Comments by SPIROLA Reviewer 1

Pulmonary function testing, primarily spirometry, plays an important role in the prevention of environmental or occupational lung disease when used in surveillance programs, research and routine clinical practice. Identification of individuals with early disease may allow removal from exposures to prevent disease progression. The analysis of spirometric data on groups of exposed workers can also be of considerable assistance in determining whether a hazard exists. Longitudinal analysis of spirometric data is potentially a extremely powerful technique when properly utilized.

An excessive decline in lung function first came to prominence when Fletcher & Peto (1) produced their diagram of the rate of decline of lung function. The rate of decline in forced expiratory volume at one second (FEV1) generally proceeds at the same rate in normal non–smoking individuals. However, this rate of decline accelerates in smokers and those exposed to occupational or environmental.

The availability of software that allows the tracking of rates of decline of lung function is long overdue. The development of SPIROLA is to be applauded and is likely to present opportunities to identify early changes in lung function allowing the application of appropriate intervention. SPIROLA also has the potential of providing a platform for longitudinal research in a wide variety of areas.

The software is relatively easy to load and the manual is clear in its instructions. There appears to be minor bugs e.g. the demonstration data supplied with the latest version caused the program to crash. This occurred in spite of using Start-> Control Panel -> Add or Remove -> Remove SPIROLA to remove the old version of Spirola. Copying of the database into the Spirola folder as a separate operation corrected this problem. It would appear that for some reason the old database was not deleted in the above operation. However, the program worked well with a small local database except for the following problems:

- Some reports where there are only two observations state that the 'rate of decline is decreasing'. This is impossible observation when there are only 2 measures available. There would need to be information at least about the slope between measure 1 and 2 versus the slope between measures 2 and 3 to make this statement.

- The Coefficients of Precision are conceptually difficult to understand. When there are only two measures at different dates 8 years apart there is likely to be a 'high' variation due to the decline of lung function over that period of time. I am not certain that comments about 'precision' are useful when you only have two values for each parameter. If the database included the minimum 3 attempts at spirometry for an individual at each date you could have some idea of the precision of the measurement for that particular date. This would allow the individual data to be tested against the international criteria (2)for repeatability (?precision?).. Statements about the need for improved quality control of the program should ideally be based on how repeatable the measures are for each individual rather than between individuals.. The number of subjects whose observations fall within the ATS/ERS criteria would provide more meaningful information about the program's quality control.

- The set of papers primarily authored by Eva Hnizdo should be required reading for anyone about to use the software(3, 4). A simplified explanation of the concepts of the methodology used to estimate the Limits of Normal Decline and the Within-person variation should be included in the manual for those of us who lack the statistical background required to understand this information.

- Clicking on 'Risk List' there is a delay when it appears that the program may have frozen. The addition of a message stating that there is a "delay of X seconds" or something with a similar meaning may be useful to users of this program. Once "Risk List" appears in the bottom left hand window there seems only limited information is available except for Overall Sp and Sr. The title "Risk List" raises the expectation of more information.

- In the reporting of the absolute and relative coefficients of precision the manual states that a ".....sample of at least 50 individuals with repeated measurements are required to obtain a reasonable estimate..." and also the within-person standard deviation are calculated on measurements within 18 months of each other. If these criteria are not met I strongly recommend that the reporting of these parameters be suppressed by the program with a message to the effect that these criteria are not met rather than relying on the user to remember that the values will be unreliable. It is not clear when '.....they will not be calculated." (Section 5, final paragraph) will actually occur.

- More explanation of the "program variation is >160ml" statement is needed. In a cohort of workers with an age range of say 20 to 55 years I would suspect that the overall variation of each of the parameters would always be greater than 160ml.

- It is acknowledged that we do not have a lot of information about the rate of decline of Forced Vital Capacity (FVC). However, a restrictive pattern for spirometry is a feature of the various fibrotic lung diseases associated with occupational exposures. Does the fact that FVC appears under View mean that this will be available in future version of the software. Spirola would certainly be an extremely useful tool in investigating these issues.

- Could Spirola be further developed to allow the choice of using other lung function parameters? For example airways resistance (Raw), diffusing capacity or transfer factor (D_LCO or T_f). It is acknowledged that within person and between person variation of these measures will provide a significant challenge. However, the ability of being able to plot the decline of serial measures with just the lower limit of normal would provide some valuable information.

Spirola is an exciting new tool. The authors of this program should be congratulated on providing a tool that has so much potential not only in the longitudinal decline in lung function measurements due to occupational or environmental exposures but also in increasing our understanding of the decline of lung function in general. It will provide the platform for a range of research opportunities both in the fields of

occupational and environmental health as well in allowing us to better understand the changes in lung function in relation to the ageing process and disease.

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1. Fletcher C, Peto R, Tinker C, Speizer F. The Natural History of Chronic Bronchitis and Emphysema. In. New York, Toronto: Oxford University Press; 1976.
2. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. In: Eur Respir J; 2005. p. 319-38.
3. Hnizdo E, Yu L, Freyder L, Attfield M, Lefante J, Glindmeyer HW. The precision of longitudinal lung function measurements: monitoring and interpretation. Occup Environ Med 2005;62(10):695-701.
4. Hnizdo E, Sircar K, Glindmeyer HW, Petsonk EL. Longitudinal limits of normal decline in lung function in an individual. J Occup Environ Med 2006;48(6):625-34.

Comments by SPIROLA Reviewer 2

Review of SPIROLA program for the longitudinal analysis of spirometry data.

The version of the program reviewed was v.01302007; the User Manual was version 020107.

The stated purpose of the SPIROLA program is:

- to provide the user with a method of 'quality control' to assess the precision of spirometry measurements on a group of individuals over time;
- to identify individuals who have excessive decline in lung function; and
- to monitor the effects of interventions undertaken to reduce rate of decline of lung function.

Strengths of the program:

- this is the first program of its kind that the reviewer is aware of that provides the clinician with the means to evaluate spirometry at group and individual level both objectively and quantatively;
- downloading and installing the program was relatively easy once access to the ftp server was established;
- navigating the program in the Windows environment is easy and intuitive;
- the program is applicable to any situation in which spirometry data is routinely collected, particularly for the occupational setting;
- it was a simple task for the reviewer to prepare and load spirometry data from our institution for testing (fortunate to be very familiar with MS Access environment).

Weakness/deficiencies:

- while not in itself a weakness or deficiency, it is the opinion of the reviewer that users will need to have a good understanding of the various assumptions and statistical methods in order to fully appreciate and understand the outputs;
- the User Manual would benefit from a glossary of terms for quick reference and clarification;
    - an example of the above – on page 10 reference is made to the cross sectional lower limit of normal (LLN) which is not defined, for example, as LLD_a and LLD_r are, on page 30;
    - on Individual Evaluation FEV1 screen at the bottom, the regression slope is given and next to it, 'Mean Slope' – what exactly is the mean slope and where in the User Manual is it described?
- some functions were not understood by the reviewer and/or did not appear to work as expected:
    - e.g. for custom reference equations there is no column for race, as there is for the Hankinson equations.

Summary:
There most definitely exits a need for a program like this, especially for the occupational medical practitioner. This reviewer will support its further development and refinement through continued interaction with Dr Hnizdo aimed at improving 'user-friendliness' and practicability.