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CALCULATING GAMBLING ODDS AND LUNG AGES FOR SMOKERS

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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 analyzed. We desired to calculate, for each decade of life, the odds that specific ratios of forced expiratory volume in 1-second to 6-seconds (%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 men and women.

For each decade of life, odds increase strikingly that smoking decreases %FEV1/FEV6 and %FEV1/FVC. At least for these three ethnicities, Δlung ages can be easily calculated as the product of (predicted–actual)%FEV1/FEV6 times 4 or (predicted-actual) %FEV1/FVC times 3. Through the 6th decade, smokers' Δlung ages 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: COPD, FEV1/FEV6, FEV1/FVC, lung age, spirometry

INTRODUCTION

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, counseling, referring to support groups, and prescribing drugs to mollify withdrawal effects from nicotine [8-10]. But spirometry has usually been of minimal benefit [11-13], perhaps because results are not presented optimally. Unfortunately, citing simplicity, the GOLD expert committee concluded that, even in younger individuals, all values of %FEV1/FVC above 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 limits, and p values of < 0.05 to interpret their patients' spirometry [15].

We now question whether it is necessary for $\%FEV_1/FVC$ values to be below these limits before concluding that airflow is reduced. We suggest two options for our readers' consideration: gambling odds and estimation of lung age. We can be like card players and gamblers by making decisions based on odds or probabilities without using a cut-off of $p<0.05$. Second, we can simplify the estimation of spirometric lung age [18], as initially proposed by Morris and Thomas [19] and recently used with some benefit [20].

Therefore, using analyses of FEV_1/FEV_6 and FEV_1/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] 9353 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 years. See supplement.

We had previously calculated from NHANES-3 data that $\%FEV_1/FVC$ for normal never-smoking adults =98.8–0.25xage(yrs)–1.79xFVC(L), independent of ethnicity and gender [24-25]. We now similarly developed the formula: $\%FEV_1/FEV_6$ = 96.9-0.189xage(yrs)-1.524xFEV_6(L) (SEE = 4.7%).

We measured the percent 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 5835 never-smokers about their predicted values and separately, the same for 3518 current-smokers. We could then calculate within each decade, the gambling odds that at any given deviation from mean predicted, the actual $\%FEV_1/FEV_6$ of an individual might be that of a current-smoker or never-smoker.

We developed new formula relating how the percent differences between actual and predicted spirometric values were related to changes in physiological lung age (Δlung age). (See supplement.) For each adult, we calculated that Δlung age =4x[(%predicted-%actual) $\%FEV_1/FEV_6$)] and =3x[(%predicted-%actual)$\%FEV_1/FVC$)]. Then, using the formulas of Morris and Thomas [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 $p < 0.05$ considered significant [26].

RESULTS

By GOLD categories, none of the current-smokers were 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%) [5]. See supplement and Figure 1E.

Gambling odds

Figure 1 displays the actual distribution, by 2% bins, for the 3rd through 8th decades for % FEV_1/FEV_6 for White adults. The patterns are quite similar for other ethnicities using either the %FEV_1/FVC or %FEV1/FEV6 formulas. Table 1 lists the resultant prevalence (gambling) odds that for a given difference between actual and predicted %FEV1/FVC, a value is from a current- or never-smoker. As the actual %FEV1/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 less than 1.0 tend to identify never-smokers. As seen in Figure 2E in the supplement, discrimination of reduced airflow attributable to smoking is evident at 25 years but strikingly greater at 55 years of age.

Lung age formula comparisons

Figure 2A shows the Morris and Thomas mean lung ages for White never- and current smokers by decade of age using gender, age, and FEV_1 or gender, age, and FVC. Note that the never-smokers 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 % FEV_1/FVC or % FEV_1/FEV_6 formulas, never-smokers mean lung ages approximate their actual age, while the current-smokers lung age differences increase decade by decade for both genders up to the 6^{th} decade and then level off at approximately 25 years. For all decades, current-smokers differed from never-smokers by 7 to 28 years ($p<0.0001$) 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 analyze 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 Thomas 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 % FEV_1/FEV_6 is 3% below predicted or % FEV_1/FVC is 4% below predicted, the Δlung age is +12 years. This should elicit a response and open discussion regarding the dangers of continuing cigarette smoking. Referral to support groups, educational and counseling sessions, and 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 women [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 the lack of continuing rise in airway obstruction after the 6^{th} decade in the White and Black subjects. 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. Second, the

lower number of current smokers than never-smokers in the 7th and 8th decades would support that possibility. Third, 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. Further, 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, gender, 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 supplement.

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.

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TABLES

TABLE 1– Prevalence (gambling) odds that a lower or higher % FEV_1/FVC is from a current-smoker, not a never-smoker.

% below or above predicted mean	(20-29 years) 3rd decade	(30-39 years) 4th Decade	(40-49 years) 5th Decade	(50-59 years) 6th decade	(60-69 years) 7th decade	(70-79 years) 8th decade	**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

FIGURE TITLES and LEGENDS:

FIGURE 1. A, B, C, D, E, and F: Distribution of % FEV_1/FEV_6 for White never- and current-smokers by decades 3 to 8 (ages 20-29 to 70-79 years), respectively. 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.

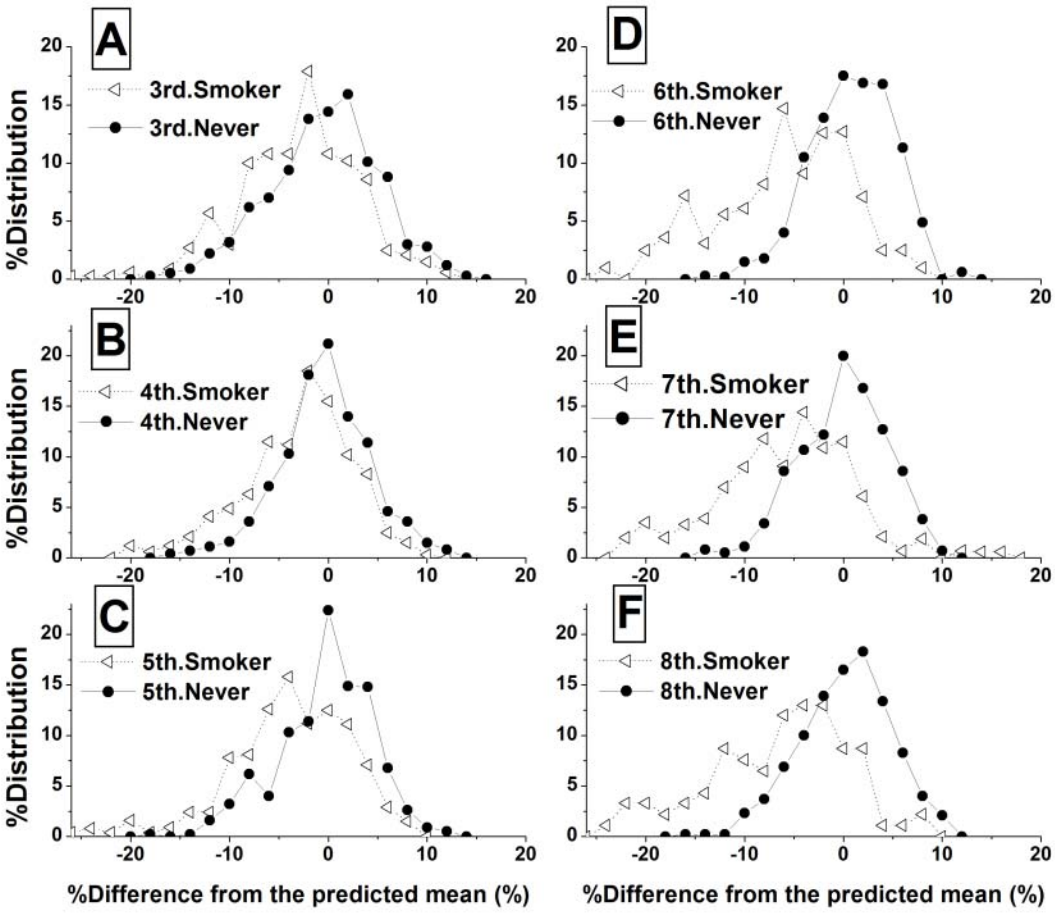
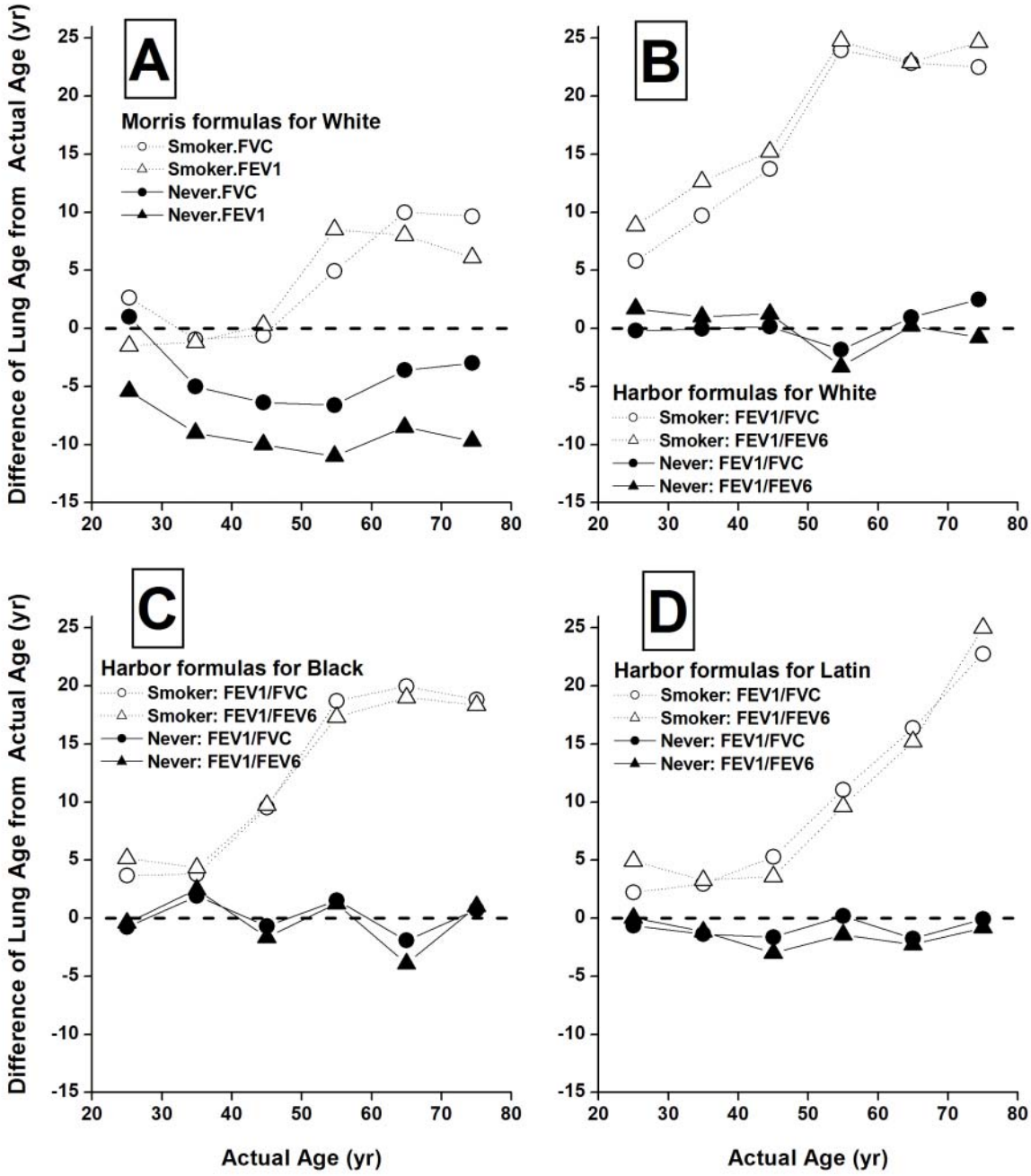


FIGURE 2. Lung age changes by decade for never-smokers and current-smokers. A: White adults with Morris formulas; B: White adults with Harbor formulas; C: Black adults with Harbor formulas; and D: Latin adults with Harbor formulas. 2A: For the 3rd decade (ages 20-29); white current- and never-smokers differed by 4 years ($p = 0.003$) using FEV_1 and 2 years ($p =$

0.43) using FVC. For older decades, FEV1 values differed by 8 to 20 years ($p<0.0001$) while FVC values varied by 5 to 14 years ($p=0.0008$ to 0.014). C: Black current-smokers differed from never-smokers by 5 to 24 years ($p<0.001$) for all but the 4th decade when the differences were only 2-3 years ($p\sim 0.08$). D: Latin current-smokers differed from never-smokers by 3 to 5 years ($p \sim 0.01$) for the 3rd and 4th decades, and 7 to 26 years ($p<0.001$) for all other decades.


A
Morris formulas for White
Smoker.FVC
Smoker.FEV1
Never.FVC
Never.FEV1
B
Harbor formulas for White
Smoker: FEV1/FVC
Smoker: FEV1/FEV6
Never: FEV1/FVC
Never: FEV1/FEV6
C
Harbor formulas for Black
Smoker: FEV1/FVC
Smoker: FEV1/FEV6
Never: FEV1/FVC
Never: FEV1/FEV6
D
Harbor formulas for Latin
Smoker: FEV1/FVC
Smoker: FEV1/FEV6
Never: FEV1/FVC
Never: FEV1/FEV6
Difference of Lung Age from Actual Age (yr)
Actual Age (yr)