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# Growth Standards for Children With Smith–Magenis Syndrome (SMS)

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## ABSTRACT

Smith–Magenis syndrome (SMS, OMIM 182290) is a complex syndromic diagnosis marked by neurobehavioral differences and distinct facial dysmorphisms, caused by haploinsufficiency of the retinoic acid-1 (*RAI1*) gene either by a pathogenic sequence variant or deletion at chromosome 17p11.2 involving a portion or all of this gene. Dysmorphisms may include a broad square face and brachycephaly, heavy eyebrows, a full mouth with an everted upper lip, and early micrognathia evolving to prognathism after excessive relative mandibular growth. All patients with SMS have variable global cognitive impairment, greatest in speech/language, disturbed sleep patterns, and distinct behaviors including self-injury, food foraging, and abnormal oral intake regulation, hyperactivity, and aggression. Short stature and central obesity are common in patients with SMS, and reference curves are needed to assess growth in clinical care and research endeavors. After IRB approval, anthropometry (including length/height, weight, head circumference) was collected via direct patient encounter, parental report from external medical encounters, and extraction from medical records. Utilizing polynomial smooth splines with a B-spline basis and variable windows depending on age, sex-specific length/height and weight curves were created, including 5th, 50th and 95th percentile lines for 0 through 15 years. Head circumference data were pooled from males and females to create 5th, 50th, and 95th percentile lines for 0 through 5 years. Nearly 6000 length/height, weight, and head circumference measurements from 190 patients with SMS from birth through adulthood were gathered. Length/height and weight data were plotted against age from birth through 15 years to create new length/height-for-age and weight-for-age curves by sex. Similar processes were employed to construct head circumference-for-age curves from birth through 5 years, combining data from both sexes into one figure. Final adult height was derived from the maximum adult height for each subject over the age of 18 years. The curves included in this article represent the first set of standardized growth curves for individuals with SMS. As such, they will permit clinicians to monitor and set expectations for linear growth, weight gain, and cranial growth in individuals with SMS.

## 1 | Introduction

Smith–Magenis syndrome (SMS, OMIM 182290) is a relatively common syndrome (prevalence 1/15,000 to 1/25,000 in the general population), characterized clinically by a distinctive facial appearance (Figure 1), minor skeletal features (brachycephaly, brachydactyly, and scoliosis), hypercholesterolemia, developmental delay of varying degrees, global cognitive impairment greatest in the speech/language realm, sleep disturbance associated with abnormal diurnal melatonin release, and a distinct behavioral phenotype. The latter includes self-injurious, stereotypic, and maladaptive behaviors, food foraging with difficulty regulating food intake, hyperactivity, and aggression (Edelman et al. 2007; Greenberg et al. 1996; Gropman et al. 2006; Smith et al. 1986, 2002). The facial appearance of SMS evolves with age and is characterized by a broad square face, heavy eyebrows, and a full mouth with everted tented appearance of the upper lip (El Allanson et al. 1999). Micrognathia is often present in early life; with time, mandibular growth exceeds maxillary, leading to midface hypoplasia and relative prognathism (El Allanson et al. 1999).

Originally SMS was described as a microdeletion syndrome of chromosome 17p11.2 (Smith et al. 1986; Greenberg et al. 1991). With refined cytogenetic analysis, the most common deletion was found to be 3.7 Mb in size and caused by non-allelic homologous recombination between low-copy number repeats (LCR). The LCRs in this region allow for additional and sometimes recurrent deletions (i.e., 4.86 and 2.13 Mb; Elsea and Girirajan 2008) and other larger contiguous gene deletions, with all affected individuals including deletion of the retinoic acid-1 (*RAI1*) gene (Rive Le Gouard et al. 2021). Pathogenic sequence variants of *RAI1*were then also associated with an SMS phenotype (Slager et al. 2003; Vilboux et al. 2011), further supporting its pathogenicity in this condition. In total, the mechanism of

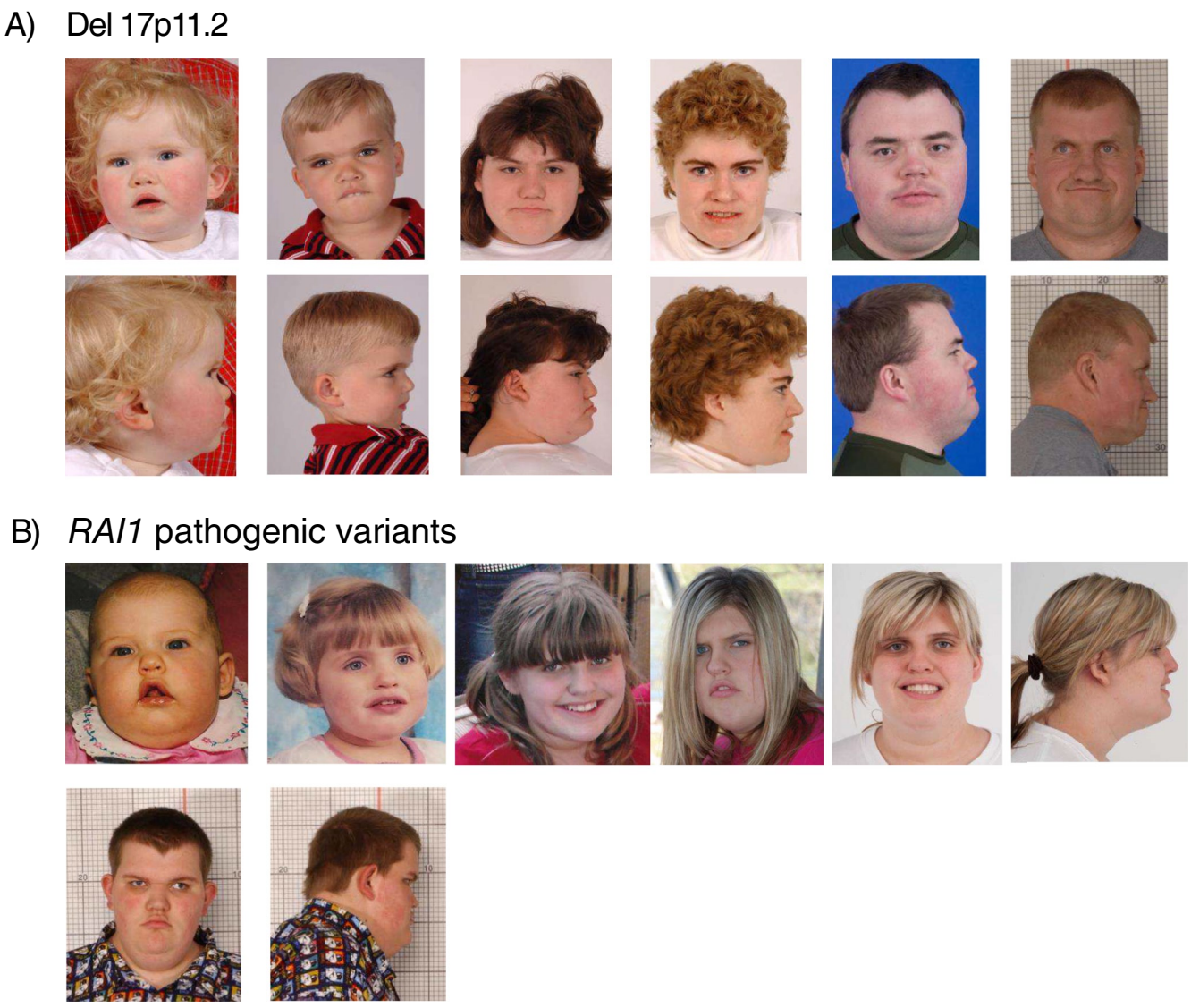


**FIGURE 1** | Smith–Magenis syndrome (SMS) patients across different ages. Craniofacial features of SMS for individuals with deletion 17p11.2 (A) and *RAI1* pathogenic variant (B) are shown. (A) Six unrelated individuals (face row 1 & profiles row 2) with del 17p11.2 at different ages from left to right: 9 months-F**; 4 years-M**; 15 years-F**, 28 years-F, 33 years-M, and 49 years-M. (B) Two unrelated individuals with de novo *RAI1* mutations include a female at different ages from left to right—Row 3: infant (< 1 year), 3 years, 12 years, 17 years, and 18 years (both face and profile); and a male at 20 years—Row 4 (face and profile). Images of deletion cases denoted with ** are used with permission of GeneReviews (Smith et al. 2022).

disease in SMS is a deletion in 90% of all affected individuals, with the remaining 10% caused by a sequence variant. SMS is typically de novo, although familial inheritance is documented in rare cases due to parental gonadal mosaicism (Zori et al. 1993; Smith et al. 2006).

*RAI1* is a transcriptional regulator, expressed at highest levels in neuronal tissue (Toulouse et al. 2003). Though it is not entirely clear how haploinsufficiency of this gene causes the recognizable physical features, developmental issues, and characteristic sleep disorder in patients with SMS, there has been progress in our understanding through study of mouse models and cell lines from affected humans with this condition. Relevant to the topic of linear growth and weight gain in this manuscript, SMS mouse models have increased abdominal obesity, particularly when fed an enriched fat or carbohydrate diet (Alaimo et al. 2014). Turco et al. (Turco et al. 2022) compared expression of lipid-producing genes and described abnormalities in lipid metabolism in cell lines from SMS patients which were not present in controls. They also observed that SMS cell lines demonstrated increased cell death attributed to mitochondrial dysfunction. More recently, Javed et al. (2023) determined that SMS (Rai1+/−) mice had disrupted brain-derived neurotrophic factor (BDNF) signaling from the hypothalamus which appeared to induce obesity. Furthermore, when they treated their SMS mouse model with a substance that stimulated neurotrophin, they delayed the onset of obesity and also ameliorated insulin intolerance and abnormal lipid profiles.

In reference to linear growth, *RAI1* insertional mutation mouse studies have shown altered transcription of multiple genes, including growth hormone, which was decreased 82.7-fold in the hypothalamus (Burns et al. 2010). Perhaps this contributes to stature in patients with SMS, which is below that expected based on parental height. In some studies, 50%–78% of patients with SMS with an *RAI1* deletion and ~10% of those with a single nucleotide pathogenic variant had height < 5th percentile (Edelman et al. 2007; Girirajan et al. 2006; Greenberg et al. 1996). Overt growth hormone deficiency also has been described in a few patients with SMS; with growth hormone treatment, they demonstrated catch-up growth (Spadoni et al. 2004; Itoh et al. 2004). With respect to weight, most infants with SMS initially appear well-nourished and comparable in size to typically developing peers (Gropman et al. 2006). However, hypotonia in patients with SMS contributes to oromotor dysfunction and feeding difficulties that often lead to failure to thrive (FTT) in infancy and childhood. Later, this often evolves to overweight and obesity as food foraging behaviors intensify and satiety with oral intake wanes.

Clearly, longitudinal patterns of height and weight acquisition in patients with SMS are not well characterized, and there currently are no standardized growth curves for this population. Though the size of the patient population from which anthropometry can be collected is somewhat limited, similar endeavors have been successful in comparably prevalent conditions such as Noonan syndrome (1/2500 people) (National Organization for Rare Disease 2019 "Noonan Syndrome"; website https://rarediseases.org/rare-diseases/noonan-syndrome/) (Malaquias et al. 2012), achondroplasia (1/25,000) (Hoover-Fong et al. 2007, 2017, 2021) and Costello syndrome (Sammon et al. 2012). Height and weight curves specific to SMS are needed for clinical care and research, as well as novel head circumference curves. The figures included in this article represent the first set of standardized growth curves for individuals with SMS against which patients can be compared to determine if an individual's growth trajectory is usual with respect to this patient population or warrants further investigation.

## 2 | Methods

### 2.1 | Participants and Approvals

A database was created from clinical data from children and adults with confirmed SMS by cytogenetic or molecular analysis. All subjects were from the US, Australia and the EU. Those from the United States and Australia were consented under the National Human Genome Research Institute (NHGRI) Institutional Review Board (IRB)-approved NIH protocol 01-HG-0109, "Natural History Study of the Clinical and Molecular Manifestations of Smith–Magenis Syndrome (SMS)". The remaining subjects were enrolled after obtaining written parental consent during PRISMS (Parents and Researchers Interested in Smith–Magenis Syndrome) conferences and/or under an approved institutional research protocol of international collaborating authors (D.M.-F.—Brazil; M.C.D.B.—France) from their clinics and/or local patient support groups.

### 2.2 | Data Collection

Demographics and anthropometry were collected through retrospective review of medical records, parental report of anthropometry at primary care provider encounters, and at face-to-face encounters at the National Institutes of Health or patient support group meetings. The anthropometry data derive from 1958 through 2020. Demographic data included date of birth, sex, date of encounter/measurement, and gestational age at birth, as well as use of growth hormone therapy. Anthropometry included length or height (cm; depending on age and ability of child), weight (kg) and head circumference (cm). A unique study ID was assigned to each participant by authors at the NIH (A.C.M.S., L.F.). Deidentified anthropometry and demographics were securely transferred for analysis to the Greenberg Center for Skeletal Dysplasias at Johns Hopkins University.

### 2.3 | Analysis

Raw data of length/height, weight, and head circumference were utilized to create growth curves for patients with SMS. Because of the relative paucity of the data at older ages, the curves presented here were truncated at 15 years. Growth percentile curves (5th, 50th, and 95th) were developed in a multistep process. First, sex-specific empirical 5th, 50th, and 95th percentiles for each month in the 0–15-year data were estimated by taking the respective percentile of values with a plus/minus window of the target age. The windows used were: +0.5 months at age 0–12 months, ±1 months at ages 12–36 months, and ±3 months for ages 37–180 months. These

empirical percentiles were then modeled as a smooth function of age (P-spline basis) separately by sex. These sex-specific smoothed height-percentile values for each age were then combined and regressed via a multivariate linear model with a smooth function of age via polynomial smooth splines with a B-spline basis, and pre-specified knots (6, 12, 18, 24, 36, 48, and 72 months) and a separate term for sex. The weight-for-age data required a stratified approach to smoothing because of the increasing skewness of weight values with increasing age. Penalized cubic smoothing splines were used to estimate sex-specific weight-for-age percentile curves separately for age intervals of birth through 3 years and 3–15 years. The number of knots were adjusted to balance model fits with enforced monotonicity of the weight-for-age percentile estimates (Rupert et al. 2003).

Data were combined for males and females for head circumference from birth through 5 years, and the empirical 5th, 50th, and 95th percentiles were estimated by taking the respective percentile of values with a plus/minus window of the target age using the same age windows as those for height and weight. The occipitofrontal circumference (OFC) for age percentile curves was estimated by regressing the empirical percentiles via a multivariate linear model with a smooth function of age via polynomial smooth splines with a B-spline basis and pre-specified knots (6, 12, and 30 months).

Sex-specific anthropometry of this SMS cohort was compared to that of typically developing children from 0 to 36 months WHO data and 36 months–15 years CDC/NCHS data (WHO Multicentre Growth Reference Study 2006). There were insufficient data to generate height and weight curves beyond 15 years. The average final adult height for males and females in our cohort was calculated by taking the maximum adult height for each subject over the age of 18 years, where more than one height measurement after the age of 18 was available. Data were combined for males and females for head circumference from birth through 5 years.

There were insufficient data to compare growth among countries of origin or *RAI1* mutation type.

Those with undocumented gestational age at birth were included in both the 0–36 growth standards and the 2–15 year growth standards with the assumption that term gestation was more likely to be omitted from the medical history than a premature birth. Anthropometry from subjects born prior to 35 weeks gestation was not included in the 0–36 month weight-for-age or length-for-age curves, but was included in the curves from 2 years of age and older as the norm in average stature growth curves when catchup growth has occurred. One individual was treated with growth hormone for 2 years; only their birth parameters and anthropometry from the period after growth hormone treatment were available and included in this analysis. All statistical analyses were performed with R Statistical Computing package (R Core Team 2021).

## 3 | Results

One hundred ninety individuals (57.4% female) with a confirmed SMS diagnosis were included in this analysis (Table 1). 178 (93.7%) had a deletion including *RAI1* and 12 (6.3%) had a sequence variant of this gene. In this retrospective data collection, the majority of subjects contributed a birth parameter. Thus the mean age of the first measurement from this cohort was quite young. The majority of subjects derived from the United States (60.0%) and Australia (24.2%) via the NIH protocol, whereas the remainder hailed from several countries including France (11), Germany and the Netherlands (9), Brazil (9) and Spain (a) as shown in Table 1. From the total cohort of 190 subjects, 149 subjects were consented under the NHGRI IRB-approved NIH protocol 01-HG-0109, "Natural History Study of the Clinical and Molecular Manifestations of Smith–Magenis Syndrome (SMS)".

**TABLE 1** | Characteristics of SMS study population, $n = 190$.

| | ***N*** |
|---|---|
| Sex | |
| Male | 81 |
| Female | 109 |
| Age at first measurement (months) | |
| Mean (SD) | 1.08 (11.28) |
| Country of origin | |
| Australia | 46 (24.2%) |
| Brazil | 9 (4.7%) |
| Germany/the Netherlands | 9 (4.7%) |
| France | 11 (5.8%) |
| Spain | 1 (0.5%) |
| USA | 114 (60.0%) |
| Gestational age, *n* (%) | |
| Term | 169 (89.0%) |
| Pre-term | 9 (4.7%) |
| Post-term | 0 |
| Unknown | 12 (6.3%) |

**TABLE 2** | Number of subjects with SMS and total anthropometry data points in each age group.

| | **Length–height** | **Weight** | **Head circumference** |
|---|---|---|---|
| | Subjects (*n*)/data points (*n*) | | |
| Total | 190/2185 | 190/2653 | 174/1035 |
| Birth | 150/150 | 177/177 | 78/78 |
| Birth–3 years | 175/1119 | 189/1356 | 131/735 |
| 3–10 years | 136/660 | 1378/761 | 96/189 |
| 3–18 years | 157/968 | 162/1132 | 1201/275 |
| > 18 years | 44/98 | 44/165 | 20/25 |

*Note:* Table includes males and females, all gestational ages, and subjects with point mutations and deletions.
Abbreviation: BMI, body mass index.

**TABLE 3** | Birth and final adult height, weight, head circumference, and BMI for subjects with SMS, by sex.

| | Length–height, cm | Weight, kg | Head circumference, cm | BMI |
|---|---|---|---|---|
| | | *N* subjects<br>Mean (SD)<br>Median [range] | | |
| Birth parameters | | | | |
| Male | 65<br>49.2 (3.2)<br>49.5 [40.0–55.0] | 74<br>3.2 (0.7)<br>3.2 [1.2–4.9] | 36<br>34.2 (2.1)<br>34.0 [31.0–42.0] | |
| Female | 86<br>49.2 (3.4)<br>49.0 [39.0–59.0] | 104<br>3.2 (0.6)<br>3.3 [1.3–4.4] | 42<br>33.7 (1.8)<br>34.0 [29.0–37.0] | |
| Adult (> 18 years) | | | | |
| Male | 17<br>165.3 (10.7)<br>163.8 [150.0–185.8] | 17<br>82.1 (29.0)<br>79.4 [40.0–167.8] | 3<br>57.0 (3.1)<br>58.0 [53.5–59.5] | 17<br>29.5 (8.0)<br>29.3 [17.8–50.8] |
| Female | 27<br>159.2 (9.7)<br>160.2 [127.0–177.0] | 27<br>79.4 (25.5)<br>75.8 [39.0–147.4] | 5<br>53.5 (2.6)<br>54.0 [49.0–55.5] | 27<br>31.2 (8.5)<br>29.9 [19.6–55.8] |

*Note:* Table includes all gestational ages and subjects with point mutations and deletions.
Abbreviation: BMI, body mass index.

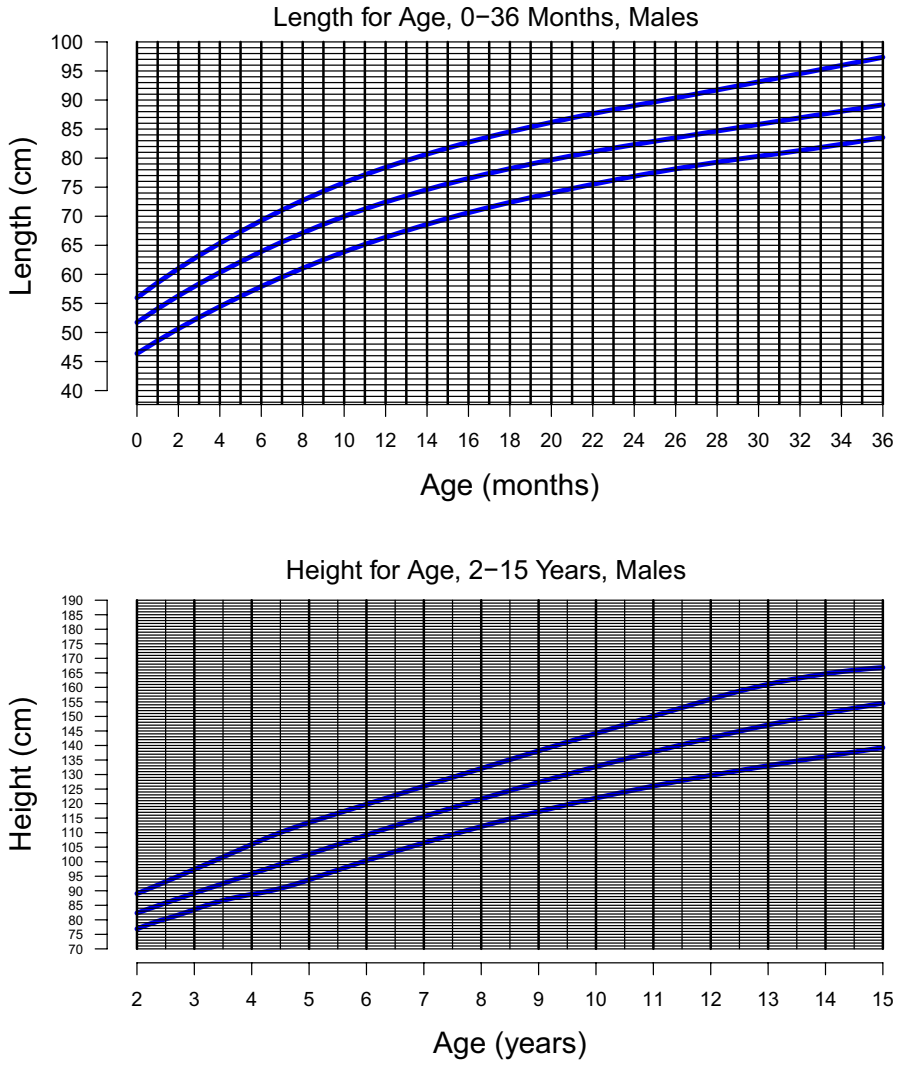


**FIGURE 2** | Length-for-age, 0–36 months and height-for-age, 2–15 years for males with SMS.

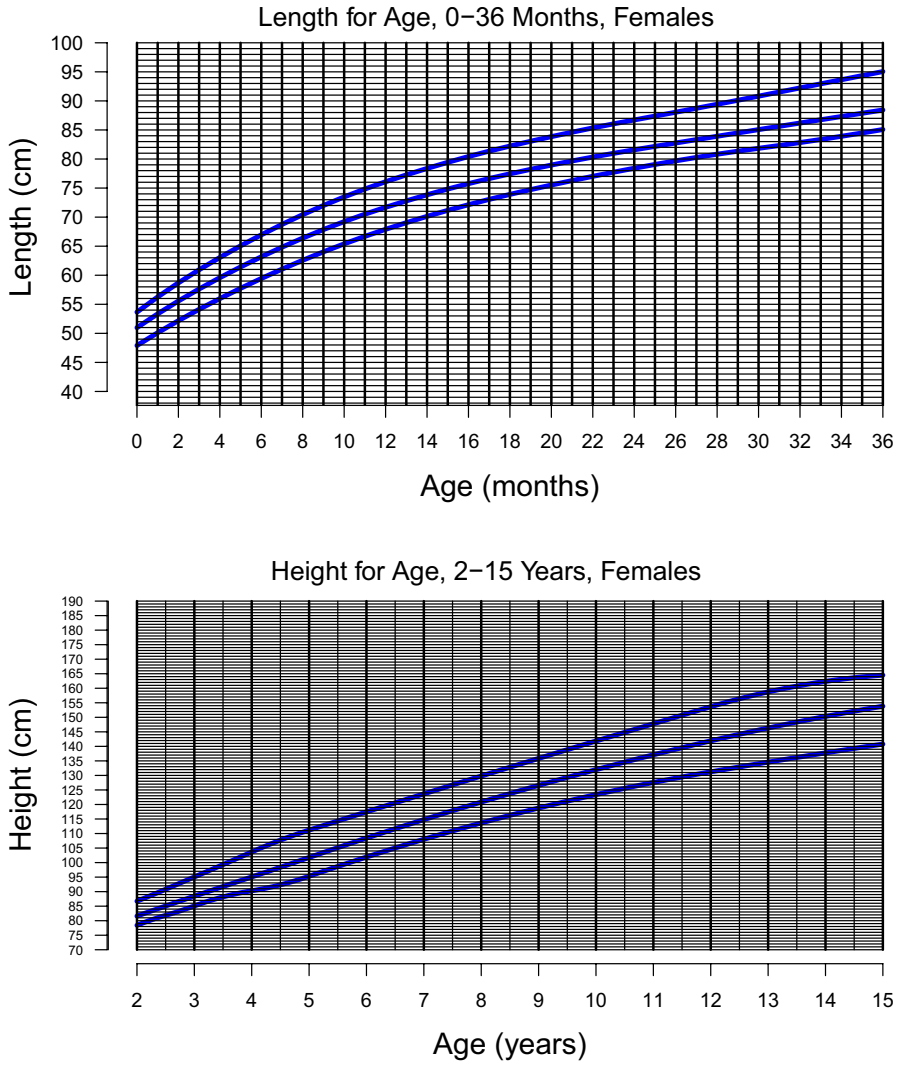


**FIGURE 3** | Length-for-age, 0–36 months and height-for-age, 2–15 years for females with SMS.

Data from an additional 21 subjects were obtained after written parental consent during PRISMS (Parents and Researchers Interested in Smith–Magenis Syndrome) conferences. The remainder of the European patients with SMS (20) were contributed by co-author M.C.D.B under an approved institutional research protocol. The majority (83.7%) were born at term and 8.5% preterm with the birth status missing and unobtainable in the remaining 6.3% ($n = 9$) of the cohort.

The total number of subjects contributing length/height, weight, and head circumference data points and the number of subjects doing so, stratified by a variety of age ranges (e.g., birth, birth–3, 3–10, 3–18, and > 18 years) are shown in Table 2. Growth parameters at birth were known in 150 (79.4%) subjects for length, 177 (93.1%) for weight, and 78 (41.1%) for head circumference. By sex, these data are shown in Tables S1 and S2.

Birth anthropometry for all infants (term and preterm) is shown in Table 3. Compared to the WHO Growth standards for term newborns, the average weight and average length were 25%–50% for males with SMS, whereas average weight was 50% and average height was 50%–75% for females with SMS. The average head circumference (OFC) at birth was 50%–75% for males and was 25%–50% for females with SMS, respectively. Final adult height data were available from 17 males and 27 females with SMS over 18 years of age. The average height at 18 years of age for males was 168.5 ± 9.3 cm (66.3″ ± 3.7″) and that for females was 154.9 ± 11.5 cm (61.0″ ± 4.5″). Compared to the average CDC height at 18 years of age, the SMS mean height represents a $Z$ score of −1.06 for males and −1.27 for females (CDC height for age percentile for Girls 2025; CDC height for age percentile for Boys 2025).

Length/height reference curves derived from 76 males between 0 and 36 months (top) and from 71 males between 2 and 15 years of age (bottom) born at 37 weeks gestation or later are shown in Figure 2. Similarly, length/height reference curves from 99 females between birth and 36 months (top) and from 97 females between 2 and 15 years (bottom) are shown in Figure 3. These sex-specific curves are suitable for clinical use for patients with SMS from birth through 15 years of age. Weight-for-age curves for 80 young males between 0 and 36 months (top) and from 72 males between 2 and 15 years (bottom) are shown in Figure 4. The same weight-for-age curves for 109 young females from birth through 36 months (top) and 102 females between 2 and 15 years (bottom) are shown in Figure 5. Figure 6 is a new reference curve for individuals with SMS from birth through 5 years

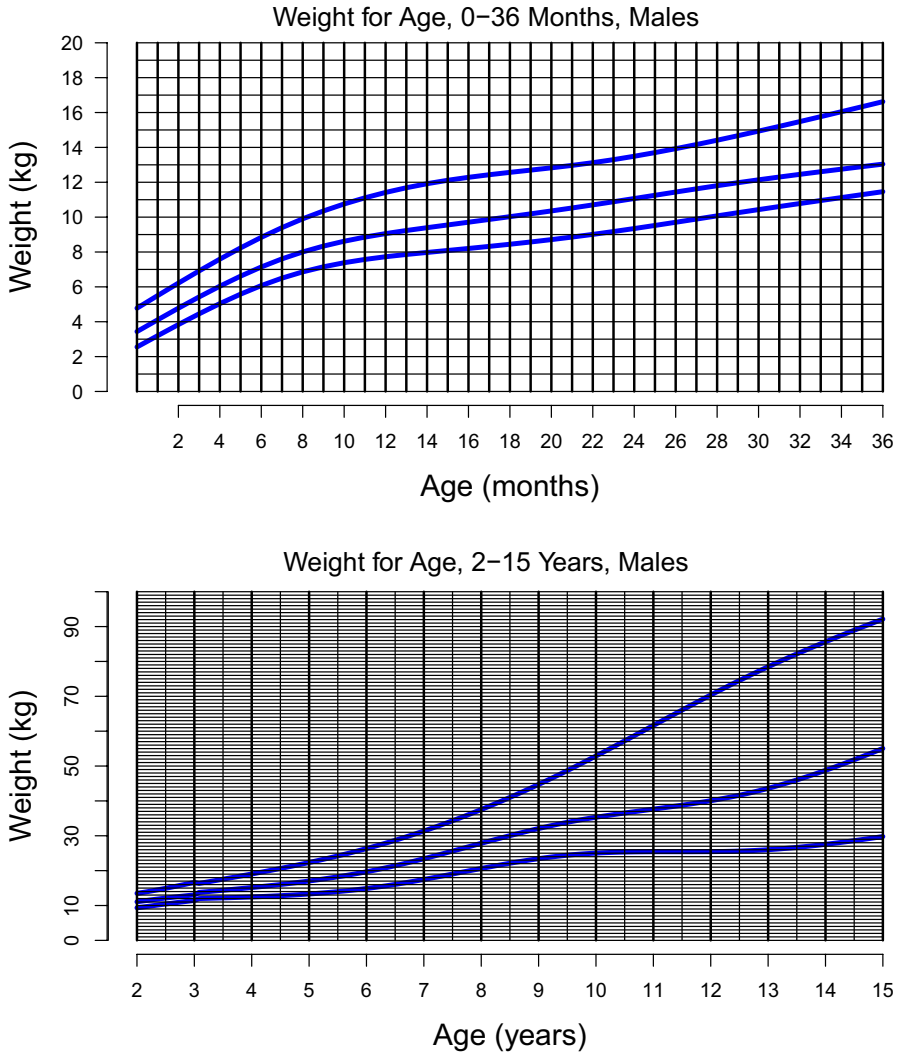


**FIGURE 4** | Weight-for-age, 0–36 months and 2–15 years for males with SMS.

of age. Due to a paucity of data and no significant sex-related differences in head circumference over the age interval, data from males and females are combined in this curve.

The raw data from which these new length/height- and weight-for-age curves were derived are also shown in Figures S1 and S3 (males) and Figures S2 and S4 (females), respectively, with reference WHO/CDC curves and the new SMS curves superimposed for comparison.

The birth weight and length for males and females with SMS at the 5th, 50th, and 95th centiles overlap that seen on the corresponding WHO centiles. Shortly after birth, however, linear growth of the SMS population is less than that of the reference population. Of the three isopleths shown in these figures (i.e., 5th, 50th, and 95th), the 5th and 50th dropped the most rapidly in the first year of life. Through age 5 years, height acquisition as seen in the 5th, 50th, and 95th centile curves paralleled, but remained below the corresponding WHO centile. There was a slight increase in height velocity observed for both males and females with SMS starting around age 5 years. By age 10 years, the 50th centile height for a male or female with SMS was at about the 25th centile on the WHO curve, compared with the 5th centile at age 5 years.

Considering weight, there also was overlap of this birth parameter in our SMS cohort as compared to the reference WHO data. After this initial overlap though, average male SMS weight gain is less than the reference through the first 3 years of life. In the females, the lower half of the weight distribution is below that of the reference population and remains there until about 1 year of life when the trajectory increases to levels that are quite similar to that of the reference population. There are more female elevated weight outliers in the first 3 years of life that seem to "pull" the 95th percentile isopleth above that of the reference population. Starting around 7 years of age for males and 9 years of age for females, the weight distribution widens which may partially be attributable to less data available at the older ages. Alternatively, this may represent excessive weight gain in females in this cohort of patients with SMS.

## 4 | Discussion

The growth curves presented here represent the first of their kind for individuals with SMS. The birth parameters for infants with SMS are comparable to those of average stature, typically developing infants represented in the WHO reference. Similar to what is observed in other SMS population

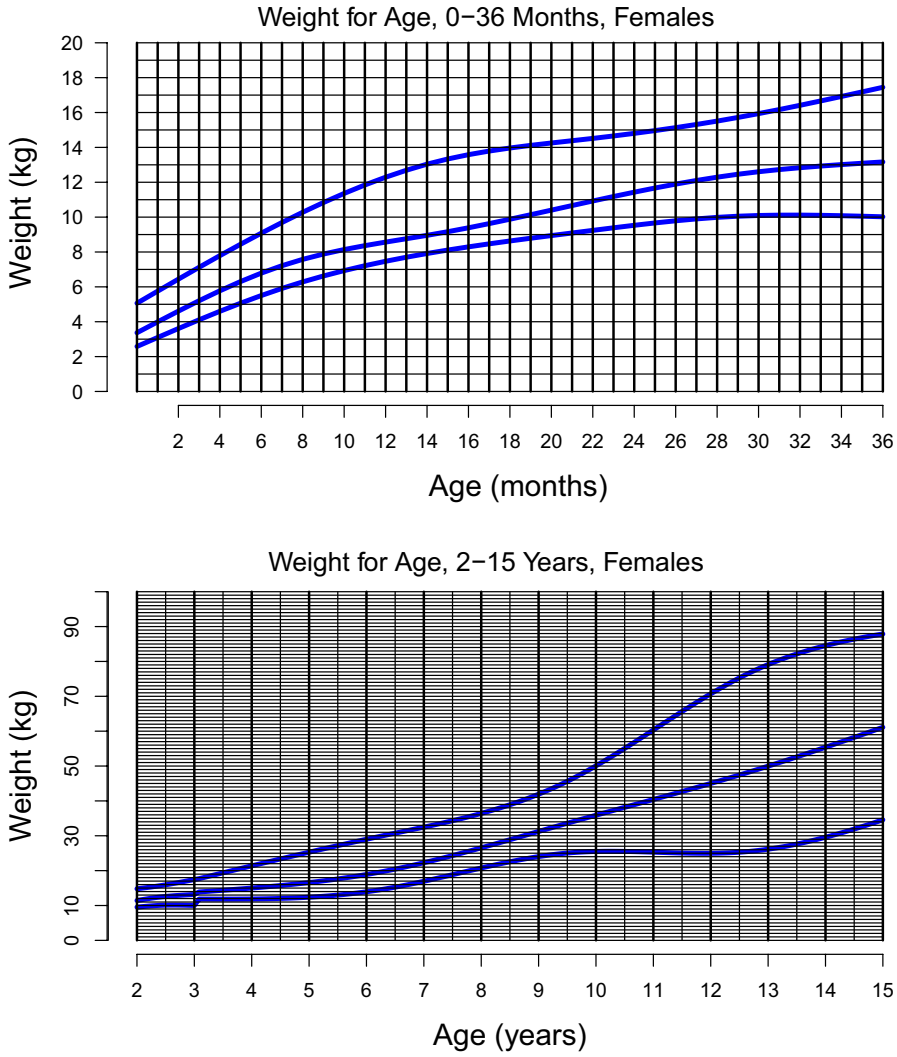


**FIGURE 5** | Weight-for-age, 0–36 months and 2–15 years for females with SMS.

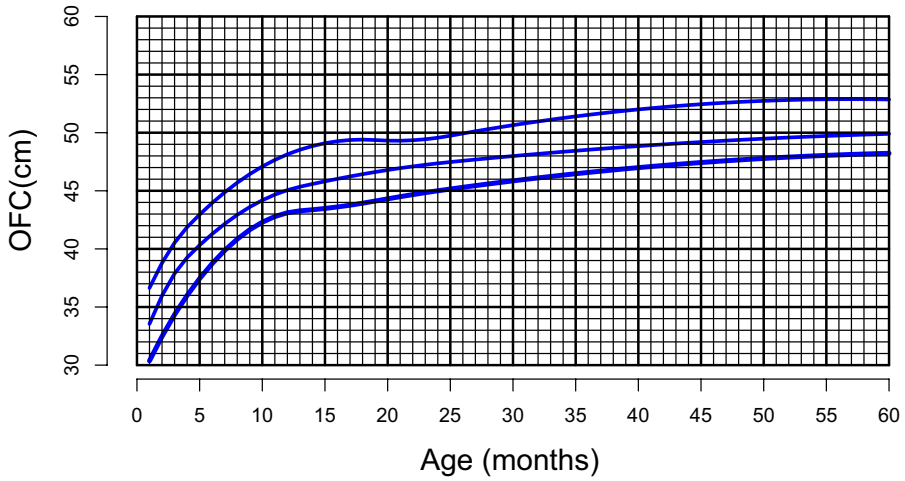


**FIGURE 6** | Head circumference for age curves for combined males and females with Smith–Magenis syndrome from birth through 5 years.

descriptions, however, (Rive Le Gouard et al. 2021; Edelman et al. 2007), we observed weight drop by centiles as compared to the reference over the first year in both sexes. Then weight gain accelerated through early childhood such that by 7 years of age, the average weight of males and females with SMS crossed above that of the CDC reference population. This is most likely reflective of the onset of overeating without apparent satiety in these patients with SMS. For comparison to Rive

Le Gouard's European population of 47 children with SMS, 60% of their population over 10 years of age were overweight, whereas 33% of Edelman's population was considered overweight or obese. With respect to linear growth, our cohort deviated from the norms over the first couple of years of life and remained there to adulthood. Again, this is comparable to the largest cohorts previously described by Le Gouard in which the height of 25% of their population was < 5% ile and 67% of Edelman's population was < 5% ile. Considering weight with respect to linear growth, this is an important observation in that excessive weight gain in children typically precedes and contributes to an acceleration of linear growth (Chung 2017; Kempf et al. 2021). But in contrast, in this and other described SMS cohorts, obesity sets in without an increase in linear growth, perhaps due to an intrinsic abnormality in growth signaling in patients with this genetic condition. Additional longitudinal growth data should be collected in patients with SMS throughout the 2nd decade of life to determine if there is a pubertal growth spurt present. In summary, linear growth in this cohort of patients is below that of average stature, typically developing children such that the average final adult height is more than −1SD below the mean for males and females. In contrast, weight gain is greater relative to linear growth, particularly in the females. Thus, the overall result is shorter than typical adults with average body mass indices in the overweight (male mean = 29.5) and obese (female mean = 31.2) categories.

The size of this patient population from which we derived the growth curves presented here is an unavoidable shortcoming of studying rare genetic conditions. This is especially difficult in the 2nd decade of life where we are currently unable to offer sufficient growth curves for clinical use. With ongoing collaboration with the patient support groups, however, more data may be gathered to refine these curves in the future. It should be noted that many of the growth parameters utilized in these curves were collected at medical centers by a small number of researchers using standardized anthropometry (e.g., wall-mounted stadiometer), thereby reducing the risk of error or unreliability of the data. Nonetheless, we admit that some of the measurements gathered were likely in error once considered in conjunction with an individual's longitudinal data and in total with the cohort. For this reason, we employed a data vetting process to target questionable datapoints and eliminate them from inclusion in the dataset if they could not be verified and corrected from the primary data collection source.

Many relatively rare genetic syndromes are associated with alteration in growth parameters when compared to age-matched, typically-developing peers. The rarity of these conditions, however, should not deter one from monitoring and trying to understand the etiology of the growth patterns in an effort to improve overall health. Perhaps an observed deviation in typical growth is common in a given condition, but the degree of deviation should not be accepted as "the norm" for that individual because it is representing the effect of a more serious underlying medical issue. Just as there are growth standards for average stature, typically-developing children (DHHS 2002), they should be available to children with rare genetic syndromes as well. The new tools presented in this manuscript can be utilized in daily care as well as future research ventures to describe and quantify growth in those participants.

### Author Contributions

**Julie Hoover-Fong:** conceptualization, methodology, data curation, writing – revision of original draft, review, editing. **John McGready:** formal analysis, data curation, methodology, writing – review and editing. **Leah Fleming:** data curation, writing – original draft, review, and editing. **Kerry Schulze:** methodology, review, and editing. **Folami Duncan:** data collection and curation, review, and editing. **Alexis Leonard:** data collection and curation, review, and editing. **Marie Christine de Blois Boucard:** data collection and curation, review, and editing. **Danilo Moretti-Ferreira:** data collection and curation, review, and editing. **Andrea L. Gropman:** data collection and curation, review, and editing. **Wendy J. Introne:** data collection and curation, review, and editing. **Ann C. M. Smith:** funding acquisition, conceptualization, methodology, data collection and curation, writing, review, and editing.

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### Conflicts of Interest

The authors declare no conflicts of interest.

### Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Figure S1:** Length-for-age (0–36 months) and height-for-age (2–15 years) for males with SMS compared to WHO (birth –36 months) and CDC norms (2–15 years). **Figure S2:** Length-for-age (0–36 months) and height-for-age (2–15 years) for females with SMS compared to WHO (birth –36 months) and CDC norms (2–15 years). **Figure S3:** Weight-for-age (0–36 months and 2–15 years) for males with SMS compared to WHO (birth –36 months) and CDC norms (3–15 years). **Figure S4:** Weight-for-age (0–36 months and 2–15 years) for females with SMS compared to WHO (birth –36 months) and CDC norms (3–15 years). **Table S1:** Number of male subjects with SMS and total anthropometry data points in each age group. **Table S2:** Number of female subjects with SMS and total anthropometry data points in each age group.