BMI trajectories between male (Fig 2A) and female (Fig 2B) during the follow-up periods (all $P < 0.001$). BMI trajectories over time of the non-LBW subjects showed significant differences compared to those of LBW or VLBW subjects (all $P < 0.001$, Fig 3). However, there were no difference in BMI trajectories between the LBW and VLBW subjects ($P = 0.36$).

Fig 2. BMI percentile curves for subjects according to sex (A, males; B, females). Lines are 1st, 3rd, 5th, 10th, 15th, 25th, 50th, 75th, 85th, 90th, 95th, 97th, and 99th percentile curves from bottom to top, in order.

Fig 3. BMI percentile curves for subjects according to birth weight. (A-C) males and (D-F) females. Lines are 1st, 3rd, 5th, 10th, 15th, 25th, 50th, 75th, 85th, 90th, 95th, 97th, and 99th percentile curves from bottom to top, in order.

The timing of adiposity rebound

Of total subjects, 63.0%, 16.6%, and 20.4% showed early, moderate, and late AR,

respectively. The number of subjects were 10,209 (5,057 males and 5,152 females) in the early AR group, 2,697 (1,390 males and 1,307 females) in the moderate AR group, and 3,301 (1,748 males and 1,553 females) in the late AR group. The median and mode of the timing of AR was 45 months (Exam-V) and 33 months (Exam-IV) of age, respectively, in all subjects. Based on cumulative prevalence rates of the timing of AR, over 79% of subjects showed AR at age 57 months (Exam-VI) regardless of sex and birth weight (Table 1). The timing of AR did not differ among the VLBW, LBW, and non-LBW groups ($P = 0.12$) or between the VLBW+LBW and non-LBW groups ($P = 0.42$). BMI trajectories over time in the late AR group showed significant differences compared to those in the early AR or moderate AR groups (all $P < 0.001$, Fig 4). However, there were no differences in BMI trajectories between the early AR and moderate AR groups ($P = 0.89$).

Table 1. Cumulative prevalence rates of the timing of adiposity rebound by sex and birth weight

Exam	Median age	Total	Male	Female	VLBW	LBW	Non-LBW
I	5 months	0.2%	0.3%	0.2%	1.5%	0.0%	0.2%
II	11 months	1.0%	1.0%	1.0%	3.1%	0.8%	1.0%
III	21 months	11.4%	10.1%	12.7%	7.7%	11.3%	11.4%
IV	33 months	39.9%	38.9%	40.9%	33.8%	39.4%	40.0%
V	45 months	63.0%	61.7%	64.3%	53.8%	63.7%	63.0%
VI	57 months	79.6%	78.7%	80.6%	83.1%	80.7%	79.5%
VII	69 months	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Abbreviations: VLBW, very low birth weight; LBW, low birth weight; non-LBW, non-low birth weight.

Fig 4. BMI percentile curves for subjects according to timing of adiposity rebound. (A-C) males and (D-F) females. Lines are 1st, 3rd, 5th, 10th, 15th, 25th, 50th, 75th, 85th, 90th, 95th, 97th, and 99th percentile curves from bottom to top, in order.

Related factors to the timing of adiposity rebound

BMI at age 57 months (Exam-VI) showed strong correlation with AR timing after controlling for birth weight ($P < 0.001$). The prevalence rates of overweight and obesity at age 57 months in the early AR group (12.6% and 12.5%, respectively) were significantly higher than those in the moderate AR (4.9% and 2.1%, respectively) and late AR (5.9% and 1.4%, respectively) groups ($P < 0.001$). The obese children at age 57 months were 3.7 times more likely than normal weight children to have AR before 57 months (Table 2).

Table 2. The distributions of BMI status at age 57 months by adiposity rebound groups and the odds ratios for adiposity rebound before 57 months

BMI at age 57 months (n=11,106)	Early AR (n=5,879)	Moderate AR (n=2,697)	Late AR (n=2,530)	Adiposity rebound before 57 months	
				Odds ratio (95% C.I.)	<i>P</i> -values*
Normal weight	73.2%	84.9%	89.1%	Reference	
Underweight	1.8%	8.2%	3.6%	0.774 (0.670-0.895)	< 0.001
Overweight	12.6%	4.9%	5.9%	1.756 (1.572-1.960)	0.0009
Obesity	12.5%	2.1%	1.4%	3.705 (3.201-4.288)	< 0.001

* by multiple logistic regression (adjustment for birth weight)

Based on questionnaires, weaning after 4 months of age (Exam-II, $P < 0.001$), sugar-

sweetened beverage intake at 21 months (Exam-III, $P = 0.02$), and no-exercise habit at 57 months (Exam-VI, $P < 0.001$) demonstrated higher values in the early AR group than in the moderate AR and late AR groups. However, breastfeeding at 11 months (Exam-II) showed no significant correlations with AR timing ($P = 0.20$), and screen time at 57 months (Exam-VI) showed contradictory results (Table 3).

Table 3. Related factors to timing of adiposity rebound

Variables	Age at survey	N	Category	Early AR	Moderate AR	Late AR	<i>P</i> -values*
Breastfeeding	11 months	13,685	Breast milk only	39.4%	40.2%	37.9%	0.20
			Formula, others	60.6%	59.8%	62.1%	
Timing of weaning	11 months	13,843	Before 4 months	3.9%	6.4%	7.9%	< 0.001
			After 4 months	96.1%	93.6%	92.1%	
Sugar-sweetened beverage	21 months	14,311	< 200 cc/day	92.7%	93.9%	94.1%	0.02
			≥ 200 cc/day	7.3%	6.1%	5.9%	
	33 months	14,351	< 200 cc/day	93.6%	94.0%	93.4%	0.71
			≥ 200 cc/day	6.4%	6.0%	6.6%	
45 months	12,777	< 200 cc/day	93.4%	93.5%	93.9%	0.71	
		≥ 200 cc/day	6.6%	6.5%	6.1%		
Add salt to baby's food	21 months	14,385	Yes	84.2%	83.8%	83.5%	0.69
			No	15.8%	16.2%	16.5%	
Meal with parents	33 months	14,392	≥ 5 days/week	73.5%	75.5%	74.5%	0.12
			≤ 4 days/week	26.5%	24.5%	25.5%	
Having breakfast	69 months	8,460	Yes	95.7%	95.7%	95.8%	0.98
			No	4.3%	4.3%	4.2%	
Screen time	57 months	9,382	≤ 2 hours/day	76.4%	72.1%	71.1%	< 0.001
			≥ 3 hours/day	23.6%	27.9%	28.9%	

Exercise habit	57 months	9,379	Yes	86.5%	98.7%	99.0%	< 0.001
			No	13.5%	1.3%	1.0%	
Family history of metabolic syndrome	57 months	8,087	Yes	45.0%	42.8%	45.4%	0.12
			No	55.0%	57.2%	54.6%	

*by multiple logistic regression (adjustment for birth weight)

Rapid weight gain and adiposity rebound in low birth weight subjects

Greater weight gain during the first 11 months was observed in the VLBW group (mean 7.7 kg) than in the LBW (6.9 kg) and non-LBW (6.5 kg) groups ($P < 0.001$), and the increment was prominent in the first 5 months (VLBW, 5.7 kg; LBW, 5.1 kg; and non-LBW, 4.8 kg). After 11 months (Exam-II), weight gain velocity did not differ between the VLBW and LBW groups.

Of the 1,129 VLBW and LBW subjects, 569 (50.4%) subjects were included in the rapid weight gain group in the first 5 months. There were no significant differences of timing of AR between the rapid and non-rapid weight gain groups ($P = 0.63$). However, the rapid weight gain group showed greater obesity at age 57 months (Exam-VI, 5.8%) and less breastfeeding at 11 months (Exam-II, 20.4%) than the non-rapid weight gain group (obesity at age 57 months, 1.7%, $P < 0.001$; breastfeeding at 11 months, 28.1%, $P = 0.0003$).

Discussion

In this study, we demonstrated the BMI trajectories of infants and children born between 2008 and 2012 in Korea. In all subjects, the median time point of AR was 45 months of age, and 79.6% of subjects showed AR before 57 months. And as expected, the LBW and VLBW groups showed different BMI trajectories compared to the non-LBW group. BMI at age 57 months along with diet and exercise habits had close relationships with early AR. Rapid weight gain during the first 5 months in the LBW and VLBW groups showed significant correlations with BMI at age 57 months and breastfeeding; however, AR timing was not relevant.

The timing of AR in the Korean growth standards, which was developed using cross-sectional data from the National Anthropometric Survey in 1997 and 2005 [16], was estimated as 5.5 years (66 months) in both sexes [11]. Considering that we had insufficient frequency of measured data in this study, the median timing of AR would be between 3.8 years (Exam-V) and 4.8 years (Exam-VI) of age, regardless of birth weight and sex. This is about one year earlier than that seen in the Korean standards, which may coincide with the global shifts in AR timing to an earlier age [12,17-19]. The most recent survey conducted in Poland in 2010 showed AR timing of subjects (with median BMIs) as 5.2 years in boys and 3.0 years in girls, which was 2.3-4.4 years earlier than the values obtained in 1983 [17,18].

Interestingly, BMI value at the age of AR was higher and BMI velocity after AR was greater in our subjects than those in the Korean standards [16]. In boys, BMI values at the age of AR for our subjects in the 50th percentile and in the corresponding Korean standard were 16.0 and 15.7 kg/m², respectively. And for those in the 95th percentile and in the corresponding Korean standard were 18.1 and 17.8 kg/m², respectively. BMI changes between 45 months of age

(Exam-V, median AR timing) and 69 months of age (Exam-VII) were greater in male subjects in the 95th percentile (1.2 kg/m²) than in the corresponding Korean standard (0.8 kg/m²). Differences in minimum BMI values and BMI velocity after AR between our female subjects and the corresponding Korean standards showed similar results to that seen in males. Altogether, these results (AR before 4.8 years of age, higher minimum BMI values, and greater BMI velocity after AR) are in line with increasing obesity, which was also seen in the Fels Longitudinal study [20]. If children have similar genetic background, current environmental issues (such as decreased physical activity, increased screen time, inappropriate feeding practices, and abundant fast foods) compared to that in the past [21], may be held responsible for these results.

Currently, beyond the role of predicting obesity, earlier AR over time may imply the acceleration of growth and development compared to the past. Based on a longitudinal study, shifting of AR timing was observed not only for children with normal weight, overweight, and obesity, but also in underweight children [12,17,18]. Unfortunately, minimum BMI in underweight subjects of the 5th percentile was not confirmed during this period, because follow-up period (69 months) was short to confirm AR timing of all subjects in this study. However, Luo *et al.* also reported that earlier AR timing was observed in heavier and taller children compared to lighter and shorter children [22].

A positive relationship between small size at birth and early AR is well known [23]. Around 80% of children born small for gestational age show catch-up growth during the first year of life [24]. Accelerated growth of the entire body contributes to the accelerated growth of fat cells, and this is a critical period for later body composition and fat deposition [1]. In this study, differences of BMI trajectories during 69 months between the non-LBW subjects and the LBW or VLBW subjects were significant. However, contrary to our expectation, AR

timing showed no differences between the birth weight groups. There may be several reasons. First, regarding body compositions, thin children are predisposed to a smaller lean mass [25], which may rebound later than children with proper lean mass. Second, the number of subjects in the LBW and VLBW groups was small, relative to those in the non-LBW group in this study; therefore, this may attenuate the differences in AR timing. Third, gestational age is also an important factor for catch-up growth with a boundary of 37 weeks gestational age [10], but data of gestational period was unavailable in this study.

Gardner *et al.* suggested that by age 5 years, childhood obesity appears relatively resistant to change [26]. In this study, BMI at age 57 months (around 5 years) had a strong relationship with AR timing, and BMI trajectories between the early AR (cutoff 45 months) and moderate AR (cutoff 57 months) groups did not differ significantly. Therefore, taken together, these results support the importance of obesity at age 5 years [27,28]. Moreover, BMI at age 57 months was linked to the rapid weight gain group especially to the LBW and VLBW groups, in this study. This confirms existing evidences that weight gain during infancy is a predictor of later obesity [29]. Botton *et al.* reported that regardless of birth weight, rapid weight gain even in the first 6 months is associated with obesity [30]. Breastfeeding, the only factor known to have protective effect against obesity [11], showed negative correlation with early weight gain during the first 11 months in our study. Therefore, the benefits of breastfeeding in LBW and VLBW infants cannot be overestimated [8].

Among other factors related to early AR, parental BMIs, especially BMI of the mother, who mostly share an environment of diet habit or activity, was closely associated [20,27,31,32]. However, the relationship between early AR and screen time [33], protein intake [34], or socioeconomic status [19,27,32] remains uncertain. Factors related to early AR such as later weaning, additional sugar-sweetened beverage intakes, and no-exercise habit showed

expected results in this study, but as there are many confounding factors within the survey data, verifications are required.

A major limitation in this study is that the exact timing of AR is difficult to judge. The best way is to trace an individual's adiposity plot through visual inspection [2,35]; however, most often, there is insufficient frequency of measured data to allow the use of this method. To compensate for this problem, various statistical approaches [5,7,35-37] or the researchers' own definitions [10,27,38] were used. Second, definitions of early AR also varied according to literatures. Generally early AR was defined before 5 years of age [2], however, over 75% of subjects had AR before 57 months in this study, so we defined early AR as before 45 months (around 4 years of age) which time was the median value of AR timing. Therefore, while comparing AR timing between contemporary studies, methods of determining AR should be carefully considered. Third, the small sample size at age 69 months (Exam-VII) and no data of gestational age could be limitations. The NHID only included 5% of total population and after deleting outliers, about 30% of initial subjects were finally included. However, this is the first national cohort study on infancy and early childhood based on individual longitudinal data; this may be sufficient to overcome any drawbacks of this study.

One of the critical periods in life for the development of obesity is the period of AR [39]. Most of Korean children in the 21st century showed early AR before 57 months and their diet and exercise habits may be related to early AR or early weight gain during infancy. This may be a warning sign for later obesity or early maturation problems, such as precocious puberty. Therefore, our results support the need of population-based preventive interventions.

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Disclosure statement

The authors declare no conflict of interest.

Author Contributions

Conceptualization: Min Jae Kang

Data curation: Min Jae Kang

Formal analysis: Young-Su Ju, Min Jae Kang

Funding acquisition: Il Tae Hwang, Min Jae Kang

Investigation: Il Tae Hwang, Young-Su Ju, Min Jae Kang

Methodology: Il Tae Hwang, Young-Su Ju, Hye Jin Lee, Young Suk Shim, Hwal Rim Jeong,
Min Jae Kang

Project administration: Min Jae Kang.

Resources: Il Tae Hwang, Young-Su Ju, Min Jae Kang

Software: Young-Su Ju.

Supervision: Il Tae Hwang, Young-Su Ju, Hye Jin Lee, Young Suk Shim, Hwal Rim Jeong,
Min Jae Kang

Validation: Il Tae Hwang, Young-Su Ju, Hye Jin Lee, Young Suk Shim, Hwal Rim Jeong,
Min Jae Kang

Visualization: Il Tae Hwang, Min Jae Kang

Writing – original draft: Min Jae Kang

Writing – review & editing: Il Tae Hwang, Young-Su Ju, Hye Jin Lee, Young Suk Shim,

Hwal Rim Jeong

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Late AR

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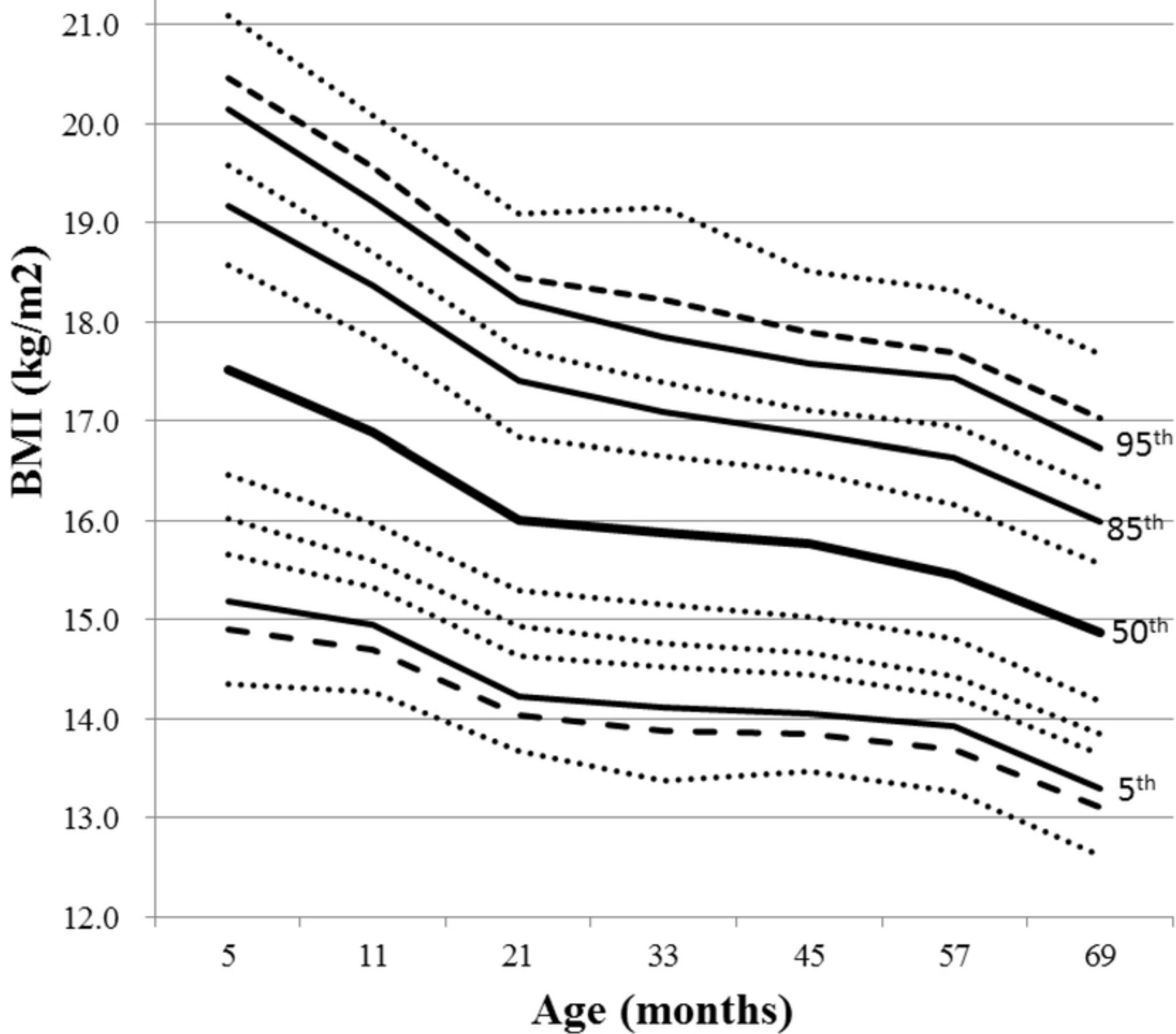


Fig 4F

Initial number of data points = 357,414							
Exam	I	II	III	IV	V	VI	VII
Exam age (month)	4-6	9-12	18-24	30-36	42-48	54-60	66-71
Median age (month)	5	11	21	33	45	57	69
N of total subjects	67,301	65,591	63,522	63,674	47,730	31,357	18,239

Inclusion criteria

$0.5 \text{ kg} \leq \text{birth Wt} \leq 5.0 \text{ kg}$

$\text{Birth Wt} < \text{Wt-I} < \text{Wt-II} < \text{Wt-III} < \text{Wt-IV} < \text{Wt-V} < \text{Wt-VI} < \text{Wt-VII} < +3 \text{ z-score of 69 months}$

$25 \text{ cm} < \text{Ht-I} < \text{Ht-II} < \text{Ht-III} < \text{Ht-IV} < \text{Ht-V} < \text{Ht-VI} < \text{Ht-VII} < +3 \text{ z-score of 69 months}$

At least 5 valid Ht, Wt, and BMI measurements during 7 times of health check-ups

Final number of data points = 153,261							
Exam	I	II	III	IV	V	VI	VII
N of total subjects	27,143	23,983	24,662	24,867	24,804	17,590	10,212
N of male	13,841	12,226	12,554	12,721	12,631	8,944	5,191
N of female	13,302	11,757	12,108	12,146	12,173	8,646	5,021

Fig 1

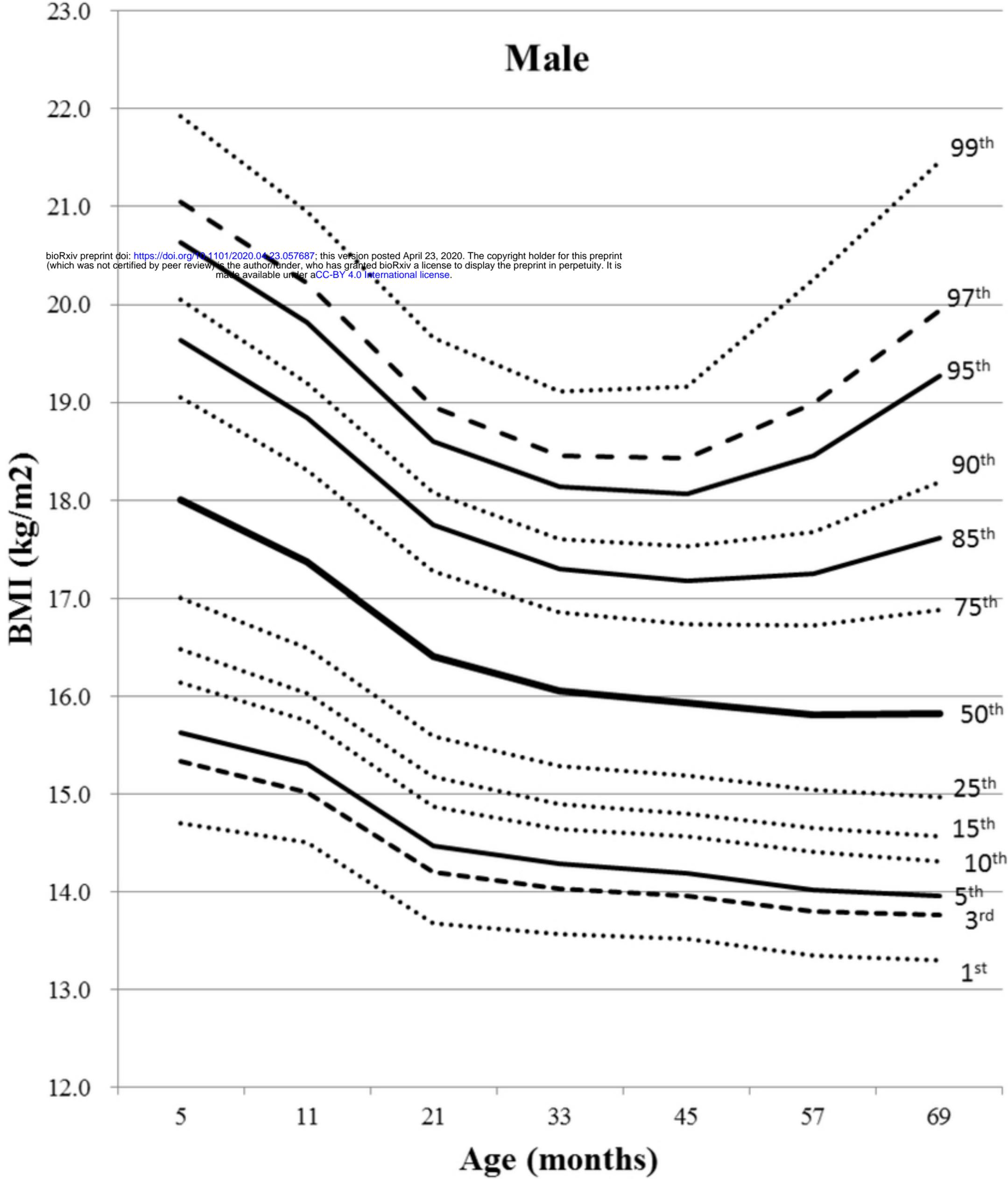


Fig 2A

Female

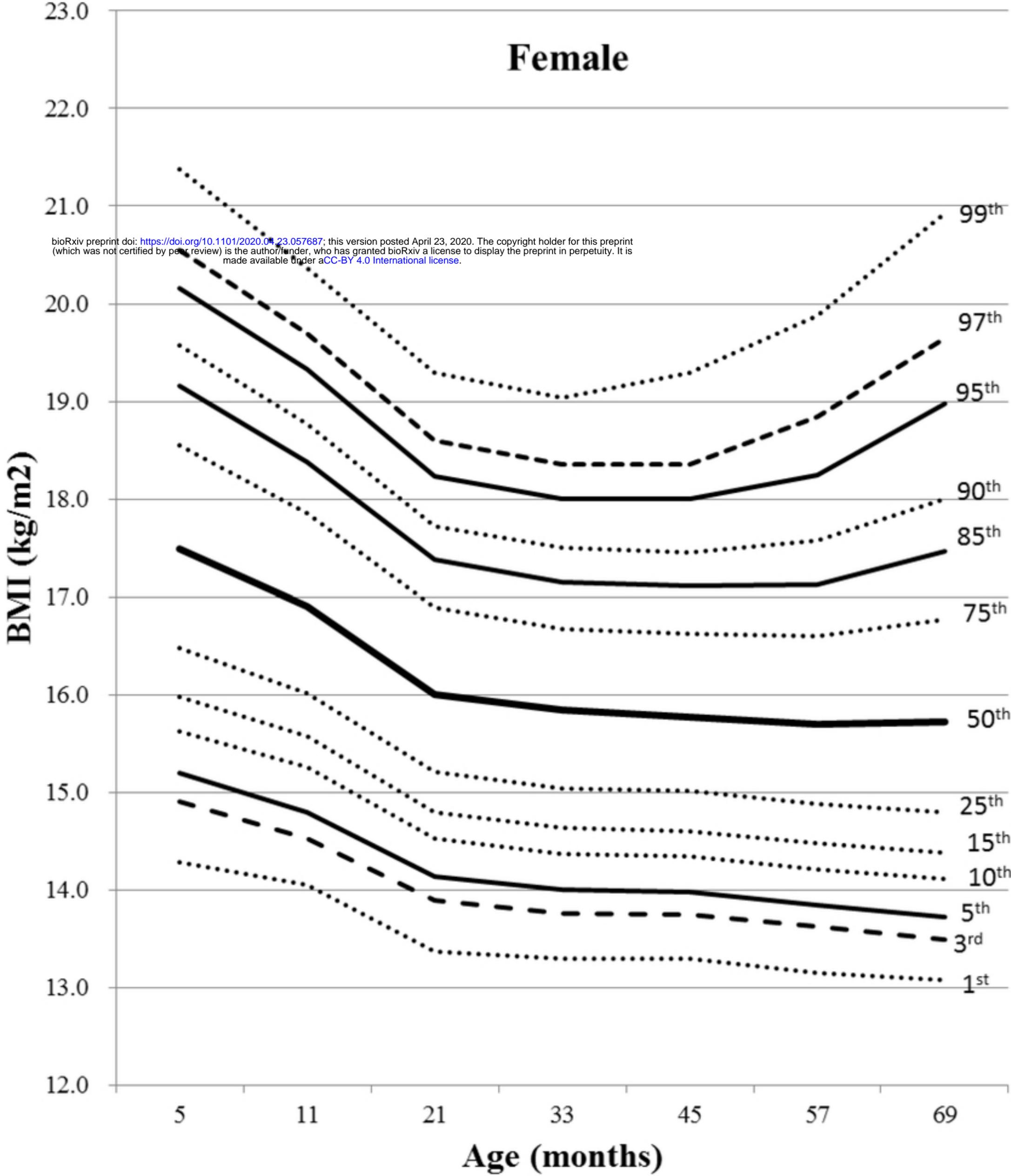
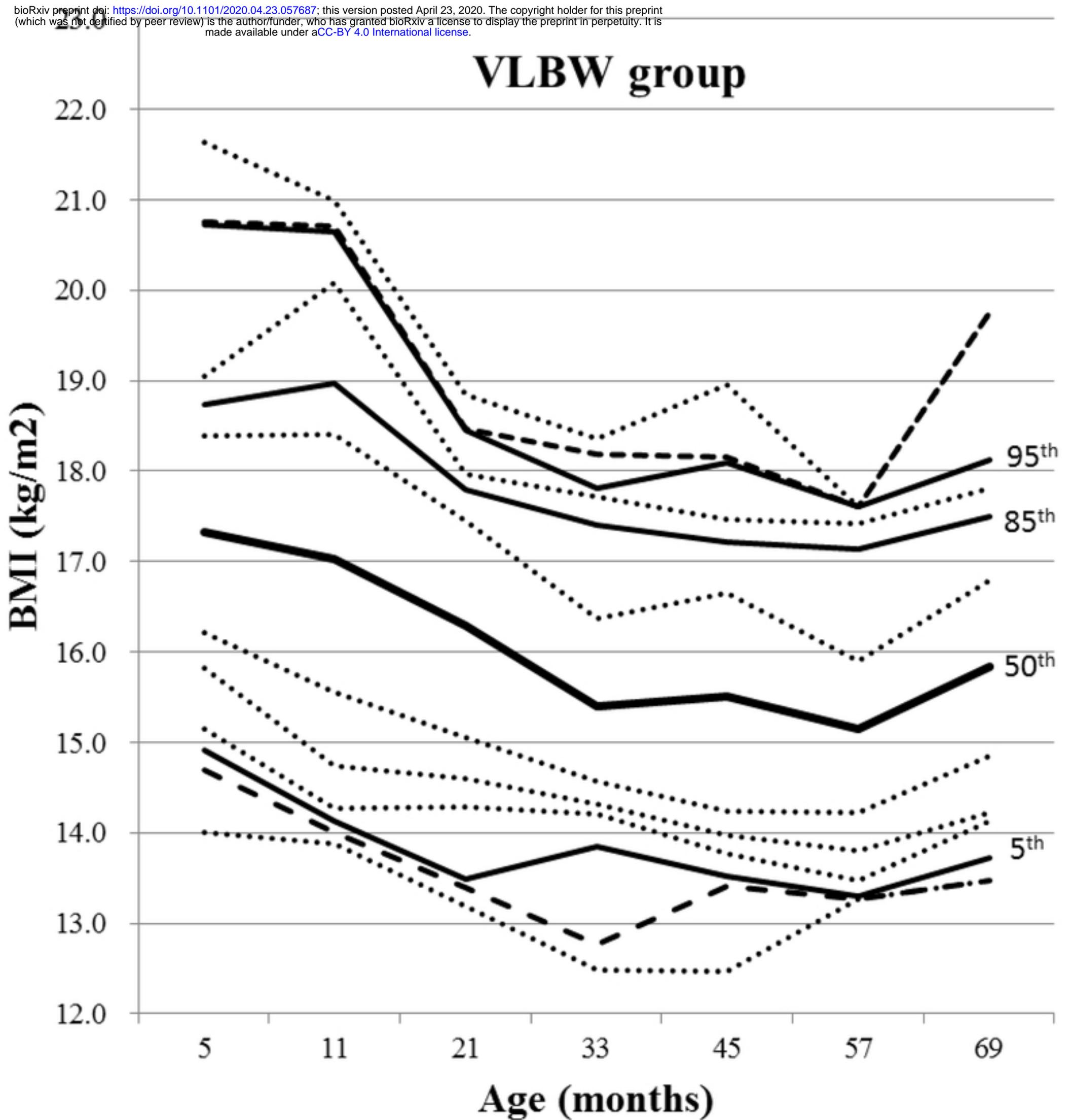


Fig 2B



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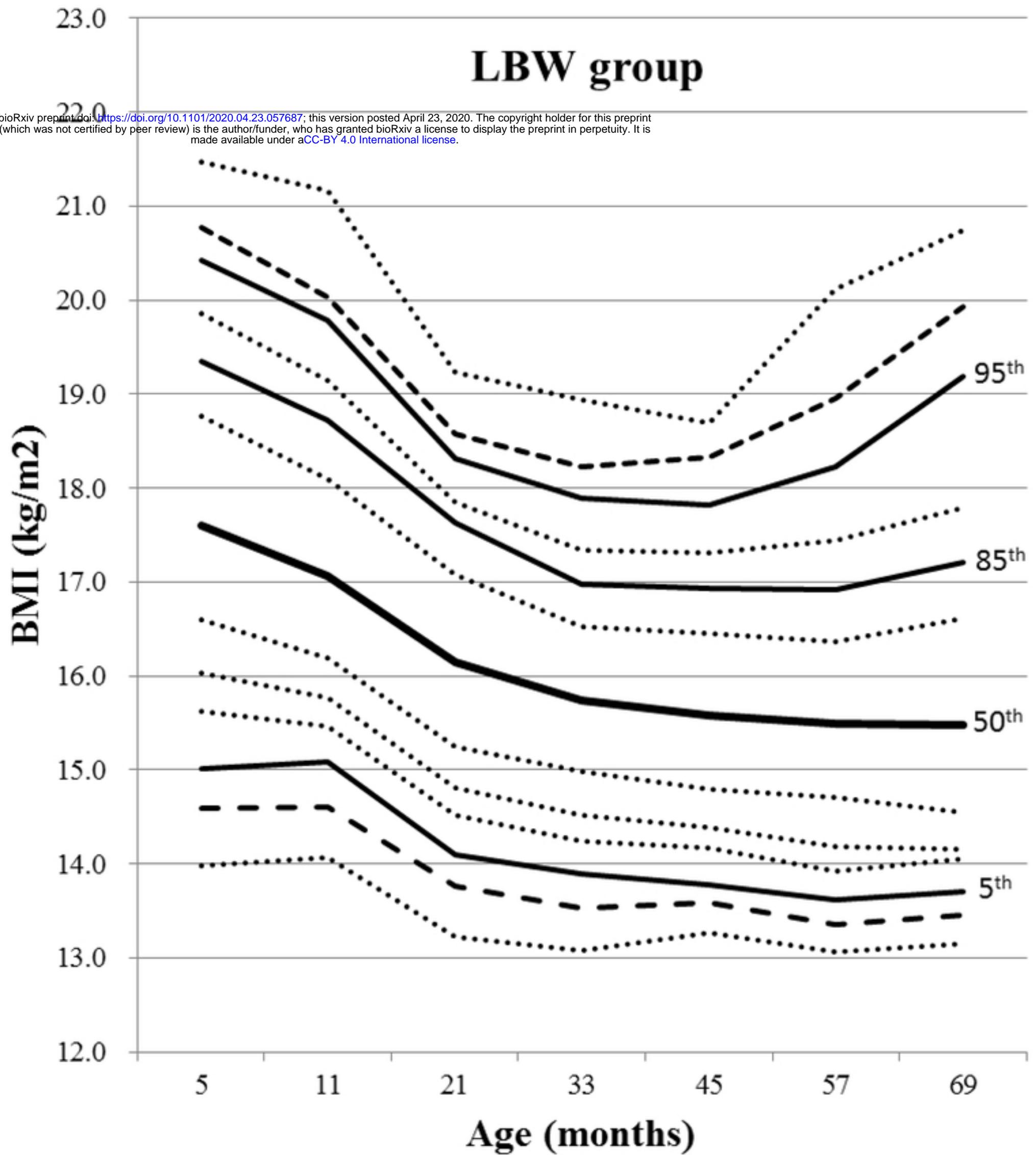


Fig 3B

non-LBW group

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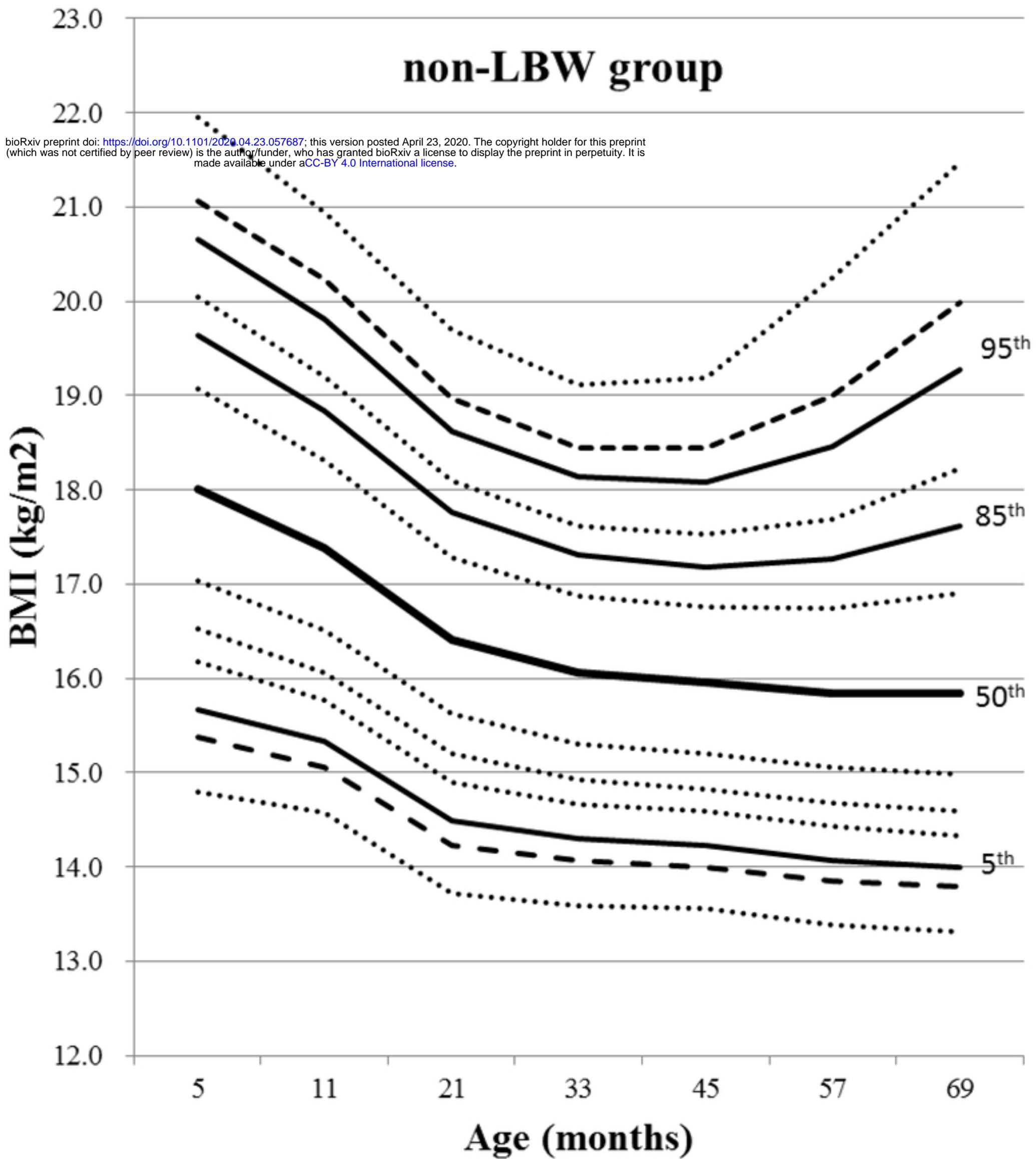


Fig 3C

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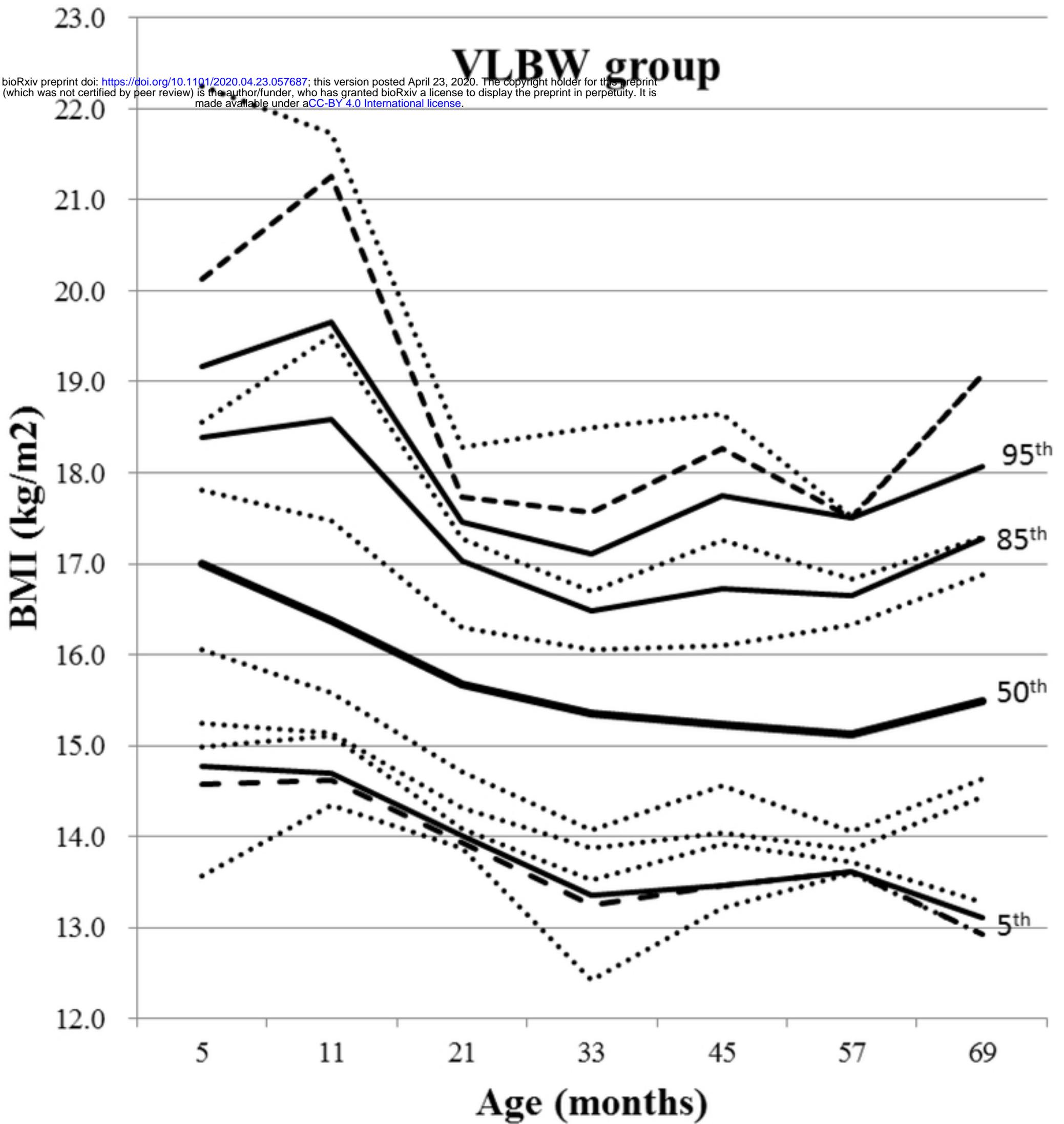


Fig 3D

LBW group

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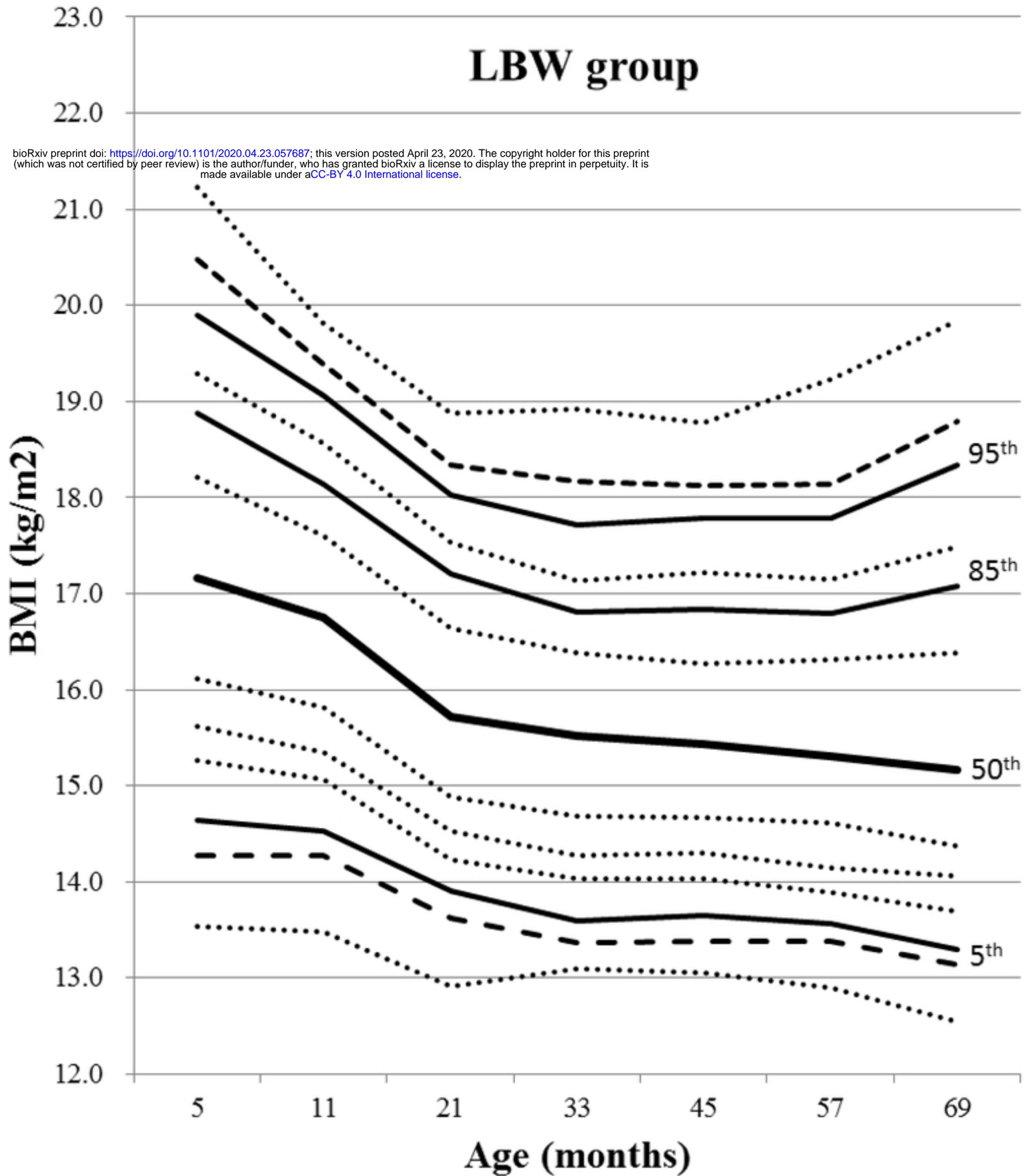


Fig 3E

non-LBW group

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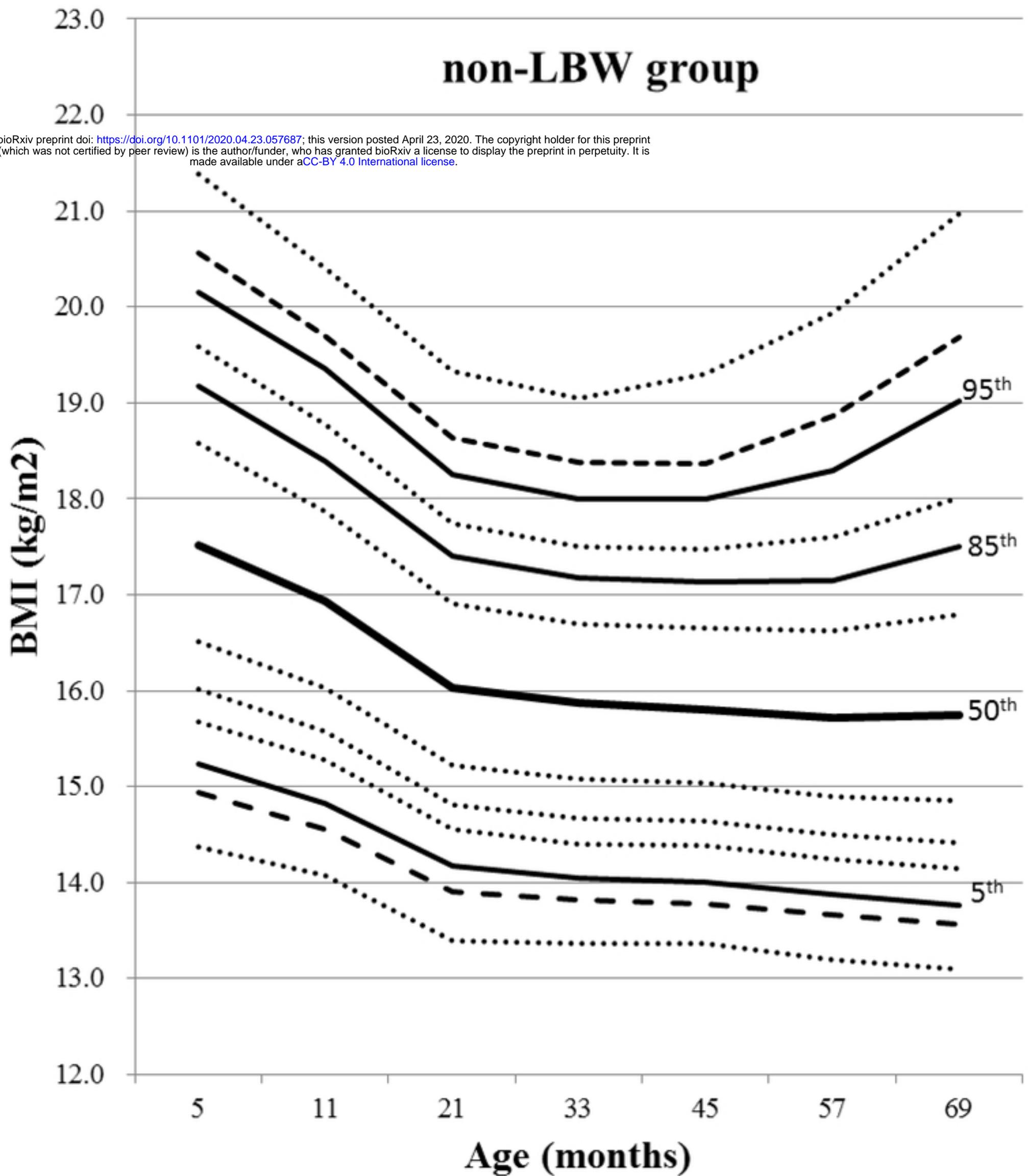


Fig 3F

Early AR

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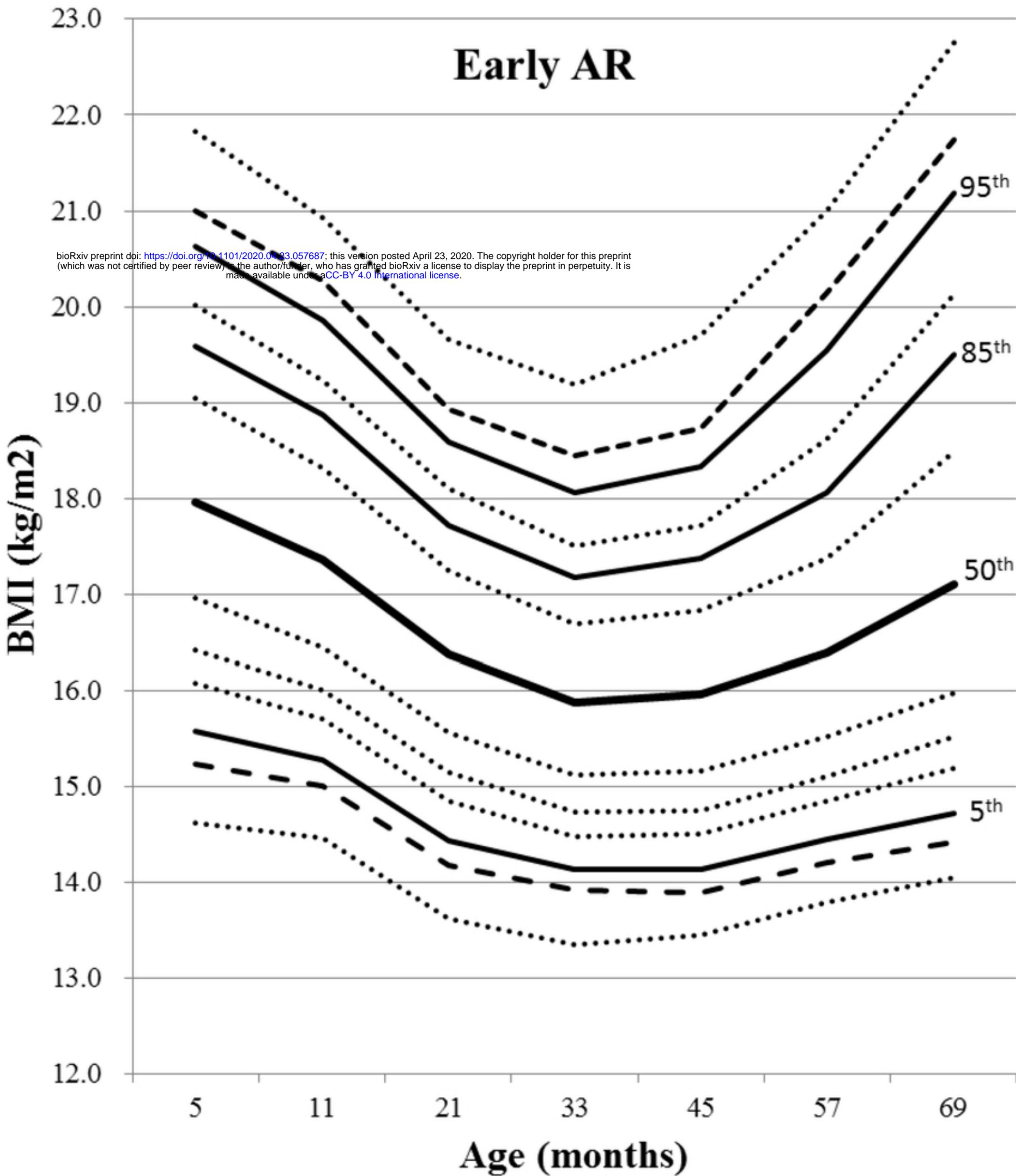


Fig 4A

Moderate AR

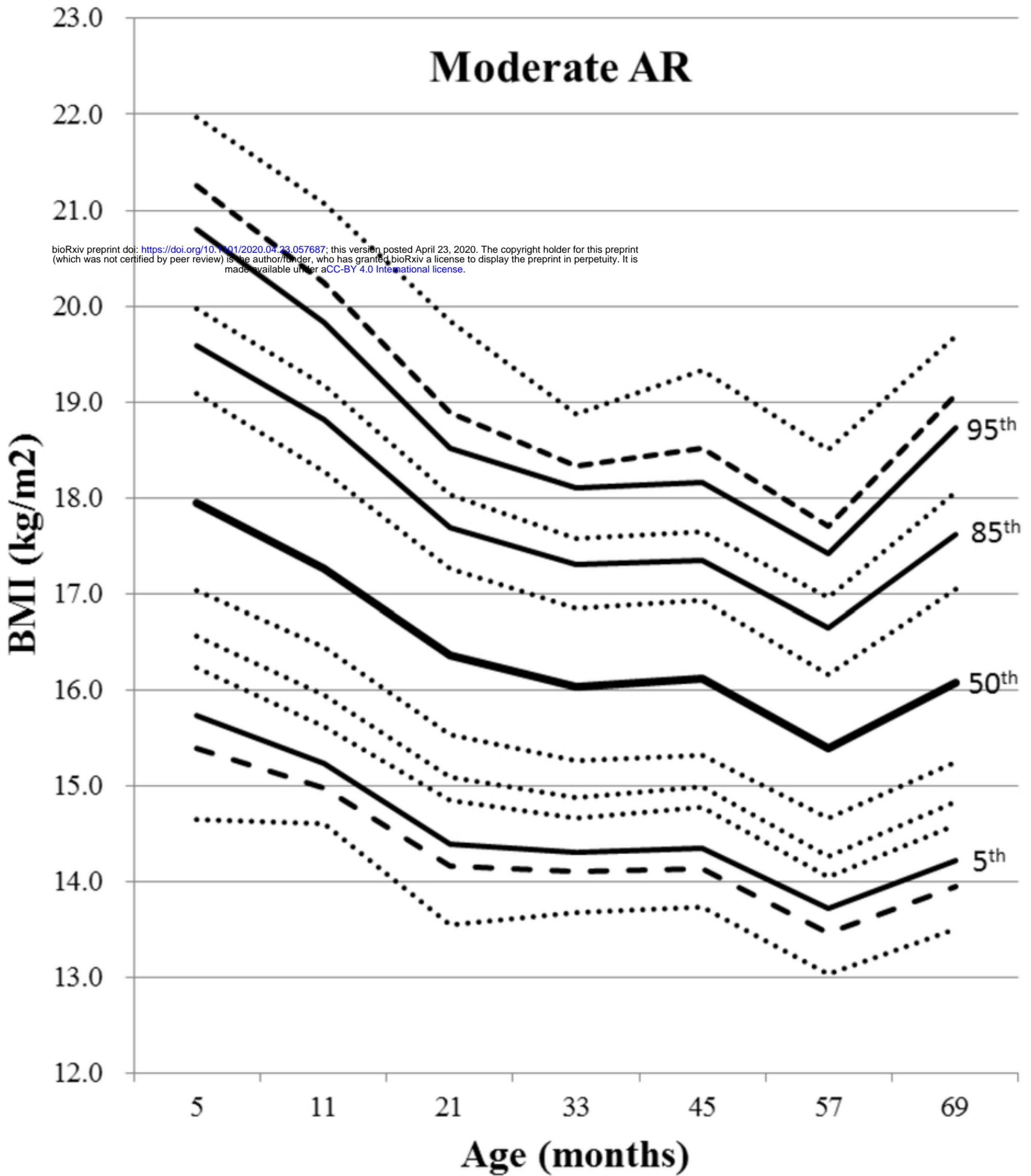


Fig 4B

Late AR

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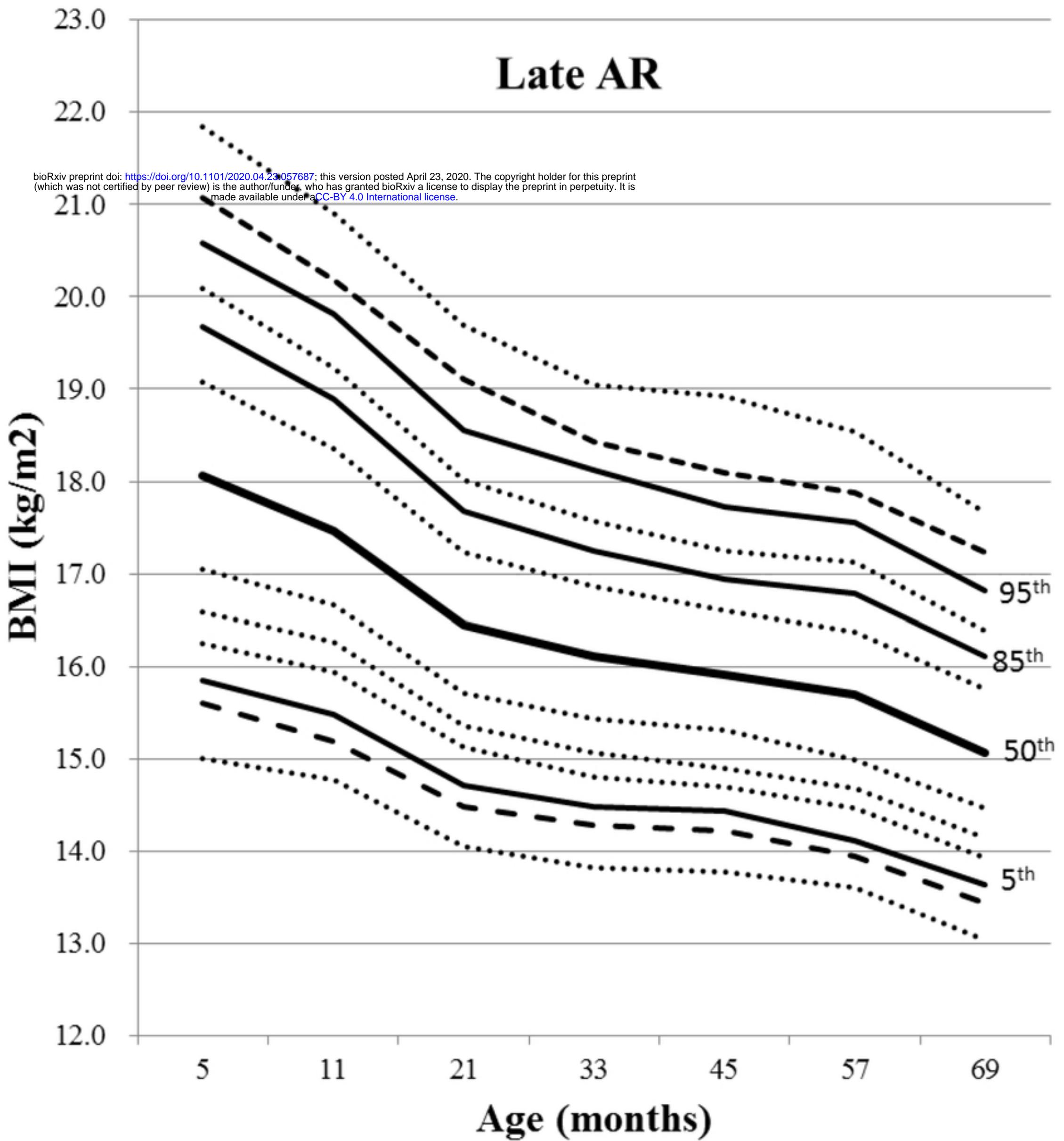


Fig 4C

Early AR

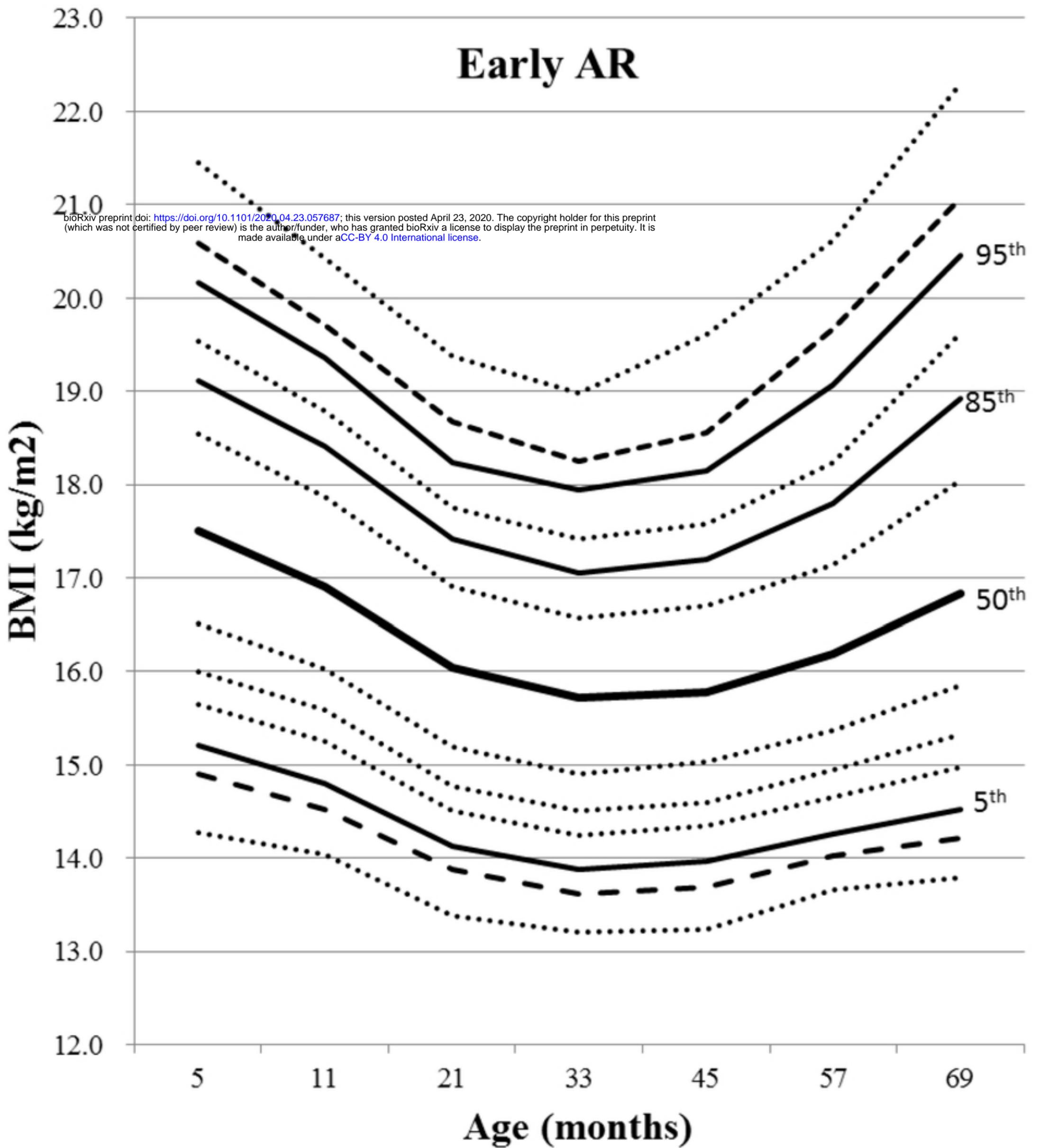


Fig 4D

Moderate AR

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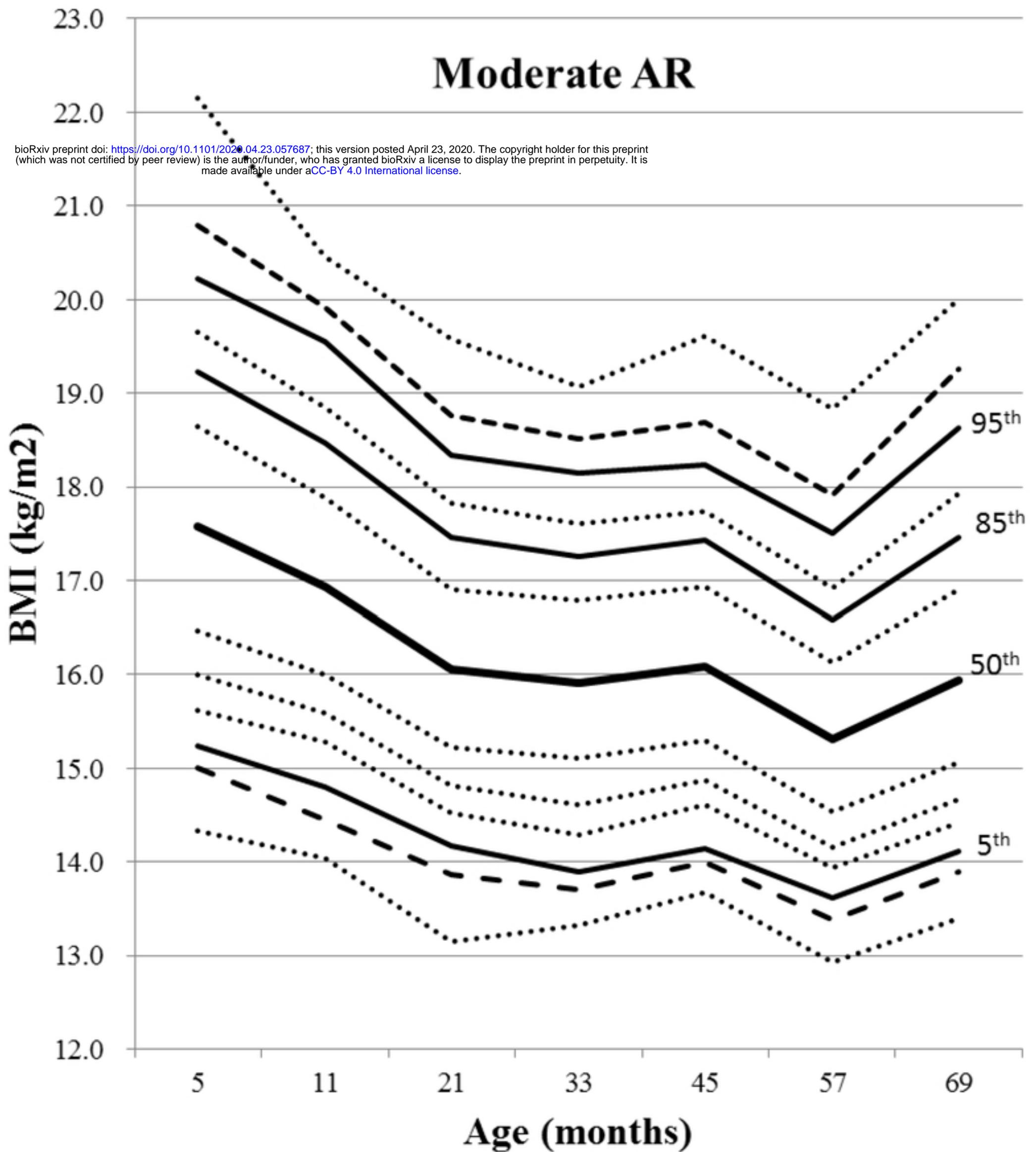


Fig 4E