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Reference values of respiratory impedance with impulse oscillometry in healthy Chinese adults

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Research

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Abstract

Background: Impulse oscillometry (IOS) is a non-invasive pulmonary function test for measuring respiratory impedance. Available reference equations of IOS indices for adults are limited. The aim of this study was to develop reference equations of IOS indices for Chinese adults.

Methods: In a multicentral, cross-sessional study of impulse oscillometry in Chinese adults, IOS data from healthy subjects were collected from 19 general hospitals across China was between 2016 and 2018. IOS measurements were conducted in accordance with recommendations of the European Respiratory Society. Multiple linear regression was performed to develop sex-specific reference equations of IOS indices.

Results: IOS measurements were performed in 1318 subjects, of which 567 subjects were defined as healthy normal individuals with acceptable IOS data and were included in the final analysis. Reference equations and limits of normal (LLN/ULN) of IOS indices were developed separately for males and females. Height but not age was shown to be the most influential contributor to IOS indices. The reference equations currently used in lung function laboratories predicted higher $R5$ and $X5$. Normal ranges of $R5$ and $X5$ recommended by the equipment manufacturer were clearly different from the ULN/LLN derived from the reference equations.

Conclusions: Reference equations of IOS indices for Chinese adults from a wide region were provided in this study. It is necessary to update new IOS reference equations and adopt ULN/LLN as normal ranges of IOS indices.

Clinical Trial Registration: This study was registered at www.clinicaltrials.gov as part of a larger study NCT03467880.

Background

Impulse oscillometry is a non-invasive method of measuring respiratory impedance based on the forced oscillation technique (FOT) [1]. IOS is regarded as a complementary tool to conventional lung function tests due to its minimal demand for cooperation and sensitivity in the evaluation of small airway function [2]. Reports of IOS as a useful tool in the assessment of asthma [3–6], chronic pulmonary obstructive diseases [7] and bronchiectasis [8] have increased its application in research and clinical settings.

In accordance with other lung function tests, choosing optimal reference values is crucial for the interpretation of IOS. The first and also the most widely used reference equation of respiratory impedance with IOS is the one proposed by Vogel et al. in 1994 [9]. The sample population of Vogel's equations was from a German industrial city that suffered from air pollution and included smokers, which obviously did not meet the American Thoracic Society (ATS) recommended criteria for the data source of lung function reference values [10]. Furthermore, the study only used age as predictor of the respiratory impedance, where later studies [11–17] have demonstrated that respiratory impedance is more associated with height and weight rather than age. This may have an impact on the predictive value and normal ranges of IOS indices, thus decreasing the capacity for IOS to identify respiratory abnormality. Although some studies had focused on developing new reference equations of respiratory impedance by FOT or IOS, the available reference equations of IOS indices for adults are limited [11–16, 18–21]. The lack of appropriate reference equations and normal ranges of IOS have hindered the application of IOS in clinical practice.

The aim of the present study was to develop reference equations of IOS indices that: 1) are based on data from healthy Chinese adults collected a wide region and under standardized quality control; 2) provide normal limits of IOS indices with up-to-date criteria for clinical use.

Methods

The study of impulse oscillometry in Chinese was a multicenter, cross-sectional and observational, and collected IOS and spirometry reports from healthy subjects and patients with respiratory diseases in 20 general hospitals from 15 provincial regions throughout China (details of these hospitals are shown in Additional File 2). IOS data from healthy subjects were used to develop reference equations of IOS in the present study.

Subject

Subjects were recruited mainly from individuals who have regular check-ups in hospitals, volunteer students at colleges and the relatives of hospital patients. Self-reported questionnaire was used to collect medical history, history of smoking and occupational exposures, respiratory symptoms, and results of chest radiography within the last 6 months. Subjects who met the following criteria were included as healthy subjects: no history of smoking or smoked < 100 cigarettes in their lifetime; no occupational exposures; no respiratory tract infections in the last 4 weeks; no chronic or recurrent respiratory symptoms including cough, expectoration, wheezing, or shortness of breath; reported no severe cardiopulmonary diseases or systematic diseases. Those who had abnormalities on chest radiography or spirometry were excluded.

IOS measurement

A Masterscreen IOS device (CareFusion, Hoechberg, Germany) was used for IOS measurements in this study. IOS measurements were conducted following the official technical recommendations for FOT from the European Respiratory Society (ERS) [22]. Verification of impedance was performed daily and a criterion of error ≤ 10% or 0.1 $kPa \cdot s \cdot L^{-1}$ was adopted. Measurements were performed in the sitting position with head in a neutral or slightly extended position, and the nose was closed by a nose clip. The cheeks were firmly supported by hands to reduce the effects of upper airway shunt. The subject was instructed to breath quietly at functional residual capacity level for 45–60 s. Measurements were repeated until 3 acceptable measurements were achieved, and the average of the 3 measurements was used for analysis. An acceptable measurement had a data acquisition of at least 30 s and included 5 normal breaths without obvious artifacts like spikes in Z-time tracing or drifts in the volume-time tracing. The coherence of each measurement was ≥ 0.8 at 5 Hz and ≥ 0.9 at 20 Hz. Unacceptable data were excluded from the analysis.

Based on the fundamentals of FOT, IOS measures respiratory impedance (Z) by superimposing pressure wave on the normal breathing [1]. Z includes resistance (R) and reactance (X). R represents the resistive properties of respiratory system, and X represents the capacitive and inert properties of respiratory system.

IOS indices analyzed in this study included R and X at different frequencies (5–35 Hz), the difference between and $R5$ and $R20$ ($R5–R20$), resonant frequency ($f$res), and low-frequency reactance area (AX). The key indices for the normal limits analysis were $R5$ and $X5$, which are respectively recognized as total resistance and capacitance of respiratory system.

Spirometry

Spirometry (CareFusion, Hoechberg, Germany) was performed immediately after the IOS measurements as per the ATS/ERS guidelines for spirometry [23]. If spirometry was performed before the IOS, at least 3 min of rest was allowed for rest [22]. Three acceptable measurements that met the quality control criteria of the ATS/ERS guidelines [24] were acquired and the best one was used in the analysis. Spirometric indices analyzed in this study were FEV_1 (forced expiratory volume in the first second), FVC (forced vital capacity), FEV_1/FVC and MMEF (maximal mid-expiratory flow). Reference values of spirometry were derived from the study of reference values for spirometry in Chinese aged 4–80 years [25].

Statistical analysis

As IOS indices exhibited skewness distribution, the results were presented as median with interquartile range. Mann-Whitney U tests were performed for the comparison of continuous indices. A P-values < 0.05 was considered statistically significant.

Reference equations were calculated separately for males and females using multiple linear regression analysis. Scatter plots (see Additional File 1) were drawn to observe the linear relationship between IOS indices and predictor variables. Normal P-P plots and residual plots were drawn to examine the normality and equal variance of the residuals. As the residuals of $f$res and AX only displayed normality and equal variance after $f$res and AX were log transformed, thus $f$res and AX were calculated as $\log_{10}$ transformation (lg$f$res and lgAX) in the equations. Predictor variables (height, weight and age) were selected using the stepwise method, in which predictors would enter the model if $P < 0.05$ and were removed if $P > 0.10$. Fitness of the model was assessed by the coefficient of determination (R^2). Normal limits of IOS indices were calculated as followed: ULN (upper limit of normal) of R = predictive value + 1.645 × RSD (residual standard deviation), LLN (lower limit of normal) of X = predictive values − 1.645 × RSD.

Results

In this study, a total number of 1318 of subjects were recruited and finished the IOS measurements between 2016 and 2018 in 19 hospitals across China, 567 subjects from 13 hospitals were included in the final analysis (see Fig. 1 and a-Table 1 in Additional File 3). The baseline characteristics are presented in Table 1 and Fig. 2. Height range is 154–186 cm in males and 142–176 cm in females. The spirometric indices FEV_1, FVC, FEV_1/FVC and MMEF from the analyzed population were all within normal limits.

Table 1
Baseline characteristics of the study population.

	Male	**Female**	***P*-value**
	(N = 270)	(N = 297)	
Age (years)	36.0 (23.8)	34.7 (23.0)	0.065
Height (cm)	170.0 (9.0)	159.0 (7.0)	< 0.001
Weight (kg)	69.0 (15.1)	56.0 (12.0)	< 0.001
BMI (kg/m^2)	23.7 (4.4)	21.9 (4.4)	< 0.001
FEV_1 (L)	3.88 (0.87)	2.86 (0.55)	< 0.001
FEV_1 z score	0.28 (1.24)	0.16 (1.16)	0.213
FVC (L)	4.66 (0.99)	3.34 (0.62)	< 0.001
FVC z score	0.23 (1.31)	0.17 (1.27)	0.211
FEV_1/FVC	0.83 (0.07)	0.84 (0.07)	0.002
FEV_1/FVC z score	-0.05 (1.10)	-0.05 (1.17)	0.839
MMEF (L/s)	3.86 (1.51)	2.95 (1.21)	< 0.001
MMEF z score	0.12 (1.23)	0.05 (1.26)	0.461

Data are presented as median (interquartile range). BMI: body mass index, FEV_1: forced expiratory volume in the first second, FVC: forced vital capacity, MMEF: maximum mid-expiratory flow.

For the whole population, the median (interquartile range) of *R*5 was 0.29 (0.09) kPa·s·L^{-1}, *R*20 was 0.27 (0.08) kPa·s·L^{-1}, and *X*5 was − 0.10 (0.04) kPa·s·L^{-1}. Resistance at all frequencies in females were significantly higher than in males, while reactance at all frequencies (except for *X*15) were more negative in females than in males (details are shown in a-Table 2 in Additional File 3).

Results of the reference equations for main IOS indices are shown in Table 2 (complete results of other IOS indices are shown in a-Table 3 and a-Table 4 in Additional File 3). Except for *R*35 in males, all IOS indices in this study derived significant reference equations with height and/or weight as predictors. R^2 of the equations ranged from 0.0154 to 0.250 and tended to be smaller in equations of the impedance at higher frequencies. Shunt effect of the upper airway may account for the less fitness of models of impedance at high frequencies.

Table 2
Reference equations of the main IOS indices

		Equations	**RSD**	R^2
*Z*5	M	0.6811–0.0032 × H + 0.0019 × W	0.0415	0.1877
	F	0.9110–0.0042 × H + 0.0023 × W – 0.0008 × A	0.0493	0.1673
*R*5	M	0.6275–0.0030 × H + 0.0019 × W	0.042	0.1789
	F	0.8103–0.0038 × H + 0.0024 × W–0.0005 × A	0.0491	0.1606
*R*20	M	0.5038–0.0019 × H + 0.0010 × W – 0.0004 × A	0.0401	0.0668
	F	0.5042–0.0013 × H	0.0442	0.0282
*R*5– *R*20	M	0.2485–0.0018 × H + 0.0010 × W	0.0205	0.2249
	F	0.2360–0.0019 × H + 0.0017 × W	0.0306	0.1865
*X*5	M	–0.3100 + 0.0013 × H + 0.0002 × A	0.0195	0.1105
	F	–0.3605 + 0.0015 × H + 0.0004 × A	0.0236	0.1233
lg*f*res	M	1.9238–0.0068 × H + 0.0033 × W	0.0801	0.1963
	F	1.8261–0.0067 × H + 0.0051 × W	0.0805	0.2505
lgAX	M	1.3268–0.0142 × H + 0.0043 × W	0.2124	0.1179
	F	1.6639–0.0166 × H + 0.0089 × W – 0.0029 × A	0.2037	0.154

*Z*5: Total respiratory impedance at 5 Hz; *R*5: resistance at 5 Hz; *R*20: resistance at 20 Hz; *R*5–*R*20: *R*5 minus *R*20; *X*5: reactance at 5 Hz; AX: low-frequency reactance area; *f*res: resonant frequency. R^2: coefficient of determination; RSD: residual standard deviation.

In the equations of most IOS indices, height was shown to be the most influential predictor as it contributed the largest R^2 changes in the prediction models. Height was negatively associated with *R*, *f*res and AX, and positively associated with *X*. On the contrary, weight showed a positive association with *R*, *f*res and AX, and negative association with *X*. Age was shown to be predictor to some indices including *X*5, *X*25, and *X*35 in both genders and *Z*5, *R*5, and lgAX in females (see a-Table 3 and a-Table 4 in Additional File 3). However, the scatter plots (Additional File 1) between these indices and age did not display notable linear relationships.

Discussion

Sex-specific reference equations for respiratory impedance were developed based on large-scale data from healthy Chinese adults from a wide region in a multicenter IOS study.

Contributors to the respiratory impedance

As pulmonary function is associated with physiological changes during growth and aging, reference equations of pulmonary function commonly include anthropometric variables such as sex, age, height and weight, in order to justify the contributory effects of these factors to lung function. Our study found that height was the most influential contributor to respiratory impedance measured with IOS, with that taller individuals had higher R and less negative X. This finding is consistent with the previous studies [11–17, 19, 21, 26]. As shown in Table 3, though the coefficients or forms of the predictors in the IOS equations were different, the tendency of the effect of predictors in most equations remained the same; that is, height was negatively correlated with $R5$ and $R20$, and positively correlated with $X5$. The association between height and respiratory resistance can be explained by the effect that height contributes to the diameter of the airways and lung volume. This could also explain the discrepancies of respiratory impedance between males and females. In contrast, weight displayed a positive association with R. The decreased lung volume and ventilation heterogeneity reported in the obese subjects [27, 28] may account for the higher respiratory resistance in the obese. However, the mechanism behind how body weight affects respiratory impedance in subjects with normal weight is still not clear since most studies have focused on overweight or obese individuals. Although age did not appear to be a marked contributor to R in adults in our study, a negative dependence on age for R has been reported in studies of children and adolescences [29, 30]. Thus, the effect of age on R may be related to the rapid physiological changes during growth, especially on the growth of the respiratory system in children and adolescences.

Table 3
Summary of the reference equations of IOS indices for adults

Equations	Area	N	F/M	Age range (years)	Ethnicity	Predictors				
							*R*5	*R*20	*X*5	*f*res
Present study	China	567	1.10	18–82	99.3% Han	M	-H, W	-H, W	H, A	-H, W
						F	-H, W, -A	-H,	H, A	-H, W
Vogel et al. [9], 1994	Germany	506	0.70	18–69	NA	M	A	A	-A	NA
						F	A	A	-A	NA
Zhao et al. [11], 2002	Xinjiang, China	457	0.80	16–81	Han, Uygur	M	W, -H	W, -H, -A	H	W, -H
						F	W, -H	-H, -A	H, W	W, -H
Fan et al. [12], 2005	Kunming, China	185	0.73	19–68	NA	M	-W *H	-W *H	NA	$-e^{H}$
						F	$-e^{W}$	$-e^{W}$	NA	-LogH, LogW
Satomi et al. [13], 2005	Japan	166	1.40	20–83	NA		-LogH	-LogH	LogH, -A	
Ni et al. [14], 2006	Nantong, China	120	0.69	20–79	Han	M	-H, W, A	-H, W, A	H, W, A	H, W, A
						F	H, W, A	H, W, -A	H, W, A	H, W, A
Newbury et al. [15], 2008	Australia	125	1.12	25–74	Caucasian	M	-H, W, -A	-H, W, -A	H, A	NA
						F	-H, A	-H, A	H, -A	NA
Wang et al. [16], 2011	Shenyang, China	100	0.69	19–80	NA	M	-lgH, -lgA	$-H^2$, $-e^A$	$-A^2$	A^2
						F	-lgH	$-H^2$	H^2, $-e^A$	-lgH, A*W
Li et al. [26], 2012	Lanzhou, China	920	1.04	>18	NA	M	-lgH, W	-H, W	$-A^2$	-H, W
						F	-H, W	W	$-A^2$	-H, W

N: the number of the study sample; F/M: ratio of female subjects to male subjects; *R*5: resistance at 5 Hz; *R*20: resistance at 20 Hz; *X*5: reactance at 5 Hz; *f*res: resonant frequency; NA: information was not available in the published paper; H, W, A respectively indicate height, weight and age as predictors of the equations, "-" indicates a negative effect of the predictor. M: equations for males; F: equations for female.

Equations	Area	N	F/M	Age range (years)	Ethnicity	Predictors				
							*R*5	*R*20	*X*5	*f*res
Schulz et al. [18], 2013	Germany	397	1.58	45–85	Caucasian	M	-H, W, -A	-H, W, -A	H, -W, -A	-H, W, A
						F	-H, W, -A	-H, W, -A	H, -W, -A	-H, W, A
Zhang et al. [19], 2015	Macau, China	362	1.02	18–78	Han	M	W, -H	-H	H	A, -H
						F	CW, -W, A	-H	H, A	A, CW, -W
Shu et al. [20], 2016	Jianghan Plain, China	431	1.03	18–79	NA	M	-AH, A, -A^2, e^W, -e^A	-AH, A, -A^2, -lgA	A*H, -A	-H^2, W^2
						F	-H^2, W, -e^W	W, -H^2	H^2	W, -H^2, -e^W

N: the number of the study sample; F/M: ratio of female subjects to male subjects; *R*5: resistance at 5 Hz; *R*20: resistance at 20 Hz; *X*5: reactance at 5 Hz; *f*res: resonant frequency; NA: information was not available in the published paper; H, W, A respectively indicate height, weight and age as predictors of the equations, "-" indicates a negative effect of the predictor. M: equations for males; F: equations for female.

Table 3 **(See the end of the document text file)**

Reference equations of respiratory impedance with IOS

Figure 3 displays the comparisons of reference values of *R*5 and *X*5 produced by different IOS reference equations. Since age is shown to have little impact on respiratory impedance in adults, it is no surprise that marked differences of predictive values were found between the Vogel's equations and the equations from other three representative studies (Newbury et al. [15], Schulz et al. [18] and the present study), as age is the only predictor in Vogel's equations [9]. Given that many lung function laboratories are still using Vogel's equations, it is important for the physicians to note that Vogel's equations predict higher *R*5 and *X*5 than other equations, especially for *X*5, and the differences are greater in tall subjects for *R*5 and in short subjects for *X*5. Undoubtedly, developing a more appropriate equation is imperative.

As summarized in Table 3, since Vogel's equations were developed, 10 studies have developed new equations of IOS indices in adults, and 7 of these were from China. However, most of these studies have limitations such as lack of quality control of IOS data or small sample sizes (Fan et al. [12], Satomi et al. [13], Newbury et al. [15], Ni et al. [14], Wang et al. [16]). Among these studies, only 6 studies had mentioned the number of IOS measurements for each subject, only 4 studies (Wang et al. [16], Schulz et al. [18], Zhang et al. [19], Shu et al. [20]) had mentioned the requirements of repeatability, and 3 studies (Satomi et al. [13], Newbury et al. [15], Schulz et al. [18]) had mentioned the acceptable criteria for the IOS measurements. As the variations of IOS indices are greater than spirometric indices [31], multiple measurements and strict quality control are particularly important in IOS measurements to ensure the repeatability and reliability of the data. Regarding sample size, studies from Satomi et al. [13] and Newbury et al. [15] were based on small sample sizes, with 166 and 125 subjects, respectively. This may decrease the reliability and applicability of their equations as a study have shown that at least 150 males and 150 females are required to validate reference equations of lung function tests in individual laboratories [32]. Also, Satomi's equation did not take sex into account, whereas sex-related differences in IOS indices have been reported in the present and former studies [21]. Schulz's study [18] was based on data from a relatively large sample size and clear quality control criteria. Similar values of *R*5 and *X*5 produced by Schulz's study and the present study in Fig. 3 provide evidence of the reliability of our reference equations.

Although 7 studies from China have developed reference equations of IOS indices [11, 12, 14, 16, 19, 20, 26] (Table 3), all of these studies were based on local sample populations, which may be less representative of the whole population of China, as China is a country with large territory and population. Heterogeneity in the inclusion criteria of participants and quality control also hinder the integration of these databases. Our study was a multicenter study that included data from a wide region across China, with uniform inclusion criteria and standardized quality control. Therefore, this study is more representative of the general population and produced more reliable data.

Normal ranges of IOS indices

Despites the fact that ERS had published official recommendations for the application of FOT in the clinical practice [22],[33], there are no acknowledged criteria for the normal ranges of respiratory impedance with FOT or IOS, probably due to the lack of systematic studies concerning on normative values of respiratory impedance. The IOS equipment manufacturer recommends using 150% of the predicted value as the normal limit for *R*5 and *R*20, and predicted value minus 0.2 kPa·s·L^{-1} as the normal limit of *X*5. The former was derived from reports from a bronchial challenge showing that a 20% decrease in FEV_1 was comparable to a 50% increase in airway resistance [1]. However, ATS guidelines for pulmonary function tests reported in 2017 have recommended using LLN/ULN as the criteria of abnormal of pulmonary function [10]. As is shown in Fig. 4, predicted *X*5 minus 0.2 kPa·s·L^{-1} (*X*5P–0.2 kPa·s·L^{-1}) was significantly more negative than the LLN of *X*5, regardless of the equation used. The 150% of predicted *R*5 (150%*R*5P) was much higher than the ULN of *R*5 produced by our equations, and marked differences were also shown in the comparison of ULN of *R*5 and 150%*R*5P produced by Newbury' equations in males and Schulz's equations in females. The above differences between the ULN/LLN and the normal limits currently used in laboratories will apparently increase the risk of misdiagnosis. Under the increasing application of IOS in clinical practice, it is necessary to update new equations and normal ranges of IOS. The validation of our new equations and normal ranges of IOS in patients with respiratory diseases will be further analyzed and discussed in our later reports.

Limitations

There were limitations to the present study. First, due to the practical limitations, our study population was not a random sample and may be less representative of the whole healthy population. Nevertheless, multicenter sources of data and strict inclusive criteria for healthy subjects in this study provide a guarantee of the representativeness of a healthy population. To date, our equations are the most representative and reliable for healthy Chinese adults. Second, our equations are based on the data of Chinese population, its use in other populations or ethnicities may be limited. However, we believe that these data may be a foundation or promotion to the development of multiethnic reference equations of IOS in the future, and our findings about the inappropriateness of the current normal ranges of IOS indices may provide evidences for the update of the internationally technical standards. Third, as the IOS data from children and adolescents in multicenter study of impulse oscillometry in Chinese were not enough to develop reference equations, we failed to develop continuous reference equations with a full age range. Studies containing a larger number of healthy children and adolescents with a randomized sample are needed in the future.

Conclusions

In summary, based on the data of a large-scale healthy population in the multicenter IOS study in China, we developed new reliable reference equations of respiratory impedance with IOS. Also, we found that the normal ranges of IOS indices wildly used in laboratories were clearly different from the ULN/LLN derived from the reference equations. It is necessary to update new IOS reference equations and adopt ULN/LLN as normal ranges of IOS indices for better use of IOS in clinical practice.

Abbreviations

Abbreviation	Full definition
ATS	American Thoracic Society
AX	Low-frequency Reactance Area.
BMI	Body Mass Index
ERS	European Respiratory Society
FEV_1	Forced Expiratory Volume in the First Second
FOT	Forced Oscillation Technique
$f$res	Resonant Frequency
FVC	Forced Vital Capacity
IOS	Impulse Oscillometry
LLN	Lower Limit of Normal
MMEF	Maximum Mid-expiratory Flow
Pred	Predictive value
$R5$	Resistance at 5 Hz
$R10$	Resistance at 10 Hz
$R15$	Resistance at 15 Hz
$R20$	Resistance at 20 Hz
$R25$	Resistance at 25 Hz
$R35$	Resistance at 35 Hz
R	Resistance
R^2	Coefficient of Determination
RSD	Residual Standard Deviation
ULN	Upper Limit of Normal
$X5$	Reactance at 5 Hz
$X10$	Reactance at 10 Hz
$X15$	Reactance at 15 Hz
$X20$	Reactance at 20 Hz
$X25$	Reactance at 25 Hz
$X35$	Reactance at 35 Hz

Abbreviation	Full definition
X	Reactance
Z	Impedance
95%CI	95% Confidence Interval

Declarations

Ethics approval and consent to participate

This study was approved by the medical ethics committee of the First Affiliated Hospital of Guangzhou Medical University - approval: MEC-2015-37.

Consent for publication

All subjects in this study gave their written informed consent.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

YG and J-PZ conceive and design the study. XLL, JD, LD, WH, JML, YL, YP, BRZ and TW collected the data. XLL analyzed the data and draft manuscript drafting. YG, WJG, JPZ, JD, LD, WH, JML, YL, YP, BRZ and TW critically review and revision of the manuscript. All authors have read and approved the final manuscript.

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References

1. Smith HJ, Reinhold P, Goldman MD. Forced oscillation technique and impulse oscillometry. Eur Respir Mon. 2005;72–105.
2. Galant SP, Komarow HD, Shin H-W, Siddiqui S, Lipworth BJ. The case for impulse oscillometry in the management of asthma in children and adults. Ann Allergy Asthma Immunol. 2017;118:664–71.
3. Shi Y, Aledia AS, Tatavoosian AV, Vijayalakshmi S, Galant SP, George SC. Relating small airways to asthma control by using impulse oscillometry in children. J Allergy Clin Immunol. 2012;129:671–8.
4. Shi Y, Aledia AS, Galant SP, George SC. Peripheral airway impairment measured by oscillometry predicts loss of asthma control in children. J Allergy Clin Immunol. 2013;131.
5. Shin YH, Yoon JW, Choi SH, Baek JH, Kim HY, Jee HM, et al. Use of impulse oscillometry system in assessment of asthma severity for preschool children. J Asthma. 2013;50:198–203.
6. Schulze J, Biedebach S, Christmann M, Herrmann E, Voss S, Zielen S. Impulse Oscillometry as a Predictor of Asthma Exacerbations in Young Children. Respiration. 2016;91:107–14.
7. Liu Z, Lin L, Liu X. Clinical application value of impulse oscillometry in geriatric patients with COPD. Int J Chron Obstruct Pulmon Dis. 2017;12:897–905.
8. Guan W, Gao Y, Xu G, Lin Z, Tang Y, Li H, et al. Impulse Oscillometry in Adults with Bronchiectasis. American Thoracic Society; 2015;12:657–65. http://www.atsjournals.org/doi/10.1513/AnnalsATS.201406-280OC. Accessed Dec 24 2019.
9. Vogel J, Smidt U. Impulse oscillometry: analysis of lung mechanics in general practice and the clinic, epidemiological and experimental research. Frankfurt: Pmi Verlagsgruppe; 1994.
10. Culver BH, Graham BL, Coates AL, Wanger J, Berry CE, Clarke PK, et al. AMERICAN THORACIC SOCIETY DOCUMENTS Recommendations for a Standardized Pulmonary Function Report An Official American Thoracic Society Technical Statement. 2017;196:1463–72.
11. Zhao M, Han A, Fang J. Determination of respiratory impedance of healthy adults by pulsating pulmonary function. Chin J Tuberc Respir Dis. 2002;25:636.
12. Fan M, Chen Y, Liu A, Yang W, Li S, Li Y. Measurement of respiratory impedance by means of impulse oscillometry in healthy adults in the Kunming area. Clin Pulmonol. 2005;9:565–7.
13. Shiota S, Katoh M, Fujii M, Aoki S, Matsuoka R, Fukuchi Y. Predictive equations and the reliability of the impulse oscillatory system in Japanese adult subjects. Respirology. 2005;10:310–5.
14. Ni S, Lv X, Feng J, Zhu A. Respiratory impedance measured with impulse oscillometry in healthy adults in Nantong area. Chinese Med J Commun. 2006;1:58–9 + 61.
15. Newbury W, Crockett A, Newbury J. A pilot study to evaluate Australian predictive equations for the impulse oscillometry system. Respirology. 2008;13:1070–5.
16. Wang T, Tan M, Zheng H. Analysis of the normal values of pulmonary function by impulse oscillometry in healthy adults in Shenyang. J China Med Univ. 2011;40:340–2.

17. Oostveen E, Boda K, Van Der Grinten CPM, James AL, Young S, Nieland H, et al. Respiratory impedance in healthy subjects: Baseline values and bronchodilator response. Eur Respir J. 2013;42.
18. Schulz H, Flexeder C, Behr J, Heier M, Holle R, Huber RM, et al. Reference values of impulse oscillometric lung function indices in adults of advanced age. PLoS One. 2013;8:e63366.
19. Zhang X, Jin-ping Z, Chen Y, Cheng K, Yang K, Dong Q, et al. Investigations of impulse oscillation technique and predictive equations in Macao healthy adults. Chinese J Pract Intern Med. 2015;35:431–5.
20. Shu Y, Li J. Analysis of normal values of pulmonary function with impulsive oscillation in healthy adults in jianghan plain. Med Inf. 2016;29:108–9.
21. Kalchiem-Dekel O, Hines SE. Forty years of reference values for respiratory system impedance in adults: 1977–2017. Respir Med. 2018;136:37–47.
22. Oostveen E, Macleod D, Lorino H, Farré R, Hantos Z, Desager K, et al. The forced oscillation technique in clinical practice: methodology, recommendations and future developments on behalf of the ERS Task Force on Respiratory Impedance Measurements. Eur Respir J. 2003;22:1026–41.
23. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J. 2005;26:319–38.
24. Graham BL, Steenbruggen I, Barjaktarevic IZ, Cooper BG, Hall GL, Hallstrand TS, et al. Standardization of spirometry 2019 update an official American Thoracic Society and European Respiratory Society technical statement. Am J Respir Crit Care Med. 2019;200:E70–88.
25. Jian W, Gao Y, Hao C, Wang N, Ai T, Liu C, et al. Reference values for spirometry in Chinese aged 4–80 years. J Thorac Dis. 2017;9:4538–49.
26. Li F, Wang X, Wan Y, Wei H, Wang H, Tao H, et al. Analysis of the normal Values of pulmonary function by impulse oscillometry in healthy adults in Lanzhou. Prog Microbiol Immunol. 2012;40:34–7.
27. Salome CM, King GG, Berend N. Physiology of obesity and effects on lung function. J Appl Physiol. 2010;108:206–11.
28. Pellegrino R, Gobbi A, Antonelli A, Torchio R, Gulotta C, Pellegrino GM, et al. Ventilation heterogeneity in obesity. J Appl Physiol. 2014;116:1175–81.
29. Amra B, Soltaninejad F, Golshan M. Respiratory resistance by impulse oscillometry in healthy Iranian children aged 5–19 years. Iran J Allergy Asthma Immunol. 2008;7:25–9.
30. Gochicoa-Rangel L, Torre-Bouscoulet L, Martinez-Briseno D, Rodriguez-Moreno L, Cantu-Gonzalez G, Vargas MH. Values of Impulse Oscillometry in Healthy Mexican Children and Adolescents. Respir Care. 2014;60:119–27.
31. Timonen KL, Randell JT, Salonen RO, Pekkanen J. Short-term variations in oscillatory and spirometric lung function indices among school children. Eur Respir J. 1997;10:82–7.
32. Quanjer PH, Stocks J, Cole TJ, Hall GL, Stanojevic S. Influence of secular trends and sample size on reference equations for lung function tests. Eur Respir J. 2011;37:658–64.
33. King GG, Bates J, Berger KI, Calverley P, de Melo PL, Dellacà RL, et al. Technical standards for respiratory oscillometry. Eur Respir J. 2020;55:1–21.

Figures

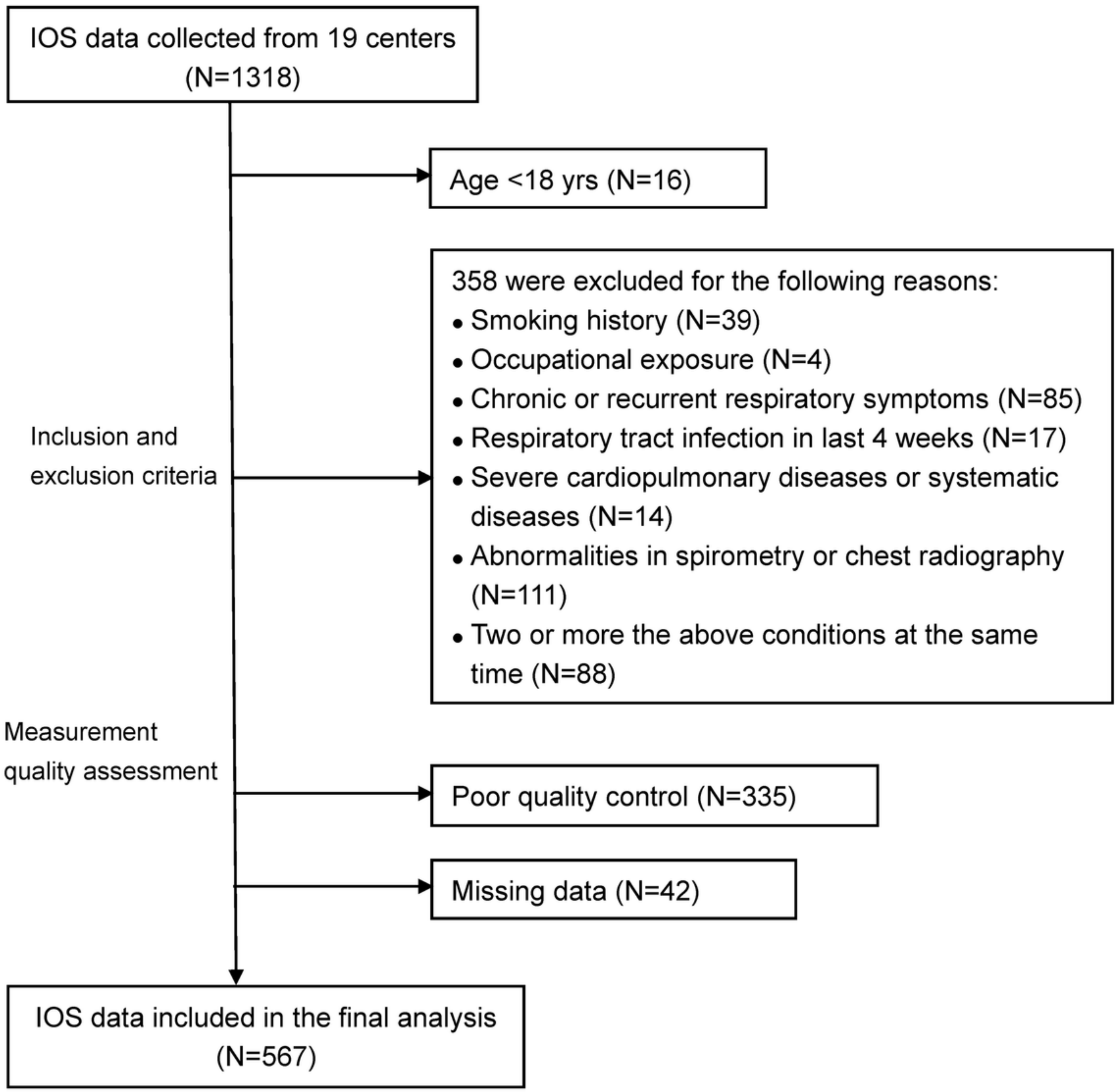

Figure 1

Flow chart of the inclusion and exclusion criteria for analyzed data.

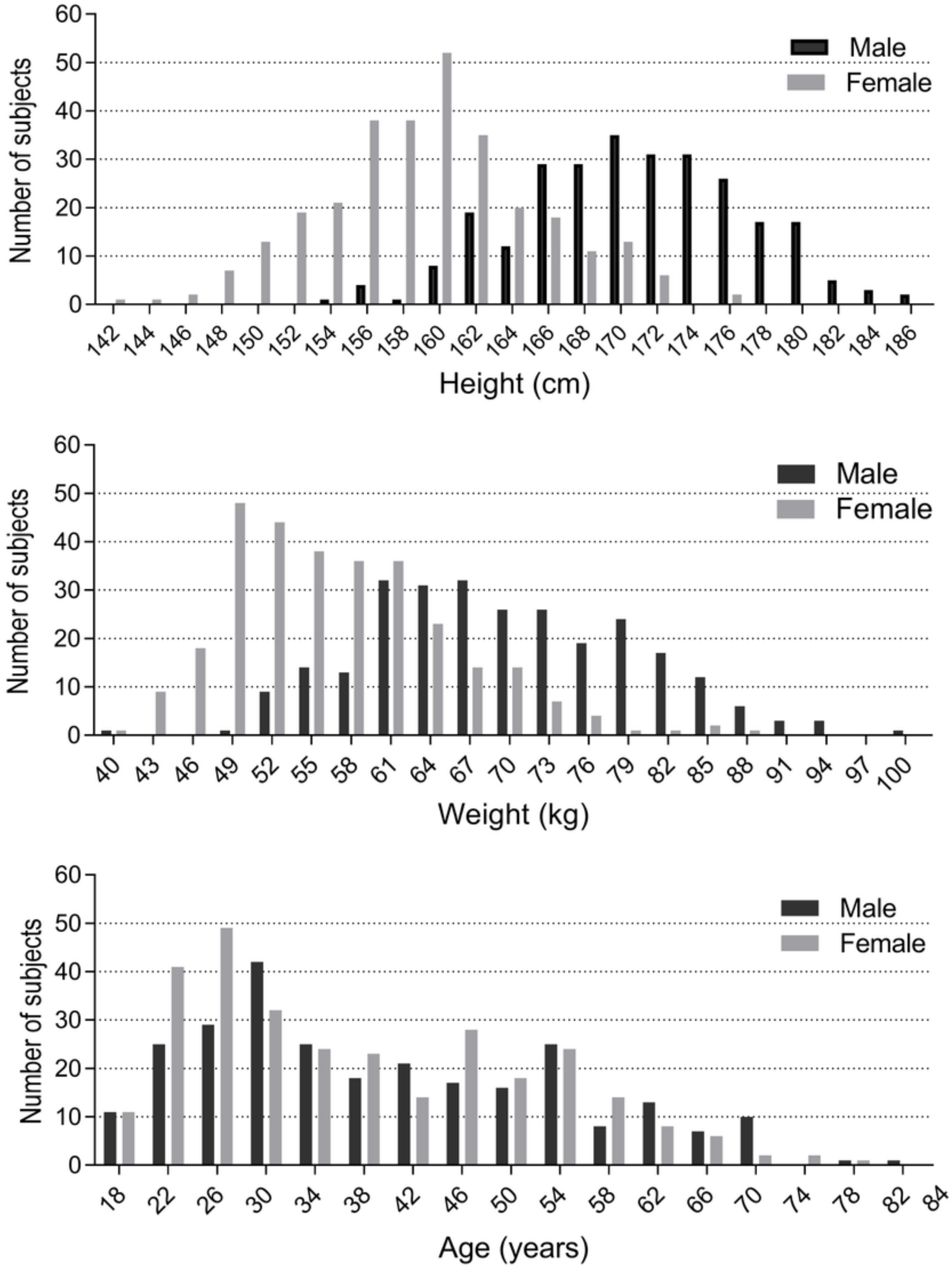

Figure 2

Distribution of height, weight and age of the study population by gender.

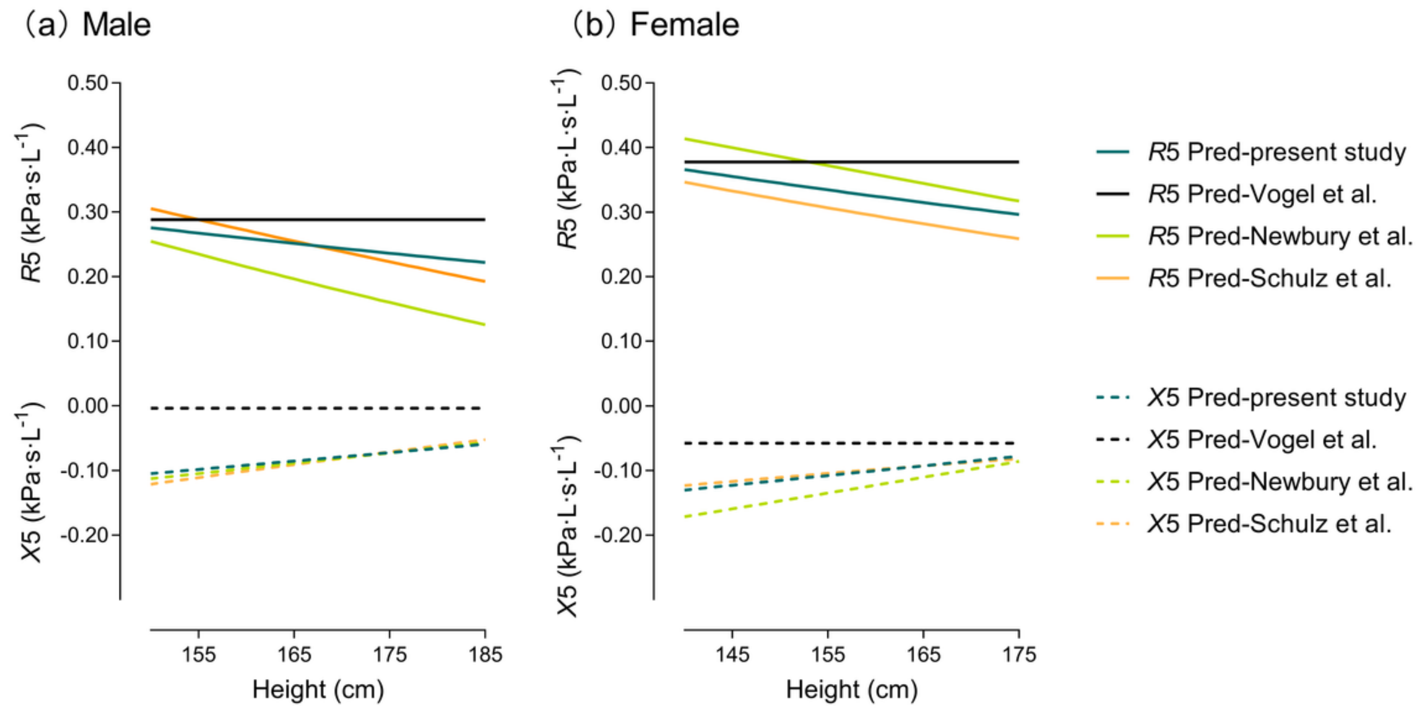

Figure 3

Comparison of the predictive values (Pred) of R5 and X5 predicted by different equations. Results are shown as a function of height, with age fixed at 50 years, and weight was calculated by a fixed BMI of 23 kg/m2 (the median of our study population). Solid lines indicate Pred of R5, and dashed lines indicate Pred of X5.

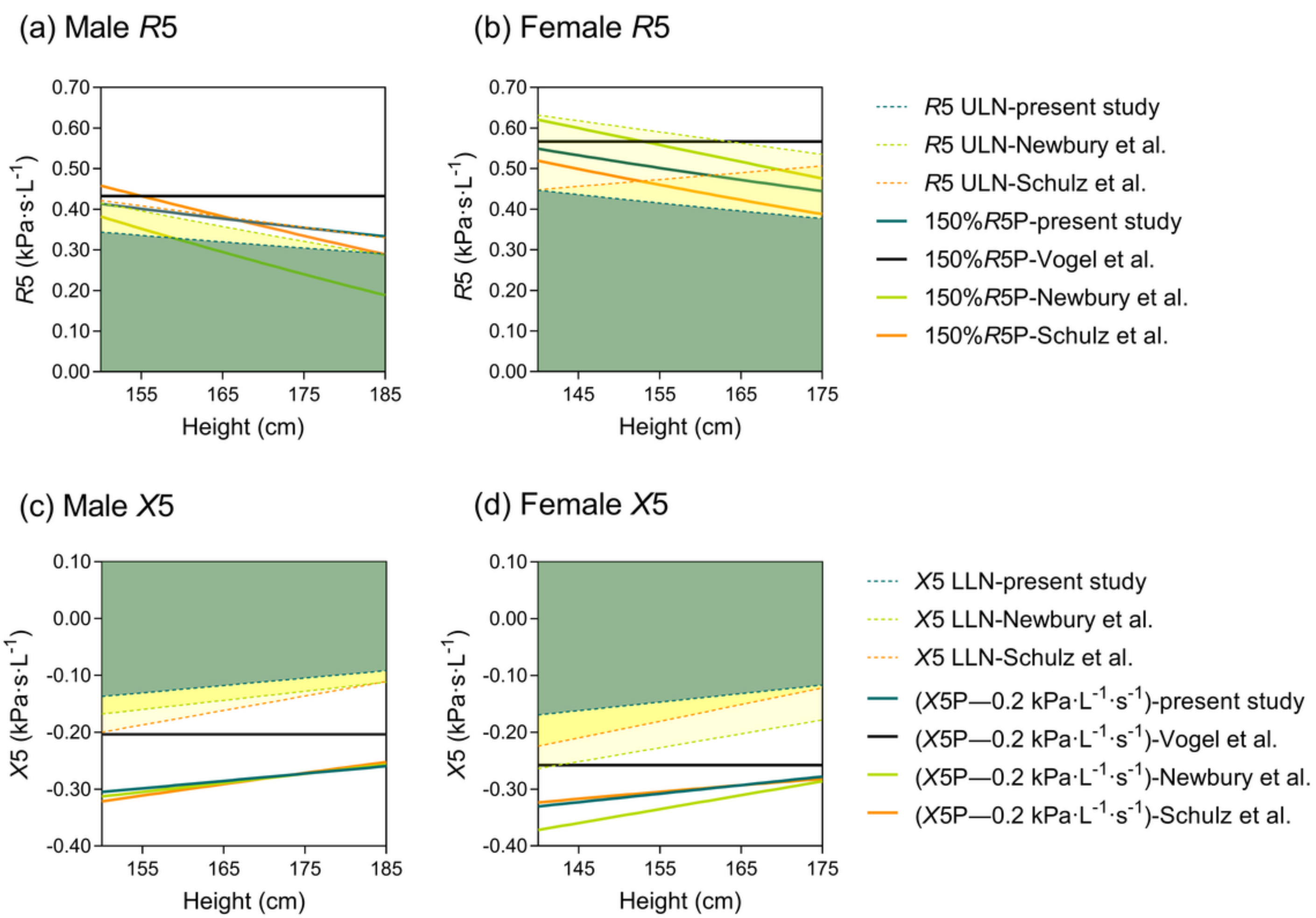

Figure 4

Comparisons of the normal ranges of R5 and X5 derived by different equations. Colored area under the dotted lines indicates ULN of R5 or LLN of X5. Solid lines indicate 150% of the predictive values of R5 (150% R5P) or the predictive values of X5 minus 0.2 kPa·s·L-1 (X5P−0.2 kPa·s·L-1). As the RSD of Vogel's equations is not available, the ULN/LLN with Vogel's equations is not shown.

Supplementary Files

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