Is the World Health Organization’s multicentre child growth standard an appropriate growth reference for assessing optimal growth of South African mixed-ancestry children?

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In South Africa (SA), it has been estimated that one-third of boys and 25% of girls under the age of 5 years are stunted, according to the World Health Organization (WHO) Multicentre Growth Reference Study. During the past decade, research in developed and developing countries has shown that the international growth standard overestimates stunting and/or wasting when compared with population-specific growth references. Population-specific growth references typically incorporate genetic and environmental factors and can therefore better inform public health by identifying children who may be at risk for malnutrition, or who may be ill. Using the universal growth standard in SA may not be accurately assessing growth. In this article, environmental and genetic factors, and their influence on growth, are reviewed. These points are illustrated through a brief history of the peopling of SA, with an understanding of the socioeconomic and political climate – past and present. We discuss the uniqueness of certain population groups in SA, with contributions regarding some of the shortest peoples in the world and a history of sociopolitical inequities, which may mean that children from certain population groups who are perfectly healthy would underperform using the universal growth standard. Therefore, we suggest that a local population-specific growth reference would serve to better inform public health policies, and address childhood health equity and physical developmental pathways to adult health risk status.


The World Health Organization (WHO) international growth standard was intended as an indication of how children should be growing under the best possible circumstances, irrespective of genetic influences.1-2 These circumstances would include: no health, environmental or economic constraints; non-smoking before or after birth; minimum of exclusive 6 months’ breastfeeding; term births (≥37 - <42 weeks); and single births.3 To understand where growth faltering does occur within the growth period, and the explanatory factors that influence the faltering, local research such as that by Norris et al.4 and Schoeman et al.5 is important to understand growth within certain South African (SA) population groups. The current article intends to expand the knowledge base of growth in a different region of SA. The article aims to highlight why there may be plausible reasons (genetic and environmental conditions) to review the WHO growth standard, adopted in SA in 2011,5 as an appropriate tool to analyse the growth of mixed-ancestry children younger than 5 years in SA. Although many factors influence pre- and postnatal growth, this paper focuses on ancestral genetic influences and environmental living conditions.

Currently, <100 countries worldwide use the WHO Multicentre Growth Reference Study (MGRS), which was developed from longitudinal and cross-sectional data between 1997 and 2003. The aim of the WHO was to provide a universal human growth standard to globally track the general health of children.5 It was developed using children from six major regions of the world (including the USA, Brazil, Ghana, Oman, India and Norway) to determine whether children grew at the same rate (growth trajectory) under the best possible circumstances (optimal living conditions), irrespective of genetic influences.6 Although the WHO growth standard is an indication of how children should grow, it is also important to determine how children do grow within a specific set of environmental and genetic influences, i.e. growth reference.3,5 It may be the case that many countries, especially developing nations, possibly do not have the necessary resources (money, time, trained personnel) to develop population-specific growth references, and therefore have had to rely on the WHO growth standard.

In 2011, the SA government adopted the MGRS growth standards5 as part of a new policy called the Strategic Plan for Maternal, Newborn, Child and Women’s Health (MNCWH) and Nutrition in SA 2012 - 2016.6 This was to enable fulfilment of some of the key health-related millennium development goals (MDGs),7 which specifically dealt with health systems, child survival, maternal health, building effective primary health systems and family planning.3 Therefore, the overarching aim of the 2011 SA policy was to improve primary healthcare for mothers and children, and for the prevention or early diagnosis of diseases/health issues. The revised Road-to-Health Booklet (RtHB) contained the MGRS 2006 growth charts (section D, point 2 of the policy).6 The RtHB was designed to track the health of mothers and their children more holistically by including all vaccinations, booster
shots, HIV and TB testing, and growth tracing. It also includes advice for primary caregivers regarding breastfeeding practices, maternal interaction with children and milestones for cognitive and motor skills development (National Department of Health, 2012). It was created as an all-inclusive summary of a child’s development from birth to 59 months (~5 years).

Although many countries use the MGRS, several studies in India, Peru and Vietnam, China and a number of other countries have shown a significant difference in growth patterns of children from birth to 5 years compared with the MGRS growth standard. Studies have demonstrated that population-specific growth references are more accurate measures of growth. Singhul noted that while the prevention of stunting, as well as the promotion of linear growth in small-for-gestational-age or preterm children, has been shown to be beneficial for neurodevelopmental and other health outcomes, the optimal pattern of infant weight gain is likely to differ depending on the population. Natale and Rajagopalan emphasise that otherwise healthy children who do not conform to the MGRS growth standard have a higher probability of misdiagnosis of malnutrition or growth disorders, and their subsequent treatment may lead to an additional burden of disease later in life. Rapid weight gain and postnatal growth acceleration in healthy, full-term infants, often in low- and middle-income country settings, have been associated with a greater risk for obesity and non-communicable diseases later in life. These findings emphasise the importance of applying an appropriate growth reference for infants and children within a specific set of environmental conditions and genetic influences, to mitigate the risks of stunting and obesity.

Therefore, there may be a case for developing population-specific growth charts to better inform SA’s healthcare system and policy development, to optimise child health and future preventive healthcare for at-risk populations. In this article, we address whether the MGRS is an appropriate standard for assessing the optimal growth of mixed-ancestry children younger than 5 years in an SA population group. To provide background and context, we begin with a discussion of the impact of genetic and environmental influences on early childhood growth, followed by a discussion of these factors within SA’s mixed-ancestry population.

**Factors that affect growth: Genetic and environmental influences**

Growth is part of human development and is partly defined as the increase of bone size and body mass. It is influenced by various interrelated factors such as genetics and the living environment. Genetic influences are the causal mechanisms that influence biological growth, resulting in the expression of certain phenotypic traits such as height and weight. These are the result of generations of factors that affect genetic admixture, including sexual selection, gene flow, genetic drift, intergenerational effects and micro-evolutionary adaptations. The ancestral influences include micro-evolutionary causal mechanisms and intergenerational effects that may drive differences in height-for-age and weight-to-height-for-age among population groups in various ecogeographical regions of the world. One major mechanism driving body shape was thermoregulation. In warmer climates, humans have adapted a more linear shape (arms and legs) in warmer climates but a stockier body shape (broader chest and shoulders) in colder climates. Another causal mechanism is the amount of exposure to ultraviolet (UV) radiation, which can affect population groups in the same topographical area. For example, within sub-Saharan Africa, the Maasai (Kenya and Tanzania) are among the tallest people in the world, whereas African pygmies (Cameroon, Gabon, Central African Republic, Democratic Republic of Congo, southern Rwanda and Nigeria) are the shortest. According to O’dea, the difference in body size between these two groups is most likely due to UV exposure. Both groups have biological adaptations that improved their survival over generations in a unique ecogeographical habitat. If different population groups have significant variation in adult height, there may be a need to further explore growth within an SA context to expand on the research of Norris et al. Growth deviation among SA mixed-ancestry children from the WHO growth standard could be informative to the health sector if regression analyses of anthropometrical measurements and explanatory variables can highlight why growth deviations exist within an SA context.

In addition to genetic influences, environmental (living) conditions can impact the growth trajectory, including nutritional adequacy, hygiene and/or exposure to disease. During adverse living conditions, physiological maintenance is more important in lieu of growth. Most of our height comes from the growth and development of our skeleton. However, when the primary functions of the body are prioritised to sustain life, skeletal growth is retarded, while the individual survives. While accepting the influence of genetic and intergenerational effects on linear growth, Steckel has described stature as a function of access to resources, and human growth as a net measure of nutrient input (food) v. metabolic output (physical activity and disease). It has been shown that in a hostile (nutrient-deficient, disease-prone and/or high metabolic output) environment, the infancy-childhood transitional age (2 - 3 years) is deferred. During this transitional change, increased growth hormone insulin-like growth factor 1 (IGF1) is released into the body. This growth-stimulating hormone is known to trigger the activity of osteoblasts (bone) and chondrocytes (cartilage) to promote growth. If living conditions are inadequate, the amount of IGF1 for bone and cartilage growth is reduced, negatively impacting skeletal maturation and consequently height potential. If a child’s environmental conditions improve before fusion of the epiphyseal plates of their bones, they may still reach their full height potential. This is known as catch-up growth, when the body accelerates growth and the child’s growth trajectory is more rapid than average, making up for loss of linear growth during adverse conditions, and hence returning children to their normal growth curve.

**SA and the international growth standard: A case study**

We explore the implications for discrepancies between the MGRS growth standard and population-specific growth trajectories, particularly for the mixed-ancestry population in SA. Genetic admixture, in combination with unique sociopolitical and socioeconomic conditions, has created a unique population. Together, these factors possibly influence growth rates and development patterns of SA children. Using the WHO growth standard, ~40% of SA children younger than 5 years of age are stunted. Conversely, the percentage of children classified as overweight in SA was twice the international average (6.1%) for the same age group. The specific concern with the use of the international MGRS in SA is the percentage of children younger than 5 years in the middle- and top-wealth quintiles
(24% and 13%, respectively), who are estimated to be stunted (below the 3rd percentile). The latest SA demographic and health survey based on the MGRS growth standard, reported stunted growth for 1 in 3 boys and 1 in 4 girls. It is doubtful that these children do not have access to adequate nutritional resources to sustain their growth, considering that many of them fall in the middle- and upper-wealth quintiles. It is also unlikely that stunting in these children can be attributed to daily living conditions, i.e. disease-prone areas, inadequate sanitation/hygiene or limited access to healthcare. Rather, there might be a predisposition for shorter stature in particular population groups in SA.

In contrast to the stunting phenomenon, SA also has one of the highest obesity prevalences (twice the international average) for children younger than 5 years of age. Is this because children eat poorly balanced meals or have a higher intake of energy-dense, nutrient-poor foods? According to Statistics SA, in 2015 two-thirds of the population lived below the upper-bound poverty line of ZAR992 (USD70) per person per month. With such little purchasing power, most would buy cheaper staple foods such as potatoes, rice, wheat and maize products. Could this impact children's and hence adults' rates of obesity? Is there a correlation between the high percentage of obesity and an international growth standard suggesting children are stunted; i.e. are the caregivers of children who are estimated to be stunted advised to increase the children's daily food intake, thus creating a greater weight-to-height-for-age ratio? To shed light on these matters, it is important to consider factors that influence the growth of children in SA.

According to the government classification system, the people of SA are divided into five population groups, i.e. black, coloured, white, Indian/Asian and other. The original inhabitants of southern Africa were click-speaking foragers, generally known today as San and Khoe. These inhabitants were later joined by the southern migrating agropastoral Bantu-speaking peoples (in reference to the Niger-Kordofanian phylum of African languages) from west and central Africa. Genetic research shows admixture between these migrants and the people from the Niger-Congo, east Africa, the rainforest pygmies, and finally the San and Khoe in southern Africa. Several different population groups reside in SA, and based on their geographical location, they have diverse genetic contributions from these four main groups. A thousand years later, colonists from Europe (e.g. Dutch, British, French, German, Spanish) joined the genetic melting pot that forms part of the contemporary population of SA.

With the arrival of Europeans and colonial rule, admixture with the local inhabitants was initially not forbidden. Later, racial segregation was introduced – first socially and then by law under apartheid. When racial segregation became law (the Prohibition of Mixed Marriages Act No. 55 of 1949 and the Immorality Act No. 21 of 1950), the descendants from this admixture were known as coloured, a term still used by the democratically elected SA government. For the purposes of this discussion, this population group will be referred to as South Africans of mixed ancestry. This term was decided upon, as their genetic heterogeneity is a more recent (c. 360 years) result of admixture. Petersen described this population group as having the highest (30%) heterozygosity in the world, with the most diverse genetic admixture between individuals within the same population. They have varied genetic contributions from southern Africa – the indigenous San and Khoe, Bantu-speaking Africans, the colonial descendants and the descendants of slaves and indentured labourers brought to the region. Geographically distinct communities also vary in the percentage contribution from the ancestral genetic input. Some individuals sampled by Petersen showed ~64% San and/or Khoe genes.

Individuals with a high contribution of indigenous San and/or Khoe genes may be predisposed to shorter stature, as genetically these people have short stature, with men reaching an average adult height of 1.5 m. Their linear shape and short stature have been described as biological adaptations to their ecoregographical habitat and food availability. Contemporary San and/or Khoe children have a slow growth period in the first 10 years of their life (40% of adult body size), which is said to be a nutritional adaptation, with a notable adolescent growth spurt. Therefore, their growth trajectory would be expected to differ from the MGRS growth standard. In addition to a genetic predisposition to short stature, many people in SA live in poor socioeconomic conditions. From the mid-19th century to its end, sociopolitical circumstances led to severe socioeconomic inequalities between the SA government's bureaucratically classified population groups. Consequently, many people have been impacted regarding, e.g. quality of education, income prospects, healthcare accessibility, spatial restriction and legalised marital segregation between the population groups (i.e. no admixture). Of the 40% of South Africans who lived below the lower-bound poverty line of ZAR647 per person per month in 2015, 23% were individuals of mixed ancestry.

Urbanisation of people may have increased their accessibility to readily available nutrient-rich food and/or medical facilities, but income levels promoting power-of-purchase have not. Currently, health inequities or disparities are still commonly found among South Africans. This situation is due to social determinants of health, including social, environmental, cultural and physical factors that they are born into, grow up in, and function in throughout their lifetimes. In summary, the lack of, or limited access to resources may have created an intergenerational effect of shorter stature among certain SA population groups, even if at present the children are reared in better living conditions than in the past.

Conclusion

Many factors that affect growth and the use of growth standards or references may not have been included in this article; however, the overarching aim was to stimulate a discussion pertaining to the WHO standards and its use regarding mixed-ancestry children. The data presented show the diversity of the mixed-ancestry population in SA, and that even a single local growth reference to encompass this broad genetic diversity is unlikely to be effective. Implementation of yet another growth reference will be costly; however, we suggest the need to expand the knowledge base of anthropometric data for different regions in SA in addition to factors that contribute to linear growth, and those that negatively affect it, by conducting further research in other ecoregographical areas, as demonstrated by Norris and Schoeman. Such research can inform the health sector as to why, based on specific explanatory variables, children of mixed ancestry, for example, are under-performing in growth – as the MGRS states. Are these children merely predisposed to a normal shorter stature or is it truly a stunting phenomenon? If the former, using the MGRS growth standard, mixed-ancestry children could possibly have a high probability of being diagnosed as undernourished and their parents may be encouraged to increase their food intake, a factor which may contribute to the high percentage of overweight children and the possibility of an increased burden of disease later in life. Each research puzzle piece regarding children’s growth can further assist paediatric clinicians and forensic pathologists with their daily duties. All things considered, these data...
show that investigating the optimal growth of SA mixed-ancestry children and understanding population-specific growth references would serve to better inform public health policies to address childhood health equity and developmental pathways to adult health risk status according to the MDGs in Africa.

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