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Lung function reference values in different German populations

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Reference values;
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Summary

Background: Spirometry is a frequently performed lung function test and an important tool in medical surveillance examinations of pulmonary diseases. The interpretation of lung function relies on the comparison to reference values derived from a healthy population.

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The study aim was to compare the lung function data of three representative population-based German studies (Study of Health in Pomerania [SHIP-1], Cooperative Health Research in the Region of Augsburg [KORA-S3] and European Community Respiratory Health Survey Erfurt [ECRHS-I Erfurt]) with existing European spirometry reference values and to establish a new set of comprehensive German prediction equations.

Methods: Spirometry was performed in 4133 participants of three population-based surveys using almost identical standardised methods. Current and former smokers, subjects with cardiopulmonary disorders or on medication with potential influence on lung function were excluded. Sex specific prediction equations were established by quantile regression analyses. Comparison was performed to existing European reference values.

Results: The healthy reference sample consisted of 1302 (516 male) individuals, aged 20–80 years. Sex specific comprehensive prediction equations adjusted for age and height are provided. Significant differences were found in comparison to previous studies with pronounced lower values of the current population if applying historic prediction equations.

Conclusion: The results contribute to the interpretation of lung function examination in providing a comprehensive set of spirometry reference values obtained in a large number of healthy volunteers. Whereas the differences in between the investigated studies are negligible, striking divergence was detected in comparison to historic and recent European spirometry prediction values.

Introduction

Spirometry is the most frequently performed lung function test and considered as an important tool in medical surveillance examinations of pulmonary diseases. Furthermore, spirometric parameters such as forced expiratory volume over 1 s (FEV1) are independently correlated to the risk of myocardial infarction, congestive heart failure, stroke[1,2] and mortality.[3,4] The interpretation of lung function results usually relies on the comparison to reference values derived from a healthy population. Variations in these available data may be, above all, explained by the kind of selection criteria applied. Furthermore, as for other anthropometric measures such as height, cohort effects have been described – that is, mean values within each age group increase over time.[5] A number of sets of prediction equations are currently available for different populations. Those most widely used in Europe are based on studies published in the eighties and nineties of the last century,[5–8] and may not represent the findings obtained in recent populations. Recommendations on the establishment of spirometric reference values propose data from cross-sectional studies of non-smokers.[9,10] Arguments for updating reference values on a regular basis and with respect to elderly people are, amongst others, cohort effects and newer technical equipment.[11]

The objectives of our study were (1) to calculate age and sex specific German spirometric prediction equations on the basis of apparently healthy individuals of three representative population-based German studies (Study of Health in Pomerania-1 [SHIP-1]), KORA-S3 Augsburg [*Cooperative Health Research in the Region Augsburg*] and ECRHS-I Erfurt [(*European Community Respiratory Health Survey in Adults*)], (2) to compare the lung function data of the present sample to historic and recent European prediction equations for lung function, and[12] to decide on the validity and feasibility of the current spirometric reference values as comprehensive German normative equations.

Material and methods

Study population

Three population-based studies were performed in different German regions (northeast, central, south). Of the adult population living in these areas defined samples were selected from the population registration offices, where all Germans inhabitants are registered. A two-stage cluster sampling method was adopted from the WHO MONICA Project Augsburg, Germany.[13] Representative samples of equally distributed sex and age groups were drawn. Eventual participation was voluntary.

SHIP-1

SHIP is a population-based survey in a region in the Northeast of Germany. Study details are given elsewhere.[14–16] A first 5-year follow-up was performed (SHIP-1) 2003–2006. The sample (without migrated, deceased and non-responding people) compromised 3300 subjects (1584 males) aged 25–85 years. Lung function examination was performed on a sub-sample consisting of 1809 individuals (885 males). 1783 were younger than 80 years and had complete data on lung function. Of these, 513 subjects with self-reported bronchial asthma, chronic obstructive bronchitis or other pulmonary diseases or use of specific pulmonary and cardiac medication were excluded. Furthermore, 35 subjects with fractional shortening $<$20% and 687 current or ex-smokers were excluded. Altogether data of 541 individuals were available for the present analyses.

KORA-S3 Augsburg

The population-based study KORA-S3 is based on the third MONICA survey, which was performed in Augsburg, Germany, 1994–1995. The objective and protocol of the underlying MONICA surveys have been published earlier.[17] For the KORA-S3 survey an enriched sample of the 3rd MONICA survey was drawn according to the presence of specific IgE-antibodies and reported allergy symptoms. Details on the sampling procedure have been published elsewhere.[18] In the subproject "KORA-C", which specifically focussed on allergic diseases, lung function tests were performed from 1997 to 1998 in a total of 1093 subjects, where 1085 participants had complete data. Of these, 185 subjects with self-reported asthma, or cough or use of specific pulmonary and cardiac medication were excluded. Furthermore, 17 subjects with heart failure and 557 current or ex-smokers were excluded. Altogether data of 326 individuals were available for the present analyses.

ECRHS-I Erfurt

The cross-sectional study ECRHS-I Erfurt was performed from 1991 to 1992 in Erfurt, Germany. The study design has been described in detail before.[19,20] In a two-step approach 6291 randomly chosen individuals were asked to reply to a short questionnaire on respiratory symptoms (stage I). A random sample of the 4332 stage I-responders, aged 20—65, were invited to perform lung function measurement and to answer a detailed questionnaire (stage II). Ultimately, 1231 lung function tests were available and complete data were present of 1161 subjects. Of these, 161 subjects with self-reported asthma, or cough or use of specific pulmonary and cardiac medication were excluded. Furthermore, 565 current or ex-smokers were excluded. Altogether data of 435 individuals were used for the present analyses.

Computer-assisted standardised interviews and questionnaires were part of the three studies. Besides, data on age and sex, information on sociodemographic parameters and medical histories were assessed and anthropometric measurements performed.

Lung function examinations were based on the ATS and ERS quality standards.[6,7,10] The standard operating procedures of the three studies are very similar regarding technical equipment, examination and measurement procedures as well as quality control. The operations were conducted by experienced, trained and certified staff. All examiners were trained in an experienced clinical department before entering the study. Initial certification was awarded to potential observers, who were held to strict quality criteria. The follow-up quality was assured. External observers were regularly invited to participate in certification procedures. The data collection phase was monitored by a Data Safety and Monitoring Committee.

Participants of all studies were investigated in health examination centres established for the purpose of the study and gave written informed consent. The studies conformed to the principles of the Declaration of Helsinki as reflected by approvals of the Ethics Committees.

Pre-diagnostics and exclusion criteria

The definition of pulmonary disorders was based on self-reported physician's diagnosis and the use of specific medication (based on the anatomic, therapeutic, and chemical [ATC] code).[21]

Height and weight were measured without shoes according to the ATS recommendations on preparing the participants.[9] The medication was recorded by a computer-aided method using the ATC code. The smoking status (current, former, or never-smoker) was assessed by self-report. Chronic bronchitis was defined as productive cough in the past 12 months for at least 3 months. Bronchial asthma and pulmonary disease were based on self-report.

Subjects fulfilling the following self-reported criteria were excluded from the present study: current smoking, any pulmonary diseases, bronchial asthma, chronic obstructive bronchitis, or the use of specific pulmonary and cardiac medication.

Spirometry and lung function variables

In all three studies lung function examinations were conducted using comparable equipment produced by Jaeger, Hoechberg, Germany, that meets the American Thoracic Society (ATS) criteria[22] and the recommendations of the ECCS.[6] The volume signal of the equipment was calibrated with a 3.0 L syringe connected to the pneumotachograph in accordance with the manufacturers' recommendations and at least once on each days' testing. Barometric pressure, temperature and relative humidity were registered every morning. Calibration was examined under ambient temperature and pressure conditions (ATP) and the integrated volumes were BTPS (Body Temperature Pressure Saturated) corrected.[10,22]

The participants performed at least three forced expiratory lung function manoeuvres in order to obtain a minimum of two acceptable and reproducible values.[6] Immediate on-screen error codes indicated the major acceptability (including start, duration and end of test) and reproducibility criteria. The procedure was continuously monitored by a physician. Before the tests the required manoeuvres were demonstrated by the operator and the individuals were encouraged and supervised throughout the performance of tests. Lung function variables were measured continuously throughout the baseline breathing and the forced manoeuvres. Spirometry flow volume loops were conducted in accordance with ATS recommendations[10] in a sitting position and with wearing noseclips.

The best results for forced vital capacity (FVC) and FEV_1 were taken. The ratio of FEV_1 to FVC (expressed as a percentage) was calculated from the largest FEV_1 and FVC.

Statistical analyses

Continuous data are expressed as median (25th and 75th percentiles). For unadjusted bivariate analyses, Kruskal—Wallis tests were used to compare SHIP-1, KORA-S3, and ECRHS-I Erfurt separately in men and women. To account for the different age distributions, comparisons were also performed by Analysis of Covariance with age and weight as covariates. Quantile regression[23] was used for the evaluation of prediction equations in men and women separately. In comparison to linear regression, quantile regression represents a more adequate method to calculated reference ranges because it makes no distributional assumption and allows an independent estimation of conditional quantile functions resulting in reference limits which are independent of global parameters like the standard deviation.[21] Furthermore, the quantile regression shows a high robustness to outlier observations. Models adjusted for age and height were developed in order to estimate the 5th, 50th, and 95th percentile. Likelihood ratio tests were used to compare the fit of models with different polynomials for the parameters age and height. Since quantile regression makes no distributional assumption, an initial transformation of the original data was not necessary. The determined prediction equations for FEV_1 and FVC were compared to formerly stated equations.[5,6,24–27] For these, differences between observed and predicted values are given as mean difference, root mean square error of prediction, and residual prediction deviation. Furthermore, Bland Altman plots were calculated to present differences between predictions form the present study and other equations. Moreover, graphical comparisons were performed by dummy calculations across all ages and with fixed heights (women 165 cm, men 180 cm) of the lower reference limit. Bland Altman plots and dummy calculations were only presented for the European studies of Falaschetti et al.,[24] the European Community for Coal and Steel [ECCS],[6] Langhammer et al.,[27] and Kuster et al.[26] Statistical analyses were performed with PROC QUANTREG in SAS 9.1.3 (SAS Institute Inc., Cary, NC, USA). A value of $p < 0.05$ was considered statistically significant.

Results

The study population consisted of 1302 individuals (516 male, 786 female) distributing on the studies as follows: SHIP-1 541 subjects (186 male), KORA-S3 326 individuals (172 male) and ECRHS-I Erfurt 435 participants (158 male).

Anthropometric and lung function data of the subjects included in the present study are given in Table 1. Significant differences between the study centres were evident in both sexes for weight, body mass index (BMI), FEV_1, FVC, and FEV_1/FVC. After adjustment for age and weight differences were still apparent for FEV_1/FVC in both men and women as well as for FEV_1 in women only.

Sex specific spirometry prediction equations from the healthy individuals for the 5th, 50th, and 95th percentile of FEV_1, FVC, and FEV_1/FVC are presented in Table 2 and Fig. 1. The threshold limit value of a lung function parameter stipulates that 90% of healthy subjects are in the range of normality. Fig. 1 illustrates that both age and height account for variation in the reference limits except for FEV_1/FVC where the effect of height is less pronounced.

Table 1 Descriptive statistics of the study population.

	SHIP-1	KORA-S3	ECRHS-I	p*	p**
Men, *N*	186	172	158		
Age (years)	47 (37; 60)	48 (39; 55)	38 (27; 50)	<0.01	–
Age (years, %)				<0.01	–
20–29	5.4	2.9	30.4		
30–39	29.1	25.0	22.1		
40–49	21.5	26.7	20.9		
50–59	17.7	43.6	23.4		
60–69	23.1	1.2	3.2		
≥70	3.2	0.6	–		
Weight (kg)	82 (75; 93)	82 (76; 90)	78 (71; 86)	<0.01	–
Height (cm)	178 (171; 181)	178 (174; 182)	178 (172; 182)	0.59	0.43
BMI (kg/cm^2)	26.7 (24.3; 29.0)	26.2 (24.6; 27.8)	24.9 (23.1; 27.3)	<0.01	0.49
FEV_1 (l)	4.0 (3.6; 4.7)	4.1 (3.5; 4.6)	4.3 (3.8; 4.7)	<0.01	0.73
FVC (l)	4.7 (4.2; 5.3)	5.0 (4.4; 5.6)	5.3 (4.6; 5.7)	<0.01	0.08
FEV_1/FVC	0.86 (0.82; 0.89)	0.82 (0.79; 0.86)	0.84 (0.80; 0.87)	<0.01	<0.01
Women, *N*	355	154	277		
Age (years)	54 (44; 64)	44 (39; 50)	45 (36; 55)	<0.01	–
Age (years, %)				<0.01	–
20–29	3.4	1.3	14.8		
30–39	15.8	30.5	19.9		
40–49	15.2	39.6	24.9		
50–59	25.4	27.3	27.8		
60–69	30.4	1.3	12.6		
≥70	9.8	–	–		
Weight (kg)	70 (61; 80)	62 (57; 70)	65 (58; 75)	<0.01	–
Height (cm)	163 (159; 167)	164 (160; 167)	163 (159; 168)	0.99	0.11
BMI (kg/cm^2)	26.3 (23.3; 30.3)	23.5 (21.5; 26.0)	24.2 (22.1; 28.1)	<0.01	0.14
FEV_1 (l)	2.7 (2.4; 3.2)	3.1 (2.8; 3.4)	3.0 (2.6; 3.3)	<0.01	<0.01
FVC (l)	3.2 (2.8; 3.7)	3.6 (3.2; 4.0)	3.6 (3.2; 4.0)	<0.01	0.14
FEV_1/FVC	0.87 (0.83; 0.90)	0.85 (0.82; 0.88)	0.83 (0.79; 0.86)	<0.01	<0.01

Continuous data are given as median (25th; 75th percentile). *Kruskal–Wallis test. **Comparisons from Analysis of Covariance with age and weight as a covariate. BMI (kg/m^2): body mass index; FEV_1 (l): forced expiratory volume in 1 s; FVC (l): forced vital capacity; FEV_1/FVC: ratio of FEV_1 to FVC.

Table 2 Prediction equations for spirometric parameters in men and women.

Variable	Men	Women
95th percentile		
FEV_1	$-3.82483 - 0.02728 \times A+0.05706 \times H$	$-2.41455 - 0.02304 \times A+0.04299 \times H$
FVC	$-5.40368 - 0.02821 \times A+0.07144 \times H$	$-4.62277 + 0.00772 \times A - 0.00032 \times A^2 + 0.05625 \times H$
FEV_1/FVC	$0.99017 - 0.00080 \times A - 0.00014 \times H$	$1.42200 - 0.00660 \times A + 0.00005 \times A^2 - 0.00171 \times H$
50th percentile		
FEV_1	$-3.20190 - 0.02358 \times A + 0.04746 \times H$	$-1.54700 - 0.02401 \times A + 0.03463 \times H$
FVC	$-5.23148 - 0.02426 \times A + 0.06383 \times H$	$-3.38781 + 0.00577 \times A - 0.00032 \times A^2 + 0.04504 \times H$
FEV_1/FVC	$1.01247 - 0.00056 \times A - 0.00085 \times H$	$1.14288 - 0.00507 \times A + 0.00004 \times A^2 - 0.00099 \times H$
5th percentile		
FEV_1	$-3.48761 - 0.02085 \times A + 0.04409 \times H$	$-0.02351 - 0.02644 \times A + 0.02190 \times H$
FVC	$-4.48344 - 0.02125 \times A + 0.05390 \times H$	$-2.02079 + 0.01622 \times A - 0.00049 \times A^2 + 0.03214 \times H$
FEV_1/FVC	$1.02786 - 0.00078 \times A - 0.00148 \times H$	$1.44424 - 0.00523 \times A + 0.00004 \times A^2 - 0.00330 \times H$

A = age [years], H = height [cm].

The calculated reference equations for FEV_1 and FVC were compared to established equations provided by different studies: (a) Brändli et al.,[5] (b) Falaschetti et al.,[24] (c) Langhammer et al.,[27] (d) Kuster et al.,[26] (e) ECCS,[6] and (f) National Health and Nutrition Examination Survey III [NHANES III].[25] Differences between observed and predicted values of FEV_1 and FVC are shown in Table 3. In both women and men, equations from Brändli et al.[5] and Langhammer et al.[27] showed the best fit to the present FEV_1 data. Whereas equations of Falaschetti et al.,[24] Kuster et al.,[26] and the ECCS[6] underestimated FEV_1 resulting in a lower proportion of subjects below the lower limit of normal range (LLN) with the most profound difference to the ECCS equation. The Bland Altman plots (Figs. 2 and 3) confirm these findings and dummy calculations showed graphically that the lower values become even more pronounced in older male subjects.

Regarding FVC, the closet agreement was with Falaschetti et al.[24] and Kuster et al.[26] in women and men (Table 3). Whereas the ECCS[6] again underpredicted the FVC, equations from Langhammer et al.,[27] Brändli et al.,[5] and NHANES[25] overestimated FVC (Figs. 2 and 3). Also for

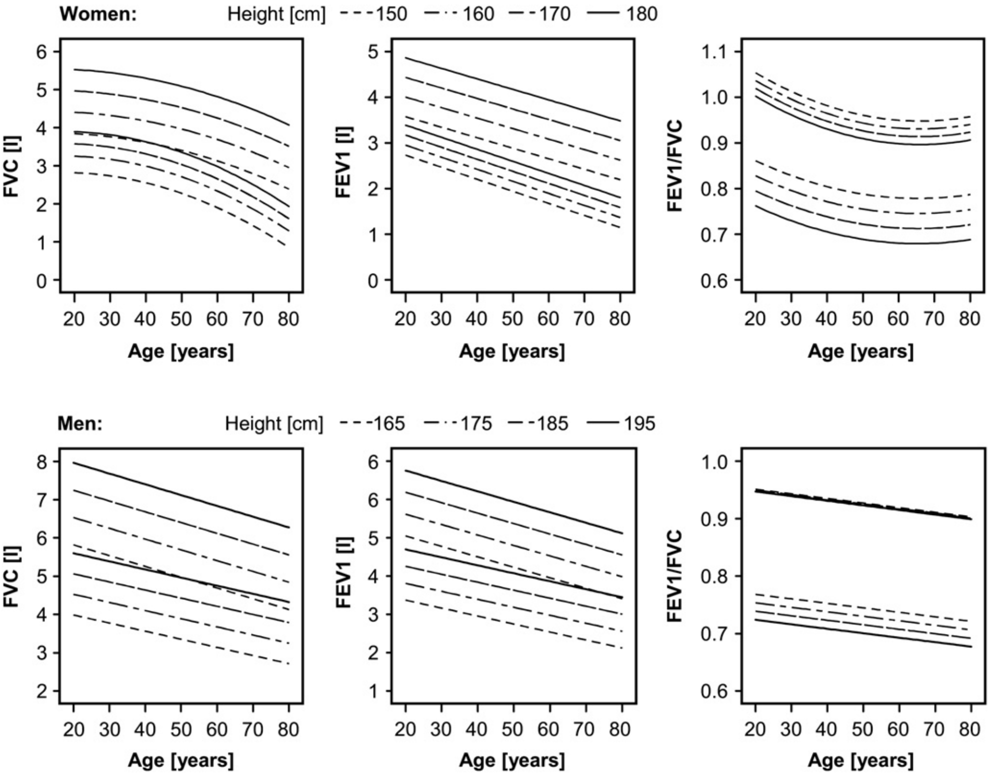

Figure 1 Upper (95th percentile) und lower reference (5th percentile) limits for forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC) and FEV_1/FVC ratio depending on age in women and men for selected heights.

Table 3 Comparison of observed values of forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) with predicted values by different studies.

	Men (*n* = 516)				Women (*n* = 786)			
	Mean difference (%) ± SD	Root mean square error of prediction	Residual prediction deviation	Observed values below the LLN *N* (%)	Mean difference (%) ± SD	Root mean square error of prediction	Residual prediction deviation	Observed values below the LLN *N* (%)
FEV_1								
Present study	0.060 ± 12.331	0.511	1.405	24 (4.7)	−1.948 ± 13.879	0.370	1.540	41 (5.2)
Brändli et al.	0.970 ± 12.369	0.515	1.393	23 (4.5)	1.017 ± 13.814	0.370	1.538	33 (4.2)
Falaschetti et al.	3.431 ± 12.746	0.543	1.323	13 (2.5)	3.733 ± 13.899	0.388	1.469	32 (4.1)
Langhammer et al.	−0.263 ± 12.413	0.513	1.400	29 (5.6)	−1.114 ± 13.847	0.367	1.550	53 (6.7)
Kuster et al.	4.871 ± 12.457	0.560	1.282	9 (1.7)	4.444 ± 13.848	0.398	1.431	31 (3.9)
NHANES	3.260 ± 12.584	0.537	1.336	15 (2.9)	1.710 ± 13.924	0.376	1.513	32 (4.1)
ECCS	8.320 ± 12.548	0.624	1.150	3 (0.6)	9.541 ± 14.188	0.463	1.231	14 (1.8)
FVC								
Present study	0.072 ± 11.743	0.590	1.419	25 (4.8)	−0.853 ± 12.813	0.418	1.562	41 (5.2)
Brändli et al.	−5.614 ± 11.911	0.645	1.299	49 (9.5)	−6.496 ± 13.156	0.466	1.403	52 (6.6)
Falaschetti et al.	−0.985 ± 11.878	0.596	1.406	12 (2.3)	0.157 ± 12.781	0.418	1.564	30 (3.8)
Langhammer et al.	−2.202 ± 11.926	0.609	1.375	34 (6.6)	−3.515 ± 12.800	0.427	1.530	59 (7.5)
Kuster et al.	2.133 ± 11.902	0.614	1.364	10 (1.9)	1.069 ± 12.985	0.430	1.521	25 (3.2)
NHANES	−2.398 ± 11.776	0.597	1.402	34 (6.6)	−3.863 ± 13.173	0.439	1.488	59 (7.5)
ECCS	6.071 ± 11.765	0.675	1.240	8 (1.6)	10.639 ± 12.977	0.560	1.167	10 (1.3)

SD = standard deviation; LLN = Lower limit of normal range.

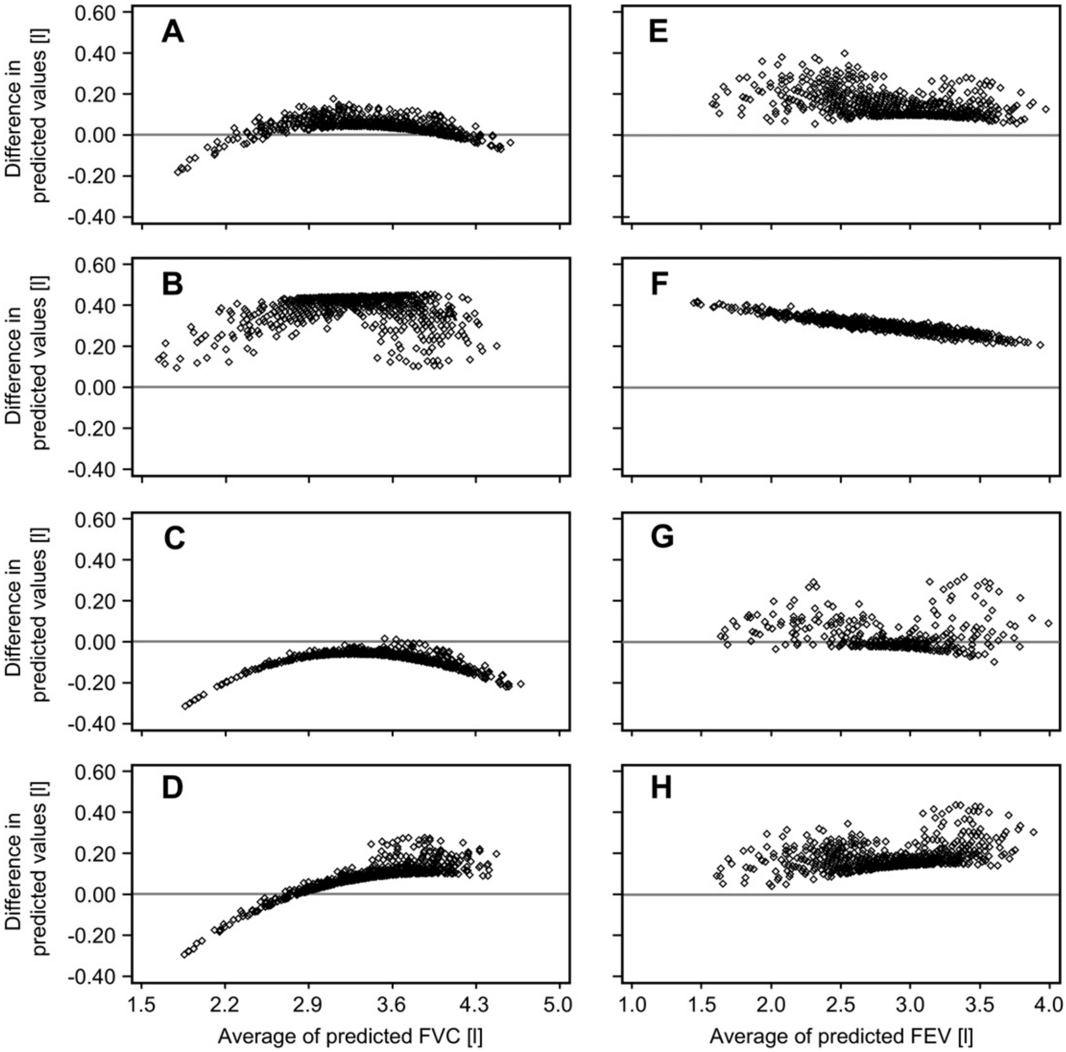

Figure 2 Differences between mean forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) predicted by the present study compared to Falaschetti et al.[24] (A, E), ECCS[6] (B, F), Langhammer et al.[27] (C, G), and Kuster et al.[26] (D, H) in women.

FVC, dummy calculations revealed that the lower values by ECCS[6] in men and the higher values by Langhammer et al.[27] in women were more striking in older age (Fig. 4).

Discussion

The current study provides reference equations for predicting lung function values of three population-representative studies of volunteers using the platform of population-based German studies — SHIP-1, KORA-S3 and ECRHS-I Erfurt. By excluding subjects with known cardiopulmonary disorders, certain cardiovascular risk factors, such as current and former smoking, or the use of specific pulmonary medication, and applying the ATS test performance criteria during data collection[10] an apparently disease-free population was created and reproducible values were obtained in the present analyses.

The present study, as others before,[5,24–27] confirms that the ECCS[6] prediction equations, which are still the most commonly used in Europe, significantly underestimate FEV_1 and FVC. As FEV_1 in percent of predicted still most commonly reflects the severity of airflow limitation, the choice of reference values may therefore be of clinical importance.

Whereas the results of the three studies showed remarkable equation conformity if analysed separately, striking discrepancies were observed not only in comparison to historic but also to recent European prediction equations. These can, to some extent, be explained by methodological, technical and personnel (e.g. equipment, observers) factors influencing spirometric measurements.[9,28] The contribution of a cohort effect cannot be completely ruled out.[29] In case of changes in individual, behavioural and environmental factors over decades, cross-sectional lung function will increase by up to 5 ml/year for FEV_1 and FVC.[30] Further, the emphasis on quality control in the current study might be an explanation for the higher values in comparison to previous studies. However, regarding standardised preparing and measuring procedures according to the ERS and ATS guidelines good conformity should be evident at least among recent European studies, where ethnical differences do not

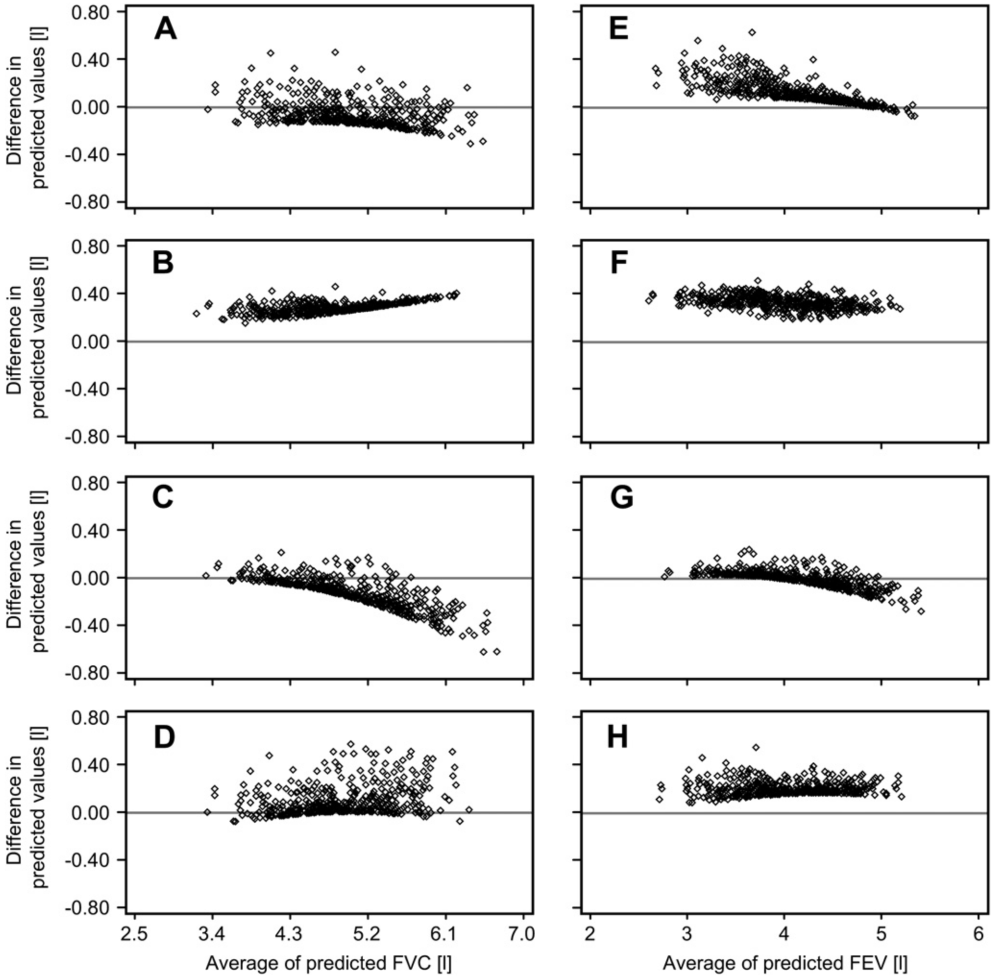

Figure 3 Differences between mean forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) predicted by the present study compared to Falaschetti et al.[24] (A, E), ECCS[6] (B, F), Langhammer et al.[27] (C, G), and Kuster et al.[26] (D, H) in men.

seem to play a major role.[8] In both women and men, equations from Brändli et al.[5] and Langhammer et al.[27] showed the best fit to the present FEV_1 data, whereas equations of Falaschetti et al.[24] and Kuster et al.[26] underestimated FEV_1.

The definition of cardiorespiratory health is quite difficult to agree upon. The ATS spirometry interpretation workshop only states that subjects should be "never-smokers, free of respiratory symptoms and disease".[9] In accordance to these guidelines, all individuals with known pulmonary dysfunction or disease, specific medication as well as former and current smokers were excluded. The exclusion of former and current smokers is justified by epidemiological and clinical experience that has shown a decline of lung function in smokers.[12,31]

A recent study on prediction models of lung function, based on the same three German populations has shown, that besides age and height, body weight, and the presence of obesity were associated with changes in lung function.[35] However, as these analyses indicated, simple models with gender, age and height explain a substantial part of lung function variance whereas further determinants add less than 5% to the total explained r-squared, at least for FEV_1 and FVC, only age and height were included into the presented prediction equations.

Differences between the studies on spirometric normative values lie, above all, in the selection of participants. The ECCS reference equations were obtained by summarising published regression equations from a survey published between the 1950s an 1980s, including different populations and using different spirometers and techniques.[6] The population-based design of recent European studies on lung function reference values[5,24–27] makes the data reasonably comparable to the current investigations. The differences between the prediction equations from the ECCS[6] and later studies, including the present, may be the result of an increase in lung function,[30] different exclusion criteria for the reference sample and the use of quality controls, such as feedback on acceptability and reproducibility[5] in recent investigations. It might even be possible that an increased awareness of respiratory symptoms among the population results in the selection of a healthier population in recent reference samples. A selection bias towards a healthier population in the elderly group in recent European studies might additionally be responsible for the differences found in comparison to historic data.

The associations between FEV_1, FVC and age found in this population are similar to results from previous cross-sectional studies.[24,25,32,33] However, as for most of the

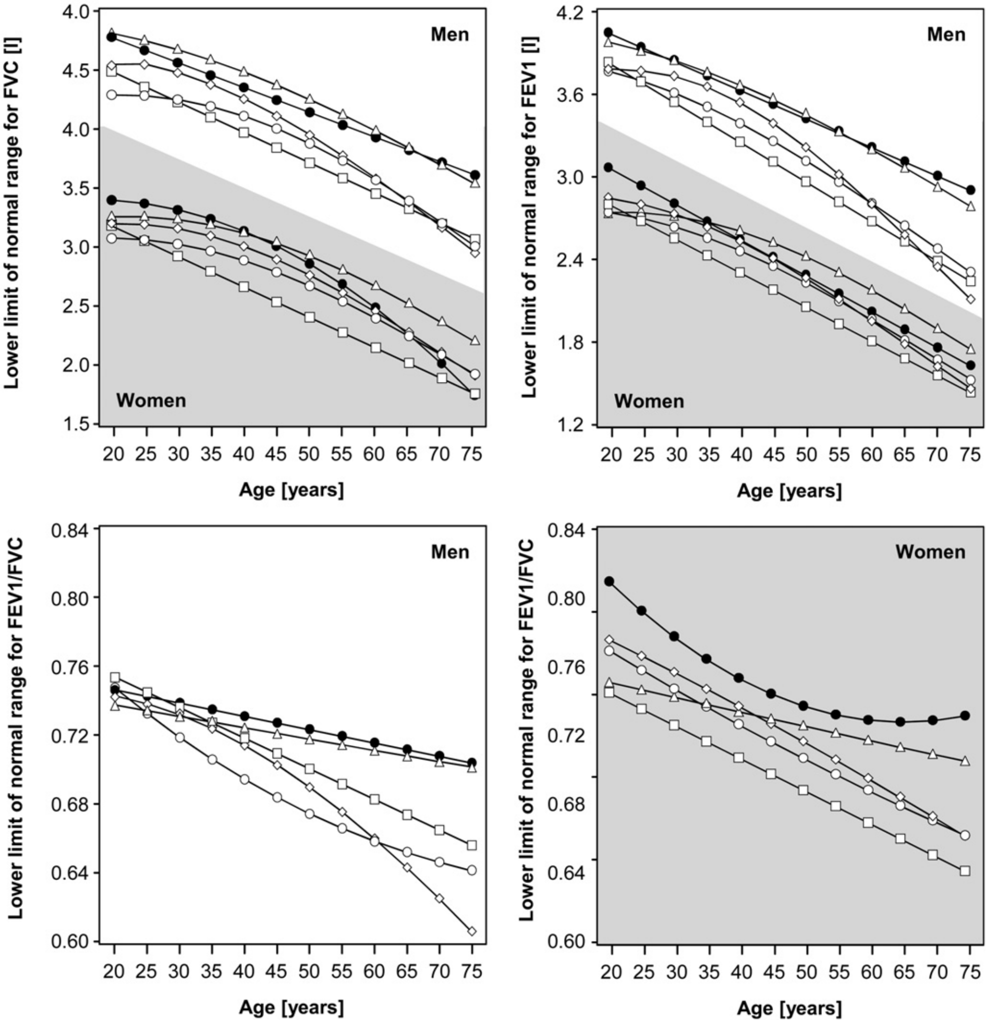

Figure 4 Lower limits of normal range for forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC) and FEV_1/FVC ratio predicted by different studies in men (fixed height at 180 cm) and women (grey shaded: fixed height at 165 cm): ● present study, ◆ Falaschetti et al.,[24] □ ECCS,[6] △ Langhammer et al.,[27] and ○ Kuster et al.[26]

compared European studies, the levels were higher across all ages in the present analyses.

The major strengths of the preset study lie in the use of data from large population-based samples of adults, in excluding subjects with relevant influencing diseases and in the application of almost identical methods for lung function testing across the different study regions.

However, the present study has some limitations as data show a selection bias towards including younger and healthier individuals due to voluntariness. The ranges of response patterns indicate that individual responses vary widely. This has to be taken into account when analysing spirometry data. A further limitation may lie in slightly different software versions used among the three studies. However, the pneumotachographs and the calibration procedures were identical.

Moreover, no chest radiographical examinations were performed, which may result in the inclusion of patients with unknown asymptomatic lung disease. Further, cohort effects because of examination time diversities as well as differences in participant selection are not negligible. It remains unclear how environmental characteristics did influence our lung function results. There might be an increased exposure to environmental and occupational pollution, including ozone, nitrogen dioxide, sulfur dioxide, dust, chemicals and gases, all of which are known to have adverse effects on lung function,[34] especially in those participants from urban areas. However, recent analyses on prediction models of lung function have indicated, that gender, age and height were the major determinants of lung function in the three presented German populations and their effect was similar across the study areas.[35]

Additionally, a bias due to a small number of included individuals above the age of 70 years and available only from SHIP as well as only few participants of KORA an ECRHS above the age of 60 years limits the applicability of the prediction equations in older subjects. Further studies in these age groups are urgently needed.

Conclusion

In summary, this study details lung function responses in healthy subjects. The present results demonstrate that especially sex, age, and behavioural characteristics should be considered in the assessment of normalcy. We have presented the results of this study in several ways, partly to allow the investigator to compare studies in other laboratories with those of the present study and to permit a flexible approach to the interpretation of lung function.

Our data indicate that the use of the ECCS prediction values may provoke lower spirometric values in recent populations. Therefore, healthcare providers are encouraged to reconsider their choice of prediction equations of spirometry. Reflecting on the present analyses, the establishment of nationwide prediction equations seems advisable. However, the results underscore that spirometric prediction equations should be derived from a population most similar to that for which the equations are to be used and based on measurements obtained by the same instruments and testing procedures as well as for the specific age range.

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Conflict of interest statement

No other competing financial or non-financial interests have to be stated. All contributers were independent from the sponsors.

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