Eur Respir J 2010; 35: 776–780
DOI: 10.1183/09031936.00107709

Calculating gambling odds and lung ages for smokers

J.E. Hansen, X-G. Sun and K. Wasserman

ABSTRACT: **Interpreting spirometry as normal or abnormal using 95% confidence limits can obscure milder airflow decreases. Other analyses might better persuade cigarette smokers to quit.**

High-quality spirometric data of ambulatory never- and current-smokers of African-, European- and Latin-American ethnicity from the Third National Health and Nutrition Evaluation Survey (n>9000) were analysed. We desired to calculate, for each decade of life, the odds that specific ratios of forced expiratory volume in 1 s to 6 s (%FEV1/FEV6) and to forced vital capacity (%FEV1/FVC) values came from a current- or never-smoker. We also desired to develop new, simpler and better formulas to estimate changes in physiological lung age (Δlung age) for males and females.

For each decade of life, odds increase strikingly that smoking decreases %FEV1/FEV6 and %FEV1/FVC. At least for these three ethnicities, Δlung age can be easily calculated as the product of (predicted - actual) %FEV1/FEV6 $\times$ 4 or (predicted - actual) %FEV1/FVC $\times$ 3. Through the sixth decade of life, smokers' Δlung age increase rapidly but little thereafter, presumably due to the inabilities of older smokers to participate in the survey or their deaths.

Using odds and Δlung ages rather than traditional 95% confidence limits might better persuade smokers to quit.

KEYWORDS: **Chronic obstructive pulmonary disease, lung age, ratio of forced expiratory volume in 1 s to 6 s, ratio of forced expiratory volume in 1 s to forced vital capacity, spirometry**

AFFILIATIONS
Los Angeles Biomedical Research Institute and Division of Respiratory and Critical Care Physiology and Medicine; Dept of Medicine at Harbor-UCLA Medical Center, University of California David Geffen School of Medicine, Torrance, CA, USA.

CORRESPONDENCE
J.E. Hansen
Box 405
Dept of Medicine Harbor-UCLA Medical Center
Torrance
CA 90502
USA
E-mail: jhansen@labiomed.org

Received:
July 10 2010
Accepted after revision:
Aug 31 2009
First published online:
Sept 24 2009

It is incumbent upon us to help persuade cigarette smokers to quit smoking and reduce suffering, pain, and premature deaths [1–5]. Increasing cigarette taxes, reducing locations where smoking is allowed, litigating, advertising the effects of tobacco smoking and increasing the stigma of smoking have all been helpful [6, 7]. Health practitioners have assisted their patients by listening, counselling, referring to support groups and prescribing drugs to mollify withdrawal effects from nicotine [8–10]. However, spirometry has usually been of minimal benefit [11–13], perhaps because results are not presented optimally. Unfortunately, citing simplicity, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) expert committee concluded that, even in younger individuals, all values of % forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) >70% are normal [5, 14], despite strong evidence and opposition to the contrary [15–17]. Alternatively, others rely on classical statistical analyses with 95% confidence intervals and p-values of <0.05 to interpret their patients' spirometry [15]. We now question whether it is necessary for %FEV1/FVC values to be below these limits before concluding that airflow is reduced. We suggest two options for consideration: gambling odds and estimation of lung age. First, we can be like card players and gamblers by making decisions based on odds or probabilities without using a cut-off of $p<0.05$; and secondly, we can simplify the estimation of spirometric lung age [18], as initially proposed by MORRIS and TEMPLE [19] and recently used with some benefit [20].

Therefore, using analyses of FEV1/ forced expiratory volume in 6 s (FEV6) and FEV1/FVC data from the Third National Health and Nutrition Evaluation Survey (NHANES-3) [21, 22], we relate airflow to gambling odds and lung age.

METHODS

We selected, from the NHANES-3 database [23], 9,353 self-identified European-American (white), African-American (black), and Mexican-American (Latin) adults with satisfactory spirometry [21, 22] between the ages of 20 and 80 yrs (see supplementary material).

This article has supplementary material available from www.erj.ersjournals.com

European Respiratory Journal
Print ISSN 0903-1936
Online ISSN 1399-3003

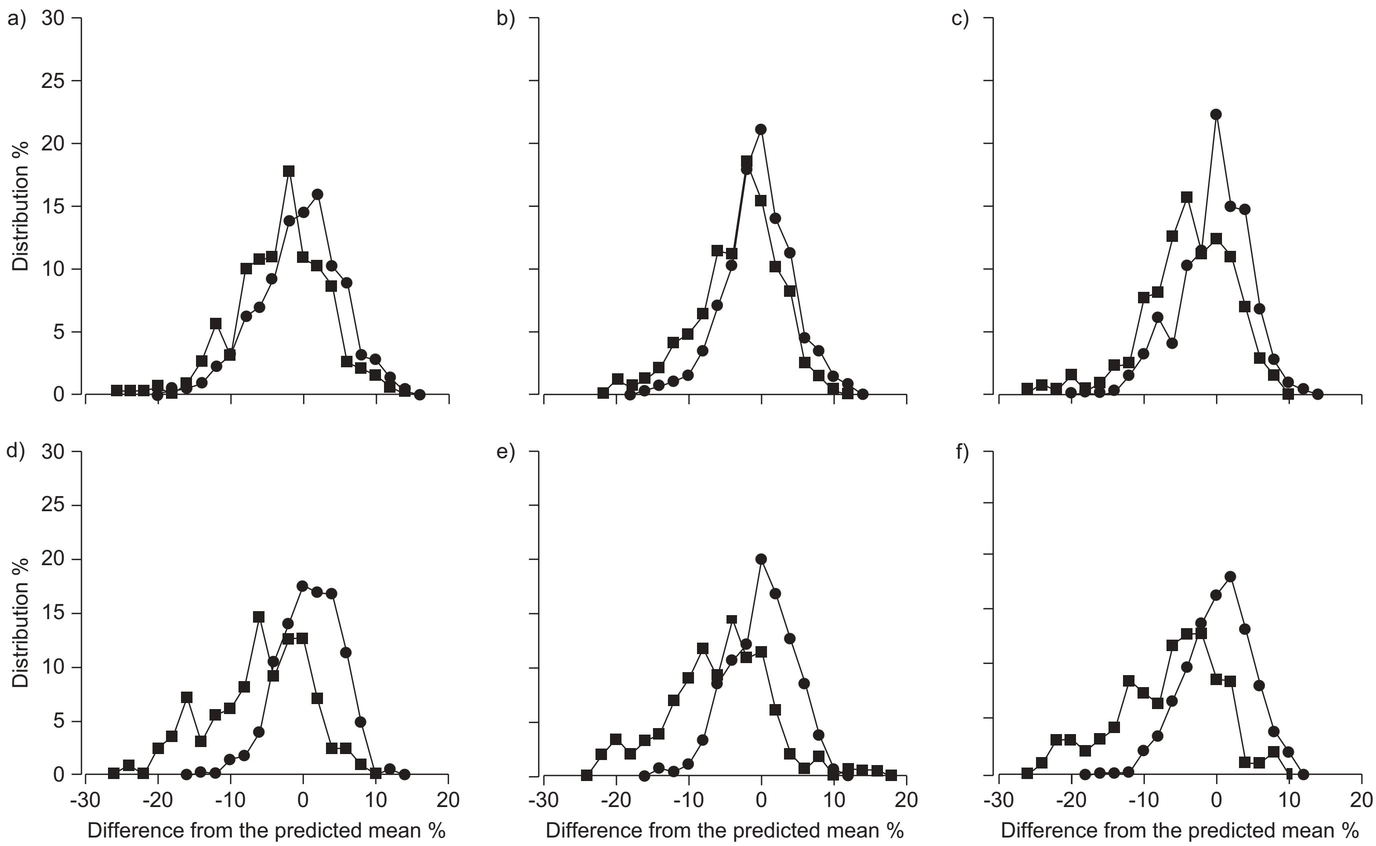

FIGURE 1. Distribution of % forced expiratory volume in 1 s/forced expiratory volume in 6 s for white never-smokers (●) and current-smokers (■) by age: a) 20–29 yrs; b) 30–39 yrs; c) 40–49 yrs; d) 50–59 yrs; e) 60–69 yrs; f) 70–79 yrs. Each never-smoker curve is normally distributed. The left-shifted curves of current-smokers, especially as ages increase, indicate increasing odds for current-smoking status.

We have previously calculated from NHANES-3 data that, for normal never-smoking adults, $\%FEV_1/FVC = 98.8-0.25 \times age$ (in yrs)$-1.79 \times FVC$ (in L), independent of ethnicity and sex [24, 25]. We now similarly have developed the formula: $\%FEV_1/FEV_6 = 96.9-0.189 \times age$ (in yrs)$-1.524 \times FEV_6$ (in L) (standard error of estimate 4.7%).

We measured the percentage differences between predicted and actual $\%FEV_1/FEV_6$ in each subject, which allowed us to graph, for each decade, the distribution of the $\%FEV_1/FEV_6$ of 5,835 never-smokers about their predicted values and, separately, the same for 3,518 current-smokers. We could then calculate within each decade, the gambling odds that, at any given deviation from mean predicted value, the actual $\%FEV_1/FEV_6$ of an individual might be that of a current-smoker or never-smoker.

We developed a new formula relating how the percentage differences between actual and predicted spirometric values were related to changes in physiological lung age (Δlung age) (see supplementary material). For each adult, we calculated that Δlung age $= 4 \times$ ((%predicted-%actual) $\%FEV_1/FEV_6$) and $= 3 \times$ ((%predicted-%actual) $\%FEV_1/FVC$). Then, using the formulas of MORRIS and TEMPLE [19], we calculated the lung ages for each white adult. This allowed both sets of formula to be compared for never- and current-smokers for each decade by two-tailed unpaired t-tests with a p-value <0.05 being considered significant [26].

RESULTS

By GOLD categories, none of the current-smokers was very-severe GOLD (FEV_1 <30%), 0.8% were severe category (FEV_1 = 30–50%), 6.5% were moderate GOLD (FEV_1 = 50–80%) and 10.4% were mild GOLD (FEV_1 >80%) (see fig. 1e and supplementary material) [5].

Gambling odds

Figure 1 displays the actual distribution, by 2% bins, for the third to eighth decade of life for % FEV_1/FEV_6 for white adults. The patterns were quite similar for other ethnicities using either the % FEV_1/FVC or % FEV_1/FEV_6 formulas. Table 1 lists the resultant prevalence (gambling) odds that, for a given difference between actual and predicted $\%FEV_1/FVC$, a value is from a current- or never-smoker. As the actual $\%FEV_1/FVC$ decrease a few percentages from mean predicted, the odds increase above 1.0, tending to identify current-smokers rather than never-smokers. Conversely, odds of <1.0 tend to identify never-smokers. As seen in figure 2e in the supplementary material, discrimination of reduced airflow attributable to smoking is evident at age 25 yrs but strikingly greater at age 55 yrs.

Lung age formula comparisons

Figure 2a shows the Morris and Temple mean lung ages for white never- and current smokers by decade of age using sex, age and FEV_1 or sex, age and FVC. Note that the never-smokers'

TABLE 1 Prevalence (gambling) odds that a lower or higher % forced expiratory volume in 1 s/forced vital capacity is from a current-smoker and not a never-smoker

% below or above predicted mean	Third decade age 20–29 yrs	Fourth decade age 30–39 yrs	Fifth decade age 40–49 yrs	Sixth decade age 50–59 yrs	Seventh decade age 60–69 yrs	Eighth decade age 60–69 yrs	All decades mean	All decades SD
≤-14	4.2	4.6	12.3	45.3	92.5	77.1	**39.3**	38.6
-12	2.3	6.0	1.7	9.7	3.5	2.9	**4.4**	3.0
-10	1.3	4.1	1.4	7.5	3.8	0.7	**3.1**	2.6
-8	1.8	1.5	3.3	1.5	1.3	1.8	**1.9**	0.7
-6	1.4	1.7	2.0	2.0	1.4	0.7	**1.5**	0.5
-4	1.2	1.0	1.5	1.3	0.5	1.4	**1.2**	0.4
-2	1.4	1.2	1.0	0.5	1.6	0.8	**1.1**	0.4
0	0.6	0.7	0.7	0.6	0.3	0.5	**0.6**	0.2
2	0.7	0.7	0.6	0.4	0.1	0.4	**0.5**	0.2
4	0.7	0.7	0.4	0.6	0.3	0.3	**0.5**	0.2
6	0.5	0.6	0.3	0.2	0.2	0.2	**0.3**	0.2
≥8	0.5	0.2	0.4	0.1	0.4	0.4	**0.3**	0.2
If ≤-8	2.1	2.9	2.8	5.4	4.3	4.1	**3.6**	1.2
If ≤-6	1.8	2.4	2.6	4.0	3.0	2.8	**2.8**	0.7
If ≤-4	1.7	1.7	2.2	3.0	2.1	2.3	**2.2**	1.5

mean lung ages are usually considerably less than their actual ages while the current-smokers' mean lung ages exceed their actual ages. In the same population, figure 2b shows that for either the Harbor % FEV1/FVC or % FEV1/FEV6 formulas, never-smokers' mean lung ages approximate their actual age, while the current-smokers lung age differences increase decade by decade for both sexes up to the sixth decade of life. Thereafter, the lung age differences levelled off at ~25 yrs. For all decades, current-smokers differed from never-smokers by 7–28 yrs ($p<0.0001$) with either Harbor formula. Figures 2c and 2d show the lung age findings in black and Latin adults using the Harbor formulas, sometimes with lesser but still statistically significant difference between never- and current-smokers.

DISCUSSION

Subtle reductions in airflow should be discernible well before a clinical diagnosis of COPD can be made [27, 28]. The presentation of gambling odds is used to challenge the deeply held belief that 95% confidence limits should be the primary criteria to decide whether a patient has reduced airflow. 95% confidence limits are appropriate to analyse treatment differences but are not ideal in distinguishing the effects of whether or not exposure to a substance is harmful. Gambling odds remind us that probabilities other than 5% or 20 to 1 can be useful. For example, a family may decide to live in site A, not because it is 20-times better than site B, but because site A is 10% or 20% or 30% safer (or cleaner, or more attractive) than site B. These odds are 1.1, 1.2, or 1.3 for choosing site A. Although airflow is influenced by health, genetics, nutrition, motivation and environmental factors, a Bayesian approach tells us that the influence of cigarette smoking on airflow need not be ignored with relative odds of 1.1, 1.2, and 1.3, to say nothing when relative odds of 2 or 5 are found.

MORRIS and TEMPLE [19] deserve credit for introducing the concept of lung age to assess airflow obstruction. PARKES *et al.* [20] found their lung ages useful, but they are not routinely calculated. Using the new formulas presented here, anyone can easily manually calculate and inform patients of their Δlung ages from any spirometric report. For example if a patient's actual %FEV1/FEV6 is 3% below predicted, or %FEV1/FVC is 4% below predicted, the Δlung age is +12 yrs. This should elicit a response and open discussion regarding the dangers of continuing cigarette smoking. Referral to support groups, educational and counselling sessions, and the use of newer pharmaceuticals all offer avenues for success [8, 9, 20, 29, 30].

Cigarette smoking is the leading cause of preventable morbidity and mortality [1, 2, 5]. Airway and vascular obstruction, both worsened by smoking, are usually parallel processes [4, 13, 31–35], but airway obstruction is cheaper and quicker to assess. There have been significant declines in death rates and morbidity from cardiovascular diseases [36], but a parallel decline in airway diseases and lung cancer attributable to cigarette smoking is not yet obvious, especially in females [1, 2, 5]. Simple and compelling advocacy is even more necessary where cigarette smoking is more openly tolerated and promoted.

Limitations

We believe our analysis of the cross-sectional NHANES-3 data underestimates the significance of the effect of cigarette smoking on airflow, morbidity, and mortality. One factor is

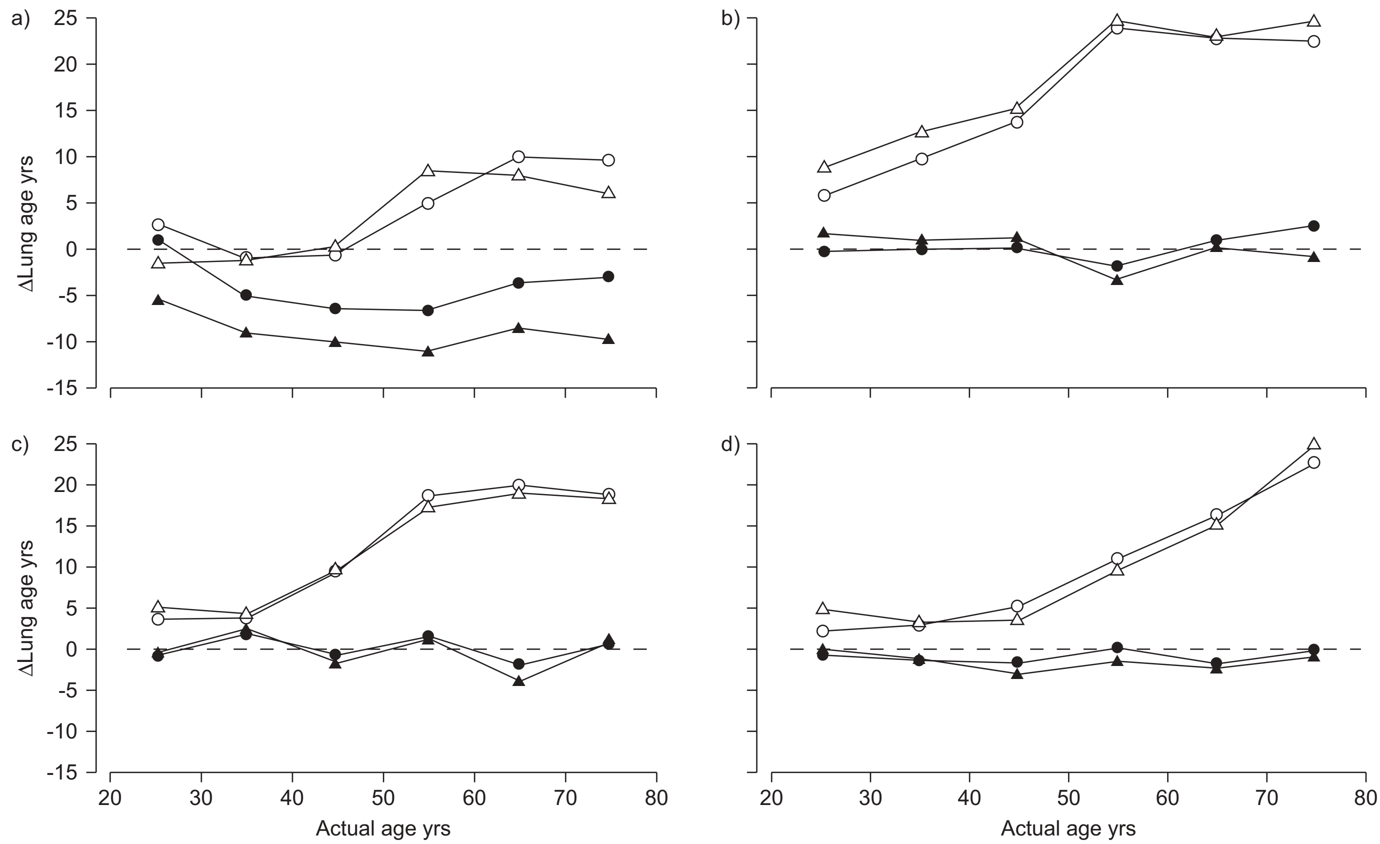

FIGURE 2. Lung age changes by decade for never-smokers (●, ▲) and current-smokers (○, △) measured. a) White adults with the Morris formula. ▲ and △: forced expiratory volume in 1 s (FEV_1); ● and ○: forced vital capacity (FVC). Harbor formula for b) white adults, c) black adults and d) Latin adults. ▲ and △: FEV_1/FEV_6; ● and ○: FEV_1/FVC. a) For the third decade (ages 20–29 yrs); white current- and never-smokers differed by 4 yrs ($p=0.003$) using FEV_1 and 2 yrs ($p=0.43$) using FVC. For older decades, FEV_1 values differed by 8–20 yrs ($p<0.0001$) while FVC values varied by 5–14 yrs ($p=0.0008–0.014$). c) Black current-smokers differed from never-smokers by 5–24 yrs ($p<0.001$) for all but the fourth decade (ages 30–39 yrs) when the differences were only 2–3 yrs ($p=\sim0.08$). d) Latin current-smokers differed from never-smokers by 3–5 yrs ($p=\sim0.01$) for the third and fourth decades, and 7–26 yrs ($p<0.001$) for all other decades.

the lack of continuing rise in airway obstruction after the sixth decade in the White and Black subjects. First, we suggest that increased mortality (due to malignancies, COPD, or cardiovascular diseases) plus the severe morbidity and lack of mobility in older smokers was likely responsible. Secondly, the lower number of current smokers than never-smokers in the seventh and eighth decades would support that possibility. Thirdly, considering the high morbidity associated with COPD, malignancies, and cardiovascular diseases, the finding that no one in the never-smoking population met the GOLD criteria [5] of very severe COPD (%FEV_1/FVC <70% and FEV_1 <30% of predicted), and <1% had severe COPD (%FEV_1/FVC <70% and FEV_1 ⩾30% and <50%) supports this under-representation of disease. Furthermore, exposure of many never-smokers to second-hand smoke or to other important pollutants may have reduced differences between the never-smoking and current-smoking groups [37].

Because there is marked variability in the spirometric ratios of normal individuals, unexplained by height, age, sex or ethnicity, not all current-smokers have lower than mean predicted %FEV_1/FEV_6 or %FEV_1/FVC, and not all never-smokers have higher than mean predicted %FEV_1/FEV_6 or %FEV_1/FVC (see supplementary material).

Conclusion

Simple formulas for assessing normality of %FEV_1/FEV_6 and %FEV_1/FVC values are presented. They allow any health professional receiving a spirometry report to calculate some of the detrimental effects of cigarette smoking on airflow and lung age and thus better inform, challenge, and support their patients to quit smoking.

STATEMENT OF INTEREST

None declared.

ACKNOWLEDGEMENTS

The authors would like to thank the USA government agencies, investigators, technicians and subjects of NHANES-3 who together acquired the data and made it available to us for further analyses.

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