Spirometric standards for healthy adult lifetime nonsmokers in Australia


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 (FEV1), forced vital capacity (FVC), peak expiratory flow rate (PEFR), forced mid-expiratory flow (FEF25–75%) and FEV1/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 FEV1, FEV1/FVC and FEF25–75% in diagnostic testing.

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

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 measured height and measured 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).

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 FEV1, regardless of the technically satisfactory trial from which they were obtained. PEFR and FEF25–75% were recorded from the trial with the largest sum of FVC and FEV1. In addition to these measured parameters, the ratio of FEV1 to FVC (FEV1/FVC, expressed as a percentage) was calculated from the largest FEV1 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 regres-
sion 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 \(\times\) height (AH); and age \(\times\) 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 for 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?" (TGTCH EST). 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 (ADF-TIGHT); "Have you ever had an attack of asthma?" (ASTHMAEV); "Have you ever had an attack of asthma in the last 12 months?" (ASTHMAAR) 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

<table>
<thead>
<tr>
<th>Age group yrs</th>
<th>n</th>
<th>%</th>
<th>Height m</th>
<th>Mass kg</th>
<th>FEV1 L</th>
<th>FVC L</th>
<th>PEFR L·s⁻¹</th>
<th>FEF25-75% L·s⁻¹</th>
<th>FEV1/FVC %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–24</td>
<td>18</td>
<td>7.2</td>
<td>20</td>
<td>1.67</td>
<td>62</td>
<td>3.58</td>
<td>3.96</td>
<td>7.56</td>
<td>4.29</td>
</tr>
<tr>
<td>25–34</td>
<td>45</td>
<td>18.1</td>
<td>30</td>
<td>1.65</td>
<td>63</td>
<td>3.32</td>
<td>3.91</td>
<td>7.11</td>
<td>3.78</td>
</tr>
<tr>
<td>35–44</td>
<td>54</td>
<td>21.7</td>
<td>40</td>
<td>1.63</td>
<td>64</td>
<td>3.08</td>
<td>3.74</td>
<td>7.09</td>
<td>3.34</td>
</tr>
<tr>
<td>45–54</td>
<td>58</td>
<td>23.3</td>
<td>50</td>
<td>1.63</td>
<td>66</td>
<td>2.67</td>
<td>3.31</td>
<td>6.40</td>
<td>2.83</td>
</tr>
<tr>
<td>55–64</td>
<td>44</td>
<td>17.7</td>
<td>60</td>
<td>1.61</td>
<td>63</td>
<td>2.37</td>
<td>3.03</td>
<td>5.96</td>
<td>2.24</td>
</tr>
<tr>
<td>≥65</td>
<td>30</td>
<td>12.0</td>
<td>70</td>
<td>1.60</td>
<td>68</td>
<td>2.18</td>
<td>2.68</td>
<td>6.04</td>
<td>2.11</td>
</tr>
<tr>
<td>All ages</td>
<td>249</td>
<td>100</td>
<td>46</td>
<td>1.63</td>
<td>64</td>
<td>2.83</td>
<td>3.44</td>
<td>6.64</td>
<td>3.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–24</td>
<td>14</td>
<td>8.5</td>
<td>21</td>
<td>1.81</td>
<td>78</td>
<td>4.79</td>
<td>5.49</td>
<td>10.25</td>
<td>5.26</td>
</tr>
<tr>
<td>25–34</td>
<td>30</td>
<td>18.2</td>
<td>29</td>
<td>1.77</td>
<td>76</td>
<td>4.54</td>
<td>5.54</td>
<td>11.15</td>
<td>4.71</td>
</tr>
<tr>
<td>35–44</td>
<td>42</td>
<td>25.5</td>
<td>39</td>
<td>1.76</td>
<td>75</td>
<td>4.19</td>
<td>5.18</td>
<td>10.43</td>
<td>4.25</td>
</tr>
<tr>
<td>45–54</td>
<td>38</td>
<td>23.0</td>
<td>49</td>
<td>1.76</td>
<td>80</td>
<td>3.93</td>
<td>4.93</td>
<td>10.19</td>
<td>3.80</td>
</tr>
<tr>
<td>55–64</td>
<td>27</td>
<td>16.4</td>
<td>59</td>
<td>1.73</td>
<td>76</td>
<td>3.50</td>
<td>4.48</td>
<td>9.55</td>
<td>3.23</td>
</tr>
<tr>
<td>≥65</td>
<td>14</td>
<td>8.5</td>
<td>70</td>
<td>1.69</td>
<td>71</td>
<td>2.98</td>
<td>3.78</td>
<td>8.73</td>
<td>2.78</td>
</tr>
<tr>
<td>All ages</td>
<td>165</td>
<td>100</td>
<td>44</td>
<td>1.75</td>
<td>76</td>
<td>4.03</td>
<td>4.98</td>
<td>10.20</td>
<td>4.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean data are presented. FEV1: forced expiratory volume in one second; FVC: forced vital capacity; PEFR: peak expiratory flow rate; FEF25-75%: forced mid-expiratory flow.
taking any medicine, pills or inhaler for asthma?" (ASTHMAE).
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 ASTHMAE. It was decided that an adequate set of exclusion variables was given by the union of the above two sets, namely: BDALWAYS; ASTHMAEV; ASTHMAE; WHEEZE; TGTCHTEST; ADFTIGHT; ASTHMAR and SBNIGHT.

The nine physical variables A, A², H, H², H³, M, M², 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 FEV₁ and FEF twenty-five–seventy-five 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.

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Equation</th>
<th>ND p-value</th>
<th>Constant (5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁ L</td>
<td>1.597 + 0.5552 H⁻¹ - 0.01574 AH</td>
<td>0.68</td>
<td>0.560</td>
</tr>
<tr>
<td>FVC L</td>
<td>-3.598 - 0.0002525 A² + 4.680 H</td>
<td>0.13</td>
<td>0.629</td>
</tr>
<tr>
<td>PEFR L⁻¹</td>
<td>3.364 - 0.02654 A + 1.036 H³</td>
<td>0.83</td>
<td>2.230</td>
</tr>
<tr>
<td>FEFtwenty-five–seventy-five L⁻¹</td>
<td>-556.706 + 1036.012 H⁻² - 637.715 H² + 131.013 H⁻³ - 0.02708 AH</td>
<td>0.32</td>
<td>1.271</td>
</tr>
<tr>
<td>FEV₁/FVC %</td>
<td>-4068.039 + 0.7137 A + 0.002234 A² + 7675.039 H⁻¹ - 94719.018 H² + 967.776 H³ - 0.6946 AH</td>
<td>0.45</td>
<td>8.016</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁ L</td>
<td>2.081 + 0.5846 H⁻¹ - 0.01599 AH</td>
<td>0.59</td>
<td>0.798</td>
</tr>
<tr>
<td>FVC L</td>
<td>12.675 - 0.0002764 A² - 10.736 H² + 4.790 H³</td>
<td>0.56</td>
<td>1.035</td>
</tr>
<tr>
<td>PEFR L⁻¹</td>
<td>-6.099 - 0.0003425 A² + 9.708 H</td>
<td>0.96</td>
<td>2.896</td>
</tr>
<tr>
<td>log₁₀ FEFtwenty-five–seventy-five L⁻¹</td>
<td>0.5707 - 0.0005695 A² + 0.025818 H³</td>
<td>0.44</td>
<td>0.180</td>
</tr>
<tr>
<td>FEV₁/FVC %</td>
<td>92.963 + 0.0002487 A² - 0.2260 AH</td>
<td>0.86</td>
<td>7.74</td>
</tr>
</tbody>
</table>

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.

### 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 r² and SEE for the present study and from six previous studies are shown in table 3. For the present study, r² 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 FEV₁/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 twenty-five–seventy-five 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 FEV₁, FEF twenty-five–seventy-five and FEV₁/FVC for females and for FEV₁ and FEV₁/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 FEV₁, FEF twenty-five–seventy-five and FEV₁/FVC for males.
Table 3. Comparison of prediction equations, sample sizes and values of $r^2$ and SEE

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study [Ref]</th>
<th>Female</th>
<th>C</th>
<th>A</th>
<th>H</th>
<th>n</th>
<th>$r^2$</th>
<th>SEE</th>
<th>Male</th>
<th>C</th>
<th>A</th>
<th>H</th>
<th>n</th>
<th>$r^2$</th>
<th>SEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1</td>
<td>Present</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>249</td>
<td>0.694</td>
<td>0.338</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>165</td>
<td>0.617</td>
</tr>
<tr>
<td></td>
<td>CRAPO [2]</td>
<td>-1.578</td>
<td>-0.025</td>
<td>3.42</td>
<td>126</td>
<td>0.80</td>
<td>0.326</td>
<td>-2.19</td>
<td>-0.0244</td>
<td>4.14</td>
<td>125</td>
<td>0.64</td>
<td>0.486</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>GIBSON [5]</td>
<td>-0.835</td>
<td>-0.025</td>
<td>2.9</td>
<td>6275</td>
<td>0.68</td>
<td>0.42</td>
<td>-2.098</td>
<td>-0.032</td>
<td>4.4</td>
<td>6511</td>
<td>0.67</td>
<td>0.59</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HANNA [6]</td>
<td>-4.3</td>
<td>-0.025</td>
<td>5.0</td>
<td>34</td>
<td>-</td>
<td>0.48</td>
<td>-4.3</td>
<td>-0.025</td>
<td>5.2</td>
<td>48</td>
<td>-</td>
<td>0.48</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MORRIS [7]</td>
<td>-1.932</td>
<td>-0.025</td>
<td>3.504</td>
<td>471</td>
<td>0.53</td>
<td>0.47</td>
<td>-1.260</td>
<td>-0.032</td>
<td>3.622</td>
<td>517</td>
<td>0.53</td>
<td>0.55</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>QUANJER [8]</td>
<td>-2.604</td>
<td>-0.025</td>
<td>3.953</td>
<td>-</td>
<td>0.88</td>
<td>0.38</td>
<td>-2.492</td>
<td>-0.029</td>
<td>4.301</td>
<td>-</td>
<td>0.86</td>
<td>0.51</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>WITHERS [3, 4]</td>
<td>-3.097</td>
<td>-0.2477</td>
<td>4.405</td>
<td>161</td>
<td>0.738</td>
<td>0.336</td>
<td>-1.362</td>
<td>-0.03235</td>
<td>3.857</td>
<td>162</td>
<td>0.680</td>
<td>0.466</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FVC</td>
<td>Present</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>249</td>
<td>0.657</td>
<td>0.380</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>165</td>
<td>0.565</td>
</tr>
<tr>
<td></td>
<td>CRAPO [2]</td>
<td>-3.59</td>
<td>-0.0216</td>
<td>4.91</td>
<td>126</td>
<td>0.74</td>
<td>0.393</td>
<td>-4.65</td>
<td>-0.0214</td>
<td>6.00</td>
<td>125</td>
<td>0.54</td>
<td>0.644</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>GIBSON [5]</td>
<td>-1.652</td>
<td>-0.023</td>
<td>3.7</td>
<td>6275</td>
<td>0.64</td>
<td>0.48</td>
<td>-4.169</td>
<td>-0.031</td>
<td>6.1</td>
<td>6511</td>
<td>0.68</td>
<td>0.67</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HANNA [6]</td>
<td>-</td>
<td>-0.02</td>
<td>2.6</td>
<td>34</td>
<td>-</td>
<td>0.57</td>
<td>-8.69</td>
<td>-0.02</td>
<td>8.2</td>
<td>48</td>
<td>-</td>
<td>0.57</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MORRIS [7]</td>
<td>-2.852</td>
<td>-0.024</td>
<td>4.528</td>
<td>471</td>
<td>0.50</td>
<td>0.52</td>
<td>-4.241</td>
<td>-0.025</td>
<td>5.827</td>
<td>517</td>
<td>0.42</td>
<td>0.74</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>QUANJER [8]</td>
<td>-2.887</td>
<td>-0.026</td>
<td>4.426</td>
<td>-</td>
<td>0.86</td>
<td>0.43</td>
<td>-4.345</td>
<td>-0.026</td>
<td>5.757</td>
<td>-</td>
<td>0.85</td>
<td>0.61</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>WITHERS [3, 4]</td>
<td>-5.634</td>
<td>-0.00000258</td>
<td>A^2</td>
<td>161</td>
<td>0.655</td>
<td>0.403</td>
<td>2.381</td>
<td>-0.0003307</td>
<td>A^2</td>
<td>162</td>
<td>0.629</td>
<td>0.575</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
+5.9294 H

| 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|
| FEF25–75%    | 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|
| FEV1/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 | - | 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], FEF25–75%). No standard error is given for FEF25–75% 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.
For each of these three variables, the mean of the asymptomatic ex-smokers (3.70 L, 3.26 L·s⁻¹ and 78.0%, respectively) was significantly less than the corresponding mean for the asymptomatic, lifetime nonsmokers (3.90 L, 3.71 L·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 FEV₁ and FEV₁/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 FEV₁ for the asymptomatic, lifetime nonsmoking
female of that age and height. The constant corresponding to 5% tolerance for FEV1 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 FEV1 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% (FEF25–75% for males), and the percentage of smokers below their 5% tolerance limit ranged from 6% (FVC for females) to 28% (FEF25–75% 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 asymptomatic female ex-smokers were below the 5% tolerance limit for FEV1. The estimated sensitivity of the test based on FEV1 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 FEV1, 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.
predicted values. No such comparisons have been report-
ed 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, FEV1, PEFR and FEF25–75% 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 equa-
tions are preferable to equations derived in the past for
predicting the lung function of Australian subjects, or
Caucasian subjects from a population with similar char-
acteristics 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 asso-
ciated with increased reactivity were BDALWAYS,
WHEEZER, ADFTIGHT and SBINIGHT. A positive
response to one or more of those variables was sufficient
for a subject to be classified as being reactive to the his-
tamine challenge. The four variables identified by
Burney et al. [26] were all among the eight critical vari-
able 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 hav-
ing been "nonreactive" and "reactive" to a histamine chal-
lenge of the type administered by Burney et al. [26].

The ATS [19] recommend that FVC, FEV1 and the
FEV1/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 FEF25–75%
as for FVC, FEV1 or FEV1/FVC. The estimated specific-
ities were also relatively constant across lung function
variables; and on the basis of predicative ability or speci-
ficity 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 pre-
dictive 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 vari-
able in the proportion of subjects who were below their
5% tolerance limits, and in sensitivity (table 5). The
sensitivity of FEF25–75% was generally superior to that
of FEV1/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 sen-
sitivities given in table 5 that FEF25–75% is the most
favoured variable for both male and female smokers and
ex-smokers, closely followed by FEV1/FVC. The apparent
diagnostic superiority of FEF25–75% for investigating
ex-smokers and smokers may warrant further explora-
tion. Similarly, Marco and Minette [27] have demon-
strated the value of FEF25–75% to screen smokers with
normal conventional spirometry for FVC, FEV1 and the
FEV1/FVC ratio. Quanjer et al. [8] also note that
FEF25–75% has good sensitivity for diagnosing minimal
airflow limitation, but caution that interpretation is dif-
ficult if the vital capacity is abnormal. Our results on
a sample of smokers and ex-smokers are, therefore, con-
sistent with the recommendations of Quanjer et al. [8].

In conclusion, we have presented a statistical proce-
dure for developing and testing spirometric prediction
equations that may be suitable in other cross-sectional
surveys. The statistical analysis used to identify symp-
tomatic 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 asympto-
matic 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.

Acknowledgement: Funding support from the Australian
Department of the Arts, Sport, the Environment and Territories
is gratefully acknowledged.

References
1. American Thoracic Society. Standardization of spiro-
1285–1298.
2. Crapo RO, Morris AH, Gardner RM. Reference spiro-
metric values using techniques and equipment that meet
ATS recommendations. Am Rev Respir Dis 1981; 123:
659–664.
3. Withers RT, Bourdon PC, Crockett A. Spirometric stan-
dards for healthy men lifetime nonsmokers. Human Biol
4. Withers RT, Lemmey AB. Lung volume and spiromet-
ric standards for healthy women lifetime nonsmokers. Human Biol
5. Gibson J, Gallagher H, Johansen A, Webster L. Lung
function in an Australian population. I. Spirometric
standards for nonsmoking adults. Med J Aust 1979; 1:
292–295.
6. Hanna G. Normal lung function values in an Australian
7. Morris JF, Koski A, Johnson LC. Spirometric standards
103: 57–67.
8. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF,
Peslin R, Yernault JC. Lung volume and forced expira-

tory flows: Report Working Party Standardization of
Lung Function Tests European Community for Steel and
affecting normal values for ventilatory lung function.
10. Gore CJ, Owen N, Bauman A, Booth M. Methods of the
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 breathing, 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?"