

Evaluating growth curves in physically active or not people with Down Syndrome: a literature review

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Published online: August 31, 2020

(Accepted for publication: August 22, 2020)

DOI:10.7752/jpes.2020.s4308

Abstract

Growth curves are useful for clinicians in order to monitor children health and growth. They become even more important in disease involving growth disturbances, such as for individuals with Down Syndrome (DS). Their role in DS people practicing physical activity or sport is fundamental for monitoring health benefits and their evolution during time. Several countries developed their own curves, by using different control population, different inclusion/exclusion criteria, different numbers and analysis, thus achieving quite different results. In this context, we conducted a literature search of original articles on growth curves published between 2010 and 2019. We found 11 articles from almost all continents, investigating height, weight, head circumference and BMI in people with DS. For each work we analysed nation, number of participants and observations, considered age range, type of study, considered population, outcomes, control and main results. In the complex, the included studies reported for general DS population shorter heights and head circumferences and higher BMI and weight/height ratio in both male and female with DS when compared to their peers. Although it is known that most of these differences in reference to general population may be due to lower physical activity, none of the selected studies dealt with this aspect. Indeed, no study focused on physically active people with DS, that could result having different growth pattern than inactive or general population with DS. In conclusion, further investigation is needed in order to achieve the complete, updated, methodologically strong, nation and subgroup-specific growth curves, so that they could become a reliable tool for clinical practice.

Keywords: Down Syndrome; Growth Curves; Anthropometry; physical activity.

Introduction

Down Syndrome (DS) is a neurodevelopmental disorder based on the presence of an extra (partial or total) copy of chromosome 21. It represents the most common genetic cause of intellectual disability, with a prevalence of about 1 on 400-1500 new-borns in different nations [Kazemi et al, 2016] and involves multiple systems, affecting not only mental health but even provoking physical and behavioural disorders. Indeed, it usually takes to a high prevalence of health-related problems, such as cardiac, gastrointestinal, immunological, respiratory, endocrine, dental, sensory, and orthopaedic issues [Bittles et al, 2007].

A growth curve is a useful tool to evaluate physical growth for preventing or screening health-related problems [Khadilkar & Khadilkar, 2011] and for monitoring health and nutritional status of general population [Ziegler & Nelson, 2012]. Specific growth curves are indispensable for disease leading to growth alteration, such as DS, in order to direct clinical practice and research planning. Indeed, clinicians need to have updated nation specific growth curve in order to monitor their patients' growth and to provide indications to their families [Barg & Hetman, 2018], even if their usefulness is still debated [Marcason, 2016]. The role of growth curves in DS people practicing physical activity or sport is fundamental for monitoring health benefits and their evolution during time.

A previous systematic review [Bertapelli et al, 2014] analysed articles dealing with DS growth curves published between 1978 and June 2013. They included papers considering DS people with and without comorbidities and put together results. Authors found lower heights (ranging from -0.4 to -4.0 standard deviation scores from reference populations) and reduced growth rates. Differences are underlined between DS results in different studies, maybe due to population differences, secular trends, different comorbidities or study limitation. They concluded that new specific curves should be developed, with national and international reproducibility, in order to help parents, healthcare professionals, and researchers in improving quality of life in children and adolescents with DS [Bertapelli et al, 2014]. Another review by Bertapelli and colleagues found a higher rate of obesity and overweight in people with DS, maybe due to metabolic alterations, comorbidities, inactivity and diet [Bertapelli et al, 2016].

Despite the main results shown by previous literature reviews, the major limitations are: (i) lack of availability of complete quantitative data for each of the outcomes considered; (ii) results were not always

representative for general DS population. In this context, starting from a systematic literature review focusing on the original articles published in the last ten years, the present study aims to investigate: (i) the main growth curves about height (H), weight (W), BMI (or W/H ratio) and head circumference (HC) in general population of DS people available and the comparisons with the normal population ones; (ii) the comparison between results from different nations.

Methods

We searched different online databases: PubMed (PM), Web of Science (WoS), and SciELO Citation Index. The selection of articles was made through ("Down Syndrome") AND "Growth Charts"[Mesh] for PM database and through ("Down Syndrome") AND (("Growth Charts") OR ("Growth Curves")) for the other databases.

Papers Selection Criteria

The analysis of the databases was made through the following criteria: (i) articles published between 2010 and 2019, in order to overview the most recent evidence; (ii) original articles, excluding reviews, commentaries, posters and proceeding papers; (iii) only full paper English written articles. After the first screening, two authors reviewed independently the founded articles with their title and abstract, in order to check the matching with the research aim. They selected papers aiming at constructing W, H, BMI and HC curves in people with DS and combined the articles obtained by the databases. Then, they checked the long paper of every of these articles excluding: (i) articles dealing with people with DS and other severe comorbidity (such as heart disease, potentially influencing results); (ii) articles dealing with intellectual disability including DS in which results about participants with DS were not presented and analysed separately; (iii) articles in which anthropometric measures are referred to people with DS in a single moment of life (e.g., in new-borns); (iv) articles considering a subclass of people with DS (for example with a specific chromosomic deletion); (v) articles comparing clinical measures with instrumental measures in the same patient (such as body composition through DXA).

Data extraction

From the selected papers the following data were extracted: (i) year of publication; (ii) participant characteristics (number, nationality, age, sex); (iii) number of observations; (iv) assessed outcome(s); (v) control; (vi) type of study; (vii) results.

Results and discussion

The review process is shown in the flow chart in Figure 1.

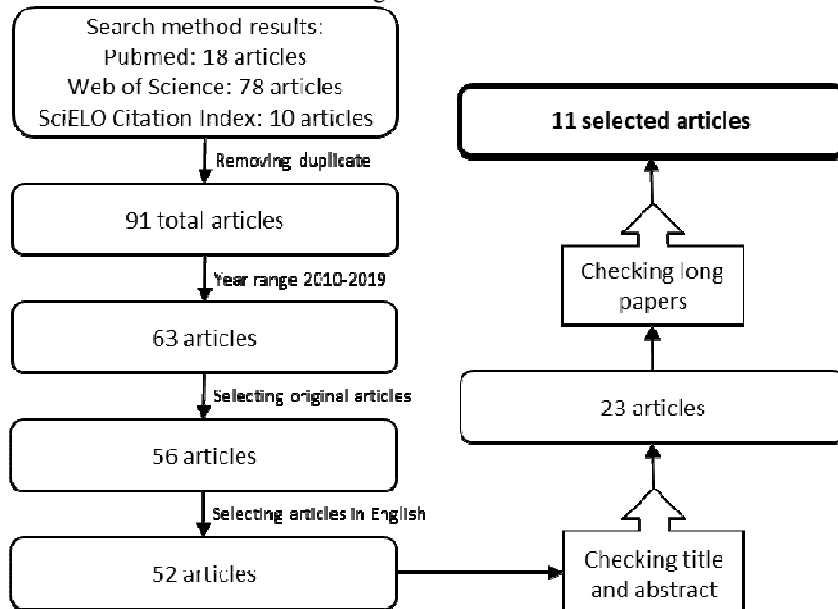


Figure 1: Flow chart representing the literature review process

After applying the paper selection criteria mentioned before (in Figure 1), we checked 23 long papers and excluded: 1 article dealing with people with DS and other severe comorbidity (influencing results); 2 articles dealing with intellectual disability including DS, in which it was not possible to extract results about participants with DS; 5 articles in which anthropometric measures are referred to people with DS in a single moment of life; 1 article considering a subclass of people with DS; 3 articles comparing clinical measures with instrumental measures in the same patient. Finally, the selected articles were 11. It is worth to notice that 3 of the studies overlap with the last review [7], we decided not to discard them because we are doing a different kind of analysis.

Table 1: selected articles main characteristics

Author and year	Nation(s) of participants	Total DS Participants Number (percentage of M: males)	Total Observations Number	Age range	Type of study
Van Gamen-Oosterom et al., 2012	Netherlands	1,596 (55.8% M)	12,336	0-26 years	Longitudinal (retrospective) study
Afifi et al., 2012	Egypt	434 (54.4% M)	1,955	0-36 months	Cross-sectional study
Tuysuz et al., 2012	Turkey	1,726 (57.4% M)	24,113	0-18 years	Longitudinal (retrospective) study
Su et al., 2014	Hong Kong	425 (57% M)	4,987	0-14 years	Mixed longitudinal (retrospective) and cross-sectional study
Aburawi et al., 2014	United Arab Emirates	182 (62.1% M)	1,263	0-18 years	Mixed longitudinal (retrospective) and cross-sectional study
Peña Rivera et al., 2015	Mexico	235 (57% M)	n.a.	45 days-16 years	Cross-sectional study
Zemel et al., 2015	United States of America	637 (51% M)	1,520	0-20 years	Longitudinal (retrospective) study
Bertapelli et al., 2017a	Brazil	706 (56.7% M)	1,986	2-18 years	Mixed longitudinal (retrospective) and cross-sectional study
Bertapelli et al., 2017b	Brazil	938 (53.7% M)	10,516	0-20 years	Mixed longitudinal (retrospective) and cross-sectional study
Mircher et al., 2018	France	2,598 (55% M)	36,416	0-20 years	Mixed longitudinal (retrospective) and cross-sectional study
Pierce et al., 2018	United States of America	412 (53.2% M)	823	2-18 years	Longitudinal (retrospective) study

As we can see from Table 1, available studies cover most of the continents, but no study from Australia fulfilled our search. Five of the selected studies were mixed longitudinal (retrospective) and cross-sectional, four are longitudinal (retrospective) studies and two cross-sectional. The previous review [Bertapelli et al., 2014] included 7 mixed studies, 4 longitudinal and 5 cross-sectional. The total number of participants ranged from 182 to 2,598 (with a mean value of 899). It can be considered suitable, considering the number of participants of the previous review [Bertapelli et al., 2014] going from 85 to 1,726, with a mean value of about 575. Male patient represented from the 51% to the 62.1% of the total considered patients. The number of observations ranged from 823 to 36,416 (mean value: 9,591), much more than the ones reported by Bertapelli et al. [Bertapelli et al., 2014], that were between 540 and 24,113 (mean value: 4,862). Most of the studies focused on children and adolescents covering the whole growth period, considering the first 14-26 years of life, only one study [Afifi et al., 2012] focused on the first three years. The previous review included 6 studies analysing the first 3 to 5 years of life [Bertapelli et al., 2014]. Table 2 shows the main detailed information of the selected studies.

Table 2: detailed information of the selected studies, with outcome(s), control and main results

Author and year	Outcome(s) (W: weight; H: height, HC: head circumference)	Control	Main results (M: male, F: female, m: smoothed median, z= z-scores compared to control; Co: control)
Van Gamen-Oosterom et al., 2012	H, HC (0-5 years)	General population (Dutch curves)	H: birth z=-1.1; 3-12 years z=-2.2; 13-26 years z=-3.0 HC: z= (-1.3) - (-2.0)
Afifi et al., 2012	W, H, HC	General population (Egypt)	W: birth 2.98kg ± 0.8 (Co: 3.9kg ± 0.48), 1 year 8.4kg ± 1.2 (Co: 9.8kg ± 1.18), 2 year 10.9kg ± 1.6 (Co: 12.9kg ± 1.38), 3 years 13.1kg ± 1.2 (Co: 15.4kg ± 1.75) H: birth 48.9cm ± 3.10 (Co: 50.6cm ± 2.20), 1 year 69.3cm ± 4.12 (Co: 75.8cm ± 3.24), 2 year 77.3cm ± 4.11 (Co: 87.2cm ± 2.96), 3 years 84.9cm ± 4.20 (Co: 94.2cm ± 4.12) HC: birth 33.6cm ± 2.50 (Co: 34.9cm ± 1.29), 1 year 42.1cm ± 1.23 (Co: 45.3cm ± 1.42), 2 year 44.4cm ± 1.40 (Co: 47.0cm ± 2.46), 3 years 45.9cm ± 2.31 (Co: 48.3cm ± 1.23)
Tuysuz et al., 2012	W, H, HC	General population (Turkish)	W: birth z=0.8; 6 months z=-1.0; 3 years z=-0.7; 5 years z= -0.5; 18 years M z= -0.3 F z= +0.5 H: birth z=-0.5; 6 months z=-0.7; 3 years z=-1.9; 8 years z=-2.2; 18 years M z= -2.56 F z= -3.06

		standards)	HC: birth z=-0.9; 6 months z<-2, 18 years M z= -1.02 F z= -2.21
Su et al., 2014	W, H, BMI, HC (0-4 years)	General population (Hong Kong - HK)	M: W: birth m=3.0 kg (HK: 3.4 kg); 5 years m=15.3 kg (HK: 17.3 kg); 10 years m=26.9 kg (HK: 30.5 kg); 14 years m=43.5 kg (HK: 47.0 kg). H: birth m=49.8 cm (HK: 50.8 cm); 5 years m=98.5 cm (HK: 109.1 cm); 10 years m=125.3 cm (HK: 136.0 cm); 14 years m=146.7 cm (HK: 162.1 cm). BMI: birth m=13.1 kg/m ² (HK: 13.4 kg/m ²); 5 years m=16.0 kg/m ² (HK: 15.1 kg/m ²); 10 years m=17.1 kg/m ² (HK: 16.2 kg/m ²); 14 years m=19.9 kg/m ² (HK: 18.2 kg/m ²). F: W: birth m=2.9 kg (HK: 3.4 kg); 5 years m=14.8 kg (HK: 16.5 kg); 10 years m=26.7 kg (HK: 30.6 kg); 14 years m=40.4 kg (HK: 44.1 kg). H: birth m=49.5 cm (HK: 50.2 cm); 5 years m=96.8 cm (HK: 107.4 cm); 10 years m=126.1 cm (HK: 137.0 cm); 14 years m=142.1 cm (HK: 155.7 cm). BMI: birth m=12.8 kg/m ² (HK: 13.1 kg/m ²); 5 years m=15.8 kg/m ² (HK: 14.8 kg/m ²); 10 years m=17.0 kg/m ² (HK: 16.0 kg/m ²); 14 years m=19.4 kg/m ² (HK: 18.3 kg/m ²).
Aburawi et al, 2014	W, H, HC (0-6 years)	General population (United Arab Emirates)	W: birth F 2.83 ± 0.71 (Co 3.56), M 3.11 ± 0.71 (Co 3.63); 3 years F 11.05 ± 1.32 (Co 13.32), M 11.45 ± 1.44 (Co 13.33); 6 years F 17.53 ± 3.33 (Co 17.8), M 17.30 ± 3.38 (Co 18.08); 9 years F 27.90 ± 4.20 (Co 23.96), M 23.49 ± 3.56 (Co 24.19); 12 years F 45.83 ± 5.89 (Co 35.29), M 39.22 ± 13.23 (Co 34.25). H: birth F 48.97 ± 3.8 (Co 52.5), M 49.81 ± 3.97 (Co 51.58); 3 years F 83.63 ± 3.99 (Co. 93.53), M 84.96 ± 4.42 (Co 94.14); 6 years F 103.99 ± 5.88 (Co 111.32), M 103.41 ± 7.39 (Co 111.54); 9 years F 122.41 ± 3.03 (Co 126.7), M 118.52 ± 5.15 (Co 127.68); 12 years F 133.92 ± 3.11 (Co 142.37), M 136.02 ± 8.96 (Co 140.32). HC: birth F 33.1 ± 2.04 (Co 34.82), M 33.98 ± 2.32 (Co 35.7); 3 years F 45.76 ± 1.27 (Co 48.16), M 45.37 ± 1.51 (Co 49.01); 6 years F 46.20 ± 1.30 (Co 49.91), M 47.35 ± 1.85 (Co 50.76).
Peña Rivera et al., 2015	W, H, W/H, BMI	General population (American, Spanish and WHO reference patterns)	American anthropometric reference: W: 54% below the 50th percentile; H: 43% below the 50th percentile Spanish anthropometric reference: W: 77.4% below the 50th percentile; H: 76.7% below the 50th percentile WHO reference: W/H: 48.5% below the 50th percentile, 12.3% below the 3rd percentile; H: 63.8% below the 3rd percentile; BMI: 50.1% below the 50th percentile, 14% below the 3rd percentile and 20.4% above the 85th percentile
Zemel et al., 2015	W, H, W/H, HC, BMI	General population (WHO and CDC)	WHO reference (0-3 years): W: z=-0.8; H: z= -1.7; W/H: z=0.2; HC: z=-1.6 CDC reference (2-20 years): W: z=-0.5; H: z=-2.1; BMI: z=0.9
Bertapelli et al., 2017a	BMI	General population (CDC)	BMI: 2 years: z=-0.2; 3-18 years: z=0.2-1.3
Bertapelli et al., 2017b	W, H, HC (0-2 years)	General population (WHO) and previous DS studies	WHO standards: W: z= (-0.8) - (-1.4); H: z= (-1.1) - (-3.2); HC: z= (-1.0) - (-1.9). Previous DS studies: W: z= (-0.8) - (+1.0); H: z= (-1.7) - (+1.3); HC: z= (-1.0) - (+1.2).
Mircher et al., 2018	W, H, HC, BMI	General population (WHO and French population standards) and previous DS studies	M: H: 5 years m=100.4 cm (WHO: 112.4 cm); 15 years m=153.8 cm (WHO: 169.0 cm); 18 years m=157.4 cm (WHO: 176.1 cm). HC: 1 year m=43.9 cm (WHO: 46.1 cm) z=-2; 3 years m=47.0 cm (WHO: 49.5 cm); 4 years m=47.7 cm (WHO: 50.2 cm); 1-12 years: z=(-2) - (-3). BMI: 4 years m=15.9 kg/m ² (WHO: 15.3 kg/m ² , French: 15.5 kg/m ²); 15 years m=21.0 kg/m ² (WHO: 20.1 kg/m ²); 18 years m=23.2 kg/m ² (WHO: 21.7 kg/m ² French: 21.3 kg/m ²); 20 years m=24.3 kg/m ² (WHO: 22.2 kg/m ²). F: H: 5 years m=99.4 cm (WHO: 109.4 cm); 15 years m=145.2 cm (WHO: 161.8 cm); 18 years m=147.0 cm (WHO: 163.1 cm). HC: 1 year m=43.2 cm (WHO: 44.9 cm); 3 years m=46.2 cm (WHO: 48.5 cm); 4 years m=47.0 cm (WHO: 49.3 cm); 0-12 years: z=-2. BMI: 4 years m=15.9 kg/m ² (WHO: 15.3 kg/m ² , French: 15.4 kg/m ²); 15 years m=21.5 kg/m ² (WHO: 20.2 kg/m ²); 18 years m=23.5 kg/m ² (WHO: 21.3 kg/m ² French: 19.8 kg/m ²); 20 years m=24.6 kg/m ² (WHO: 21.4 kg/m ²). H: 3 years: z=-1; 13 years: z=-2
Pierce et al., 2018	W, H, BMI	General population (CDC) and previous DS studies	Median W percentile (previous DS study): 2-4 years: 62; 5-7 years: 55; 8-10 years: 51; 11-13 years: 67; 14-18 years: 62; total: 59 Median H percentile (previous DS study): 2-4 years: 77; 5-7 years: 69; 8-10 years: 47; 11-13 years: 76; 14-18 years: 76; total: 73 Median BMI percentile (CDC): 2-4 years: 73; 5-7 years: 83; 8-10 years: 81; 11-13 years: 85; 14-18 years: 86; total: 79

Table 2 underlines that 9 out of 11 studies assessed H and W, 5 of which considered even BMI. Some of the studies assessed HC in the first years of life [Van Gasteren-Oosterom et al, 2012; Afifi et al, 2012; Su et al, 2014, Aburawi et al, 2015, Bertapelli et al, 2017], but others extended this measurement to the whole considered age range [Tüysüz et al, 2012, Zemel et al, 2015, Mircher et al, 2018]. One study only assessed BMI [16], while another one only considered H and HC [Van Gasteren-Oosterom et al, 2012]. The main control population was general population. Most of the studies [Pena Rivera et al, 2015; Zemel et al, 2005; Bertapelli et al, 2017a; Bertapelli et al, 2017b; Mircher et al, 2018; Pierce, 2019] used reference population by WHO [2007] or CDC [Kuczmarski, 2002], as recommended by the American Academy of Pediatrics [Leonberg, 2020], even if some of them concluded they were not the best reference for DS people [Pena Rivera et al, 2015]; other studies referred to national population standards [Van Gasteren-Oosterom et al, 2012; Afifi et al, 2012; Tüysüz et al, 2012; Su et al, 2014; Aburawi et al, 2015]; the study by Peña Rivera and colleagues [Pena Rivera et al, 2015] used the American and Spanish reference populations, in particular the American one was found to better fit for the considered population. Few studies made a comparison with previous DS reference studies [Bertapelli et al, 2017; Mircher et al, 2018; Pierce et al, 2019]. No study focused on physically active people with DS, that could result having different growth pattern than inactive or general population with DS. Results are presented in different ways: 5 studies express them in z-score, or standard deviations (SD) below or above the reference population mean; 3 studies [Su et al, 2014; Mircher et al, 2018; Pierce et al, 2019] reported a comparison between medians in the considered population and in the control one; 2 studies [Afifi et al, 2012; Aburawi et al, 2015] express results as mean and standard deviation of both populations; one study [Pena Rivera et al, 2015] reported percentages above or under a certain percentile of control population. In the previous review most of the comparisons were done by superimposition of centile distribution curves, not providing data in terms of SD differences. In the selected studies, reporting results in terms of z-scores, H in new-borns ranges between 1.1 and 0.5 SD under general population [Van Gasteren-Oosterom et al, 2012; Tüysüz et al, 2012]; at 6 months -0.7 SD [Tüysüz et al, 2012], at 3 years of age -1.9 DS [Tüysüz et al, 2012], from 3 to 12 years -2.2 SD [Van Gasteren-Oosterom et al, 2012; Tüysüz et al, 2012], at 18 years of age -2.56 SD in male and -3.06 SD in female [Tüysüz et al, 2012]. The highest deviation from general population is reported by Bertapelli [Bertapelli et al, 2017] and it reaches -3.2 SD. The previous review [Bertapelli et al, 2014] reported final H going from -0.4 and -4 SD. As for W, at birth it is reported to be -0.8 SD from general population [Tüysüz et al, 2012, 15], at 6 months -1 SD [Tüysüz et al, 2012], at 3 years -0.7 SD [Tüysüz et al, 2012], at 5 years -0.5 SD [Tüysüz et al, 2012], reaching -0.3 SD in male and +0.5 SD in female at 18 years [Tüysüz et al, 2012]. About HC, at birth it is at -0.9 SD [Tüysüz et al, 2012], from 0 to 3 years -1.6 SD [Zemel et al, 2015] and at 18 years -1 SD in male and -2.2 SD in female [Tüysüz et al, 2012]. W/H ratio from 0 to 3 years is +0.2 SD from general population [Zemel et al, 2015]. BMI at 2 years is -0.2 SD and ranges from 0.2-1.3 SD from 3 to 18 years [Bertapelli et al, 2017]. In sum, the included studies reported shorter H and HC and higher BMI and W/H ratio in both male and female with DS when compared to general population. Sometimes W appears to be lower than general population, but it should be considered relatively to the lower H. About the achieved results in comparison with previous DS studies, French girls and boys with DS appear to be taller than U.S. ones, with lower BMI [Mircher et al, 2018]. Another study [Bertapelli et al, 2017] found similar heights in Brazilian with DS to other DS studies in the first two years of life and shorter H at the end of growth period than Dutch people with DS [Van Gasteren-Oosterom et al, 2012], similar to the U.S. ones [Cronk et al, 1988], maybe due to genetic similarities or variations between populations. Even the previous review [Bertapelli et al, 2014] found differences in W, H and HC between studies with DS. All the considered studies used manual measurements, sometimes taken by different raters and requiring time and a certain compliance by the patients. In recent years some measurement systems using photogrammetry appeared in literature [Grazioso et al, 2019; 2019 June]. They allow an instantaneous (50 ms) and accurate (0.2 mm of accuracy) 3D measure of whole or specific body sites, augmenting patients compliance (that may be relevant in people with disabilities, such as DS).

Conclusions

There is growing interest in realising and updating growth curves in people with DS, for monitoring their health and nutritional status. The available results show for general DS people shorter heights and head circumferences and higher BMI and weight/height ratio in both male and female with DS when compared to peers. However, differences appeared between studies on DS, maybe due to genetic or methodological differences. Although it is known that most of these differences in reference to general population may be due to lower physical activity, none of the selected studies dealt with this aspect. Further investigation is needed in order to achieve the updated and methodologically strong nation-specific growth curves, so that they could become a reliable tool for clinical practice. In particular, future studies on growth curves in people with DS should: focus on H, W, HC and BMI (or W/H), in order to have a full description of DS growth; take their national growth curves as reference population, in order to overcome biases related to genetic and environmental differences between nations; express results in terms of z-scores or SD from reference population, so that they may be compared in an easier way; possibly use technological measurement systems (such as photogrammetric systems). Particular attention is needed on achieving growth curves adapted to important sub-groups of DS population, such as the ones regularly making physical activity or sport.

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