Longitudinal effects of change in body mass on measurements of ventilatory capacity

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Abstract

Background – In several longitudinal studies changes in body mass and in forced expiratory volume in one second (FEV₁) have been found to be negatively correlated. This paper tests the hypothesis that failure to allow for the association can lead to error in the interpretation of longitudinal measurements of ventilatory capacity.

Methods – Male shipyard workers (n = 1005) were assessed on two occasions with an average interval between measurements of 6.9 years. A respiratory symptoms questionnaire, detailed anthropometric measurements, and dynamic spirometric tests were undertaken. Multiple regression analysis was used to identify variables which contributed to the changes in lung function.

Results – After allowing for age and growth in stature, a change in body mass of 1 kg was, on average, associated with a mean (SE) converse change in FEV₁ of 17.6 (2.0) ml, and in forced vital capacity (FVC) of 21.1 (2.5) ml. Neglect of changes in body mass (which in this context reflected changes in body fat) led to underestimation of the longitudinal decline in FEV₁ with age and failure to detect significant improvements in FEV₁, both in smokers following discontinuation of smoking and in shipyard welders and caulker/burners as a consequence of leaving their employment. The estimated peak ages and associated peak levels of the indices were found to differ, depending on whether or not they were expressed at constant body mass.

Conclusions – Neglect of changes in body mass can lead to erroneous conclusions being drawn from longitudinal measurements of FEV₁.

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Understanding the factors that influence longitudinal change in ventilatory capacity is important for the interpretation of many clinical, epidemiological, and occupational studies. Hence, the potential confounding factors that influence the annual change in ventilatory capacity need to be identified. One such factor which has been relatively overlooked is change in body mass which, in three different studies, for a man aged 40 years, has been found to be associated with reductions in forced expiratory

volume in one second (FEV₁) per kg gain in mass of, on average, 21.4 ml/kg, 13.9 ml/kg, and 23 ml/kg.¹⁻³ Since the magnitude of this change is of the same order as the annual change in FEV₁, this could be an important confounding influence because a change in exposure to tobacco smoke or to an occupational pollutant can be accompanied by a change in body mass. Similarly, since body mass usually increases from youth to middle age and then diminishes,⁴ some of the age-related decline in lung function could be due to the associated changes in body mass.^{5,6} This paper explores these interrelationships using data obtained from longitudinal studies of shipyard workers, and attempts to answer the question "Can neglect of changes in body mass, standardised for stature, materially affect the interpretation of longitudinal measurements of FEV₁ and FVC?"

Methods

SUBJECTS

The men were current or ex-employees of a shipyard on the river Wear (yard 1) and a group of shipyards on the river Tyne (referred to collectively as yard 2). At yard 1 the men were recruited in 1979 as a stratified sample of the workforce, including all present and past welders and caulker/burners aged 45-70 years, and a sample of all other tradesmen, most of whom were electricians. Six hundred and eighty six men were identified and 607 attended the initial assessment; their mean age was 46.0 years.⁷ Subsequently 53 men died, 66 were lost to follow up, and 488 were reassessed.⁸ At yard 2, men in two age groups were seen. The younger cohort (initial ages 17-30 years, mean 23.1 years) was recruited between August 1980 and September 1984 by which time 222 welders and 194 caulker/burners had been assessed; they comprised, respectively, 95% and 85% of the defined populations. Electricians identified from the works list were chosen as the control group, but volunteers from other trades were also accepted (n = 239). Three welders and four caulker/burners were subsequently excluded because the results were of poor technical quality or because of incomplete data or unrelated medical conditions. A clinical history of asthma led to the exclusion of a further 24 men (six welders, six caulker/burners, and 12 other tradesmen) leaving 624 men for inclusion in the study. The older cohort comprised 239 men who were apparently healthy and gave no history of asthma (mean age 41.7 years, range 23-47 years); they were recruited for assessment of the physiological response to exercise.⁹ Follow up of both groups

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from yard 2 ($n = 863$) was undertaken between 1987 and 1991, during which time 548 men were reassessed.¹⁰ Lapses to follow up occurred in seven men who had died, 285 who had left the area and could not be retrieved, and 23 who refused.

In all, 1470 men were included in the study, of whom 60 died before reassessment. Complete information was available for 1005 men (71%), of whom 73% had discontinued work in the shipyard during the average 6.9 years of follow up. The study was approved by relevant ethical committees in the Northern Region.

MEASUREMENTS

At each attendance the MRC questionnaire on respiratory symptoms (1976), with additional questions about employment and habitual leisure time activity, was completed.¹¹ Anthropometric measurements included stature, body mass, fat free mass, and percentage fat; these quantities were measured using a Harpenden stadiometer and skin calipers (Holtain Ltd, Crosswell, Pembs, UK) and beam balance (Avery GEC Ltd, Smethwick, West Midlands, UK). The equipment was calibrated and used in the manner recommended for the International Biological Programme.¹² The skinfolds were taken over the biceps and triceps muscles midway between the olecranon and acromion processes, below the angle of the scapula and just above and medial to the anterior superior iliac spine; details of the measurements are given elsewhere.⁵ The fat free mass and percentage fat were calculated from the body mass and the four skinfold thicknesses by the method of Durnin and Womersley.¹³

Dynamic spirometric tests were performed in quintuplicate while seated using a dry bellows digital spirometer (McDermott, Garw Electronic Instruments Ltd, Llantrisant, Glamorgan, UK); the volume/time information was encoded in real time on cassette tape as the number of 10 ml increments of volume expired every 10 ms.¹⁴ After each blow the flow-volume curve was plotted and the FEV₁ and forced vital capacity (FVC) were calculated by the microprocessor on the spirometer and recorded. The highest of the first three technically satisfactory blows was accepted for analysis. The selection criteria were that the FVC was within 5% of the maximum, the flow-volume curves were of similar overall shape, and that the peak expiratory flow was within 10% of the maximal observed value.⁶

For the microprocessor calculation of FEV₁ the expiration was considered to have started when 0.1 litres had been expired. Subsequently, the tape records were reprocessed using a portable computer and the start of forced expiration was redefined by back extrapolation to zero time of the steepest part of the volume-time curve.

ANALYSIS OF DATA

Multiple regression analyses were performed using the statistical package for the Social Sciences of the University of Michigan (SPSS, release 4.0). Body mass (BM) and fat free mass

(FFM) were expressed as body mass index ($BMI = BM \times St^{-2}$) and fat free mass index ($FFMI = FFM \times St^{-2}$) because, in this form, they were independent of stature (St). Multiplicative interaction terms were included if significant in the presence of their constituent variables. Shipyard trade was a categorical variable where 1 identified a man as having been a welder or caulker/burner (WCB), and 0 an electrician or other tradesman. The former trades were treated together because, although the men's occupational exposures differed, they had similar prevalences of respiratory symptoms and similar changes in lung function.^{7,8,10} "Shipyard" (SY) was used to identify men who either continued to work in one of the original shipyards or had left but had practised their trade in another shipyard for at least 85% of the available time; hence WCB·SY identified welders and caulker/burners who continued in their trade throughout the period of follow up.

Smokers (Sm) were defined as current smokers plus those who had discontinued smoking within the preceding six months, non-smokers (Non-sm) as those who had never smoked as much as one cigarette per day for as long as one year, and the remainder were ex-smokers (Ex-sm). Changes over the period of follow up were expressed as absolute change (e.g. ΔBMI), annual rate of change (e.g. ΔBMI), and percentage change.

Analysis of changes in body mass was based on all subjects, but that of FEV₁ was confined to smokers and non-smokers since a decision to discontinue smoking might have been influenced by other related variables including deterioration in lung function or loss of income following leaving the shipyard. Cross-sectional analysis with respect to age was limited to men aged 25 years and older because before this age the men were still growing,⁵ whilst the effects of discontinuing smoking were analysed for men who were smokers at the initial assessment.

In the multiple regression analyses terms were admitted in a stepwise fashion in the order which reflected their contributions to the explained variance. A 5% level of probability was accepted as significant. Reference values were those previously found appropriate for UK populations.⁵ The peak age was that at which the annual change in lung function was zero, after making allowance for change in stature and other nuisance variables.¹⁵ The analysis was performed both for the data from yard 2 and for the combined data from the two yards. The two analyses gave effectively the same results.

To explore the effects on lung function of different degrees of change in body mass, independent of age and change in stature, subjects were subdivided by level of change in body mass index (ΔBMI) into 16 subgroups; the levels were chosen to give approximately equal numbers in each subgroup. The results were adjusted to age 40 years.

Results

DESCRIPTION OF SUBJECTS

At the initial assessment the mean (SD) age of the 1005 subjects was 36.5 (12.2) years, the

Figure 1 Evolution of body mass in a typical shipyard worker; nuisance variables were allowed for, as in Eqn 1 ($n=1005$). At any age the mean increase in body mass associated with discontinuing smoking was 3.13 kg.

body mass was 74.8 (11.1) kg, and the stature 1.73 (0.07) m. The mean (SD) annual changes in body mass (ΔBM) and body mass index (ΔBMI) were, respectively, 0.26 (0.794) kg/year and 0.081 (0.264) kg/m²/year. The mean (SD) increase in stature (Stdif) was 0.13 (0.54) cm, reflecting growth in men aged 25 years and less.

EVOLUTION OF BODY MASS WITH AGE

Over the period of follow up the body mass of the younger subjects increased whilst that of the older subjects decreased. Using the data for all subjects, change in body mass was related to age during follow up and other variables according to the following relationship (Eqn 1):

$$BM_{diff} \text{ (mean 1.83 kg)} = 6.83 - 0.119 \text{ Age} + 3.13 \text{ if Ex-sm} - 0.052 \text{ initial level} + 0.468 \text{ interval} + 0.647 \text{ Stdif} \text{ (} R^2 = 0.14; \text{RSD} = 5.04 \text{)}.$$

The evolution of body mass with age in a smoker or non-smoker of 1.76 m in height and initial body mass of 68 kg at the age of 18 is shown in fig 1. The evolution of body mass index was similar.

On average, 78% of the changes in body mass (ΔBM or ΔBMI) with age were due to changes in body fat ($\Delta \%fat$, calculated from skinfold thickness) which accounted for ap-

Figure 2 Grouped data showing the average relationship of change in percentage fat to extent of change in body mass index (BMI).

proximately 50% of the variance (fig 2). Of the individual skinfolds, the change in thickness below the subscapula contributed most (approximately two thirds), with the change in thickness over the triceps muscle accounting for most of the remainder.

CHANGE IN BODY MASS AND LUNG FUNCTION

Absolute changes in FEV₁ and FVC over the period of follow up ($FEV_{1,diff}$ and FVC_{diff}) were negatively correlated with absolute changes in body mass (BM_{diff} or BMI_{diff}), and the associations persisted after making allowance for age, any change in smoking habit, occupational exposure, initial level of lung function or, in the case of FEV₁, the interval between measurements. The interaction term Age· BMI_{diff} did not make a significant contribution. The effects on lung function of a 1 kg change in body mass – that is, the partial regression coefficient of change in lung function (for example, $FEV_{1,diff}$) on change in body mass (BM_{diff}) – after allowing for the nuisance variables are given in table 1.

The relationships were independent of the extent of the change in body mass, including whether it was positive or negative, except in the group of men who had lost the most weight (fig 3). Amongst this group the increase in

Figure 3 Grouped data for men with a mean age of at least 25 years, showing the average relationship of annual change in FEV₁ (ΔFEV_1) to extent of annual change in body mass index (ΔBMI). ΔFEV_1 was standardised to age 40 years. The regression line was fitted to all points except that for subjects who lost the most weight (ΔBMI less than $-0.3 \text{ kg/m}^2/\text{year}$). The aberrant point is indicated by an arrow.

Table 1 Change in lung function per kg change in body mass after allowance for nuisance variables in shipyard workers of initial age >25 years ($n=772$)

	Mean change	Mean (SE) change per kg	Variance explained (%)	
			By BMI_{diff}	Total
$FEV_{1,diff}$ (ml)	-220.2	-17.6 (2.0)	6.9	19.3
FVC_{diff} (ml)	-124.0	-21.1 (2.5)	5.7	17.3

FEV₁=forced expiratory volume in one second; FVC=forced ventilatory capacity; BM=body mass.

Table 2 Multiple regression equations describing changes in FEV₁ and FVC (Δ FEV₁ and Δ FVC) in shipyard workers (Smokers (Sm) and non-smokers (Non-sm), n = 885) showing how estimates of the effects of continuing to weld (WCB-SY) and of peak age are influenced by including changes in body mass index (Δ BMI) amongst the reference variables

	Δ FEV ₁ (-24.8 ml/year)		Δ FVC (-7.13 ml/year)	
	Δ BMI ignored	Δ BMI allowed for	Δ BMI ignored	Δ BMI allowed for
Constant terms	51.3 (13.4)	58.4 (12.9)	93.3 (16.3)	104.7 (16.0)
Coefficient terms				
Mean age (39.6 years)	-1.00 (0.16)	-1.30 (0.16)†	-1.51 (0.18)	-1.74 (0.18)
Δ BMI (mean 0.065 kg/m ² /year)	Omitted	-40.9 (5.07)	Omitted	-38.9 (6.31)
Age.Sm (mean 18.7 years)	-0.44 (0.063)	-0.46 (0.061)	-0.37 (0.078)	-0.38 (0.076)
WCB (mean 0.708)	-7.98 (2.92)	NS	-7.93 (3.60)	-7.38 (3.53)
WCB-SY (mean 0.181)	NS	-8.21 (3.31)	NS	NS
Initial levels (mean 3.78 and 4.94 l)	-6.15 (2.11)	-5.18 (2.04)	-5.96 (2.26)	-5.86 (2.21)
Stdif (mean 0.133 cm)	6.02 (2.52)	5.06 (2.44)	9.03 (3.11)	8.16 (3.04)
R ²	0.16	0.22	0.19	0.22
Residual standard deviation	38.4	37.2	47.4	46.4
Peak age at constant stature (years)				
Non-smoker, non-welder	28.0	29.9††	42.3	43.5††
Smoker, non-welder	19.8	23.2††	37.7	39.4††

† Decrease compared with previous coefficient, p<0.05.

†† At constant BMI.

WCB = welder or caulker/burner; SY = current shipyard worker; Stdif = change in stature.

Values in parentheses are standard errors.

Δ FEV₁ was apparently less than might have been expected from the other results. The aberrant group was not exceptional with respect to age which was negatively correlated with Δ BMI over the whole range of groups, to level of FEV₁ which was close to the reference value for all groups, or to the proportion of men with regular wheeze. The proportion with chronic cough and phlegm was somewhat above average, but the difference was not significant.

EFFECTS OF DISCONTINUING SMOKING

Of 522 men who were smokers at the first assessment, 120 discontinued smoking so were ex-smokers at follow up. For these men, after adjusting for mean age, initial level of body mass, and change in stature, discontinuing smoking was associated with a mean (SE) increase in body mass of 3.37 (0.54) kg. There were associated significant increases in the subscapular and triceps skinfold thicknesses, but not in the biceps or suprailiac measurements.

In the same group of subjects the change in FEV₁ (FEV₁diff) was related to the mean age and the interval between measurements, but terms for change in stature, initial FEV₁, shipyard trade, and continuing to work in the shipyard were not significant. The term for ex-smoking was significant only after allowance had been made for change in body mass; ex-smoking was then associated with a mean increase in FEV₁ of 62.9 (29.6) ml. Discontinuing smoking did not improve the FVC.

CONTRIBUTIONS OF CHANGES IN ANTHROPOMETRIC VARIABLES TO EVOLUTION OF LUNG FUNCTION

This aspect was investigated using as subjects all 885 men who did not change their smoking habits during the period of follow up. The changes in lung function were analysed with respect to age, absolute change in stature (Stdif), smoking, shipyard trade, and working in or having left the shipyard (SY). The contribution of Δ BMI was then assessed. The results for Δ FEV₁ and Δ FVC are summarised in table 2.

Variance explained by the regressions

In the absence of allowance for Δ BMI, the proportion of the variance in Δ FEV₁ which was explained by the regression (R^2) was 0.16 (16%). This was increased by 0.06 to 0.22 by the inclusion of Δ BMI as an additional reference variable. The corresponding increase for Δ FVC was 0.04. Substituting for Δ BMI the changes in the subdivisions of body mass index, fat free mass index, and percentage body fat did not further improve the variance explained by the regressions.

Peak age

In non-smokers who were not welders or caulker/burners, the peak ages at constant stature (Stdif=0) for FEV₁ and FVC unstandardised for Δ BMI were, respectively, 28.0 and 42.3 years. The peak ages were reduced by smoking. Irrespective of smoking habit, standardisation to constant BMI increased the peak ages (table 2); in addition, the peak levels of lung function were increased. The changes in FEV₁ are illustrated in fig 4.

Figure 4 Evolution of FEV₁ in a typical non-smoking non-welder with an FEV₁ at age 18 years of 4.0 litres with and without allowance for coexisting changes in body mass.

Effect of shipyard trade

In the absence of an allowance for change in body mass, the Δ FEV₁ was related to age, smoking, initial FEV₁, change in stature during follow up, and work as a welder or caulker/burner. Discontinuing work as a welder or caulker/burner apparently did not have a beneficial effect – that is, the term WCB-SY did not make a significant contribution. However, on discontinuing welding the body mass increased ($p=0.05$) and, when this was allowed for by inclusion of Δ BMI amongst the reference variables, an amelioration of the decline in FEV₁ became apparent.

Discussion

In this longitudinal study we have shown a significant effect of change in body mass on the level of FEV₁ and FVC. Body mass is the sum of its constituents, which include body muscle and fat. The muscle component can influence the maximal respiratory pressures and, hence, inspiratory capacity, indices of which inspiratory capacity forms a part, and peak expiratory flow.^{16,17} The fat component can influence the total lung capacity and its subdivisions, the work of breathing and, in some circumstances, the airway calibre.⁵ In cross-sectional studies an atypical body mass can reflect an excess or diminution in either fat or muscle, or both. The effects of these variables on lung function have opposite signs, hence they tend to cancel out. As a result, the overall contribution of body mass to cross-sectional descriptions of ventilatory capacity is relatively small. In longitudinal studies, whether or not changes in total muscle or fat affect the lung function depends critically on where the changes occur. Hypertrophy of muscles acting on the shoulder girdle can assist inspiration, whilst that of muscles acting on the lower limbs cannot. Similarly, fat which is deposited centrally in the thorax or abdomen could displace air from the lungs, whilst that on the buttocks and thighs cannot. Amongst the subjects included in this study, on average 78% of the increase in body mass represented accumulation of fat. The relevant sites were thoracic (subscapular) rather than lower abdominal (suprailiac), but no direct measurements were made of intrathoracic and upper abdominal compartments.

Men tend to deposit fat centrally, whilst in women the deposition is often peripheral.^{18,19} The effects on the lungs of an increase in body mass due to fat should therefore be greater in men than in women, and this has been observed to be the case.³ Causality could imply that the changes were reversible but only if, in any individual, the sites of deposition and removal were the same.

Reversibility was a feature of the previous study by one of the present authors.¹ In the present study the relationship between change in FEV₁ and change in body mass standardised for stature applied to most of those subjects in whom body mass decreased during follow up, as well as to those in whom the mass increased (fig 3). By contrast, a U-shaped relationship

between the level of body mass and FEV₁ was observed by Dockery and colleagues,²⁰ with subjects who were materially overweight or underweight having the lower values. However, these results did not relate to changes in body mass.

The present effect of body mass was independent of age. In this the result resembled that of Chen *et al* in a sample from a whole population,³ but differed from those of Bande and colleagues who studied air crew,² and of Borkan *et al* who investigated patients with ischaemic heart disease;²¹ the reason for the difference is unclear. The present levels of the changes in FEV₁ and FVC of 17.6 (2.0) ml/kg and 21.1 (2.5) ml/kg were similar both to the previous results¹ and to those of Chen.³ Thus, the existence of an effect is not in doubt. The present findings suggest that it is due to changes in body fat ($\Delta\%$ Fat); however, for this index the measurement error is large and, probably on this account, the use of $\Delta\%$ Fat did not contribute more to the variance in Δ FEV₁ and related indices than Δ BMI itself.

The average effect on FEV₁ of a 1 kg change in body mass (17.6 ml) is of similar magnitude to the average annual change in FEV₁ (15–20 ml/year depending on age and smoking habit). Hence, a factor which is associated with a change in body mass will affect the evolution of lung function independent of any direct action of that factor upon the lungs. Among working populations the process of ageing, giving up smoking, and ceasing to engage in physically demanding work could fall into this category. Among patients a similar effect might be expected if the disease process, or resulting treatment, led to a change in body mass. Loss of body mass is a feature of many chronic respiratory disorders, whilst an increase can occur as a result of antitubercular or steroid therapy, or lung transplantation. The changes in body mass associated with all these situations are likely to affect the lung function.

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