Normal values of respiratory oscillometry in South African children and adolescents

Shaakira Chaya [1], Rae MacGinty[1], Carvern Jacobs[1], Leah Githinji[1], Sipho Hlengwa[1], Shannon J. Simpson[2,3], Heather J. Zar[1], Zoltan Hantos [4,5] and Diane M. Gray [1,5]

[1]Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital and SA-MRC Unit on Child and Adolescent Health, University of Cape Town, Cape Town, South Africa. [2]Wal-yan Respiratory Centre, Telethon Kids Institute, Perth, Australia. [3]School of Allied Health, Curtin University, Perth, Australia. [4]Department of Anaesthesiology and Intensive Therapy, Semmelweis University, Budapest, Hungary. [5]These authors contributed equally.

Corresponding author: Diane Gray (diane.gray@uct.ac.za)

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The first respiratory impedance reference equations for African children and adolescents are established to aid in early identification and diagnosis of respiratory impairment https://bit.ly/3HNxKvt

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Abstract

Introduction Noninvasive measurement of respiratory impedance by oscillometry can be used in young children aged from 3 years and those unable to perform forced respiratory manoeuvres. It can discriminate between healthy children and those with respiratory disease. However, its clinical application is limited by the lack of reference data for African paediatric populations. The aim of the present study was to develop reference equations for oscillometry outcomes in South African children and adolescents.

Methods Healthy subjects, enrolled in the Drakenstein Child Health Study, HIV-uninfected adolescents in the Cape Town Adolescent Antiretroviral Cohort and healthy children attending surgical outpatient clinics at Red Cross War Memorial Children's Hospital were measured with conventional spectral (6–32 Hz) and intra-breath (10 Hz) oscillometry. Stepwise linear regression was used to assess the relationship between respiratory variables and anthropometric predictors (height, sex, ancestry) to generate reference equations.

Results A total of 692 subjects, 48.4% female, median age of 5.2 years (range: 3–17 years) were included. The median (interquartile range (IQR)) for weight for age z-score and height for age z-score was −0.42 (−1.11–0.35) and −0.65 (−1.43–0.35), respectively. Stepwise regression demonstrated that all the variables were significantly dependent on height only. Comparison to previous reference data indicated slightly higher resistance and lower compliance values in the smallest children.

Conclusion We established the first respiratory oscillometry reference equations for African children and adolescents, which will facilitate use in early identification and management of respiratory disease. Our results suggest differences in oscillometry measures by ancestry but also highlight the lack of standardisation in methodology.

Introduction

Measurement of lung function in early childhood is important for the diagnosis and management of lung disease, to promote optimal lung growth and development. Early life lung function predicts later morbidity and mortality [1, 2]. Spirometry is currently the most commonly performed lung function test, but its use is limited in young children as it requires a forced expiratory manoeuvre, mostly only feasible in children ⩾5 years of age. In addition, it is relatively insensitive to detect early lung disease and is a poor measure of peripheral airway function [3].

Oscillometry is an attractive, feasible option in preschool children as it is a simple noninvasive test, requires minimal cooperation and can be used to follow lung function across the life course. Oscillometry measures the response of the respiratory system to an external small-amplitude oscillatory signal of

medium (*e.g.* 4–40 Hz) frequencies which is superimposed on tidal breathing. The oscillatory pressure–flow relationship reflects the mechanical impedance of the respiratory system (Z_{rs}), which consists of two components, namely resistance (R_{rs}) and reactance (X_{rs}) [4, 5].

The conventional multifrequency or spectral values of Z_{rs} are generally obtained for a number of consecutive whole breaths (or, more recently, as mean values for the inspiratory and expiratory phases). In contrast, the novel intra-breath measurements, collected with a single-frequency tracking signal, follow the changes in R_{rs} and X_{rs} *within* the breathing cycle [6]. In particular, intra-breath oscillometry focuses on the zero-flow points (end inspiration and expiration); these Z_{rs} values are less influenced by the breathing pattern, which is often variable in young children and reflects less the contribution of the flow-dependent extrapulmonary airways. Owing to the ability to measure R_{rs} and X_{rs} at specific points of the respiratory cycle and thus estimate the tidal changes in respiratory mechanics, intra-breath oscillometry has proved more sensitive than standard measures to assess airway obstruction, ventilation inhomogeneity, asthma control and respiratory disease risk [7–10].

Accurate interpretation of lung function measurements depends on the availability of a robust reference standard specific to the population assessed. Population differences in lung function such as anthropometric, sociocultural and environmental characteristics are well recognised [11–13]. Most oscillometry reference standards are specific for Caucasian populations from Europe, North America and Australia between the ages of 2 and 16 years [14–27]. Studies of non-Caucasian participants include Mexican, Thai, Emirati, Korean, Taiwanese, Turkish and Indian population groups with an age range between 3 and 17 years [28–34]. While reference equations derived from Caucasian data may be adequate for Caucasian South Africans, the most recent census describes the South African population as multi-ancestry: 80.7% Black African, 8.8% mixed ancestry (which would include African ancestries, Asian, Caucasian, amongst others) and 2.6% Indian/Asian [35]. Currently, no oscillometry reference equations exist for African populations, despite the high burden of respiratory disease in the region. Additionally, normative data on the novel intra-breath oscillometry measures are scant [8] and are not available for paediatric populations beyond infancy [9, 36]. Recent technical standards for oscillometry equipment and testing, developed by a European Respiratory Society (ERS) task force have highlighted the lack of appropriate paediatric reference standards, especially for underrepresented populations [37].

The aim of this study was to develop reference values for spectral and intra-breath oscillometry measures in healthy South African children and adolescents.

Methods

Participants

Healthy children and adolescents were enrolled from three South African groups: the Drakenstein Child Health Study (DCHS), a birth cohort study [38]; the Cape Town Adolescent Antiretroviral Cohort (CTAAC), including a healthy HIV-uninfected control group [39]; healthy children with no history of respiratory illnesses attending surgical outpatient clinics at Red Cross War Memorial Children's Hospital, Cape Town (HCSOC). Participants from the DCHS birth cohort were tested annually (collected 2015–2020) from 3 to 7 years, with one randomly selected time point per individual included in this study to remove any bias in the sample. Participants from CTAAC (11–15 years) and HCSOC (8–17 years) were tested between 2018 and 2020. All participants were of African ancestry, self-identifying as either Black African or mixed ancestry and from predominantly low socioeconomic communities [38, 39]. Socioeconomic status was determined from questionnaires completed at study visits and was based on household income, including accessed social grants. Household smoking was self-reported.

All children were healthy at the time of testing. Prior to testing they were screened for respiratory symptoms (cough, wheeze, difficult breathing) using a clinical and symptom study questionnaire based on the validated International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. Those with acute lower respiratory tract illness (LRTI) or any respiratory illnesses in the previous month were excluded from testing. LRTI was defined as per the World Health Organization (WHO) case definition [40]. Children with any chronic respiratory conditions (self-reported or doctor diagnosed) including recurrent or persistent wheeze as well as chronic illnesses such as HIV infection, cardiac or neurological disorders were also excluded.

Ethics

The study was approved by the University of Cape Town Faculty of Health Sciences (048/2020; 082/2018; 423/2012). Parents or legal guardians gave written informed consent in their first language and assent was given by all youth 7 years and older.

Lung function measurements

Oscillometry data were obtained using the same custom-made equipment (INCIRCLE wavetube system, University of Szeged, Hungary) [41, 42] by a trained team of three technologists. Measurements were made with the individual sitting comfortably, breathing through a mouthpiece and filter, nose clip in place and the cheeks firmly supported, in accordance with published consensus guidelines [37]. The oscillometry system operated with either a pseudo-random signal in the 6–32 Hz range (conventional oscillometry) or a 10 Hz intra-breath tracking frequency; the latter corresponds to a 0.1-s temporal resolution allowing identification of the zero-flow Z_{rs} values (see below). Measurements consisted of a maximum of five 16-s epochs of multifrequency oscillations to yield a minimum of three acceptable measurements and one 16-s intra-breath recording, repeated if necessary to obtain a minimum of five regular breaths, *i.e.* without any vocal cord noise, apnoea, irregular breathing pattern, glottic closure, leak or sighs.

Conventional oscillometry measures included R_{rs} at 6 Hz (R_6), 8 Hz (R_8) and 10 Hz (R_{10}), X_{rs} at 6 Hz (X_6), 8 Hz (X_8) and 10 Hz (X_{10}), frequency dependence of R_{rs} (R_6–R_{20}), resonance frequency (F_{res}) and the absolute area of the X_{rs} *versus* frequency plot between 6 Hz and F_{res} (A_x). Additionally, mean respiratory system resistance (R), inertance (I) and compliance (C) were determined from model fitting to the measured Z_{rs} data in the frequency range 10–20 Hz for R and 6–32 Hz for I and C [41–43]. This procedure is illustrated in supplementary figure S1.

The intra-breath measurements were characterised by R_{rs} at end inspiration (R_{eI}) and at end expiration (R_{eE}), X_{rs} at end expiration (X_{eE}) and end inspiration (X_{eI}), and their tidal changes R_{eE}–R_{eI} (ΔR) and X_{eE}–X_{eI} (ΔX).

Statistical analysis

Data were analysed using STATA 14.1 (STATA Corporation, College Station, TX, USA) and presented as frequencies, proportions, median and interquartile range (IQR) as appropriate. A natural logarithmic transformation was used for R, R_6, R_8, R_{10}, C, F_{res}, Ax, R_{eE} and R_{eI}. The effect of sex on oscillometry outcomes was investigated using Wilcoxon rank-sum test (Mann–Whitney U-test), and the relationship between the oscillometry outcomes and anthropometric covariates (sex, height (Ht) and ancestry) were explored using a backward stepwise linear regression. A reference equation for each outcome was generated and presented with the adjusted R^2 and standard error of the estimate (SEE) to allow z-score calculation: z-score=(measured value − predicted value)/SEE.

In order to assess the effect of puberty (particularly as numbers in this age group were relatively low) on the reference equation, backward stepwise regressions with anthropometric data for sex, Ht and ancestry were used to generate a reference equation in children between 3 and 7 years of age from the DCHS cohort.

Bayesian Information Criteria (BIC) models were used to select the best model fit for each of the oscillometry outcomes. In addition, diagnostic checks were done to ensure that the assumptions of linear regression were not violated. This included testing for the presence of multicollinearity using variance inflation factor, normality of residuals using histograms, kernel density and quantile–quantile plots, and homoscedasticity using residual *versus* fitted plots.

Results

A total of 692 children between the ages of 3 and 17 years were included in the study; 573 (82.8%) were from the DCHS cohort, 38 (5.5%) and 81 (11.7%) from the CTAAC and HCSOC sites, respectively, all representative of the same population group. All were of African ancestry, 361 (52%) were self-identified Black Africans and 331 (48%) of mixed ancestry. Demographic details and anthropometry of cohort including the weight for age z-score and Ht for age z-score data are summarised in table 1 and detailed in supplementary table S1. A total of 13 children (2%) were severely stunted (⩽3 standard deviations below the mean) and four children (0.6%) were severely underweight (⩽3 standard deviations below the mean). Six children (0.9%) were obese (⩾3 standard deviations above the mean). Notably, 29% of mothers self-reported smoking.

The conventional and intra-breath impedance measures are shown for all age groups in supplementary table S2. Values of F_{res} were available (*i.e.* fell in the 6–32 Hz range) in 514 (74.3%), less in the youngest and in most of the older children. The R and C data exhibited marked Ht dependences (figure 1); the compensatory parameter I has less physiological importance, and its values are not reported here. In figure 1, regressions on R and C *versus* Ht established in earlier work using model fitting are also plotted for comparison. The changes in various Z_{rs} measures with Ht are represented in supplementary figures S2a and b, exhibiting a decrease in R_6 and increase in X_6 with Ht. As shown in supplementary figure S2c–e, F_{res}, Ax and R_6–R_{20} decreased with increasing Ht. The intra-breath measures are plotted against Ht in

TABLE 1 Demographics of all children and adolescents (n=692)

Individual characteristics	
Sex, female	335 (48.4)
Age years	5.2 (4.2–7.2)
Site	
CTAAC	38 (5.5)
Healthy surgical (HCSOC)	81 (12.7)
DCHS	573 (82.8)
Ancestry	
Black African	361 (52.2)
Mixed ancestry	331 (47.8)
Weight kg	18.20 (15.25–23.10)
WAZ	−0.42 (−1.11–0.35)
Height cm	110 (101–120)
HAZ	−0.65 (−1.43–0.05)
BMI kg·m^{-2}	15.50 (14.53–17.04)
BMI-Z	−0.04 (−0.70–0.76)
Housing, informal settlement[#,¶]	255/611 (58.3)
Maternal smoking[#]	179/611 (29.3)

Data are presented as median (IQR) or n (%). CTAAC: Cape Town Adolescent Antiretroviral Cohort; HCSOC: Healthy Children at Surgical Outpatient Clinics; DCHS: Drakenstein Child Health Study; BMI: body mass index; WAZ: weight for age z-score; HAZ: height for age z-score; BMI-Z: body mass index z-score. [#]: information not available for HCSOC. [¶]: shelter constructed outside of the formal housing delivery system [46]; remainder classified as urban.

supplementary figure S3. ΔR and ΔX exhibited large scatters but were predominantly positive (supplementary figure S3c and f, respectively).

Stepwise regression analysis demonstrated the significant association with Ht for all variables; R_6, X_8, X_{eE} and X_{eI} were also found to be associated with sex; X_8 and X_{10} with ancestry. However, as demonstrated by the BIC model (supplementary table S3), these additional associations offered negligible contribution to predictive models. Thus, only Ht was included in all regression models. The reference equations are compiled in table 2. An online tool using these equations for z-score calculation is available from supplementary material. The limits of normal are +1.64 z-score for R values, F_{res}, Ax, $R_{6–20}$, and −1.64 z-score for X values.

To assess the effect of puberty on the reference range equations, stepwise regression in children from the DCHS cohort was done; the coefficients obtained (supplementary table S4) remained very close to that of the reference equations for the entire cohort, with a moderate decrease in adjusted R^2 attributable to the narrower Ht range. The consistency of reference equations between the full and reduced ranges in Ht is also illustrated in figure 1 and supplementary figures S2 and S3. Overall, the deviations between the full and reduced Ht range predictions are significant only in ΔR (Figure S2), and mild in C (figure 1), X_6 and Ax (supplementary figure S2), R_{eI}, X_{eE} and X_{eI} (supplementary figure S3). Excellent agreements were found for R and R_6 between the full and reduced Ht range predictions.

The comparison between R_6 predicted with the current equation and other published reference equations for different populations is illustrated in figure 2 [14–26, 30, 34]. Initially, we considered reference data from previous studies only if 1) R_{rs} values at around 5–6 Hz were analysed, 2) Ht was the single independent variable and 3) higher-order than linear relationship to Ht was assumed. The main features of these studies are summarised in table 3. Our R_6 values are similar to the R_{rs} plots of the other studies at the medium Ht range. Data from nine additional studies that assumed the linear R_{rs} *versus* Ht relationship (supplementary table S5) are shown in supplementary figure S4; these reference lines are rather scattered and fall outside the nonlinear regressions and illustrate the inadequacy of the linear Ht dependence, especially in the wide Ht range.

Discussion

This is the first study to report oscillometry data in healthy African children and adolescents that includes both conventional and intra-breath measures. Our findings compare favourably with previously published

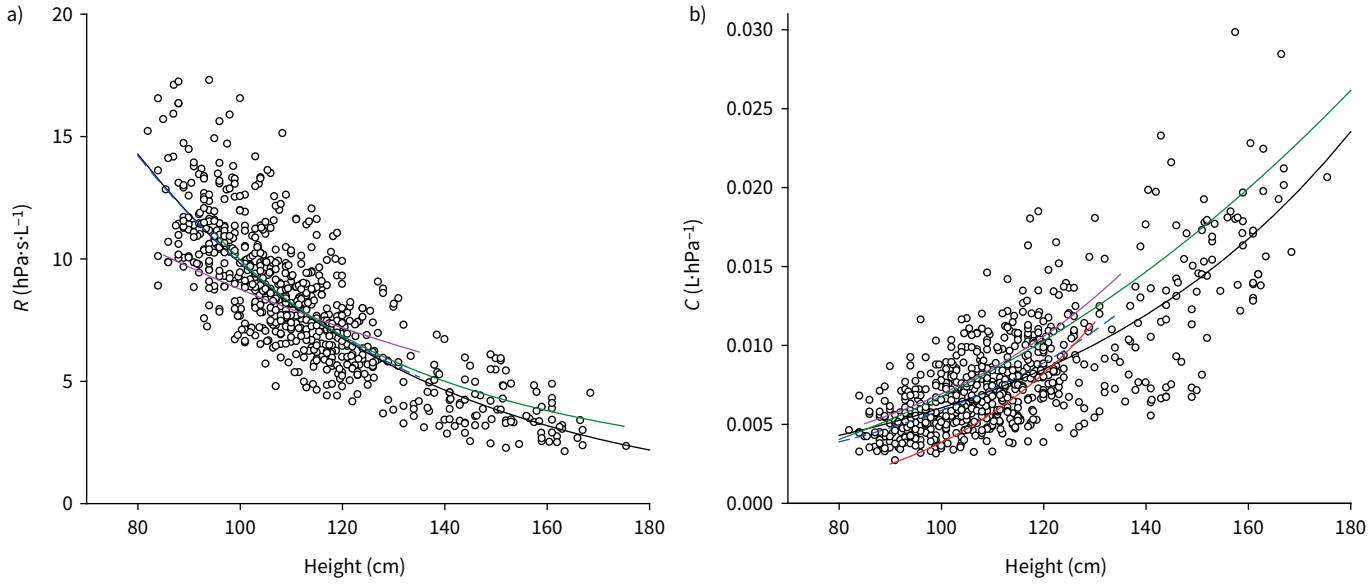

FIGURE 1 a) Respiratory system resistance (*R*) and b) compliance (*C*) *versus* height in healthy children and adolescents. Black solid and blue dashed lines indicate the regressions on the total population (n=692) and the 3- to 7-year age range (n=573), respectively. *R* and *C versus* height regressions from previous work are also plotted for comparison: Hantos *et al.* [22] (green), Mazurek *et al.* [25] (red) and Shackleton *et al.* [41] (pink).

normative data from other populations, suggesting that standardisation of methodology is a key factor accounting for cohort differences, while indicating the role of population differences.

The vast majority of normative data derived since 1972 includes predominantly Caucasian populations, covering various age ranges, and utilises a variety of oscillometry equipment. Additionally, the predictions employed different statistical models and anthropometric variables, further hindering direct comparison.

TABLE 2 Reference equations for children and adolescents 3 to 17 years of age

Outcome	Equation	Adj R^2	SEE
R_6 hPa·s·L^{-1}	exp(4.34–0.0189·Ht)	0.723	0.214
R_8 hPa·s·L^{-1}	exp(4.29–0.0190·Ht)	0.735	0.210
R_{10} hPa·s·L^{-1}	exp(4.27–0.0191·Ht)	0.747	0.204
X_6 hPa·s·L^{-1}	3.46–727·Ht^{-1}	0.405	1.168
X_8 hPa·s·L^{-1}	3.31–647·Ht^{-1}	0.425	0.995
X_{10} hPa·s·L^{-1}	2.73–531·Ht^{-1}	0.359	0.938
F_{res} Hz	exp(3.74–0.0062·Ht)	0.230	0.211
R_6–R_{20} hPa·s·L^{-1}	5.67–0.0311·Ht	0.177	1.227
Ax hPa·L^{-1}	exp(6.35–0.0287·Ht)	0.416	0.624
R hPa·s·L^{-1}	exp(4.16–0.0187·Ht)	0.739	0.205
C L·hPa^{-1}	exp(0.099 +0.0168·Ht)	0.523	0.295
R_{eE} hPa·s·L^{-1}	exp(4.36–0.0204·Ht)	0.734	0.225
R_{eI} hPa·s·L^{-1}	exp(4.32–0.0208·Ht)	0.729	0.233
X_{eE} hPa·s·L^{-1}	2.17–409·Ht^{-1}	0.174	1.178
X_{eI} hPa·s·L^{-1}	3.22–577·Ht^{-1}	0.397	0.943
ΔR hPa·s·L^{-1}	2.26–0.0144·Ht	0.040	1.272
ΔX hPa·s·L^{-1}	1.80–0.0117·Ht	0.050	0.928

Adj R^2: adjusted R^2; SEE: standard error of the estimate; R_6, R_8 and R_{10}: resistance at 6, 8 and 10 Hz; X_6, X_8 and X_{10}: reactance at 6, 8 and 10 Hz; F_{res}: resonance frequency; R_6–R_{20}: difference between resistance at 6 Hz and resistance at 20 Hz; *Ax*: area under the reactance curve; *R*: resistance from model fitting; *C*: compliance from model fitting; R_{eI}: resistance at end inspiration; R_{eE}: resistance at end expiration; ΔR: R_{eE}–R_{eI}; X_{eI}: reactance at end inspiration; R_{eE}: reactance at end expiration; ΔX: X_{eE}–X_{eI}.

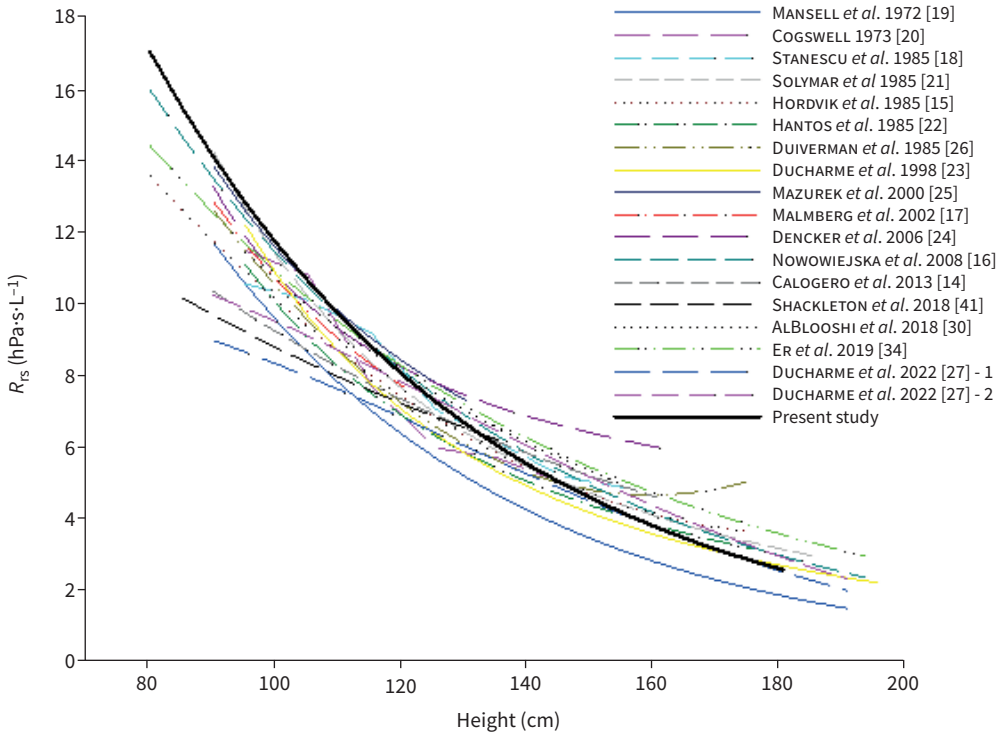

FIGURE 2 Comparison of respiratory resistance (R_{rs}) *versus* height relationships established in the present and previous studies (see table 3 for details).

TABLE 3 Summary of reference studies on resistance (R) *versus* height (Ht) relationships[#]

Author(s)	Year	Frequency Hz	Device	Country/race	No. of subjects	Age range years	Reference equation
Mansell *et al.* [19]	1972	5	Custom made	Canada	79	3–17	R_5=exp(1.877–0.0089·Ht)
Cogswell [20]	1973	5–7	Custom made	UK	204	3–12	$R_{5–7}$ *versus* Ht range data
Stanescu *et al.* [18]	1979	4–9	Custom made	Belgium	130	3–14	R_4 *versus* Ht range data
Solymar *et al.* [21]	1985	2–12	Custom made	Sweden	218	2–18	R_4=antilog(1.053–2.18·log(Ht))
Hordvik *et al.* [15]	1985	2–26	Jones Oscillaire	USA/C	138	2–16	R_6=9.2·Ht^2–34.1·Ht+35.2
Hantos *et al.* [22]	1985	3–10	Custom made	Hungary	121	4–16	R(3–10)=1.28·10^5·Ht$^{-2.05}$
Duiverman *et al.* [26]	1985	2–26	Custom made	The Netherlands/C	255	2.3–12.5	R_6=0.0017·Ht^2–0.541·Ht+47.73
Ducharme *et al.* [23]	1998	8–16	Custo Vit R	Canada/mixed	199	3–17	R_8=exp(10.99–2.37·ln(Ht))
Mazurek *et al.* [25]	2000	4–32	Custom made	Poland	127	2.5–7.5	R_6=exp(2.4422–1.7447·ln(Ht))
Malmberg *et al.* [17]	2002	5–35	Jaeger IOS	Finland	109	2–7	R_5=exp(2.115–1.786·ln(Ht))
Dencker *et al.* [24]	2006	5–35	Jaeger IOS	Finland-Sweden/C	360	2–11	R_5 *versus* Ht curve
Nowowiejska *et al.* [16]	2008	5–35	Jaeger IOS	Poland	626	3–18	R_5=exp(–0.0169·Ht+1.818)
Calogero *et al.* [14]	2013	4–48	Chess i2M	Australia–Italy/C	760	2–13	R_6=exp(3.3738–0.01155·Ht)
Shackleton *et al.* [41]	2018	6–26	Custom made[¶]	Australia/Hungary/C	319	3–6	R_6= exp(3.3501–0.01033·Ht)
AlBlooshi *et al.* [30]	2018	5–37	Tremoflo C-100	UAE/Emirati	291	4–12	R_5=exp(3.786–0.014·Ht)
Er *et al.* [34]	2019	5–35	Jaeger IOS	Turkey/Turkish	151	3–7	R_5=antilog(0.527–0.005·Ht)
Ducharme *et al.* [27] – 1	2022	5–37	Resmon Pro	Canadian/mixed	271	3–17	R_5=exp(–0.1509+0.00809·Ht-0.0000824·Ht^2)
Ducharme *et al.* [27] – 2	2022	5–37	Tremoflo C-100	Canadian/mixed	292	3–17	R_5=exp(–0.0252+0.00809·Ht-0.0000817·Ht^2)

Units in the reference equations are as originally reported: R in cmH_2O·s·L^{-1}, hPa·s·L^{-1} or kPa·s·L^{-1}; Ht in cm or m. C: Caucasian (when stated). [#]: only studies that used nonlinear formulae are included; those assuming linear relationship are added in supplementary table S5. [¶]: identical device to that used in the present study.

We therefore limited the comparison of the present data to studies that reported Ht as the only independent variable and used a nonlinear Ht dependence of Z_{rs} measures, as appropriate. The inappropriateness of the linear R_{rs} *versus* Ht relationship is highlighted in supplementary figure S4.

To our knowledge, figure 2 represents the most comprehensive survey on the Ht dependence of R_{rs} values in children and adolescents, although the permissive inclusion of the different lowest frequencies (4, 5 or 6 Hz) or frequency ranges for model fitting increases the variability. The roughly inverse relationships between R_{rs} and Ht exhibit some variability between the normative studies, and our data, which covers one of the widest Ht ranges, is consistent with this (see figure 2). We note that some nonlinear models, such as polynomial regressions, may predict unrealistic inflections in the R_{rs} *versus* Ht relationships towards lower Ht [27] or higher Ht [26]. Apart from this, in the lowest Ht range (<120 cm), our 6-Hz R_{rs} values are among the highest, together with lower-frequency (4 and 5 Hz) measurements expected to result in higher R_{rs} [16, 21], and that obtained with a special (head generator) device [25] leads to higher values than the uncorrected R_{rs}. A more rigorous comparison covering only Z_{rs} data at 10 Hz is presented in supplementary figure S5; the relative position of our R_{10} values remains similar to that shown in figure 2, whereas our X_{10} data are rather in the middle of the smaller set of available X_{10} predictions. There appears to be a systematic difference between our predictions and those based on the same oscillometry setup employed in a population of Caucasian children [41]. Comparison of F_{res} *versus* Ht regressions reveal a wide scatter between studies, in which our data take a midposition.

Ethnic differences in oscillometry measurements obtained with the same device have been noted [28]; ancestry, environmental and body habitus differences, which influence Ht, were the most likely suggested reasons accounting for this discrepancy. Moreover, differences in Ht between populations appear to be greatest in preschool years [44]. The fact that our cohort had a higher R_{rs} at Ht <120 cm possibly indicates that the younger children in our study may have smaller lungs for a given Ht compared to other healthy reference populations. We noted a higher R_{rs} with a predominantly lower X_{rs} in oscillometry variables in females compared to males, similar to findings by others [9, 14]. However, we found that sex was not independently predictive after adjusting for Ht. Difference in Z_{rs} between females and males in childhood and adolescence may be primarily driven by smaller lung volumes and narrower airways in females compared to males [45, 46].

Many early life factors influence lung growth and development, including environmental smoke exposure and socioeconomic status (SES) [11, 38]. Our study population was from a predominantly low SES community with high smoke exposure; 29% of mothers in our cohort smoked [38, 39]. However, this subtle difference in R_{rs} at small Ht should be interpreted with care as measurement accuracy has been shown to be rather variable between commercial oscillometry devices at high load impedances, such as Z_{rs} in small children [47]. It is worth noting that the reference equipment in this device comparison study [47] was the wavetube setup [41, 42] employed in the present investigation. Efforts are underway to align and standardise equipment signalling and processing, including the development of consensus guidelines [37, 41, 47, 48].

In addition to the conventionally reported R_{rs} and X_{rs} values at the oscillation frequencies, F_{res} and *Ax* are increasingly used to determine the elasticity and ventilation inhomogeneity of the respiratory system, whereas $R_{6–20}$ reflects peripheral inhomogeneity and airway obstruction [47]. With the exception of F_{res}, these measures are very sensitive to the value of the lowest oscillation frequency, which is rather variable between devices and hence different studies; this is another argument calling for urgent standardisation effort. We have added the mean R_{rs} (R) and C parameters from model fitting [42, 43] and propose these measures as more robust descriptors of the resistive and reactive behaviour of the respiratory system than the R_{rs} and X_{rs} readings at individual frequencies. Reports on R and C in paediatric populations are scant in the literature [22, 25]; the most important comparison with a previous study [41] that employed the same oscillometry device and evaluation procedure (figure 1) reinforces the single-frequency findings on the relatively high resistance and low compliance values in our preschooler population.

This study is one of the first to develop comprehensive reference equations for the novel intra-breath oscillometry measurements in the paediatric population [7–9]. Intra-breath measures have been shown to be a measure of airway obstruction in preschool children with wheezing and altered in children with asthma [7]. We have also previously shown that these measurements were able to predict healthy infants at risk for lower respiratory tract infections [9]. The clinical utility of the intra-breath measures together with standardised conventional spectral variables in children need to be fully established, and ongoing work is recommended in this area to facilitate diagnosis of respiratory disease with more precision.

Strengths of this study include the large sample of healthy children with data collected using the same equipment and methodology. The age range of children extended from preschool to adolescence provides us with a tool useful through childhood and adolescence. The availability of an online tool for calculation of the lower/upper limits of normal and z-score simplifies this further, facilitating its use for users in the field.

A limitation of this study is the relatively small sample size in the 8- to 17-year-old age interval, a time of variable lung growth particularly between sexes, thus assessing the impact of puberty was limited. Since there is a remarkable consistency in the Ht dependencies of the major oscillometry measures between the full (3–17 years) and the lower (3–7 years) age ranges, these reference equations aim to guide clinical practice until they are updated by using more balanced patient cohorts. In addition, these normative values are based only on data from a single province, the Western Cape, of South Africa; therefore this may not necessarily be generalisable to the rest of the Southern Africa region, although recent multi-province data collection in healthy individuals shows concordance in spirometry measurements [45].

In conclusion, we have established the first respiratory impedance reference equations for South African children and adolescents with an online tool to facilitate its use in early identification and management of respiratory disease. While our results reveal differences in oscillometry measures by ancestry, they also highlight the lack of standardisation in methodology.

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