Lung function in mid-life compared with later life is a stronger predictor of arterial stiffness in men: The Caerphilly Prospective Study

Charlotte E Bolton,1* John R Cockcroft,2 Ramsey Sabit,1 Margaret Munnery,1 Carmel M McEniery,3 Ian B Wilkinson,3 Shah Ebrahim,4 John E Gallacher,7 Dennis J Shale1 and Yoav Ben-Shlomo6

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Background Increased arterial stiffness predicts future cardiovascular disease and in some cross-sectional studies it is related to worse lung function and obstructive pulmonary disease. We assessed the predictive value of lung function measured in mid-life as compared with later life on arterial stiffness in the Caerphilly Prospective Study (CaPS).

Methods Men aged 47–67 years had lung function measured between 1984 and 1988 and repeated between 2002 and 2004 (n = 827) as well as having carotid-femoral pulse wave velocity (PWV) measured.

Results Both forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) in mid-life and later life were inversely associated with PWV (P < 0.0001) but mid-life measures were stronger predictors. Only mid-life measures remained predictors after mutual adjustment (FEV1 mid-life β coeff. −0.65, 95% CI −1.04, −0.26, P < 0.0001; FVC mid-life β coeff. −0.52, 95% CI −0.82, −0.23, P < 0.0001). Adjustment for smoking status, early life, inflammatory and metabolic factors in sub-groups did not markedly change the associations.

Conclusions Mid-life lung function is a stronger risk factor than in later life for arterial stiffness in men. It is possible that developmental factors influence both lung function and arterial stiffness. Lung function assessment in mid-life may identify individuals at greater risk of their future cardiovascular disease.

Keywords Epidemiology, cardiovascular disease, lung function, arterial stiffness

Introduction Increasing airways obstruction and impaired lung function are related to the presence of cardiovascular disease and mortality.1–3 This relationship is independent of potential confounding factors such as smoking and is reinforced by an association between lung function and cardiovascular disease even in non-smokers.4 Meanwhile, in those with a smoking

1 Department of Respiratory Medicine, School of Medicine, Cardiff University, Cardiff, South Wales, UK.
2 Wales Heart Research Institute, School of Medicine, Cardiff University, Cardiff, South Wales, UK.
3 Department of Clinical Pharmacology, University of Cambridge, Addenbrooke’s Hospital, Cambridge, UK.
4 London School of Hygiene and Tropical Medicine, University of London, London, UK.
5 Department of Epidemiology, Statistics and Public Health, Centre for Health Sciences Research, Cardiff University, Cardiff, UK.
6 Department of Social Medicine, University of Bristol, Bristol, UK.
* Corresponding author. Department of Respiratory Medicine, School of Medicine, Cardiff University, Academic Centre, Llandough Hospital, Penlan Road, Cardiff CF64 2XX, South Wales, UK. E-mail: boltonce@cf.ac.uk
history, cardiovascular events and death are greatest in those with a greater decline in lung function.4,5

Underlying causes for the association between lung function and cardiovascular disease are unknown but could include both atherosclerosis and arterial stiffness (a measure of vascular compliance). Increased arterial stiffness is a predictor of cardiovascular disease in both healthy subjects and in a number of different populations, including the elderly and in disease states such as hypertension and renal disease.6–12 There are a number of methods to determine arterial stiffness, which include non-invasive aortic pulse wave velocity (PWV). This independently predicts cardiovascular risk.11,12 Cross-sectional analysis of arterial stiffness demonstrated an inverse association with lung function parameters in men13 and more recently, arterial stiffness in patients with chronic obstructive pulmonary disease (COPD) was greater compared with age- and gender-matched smoking exposed controls.14–16 In cross-sectional study of Sabit et al., aortic PWV was inversely related to spirometric parameters of lung function and was independent of smoking,14 whilst others report association to severity of emphysema.15 A positive association between circulating interleukin (IL-6), an inflammatory mediator and aortic PWV has also been reported.16 COPD confers a persisting elevated chronic systemic inflammatory state but it is unclear whether this is causally related to arterial stiffness or simply an epiphenomenon.17 A similar relationship of aortic PWV with circulating inflammatory mediators has also been described in other populations including those with chronic inflammation and also in healthy subjects.18–20 Alternatively, metabolic and early life factors could be implicated in the association of PWV and lung function seen in later life.21,22

It is therefore possible to hypothesize that arterial stiffness may be a consequence of poor lung function, possibly through inflammatory or metabolic pathways, or that both arterial stiffness and poor lung function are the long-term consequences of other factors acting in early life and across the life course. We have explored these hypotheses in the Caerphilly Prospective Study (CaPS), a population-based cohort study, which has repeat measures of lung function over a 20-year period and also aortic PWV arterial stiffness measured more recently. We assessed the predictive value of lung function measured in mid-life as compared with that in later life on arterial stiffness and whether this was independent of early life and/or socio-economic factors, inflammatory markers or metabolic factors.

Methods

Subjects

CaPS is a population-based male cohort study of all men aged between 45 and 59 years who resided in the small South Wales town of Caerphilly.23 The initial examination (phase 1) took place between 1979 and 1983. Of the 2818 eligible men, 2512 (89%) were recruited. An additional 447 patients were recruited at phase 2 so that some men did not have phase 1 data. Men were re-invited for further follow-up approximately every 5 years. The last follow-up (phase 5) occurred between 2002 and 2004.

Subjects gave written informed consent and the study had the approval of the local research ethics committee. At commencement, a detailed questionnaire was administered and review of their personal and medical history was collected. Items included their fathers’ and own occupational social class (grouped as an ordinal variable: I, II, IIINM; IIIM; IV, V in such a way that social class I is skilled professionals such as doctors and social class V is unskilled manual labourers), self-reported birth weight and their smoking habit. Smoking status was categorized according to never, ex, pipe smokers, current smoker 1–24 cigarettes per day, or current smoker 25 or more cigarettes per day.

Clinic measures

Height in bare feet was measured using a Holtain stadiometer and weight in light clothes using standardized scales. From this, body mass index (BMI, kg/m²) was calculated as a measure of obesity.

Spirometry

Spirometry was performed at phase 1, 2 and 5. At phases 1 and 2, spirometry was performed using the McDermott spirometer in the standing position. The forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC) and their ratio (FEV₁/FVC) were calculated. An acceptable result was only included if the two valid, best traces of the three performed had less than 100 ml variability in FEV₁ and FVC. At phase 5, spirometry was performed using the Vitalograph spirometer (Vitalograph, Bucks, UK) with the same strict criteria. Subjects were not given any bronchodilator therapy prior to testing.

Blood pressure (BP)

Peripheral BP was measured in duplicate using a Hawksley random zero sphygmomanometer at phases 1 and 2 and Omron 711 automatic at phase 5.

Aortic PWV

Aortic PWV was measured at phase 5 only. All tests were performed in duplicate in the supine position after 10 min rest according to standardized methodology.8,24 Men were asked to refrain from smoking and caffeinice drinks for at least 3 hours prior to the procedure.8 Aortic PWV was measured by sequentially recording ECG gated carotid and femoral artery waveforms. Wave transit time was calculated by the system software, using the R wave of a
simultaneously recorded ECG as a reference frame (Sphygmocor; AtCor Medical, Sydney, Australia). Aortic PWV was determined by dividing the distance between the two recording sites by the wave transit time.

**Venous blood samples**

At phase 2, subjects attended an early morning clinic not having eaten breakfast, and a blood sample was taken with minimal venous stasis. This was assayed for blood viscosity, white blood cell count (WBC), C-reactive protein (CRP), triglycerides, insulin and glucose. Insulin resistance [modified homeostatic model assessment (insulin resistance) (HOMA) score] was calculated as the product of fasting glucose and fasting insulin divided by 22.5. The higher the HOMA value, the greater the level of insulin resistance.25

**Statistics**

We decided to use the phase 2 cohort (2398 subjects) as our sample of men. This was because this cohort provided the largest sample size of men contributing data at both phases 2 and 5 as compared with phases 1 and 5. We calculated the strength of the association between lung function and aortic PWV by using linear regression. We z-scored all lung function data (this rescales the observed value by the difference between it and the mean which is then divided by the standard deviation, so that the mean value is now 0). This enables one to directly compare the regression coefficients which indicate the effect on PWV for a 1 SD increase in lung function compared with the average value. We log-transformed variables that were positively skewed (e.g. white cell count, triglycerides, HOMA, CRP). Age at phase 5 was modelled as a three level factor (63–69.9, 70–74.9, 75+ years). All the simple models were adjusted for current age, height, mean arterial pressure and heart rate at phase 5 as these are all strong predictors of PWV. We subsequently stratified and adjusted our results for smoking status to see if these results were independent of smoking status. A possible interaction between smoking and lung function was examined using the Wald test. We then specified, a priori, three specific models that could either confound or mediate any observed association: (a) early life and socioeconomic model—this assumes that both lung function and arterial stiffness may have common origins in prenatal development (birth weight is used as a proxy marker) and social circumstances acting across the life course as measured by childhood and adult socioeconomic status (Figure 1). These covariates are therefore potential confounders. (b) Inflammatory model—this assumes that an association between mid-life lung function and later stiffness may be mediated by low-grade chronic inflammation. To test this hypothesis we added CRP, blood viscosity and white cell count into our model. (c) Metabolic syndrome model—this assumes that an association between mid-life lung function and later stiffness may be mediated by metabolic factors such as insulin resistance. To test this we added BMI, HOMA, triglycerides, systolic BP in mid-life into our model. If inflammatory or metabolic pathways mediate the association between lung function and arterial stiffness, then adjustment should attenuate or abolish the association. We tested whether the addition of extra covariates in each model improved the goodness of fit by deriving the P-value from the Wald test. The number of subjects across these different models differed due to missingness so the subgroups of subjects that are being examined are different. We also repeated the simple model using a complete case analysis so that the number of observations remains constant when comparing the lung function coefficients with and without the additional variables.

**Results**

Of the 2398 members from phase 2, 906 men (37.8%) had died before we could undertake measurement of their PWV. One hundred and three men were known to have moved out of the area, hence were not invited leaving 1389 potential men. One hundred and twenty-four men could not be found from their last known address and 438 men either refused to take part or were unable to attend the clinic resulting in 827 phase 2 men of whom 790 had valid measures of PWV (62.5% of men contacted). Descriptive data are presented in Table 1. Acceptable spirometry was available for 729–770 subjects in mid-life who also had PWV measures and around 720 subjects in later life. Subjects who were lost to follow up were more likely to be older, of lower socioeconomic status, had worse measures of inflammation (WBC, CRP, viscosity) and
### Table 1
Summary statistics on exposures, confounders, intermediaries and outcomes for men including and lost to follow up

<table>
<thead>
<tr>
<th>Phase 2 characteristics</th>
<th>Men with PWV</th>
<th>Men without PWV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sample size</td>
<td>Mean or percent</td>
</tr>
<tr>
<td></td>
<td>Mean or percent</td>
<td>SD or interquartile range</td>
</tr>
<tr>
<td>Age (years)</td>
<td>790</td>
<td>56.1***</td>
</tr>
<tr>
<td>Father’s social class (%)</td>
<td>621</td>
<td>15.5***</td>
</tr>
<tr>
<td>I, II, IIIINM</td>
<td></td>
<td>65.4</td>
</tr>
<tr>
<td>IIIM</td>
<td></td>
<td>19.2</td>
</tr>
<tr>
<td>IV &amp; V</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current social class (%)</td>
<td>654</td>
<td>43.7***</td>
</tr>
<tr>
<td>I, II, IIIINM</td>
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<td>46.5</td>
</tr>
<tr>
<td>IIIM</td>
<td></td>
<td>9.8</td>
</tr>
<tr>
<td>Self-reported birth weight (kg)</td>
<td>377</td>
<td>3.61</td>
</tr>
<tr>
<td>Blood viscosity</td>
<td>757</td>
<td>1.65***</td>
</tr>
<tr>
<td>White blood cell count (10^9/l)^a</td>
<td>758</td>
<td>6.09***</td>
</tr>
<tr>
<td>C-reactive protein (mg/l)^a</td>
<td>533</td>
<td>1.32***</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
<td>785</td>
<td>26.4</td>
</tr>
<tr>
<td>HOMA score^a</td>
<td>362</td>
<td>1.01</td>
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<tr>
<td>Triglycerides^a (mmol/l)</td>
<td>770</td>
<td>1.65***</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>784</td>
<td>142.7***</td>
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<tr>
<td>Smoking status</td>
<td>825</td>
<td>24.5***</td>
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<tr>
<td>Never</td>
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<td>42.4</td>
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<tr>
<td>Ex-smoker</td>
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<tr>
<td>Pipe/cigar</td>
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<td>18.7</td>
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<tr>
<td>Smoker 1–24/day</td>
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<td>4.0</td>
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<tr>
<td>Smoking status</td>
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<td></td>
</tr>
<tr>
<td>FEV₁ (l)</td>
<td>729</td>
<td>3.08***</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>770</td>
<td>3.89***</td>
</tr>
<tr>
<td>FEV₁/FVC ratio</td>
<td>729</td>
<td>0.79***</td>
</tr>
<tr>
<td>FEV₁ change (ml/year)^b</td>
<td>665</td>
<td>−40.1</td>
</tr>
<tr>
<td>FVC change (ml/year)^b</td>
<td>706</td>
<td>−24.3</td>
</tr>
<tr>
<td>Ratio change (%/year)^b</td>
<td>665</td>
<td>−0.59</td>
</tr>
<tr>
<td>Phase 5 characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>790</td>
<td>73.8</td>
</tr>
<tr>
<td>FEV₁ (l)</td>
<td>721</td>
<td>2.36</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>720</td>
<td>3.44</td>
</tr>
<tr>
<td>FEV₁/FVC ratio</td>
<td>719</td>
<td>0.68</td>
</tr>
<tr>
<td>PWV (m/s)</td>
<td>790</td>
<td>11.5</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>771</td>
<td>102.2</td>
</tr>
<tr>
<td>Heart rate per minute</td>
<td>771</td>
<td>64.3</td>
</tr>
</tbody>
</table>

BMI: body mass index; FEV₁: forced expiratory volume in first second; FVC: forced vital capacity; HOMA: homeostatic model assessment (insulin resistance).

^aGeometric mean.

^bDerived by the difference in phase 5 and phase 2 divided by the follow-up time.

^*P*-value between 0.02 and 0.05; **P*-value between 0.002 and 0.01; ***P*-value ≤ 0.001.
greater levels of triglycerides and systolic BP (all \( P \)-values <0.01) at phase 2 than those who survived and re-attended our clinic ('healthy survivor effect'). The attendees also had better lung function at phase 2 and re-attended our clinic.

We compared the strength of the standardized (z-score) lung function tests in mid and later life (Table 2). Baseline lung function was a stronger predictor than the later measures (all \( P \)-values <0.001). Not surprisingly, lung function measures were strongly correlated across time (FEV1 0.84, FVC 0.75, ratio 0.54). When we entered both the mid-life and later life measures together into our multivariable models, the earlier spirometry remained a significant predictor whilst the later measure was markedly attenuated (FEV1 mid-life \( \beta \) coeff. \(-0.65\), 95% CI \(-1.04\) to \(-0.26\), \( P < 0.0001\), FEV1 later life \( \beta \) coeff. 0.00, 95% CI \(-0.35\) to \(-0.37\), \( P = 0.97\); FVC mid-life \( \beta \) coeff. \(-0.52\), 95% CI \(-0.82\) to \(-0.23\), \( P < 0.0001\), FVC later life \(-0.09\), 95% CI \(-0.39\) to \(-0.21\), \( P = 0.55\)).

We repeated these analyses adjusting for smoking status (Table 2). This hardly altered the results. In stratified analyses, the association of lung function with PWV was weaker in never smokers as compared with ex or current smokers but the interaction tests showed this was compatible with chance variation (all \( P \)-values >0.30).

Inclusion of birth weight and socioeconomic data marginally improved our model prediction (\( P = 0.06\), but did not alter the association between FEV1 and FVC with PWV. The differences between coefficients in Tables 2 and 3 reflect different subgroups of subjects due to missing data. Inclusion of our inflammatory markers enhanced our model fit for predicting PWV (\( P = 0.004\)), but again hardly altered the strength of association between lung function and PWV. Our insulin resistance model did not appear to improve the model (\( P = 0.15 \) and 0.12) and did not change the lung function results.

### Table 2 Associations between lung function and aortic PWV with and without adjustment for smoking status

<table>
<thead>
<tr>
<th>Variable</th>
<th>All subjects*</th>
<th>Adjusted for smokingb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( n )</td>
<td>( \beta ) coeff</td>
</tr>
<tr>
<td>Phase 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1</td>
<td>665</td>
<td>(-0.66)</td>
</tr>
<tr>
<td>FVC</td>
<td>706</td>
<td>(-0.60)</td>
</tr>
<tr>
<td>FEV1/FVC ratio</td>
<td>665</td>
<td>(-0.14)</td>
</tr>
<tr>
<td>Phase 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1</td>
<td>704</td>
<td>(-0.39)</td>
</tr>
<tr>
<td>FVC</td>
<td>703</td>
<td>(-0.42)</td>
</tr>
<tr>
<td>FEV1/FVC ratio</td>
<td>702</td>
<td>(-0.11)</td>
</tr>
</tbody>
</table>

FEV1: forced expiratory volume in first second; FVC: forced vital capacity.
*All linear regression models have adjusted for age group, height, mean arterial pressure and heart rate at phase 5.
*bAll linear regression models have adjusted for smoking, age group, height, mean arterial pressure and heart rate at phase 5.

**Discussion**

Recognition of the association between cardiovascular disease and impaired lung function has strengthened over the last few years. In this large prospective study of male subjects, we demonstrated an inverse relationship between arterial stiffness and lung function. Importantly, we demonstrated lung function parameters performed nearly two decades earlier were a stronger predictor of arterial stiffness than contemporaneous lung function. These associations were independent of smoking, early life factors, and inflammatory and metabolic mediators. To put our results in clinical context, a 1 SD decrease in FEV1 in mid-life was associated with stiffer arteries equivalent to being around 5 years older in age, based on the age associations described in the ACCT study.24
Similarly a 500ml reduction in FEV1 and FVC in mid-life was associated with an increase of PWV of 0.52 m/s and 0.42 m/s, respectively.

Loss of lung function, as evidenced by a decline in FEV1 and FVC occurs with age and in a number of common respiratory conditions. This decline is accelerated in patients who smoke, which may or may not lead to clinical disease.26,27 Causes for this age-related deterioration in the lung parameters include impaired alveolar anatomy with loss of lung elastic recoil and impaired gas transfer. Weaker respiratory muscles are also likely to have additional impact. These, together with systemic involvement such as an impaired immune response also increase the susceptibility of and potential for sustained parenchymal damage following respiratory insults such as lower respiratory infection. Our findings of an association of arterial stiffness with loss of both FEV1 and FVC but not with the FEV1/FVC ratio would reflect this and parallels the findings of the cross-sectional COPD study by Sabit et al. where PWV was related to the individual components, this time in an obstructed group of subjects (but was not related to their ratio).14 Similarly, age-related increases in arterial stiffness occur within the cardiovascular system due to loss of arterial elasticity and vascular remodelling, and this is a major cause of cardiovascular events in the elderly.24 In this study, we report that lung function predicted aortic PWV over and above age. A Japanese study by Taneda et al.28 failed to report a relationship between lung function and PWV. However, it is clear from the crude results that such an association existed before adjustment. In addition, the analysis was based on dichotomizing both exposure and outcome variables rather than treating them as continuous measures. Finally, this study included women and men though no sex-specific results are presented so it is unclear whether this may have affected the results.

There are several possible causes for the association. First, lung function and arterial stiffness may track each other throughout life or be influenced by a genetic susceptibility or inherited factors.29 Alternatively, one may exert an influence on the other or they are affected by an external third factor, such as inflammation, body habitus, environmental factors such as smoking or metabolic disruption. We failed to find any interaction, for example, between smoking status and lung function on PWV (P-value for interaction = 0.30); however, given the sample size, we may have been underpowered to find such an effect unless it was very large.

One plausible explanation for the findings may be a simultaneous loss of elasticity in both the connective tissue of the alveoli and arterial wall due to genetic or proteolytic process. This remains an important consideration yet beyond the remit of this study. Possible culprits include alterations in elastase or matrix metalloproteases (MMP), through genetic or environmental influences. Yasmin et al. reported the association of artery stiffness with MMP-9 polymorphisms in
a healthy population.\textsuperscript{30} MMP-9 is elevated in the airways compartment and increased circulating levels have been detected in patients with COPD.\textsuperscript{31–34} Genetic susceptibility remains an evolving area and could be implicated in the association of lung function decline and arterial stiffness.\textsuperscript{35}

Factors affecting early life may contribute to the development of both lung and cardiovascular complications. In this study, the participants’ social status, reported birth weight and fathers’ social status were included into regression models in an attempt to consider the early life factors and environmental exposure. A low birth weight has been inversely associated with individual outcomes of lung function,\textsuperscript{36} BP and arterial stiffness.\textsuperscript{37–39} Despite the inclusion of these parameters into the models, lung function maintained its independent effect on arterial stiffness. However, we only had limited information on early life. Our measure of birth weight was self-reported, however, the same variable has previously shown an inverse association with cardiovascular disease similar to studies with documented birth weights.\textsuperscript{40}

Additional developmental and nutritional factors such as growth during the post-natal and childhood period or the influence of childhood infections may be of more relevance.\textsuperscript{41,42} Alveolization occurs predominantly from the later stages of embryonic development and then in early life, particularly the first 2 years, whilst the majority of airway development has occurred throughout foetal life. Our observation that, conditional or mid-life lung function—there is no added predictive value of later life lung function, is consistent with a hypothesis that common developmental factors may be of greater importance than determinants of age-related deterioration.

Many respiratory conditions, such as COPD or asthma are associated with a persisting systemic inflammatory response.\textsuperscript{43–45} Such patients may have chronic or intermittent hypoxia (the latter may not be clinically overt, especially if at the cellular level) with increasing lung impairment. In addition, in a general population, lung function is inversely associated with such inflammatory mediators.\textsuperscript{46,47} Fogarty\textsuperscript{46} reported no faster rate of decline in lung function in the general population with elevated CRP levels over a 9-year period. There are reports of foetal and early life growth relationship to inflammatory mediators, which may have an influence on peak lung volumes.\textsuperscript{48}

Cardiovascular disease has also been associated with inflammation. Both CRP and IL-6 have been reported to have a predictive role for subsequent cardiovascular disease.\textsuperscript{17} Debate remains as to whether this is cause or effect. Using a Mendelian randomization approach, Timpson and colleagues showed that circulating CRP, but not functional CRP polymorphisms, were associated with the metabolic syndrome suggesting that the former is due to reverse causality and a surrogate measure of pathology.\textsuperscript{49} However, the association of systemic inflammation and arterial stiffness has been demonstrated in a number of disease states.\textsuperscript{50–52} In rheumatoid arthritis, a disease without the classical cardiovascular risk factors, arterial stiffness was directly and independently related to CRP. In addition, there was a reciprocal attenuation in aortic PWV with anti-tumour necrosis factor-\textalpha\ therapy in these patients.\textsuperscript{18} Patho-mechanisms underlying the inflammatory/arterial stiffness link may be through endothelial dysfunction and increased atherogenesis.

Another possible pathway that we examined was through metabolic factors. Obesity and hypercholesterolaemia are risk factors for cardiovascular disease.\textsuperscript{53,54} Hypercholesterolaemic patients have elevated arterial stiffness.\textsuperscript{55} Meanwhile, obesity has been implicated in lung function impairment and the development of asthma.\textsuperscript{56,57} There is increasing recognition of the association of insulin resistance with both impaired lung function, specifically FVC decline and COPD\textsuperscript{58,59} and is thought to be a factor for the increased cardiovascular risk. Our results however did not suggest this metabolic pathway was the potential causal pathway as the effects estimates were hardly altered after adjustment.

**Strengths and limitations**

This is the first population-based cohort study to examine the role of lung function measured around 20 years prior as a predictor of arterial stiffness. We have also attempted to examine a range of hypotheses that may explain the association. Because of the prospective nature of the study there are no issues relating to recall bias as found in case–control or cross-sectional studies.

Our population was limited to men so we cannot generalize our results to women. Our multivariable models attempted to adjust for either confounders or intermediaries. It is possible that our measures were poor proxies and so we cannot exclude the possibility of residual confounding. We had reduced power for the models we used to investigate specific hypotheses, however in each case we found evidence that the association between lung function and PWV was unlikely to be due to chance and there was remarkably little attenuation of effect estimates. We feel that the pattern of missingness is most likely to be: missing at random or completely at random. For example, an additional 447 men were recruited at phase 2 who were not in phase 1, and did not have data on variables such as birth weight that were only asked at phase 1. We are not aware that these men differed in any way to men who were recruited at phase 1. Finally, it is important to recall that our sample reflects the healthy survivors who were able to be re-screened. This is inevitable in any long-term follow-up study. We showed that the men who were lost to follow up had worse lung function and cardiovascular risk factors. It is likely that the
association between lung function and PWV in this group of men is either the same or stronger than in the survivors. This implies that our results are probably an underestimate of the true association.

Spirometry was conducted according to the same strict criteria in the standing position on both occasions. External validation measures and calibration were conducted and the standard deviation of the measurements is comparable to other epidemiological papers.

Whilst the Caerphilly cohort are generally considered to be comparable to other European male cohorts; particularly in respect to lung function, Caerphilly was a mining town and occupational exposure may have contributed to any lung function impairment.

In conclusion, mid-life lung function is a stronger risk factor than later-life lung function for arterial stiffness in men, even after taking traditional risk factors into account. This may be explained by developmental factors that influence both lung function and arterial stiffness. Currently, lung function assessment is not a component of cardiovascular risk stratification. Yet, given the greater predictive value of early lung function on arterial stiffness and the independent predictive value of aortic PWV on future cardiovascular disease, it may offer a useful role in identifying those at greatest risk for future morbidity and hence be used for targeting interventions.

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**Acknowledgement**
Caerphilly Prospective Study was established by the former MRC Epidemiology Unit (Cardiff).

**Conflict of interest:** None declared.

### KEY MESSAGES
- Arterial stiffness is inversely associated with lung function impairment in men.
- Lung function in mid-life compared to later life is a stronger predictor of arterial stiffness.
- Lung function assessment in mid life may identify individuals at greater risk of their future cardiovascular disease.

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