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Spirometric reference standards for preschool children in Hong Kong

Key Messages

1. Prediction equations and normograms are established using incentive spirometry in a community cohort of 770 Hong Kong Chinese children aged 2 to 6 years.
2. All spirometric parameters depend mainly on standing height. Boys have higher values than girls.
3. Forced expiratory volumes depend on birth weight, place of birth, history of wheezing, and environmental tobacco smoke (ETS) exposure.
4. High urinary cotinine level as a biomarker of ETS exposure is noted in about one tenth of the children.
5. Urinary cotinine level is inversely associated with all spirometric parameters. This supports implementation of the smoking cessation programme.

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Introduction

Spirometry is a standard clinical procedure for assessing the respiratory health of adults and older children. Preschool children have difficulty performing spirometry because of difficulty producing consistent flow volumes, short attention span, low frustration tolerance, and inability to inspire consistently to total lung capacity and exhale completely and consistently to zero flow. Nonetheless, advances in spirometry techniques enable measurements for children as young as 3 years of age.[1,2] The use of animation programmes is one of these technological improvements. The Asthma UK Collaborative Initiative has collated spirometric data from 53 777 healthy children aged 3 to 7 years old from 15 centres across the United States and Europe, in order to establish reference standards for spirometry in Caucasian preschool children.[3] There were only two small reports on spirometric testing in Chinese preschoolers, one in Shenzhen and another in Taiwan. These studies were performed before the availability of any international guideline.[2] This study aimed to establish the spirometric reference standards in Chinese preschool children in Hong Kong and investigate how demographic, anthropometric, and environmental factors influence the reference standards.

Methods

This study was conducted from January 2009 to September 2010 and was approved by the ethics committee of our university. Sample selection was based on stratified (by districts) and clustered (all subjects within a class) random sampling. Nurseries and kindergartens registered under the Education Bureau were randomly selected in proportion to the childhood population residing in the four geographical regions in Hong Kong. Parents of children completed a questionnaire on demographics, environmental exposure, and respiratory health. Our research staff were blind to such information when measuring the children's lung function by incentive spirometry. Exclusion criteria for spirometric references were premature birth (<37 weeks), birth weight <2.5 kg, reported having current wheeze or any history of asthma, congenital cardiorespiratory diseases warranting surgery or long-term medication, and respiratory tract infection within the last 4 weeks.

Each subject's weight, height (standing and sitting), and waist circumference were measured. Lung function was measured using incentive spirometry (Master Screen, Jaeger GmbH, Würzburg, Germany) according to international guidelines.[2] The spirometer was calibrated on-site daily using a 1-litre calibration syringe. Each subject performed at least three forced vital capacity (FVC) manoeuvres. Following data acquisition, the same staff reviewed all computer-derived flow-volume curves for technical acceptability.[2] Spirometric parameters recorded were forced expiratory volume in 0.5 second ($FEV_{0.5}$), $FEV_{0.75}$, FEV_1, FVC, forced expiratory flow at 50% of exhalation (FEF_{50}), and peak expiratory flow (PEF). The highest value of the parameters that were technically satisfactory were reported. Fifteen of the children repeated spirometry within 3 weeks to evaluate between-day reproducibility.

Urine samples of half of the children (randomly chosen) were collected and stored within 4 hours at -20ºC until analysis for cotinine (Calbiotech, Spring Valley, CA, USA) and creatinine (Jaffe method, Roche Diagnostics GmbH,

Mannheim, Germany). Urinary cotinine-to-creatinine ratios were log-transformed. Significant exposure to environmental tobacco smoke (ETS) was defined as cotinine ≥30 ng/mg creatinine.[4]

Spirometric parameters were compared between subgroups using the Student's *t* test or ANOVA as appropriate, and confirmed by linear regression. Multiple regression analysis was used to determine relationship between subjects' best spirometric parameters and physical traits. The regression models were tested for deviation from linear effects of age, height, and weight by means of additive models. Alternative models in which lung function measures and/or the explanatory variables were log-transformed or square-rooted were also carried out. Prediction equations for different spirometric parameters were derived, and sex-specific normograms were constructed using the LMS method.

Results

Out of 4168 eligible preschool children, 2833 (68%) were recruited. In the training phase, 911 (66.4%) of 1371 eligible children consented to participate. Of them, 832 children attempted spirometry and 79 refused testing (Table 1). Only 123 children met ATS/ERS criteria for valid spirometric measurement, 79 of them fulfilled our inclusion criteria. This high failure rate was not unexpected, as all the research staff were new to incentive spirometry. Spirometric data from this phase was not included in the analysis of reference standards. In the research phase, 1922 (68.7%) of 2797 children from 19 nurseries and kindergartens consented to participate. Of them, 12.7% (from four schools) resided in Hong Kong Island, 52.8% (from 10 schools) resided in Kowloon, 22.8% (from four schools) resided in the New Territories East, and 11.8% (from one school) resided in the New Territories West. Excluding subjects with medical and technical problems, a subgroup of 770 (40.1%) could provide spirometric data to establish the reference standards.

The success rates of spirometry varied from 40.6% for those aged <3 years to 95.7% for those aged 6 years. Compared with girls, boys had higher $FEV_{0.5}$, $FEV_{0.75}$, FEV_1, FVC, and PEF values (P<0.001 to 0.010), whereas FEF_{50} and $FEV_{0.5}$/FVC values were independent of gender. The reference standards for individual parameters were thus separately analysed for boys and girls. FEF_{50} was not analysed because of an unsatisfactory R^2 by linear regression. Standing height without any data transformation was the strongest predictor for $FEV_{0.5}$, $FEV_{0.75}$, FEV_1, FVC, and PEF. Table 2 summarises the prediction equations for different spirometric parameters. Bland-Altman plots revealed good between-day agreement for $FEV_{0.5}$ and FVC, with the respective Cronbach's α being 0.985 (95% CI, 0.956-0.995) and 0.995 (95% CI, 0.987-0.998) [P<0.001 for both].

Table 1. Demographic and clinical features of subjects in training and research phases

Characteristic	All children in the training phase (n=946)*	Research phase	
		All children who consented (n=1922)	Children providing spirometric data (n=770)
Mean±SD age (years)	4.5±1.0	4.4±1.0	4.8±0.9†
No. (%) of males	489 (51.7)	1053 (54.8)	417 (54.2)
Anthropometric parameters (mean±SD)			
Body weight (kg)	17.7±3.9	17.5±3.6	18.4±3.9
Standing height (cm)	105.1±8.4	105.2±8.3	107.3±7.7†
Sitting height (cm)	-	58.1±5.6	58.8±5.8
Waist circumference (cm)	49.5±4.5	49.2±4.9	49.8±5.1
Birth history (no. [%] of subjects)			
Born <37 weeks of gestation	70 (7.9)	154 (8.0)	-
Birth weight <2.5 kg	57 (6.4)	160 (8.3)	-
Born outside Hong Kong	64 (6.8)	142 (7.4)	71 (9.2)
Breastfeeding ever (no. [%] of subjects)	462 (48.7)	996 (51.8)	402 (52.2)
Daycare attendance ever (no. [%] of subjects)	129 (13.6)	337 (17.5)	131 (17.0)
Current domestic tobacco smoke exposure (no. [%] of subjects)	382 (40.3)	770 (40.1)	304 (39.5)
Maternal tobacco smoking (no. [%] of subjects)			
During pregnancy	32 (3.5)	76 (4.0)	29 (3.8)
During infancy	79 (8.5)	157 (8.2)	56 (7.3)
Over past 12 months	90 (9.5)	190 (9.9)	66 (8.6)
Dog/cat keeping at home (no. [%] of subjects)			
During infancy	155 (16.3)	192 (10.0)	73 (9.5)
Over past 12 months	129 (13.6)	122 (6.3)	45 (5.8)
History of atopic disorders (no. [%] of subjects)			
Asthma ever	64 (6.8)	99 (5.2)	-
Current wheeze	89 (9.4)	204 (10.6)	-
Rhinitis ever	235 (24.8)	543 (28.3)	197 (25.6)
Eczema ever	299 (31.5)	668 (34.8)	239 (31.0)

* Including 911 consented children and 35 children who returned questionnaires but did not consent for spirometry

† Age distribution for boys: 2 years (n=15), 3 years (n=82), 4 years (n=131), 5 years (n=161), and 6 years (n=28). Age distribution for girls: 2 years (n=13), 3 years (n=75), 4 years (n=120), 5 years (n=110) and 6 years (n=35). Standing height distribution for the 417 boys: <95 cm (n=24), 95-99 cm (n=45), 100-104 cm (n=91), 105-109 cm (n=98), 110-114 cm (n=84), 115-119 cm (n=56), and ≥ 120 cm (n=19). Standing height distribution for the 353 girls: <95 cm (n=23), 95-99 cm (n=38), 100-104 cm (n=75), 105-109 cm (n=94), 110-114 cm (n=68), 115-119 cm (n=43), and ≥120 cm (n=12).

Table 2. Prediction equations for spirometric parameters in Chinese preschool children as a function of: Spirometric index=α + β x standing height

Spirometric index	Height (cm)	α	β	R^2	Residual SD
Forced expiratory volume in 0.5 second ($FEV_{0.5}$) [L]					
Boys (n=417)	83.1-130.0	-1.267	0.019	0.623	0.116
Girls (n=353)	83.0-128.1	-1.387	0.020	0.652	0.109
$FEV_{0.75}$ (L)					
Boys (n=414)	83.1-130.0	-1.534	0.023	0.668	0.126
Girls (n=347)	83.0-128.1	-1.644	0.024	0.703	0.114
FEV_1 (L)					
Boys (n=388)	83.1-130.0	-1.767	0.026	0.700	0.130
Girls (n=327)	83.0-128.1	-1.769	0.025	0.718	0.117
Forced vital capacity (L)					
Boys (n=417)	83.1-130.0	-2.211	0.031	0.727	0.149
Girls (n=353)	83.0-128.1	-2.115	0.030	0.723	0.136
Peak expiratory flow (L/s)					
Boys (n=417)	83.1-130.0	-3.971	0.058	0.530	0.428
Girls (n=353)	83.0-128.1	-4.782	0.065	0.561	0.429

Urine samples were collected from 861 (44.8%) subjects. The cotinine level was high in 92 (10.7%) samples, which were from 77 (23.4%) of 329 children who reported current ETS exposure and 15 (2.8%) of 532 children who reported no such history (P<0.001).

High ETS exposure (high urinary cotinine level) was associated with lower values for all parameters, whereas subjects with parent-reported ETS exposure had higher $FEV_{0.5}$, $FEV_{0.75}$, FVC, and PEF values. An inverse trend was noted between urinary cotinine levels (from lowest to highest quartiles) and values of $FEV_{0.5}$ (P=0.002), $FEV_{0.75}$ (P=0.001), FEV_1 (P=0.016), FEF_{50} (P=0.009), and PEF (P<0.001), but not FVC (P=0.098). Children with recent respiratory tract infections (n=397) had lower $FEV_{0.5}$ values than those without (mean±SD, 0.70±0.21 vs 0.77±0.19 L; P<0.001). Similar findings were observed for $FEV_{0.75}$, FEV_1, FVC, and PEF (P<0.001 for all), but not FEF_{50} (P=0.079) values. Table 3 summarises the effects of demographic, anthropometric, and early-life factors on spirometric variables. Stepwise linear regression revealed that $FEV_{0.5}$ was associated with place of birth (β=0.027; 95% CI, 0.004-0.050; P=0.021) and history of current wheeze (β=0.002; 95% CI, 0.001-0.004; P=0.034), after adjustment for age, sex, residence, standing height, and respiratory tract infection as covariates. A history of asthma was associated with low FEF_{50} (β=0.192; 95% CI, 0.104-0.280; P≤0.001) and $FEV_{0.5}$/FVC (β=4.731; 95% CI, 2.664-6.799; P<0.001) values.

Discussion

Spirometric parameters in Chinese school-age children were up to 12% lower than in Caucasians. This difference may have been due to body size and shape. Chinese newborns had smaller chest circumferences than Caucasian babies, and probably have smaller lungs. However, by superimposing medians and 5th percentile lines for FEV_1 and FVC of Caucasians[3] on our normograms, these parameters were in fact higher in Chinese than Caucasian preschool children. This observation might be attributed to our use of animation programmes as an incentive.

As in other populations, standing height was the best predictor of different spirometric outcomes. Lung function parameters ($FEV_{0.5}$, FEV_1, and FVC) were higher in boys than girls, which was consistent with reports in Caucasian populations.[3,5] Because of small sample sizes, caution is needed when applying the prediction equations to children at extremes of age or standing height.

The Asthma UK Collaborative Initiative lacked sufficient data relevant to the present prediction equations for $FEV_{0.5}$, and the smaller sample size for $FEV_{0.75}$ also limited appropriate interpretation of any sex difference for this parameter.[3] This may be partly due to unavailability of international guidelines at that time. Our study focused on the measurement of FEV_t, as it is more clinically relevant for children, whereas $FEV_{0.5}$ could be measured in all recruited subjects who provided valid spirometric data.

This study had several limitations. Like other preschool spirometric references,[1,3,5] this cross-sectional study had limited interpretation of longitudinal changes in lung function. The retrospective nature of the study made it difficult to distinguish differences in lung function attributable to equipment and measurement techniques from genuine differences. Nonetheless, we performed incentive spirometry according to international guidelines,[2] which should have minimised intra- and inter-observer variability. In terms of subject selection, it was impossible to accurately define the presence of respiratory tract infections unless respiratory samples had been collected to screen for common respiratory pathogens. To overcome this problem, we excluded subjects with fever of ≥38ºC, cough, rhinorrhoea, and sore throat within 4 weeks. Our study population might have over-represented Kowloon children and under-represented those from Hong Kong Island and the New Territories West, when compared with 2006 population by-census statistics. This discrepancy was due to the high refusal rate from schools in the New Territories West, small student numbers in schools on

Table 3. Association between spirometric parameters and potential risk and protective factors in 1402 children with valid spirometric data

Characteristic	Forced expiratory volume in 0.5 second ($FEV_{0.5}$) [L]	P value	Forced expiratory flow at 50% of exhalation (FEF_{50}) [L/s]	P value	$FEV_{0.5}$/ forced vital capacity (%)	P value
Sex		0.002		0.552		0.001
Male (n=770)	0.762 (0.199)		1.352 (0.449)		70.8 (9.1)	
Female	0.730 (0.188)		1.370 (0.685)		72.5 (9.1)	
Born <37 weeks gestation		0.787		0.304		0.353
Yes (n=103)	0.743 (0.179)		1.305 (0.396)		70.8 (9.9)	
No	0.748 (0.196)		1.364 (0.578)		71.6 (9.1)	
Low birth weight <2.5 kg		0.001		0.009		0.434
Yes (n=107)	0.690 (0.195)		1.222 (0.446)		70.8 (10.6)	
No	0.753 (0.194)		1.372 (0.575)		71.6 (9.0)	
Born outside Hong Kong		<0.001		<0.001		0.695
Yes (n=115)	0.855 (0.187)		1.528 (0.472)		71.3 (7.6)	
No	0.738 (0.192)		1.345 (0.573)		71.6 (9.3)	
Breastfeeding ever		0.988		0.236		0.118
Yes (n=722)	0.748 (0.197)		1.377 (0.664)		71.9 (9.1)	
No	0.748 (0.192)		1.342 (0.442)		71.2 (9.2)	
Daycare attendance ever		0.204		0.206		0.257
Yes (n=242)	0.733 (0.202)		1.318 (0.455)		70.9 (9.8)	
No	0.751 (0.193)		1.369 (0.588)		71.7 (9.0)	
Current domestic tobacco smoke exposure		0.520		0.881		0.846
Yes (n=582)	0.752 (0.189)		1.357 (0.436)		71.5 (8.8)	
No	0.745 (0.198)		1.362 (0.645)		71.6 (9.4)	
Maternal tobacco smoking during pregnancy		0.355		0.847		0.663
Yes (n=57)	0.771 (0.178)		1.374 (0.352)		72.1 (8.1)	
No	0.747 (0.195)		1.359 (0.575)		71.5 (9.2)	
Maternal tobacco smoking during infancy		0.984		0.643		0.382
Yes (n=113)	0.748 (0.201)		1.336 (0.453)		70.8 (8.4)	
No	0.747 (0.194)		1.362 (0.577)		71.6 (9.2)	
Maternal tobacco smoking over past 12 months		0.783		0.379		0.069
Yes (n=141)	0.752 (0.193)		1.320 (0.430)		70.4 (8.1)	
No	0.747 (0.195)		1.364 (0.581)		71.7 (9.3)	
Dog/cat keeping at home during infancy		0.259		0.297		0.822
Yes (n=125)	0.746 (0.171)		1.346 (0.393)		71.7 (9.2)	
No	0.748 (0.196)		1.361 (0.579)		71.5 (9.1)	
Dog/cat keeping at home over past 12 months		0.004		0.031		0.493
Yes (n=73)	0.721 (0.177)		1.329 (0.423)		72.1 (9.5)	
No	0.750 (0.196)		1.363 (0.580)		71.5 (9.1)	
History of asthma ever		0.608		0.018		<0.001
Yes (n=76)	0.737 (0.181)		1.210 (0.430)		66.7 (10.4)	
No	0.748 (0.195)		1.369 (0.573)		71.8 (9.0)	
History of wheezing ever		0.431		0.674		0.002
Yes (n=241)	0.739 (0.206)		1.346 (0.954)		69.9 (9.6)	
No	0.750 (0.192)		1.363 (0.448)		71.9 (9.0)	
Current wheezing		0.042		0.369		0.255
Yes (n=153)	0.718 (0.214)		1.321 (1.153)		69.3 (10.3)	
No	0.771 (0.190)		1.379 (0.434)		70.7 (8.2)	
History of rhinitis ever		0.002		0.296		0.469
Yes (n=405)	0.773 (0.197)		1.385 (0.448)		71.3 (9.1)	
No	0.738 (0.193)		1.350 (0.610)		71.7 (9.2)	
History of eczema ever		0.324		0.590		0.972
Yes (n=476)	0.741 (0.197)		1.371 (0.755)		71.5 (9.2)	
No	0.752 (0.193)		1.354 (0.442)		71.6 (9.1)	

Hong Kong Island, and large student numbers in schools in Kowloon. Nonetheless, the body anthropometry (and thus lung volume) of preschoolers in the four geographical regions was similar. As all the subjects did not have asthma/wheezing, they should not have been vulnerable to environmental exposures (eg ambient pollution) that might have differed in these regions.

Conclusions

This territory-wide community study established normograms and prediction equations by incentive spirometry for Chinese children in Hong Kong. Standing height was the best predictor for FEV, which was higher in boys than girls. High ETS exposure (high urinary cotinine level) was associated with lower values for all measured parameters; FEV were influenced by intercurrent respiratory tract infection, birth weight, place of birth, and a history of wheezing.

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