Lung function development in young adults: is there a plateau phase?

D.R. Robbins, P.L. Enright, D.L. Sherrill

ABSTRACT: Numerous population studies have reported that pulmonary function following the adolescent growth phase appears to be in a steady-state, where there is little or no growth occurring up to 40 yrs of age. We examined longitudinal forced expiratory volume in one second (FEV1), changes using three different statistical approaches to determine which subjects actually have significant trends during this period.

Participants, who were employees at a metal processing plant, underwent quarterly spirometry for up to 10 yrs. Test results up to 33 yrs of age were included in the analysis. Each subject's FEV1 data was first analysed using simple linear regression (SLR) to test for a statistically significant linear slope. Next, each subject's data were fitted using bootstrap sampling (BSS) of their original data, to yield reduced estimates of the slope variances and increase the power of detecting a significant trend. And thirdly, we fitted a regression breakpoint (BKPT) model to the data to find those subjects who may have piecewise linear growth or decline in function. All analyses were stratified, based on smoking status.

Subjects included 111 nonsmokers and 110 smokers. Among the nonsmokers, 34 subjects had significant slopes using SLR, an additional three using BSS, and only two with BKPT. Among the smokers, 36 had a significant trend using SLR, 7 were added using BSS, and no additional subjects with BKPT.

We conclude that in young adult males lung function is not in a steady-state and that as many as 40% have a significant slope, either positive or negative. In addition, the proportion of subjects with a positive slope was less among lifetime nonsmokers, suggesting that smokers may start to lose function at an earlier age than non-smokers.

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Several studies have examined development of lung function in young adults [1–8]. Some reported continued growth of lung function into early adulthood, followed by decline beginning at approximately 35 yrs of age [4], whilst others have described this early adult phase as a steady-state period, where there is little or no growth occurring. It is often called the "plateau phase" of lung function development [1, 5, 6]. The age interval defining the plateau phase depends on the study population, the pulmonary function measure of interest, smoking status, and the respiratory health status of the study participants. Tagg et al. [1] reported peak forced expiratory volume in one second (FEV1) levels at approximately 20–23 yrs of age, and a plateau phase that extended to 45 yrs of age. Their results also suggested that current smokers had shortened plateau phases followed by rates of decline similar to lifetime nonsmokers. In contrast, Sherrill et al. [6] found a shorter plateau phase for FEV1 in asymptomatic nonsmoking subjects that began at 17.4 yrs and ended at 25.9 yrs of age. Both studies also found gender differences, with females generally starting the plateau earlier than males and having longer plateau phases.

Most investigators agree that the onset of the plateau phase, if it exists, is related to the "adolescent growth spurt", perhaps with a lag period of around one year [9], but the interpretation of the end is less clear. Studies of this nature require that the subjects be followed longitudinally and have sufficient follow-up to yield accurate slope estimates, which generally requires around 5 yrs of data [10], depending on sample intervals. In most analyses of these data, subjects are grouped together to yield an overall mean trend. This process essentially ignores individual trends in favour of what the group as a whole is doing. If a number of these slopes are in opposing directions this could result in "regression to the mean", where in fact some subjects are continuing to increase lung function, whilst others may have already started to lose lung function, and still others may indeed be in a steady-state or plateau phase, but the net result indicates no apparent trend.

Characterizing lung function development during this
age interval poses several problems from an epidemiological perspective. Firstly, adolescents and young adults tend to move away from home and are less likely to remain active in population studies. Secondly, because this phase is relatively short, frequent pulmonary function testing must be performed to ensure adequate data for accurate modelling or statistical testing.

In this study, we examined the pulmonary function of subjects who were participants in a workplace monitoring study, where they were tested at least every 3 months for up to 10 yrs. We applied three different statistical methods, in an attempt to characterize the various patterns of growth or decline that might occur and to compensate for subjects who might have more variable or noisier observations.

**Methods**

**Population**

Beginning in 1975, all employees of a metal processing plant (blue collar, white collar and clerical) received quarterly medical examinations which included spirometry. Nurses performing the tests were certified by the National Institute of Occupational Safety and Health (NIOSH) approved training, and spirometers were calibrated daily using a 3.0 L syringe. A short respiratory history and at least 3 acceptable forced vital capacity (FVC) manoeuvres (as judged by observation of the flow-volume display) were obtained at each visit.

Subjects were selected for this analysis if they had five or more observations under 33 yrs of age and had at least 1.5 yrs of follow-up. The upper age limit was selected by fitting a piecewise linear regression model to the combined FEV1 versus age data of all male subjects under 50 yrs of age. A breakpoint (BKPT) or junction at 33 yrs of age was found to yield the best fit, where prior to 33 yrs of age subjects’ FEV1 appeared to be in a steady-state period, and after this age it started to decline more rapidly. The BKPT analysis is described in more detail in the statistical methods section. Observations obtained beyond 33 yrs of age were then excluded. Subjects were classified as “smokers” if they ever reported a non-zero number of cigarettes smoked per day, and otherwise as “nonsmokers”.

Since females are known to have different temporal patterns of pulmonary function growth than males [9] and there were only 25 females that met the selection criteria, they were excluded from the current analysis.

**Statistical methods**

The first step in the data analysis was to fit a simple linear regression (SLR) to each subject’s FEV1 versus age data, and test for statistically significant slopes. There could be several reasons why a subject did not have a significant slope. The most obvious would be that they were indeed in a steady-state or plateau phase of lung development. However, they could have had noisy observations that prevented detection of a linear trend due to large slope variance estimates, or they could have had a trend that was nonlinear. To determine if the former was true, we performed bootstrap sampling analysis (BSS) on all subjects’ data. This procedure served as a variance reduction technique. For this analysis, each subject’s FEV1 data were randomly sampled with replacement to generate 100 permuted samples or bootstrap samples, each of the same size as the original sample [11, 12]. Each bootstrap sample was then analysed using SLR to yield 100 bootstrap slope estimates. The standard deviation of these 100 slopes is the standard error estimate of the slope and can be used to test for statistical significance. This robust procedure was intended to detect subjects who had a linear trend in their data, but noisy or too few observations prevented their slope from reaching significance.

The breakpoint analysis (BKPT) fits two lines to the data that join at a common junction called a breakpoint. This technique is well-suited to fitting data that display a “hockey stick” or “dog leg” pattern. For example, the BKPT model would be expected to give the best fit for a subject who initially has increasing FEV1 followed by a plateau phase, or a subject who is initially in a steady-state period of development, and then has a period of more rapid decline. All analyses were stratified by smoking status, and hypothesis testing was performed at α=0.05 significance level. For our purposes, subjects were classified as having a statistically significant trend if any one procedure was significant. A statistically significant BKPT indicated that a piecewise linear model fitted a subject’s data better than SLR.

**Results**

The subjects analysed included 221 males who had at least five pulmonary function tests by 33 yrs of age. Characteristics of the population at their first clinical visit are summarized in table 1. The average age at entry was 25 yrs. Figure 1 shows the number of observations for each subject, and figure 2 shows the distribution of duration of follow-up. The average duration of follow-up was 5.1 yrs, which corresponds to approximately 21 observations. Figure 3 shows the predicted FEV1 trajectories for a 20% random sample of subjects, using the results from the SLR analyses and the regression line fitted to the population as determined using longitudinal methods [6]. The trajectories display a wide range

| Table 1. – Characteristics of the subjects at their first clinical visit (n=221) |
|---|---|
| Age yrs | 25 (4) |
| Height cm | 177 (7) |
| Duration of follow-up yrs | 5.1 (1.8) |
| Weight kg | 82 (15) |
| FEV1 L | 4.50 (0.74) |
| FVC L | 5.69 (0.88) |

Data are mean (sd). FEV1: forced expiratory volume in one second; FVC: forced vital capacity.
Fig. 1. – The number of spirometry tests performed for each man (ages 18–33 yrs).

Fig. 2. – The duration of follow-up for the 221 male employees with five or more quarterly spirometry tests.

of slopes which offset each other in a combined analysis and result in a nonsignificant population slope estimate. Clearly there are subjects here who have substantial slopes, both positive and negative.

Results from the analyses are listed in table 2. There were almost equal numbers of smokers and nonsmokers, each having an average of approximately 20 pulmonary function measures. Of the 111 nonsmokers, 34 had statistically significant slopes using SLR; three more had significant slopes using BSS; and an additional two subjects had significant trends using BKPT; for a total of 39 nonsmokers with a significant trend of 35%. Of those with a significant trend, just over 50% had positive slopes, indicating continued growth during this period. Of the 110 smokers, 36 had a significant trend using the SLR analysis, but a smaller number of those (39%) had

Table 2. – Models without and with breakpoint

<table>
<thead>
<tr>
<th>Smoking status</th>
<th>Linear regression model</th>
<th>Breakpoint model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SLR</td>
<td>Bootstrap</td>
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<tr>
<td>Nonsmokers</td>
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<td>77</td>
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<tr>
<td>111</td>
<td>74</td>
<td>3*</td>
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<tr>
<td>34* (47.1%)</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>111</td>
<td>34</td>
<td>34*</td>
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<tr>
<td>33 (47.1%)</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Total significant trends</td>
<td>34</td>
<td>37</td>
</tr>
<tr>
<td>34 (47.1%)</td>
<td>37 (48.7%)</td>
<td></td>
</tr>
<tr>
<td>39 (51.3%)</td>
<td>33 (0%)</td>
<td></td>
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</tbody>
</table>

Smokers

<table>
<thead>
<tr>
<th></th>
<th>Linear regression model</th>
<th>Breakpoint model</th>
</tr>
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<tr>
<td>110</td>
<td>67</td>
<td>67</td>
</tr>
<tr>
<td>74</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>7* (28.6%)</td>
<td>35</td>
<td></td>
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<tr>
<td>74</td>
<td>36*</td>
<td></td>
</tr>
<tr>
<td>36* (38.9%)</td>
<td>36*</td>
<td></td>
</tr>
<tr>
<td>36* (38.9%)</td>
<td>1*</td>
<td></td>
</tr>
<tr>
<td>Total significant trends</td>
<td>36</td>
<td>43</td>
</tr>
<tr>
<td>36 (38.9%)</td>
<td>43 (37.2%)</td>
<td></td>
</tr>
<tr>
<td>43 (37.2%)</td>
<td>35 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

Figures are number of subjects. Numbers in brackets represent proportion with positive slope; SLR: simple linear regression; *: significant slope for linear regression models and for breakpoints to a better fit of that model compared to linear regression models.
cant trend in their FEV1 measures, when examined in-
cantly significant trends. More variability in the data among those with statisti-
cal significance (mean=0.82), implying that there was
tended to be higher (mean=1.33) than those without a
trend. The mean of the distribution for those subjects with significant trends,
those with and without significant trends. The mean of
red error (MSE from the SLR analysis) distributions of
variability among observations, we compared mean squa-
re slopes using BSS, as expected, since BSS should reduce
slope variance estimates. There was one subject in
who had a significant slope using BSS. Thus, nonsmokers who had a significant
had significantly more negative slopes than smokers.
These findings are consistent with those of TAGER
[1], who reported a "premature onset of a normal rate of
delay" in cigarette smokers. In this study, we were not
actually able to determine the inflection point or break-
point in smokers, but we do know that more of them had
negative slopes. In contrast to the findings of TAGER
et al. [1], the decline was more rapid among smokers than
among nonsmokers.

In a recent study comparing the age dependence of
cross-sectional and longitudinal changes in FEV1 using
longitudinal data and methods, VAN PELT et al. [7] showed
that young adults exhibited a plateau phase or period of
continued growth, in their study of adults in two diffe-
rrent areas in the Netherlands. In contrast, cross-sectional
data from the same subjects showed FEV1 declining
throughout young adulthood (figure 2 in [7]), illustrating
the importance of having longitudinal measures for
obtaining accurate slope estimates. The same authors
also demonstrated that the age at which FEV1 starts to
decline is earlier in smokers than in the reference/nonsmok-
ing group, in agreement with our findings.

For several men who had significantly better fits using
BKT analysis (compared to SLR), examination of the
model fit to the observed data showed that the model
was actually fitting noise or outliers in the data rather
than an actual temporal trend. These were reclassified
as "nonsignificant BKPT trend". Investigators who use
this procedure for describing pulmonary function mea-
sures should closely examine each model fit.

Since our results are from a working population of
Caucasian men, they may not be representative of the
population as a whole. However, they are similar to the
"healthy" subpopulation frequently selected for computing
spirometry reference equations. In summary, we con-
clude that one cannot assume that pulmonary function
development in young adults is in a steady-state plateau.
We have demonstrated that a large number of men are
either continuing lung growth or have already started to
lose lung function between 18–33 yrs of age.

negative slopes. The BSS analyses yielded seven more
subjects with significant slopes, and the BKPT added no
subjects not previously characterized; for a total of 43
smokers with a significant trend (slightly more than found
in nonsmokers). Among those subjects who had statistically
significant trends, there were no significant differ-
ences between the mean slope estimates of the smokers
and nonsmokers, stratified by the sign of their slopes
(table 3). A larger proportion of smokers had negative
slopes (63%) than nonsmokers (49%), however, these
differences were not statistically significant (Chi²=1.64;
p=0.2). In addition, subjects with a significant positive
slope tended to be younger at these initial tests than those
who had significant negative slopes.

The average number of observations for those included
in the different analyses were similar, except for
those nonsmokers who had a significant slope using BSS.
They had on average 13.7 observations. Nonsmokers
with significant trends using the BKPT analyses tended
to have more observations. However, the number of
subjects in these groups were small. All subjects that
had significant slopes using SLR also had significant
slopes using BSS, as expected, since BSS should reduce
the slope variance estimates. There was one subject in
each smoking category who had a significant trend using
all three methods. For this subject, the statistically best
fit to the data was the BKPT model based on "extra sum
of squares" [13].

Subjects with a larger number of observations or a
longer duration of follow-up tended to have statistically
significant trends more often. To ensure that the lack of
a statistically significant trend was not due to increased
variability among observations, we compared mean squa-
red error (MSE from the SLR analysis) distributions of
those with and without significant trends. The mean of
the distribution for those subjects with significant trends,
tended to be higher (mean=1.33) than those without a
significant trend (mean=0.82), implying that there was
more variability in the data among those with statisti-
cally significant trends.

### Discussion

Up to 37% of adult males in our study had a signifi-
cant trend in their FEV1 measures, when examined in-
dividually, in contrast to the nonsignificant slope obtained
using the combined data [6]. Some of these men had
positive slope estimates, whilst others had negative slope
estimates, suggesting continuing growth and early de-
cline, respectively. This finding is particularly important
when predicting lung function development in apparently
healthy individuals in this age range for assessment of
possible lung disease due to occupational or environ-
mental exposures. The most frequently used spirometry
reference equations for 20+ yrs of age assume that pul-
monary function declines at a constant rate throughout
adulthood [14]. The European Coal and Steel Commu-
nity (ECSC) and other recent prediction equations in-
clude a plateau period [6, 15], but even those equations
would only be appropriate for 63% of the subjects. Pre-
diction equations with no plateau (as used by most pul-
monary function laboratories in the USA), are only
appropriate for 22% of the men aged 18–33 yrs in this
study. This could lead to misclassification of disease
status and/or exposure impact in this age group.

The proportion of subjects who had a significant trend
was independent of smoking, but men who were smokers
had significantly more negative slopes than nonsmokers.
These findings are consistent with those of TAGER et al.
[1], who reported a "premature onset of a normal rate of
delay" in cigarette smokers. In this study, we were not
actually able to determine the inflection point or break-
point in smokers, but we do know that more of them had
negative slopes. In contrast to the findings of TAGER et al.
[1], the decline was more rapid among smokers than
among nonsmokers.

<table>
<thead>
<tr>
<th>Significant positive slope</th>
<th>Nonsmoker</th>
<th>Smoker</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>20</td>
<td>16</td>
</tr>
<tr>
<td>Slope L·yr⁻¹</td>
<td>0.065±0.009</td>
<td>0.056±0.007</td>
</tr>
<tr>
<td>Intercept</td>
<td>2.90±0.309</td>
<td>3.24±0.276</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Significant negative slope</th>
<th>Nonsmoker</th>
<th>Smoker</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>19</td>
<td>27</td>
</tr>
<tr>
<td>Slope L·yr⁻¹</td>
<td>-0.103±0.012</td>
<td>-0.109±0.018</td>
</tr>
<tr>
<td>Intercept</td>
<td>7.08±0.417</td>
<td>7.40±0.619</td>
</tr>
</tbody>
</table>

Data are means±sem. Comparison of the proportion of nonsmokers
and smokers with negative slopes. Chi² = 1.64; p=0.2.
Acknowledgements: The authors thank T. Markham, Brush Wellman Medical Director, for the use of the data.

References