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Spirometric standards for healthy adult lifetime nonsmokers in Australia

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Spirometric standards for healthy adult lifetime nonsmokers in Australia. C.J. Gore, A.J. Crockett, D.G. Pederson, M.L. Booth, A. Bauman, N. Owen. ©ERS Journals Ltd 1995.

ABSTRACT: The aim of this study was to develop suitable spirometric prediction equations for asymptomatic Caucasian adults in the Australian population. These equations were compared with those of previous studies and constants were presented which, when associated with the prediction equations, permitted the calculation of 5% tolerance intervals for lung function.

The 1,302 subjects (aged 18–78 yrs) who underwent pneumotachograph spirometry, using techniques recommended by the American Thoracic Society, were a sample from metropolitan Adelaide, South Australia. The variables recorded were sex, age, height, mass, forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), peak expiratory flow rate (PEFR), forced mid-expiratory flow ($FEF_{25-75\%}$) and FEV_1/FVC ratio. Complete data were obtained for 614 females and 621 males, but the sample was reduced to 249 females and 165 males when only lifetime nonsmokers with no adverse bronchial symptoms were selected. Prediction equations of normal lung function were obtained from the reduced sample by multiple regression, with age, height and functions of both age and height as predictors.

The derived equations did not differ significantly from the majority of previously reported equations and were generally superior in their ability to predict the lung function of the asymptomatic ex-smokers who were part of the original sample. Analysis of the sensitivity, specificity and predictive power of 5% tolerance limits for the presence of symptoms revealed the important roles of FEV_1, FEV_1/FVC and $FEF_{25-75\%}$ in diagnostic testing.

The present prediction equations are recommended for use on the Australian population and on populations with similar Caucasian characteristics.

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Spirometry is used routinely to evaluate patients who have, or who are at risk of developing, respiratory diseases. Ideally, the spirometric standards used to delineate normal lung function should be obtained from a relatively large random sample of the relevant population, and should be based on measurement techniques in accordance with guidelines published by a group such as the American Thoracic Society (ATS) [1]. The common practice in recent studies has been to define the relevant population as being the portion of the total population comprising only healthy, lifetime nonsmokers [2–4].

Past studies of lung function on the Australian population have invariably fallen short of the ideal. For example, the standards reported by Gibson *et al.* [5] were derived using equipment that did not meet the contemporary guidelines of the ATS [1], and their sample was biased toward individuals of high socioeconomic status. Hanna [6] reported a study of a small sample (n=91) which included hospital patients and ex-smokers. Although other studies [3, 4] used suitable equipment and testing procedures on lifetime nonsmokers, their sample recruitment did not employ a randomized, probability selection procedure and, therefore, there remains some doubt about the relevance of their prediction equations to the Australian population.

Because of the limitations of previous Australian studies, Australian respiratory laboratories frequently use overseas prediction equations based on either North American or European populations [2, 7, 8]. However, even for the rigorous study of Crapo *et al.* [2], there is some doubt as to the population to which the standards are applicable, since more than 90% of the subjects in the sample were volunteers from the Mormon church in the state of Utah. Woolcock *et al.* [9] stated that since ethnicity, environmental and physical activity factors can effect normal lung function, prediction equations for a specific population should be derived from a random sample of the population itself.

The aim of this study was, therefore, to develop a set of prediction equations of lung function using data from a probability sample of asymptomatic Australian males and females and to compare the derived equations with those reported in previous Australian and overseas studies. A further aim was to estimate the sensitivity, specificity and predictive value of diagnostic procedures based on 5% tolerance limits of lung function variables.

Material and methods

Study subjects

The subjects (n=2,298) were those of the 1990 Pilot Survey of the Fitness of Australians [10], which was the first Australian adult fitness survey to attempt to obtain a probability sample. Subjects were randomly selected from the adult population (aged 18–78 yrs) of metropolitan Adelaide, South Australia, using a three stage systematic randomized sampling procedure [10]. Informed consent was obtained from all subjects in accordance with the requirements of the University of Adelaide Committee on the Ethics of Human Experimentation.

Study design

Each subject in the total sample (n=2,298) completed a general health and physical activity questionnaire [10], in which they reported on their smoking habits, sex, age, height and mass. The last two variables are referred to as self-reported height and self-reported mass. Spirometry was then carried out on a subsample of subjects (n=1,302), consisting of those from the total sample who volunteered to undertake a comprehensive fitness assessment. Those subjects who did not volunteer for the fitness assessment were classified as having missing data for spirometry. Immediately prior to undergoing spirometry, each subject completed a 16 item bronchial symptoms questionnaire developed by the International Union Against Tuberculosis (IUAT) [11]. The 16 questions, plus an additional question designed to identify subjects with a current respiratory infection, are shown in the Appendix. (The abbreviations corresponding to all questions are also contained in the Appendix).

Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), forced mid-expiratory flow ($FEF_{25–75\%}$) and peak expiratory flow rate (PEFR) were measured. The sex, age, standing height and body mass of each subject were also recorded, and the last two variables are referred to as measured height and measured mass.

Methods

Spirometry was conducted using a Cybermedic "Antler Pak" pneumotachograph (Louisville, Colorado, USA) interfaced to a lap-top computer (Toshiba, TS3200). The pneumotachograph, which meets ATS criteria [12], was calibrated with a Hans Rudolph 3.0 L syringe at three flow rates, in accordance with the manufacturer's recommendations, before each day's testing and after every few hours of testing. The temperature of the test room was measured with a calibrated mercury-in-glass thermometer, and barometric pressure was obtained twice daily from the Adelaide office of the Bureau of Meteorology. Barometric pressure at the test location was within 5 mmHg of that from the Bureau of Meteorology which could cause an error of approximately 0.04% in body temperature and pressure, saturated with water vapour (BTPS) correction of the spirometry values.

Spirometry flow-volume loops were conducted in accordance with ATS recommendations [1]. Seated subjects wearing a noseclip completed three trials within 3% of each other. The values analysed were the largest FVC and FEV_1, regardless of the technically satisfactory trial from which they were obtained. PEFR and $FEF_{25–75\%}$ were recorded from the trial with the largest sum of FVC and FEV_1. In addition to these measured parameters, the ratio of FEV_1 to FVC (FEV_1/FVC, expressed as a percentage) was calculated from the largest FEV_1 and FVC.

Standing height was measured using the method of Ross and Marfell-Jones [13] with a custom-built anthropometer validated against an Harpenden anthropometer. Body mass was measured barefoot and in light clothing on an A and D Mercury (Adelaide, South Australia) electronic load cell scale (130×0.05 kg).

Analysis

Only nonsmoking subjects were used in the derivation of prediction equations, with a smoker being defined as a subject who had smoked at least one cigarette a day (or one or more cigars a week, or one or more ounces of pipe tobacco a month) for as long as one year. The variables corresponding to the questions in the bronchial symptoms questionnaire supplied information on each subject's bronchial status. However, redundancy among these questions was expected, and thus the first step of the analysis was to determine the bronchial symptoms variables which were most strongly associated with low lung function, so that these variables could be used to exclude symptomatic subjects. The second step of the analysis determined the prediction equations from the sample of asymptomatic subjects, whilst the third step cross-validated the derived equations with the equations from previous studies. The fourth step in the analysis determined the 5% tolerance intervals for asymptomatic subjects and then the sensitivity, specificity and predictive values of diagnostic tests based on those limits. When multiple regression analyses were used (steps 1–3), residuals were checked for outliers [14] and for normality [15]. Unless otherwise indicated, a 5% significance level was used in all statistical tests, with the Bonferroni procedure [16] being applied where multiple tests were carried out simultaneously.

Step 1: selection of the exclusion variables. Data of females and males were combined and a multiple regression analysis was carried out for each lung function variable using the following set of independent variables: sex (S); age (A) yrs; age squared (A^2); measured height (H) metres; height squared (H^2); height cubed (H^3); measured mass (M) kg; mass squared (M^2); age × height (AH); and age × mass (AM). The bronchial symptoms variables were added to the equations in turn, to test their individual associations with lung function. In a second round of analyses, the symptom variables were permitted to enter each multiple regression equation in a forward stepwise fashion.

The results of the two rounds of analysis were amalgamated to determine a set of critical bronchial symptom variables, which were consistently associated with a significant reduction in lung function. All subjects who had responded in the affirmative to any of the critical bronchial symptom questions were defined as being symptomatic and were excluded, thus producing a sample of asymptomatic subjects. Analyses of covariance were used to compare the means of the lung function variables for the symptomatic and asymptomatic, lifetime nonsmokers. The covariates in the analyses were age, height, and mass, and the means were, therefore, adjusted to allow for variations in age, height and mass between the two groups of subjects.

Step 2: derivation of the prediction equations. Data on the asymptomatic, lifetime nonsmokers were used in multiple regression analyses, which produced the 10 prediction equations, *i.e.* prediction equations for FVC, FEV_1, PEFR, $FEF_{25-75\%}$ and FEV_1/FVC both for females and males. In each analysis, the physical predictors significantly associated with lung function were selected from among A, A^2, H, H^2, H^3, M, M^2, AH and AM. The value of C_p (the model selection criterion) [17] was calculated for each possible combination of the nine predictors, and the chosen model was that for which C_p was first less than p (the number of predictors plus the intercept) as p increased. Each model chosen in this manner had the property that the error mean square was no greater than the error mean square with all nine predictors in the model. The coefficient of determination (r^2) was used as the measure of goodness-of-fit of each equation, and the standard error of the estimate (SEE) was used as an estimate of error variation.

Step 3: cross validation against other prediction equations. Comparisons were made with similar equations derived by Crapo *et al.* [2], Withers and co-workers [3, 4], Gibson *et al.* [5], Hanna [6], Morris *et al.* [7] and Quanjer *et al.* [8]. Each equation derived in those previous studies was used to calculate predicted values, and the prediction errors (our measured minus their predicted values) were regressed linearly on our predicted values.

Another basis for comparison of the equations was the level of agreement between observed and predicted values. However, for the data on asymptomatic nonsmokers, none of the equations derived in previous studies could have produced a lower error sum of squares than the present equations, for a given number of predictors. The data for asymptomatic ex-smokers (n=270) were therefore used, where ex-smokers were defined as subjects who did not currently smoke but who had smoked for as long as one year in the past. In this way, the equations from previous studies were allowed to compete on equal terms, in a statistical sense, with our equations. Each of our equations and each equation derived by previous authors was used to predict the lung function for each asymptomatic ex-smoker and the equations were compared on the basis of the sum of the squares of the deviations between observed and predicted values.

Step 4: tolerance limits for asymptomatic subjects. For a subject of known sex, age and height, the interest is in whether the subject's measured value for a particular lung function variable is less than the lower limit of normal for the population of asymptomatic, lifetime nonsmokers. The lower limit of normal, for which the term "tolerance limit" [18] is appropriate, was defined as the fifth percentile of the population [19]. Tolerance limits may be defined in more than one way, and the definition used here was such that the lower 5% of the population was below the tolerance limit, on average [18]. With that definition, and under assumption of normally distributed residuals, the tolerance limit for a particular combination of predictor values was numerically identical to the lower end of a 90% confidence interval for the true value of a subject with those predictor values. Confidence intervals of that type, often termed "prediction intervals", are produced routinely by most statistical computer packages and increase in width as predictors move away from their means. However, as has been done in previous studies [2–5], a single constant was determined for each prediction equation which, when subtracted from a predicted value, gave a lower 5% tolerance limit. In this case, the constant was one-half of the width of the 90% confidence interval when all predictors were fixed at their mean. Since this was the minimum of all possible constants, the actual percentage of a population below a calculated tolerance limit may slightly exceed the nominal 5%.

The constants required for the calculation of 5% one-sided tolerance intervals were determined and then applied to the sample of asymptomatic, lifetime nonsmokers to see whether the observed percentages below the tolerance limits agreed with the nominal percentages. The constants were also applied to the sample of ex-smokers and the sample of smokers, who were part of the total 1,302 subjects tested, to estimate the proportions of those subject groups which fell below the tolerance limits.

By defining the aim of a procedure as being to identify subjects who are symptomatic rather than asymptomatic, the characteristics of diagnostic procedures based on the tolerance intervals were investigated. A positive test was considered to be one for which the subject's measured value was below the 5% tolerance limit and estimates of sensitivity, specificity and the predictive value of both a positive and negative test were obtained for both the ex-smokers and smokers in the sample.

Results

The exclusion of subjects with missing values reduced the sample size from 2,298 to 1,235, and the restriction to lifetime nonsmokers reduced it further to 560 subjects. These three groups of subjects were similar in age as well as both in self-reported and measured height and mass characteristics. For example, the mean ages (±SD) of females were 46 (±16) yrs for the complete sample, 45 (±15) yrs for the sample with missing values excluded, and 46 (±15) yrs for the lifetime nonsmokers. The corresponding values for males were 46 (±16) 45 (±15) and 42 (±15) yrs. Both for measured and self-reported height, the means and standard deviations were constant across the three groups for females and males. Thus, no bias was introduced for age and self-reported height and mass for the subsamples compared with the original sample.

Selection of the exclusion variables

Among the lifetime nonsmokers, 156 females and 92 males responded "yes" to one or more of the bronchial symptoms questions. If all of those subjects had been excluded from subsequent analyses, then the sample sizes would have been 186 females (46% less than the original sample size of 342) and 126 males (42% less than the original sample size of 218). In order to retain as many subjects as possible who did not have reduced lung functions, analyses were, therefore, carried out to identify the bronchial symptoms variables most strongly associated with low lung function. The correlations between the bronchial symptoms variables may be demonstrated by considering the first two in the list of questions: "Have you had wheezing or whistling in your chest, at any time in the last 12 months?" (WHEEZE) and "Have you woken up with a feeling of tightness in your chest first thing in the morning, at any time in the last 12 months?" (TGTCHEST). Among females, 47 out of 342 (13%) responded "yes" to WHEEZE, but among the females who responded "yes" to TGTCHEST the number who responded "yes" to WHEEZE was 21 out of 31 (68%). The corresponding numbers for males were 28 out of 218 (13%) and 11 out of 17 (65%), respectively.

When the symptom variables were included one at a time as covariates in multiple regression equations, the variables which showed a significant association ($p<0.001$) with a decrease in lung function for at least two of the lung function variables were: WHEEZE; TGTCHEST; "My breathing is never quite right" (BDALWAYS), "When you are in a dusty part of the house or with animals (for instance dogs, cats or horses) or near feathers (including pillows, quilts and eiderdowns) do you ever get a feeling of tightness in your chest (ADFTIGHT); "Have you ever had an attack of asthma?" (ASTHMAEV); "Have you ever had an attack of asthma in the last 12 months?" (ASTHMAR) and "Are you currently

Table 1. – Descriptive statistics of the 249 women and the 165 men, all asymptomatic, lifetime nonsmokers, used to derive prediction equations

Age group yrs	n	%	Age yrs	Height m	Mass kg	FEV_1 L	FVC L	PEFR $L \cdot s^{-1}$	$FEF_{25-75\%}$ $L \cdot s^{-1}$	FEV_1/FVC %
Females										
18–24	18	7.2	20	1.67	62	3.58	3.96	7.56	4.29	90
25–34	45	18.1	30	1.65	63	3.32	3.91	7.11	3.78	84
35–44	54	21.7	40	1.63	64	3.08	3.74	7.09	3.34	83
45–54	58	23.3	50	1.63	66	2.67	3.31	6.40	2.83	81
55–64	44	17.7	60	1.61	63	2.37	3.03	5.96	2.24	78
≥65	30	12.0	70	1.60	68	2.18	2.68	6.04	2.11	79
All ages	249	100	46	1.63	64	2.83	3.44	6.64	3.03	82
		SD	15	0.07	11	0.61	0.65	1.54	1.04	5.8
		Min	18	1.45	45	1.08	1.87	2.27	0.51	69
		Max	78	1.87	124	4.72	4.96	10.99	6.37	96
Males										
18–24	14	8.5	21	1.81	78	4.79	5.49	10.25	5.26	87
25–34	30	18.2	29	1.77	76	4.54	5.54	11.15	4.71	83
35–44	42	25.5	39	1.76	75	4.19	5.18	10.43	4.25	81
45–54	38	23.0	49	1.76	80	3.93	4.93	10.19	3.80	80
55–64	27	16.4	59	1.73	76	3.50	4.48	9.55	3.23	79
≥65	14	8.5	70	1.69	71	2.98	3.78	8.73	2.78	79
All ages	165	100	44	1.75	76	4.03	4.98	10.20	4.02	81
		SD	14	0.07	10	0.77	0.94	1.98	1.24	5.2
		Min	19	1.58	55	2.04	2.67	4.53	1.66	63
		Max	78	1.95	111	6.50	8.13	15.89	7.44	94

Mean data are presented. FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; PEFR: peak expiratory flow rate; $FEF_{25-75\%}$: forced mid-expiratory flow.

taking any medicine, pills or inhaler for asthma?" (ASTHMAME). When the symptom variables were permitted to enter multiple regression equations in a forward stepwise fashion, the variables which entered at the 5% level for at least two of the lung function variables were: "Have you, at any time in the last 12 months, been woken at night by an attack of shortness of breath?" (SBNIGHT); BDALWAYS; ASTHMAEV; and ASTHMAME. It was decided that an adequate set of exclusion variables was given by the union of the above two sets, namely: BDALWAYS, ASTHMAEV, ASTHMAME, WHEEZE, TGTCHEST, ADFTIGHT, ASTHMAR and SBNIGHT.

The nine physical variables A, A^2, H, H^2, H^3, M, M^2, AH and AM and the eight exclusion variables were forced into a separate multiple regression equation for each lung function variable and each sex. The remaining eight bronchial symptoms variables were given the opportunity to enter each equation in a forward stepwise manner, but none did. The eight symptom variables listed in the previous paragraph, rather than the full set of 16 variables, were, therefore, used in subsequent analyses to exclude individuals because of their bronchial symptoms.

Excluded subjects, were, therefore, those who had responded "yes" to one or more of the eight exclusion variables. The effect was to reduce the sample size of females from 342 to 249, a 27% reduction, and the sample size of males from 218 to 165, a 24% reduction. In each case, the mean for the excluded subjects was less than the mean for the retained subjects. The difference was significant for one-tailed tests ($p<0.005$) for PEFR for females and for FEV_1 and $FEF_{25-75\%}$ for both females and males. The descriptive statistics for the 414 retained subjects, all of whom were asymptomatic, lifetime nonsmokers, are presented in table 1. The "retained" sample was mostly of Caucasian descent; 99.6% of females and 98.6% of males were born in Australia, the United Kingdom, Ireland or Europe.

Derivation of the prediction equations

The derived prediction equations, including tests of normality for residuals, are given in table 2.

Comparisons with equations from previous studies

Values of r^2 and SEE for the present study and from six previous studies are shown in table 3. For the present study, r^2 was never greater than the value for the other studies but it was also the case that the present study gave the smallest value only for FEV_1/FVC for males. For the present study, SEE was smaller than the value for the other studies in four of the nine cases where a comparison was possible. In the linear regression analyses of residuals, the regression slope was significantly different from zero ($p<0.001$) for the FVC predictions of Hanna [6] and for the $FEF_{25-75\%}$ predictions of Morris *et al.* [7] and of Quanjer *et al.* [8]. In each of those three cases, the positive slope indicated that the equation derived by the previous author tended to overpredict when our predicted value was low and/or underpredict when our predicted value was high. It is noteworthy that the equations derived by Crapo *et al.* [2] gave the second smallest sum of squares of deviations between our measured and their predicted values for FEV_1, $FEF_{25-75\%}$ and FEV_1/FVC for females and for FEV_1 and FEV_1/FVC for males, and the third smallest sum of squares of deviations for FVC for both females and males. This indicates a general superiority of the Crapo *et al.* [2] equations over the equations derived by other researchers with respect to our data.

It was expected that the asymptomatic ex-smokers would have means which were either equal to or less than the means for asymptomatic, lifetime nonsmokers. In fact, the two means were not significantly different except for FEV_1, $FEF_{25-75\%}$ and FEV_1/FVC for males.

Table 2. – Equations for predicting lung function from age (yrs) and height (m)

Variable	Equation	ND p-value	Constant (5%)
Females			
FEV_1 L	$1.597 + 0.5552\ H^3 - 0.01574\ AH$	0.68	0.560
FVC L	$-3.598 - 0.0002525\ A^2 + 4.680\ H$	0.13	0.629
PEFR $L \cdot s^{-1}$	$3.364 - 0.02654\ A + 1.036\ H^3$	0.83	2.230
$FEF_{25-75\%}$ $L \cdot s^{-1}$	$-556.706 + 1036.012\ H - 637.715\ H^2 + 131.013\ H^3 - 0.02708\ AH$	0.32	1.271
FEV_1/FVC %	$-4068.039 + 0.7137\ A + 0.002234\ A^2 + 7675.039\ H - 4719.018\ H^2 + 967.776\ H^3 - 0.6946\ AH$	0.45	8.016
Males			
FEV_1 L	$2.081 + 0.5846\ H^3 - 0.01599\ AH$	0.59	0.798
FVC L	$12.675 - 0.0002764\ A^2 - 10.736\ H^2 + 4.790\ H^3$	0.56	1.035
PEFR $L \cdot s^{-1}$	$-6.099 - 0.0003425\ A^2 + 9.708\ H$	0.96	2.896
$\log_{10} FEF_{25-75\%}$ $L \cdot s^{-1}$	$0.5707 - 0.00005695\ A^2 + 0.025818\ H^3$	0.44	0.180
FEV_1/FVC %	$92.963 + 0.002487\ A^2 - 0.2260\ AH$	0.86	7.74

ND: p-value of the Shapiro-Wilk test of normality; Constant (5%): the constant which, when subtracted from a predicted value, gives the lower fifth percentile. For further abbreviations see legend to table. 1.

Table 3. – Comparison of prediction equations, sample sizes and values of r^2 and SEE

			Female						Male					
Variable	Study	[Ref]	C	A	H	n	r^2	SEE	C	A	H	n	r^2	SEE
FEV_1	Present	-	-	-	-	249	0.694	0.338	-	-	-	165	0.617	0.481
	Crapo	[2]	-1.578	-0.0255	3.42	126	0.80	0.326	-2.19	-0.0244	4.14	125	0.64	0.486
	Gibson	[5]	-0.835	-0.025	2.9	6275	0.68	0.42	-2.098	-0.032	4.4	6511	0.67	0.59
	Hanna	[6]	-4.3	-0.025	5.0	34	-	0.48	-4.3	-0.025	5.2	48	-	0.48
	Morris	[7]	-1.932	-0.025	3.504	471	0.53	0.47	-1.260	-0.032	3.622	517	0.53	0.55
	Quanjer	[8]	-2.604	-0.025	3.953	-	0.88	0.38	-2.492	-0.029	4.301	-	0.86	0.51
	Withers	[3, 4]	-3.097	-0.2477	4.405	161	0.738	0.336	-1.362	-0.03235	3.857	162	0.680	0.466
FVC	Present	-	-	-	-	249	0.657	0.380	-	-	-	165	0.565	0.623
	Crapo	[2]	-3.59	-0.0216	4.91	126	0.74	0.393	-4.65	-0.0214	6.00	125	0.54	0.644
	Gibson	[5]	-1.652	-0.023	3.7	6275	0.64	0.48	-4.169	-0.031	6.1	6511	0.68	0.67
	Hanna	[6]	-	-0.02	2.6	34	-	0.57	-8.69	-0.02	8.2	48	-	0.57
	Morris	[7]	-2.852	-0.024	4.528	471	0.50	0.52	-4.241	-0.025	5.827	517	0.42	0.74
	Quanjer	[8]	-2.887	-0.026	4.426	-	0.86	0.43	-4.345	-0.026	5.757	-	0.85	0.61
	Withers	[3, 4]	-5.634	-0.00000258 A^3	+ 5.9294 H	161	0.655	0.403	2.381	-0.0003307 A^2	+0.6246 H^3	162	0.629	0.575
PEFR	Present	-	-	-	-	249	0.243	1.35	-	-	-	165	0.234	1.75
	Hanna	[6]	8.0	-0.059	-	34	-	1.6	-9.1	-0.018	10.0	48	-	1.6
	Quanjer	[8]	-1.106	-0.030	5.501	-	0.48	0.90	0.154	-0.043	6.146	-	0.55	1.21
$FEF_{25-75\%}$	Present	-	-	-	-	249	0.466	0.768	-	-	-	165	0.370	-
	Crapo	[2]	2.683	-0.046	1.54	126	0.60	0.792	2.133	-0.038	2.04	125	0.42	0.962
	Hanna	[6]	-3.07	-0.043	5.0	34	-	0.96	-3.07	-0.043	5.0	48	-	0.96
	Morris	[7]	0.551	-0.030	2.362	471	0.31	0.80	2.513	-0.045	1.850	517	0.28	1.12
	Quanjer	[8]	2.924	-0.034	1.252	-	0.53	0.85	2.699	-0.043	1.944	-	0.44	1.04
	Withers	[3, 4]	4.117	-0.05695 A	+0.02333 M	161	0.568	0.802	6.231	-0.05248	-	162	0.443	0.997
FEV_1/FVC	Present	-	-	-	-	249	0.319	4.83	-	-	-	165	0.207	4.66
	Crapo	[2]	126.58	-0.252	-20.2	126	0.43	5.26	110.49	-0.152	-13	125	0.26	4.78
	Hanna	[6]	100.76	-0.186	-4.8	6275	0.28	7.52	106.28	-0.14	-10.7	6511	0.24	6.76
	Morris	[7]	95	-0.30	-	34	-	6	85.0	-0.15	-	48	-	6
	Quanjer	[8]	89.10	-0.192	-	-	0.35	6.51	87.21	-0.179	-	-	0.28	7.17
	Withers	[3, 4]	92.911	-0.29	-	161	0.398	5.8	112.13	-0.19	-14.0	162	0.259	5.04

Regression coefficients (r^2) are shown for the constant (C), age (A) and height (H). Mass (M; kg) is a predictor in one equation (Withers [3,4], $FEF_{25-75\%}$). No standard error is given for $FEF_{25-75\%}$ for males in the present study because a logarithmic transformation was used. SEE: standard error of the estimate. For further abbreviations see legend to table 1.

Table 4. – Comparisons of the present equations with those of previous studies using data from asymptomatic ex-smokers

Variable	Study	[Ref]	Females Mean	Females USS	Females Rank	Males Mean	Males USS	Males Rank
FEV_1	Present	-	0.02	13.6	1	-0.22	41.9	5
	CRAPO	[2]	0.03	13.9	2	-0.22	44.9	6
	GIBSON	[5]	0.12	15.4	4	-0.38	58.1	7
	HANNA	[6]	0.15	16.3	6	0.06	36.3	2
	MORRIS	[7]	0.23	18.6	7	0.14	36.8	4
	QUANJER	[8]	0.17	16.3	5	0.03	33.7	1
	WITHERS	[3, 4]	-0.09	14.6	3	-0.15	36.6	3
FVC	Present	-	0.10	18.9	1	-0.15	49.7	2
	CRAPO	[2]	0.13	20.3	2	-0.14	50.2	4
	GIBSON	[5]	0.23	24.9	5	-0.30	59.0	7
	HANNA	[6]	0.24	27.8	6	-0.02	49.7	3
	MORRIS	[7]	0.13	20.4	3	-0.06	45.4	1
	QUANJER	[8]	0.17	35.6	7	0.22	52.8	6
	WITHERS	[3, 4]	-0.17	20.8	4	-0.20	50.4	5
PEFR	Present	-	0.17	181	1	-0.28	701	1
	HANNA	[6]	1.59	431	3	2.17	1581	3
	QUANJER	[8]	0.36	187	2	0.94	828	2
$FEF_{25-75\%}$	Present	-	-0.10	65.9	1	-	-	-
	CRAPO	[2]	-0.16	69.1	3	-	-	-
	HANNA	[6]	-0.20	71.9	4	-	-	-
	MORRIS	[7]	-0.12	65.9	2	-	-	-
	QUANJER	[8]	-0.49	87.5	6	-	-	-
	WITHERS	[3, 4]	-0.09	74.7	5	-	-	-
FEV_1/FVC	Present	-	-1.20	3120	2	-2.23	7690	5
	CRAPO	[2]	-1.67	3230	4	-2.47	7740	4
	GIBSON	[5]	-4.08	4440	6	-2.90	8180	6
	HANNA	[6]	-0.87	3270	5	0.15	6650	3
	QUANJER	[8]	0.02	2944	1	-0.58	6604	2
	WITHERS	[3, 4]	0.75	3210	3	-0.42	6560	1

Values shown are the means and uncorrected sum of squares (USS) of the differences between observed and predicted values. No results are shown for $FEF_{25-75\%}$ for men since a logarithmic transformation was used in the present study. The ranks of USS values are shown, from smallest to largest. For abbreviations see legend to table. 1.

For each of these three variables, the mean of the asymptomatic ex-smokers (3.70 L, 3.26 $L \cdot s^{-1}$ and 78.0%, respectively) was significantly less than the corresponding mean for the asymptomatic, lifetime nonsmokers (3.90 L, 3.71 $L \cdot s^{-1}$ and 80.3%) ($p<0.005$). The female ex-smokers were, therefore, regarded as having the same lung function as the female nonsmokers, and the male ex-smokers were regarded as being the same as the male nonsmokers for the variables FVC and PEFR. When our derived equations and those of previous researchers were applied to the data from asymptomatic ex-smokers, the present equations gave the lowest sum of squares of deviations between the observed and predicted values for four of the five lung function variables for females and the lowest sum of squares for PEFR for males (table 4). Therefore, the present equations were more accurate than the equations of the previous researchers at predicting unimpaired lung function, as would be observed in an asymptomatic, lifetime nonsmoker or in a subject with similar lung function to that of an asymptomatic, lifetime nonsmoker, for the population from which our samples were drawn. The superiority of the equations of HANNA [6], WITHERS *et al.* [3] and QUANJER *et al.* [8] at predicting FEV_1 and FEV_1/FVC for male ex-smokers was due to their tendency to under-predict.

Tolerance limits

The constants to be subtracted from predicted values to produce lower 5% tolerance limits for the population of asymptomatic, lifetime nonsmokers are presented in table 2. To illustrate the use of the constants, suppose that a subject was a female, aged 30 yrs and 1.7 m in height: the equation in table 2 gives 3.52 L for the predicted FEV_1 for the asymptomatic, lifetime nonsmoking

Table 5. – Sensitivity, specificity and predictive value of a positive and a negative test for a diagnostic procedure in which the aim is to identify symptomatic subjects

Variable	Sensitivity Ex	Sensitivity Sm	Specificity Ex	Specificity Sm	Predictive value (+ve) Ex	Predictive value (+ve) Sm	Predictive value (-ve) Ex	Predictive value (-ve) Sm
Female								
FEV_1	0.08	0.15	0.96	0.89	0.43	0.50	0.72	0.58
FVC	0.08	0.12	0.96	0.98	0.43	0.78	0.72	0.59
PEFR	0.05	0.12	0.97	0.89	0.40	0.44	0.71	0.57
$FEF_{25-75\%}$	0.16	0.26	0.96	0.81	0.60	0.52	0.74	0.59
FEV_1/FVC	0.14	0.27	0.88	0.75	0.31	0.44	0.72	0.57
Male								
FEV_1	0.23	0.28	0.90	0.81	0.45	0.55	0.78	0.56
FVC	0.08	0.12	0.96	0.90	0.42	0.50	0.75	0.53
PEFR	0.18	0.21	0.90	0.86	0.38	0.57	0.76	0.55
$FEF_{25-75\%}$	0.40	0.33	0.79	0.76	0.40	0.54	0.79	0.56
FEV_1/FVC	0.36	0.24	0.83	0.80	0.40	0.50	0.80	0.56

Subjects with a positive test are those who fall below the 5% tolerance limit of a lung function variable. Results are given for ex-smokers (Ex) and smokers (Sm). For abbreviations see legend to table 1.

female of that age and height. The constant corresponding to 5% tolerance for FEV_1 of females is 0.560 L (table 2); and it may, therefore, be concluded that 5% of asymptomatic, female, lifetime nonsmokers of that age and height would be expected to have an FEV_1 below (3.52 - 0.560) = 2.96 L.

For all five lung function variables, both for females and males, either 4 or 5% of asymptomatic, lifetime nonsmokers were below their 5% tolerance limit, which is an acceptable level of agreement. However, the percentage of ex-smokers below their 5% tolerance limit ranged from 4% (PEFR for females) to 26% ($FEF_{25-75\%}$ for males), and the percentage of smokers below their 5% tolerance limit ranged from 6% (FVC for females) to 28% ($FEF_{25-75\%}$ for males).

The proportion of subjects who were symptomatic was 38 out of 131 (0.29) and 61 out of 141 (0.43) for female ex-smokers and smokers, respectively, and 62 out of 239 (0.26) and 77 out of 164 (0.47) for male ex-smokers and smokers, respectively. Three of the 38 symptomatic female ex-smokers were below the 5% tolerance limit for FEV_1. The estimated sensitivity of the test based on FEV_1 for female ex-smokers was, therefore, 3 in 38 (0.08). Eighty nine of the 93 asymptomatic female ex-smokers were above the 5% tolerance limit for FEV_1, giving an estimated specificity of 89 in 93 (0.96). The estimated predictive value of a positive test was therefore 3 in 7 (0.43) and the estimated predictive value of a negative test was 89 in 124 (0.72). The complete set of sensitivities, specificities and predictive values are given in table 5. However, these predictive values are specific to the population used in this study and in another population where the prevalence of respiratory symptoms is different, the predictive power may not be the same.

Discussion

This study reports predicted normal values for spirometric parameters derived from an attempted probability-based random sample using a pneumotachograph coupled to a computer. Many previous studies that have reported normal values [2–7] have not used such a methodologically-sound approach for sample selection. However, it is likely that the current sample is not a true probability sample because this study of lung function was a subset of a study of community fitness levels. Nevertheless, our sampling procedure was similar to that of Miller *et al.* [20], who also used volunteers, and our response rates were comparable. Miller *et al.* [20] scheduled an examination for 62% of their volunteers, of whom 68% completed all tests. In the present study 72% of the volunteers booked for a physical health assessment and 57% of these people completed spirometry. Furthermore, no bias was introduced by the subsampling procedure of the current study for the lung function predictor variables, since there were only minor differences between the self-reported age, height and mass of the total sample (n=2,298), spirometry sample (n=1,302) and lifetime nonsmoking sample (n=560).

Like the majority of similar studies carried out in the past, the study was cross-sectional rather than longitudinal. Differences between cross-sectional and longitudinal studies in relation to decline in lung function parameters with age are not well-established [21–25]. Nevertheless, cross-sectional studies are more economical, easier to perform, require less time, and provide useful information even within their limitations.

Comparisons of coefficients of determination (table 3) for the present and past predictive equations revealed the relative superiority of the equations of Quanjer *et al.* [8]. However, a cross-validation technique based on linear regression demonstrated that the equations presented by Crapo *et al.* [2] gave better prediction than other previous studies for the present population. However, the best test of a prediction equation is how well the observed value of a subject agrees with the predicted value given by the equation. If alternative prediction equations were compared, the best would be the equation for which there was the closest overall agreement between observed and predicted values. No such comparisons have been reported by previous authors, presumably because of a lack of suitable data sets, but in the present study the data from ex-smokers who reported no adverse bronchial symptoms were available. The present equations produced closer agreement between observed and predicted values for FVC, FEV_1, PEFR and $FEF_{25-75\%}$ for females and for PEFR for males. These were five of the seven variables for which the differences between the means of lifetime nonsmokers and ex-smokers were not significant. This result lends strength to the assertion that the present equations are preferable to equations derived in the past for predicting the lung function of Australian subjects, or Caucasian subjects from a population with similar characteristics to the Australian population.

Burney *et al.* [26] tested the IUAT questionnaire for its ability to predict the bronchial response to histamine in adults aged 18–64 yrs living in two areas of southern England. Four variables found to be independently associated with increased reactivity were BDALWAYS, WHEEZE, ADFTIGHT and SBNIGHT. A positive response to one or more of those variables was sufficient for a subject to be classified as being reactive to the histamine challenge. The four variables identified by Burney *et al.* [26] were all among the eight critical variables identified in the present study. Of the 192 women who were symptomatic in the present study, among the 614 who responded to the IUAT questionnaire, 137 (71%) would have been classified as being reactive according to the criteria of Burney *et al.* [26]. Of the 192 men who were symptomatic, among the 621 who responded to the IUAT questionnaire, 150 (78%) would have been classified as being reactive according to the criteria of Burney *et al.* [26]. With a high degree of certainty, the subjects classified as "asymptomatic" and "symptomatic" in the present study may, therefore, be regarded as having been "nonreactive" and "reactive" to a histamine challenge of the type administered by Burney *et al.* [26].

The ATS [19] recommend that FVC, FEV_1 and the FEV_1/FVC ratio should be used for overall clinical diagnosis of lung dysfunction. Our results (table 5) for a sample both of female and male smokers and ex-smokers, indicate similar predictive ability for $FEF_{25-75\%}$ as for FVC, FEV_1 or FEV_1/FVC. The estimated specificities were also relatively constant across lung function variables; and on the basis of predicative ability or specificity there is little reason to favour one lung function variable over the others. For example, for male ex-smokers the specificities ranged 0.79–0.96 and the predictive values of positive and of negative tests ranged 0.38–0.45 and 0.75–0.80, respectively. However, there was considerable variability across lung function variables in the proportion of subjects who were below their 5% tolerance limits, and in sensitivity (table 5). The sensitivity of $FEF_{25-75\%}$ was generally superior to that of FEV_1/FVC for female and male ex-smokers and smokers in our sample. High sensitivity is an important feature of a test procedure and it follows from the sensitivities given in table 5 that $FEF_{25-75\%}$ is the most favoured variable for both male and female smokers and ex-smokers, closely followed by FEV_1/FVC. The apparent diagnostic superiority of $FEF_{25-75\%}$ for investigating ex-smokers and smokers may warrant further exploration. Similarly, Marcq and Minette [27] have demonstrated the value of $FEF_{25-75\%}$ to screen smokers with normal conventional spirometry for FVC, FEV_1 and the FEV_1/FVC ratio. Quanjer *et al.* [8] also note that $FEF_{25-75\%}$ has good sensitivity for diagnosing minimal airflow limitation, but caution that interpretation is difficult if the vital capacity is abnormal. Our results on a sample of smokers and ex-smokers are, therefore, consistent with the recommendations of Quanjer *et al.* [8].

In conclusion, we have presented a statistical procedure for developing and testing spirometric prediction equations that may be suitable in other cross-sectional surveys. The statistical analysis used to identify symptomatic subjects was apparently successful since there was a high probability that the symptomatic subjects would have been reactive to a histamine challenge, and the comparison of prediction equations using asymptomatic ex-smokers led to the conclusion that the present equations are preferred for the target population of the present study. The prediction equations presented here are recommended as most suitable for the Australian population and on populations with similar Caucasian characteristics.

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Appendix

The following 17 questions were part of the IUAT Bronchial Symptoms Questionnaire. Questions 1–8 and 12–16 each required a yes/no response, and the respondent was asked to choose and respond to only one of questions 9, 10 and 11.

1. WHEEZE – "Have you had wheezing or whistling in your chest, at any time in the last 12 months?"
2. TGTCHEST - "Have you woken up with a feeling of tightness in your chest first thing in the morning, at any time in the last 12 months?"
3. SBNONST - "Have you, at any time in the last 12 months, had an attack of shortness of breath that came on during the day when you were not doing anything strenuous?"
4. SBAFTEX - "Have you had an attack of shortness of breath that came on after you stopped exercising, at any time in the last 12 months?"
5. SBNIGHT - "Have you, at any time in the last 12 months, been woken at night by an attack of shortness of breath?"
6. CNIGHT - "Have you, at any time in the last 12 months, been woken at night by an attack of coughing?"
7. CMORN - "Do you usually cough first thing in the morning?"
8. CPHLEGM - "Do you usually bring up phlegm from your chest first thing in the morning?"
9. BDNEVER - "I never or only rarely get trouble with my breathing".
10. BDREG - "I get regular trouble with my breath ing, but it always gets completely better".
11. BDALWAYS - "My breathing is never quite right".
12. ADFTIGHT - "When you are in a dusty part of the house or with animals (for instance dogs, cats or horses) or near feathers (including pillows, quilts and eiderdowns) do you ever get a feeling of tightness in your chest?"
13. ADFSHORT - "When you are in a dusty part of the house or with animals (for instance dogs, cats or horses) or near feathers (including pillows, quilts and eiderdowns) do you ever start to feel short of breath?"
14. ASTHMAEV - "Have you ever had an attack of asthma?"
15. ASTHMAR - "Have you had an attack of asthma at any time in the last 12 months?"
16. ASTHMAME - "Are you currently taking any medicines, pills or inhalers for asthma?"
17. COLDFLU - "Do you have a cold or flu at the moment?"