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Spirometry: a comparison of prediction equations proposed by Lubiński for the Polish population with those proposed by the ECSC/ERS and by Falaschetti et al.

Spirometria — porównanie polskich wartości należnych Lubińskiego z należnymi ECSC/ERS i Falaschetti

Abstract

Introduction. Prediction equations proposed by the European Community of Steel and Coal (ECSC) and the European Respiratory Society (ERS) or those proposed by Falaschetti et al. for the English population are currently recommended for use in Poland. The aim of the present study was to compare these equations with those developed by Lubiński and Gólczewski for the Polish population — both in terms of methodological correctness and appropriateness to the present Polish population.

Materials and methods. The ECSC/ERS prediction equations, the Falaschetti equations, and the Polish equations (developed on the basis of data on healthy, non-smoking Poles aged 18 to 85 years [1120 men and 1625 women] who underwent spirometry in accordance with the American Thoracic Society [ATS]/ERS recommendations) were compared in terms of methodological correctness.

Results. The main flaws in the ECSC/ERS equations include: (a) the *a priori* assumption that the age from which a given pulmonary function parameter (PFP) begins to decline is the same for all the PFPs and is equal to 25 years; (b) the fact that a single linear equation may not correctly describe age-related changes beyond the age of 25 years; (c) the fact that the lower limits of normal are defined by equations for the mean values minus 1.645 $\times$ SD (where SD is the standard deviation for differences between the observed and the expected values); and (d) the fact that the equations were developed a long time ago for previous generations and old spirometry procedures. The main flaws in the Falaschetti equations include: (a) excessive and unnecessary non-linearity of the equations; and (b) inadequate selection of the general population sample (insufficient number of elderly subjects) causing overestimation of forced expiratory volume in one second (FEV_1) to forced vital capacity (FVC) ratio in elderly subjects. The equations proposed by Lubiński and Golczewski are free from these flaws. In particular, age distribution in the sample was uniform. Moreover, with reference to each of the PFPs: (a) the age from which a given PFP began to decline was mathematically determined together with the other coefficients of the equations; and (b) the statistical significance of the non-linearity of the relationship between age and each of the individual PFPs was analysed. What is more, in the case of the oldest subjects, the Lubiński equations yielded identical results to those obtained by other authors who had thoroughly analysed PFPs in the elderly.

Conclusions. The comparison presented in this paper suggests that the equations proposed by Lubiński and Gólczewski should be used in Poland rather than those proposed by ECSC/ERS or Falaschetti et al.

Key words: spirometry, predicted values, prediction equations, pulmonary function

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Introduction

The need for early detection of obstructive diseases seems to be commonly recognised [1]. In the primary care setting, although perhaps not only, early detection is based on spirometry (forced spirometry). An assessment of a spirometry requires a comparison of measured pulmonary function parameters (PFPs) with values predicted by means of appropriate prediction equations. In Poland, the most popular equations are still those proposed by the European Community of Steal and Coal (ECSC) and the European Respiratory Society (ERS), which are almost 30 years old and are based on even older databases. The ECSC/ERS prediction equations, revised nearly 20 years ago [2], continue to be recommended, although with certain reservations, in the official Polish Respiratory Society guidelines on spirometry [3]. Taking into account the fact that the dependence of predicted PFP values on the patient's age is not only a function of the ageing process but also a function of intergenerational differences, the use of equations developed one or two generations ago may be a mistake. In addition, for the past 20–30 years, forced spirometry procedures have slightly changed (have been restrictively formalised), which may affect PFP values that should be considered as the predicted ones.

This means that the ECSC/ERS predicted values might be outdated. For this reason the prediction equations developed several years ago by Falaschetti et al. [4] have aroused considerable interest. The problem is that the data used for the development of these equations came from the English population, whereas it is now commonly accepted that predicted values for various ethnic groups may differ. Each ethnic group should therefore have their own sets of prediction equations [5]; theoretically, it would be best if each laboratory that performs spirometry had its own predicted values [6]. Hankinson et al. [7], for instance, developed prediction equations for three major ethnic groups in the United States. Therefore, even if the prediction equations proposed by Falaschetti et al. are as accurate as possible for the English population, they are not necessarily appropriate for the Polish population.

Taking into account the potential imperfections of the ECSC/ERS equations and those proposed by Falaschetti et al., Lubiński and Gólczewski developed prediction equations for the present Polish population. A detailed description of the material which had been utilised and the method used to develop the equations were published in 2010 in a paper entitled: "Physiologically interpretable prediction equations for spirometric indices" [8]. The paper also provides values of physiologically interpretable coefficients of equations defining predicted values and lower limits of normal (LLN) for forced vital capacity (FVC), forced expiratory volume in one second (FEV_1) the FEV_1/FVC ratio, as well as for peak expiratory flow (PEF), maximum expiratory flow at 75%, 50%, and 25% of the FVC (MEF75, MEF50, and MEF25, respectively), and MEF75–25. The physiological interpretability of these equations means that they are constructed in such a way that their coefficients are not only mathematical objects, i.e. numbers, but they also have a physiological interpretation. Coefficients with the following meanings are used in these equations:

1. The baseline value of a given PFP being equal to the mean value for 18 years old individuals.
2. Age from which a given PFP begins to decline with age because of both ageing process and intergenerational differences.
3. The rate of decline of a given PFP with age.
4. A coefficient of the effect of the only quantitatively assessed interpersonal difference that is taken into account during the analysis of a spirometry; namely the difference between the patient's height and the mean height for all the individuals born in the same year as this patient (the reason for this approach has been explained in the last paragraph of the Discussion section).

Thanks to this construction of equations, they may not only be used in medicine to determine predicted values and LLN but also in physiology to compare the properties of various PFPs (e.g. the order in which individual PFPs begin to decline with age) and in epidemiology, for instance, to compare various populations by means of a direct comparison of the above coefficients. That paper also included a quantitative comparison of the suitability of equations proposed by various authors for the analysed sample of the Polish population, separately for three age groups: young adults (18–40 years of age), middle-aged subjects (41–60 years of age) and the elderly (61–85 years of age). Certainly, the equations proposed by Lubiński and Gólczewski proved to be most appropriate for the sample of the Polish population used in elaboration of these equations. Among the equations developed by other authors, generally, i.e. for the greatest number of PFPs and age ranges, the equations found most suitable for the Polish population were those proposed by Hankinson et al. [7] developed for the American Caucasian population (especially in the case of males). Equations proposed by European authors were rated lower, especially for the elderly. It should be noted that the "outdated" ECSC/ERS equations proved to be the best among the European ones.

Generally, the differences between predicted values in various populations may be explained by the differences between those populations. It may well be that the Polish population differs from the other European populations more than it does from the Caucasian American population being a mixture of the European populations including the Polish population. It is also possible, however, that the European equations are not perfect from the methodological point of view.

The aims of this paper were:

— to present the Lubiński and Gólczewski equations in a simple, piecewise linear form analogous to the form of the ECSC/ERS equations;
— to compare the Lubiński and Gólczewski equations with the ECSC/ERS equations and those proposed by Falaschetti et al., including an analysis of possible mathematical or methodological imperfections.

Materials and methods

The following equations have been analysed in the present paper:

— the ECSC equations [2],
— the equations proposed by Falaschetti et al. [4],
— the equations proposed by Lubiński and Gólczewski [8].

ECSC equations

The ECSC equations [2] have a simple, piecewise linear form:

(a) for patients aged ≤ 25 years:

$$PFP_i = C_i + H_i \times \text{height} + A_i \times 25$$

(b) for patients aged > 25 years:

$$PFP_i = C_i + H_i \times \text{height} + A_i \times \text{age}$$

where: PFP_i refers to the i-th pulmonary function parameter (i = 1, 2, 3, and 4 corresponds to FEV_1/FVC, FVC, FEV_1, and MEF75–25, respectively) and C_i, A_i, and H_i are coefficients for a given PFP_i (C — the constant term, A — coefficient accompanying age, H — coefficient accompanying height).

Equations proposed by Falaschetti et al.

The equations proposed by Falaschetti et al. [4] have a very complex, non-linear form (a product of a power function and an exponential function with a squared form in the exponent):

$$PFP_i = \text{height}^{H_i} \times e^{C_i + A1_i \times \text{age} + A2_i \times \text{age}^2}$$

Moreover, in the case of males, equations were fitted separately for males aged ł25 yrs, and for those aged ≥ 25 yrs. In addition, in the sample of the English population based on which the coefficients of the equations have been determined, the number of middle-aged adults (45–64 years of age) was significantly lower than the number of young adults, and the number of elderly individuals (65–85 years of age) was very low (Table 1).

Equations proposed by Lubiński and Gólczewski

The equations proposed by Lubiński and Gólczewski [8] may also be presented in a simple, piecewise linear form (with the exception of MEF25):

(a) for patients meeting the following condition: age (years) ≤ $W1_i$:

$$PFP_i = C1_i + H1_i \times \text{height}$$

(b) for patients meeting the following condition: $W1_i$ < age (years) ≤ $W2_i$:

$$PFP_i = C2_i + H2_i \times \text{height} + A2_i \times \text{age}$$

(c) for patients meeting the following condition: age (years) > $W2_i$:

$$PFP_i = C3_i + H3_i \times \text{height} + A3_i \times \text{age}$$

where, in contrast to the ECSC/ERS equations and Falaschetti et al. equations for males, the threshold ages $W1_i$ and $W2_i$, were established using mathematical methods separately for each PFP_i together with the other coefficients.

Coefficients of these equations have been established on the basis of the results of spirometry performed as part of the project "Hope for Lungs" conducted between 2002 and 2005 by the Military Institute of Medicine (Warsaw, Poland). A total of 9846 volunteers, including 4716 men and 5130 women, were examined. Examinations were performed in 93 cities, towns, and villages all over Poland (approximately 100 examinations in each of those sites).

For the purpose of developing Polish predicted values, exclusion criteria identical to those adopted by Falaschetti et al. [4] were used. These included: (a) ex-smokers or current smokers; (b) presence of manifestations of a disease, including respiratory disease (e.g. cough); and (c) individuals who were unable to undergo correct spirometry.

On top of these, an additional unique criterion was used. It is based on the quantitative assessment of the correctness of the shape of the flow-volume curve previously developed by Gólczewski and Lubiński [9]. According to Kuziemski et al. [10], spirometry is relatively often incorrect. Checking the correctness of the measurement is one of the

Table 1. Characteristics of the samples analyzed by Lubinski and Golczewski as well as Falaschetti et al. [4] in their studies

	Males		Females	
	Lubiński	**Falaschetti**	**Lubiński**	**Falaschetti**
Total	4716	13 883	5130	16 646
After rejection (n)	1120	2479	1625	3556
Age (yrs)	55 ± 16	40 ± 16	57 ± 14	43 ± 17
Height [cm]	173 ± 7	176 ± 7	161 ± 6	162 ± 6
Age groups	n (%)	n (%)	n (%)	n (%)
18–45 lat	311 (28)	1627 (66)	316 (20)	2059 (58)
46–65 lat	472 (42)	636 (26)	766 (47)	1009 (28)
65–85 lat	337 (**30**)	208 (**8**)	543 (**33**)	463 (**13**)

Data are presented as the number of participants (n), age groups as percentages of the whole sample (%), or mean ± SD

major steps of a spirometry interpretation [11]. More experienced pneumonologists can assess the correctness of the spirometry based on factors that include a subjective assessment of the shape of the flow-volume curve, while primary care physicians may find it difficult. It therefore happens that this shape departs from the norm despite that manoeuvre is treated as correct because of repeatability of the FEV_1 and FVC measurement. In order to avoid these types of errors an objective quantitative measure of the flow-volume curve shape correctness was developed.

Based on this new criterion, results in which the deviation of the curve shape from the norm exceeded the 5th percentile upper limit of normal were rejected [9]. This means that the sizes of the analysed groups of males and females were 5% smaller than the sizes determined if the investigators limited themselves to using the widespread exclusion criteria only.

Eventually, after the rejections, spirometry results for 2745 non-smoking healthy individuals aged 18 to 85 years (1120 males and 1625 females) were analysed. The age distribution in the analysed sample was much more homogenous than in the sample analysed by Falaschetti et al. (Table 1).

Results

Table 2 provides the values of the coefficients C, H, and A for the Lubiński and Gólczewski equations presented in the conventional form described above. The equations were developed for the age range of 18 to 85 years. Only FEV_1/FVC, FVC, FEV_1, and MEF75–25 are given here, as Falaschetti et al. provided equations only for the first three parameters. The coefficients for MEF75–25 are given here due to the increasing popularity of this parameter among pneumonologists, who would like to assess both the mean initial flow (FEV1 is such a flow from the mathematical point of view) and mean mid-expiration flow. The values of the coefficients C, H, and A vary with different age ranges defined by regression methods separately for each of the PFPs. For example:

(a) if the age of a female patient is less than $W1_3$ (i.e. 29 years), then FEV_1 (the PFP_3) should be calculated from the following equation:

$$FEV_1 = -0.737 + 0.02494 \times \text{height}$$

(b) if the age of a female patient falls within the range $W1_3$–$W2_3$ (i.e. 29–35 years), then:

$$FEV_1 = 0.307 + 0.02494 \times \text{height} - 0.03601 \times \text{age}$$

(c) if the age of a female patient exceeds $W2_3$ (i.e. 35 years), then:

$$FEV_1 = 0.162 + 0.02494 \times \text{height} - 0.03191 \times \text{age}$$

Table 3 shows how much the equations proposed by Lubiński and Gólczewski, the equations proposed by Falaschetti et al., and the ECSC/ERS equations are appropriate for the analysed sample of the Polish population. Currently, the mean rather than the median (i.e. the 50th percentile) is treated as the predicted value. However, if a given variable has a distribution similar to the normal one, the mean and the median have similar values. This means that if a given equation correctly determines the predicted value of a given PFP, then the measured value should be lower than the predicted value for about 50% of the population and higher for the others. If much more than 50% of healthy individuals have PFP values lower than the calculated predicted values, the equation overestimates it. By analogy, in the case of the 5th percentile LLN: the measured value of a PFP should be lower than the LLN for 5% (neither more nor less) of the healthy population.

Table 2. Coefficients of Lubiński and Gólczewski prediction equations presented in the conventional form

	Males				Females			
	Age	**C**	**H**	**A**	**Age**	**C**	**H**	**A**
FEV_1/FVC (DGN)	< 24	81.75	–0.06811	0	< 28	70.80	0	0
	24–37	82.07	ditto	–0.01347				
	38–85	91.65	ditto	–0.26646	28–85	75.70	0	–0.17771
FVC (ref)	< 24	–4.371	0.05735	0	< 32	–1.596	0.03480	0
	24–30	–4.643	ditto	0.01134	32–35	–0.310	ditto	–0.04095
	31–85	–2.910	ditto	–0.04618	36–85	–0.513	ditto	–0.03522
FEV_1 (ref)	< 24	–2.569	0.04050	0	< 29	–0.737	0.02494	0
	24–30	–2.761	ditto	0.00801	29–35	0.307	ditto	–0.03601
	31–85	–1.197	ditto	–0.04375	36–85	0.162	ditto	–0.03191
MEF75-25 (ref)	< 24	–0.612	0.03084	0	< 30	3.614	0	0
	24–33	–0.758	ditto	0.00610				
	34–85	1.572	ditto	–0.06451	30–85	5.016	0	–0.04673

FEV_1 (ref) — forced expiratory volume in one second (reference value), FVC (ref) — forced vital capacity (reference value), FEV_1/FVC (DGN) — the lower limit of normal of FEV_1/ /FVC, MEF75–25 (ref) — maximal mid-expiratory flow (reference value); Age — the range for which the showed values of the following coefficients should be used: C, H, A — the constant term, height coefficient, and age coefficient, respectively (the predicted value or lower limit of normal should be calculated with the following form: C + H*height [cm] + A*age [yrs])

As shown in Table 3, the equations for FEV_1/FVC developed by Falaschetti et al. are extremely inappropriate for the Polish population. For example, according to these equations, more than 80% of elderly males have FEV_1/FVC values that are lower than the predicted values, and nearly 18% of healthy elderly females should be diagnosed with obstructive disease because of FEV1/FVC lower than LLN.

Discussion

ECSC/ERS equations

As shown above, the equations proposed by Lubiński and Gólczewski, for all the PFPs (with the exception of MEF25), can be reduced to a form that is similar to that of the ECSC/ERS equations. There are, however, three fundamental mathematical differences between ECSC/ERS and Lubiński's equations:

1. The fundamental difference is related to the fact that the age, at which the piecewise linear equation changes, has been arbitrarily assumed to be the same for all the PFPs and equal to 25 years. This means that PFP value alteration at age above 25 years must be approximated with a single straight line. If the actual age, at which a given PFP begins to change with age, is higher than 25 years, the straight line described by the ECSC/ERS equation cannot correctly approximate the mean value of this parameter in all age groups, e.g. in all the decades. If the ECSC/ERS straight line passed correctly through points corresponding to the mean values for a certain two decades, then it has to under- or overestimate the mean values in the other decades, which follows from the geometrical properties of the straight line. For instance, in Figure 1A, the ECSC/ERS straight line for MEF75 correctly determines the mean values for individuals 25–30 years of age and for 50-year-olds, and this means that for purely geometrical reasons it must underestimate MEF75 in 30- and 40-year-olds and overestimate MEF75 in 60-year-olds and older individuals. This is the case with most PFPs. This imperfection of the ECSC/ERS equation form is formal in nature, which means that it is impossible to be eliminated by repeated studies however recent or precise, and however numerous the populations. The Polish equations are devoid of this flaw because for each of the PFPs taken separately, the age at which this particular PFP begins to decline was established mathematically, i.e. using regression methods, in exactly the same way that all the other coefficients of the equation were established (i.e. it was established together with them). This was possible thanks to the unique form of equations proposed in the paper entitled: "Physiologically interpretable prediction equations for spirometric indices" [8].
2. The fact that a straight line cannot correctly describe age-related changes in PFP is related

Table 3. Percentages of age groups with a lung function variables below predictions (lower limits of normal) estimated with discussed authors' equations

	Males			Females		
Age range	**18–40**	**41–60**	**61–85**	**18–40**	**41–60**	**61–85**
	ref (DGN) (%)	ref (DGN) (%)	ref (DGN) (%)	ref (DGN) (%)	ref (DGN) (%)	ref (DGN) (%)
FEV_1/FVC						
Lubinski [8]	47 (4.9)	46 (5.4)	47 (5.6)	44 (5.7)	47 (4.8)	47 (5.4)
Falaschetti [4]	**75 (12.6)**	**66 (12.4)**	**81** (9.1)	**76 (21.0)**	**73 (15.3)**	**76 (17.7)**
ECSC [2]	66 (5.8)	52 (5.6)	58 (7.4)	65 (8.1)	63 (8.3)	56 (8.6)
Hankinson [7]	66 (11.2)	50 (8.6)	54 (**11.3**)	73 (16.7)	67 (11.3)	60 (12.0)
FVC						
Lubinski [8]	51 (5.8)	48 (5.4)	48 (5.0)	49 (5.2)	47 (4.9)	49 (4.7)
Falaschetti [4]	34 (2.9)	47 (6.1)	58 (**11.7**)	34 (5.7)	49 (**8.7**)	49 (**8.5**)
ECSC [2]	**18 (2.4)**	**26** (**3.7**)	**40** (5.9)	**20 (1.9)**	**21** (2.6)	**32** (2.2)
FEV_1						
Lubinski [8]	49 (4.9)	48 (6.5)	48 (4.5)	50 (4.3)	48 (6.3)	50 (4.3)
Falaschetti [4]	42 (**7.3**)	52 (**14.7**)	**65** (**16.7**)	52 (**10.0**)	**60** (**15.3**)	**62** (**17.6**)
ECSC [2]	**31** (3.9)	**39** (7.5)	53 (10.7)	**38** (6.2)	41 (7.2)	54 (7.3)
MEF25–75						
Lubinski [8]	50 (4.4)	51 (6.3)	55 (4.1)	51 (5.3)	53 (5.4)	54 (4.0)
ECSC [2]	50 (**8.3**)	58 (**10.3**)	**75** (**11.4**)	**69** (**17.3**)	**77** (**15.2**)	**87** (**18.5**)
Hankinson [7]	**40** (6.3)	**39** (4.9)	51 (1.6)	51 (10.0)	58 (6.8)	59 (1.8)

ref (DGN) — the percentages for reference values (lower limits of normal). In each age group, results that are most different from correct ones (about 50% for the predicted values and 5% for DGN) are underlined. The elderly group is restricted to the age for which equations of given authors are estimated

to non-linearity of PFP dependence on age. In the ECSC/ERS equations, an *a priori* assumption was made that this non-linearity could be sufficiently precisely represented by a piecewise linear function with a horizontal part until the age of 25 years and an inclined straight line above the age of 25 years, which reflects a constant rate of age-related PFP alteration above that age. In the case of the Lubiński and Gólczewski equations, each of the PFPs was analysed mathematically to test whether piecewise linear functions sufficiently approximate the non-linearity of age-related alteration of that particular PFP. Statistical analyses show that the piecewise linear form is sufficiently good for all the PFPs with the exception of MEF25 [8]. In the case of MEF25, acceptation of a constant rate of changes with age, like in the ECSC/ERS equations, leads to erroneous or even physically meaningless conclusions, such as a negative value of LLN for MEF25 in women over the age of 65 (Figure 1B), which would mean that forced expiration can be an inspiration (a negative expiration is an inspiration).

3. The nonsense mentioned above (the "negative expiration") is caused by the failure to take into account the decreasing rate of MEF25 decline with age and by the fact that LLN has been established as a predicted value minus $1.645 \times SD$ (where the SD is the standard deviation of the differences between the observed and expected values of a given PFP). This means that LLN is at the same distance from the predicted value across the whole age range. This is an incorrect approach, which is most strikingly revealed in the case of MEF25, where — even without mathematical analyses — one can observe that the higher the age, the closer the LLN to the predicted value (Figure 1B). In the case of most other PFPs (esp. FEV_1/FVC) the distance between the predicted value and the LLN increases with age. Lubiński and Gólczewski [8] as well asFalaschetti et al. [4], established the 5th percentile LLN using the Healy's method [12].

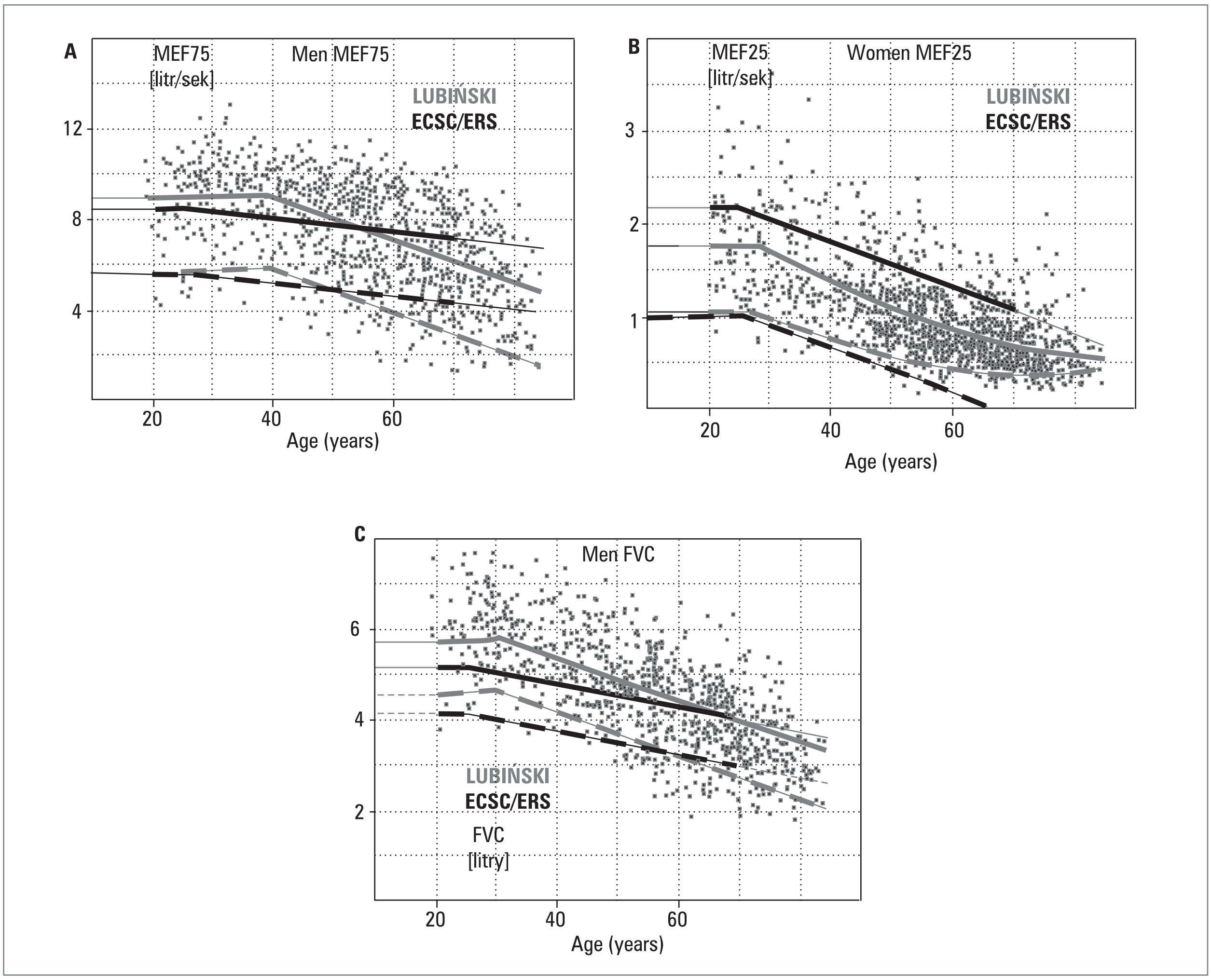

Figure 1 A–C. Predicted values (solid lines) and lower limits of normal (dashed ones): black lines — ECSC/ERS equations [2], gray ones — Lubinski and Golczewski equations [8]; thin lines — predictions beyond the age range for which equations were elaborated; light gray dots — actual results for the examined individuals. **A** — maximal expiratory flow at 75% of forced vital capacity (MEF75) for males (height 175 cm); **B** — maximal expiratory flow at 25% of forced vital capacity (MEF25) for females (height 160 cm); **C** — forced vital capacity (FVC) for males (height 175 cm)

In addition to the mathematical flaws of the ECSC/ERS equations, it seems that they do not fit well to the present generations. The FVC data may suggest that, for the present generations, the younger the person is, the more their FVC value is higher compared to the individuals examined 20–30 years ago, who were at the same age at that time (Figure 1C). It may be associated with the quite rapid change in the average standard of living in the past 20–30 years.

Equations proposed by Falaschetti et al.

The equations proposed by Falaschetti et al. for FEV_1/FVC differ considerably from those proposed by Lubiński and Gólczewski (Figures 2A and 2B). As illustrated in Table 3, well-established equations, i.e. the ECSC/ERS ones [2] and the American ones proposed by Hankinson et al. [7], seem to be much better. Among the equations proposed by other, less well-known authors, the equations by Brandli et al. [13] for males above the age of 35 years practically overlap with those of Lubiński. It is also difficult to explain the considerable differences in the Falaschetti equations for the LLN of FEV_1/FVC for elderly males and females despite the quite similar equations defining the predicted values of this parameter (Figures 2A and 2B). No such differences between the genders are observed by other authors.

In the case of the predicted value for FVC, the equations proposed by Falaschetti et al. yield results similar to those obtained with the Lubiński and Gólczewski equations (Table 3). More significant differences are only observed for young adults (the average vital capacity in young male and female Poles seems higher than that suggested by Falaschetti et al.). The equations for FVC LLN proposed by Falaschetti et al. are rated slightly wor-

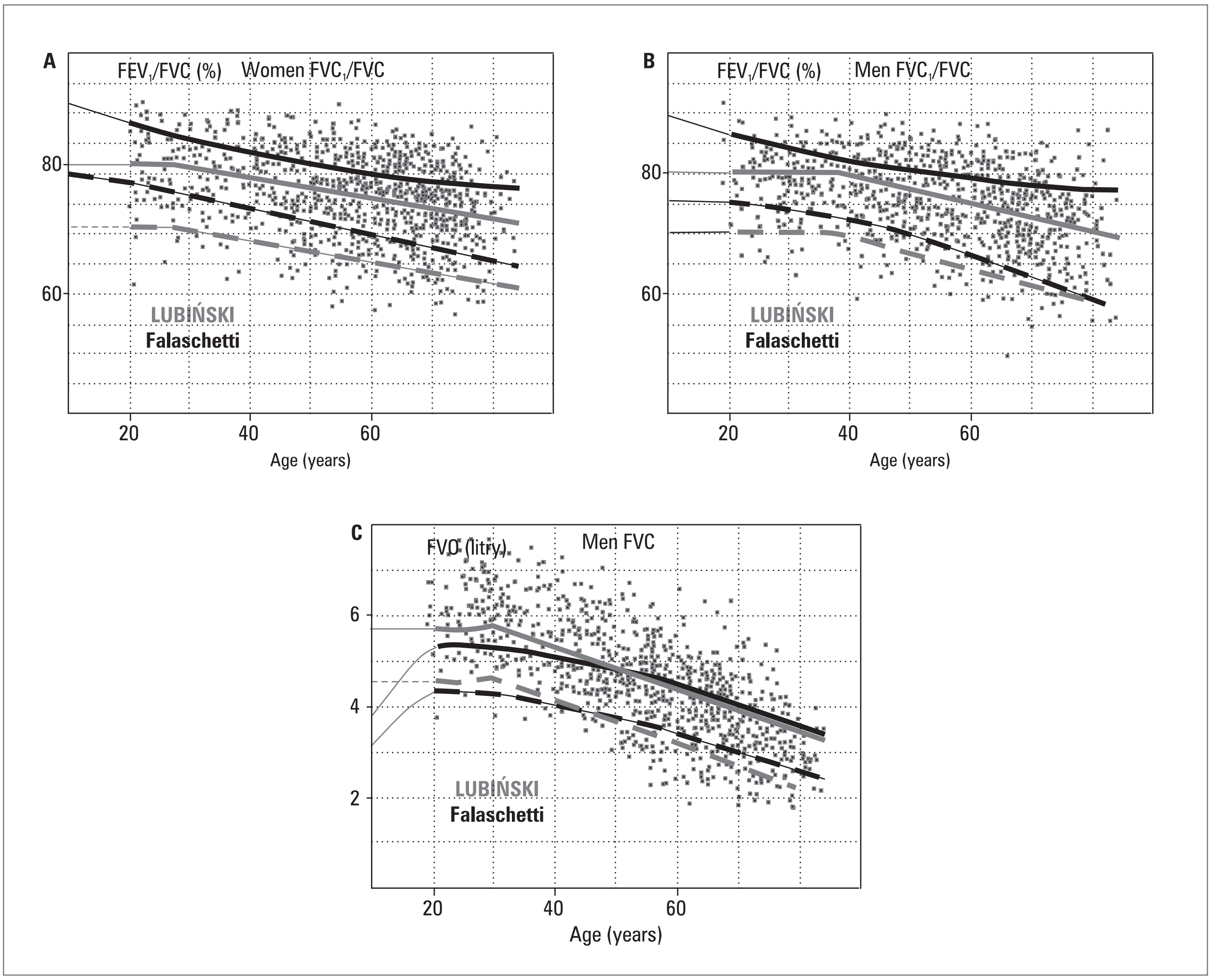

Figure 2 A–C. Predicted values (solid lines) and lower limits of normal (dashed ones); black lines — Falaschetti et al. equations [4], gray ones — Lubinski and Golczewski equations [8]; thin lines, predictions beyond the age range for which equations were elaborated; light gray dots, actual results for the examined individuals. **A** — forced expiratory volume in one second to forced vital capacity ratio (FEV_1/FVC) for females; **B** — FEV_1/FVC for males; **C** FVC for males (height 175 cm)

se, while those for FEV_1 are less suitable for the Polish population than the ECSC/ERS equations, particularly in the case of the elderly (Table 3).

Inappropriateness of the Falaschetti equations for the Polish population might be related to some differences between the Polish and English populations. It seems, however, that methodological flaws of the Falaschetti equations may result in the inappropriateness. The two following imperfections can have particular meaning:

— The form of the equations proposed by Falaschetti et al. is "excessively" non-linear. This assumption was adopted *a priori*, without any statistical analyses to investigate if and to what degree the changes in PFP with age are non-linear and, in particular, if and to what degree the rate of decline of a given PFP with age changes. As mentioned above, only the rate of MEF25 decline changes with age in a statistically significant manner [8].

— From a statistical point of view, Falaschetti et al. incorrectly selected the population sample. It is true that in general, from the point of view of Statistics, a sample should closely reflect the general population. However, this does not apply to cases in which a regression method is used to determine the average statistical relationship between a parameter and a variable treated as an independent variable; in our case: the relationship between PFPs and age. In such cases, from purely mathematical reasons, the relationship is defined most precisely for the most numerously represented age group at the expense of smaller groups. For that reason, if the relationship between a PFP and age is to be precisely defined also for the population of the elderly, their number in the

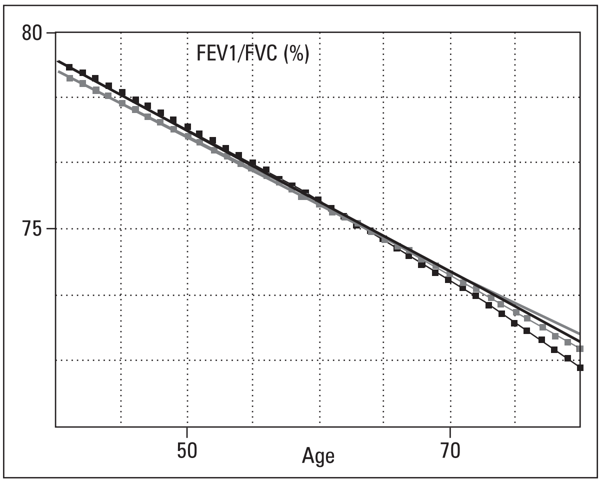

Figure 3. Sensitivity of prediction equations for FEV_1/FVC to data structure. Pointed lines — the 'doubly-nonlinear' form used by Falaschetti et al. [4], solid lines — the form proposed by Lubiński and Gólczewski [8]. Gray lines — an approximately uniform distribution of number of subjects in function of age (our original data), black lines — the distribution similar to that from [4] (small number of older subjects — tab. 1) obtained from our original data by multiplication of data related to young persons and random rejection of a part of older subjects

analysed sample must be similar to the number of younger persons, while in the study by Falaschetti et al. [4], the elderly are a small fraction of the entire study population (Table 1).

In addition, non-linear equations of the type used by Falaschetti et al. are much more sensitive than linear equations to the database used in regression. This particularly concerns the extreme ends of the analysed age range (see the rapid changes in the equation by Falaschetti et al. for the height of 175 cm and the age below 20 years in Figure 2C). Therefore, the unnecessary "excessively" non-linear form of the equations in combination with the poor representation of the elderly people in the analysed sample of the English population may be the basic source of unsuitability of the equations by Falaschetti et al. in this age range.

Figure 3 compares the stability of the equations proposed by Falaschetti et al. with that of the Polish equations. The grey lines depict the equation proposed by Falaschetti et al. and the equation proposed by Lubiński and Gólczewski for predicted values of FEV_1/FVC obtained by the regression methods for our original data, where the size of the elderly group is comparable with the sizes of the other two groups (Table 1). The black lines depict the same equations except that they have been obtained for the dataset formed from our original data through multiplication of the results for young adults and random rejection of some of the elderly individuals so that the sizes of the age groups are proportional to the sizes of these groups in the sample analysed by Falaschetti et al. (Table 1). As has been demonstrated, the non-linear equation by Falaschetti et al. has changed more than the Polish equation of a simple form. The changes are particularly significant at the upper end of the age range (70–80 years), which suggests a higher instability of the form of the equations used by Falaschetti et al. The lower differences between the equation by Falaschetti et al. and that by Lubiński and Gólczewski defined for our original data confirm the statement according to which the age distribution should generally be uniform.

It might seem that despite everything the change in the equation by Falaschetti et al. shown in Figure 3 is not large enough, even in the case of the oldest individuals, to explain the increase in the differences for the extremes of age between the original equation by Falaschetti et al. and the equation by Lubiński and Gólczewski (Figures 2A and 2B). It should, however, be taken into account that from the point of view of the mean values, in both cases presented in Figure 3, we were dealing with the same sample (neither multiplication of the young adults nor a random removal of elderly individuals changed the mean values of FEV_1/FVC in these groups, and the predicted value is the mean value). We can guess how considerable changes in the equation by Falaschetti et al. at the extremes of age might be if some actual differences were present between the populations or even between two different samples of the same population.

Equations proposed by Lubiński and Gólczewski

These equations are devoid of the above mathematical and methodological flaws. In particular:

- Such a form of prediction equations was used so that for each specific PFP treated separately, all the coefficients - also the age from which this PFP began to decline - were established mathematically from the experimental data.
- Thanks to this novel form, it was possible to test whether the non-linearity, i.e. alteration of the decline rate of a given PFP, was statistically significant (as already mentioned, only non-linearity of MEF25 decline has appeared to be statistically significant).
- The LLN was determined directly from the definition of the 5th percentile using the Healy method.
- The size of the group of the elderly was comparable with the sizes of the other groups (Table 1).

Lung ageing is associated with significant changes in the structure of the respiratory system, particularly with respect to the elastic elements of the pulmonary parenchyma. Consequently, the closing volume increases with age as a result of the tendency towards a premature significant increase in the resistance of the small airways and a more rapid closure of the small airways at low lung volumes [14]. For this reason, the first parameter that begins to decline with age is MEF25, i.e. the flow rate at low lung volumes. As ageing progresses, flow rates for higher volumes begin to decline. As FEV_1 accounts for about 70–80% of FVC, the flow rate after exhaling 75% of FVC (i.e. MEF25) affects FEV_1. Hence the age at which FEV_1 begins to decline is similar to the age at which MEF25 begins to decline (the same is true for MEF75–25). The age at which PEF begins to decline, determined by Lubiński and Gólczewski [8], is identical to the age shown in the study of Nunn and Gregg [15] both in females (about 35 years) and males (about 38 years). Thus, mathematically obtained values of age at which individual PFPs begin to decline are in line with the physiological knowledge and epidemiological studies.

It should be noted that the age at which the mean height for a given year of birth begins to decrease varies with the age at which individual PFPs begin to decline [8]. Due to these differences, when the equations are analysed for individuals of the same height, values of some PFPs increase until a certain age, at which they begin to decline. For instance, in men of the same height, MEF75 increases until the age of 39 years (Figure 1A), while FVC peaks at about the age of 30 years (Figures 1C and 2C and the positive value of coefficient A for the age range 24–30 years in Table 2). A more detailed discussion of these results and their comparison with identical results of other authors (e.g. results obtained by Nunn and Gregg [15]) is, however, beyond the scope of this paper.

Chronic obstructive pulmonary disease (COPD) is caused by a long-lasting exposure to contaminants in the inspired air (tobacco smoke is the most common contaminant). For this reason, COPD most commonly affects the elderly, in whom the diagnosis is much more complex than in younger individuals [16]. On the other hand, ageing affects PFPs in a similar way to obstructive diseases. That is why, in order to carry out a more accurate differentiation between COPD and the effects of ageing, the intention of Lubiński and Gólczewski was to determine predicted and LLN values with particular attention paid to the increasing population of the elderly. This goal seems to have been achieved, as may be evidenced by a comparison of our equations with the results obtained by those authors who analysed PFP only in the elderly but carried out the analysis in a very meticulous way. For instance, the equations discussed here give identical predicted values of FEV_1/FVC and LLN as those by Hardie et al. [17] for elderly Norwegians.

Finally, it should be noted that the creation of mathematical equations for the calculation of predicted values is a some case of relic of the times when digital technology was in its infancy. In the case of medical parameters which are not age-related, no equations are created; norms such as reference range or the mean and LLN values identical for all ages are determined. Analogously, if a parameter is age-related, then it would be natural to establish norms for each year group separately. However, taking into account the number of year groups (e.g. 90, if one were to consider an age range of 5–95 years) and the number of PFPs, several hundreds or even several thousands of norms would be required. Therefore, when a physician had to determine the reference value or LLN by himself/herself, a few equations with 2–3 coefficients were much convenient. However, present digital technology makes it possible to put all the numerical data in the microcomputer being a part of modern spirometers. The microcomputer would use these data directly to determine the degree to which the value of a PFP measured in a patient differs from the predicted (or LLN) one.

Despite the present possibility of using norms for each of the year groups separately, researchers — possibly as a result of a certain inertia — still develop equations that more or less precisely approximate norms for 90 year groups. Such equations are some method for data compression, which used to be useful but no longer is. For instance, instead of the 90 predicted values for FEV_1 for all year groups we now have two (ECSC) or three (Lubiński and Gólczewski; Falaschetti et al.) coefficients of an equation (1-2 coefficients related to age and the constant term). Such compression is, however, completely unnecessary today since microcomputer remembers the numbers and performs calculations, whereas the data can be published on and sent by the Internet. Despite this possibility, researchers continue to develop novel and more sophisticated equations and publish papers with more (e.g. [18]) or less (e.g. this paper) complex analyses of these equations and conditions in which they were developed. It seems, however, that now the only justification for developing the equations could be their application in other areas, such as physiology or epidemiology; hence our physiologically interpretable equations.

The above discussion should be complemented with two comments. Firstly, in order for an equation to approximate the norms to a more precise degree for all the 90 year groups, none of these year groups can be preferred; in particular, none of the year groups can be taken into account several times. At present, the equations are defined not on the basis of previously developed norms for particular year groups but directly from the original data for a sample of the general population. In such a case the preferredness of some year groups is equivalent to the higher number of subjects in these groups . In particular, the young group is preferential when the elderly group is much smaller like in Falaschetti et al. study.

Secondly, results for healthy individuals from a given year group are dispersed around the mean value because of interpersonal differences, i.e. deviations of various factors form the mean values for this year group. If an easily measurable factor is known, its deviation from the mean value can be taken into account in a more precise definition of the norm. In the case of spirometry, height is such an easily measurable and significant factor. Therefore not the patient's height but its deviation from the mean height for the patient's year group is taken into account in the physiologically interpretable form of the Lubiński and Gólczewski equations.

Conclusions

Interpretation of spirometry results should be based on predicted values and the lower limit of normal that were calculated from prediction equations developed for a particular population. Moreover, these equations should be correct from the formal, i.e. methodological and mathematical, points of view.

It seems that the use of norms developed by Lubiński and Gólczewski should be considered in Poland, particularly in the case of the elderly, because they have been developed for the Polish population and they have no formal imperfections which are present in the equations recommended now by the Polish Respiratory Society, i.e. in the ECSC/ERS equations and those developed by Falaschetti et al..

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