# **BMJ Open** Worldwide variation in human growth and the World Health Organization growth standards: a systematic review

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# ABSTRACT

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#### **Objective:** The World Health Organization (WHO) has established a set of growth curves for use as international standards in children up to age 5. The WHO's position is that all economically advantaged children who were breastfed as infants grow similarly. As a result, a single set of growth charts can be used to judge growth in any child, regardless of race or ethnicity. The goal of this study was to compare mean heights, weights and head circumferences from a variety of studies with the WHO's data. **Design:** We compared data from the WHO's Multicentre Growth Reference Study (MGRS) with data from studies performed in 55 countries or ethnic aroups.

**Data sources:** PubMed, WHO Global Database on Child Growth and Malnutrition, SciELO, Google Scholar, Textbooks and Ministries of Statistics and Public Health. **Eligibility criteria:** Large recent studies (1988–2013) of economically advantaged groups, including comparisons with cohorts of breastfed children wherever possible.

**Results:** Height varied somewhat among different national and ethnic groups. Means were generally within 0.5 of an SD of the MGRS means. Weight varied more than height, but the low MGRS means were seen as endorsing slenderness in the midst of an obesity epidemic. The mean head circumference varied widely. In many groups, means were consistently 0.5–1 SD above the MGRS mean. Head size in breastfed children at any age examined was far closer to local norms than to the MGRS means.

**Conclusions:** Height and weight curves may not be optimal fits in all cases. The differences between national or ethnic group head circumference means were large enough that using the WHO charts would put many children at risk for misdiagnosis of macrocephaly or microcephaly. Our findings indicate that the use of a single international standard for head circumference is not justified.

**Systematic Review Registration:** PROSPERO (# CRD42013003675).

## INTRODUCTION

The importance of growth monitoring in paediatric care is well recognised. Unduly slow

## Strengths and limitations of this study

- We found data from 55 different countries or ethnic groups (over 11 million children), making this study a large-scale comparison of growth in healthy children around the world.
- We found a relatively few studies from South America and sub-Saharan Africa. This limitation was due to the relatively few studies meeting our inclusion criteria in these areas.
- We also found extensive data comparing growth in breast- and formula-fed infants. This data facilitated comparisons with the MGRS data.

or rapid growth can indicate serious medical conditions, including genetic disorders, chronic disease, infectious disease, abuse or neglect and a variety of other problems.

Although analysis of information about an individual's growth can be complex, clinicians often look for patterns that may indicate abnormal growth. Examples include data points for a child that cross centile lines on a growth curve guickly, or values >2 SDs from the mean (below the 2.3rd and above the 97.7th centiles). Head circumference values below the 2.3rd centile may indicate poor brain growth, and height values in this range are often used to define short stature. Insurance companies and national healthcare systems often use SD cut-offs as criteria for coverage of growth hormone therapy. Thus, it is critically important that clinicians use curves with centiles that accurately reflect a child's expected pattern of growth.

The WHO's position is that unconstrained growth of economically advantaged breastfed infants and children does not vary substantially, and that a single set of growth curves can describe a human physiological norm up to age 5.<sup>1 2</sup> Accordingly, the WHO calculated a set of normative curves from the Multicentre Growth Reference Study (MGRS<sup>1 3</sup>). Study participants came from single cities in six countries (Brazil, Ghana, India, Norway, Oman and the USA).

The WHO refers to its curves as growth *standards*, or tools that provide a norm or desirable target, involve a value judgement, and describe how children 'should grow' in *all* countries.<sup>3–8</sup> Standards are different from references, which show how children are actually growing in a given place and time. The WHO notes that any deviations from its standards should be considered as evidence of 'abnormal growth'.<sup>1 3</sup> To date, >100 countries have adopted the MGRS curves.<sup>9</sup>

Many recent studies have found growth patterns of economically advantaged children that differ from the MGRS means. These studies were rigorous. Unfortunately, however, they focus on no more than two countries or ethnic groups,<sup>10–16</sup> do not compare their data with the MGRS data, were published before the MGRS curves<sup>11</sup> <sup>14</sup> <sup>17–20</sup> or are written in local languages.<sup>21–23</sup> To date, no one has carried out a large-scale comparison of data from the MGRS and different studies. As a result, the magnitude of international differences in growth is not fully evident.

In addition, the WHO has not published data supporting the idea that head circumference does not vary between nations and ethnic groups, nor has it published site-specific data for weight and head circumference from the MGRS study. Owing to the large number of countries using the WHO curves and because errors in diagnosis can occur when using growth curves with inaccurate centiles, we decided to compare the MGRS data with data from growth studies performed in different countries.

We analysed studies from 55 countries or ethnic groups, including 3 that had participated in the MGRS (India, Norway and the USA). We compared height, weight and head circumference from birth to age 5, and strove to use data from breastfed economically advantaged children. Like the WHO,<sup>2 5</sup> we defined 0.5 of an SD as a benchmark for significant differences between groups (called *outlying groups* or *outliers* here).

#### **METHODS**

The protocol for this study is registered with PROSPERO (# CRD42013003675).

#### Literature search

We searched PubMed, the WHO Global Database on Child Growth and Malnutrition, SciELO, Google Scholar and Google between May 2012 and May 2013. A final search was also performed immediately prior to publication. Our search terms were ["head circumference" OR birthweight OR weight OR length OR height OR anthropometric OR anthropometry OR "occipitofrontal" OR "growth curves" OR "length or height or stature" OR "growth charts"] alone or AND [ethnic group or nation]. Searches were performed in English, Arabic, Chinese, Czech, Dutch, French, German, Japanese, Icelandic, Italian, Korean, Norwegian, Polish, Portuguese, Russian, Spanish and Turkish. Most of the non-English papers had English abstracts. Google Translate and colleagues with knowledge of other languages aided in translation.

We scanned publication references and 'cited by' papers in Google Scholar, and contacted researchers to request information or sample size data not included in publications. Our initial screen identified ~2500 publications; ~900 that appeared to be relevant were selected for close review. 'Relevance' was defined as publications that, according to their abstracts, focused on growth, including the creation of curves and/or mean or centile values at specific ages. These included papers, books, one PhD thesis and government-made national growth curves. We reviewed these leads and determined which studies met our inclusion/exclusion criteria (see below and online supplementary figure S1). Differences of opinion were discussed until agreement was reached.

#### Study selection and data extraction

The MGRS study enrolled economically advantaged children who had been breastfed as infants.<sup>1 3</sup> We strove to find studies duplicating these conditions. The MGRS assumed that children at study sites in two developed nations (Norway and the USA) were unconstrained by economic hardship. We made this assumption for nations scoring  $\geq 0.750$  on the United Nations Human Development Index (HDI) at the time a study was performed. This approach helped us to reduce bias from growth data from children who were malnourished or afflicted with poverty-related medical conditions that affect growth. Other studies specifically cited favourable circumstances as inclusion criteria.<sup>19-21</sup> <sup>24-26</sup>

Study quality was improved by the use of peer-reviewed publications and data from national health surveys. Online supplementary table S1 has a column ranking each study by its relative risk for the biases noted above. Rankings were described on the following scale: low, low-medium, medium, medium-high and high. We used studies with rankings of low and low-medium. A study was scored low-medium if it met the conditions noted above but some uncertainties existed. An example would be the absence of a statement in a high HDI country about excluding children with diseases affecting growth. As another example, the MGRS study was scored low-medium because of potential attrition bias.<sup>27</sup>

For size at birth, we used studies reporting measurements by gestational age when possible.<sup>10</sup> <sup>22</sup> <sup>24</sup> <sup>28–51</sup> In addition, two studies defined 'term birth' in this way.<sup>52</sup> <sup>53</sup> This approach allowed us to duplicate the MGRS's 37–41 completed weeks 'term birth.' Some studies defined term birth as 37–42 weeks.<sup>12</sup> <sup>54–59</sup> A study from Sweden defined term birth as 37–43 gestational weeks.<sup>60</sup> Another study of birth size in Sweden noted deceleration of growth after 40 weeks<sup>61</sup>; thus, the studies including data from gestational ages after 41 weeks (in Sweden at least) are unlikely to skew the data significantly. The Euro-12 used data from 37–44 weeks.<sup>62</sup> Five studies noted 'term birth'.<sup>23</sup> <sup>25</sup> <sup>26</sup> <sup>63–68</sup> Our remaining birth studies simply reported size at birth.<sup>14 21 69–76</sup>

Means at the following ages were analysed: birth, 6 months (head circumference only), and 12, 18, 24, 36, 48 and 60 months. Data were transferred to Excel spreadsheets and checked and rechecked by both authors.

#### Calculation of weighted averages and composite SDs

We calculated weighted averages  $(\overline{X_t})$  and composite SDs  $(\sigma_t)$  for data at birth using standard methods. Composite SDs were calculated as follows:

$$\sigma_t = \sqrt{\left\{\sum_{i=1}^k{(n_i-1)V_i} + \sum_{i=1}^k{n_i(\overline{X}_i - \overline{X}_t)^2}\right\}} \big/ (n_t-1)$$

In this calculation, k is the number of term gestational age groups in each study (1 group/week; 37–41 weeks),  $n_i$  the sample size of each gestational age group,  $n_t$  the total number of samples in each ethnic group,  $(n_t-1)$  the degrees of freedom,  $X_i$  the mean value in each gestational age group and  $V_i$  the variance in each gestational age group. The first sum inside the root sign is the overall error sum of squares; the second sum is the group sum of squares. When added together and divided by the degrees of freedom, the result is variance. The square root of variance is SD, which we used to calculate SEs.

#### Defining significant differences

The WHO used 0.5 SD as a benchmark for clinically significant differences.<sup>2 5</sup> We adopted this cut-off. However, 0.5 SD is normally considered to be of moderate clinical significance and <0.5 SD may not be an optimal definition for not significantly different. Consequently, we also identified differences that were smaller but consistent. This was defined as a mean that was 0.25–0.49 SD from the MGRS mean in at least four of the ages noted above. Note that 0.25 SD outliers measure studies as a whole: if means at ≥4 ages were ≥0.25 SD from the MGRS mean, the country was identified as a 0.25 SD outlier.

# RESULTS

#### Study selection

This review uses studies from the following countries/ ethnic groups: Argentina,<sup>44</sup> Australia (indigenous and non-indigenous),<sup>28</sup> <sup>49</sup> <sup>75</sup> Belgium,<sup>59</sup> Brazil,<sup>41</sup> Canada (indigenous and non-indigenous),<sup>10</sup> <sup>48</sup> <sup>77</sup> China,<sup>65</sup> <sup>71</sup> Czech Republic,<sup>73</sup> Denmark,<sup>16</sup> <sup>52</sup> <sup>66</sup> Egypt,<sup>19</sup> Euro-12,<sup>62</sup> Finland,<sup>37</sup> <sup>64</sup> France,<sup>29</sup> <sup>78</sup> Germany<sup>13</sup> <sup>50</sup> <sup>79</sup> Greece,<sup>57</sup> <sup>80</sup> Hong Kong,<sup>30</sup> Iceland,<sup>53</sup> <sup>81</sup> India (birth and postnatal<sup>20</sup> <sup>33</sup> <sup>38</sup> <sup>82</sup> <sup>83</sup>), Iran,<sup>55</sup> Ireland,<sup>84</sup> Israel,<sup>34</sup> Italy,<sup>31</sup> <sup>85</sup> Japan,<sup>14</sup> <sup>39</sup> <sup>56</sup> Kuwait,<sup>43</sup> Lebanon,<sup>36</sup> Libya,<sup>86</sup> Malaysia,<sup>35</sup> Mexico,<sup>45</sup> Moroccans (in the Netherlands and Spain),<sup>22</sup> <sup>87</sup> Nepal,<sup>63</sup> the Netherlands (including Moroccans and Turks),<sup>18</sup> <sup>87-90</sup> New Zealand (indigenous and non-indigenous),<sup>58</sup> <sup>91-93</sup> Nigeria (birth<sup>26</sup>), Norway,<sup>12</sup> <sup>51</sup> <sup>67</sup> Poland,<sup>94</sup> <sup>95</sup> Portugal,<sup>46</sup> Russia,<sup>72</sup> Saudi Arabia,<sup>25</sup> Scotland,<sup>47</sup> Singapore,<sup>40</sup> <sup>69</sup> South Korea,<sup>70</sup> <sup>74</sup> Spain (birth; Caucasians, Moroccans, South Americans and sub-Saharan Africans born in Spain),<sup>22</sup> Spain (postnatal),<sup>96</sup> Sweden,<sup>60</sup> Switzerland,<sup>23</sup> Taiwan,<sup>42</sup> Turkey,<sup>21</sup> <sup>90</sup> United Arab Emirates,<sup>24</sup> the UK<sup>54</sup> and the USA,<sup>32</sup> <sup>97</sup> plus the MGRS.<sup>1 3</sup> The participants in these studies totalled roughly 11 million children (see online supplementary table S1).

#### Height

A publication authored by the MGRS showed that height means within the MGRS study sites did not vary significantly from birth to age  $5.^2$  In general, most means we analysed also fit within±0.5 SD of the MGRS means (results not shown). Groups with outlying means at three or more ages included Pacific Islanders,<sup>58</sup> the Netherlands,<sup>18</sup> Finland,<sup>98</sup> India<sup>20</sup> and Saudi Arabia.<sup>25</sup> Europeans and Pacific Islanders were above the +0.5 SD mark; other groups were below -0.5 SD.

Pacific Islander adults are not taller than other groups<sup>99</sup>; it is likely that increased height in these children is due to prematurely accelerated growth caused by increased weight (E. Rush, personal communication).<sup>100</sup> As a result, we were concerned about high weight and high body mass index (BMI). We investigated this possibility by using the Centers for Disease Control and Prevention's (CDC's) paediatric BMI calculator<sup>1</sup> to determine BMIs for Pacific Islander children aged 2-5 with weights and heights at the 50th centiles; all values came from a large recent study of this group.<sup>92</sup> The values we obtained were between the 87th and 98th centiles, with the majority >90. The CDC cutoff centile for overweight is the 85th centile. Thus, an average-sized child in that study would be overweight at a minimum, even when accounting for differences in body composition.<sup>99</sup> Alternatively, the same calculations for Dutch children ranged from the 39th to the 56th centiles, with the majority <50. These findings imply that increased linear growth in the Dutch population is not due to excess weight.

Infants in some nations were also longer than the MGRS means. For example, the average length of all children in Iceland was ~2/3 of an SD longer than the MGRS charts at birth and 12 months in a study that measured children at these two time points.<sup>53</sup> Male and female infants in Denmark were also outliers up to age 1.<sup>66</sup> The Icelandic study was small, but the Danish study was a large national survey. In addition, Moroccan infants in the Netherlands were outliers at age 1.<sup>87</sup> Finally, a large German study found that means for German girls and boys up to age 5 were at the 62nd and 60th MGRS centiles, respectively.<sup>101</sup> The authors deemed these differences to be sufficient to warrant the use of national growth curves over the MGRS curves.<sup>101</sup> Overall, 20% of the total means were  $\geq 0.5$  SD from the

<sup>&</sup>lt;sup>i</sup>http://apps.nccd.cdc.gov/dnpabmi/Calculator.aspx? CalculatorType=Metric

MGRS mean. However, the percentage of means at least  $\pm 0.25$  SD from the corresponding MGRS means at 4 or more time points was 44% for boys and 48% for girls.

#### Breastfed infants and children

Several studies have examined the effects of breastfeeding on linear growth. Although breastfed cohorts may be smaller than formula-fed cohorts,<sup>52 56</sup> in most studies we analysed, the lengths of breastfed infants and children were closer to local references than to the WHO standards<sup>12</sup> <sup>16</sup> <sup>56</sup> <sup>102</sup> <sup>103</sup> or, in pre-MGRS studies, the mean lengths of breast- and formula-fed infants were not significantly different.<sup>104 105</sup> We excluded older studies (before 1988) comparing breastfed and formula-fed infants due to changes in formula content with time. A Japanese breastfed cohort was at least 0.5 SD below the MGRS mean at every age measured; means for formula-fed children were either within 0.25 SD of the MGRS mean or not below 0.5 SD.<sup>56</sup> No pattern was found when comparing Greek breastfed infants with the national standards and MGRS data.57 80

#### Weight

We compared mean MGRS weight-for-age values with values from 24 to 54 (depending on age) countries or ethnic groups. The MGRS means were always at the low end of the range of values we obtained. Figure 1 is an example showing weight in boys and girls at age 24 months.

Overall, weight varied more than height. The percentage of outlying means in our analysis ranged 12-57%, with a peak at 30-39%. The greatest variation occurred BMJ Open: first published as 10.1136/bmjopen-2013-003735 on 8 January 2014. Downloaded from http://bmjopen.bmj.com/ on November 15, 2023 by guest. Protected by copyright.

at the age of 12 months (60% of means were outliers among boys and 44% for girls).

Importantly, ~84% of outlying mean weights were above the MGRS +0.5 SD mark. Owing to the global obesity epidemic, the low position of the MGRS means in our range can be seen as endorsing the idea that slenderness is healthy. This is a strength of the MGRS curves, particularly since overweight and obesity pose significant health risks. However, clinicians working with children from groups that are somewhat taller or shorter than average should bear differences in mind when assessing weight centiles with the MGRS charts. This is particularly important when making determinations about failure to thrive (FTT).

Online supplementary figure S2 compares birth weight in boys and girls in 54 studies and the MGRS. Although the MGRS values were closer to the middle of the range of values at birth, outliers occurred above and below the mean, with highly developed nations well above the mean (Iceland) and well below it (Japan). Thus, the charts may not be good global fits for birth weight. A study in the UK came to this conclusion for British children.<sup>106</sup>

Overall, 31% of all weight means were at least 0.5 SD from the WHO mean at any age, with 62% (boys and girls) of studies being 0.25 SD outliers as defined above. Alternatively, results for a similar comparison of Euro- $12^{62}$  weight means and national European weight means identified only four 0.5 SD outliers among 144 data points and 2/15 (13%; boys and girls) as consistent 0.25 SD outliers. We did not make this comparison for height because the Euro-12 study measured only length, and most other studies measured standing height at ages 2 and 3.

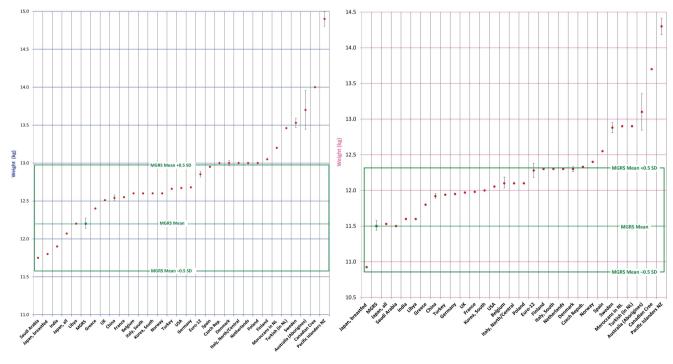


Figure 1 Weight at 2 years: 30 countries versus Multicentre Growth Reference Study (MGRS). The green box delimits the area within 0.5 SD of the MGRS mean. The green line within the box shows the MGRS mean. (A) Boys; MGRS mean: 12.2 kg; SD up: 1.55 kg, down: 1.25 kg. (B) Girls; MGRS mean: 11.5 kg; SD up: 1.65 kg, down: 1.25 kg. Error bars show 1 SE.

#### Breastfed infants and children

Weight differences between breast- and formula-fed cohorts were more substantial than for length/height. However, national breastfed means were not necessarily the same as the WHO means, and no overall pattern was found. For example, weights in Belgium and Norway were closer to the MGRS means at some ages and to local formula-fed means at other ages.<sup>12 107</sup> Alternatively, a study in the USA found consistent differences between the two cohorts.<sup>102</sup> Weights of Danish infants fed according to the WHO recommendations fluctuated but were generally <0.25 SD from the overall mean of breastfed and formula-fed infants combined.52 Mean cohort weights did not differ significantly in another Danish study, but were above the MGRS means.<sup>16</sup> This finding mirrors that of a study in Sweden, which found no differences between the two feeding groups.<sup>104</sup> Most breastfed Japanese infants up to age 2 were 0.5 SD outliers.<sup>56</sup> All were lighter than formula-fed infants, who were not generally 0.5 SD outliers.

#### Head circumference

Overall, head circumference varied far more than weight or height. Again, the MGRS mean values were at the low end of the range of values we found. Most outlying groups were European (including Turks), but Asian Indians, Australian aborigines, Canadian Cree, Japanese children at birth and Pacific Islanders were also represented. Figure 2 compares head circumference at age 24 months in 26 studies with the MGRS means. Eighteen means in each group were 0.5 SD outliers. Figure 3 shows the percentage of outlying means at each age we analysed. Outliers ranged from 32-72% of age groups from birth to age 5. Overall, 219 means of 408 total were outliers (54%). Of these, 202 (98%) were above the +0.5 SD cut-off.

A total of 51% of female means and 56% of male means were 0.5 SD outliers, and 69% of studies on boys and 78% of studies on girls were 0.25 SD outliers. The difference between the highest and the lowest mean values was  $\geq$ 1.5 MGRS SDs in the majority of ages.

Means in geographically proximal countries were closer. Figure 4 compares Euro-12 means at 24 months with European national means.<sup>62</sup> There were no 0.5 outliers. In addition, there were only eight 0.5 SD outliers of 182 data points from birth to 36 months (data not shown). Six of these points were from the UK. However, 31% of female study means from 0 to 5 and 44% of male studies were surpassed the 0.25 SD cut-off.

Data for Cree head size were included even though many Cree live in disadvantaged circumstances with a high prevalence of diabetes. Our reasons for using the data were that (1) diabetes (including gestational diabetes) apparently does not affect head circumference<sup>108</sup> and (2) different studies have found large head sizes in the Cree,<sup>77 109</sup> with their larger overall sizes dating back to a time when they maintained traditional lifestyles.<sup>110</sup>

In practical terms, these findings indicate that many children from groups analysed here would be *extreme outliers* above the 97.7th centile/2nd SD above the mean on the MGRS's curves, and few would be extreme outliers below the 2.3rd centile/2nd SD below the mean. We

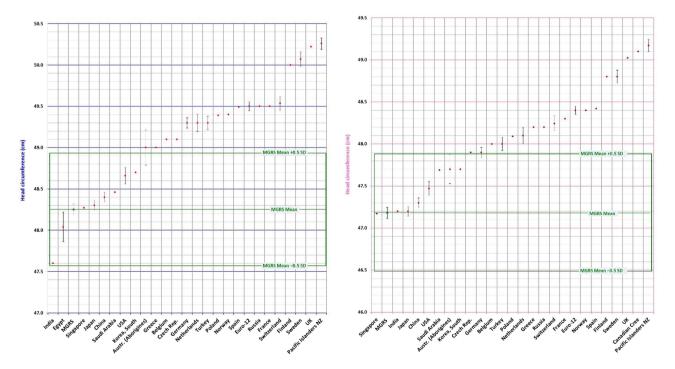
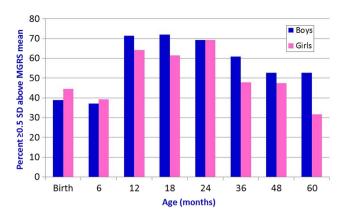


Figure 2 Head circumference at 2 years: 26 countries versus Multicentre Growth Reference Study (MGRS). The green box delimits the area within 0.5 SD of the MGRS mean. The green line within the box shows the MGRS mean. (A) Boys; MGRS mean: 48.25 cm; SD: 1.36 cm. (B) Girls; MGRS mean: 47.2 cm; SD: 1.40 cm. Error bars show 1 SE.

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**Figure 3** Percentage of head circumference outliers by age and sex. The figure shows the percentage of studies with head circumference means that were at least 0.5 SD above or below the Multicentre Growth Reference Study (MGRS) mean. Half or more of all means for boys were beyond 0.5 SD at 12 months and older; at least 40% of means for girls were in this category in 6 of 8 age groups.

addressed this question by estimating the percentage of children from different national or ethnic groups who would be extreme outliers on the MGRS curves.

To do this, we determined MGRS values that were  $\pm 2$ SDs from the MGRS mean for different ages and sexes. For example, the MGRS +2 SD value for 24-month-old boys is 51 cm. Next, we determined centiles for these values in other groups. Thus, 51 cm is roughly the 73rd centile for British boys at the same age, meaning that  $\sim 27\%$  of British boys would be above the 97.7th centile on the MGRS growth curves. Alternatively, 51 cm is approximately the 86th centile in the Euro-12 data, meaning that ~14% of European 2-year-old boys overall would be above the MGRS's 97.7th centile. This estimate fits well with the fact that the Euro-12 male mean at 24 months is ~0.9 SD above the MGRS mean. Alternatively, only 0.02% of British boys and 0.26% of Euro-12 boys would be below the 2.3rd centile on the MGRS charts. Note that the SD values for the MGRS, UK and Euro-12 studies were generally very close at all ages, especially for males, facilitating this comparison. This similarity was not the case for every country tested, and growth variation within individual nations presumably contributes to differences at the extremes when measured against the MGRS curves. Figure 5 shows percentages of extreme outliers for countries on different continents. Online supplementary figures S3 and S4 show extreme outliers for height and weight at age 2.

Euro-12 used 'strictly standardised methods of measurement' that mirrored the MGRS's,<sup>111</sup> including use of a metal measuring tape applied firmly.<sup>112</sup> Given the methodological similarities between both studies, it is unlikely that the large differences in means between the MGRS and Euro-12 studies are due to technique.

#### Breastfed infants and children

Head circumference means in breastfed infants and children were generally closer to local norms than to the MGRS standards<sup>12</sup> <sup>107</sup> or close to formula-fed groups in pre-MGRS studies.<sup>52</sup> <sup>62</sup> <sup>102</sup> <sup>105</sup> A Turkish study found fluctuations in differences between the groups, but only measured infants until the age of 6 months.<sup>113</sup> Head size in Japanese breastfed and formula-fed cohorts did not generally differ significantly at the ages tested (birth to 24 months), while differences from the MGRS means fluctuated.<sup>56</sup> A Danish study found that head circumference in breastfed infants did not differ from nonbreastfed infants, and both groups had larger mean head sizes than the MGRS means.<sup>16</sup>

#### DISCUSSION

This study is a large international comparison of height, weight and head circumference means in children up to age 5. In order to minimise effects due to secular changes in growth, we used recent growth studies published within the same general time as the MGRS study. Overall and with some exceptions as noted, mean values for linear growth examined here were within 0.5 SD from the MGRS means, although close to half of means were not consistent within 0.25-0.49 SD of the MGRS means. Among 0.5 SD outliers, Europeans were generally above 0.5 SD and some other groups (eg, Saudi Arabians and Asian Indians) were below -0.5 SD. Thus, the curves may underindicate short stature in slightly taller European populations and overindicate it in shorter ones. Clinicians should keep this fact in mind when dealing with children from these populations.

Obviously, means for groups with small average body sizes, such as the Aka, Efé and Mbuti tribes, and others, would not fit into the MGRS charts and these groups would presumably require their own charts for optimal analysis of growth. Owing to the challenges of making charts for these populations (a relatively small population size, relative isolation, etc), their situations pose unique difficulties in this regard.

Variation in weight was greater, with 57% of male means and 39% of female means being outliers at 12 months. This large percentage may have been partially due to differences in feeding methods, but without specific studies, there is no way to know. Additionally, many of the higher weights in European populations may also have been partially due to their mildly greater lengths/heights.

The MGRS weight means tended to be at the low or very low end of the range of weights we found, and 84% of outlying weight means were above the MGRS mean. The position of the MGRS means can be seen as endorsement of slenderness and is therefore a strength of the MGRS curves. However, weight centile values must still be interpreted carefully in populations that are tall or short.

In addition, 16% of the outlying mean weights identified here were below the MGRS mean. Most were from India and Saudi Arabia. As noted, Indian children tended to be short and would therefore be expected to

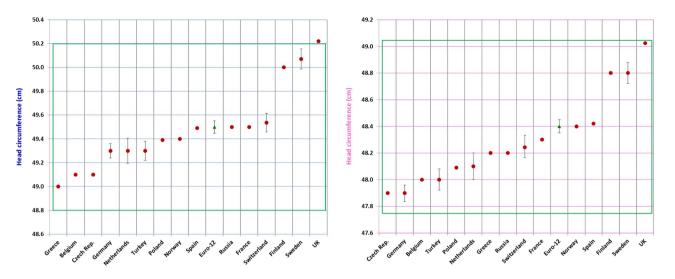


Figure 4 Euro-12 versus 15 European studies (head circumference, 24 months). (A) Boys; Euro-12 mean: 49.5 cm; SD: 1.4 cm. (B) Girls; Euro-12 mean: 48.4 cm; SD: 1.3 cm. Error bars show 1 SE. MGRS, Multicentre Growth Reference Study.

have lower weights; Saudi children were also at the low end of our height ranges.

In contrast, head circumference varied considerably. Variation between the extremes in each age/sex group was as high as ~2.5 SDs. However, as noted in the text and shown in figure 4, variation was less in geographically proximate Europeans. This was also the case for eastern Asian populations analysed here (China, Japan and Singapore). Overall, means for these groups clustered together at all ages examined.

Although the WHO examined weight and linear growth in breast- and formula-fed infants prior to beginning the MGRS, head circumference was not examined.<sup>114–117</sup> In addition, the final MGRS study did not publish site-specific head circumference data, apart from a small set of sex-pooled birth data.<sup>118</sup> We found 0.5 SD outliers in that data (Norway and Oman; not shown).

Also, studies comparing head size in breastfed and bottlefed children have found either no or modest size differences between them or found that head circumference in breastfed infants is closer to other local infants than it is to the WHO charts.<sup>12 52 102 107 119</sup> The Euro-12 study found that all size differences between breastfed and non-breastfed European children, including head size, were clinically irrelevant after the first birthday.<sup>105</sup> Taken as a whole, these findings indicate that the MGRS head circumference curves are of questionable validity for global use.

The variation found here highlights the fact that growth and growth monitoring are complex processes. Growth is affected by genes, physiology, general health, general environment, nutritional status and other factors. Growth monitoring is affected by secular changes in size, the size of each study sample and its composition, measurement errors and other things.

Just as importantly, size at any age is affected by innate differences in anatomy. As an example, the craniums in

Polynesians are shaped differently when viewed from above and behind in comparison with those of other humans, and their cranial vaults are higher and larger.<sup>120</sup> There are also differences between Chinese and Caucasian head morphology.<sup>121</sup> Finally, the highly regarded works of William White Howells describe ethnic differences in skulls that are used to aid in the identification of human remains.<sup>122</sup> <sup>123</sup> One of his works describes centuries-old Polynesian skulls as 'large'.<sup>122</sup> Many or most of the differences he described may affect head circumference.

The WHO is correct to be concerned that the potentially smaller size of breastfed infants may lead to erroneous interpretations of growth faltering, followed by premature introduction of supplemental foods. This practice can be deleterious and have significant ill effects on children living in areas where sanitation is poor. However, it is equally important to acknowledge that curves that fit poorly with a population may also lead to errors, such as regarding head growth, FTT or the need for specialist services. These errors can raise barriers to correct diagnosis when a problem exists, create unnecessary stress when one does not and increase strain on overtaxed healthcare systems. Many countries will be able to use their own curves. However, because of the lack of data on unconstrained growth in sub-Saharan Africans, growth references for this population may be beneficial. Creating them for East and West African groups could be advantageous.

Analyses of secular changes have found that average height increases incrementally over generations,  $^{124-134}$  even in affluent populations. Continued incremental increases in height continue to be documented in countries such as Denmark, Sweden and the Netherlands (albeit at reduced rates  $^{16\ 18\ 135}$ ), where socioeconomic constraints on growth have been effectively absent for decades.

Incremental increases appear to be due to physiological constraints,<sup>136</sup> and are affected by maternal

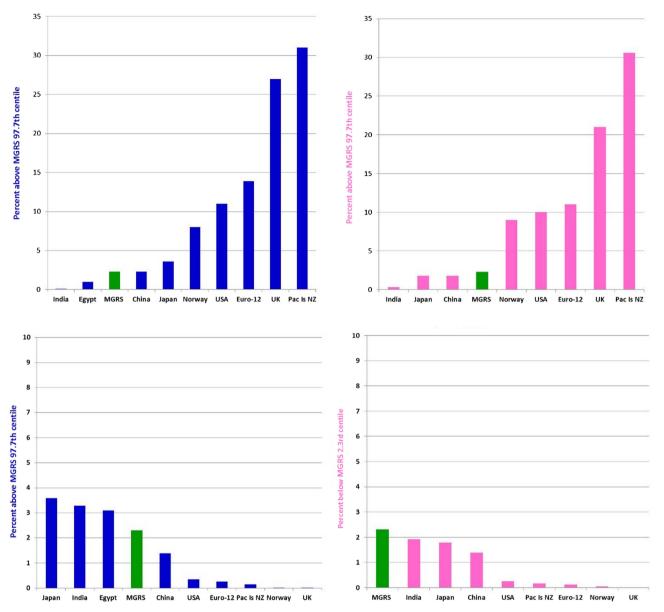


Figure 5 Estimated percentages of extreme outliers (head circumference) at age 24 months. (A) Percentage of boys (blue) or girls (pink) estimated to be above the 97.7th centile on the Multicentre Growth Reference Study (MGRS) curves. (B) Percentage of boys (blue) or girls (pink) estimated to be below the 2.3rd centile on the MGRS curves.

growth (fetal and postnatal<sup>137</sup>) and mid-parental height (reviewed in ref. <sup>138</sup>), among other factors. However, secular increases in stature have slowed considerably in some countries, yet will likely continue robustly in others for decades.<sup>136</sup> These observations imply that a population may eventually reach a maximum mean height. Clearly, however, maximum height cannot have been reached for the vast majority of the world's populations.

On the basis of this information, the advantaged children in the WHO's study may not have represented their population's maximal sizes, unless they had come from families that had been living in optimal conditions for many generations. The MGRS did not consider this factor. While Norway may have reached or be close to a growth plateau, the five other countries in the MGRS study likely have not, and all are likely in different stages of secular change. As a consequence, although the WHO notes that its curves were designed to show how children 'should grow rather than how they grew in a particular time and place',<sup>6</sup> <sup>139</sup> they may describe how advantaged children in countries at different stages of secular change were growing at a certain time.

## **Strengths and limitations**

A major strength of this study is that it is the first large-scale comparison of growth data with the MGRS data. In choosing which data to include, we were careful to select recent studies of children living in advantaged conditions. This careful selection process increased the comparability of the means reported here with the MGRS means by maximising the similarity of conditions under which the data for comparison was gathered. We

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have also compared mean head size in cohorts of breastfed children with the MGRS means wherever possible.

We attempted to reduce the risk of bias by including large studies, searching multiple sources in multiple languages and using high-quality studies. By focusing on healthy, affluent populations, we also reduced the risk of reporting on growth that had been affected by disease or poverty.

Limitations of this study include the relative lack of data from South America and Africa. Unfortunately, the majority of South American studies pooled data for both sexes, and could not be used. In addition, the dearth of studies from sub-Saharan African nations was a limitation. Although our searches were extensive, it is also possible that we may have missed publications relevant to this analysis.

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**Data sharing statement** Both authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

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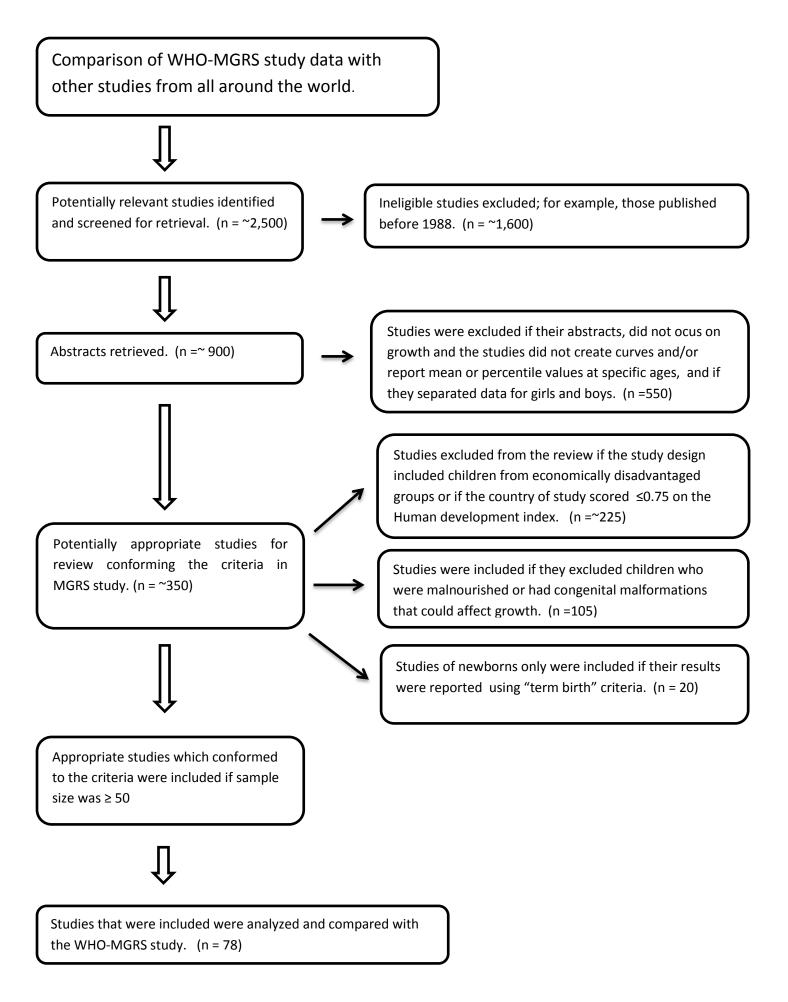
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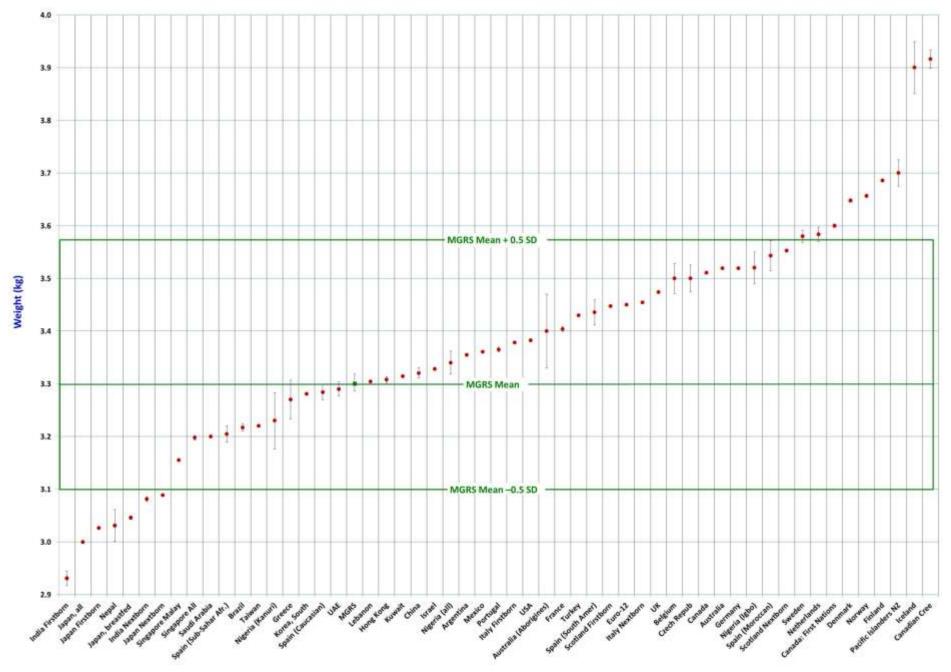
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Supplemental Figure 1. Flow diagram of study selection.

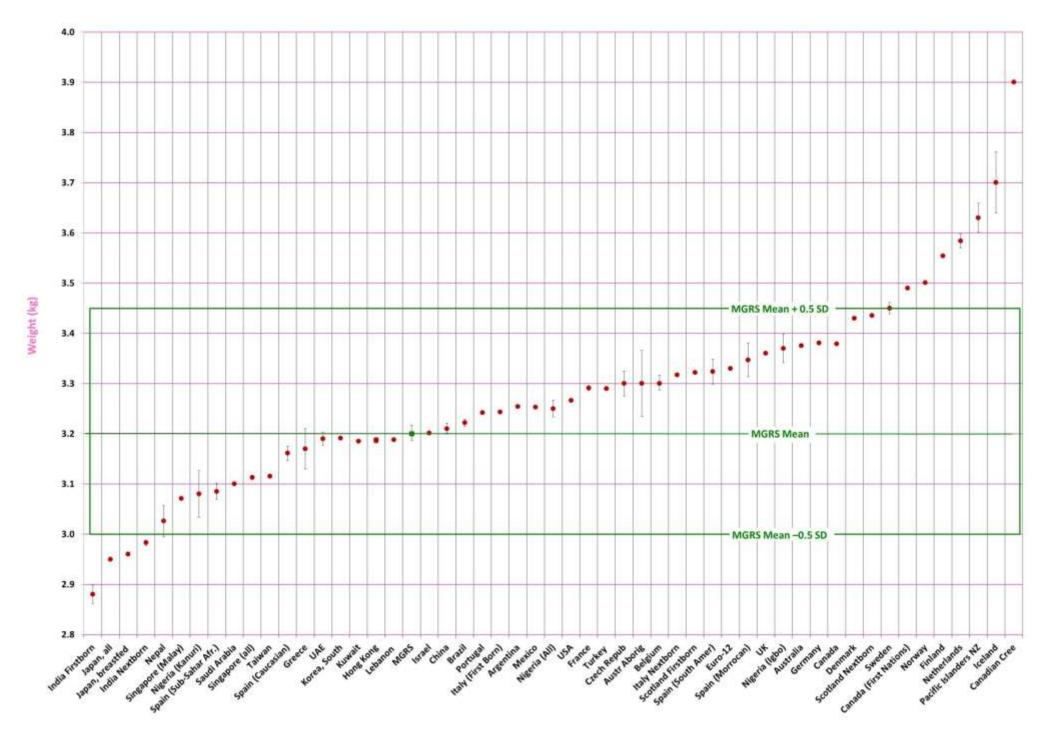


Supplemental Figure 2. Weight at birth: 54 countries vs. MGRS. The green box delimits the area within 0.5 SD of the MGRS mean. The green line in the box shows the MGRS mean. *4a. Boys.* MGRS mean: 3.3 kg; SD: 0.55 kg up; 0.40 kg down; *4b. Girls.* MGRS mean: 3.2 kg SD: 0.50 kg up; 0.40 kg down.

# **Supplemental Figure 2a**



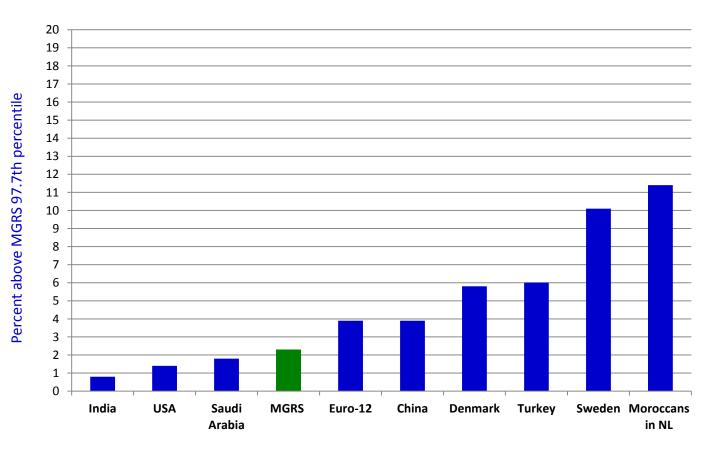
# **Supplemental Figure 2b**

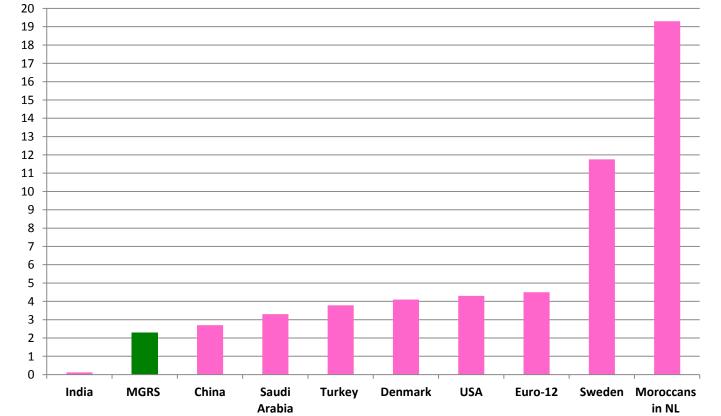


# Supplemental Figure 3. Estimated percentages of extreme outliers (weight) at age 24 months. 4a.

Percentage of boys (blue) or girls (pink) estimated to be above the 97.7<sup>th</sup> percentile on the MGRS curves. 4b. Percentage of boys (blue) or girls (pink) estimated to be below the 2.3<sup>rd</sup> percentile on the MGRS curves. Moroccans in NL = Moroccan people living in the Netherlands.

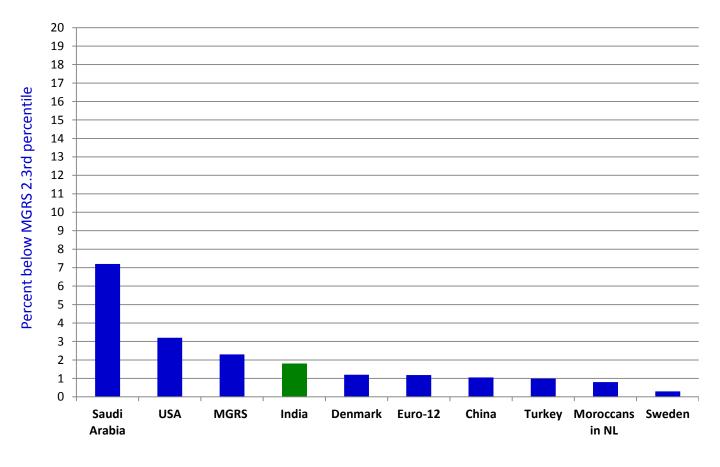


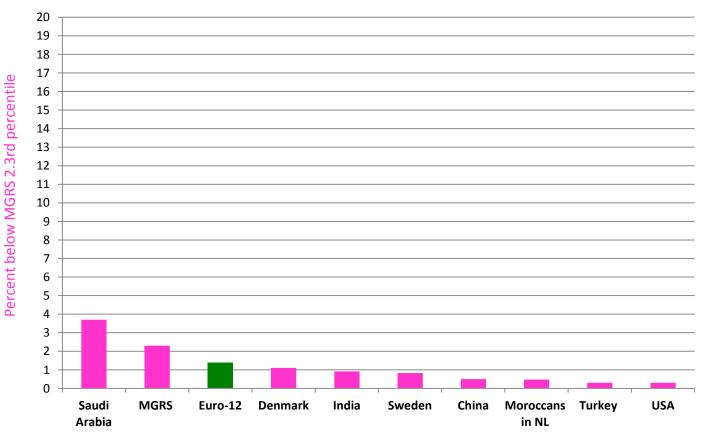




Percent above MGRS 97.7th percentile

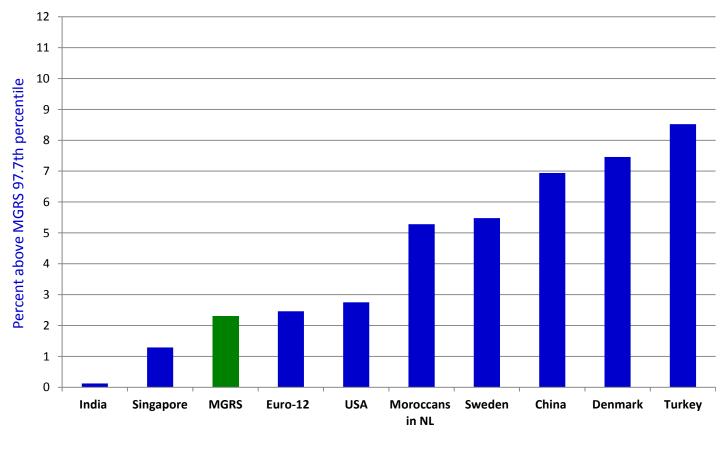




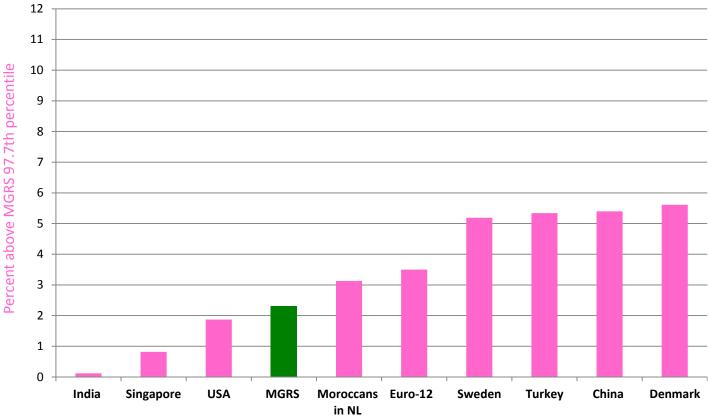


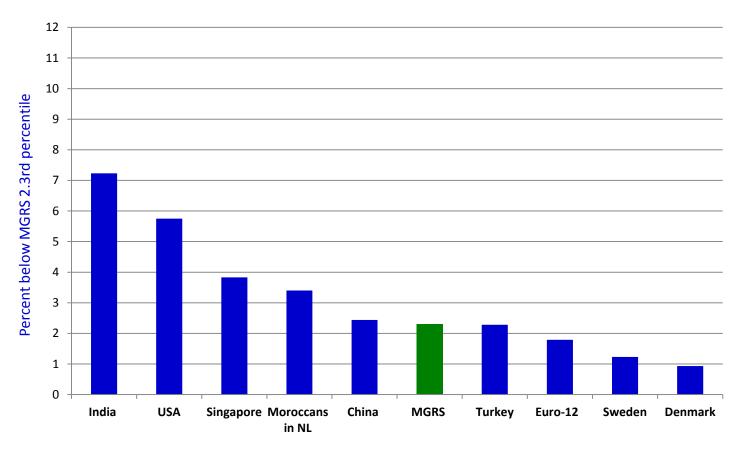
# Supplemental Figure 4. Estimated percentages of extreme outliers (height) at age 24 months. 4a.

Percentage of boys (blue) or girls (pink) estimated to be above the 97.7<sup>th</sup> percentile on the MGRS curves. 4b. Percentage of boys (blue) or girls (pink) estimated to be below the 2.3<sup>rd</sup> percentile on the MGRS curves. Moroccans in NL = Moroccan people living in the Netherlands.

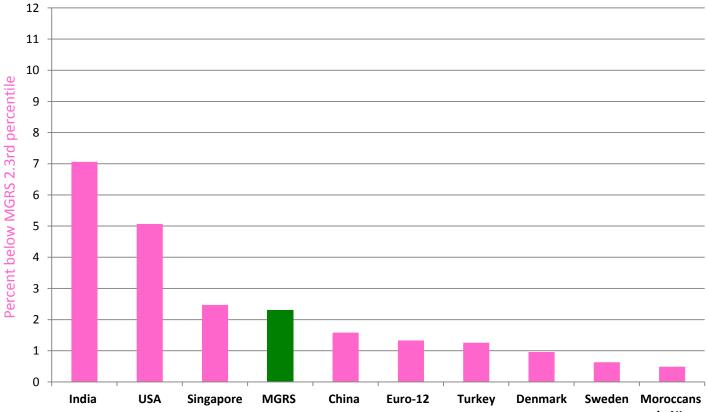


# **Supplemental Figure 4a**





# Supplemental Figure 4b



in NL

Supplemental Table 1. Studies included in this systematic review. The number of subjects reflects, to the best of our ability, the number of children included in this review and may be less than the total number of subjects in a given study. Thus, if a study of birthweight reported group sizes for each gestational age from 30 – 43 gestational weeks, we used information only for 37 – 41 weeks and reported only the number of subjects in the 37 – 41 week age groups here.

+#	First Author, year	Country or group	n, Type*	What was measured?**	Subject ages	Inclusion criteria	Exclusion criteria	Bias risk
1	Agarwal, 1994	India	2, 635; M	Wt, Ht, OFC	Birth – 6 years	Affluent according to study criteria (income, education level, other factors), well-nourished	_	Low
2	Albertsson-Wikland, 2002	Sweden	4,448; L	Wt, Ht, OFC	Birth – 18 years	Final year of school, Gotheburg, willing to provide health records	Gestational prematurity or postmaturity, chronic disease or medical treatment	Low
3	Alshimmiri, 2003	Kuwait	23.428; B	Wt	Birth	Live births in two Kuwaiti hospitals; data sorted by ethnicity, gestational age known; size data for each week from 37– 41 weeks stated in tables	Stillbirths, congenital malformations, statistically outlying measurements	Low
4	Anzo, 2002	Japan	16,621; CS	OFC	Birth – 6 years	Children measured in a national survey run by the Japanese Ministry of Health	_	Low
5	Atladottir, 2000	Iceland	138; L	Wt, Ht	Birth – 1 year	Singletons born between 37 – 41 weeks gestation to Icelandic parents	Birth defects or inborn long-term disease, mother did not receive prenatal care	Low
6	Beeby, 1996	Australia	22,309; B	Wt, Ht, OFC	Birth	Singletons born between 35 – 43 weeks; size data for each week from 37–41 weeks stated in tables	Stillbirths, extreme outliers	Low- Medium
7	Bertino, 2010	Italy	45,462, B	Wt, Ht, OFC	Birth	Singletons with two parents of Italian origin; size data for each week from 37–41 weeks stated in tables	Hydrops, major congenital anomalies, stillbirths	Low
8	Bonellie, 2008	Scotland	100,133; B	Wt	Birth	Live singletons registered in Scottish maternity data collection system; data for each week from 37–41 weeks stated in tables	Lethal/major congenital anomalies, statistically outlying measurements	Low

\* B = Birth only, L = Longitudinal, CS = Cross-sectional, M = Mixed Longitudinal

9	Bordom, 2008	Libya	1473; CS	Wt, Ht	Birth – 5 years	Healthy infants and children in two Tripoli and Al-Jabel Al-Gharbi; presence of a health establishment in the commune (quality of services assessed); methodology followed WHO methodology	Chronic disease	Low
10	Braegger, 2011	Switzerland	493; L	OFC	Birth – 19 years	Children of Swiss origin in the 1 <sup>st</sup> and 2 <sup>nd</sup> Zurich Longitudinal Study (urban populations)	-	Low- Medium
11	Cacciari, 2006	Italy	13,735; CS	Wt, Ht, BMI	2 years – 6 years	Children in infant schools (preschools) throughout Italy.	Parents not of Italian origin	Low- Medium
12	Cole, 2011	UK	9,443; B	Wt, Ht, OFC	Birth	Used existing UK90 data	-	Low
13	Copil, 2006	Spain	4,160; B	Wt, Ht, OFC	Birth	Healthy singletons born in a large hospital in Barcelona between 37 and 42 weeks gestation; size data for each week from 37–41 weeks stated in tables	Stillbirths, chronic or gestational maternal disease, maternal drug use, for non- Caucasian group, parents were non- Caucasian and were both of the appropriate ethnic group	Low
14	Cunha, 2007	Portugal	24,852, B	Wt	Birth	Singleton births at Hospital Fernando Fonseca, Amadora; size data for each week from 37–41 weeks stated in tables	Stillbirths, weight > 5 kg	Low- Medium
15	Davidson, 2008	Israel		Wt, Ht, OFC	Birth	Singletons; size data for each week from 37–41 weeks stated in tables	Stillbirths, statistically outlying measurements	Low- Medium
16	Dawodu, 2008	UAE	2,497, B	Wt, Ht, OFC	Birth	Singleton healthy UAE nationals born in at five hospitals in the UAE; size data for each week from 37–41 weeks stated in tables	Malformations, maternal diabetes, hypertension, heart failure or asthma	Low
17	El Mouzan, 2010	Saudi Arabia	35,279; CS	Wt, Ht, OFC	Birth – 19 years	Saudis living throughout the kingdom.	Birthweight <2500 g, chronic disorders including congenital malformations or syndromes known to affect growth	Low

	Fok, 2003	Hong Kong	8,557;	Wt, Ht, OFC	Birth	Singletons of ethnic Chinese origin born	Moribund condition at birth, major	Low-
18			В			between 24-43 weeks of gestation; size	congenital malformations, chromosomal	medium
						data for each week from 37–41 weeks	abnormalities, gestational age	
						stated in tables	undetermined	
	Fredriks, 2000	Netherlands	14,500;	Wt, Ht, OFC	2 weeks –	Children of Dutch origin (at least one	Diagnosed growth disorders, use of	Low
19			CS		21 years	Dutch parent, other parent western	medications known to interfere with growth	
						European)		
	Fredriks, 2004	Netherlands	2,882;	Wt, Ht, OFC	3 weeks –	Children with both parents Moroccan	Diagnosed growth disorders and children on	Low
20			CS		20 years	(99.5%) or one Moroccan parent and	medication known to interfere with growth	
						other parent born in North Africa. Living in		
						4 large cities in the Netherlands.		
	Guihard-Costa, 1997	France	16,877;	Wt, Ht, OFC	Birth	Singletons born in Hauts-de-Seine; size	One or more parents not born in France,	Low-
21			В			data for each week from 37–41 weeks	mother had undergone several prenatal	Medium
						stated in tables	exams.	
	Haschke, 2000	Europe	2,145; L	Wt, Ht, OFC	Birth –	Singletons born at term (37 – 44 weeks)	Intrauterine growth aberration, maternal	Low
22		(12 nations)			36 months		diabetes or epilepsy, father unknown,	
							birthweight <2500 g, congenital	
							malformations or metabolic diseases	
	Health and Human	United	Unknown;	Wt, Ht, OFC	Birth –	US children of different races and	Very low birthweight infants (infant charts	Low
23	Services, Dep't of	States	CS		18 years	ethnicities	ony), extreme statistical outliers	medium
	(CDC)							
	Hoey, 1990	Ireland	3,138;	OFC	5 –	Rural and urban Irish schoolchildren of	Chronic illnesses, non-Irish parents,	Low
24			CS		19 years	different SES classes (Ireland had a high	inadequate information obtained or	
						HDI ranking in 1990)	available	
	Hof, 2011	Netherlands	3871;	Wt, Ht, OFC	Birth –	For Dutch children: mother born in the	_	Low
25			L		3 years	Netherlands		medium
	Hsieh, 2006	Taiwan	1,298,389 B	Wt	Birth	Singletons with data in the Ministry of	Stillbirths, extreme outliers, registrations	Low
26						Interior birth registry, (data for each	entered > 3 months after birth	medium
						week from 37–41 weeks stated in tables)		
	Júlíusson, 2009	Norway	7,291; CS	Wt, Ht, OFC	Birth –	Children whose parents were natives of	Chronic diseases, prematurity	Low
27					5 years	Northern Europe		

28	Kandraju, 2011	India (south)	28,790 (OFC) – 31,391 (Wt); B	Wt, Ht, OFC	Birth	Singletons born in Level III hospital in South India; size data for each week from 37–41 weeks stated in tables	Major congenital anomalies, uncertain gestational age	Low- Medium
29	Kheng, 2011	Singapore	19,634; B	Wt	Birth	Singletons	Stillbirth, congenital anomalies, sex, parity, or gestational age unknown, extreme outliers, not Chinese, Malay, or Indian	Low- Medium
30	KiGGS, 2011	Germany	17,158; CS	Wt, Ht, OFC	Birth – 17 years	Nationwide study (all parts of Germany)	Prematurity (in children up to age 1), chronic renal or gastrointestinal diseases, primary or secondary short stature (e.g. Down syndrome, cystic fibrosis), tall stature due precocious puberty or disease, tuberculosis, microcephaly, macrocephaly, cancers, congenital heart disease, use of growth hormones, steroid use, ADHD-drug use, tuberculosis	Low
31	Korea Centers for Disease Control and Prevention, 2007	Republic of Korea	142,945; CS	Wt, Ht, OFC	Birth – 18 years	Children living throughout South Korea; 0- 6 years: children were enrolled in university hospitals and childcare facilities	_	Low- Medium
32	Karvonen, 2012	Finland	19,715; L	OFC	Birth – 7 years	Children born or living in Espoo; data came from an anonymized database	Diseases or medications affecting growth; measurements made outside scheduled visits, measurements outside ±5 SD	Low
33	Kramer, 2001	Canada	675,909; B	Wt	Birth	Singletons born in all provinces except Ontario (poor data quality) in a national file of information; size data for each week from 37–41 weeks stated in tables	Statistical outliers	Low- Medium
34	Kulaga, 2013	Poland	5,050	Wt, Ht	3 years – 6 years	Children throughout Poland in 81 different primary care practices	Diseases or medications affecting growth	Low
35	Kumar, 2013	India	19,501; B	Wt	Birth	Mother aged 20 – 39, early ultrasound to determine fetal age	Birthweight ±3 SD from mean, maternal hypertension or diabetes, heart disease, and other diseases	Low- Medium

36	Lavallée, 1988	Canada (Cree people)	764; CS	Wt, Ht, OFC	Birth – 5 years	Cree children living in St. James Bay, Quebec	One non-Cree parent or two non-Cree grandparents; children with proven growth problems, diabetes in the mother, congenital disorders, anemia, recent viral illness	Low- Medium
37	Lee, 2006	Republic of Korea	18,427; B	Wt, Ht, OFC	Birth	Births at 51 hospitals in South Korea	-	Low- Medium
38	Loke, 2008	Singapore	19,249	Wt, Ht, OFC	Birth – 6 years	Children attending Singapore polyclinics	-	Low- Medium
39	Marwaha, 2011	India	64,629 (3-18 years); 2,459 (3-5 years)	Wt, Ht	3 years – 18 years	Children attending private schools in 4 geographical zones of India (north, south, east, west)	_	Low
40	Mazurin, 2000	Russia	Unknown	Wt, Ht, OFC	Birth – 18 years	Russian infants, children, and adolescents	-	Low- Medium
41	McCowan, 2004	New Zealand	10,292; B	Wt	Birth	Singletons born in the National Women's Hospital, Auckland	Stillbirths, congenital abnormalities, preterm births	Low
42	Michaelsen, 1994	Denmark	156; L	Wt, Ht, OFC	Birth – 1 year	Singletons born in Hvidovre & Herlev Hospitals, Copenhagen; gestational age 37–41 weeks	Malformations or perinatal disease, parents not Danish, birthweight for gestational age between 10 <sup>th</sup> and 90 <sup>th</sup> percentiles	Low
43	Moon, 2000	Republic of Korea	142,945; CS	Wt, Ht, OFC	Birth – 18 years (used birth data only)	Children living throughout South Korea; 0- 6 years: children were enrolled in university hospitals and childcare facilities	_	Low- Medium

44	Nickavar, 2007	Iran	2,832; B	Wt, Ht, OFC	Birth	Neonates born in government hospitals in Tehran at 37 – 42 weeks' gestation whose mothers had appropriate prenatal care; suitable SES	Cigarette smoking, premature rupture of membranes, malnutrition, preeclampsia or eclampsia, chromosomal anomalies, other anomalies in the neonate, maternal hypertension, diabetes, heart failure, autoimmune problems, placental disease, infection	Low
45	Nielsen, 2010	Denmark	4,105; L	Wt, Ht	Birth – 5 years	Singletons	Preterm birth, conditions affecting growth	Low
46	Neyzi, 2008	Turkey	4,493 (Birth - 5 years); L	Wt, Ht, OFC	Birth – 18 years	Economically advantaged children in Istanbul	-	Low- Medium
47	Olafsdottir, 2005	Iceland	436; B	Wt	Birth	Singletons born at term (>37 weeks)	Pre-elampsia, hypertension, diabetes, stillbirths, preterm birth	Low
48	Olsen, 2010	United States	57,115 (37- 41 weeks); B	Wt, Ht, OFC	Birth	Singletons born at 22-42 weeks in a large pediatric medical group; size data for each week from 37–41 weeks stated in tables	Stillbirths, mortality before discharge, congenital anomalies, physiologically improbably measurements, unknown sex, missing data	Low
49	Palczewska, 2001	Poland	6,366; CS	Wt, Ht, OFC	1 month – 18 years	Children in Warsaw selected randomly from registry at Institute of Mother and Child (ages 0–3) and from local schools (ages 4–18).	-	Low- Medium
50	Patwari, 1988	Nigeria	1,530	Wt, Ht, OFC	Birth	Singletons from privileged/well-to-do families born in the University of Maiduguri Teaching Hospital	Stillbirths, preterm births, congenital malformations, maternal pre-eclampsia or eclampsia, antepartum hemorrhage, anemia, sickle cell disease	Low

	Patsourou, 2012	Greece	206;	Wt, Ht, OFC	Birth –	Breastfed infants in Thessaloniki and other	Not exclusively breastfed up to 6 months,	Low
51			L		3 years	parts of Greece, born between 38 and 42	parents not married, parents not healthy,	
						weeks gestation with normal Apgar scores	parents smokers, mother a vegan or	
							vegetarian, birthweight < 2,500 g, health	
							conditions that interfere with growth	
	Remontet, 1999	France	7,423;	Wt, Ht, OFC	Birth –	Schoolchildren living in Rhone and Isère	Preterm birth	Low-
52			L		6 years	for whom gestational age at birth and		Medium
						length, weight, and OFC had been		
						recorded in their health booklets.		
	Rios, 2008	Mexico	79,706;	Wt	Birth	Singletons born between 30-44 weeks	Stillbirths, congenital malformations,	Low
53			В			gestational age in hospitals in the state of	statistical outliers (birthweights ± 2.58 SD	
						Chihuahua; size data for each week from	from expected values)	
						37–41 weeks stated in tables		
- 4	Roberts, 1999	Australia	664024;	Wt	Birth	Singletons born throughout Australia from	Stillbirths, mother born outside Austsralia,	Low-
54			В			20-44 weeks; size data for each week	extreme statistical outliers	Medium
						from 37–41 weeks stated in tables		
	Roelants, 2009	Belgium	15,989;	Wt, Ht, OFC	Birth –	Subjects living in Flanders aged 0 – 25	Preterm birth (<37 weeks) in the group	Low
55			CS		21 years	years of age	aged 0–3 years, non-Belgian origin, growth	
							disorders, severe chronic disease, use of a	
							medication that may affect growth	
50	Rush, 2008	New	659;	Wt, Ht	Birth –	Pacific Islanders living in South Auckland	Low birthweight, baby not home within 6	Low
56		Zealand	L		4 years	(at least one parent self-identified as being	weeks of birth, maternal diabetes. <b>NOTE</b>	
						of Pacific Island descent), permanent New	(not exclusion): Subgroup analysis of WHO	
						Zealand residents.	compliant mothers (non-smoking,	
							breastfeeding)	
	Rush, 2010	New	722;	Wt, Ht	Birth –	Pacific Islanders living in South Auckland	Diabetes in the mother	Low-
57		Zealand	L		6 years	(at least one parent self-identified as being		Medium
						of Pacific Island descent), permanent New		
						Zealand residents.		

	Rush, 2013	New	1,398;	Wt, Ht, OFC	Birth –	Pacific Islanders living in South Auckland	Diabetes in the mother	Low-
58		Zealand	L		10 years	(at least one parent self-identified as being of Pacific Island descent), permanent New Zealand residents.		Medium
59	Saari, 2011	Finland	~73,000 CS-L	Ht, Wt	Birth – 20 years	Patients attending public primary care clinics in Espoo (94.4% of Finnish origin)	Diagnosis or medications affecting growth; prematurity	Low
60	Sankilampi, 2013	Finland	188922; B	Wt, Ht, OFC	Birth	Singletons or twins in the Finnish Birth Register (twin data not used in this systematic review); size data for each week from 37–41 weeks stated in tables	Stillbirths, congenital anomalies, statistical outliers, sex or gestational age unknown; triplets; maternal smoking or smoking status unknown; maternal hypertension or diabetes; in vitro fertilization	Low
61	Schienkiewitz, 2011	Germany	17,158; CS	OFC	3 months– 18 years	Part of the KiGGS study; nationwide study (all parts of Germany)	Prematurity (in children up to age 1), chronic renal or gastrointestinal diseases, primary or secondary short stature (e.g. Down syndrome, cystic fibrosis), tall stature due precocious puberty or disease, tuberculosis, microcephaly, macrocephaly, cancers, congenital heart disease, use of growth hormones, steroid use, ADHD-drug use, tuberculosis	Low
62	Segre, 2001	Brazil	7,925; B	Wt	Birth	Singletons whose mothers were from a high-income population and who had prenatal care; size data for each week from 37–41 weeks stated in tables	Infants with congenital malformations, stillbirths	Low
63	Skaerven, 2000	Norway	1,655,058; B	Wt	Birth	Singletons in the Medical Birth Registry of Norway; size data for each week from 37– 41 weeks stated in tables	Stillbirths, congenital malformations, cesarean sections	Low

64	Sobraillo, 2007	Spain	6,443: CS	Wt, Ht, OFC	Birth –	Used CS data here. Births in Hospital de		Low-
04			600: L		18 years	Basurto; hildren attending public and	-	Medium
						private pediatric clinics; students from		
						public and private schools		
~-	Sreeramareddy,	Nepal	400;	Wt	Birth	Singletons born in Western Regional	Congenital anomalies/dysmorphic features,	Low-
65	2008		В			Hospital, Pokhara	preterm birth (<37 weeks)	Medium
	Tanaka, 2013	Japan	647;	Wt, Ht, OFC	Birth –	Term birth (37 – 42 weeks), exclusive	Maternal smoking	Low-
66			L+CS		2 years	breastfeeding >4 months		Medium
	Tinnggaard, 2013	Denmark	1,792;	Wt, Ht, OFC	Birth –	High SES Caucasian children living around	Chronic diseases, use of medicines affecting	Low
67			L		20 years	Copenhagen; gestational age ≥37 and ≤42	growth	
						weeks; subset of singleton breastfed		
						children of nonsmoking mothers who		
		<u> </u>	444.000.0			were not small or large for gestational age		
68	Uehara, 2011	Japan	144,980; B	Wt	Birth	Singletons in the Japan Society of	Stillbirths, Apgar score = 0 at 1 & 5 minutes,	Low
00						Obstetrics and Gynecology Database; size data for each week from 37–41 weeks	hydrops, malformations, sex or gestational age absent	
						stated in tables	age absent	
	Urquia, 2011	Argentina	3,322,317	Wt	Birth	Singletons and twins (twins data not used	Stillbirths, records with missing information	Low-
69		-	В			here) born in Argentina at any gestational	(sex, birthweight, gestational age, mother's	Medium
						age; size data for each week from 37–41	place of residence,)	
						weeks stated in tables		
	Vignerová, 2006	Czech	18,584 (0–6	Wt, Ht, OFC	Birth –	Infants, children, and adolescents living	_	Low-
70		Republic	years);		19 years	throughout the Czech Republic		Medium
			CS					
71	Voigt, 2010	Germany	2,093,205;	Wt, Ht, OFC	Birth	Singletons born throughout Germany	Statistically outlying measurements	Low-
71			В			between 20 and 43 weeks' gestation; size data for each week from 37–41 weeks		Medium
						stated in tables		
	Webster, 2013	Australia	159;	Wt, Ht, OFC	Birth –	Aboriginal infants born and living in	Birthweight < 1,500 g	
72	WEDSIEL, 2015	Austidiid	139,		2 years	Sydney, New South Wales		Low-
, -			L		2 years	Syulley, New South Wales		Medium

#	First Author, year	Country or group	n, Type*	What was measured?**	Subject ages	Inclusion criteria	Exclusion criteria	Bias risk
_	(Same data; different languages)	(maintand)			, years		malnourishment, physical handicap	
79	Zong, 2013 Li, 2009	China (mainland)	69,760; CS	Wt, Ht, OFC	Birth – 7 years	Resident of one of seven provincial capital cities	Premature birth, Temporary residents, birthweight <2500 g, chronic illness,	Low
78	Zaki, 2008	Egypt	27,826; CS	OFC	Birth — 18 years	Children living in greater Cairo	Low SES, major genetic or organic diseases known to affect growth	Low
77	Yunis, 2007	Lebanon	23,234; B	Wt, Ht, OFC	Birth	Singletons born in 9 tertiary care centers throughout Lebanon at 28-42 weeks gestation; size data for each week from 37–41 weeks stated in tables	Stillbirths, missing data	Low- Medium
76	Wright, 2011	UK	15,910; L	OFC	Birth – 3 years	Children in the Southampton Women's Survey and the Avon Longitudinal Study	Preterm birth (<37 weeks)	Low- Medium
75	Willows, 2011	Canada	1,057; B	Wt, Ht, OFC	Birth	Cree ethnicity, singletons, term birth (37– 41 weeks)	_	Low- Medium
74	WHO MGRS, 2007	MGRS	7,551; L & M	OFC	Birth – 5 years	High SES, non-smoking mother, breastfed infants	_	Low- Medium
73	WHO MGRS, 2006	MGRS	7,551; L & M	Wt, Ht	Birth – 5 years	High SES, non-smoking mother, breastfed infants	_	Low- Medium