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Is adult height related to the risk of having Chronic Obstructive Pulmonary Disease (COPD)?

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What is already known on this subject?

Adult height is inversely related to the risk of developing a number of diseases and this association is presumed to reflect the impact of adverse living conditions in childhood. In historical studies the relationship between adult height and the risk of developing COPD has been particularly strong but what is not known is whether this effect still remains today now that living conditions have improved.

What this study adds?

In a cross-sectional study using computerized general practice records for more than a million adults we have demonstrated that adult height remains strongly associated to the risk of having COPD, and that this association was most marked in younger adults and decreased in strength with increasing age. Our findings suggest that socio-economic factors in early life remain important in the aetiology of COPD.

Abstract (words 250)

Background: A number of historical studies have suggested that early life deprivation increases the risk of developing COPD in adult life, but whether this is still true now that living conditions have improved is not known. The aim of this study is to quantify the current association between adult height (a maker of socioeconomic status in early life) and COPD, and to determine how this varies by age.

Methods: We obtained data on 1,204,110 people (aged over 35yrs old) from The Health Improvement Network – a general practice database. We used a cross-sectional analysis to quantify the odds of having doctor diagnosed COPD in relation to height using logistic regression.

Results: In our dataset we had information on adult height for 1,025,662 (85%) people and of these 2.7% had a diagnosis of COPD. The risk of having COPD decreased with each increase in quintile of height – odds ratio 0.90 (95% confidence interval 0.89 to 0.91). There was evidence of effect modification by age group such that this association was strongest in people aged 35 to 49 years (odds ratio 0.86, 95% confidence interval 0.82 to 0.89) and decreased progressively with age.

Conclusions: The risk of developing COPD is still strongly associated with adult height. This association is strongest in the youngest age category suggesting that early life experience will remain an important risk factor for COPD for some time to come and possibly that COPD related to early life deprivation is more severe and tends to present at a younger age.

Introduction (267 words)

Although cigarette smoking remains the most important risk factor for developing COPD there are other risk factors, particularly socioeconomic deprivation which may exert its effect both in adulthood and during early life.^{1-4;5} Adult height is influenced by socioeconomic status in childhood and so has been used by epidemiologists to determine whether socioeconomic deprivation early in life is a risk factor for adult disease.⁶⁻⁸ In previous studies of adult height and disease specific mortality the associations with respiratory disease have generally been amongst the strongest.^{6;8;9} For example in an analysis of the Renfrew and Paisley cohort the rate ratio per quintile of adult height for mortality from respiratory disease was 1.35 for males, whilst that for stroke was 1.30 and that for cardiovascular disease was 1.12.⁸ Similarly in an analysis of the Whitehall 1 dataset Leon et al found that for each 6 inches decrease in height the risk of dying from COPD increased 1.58 times - the equivalent figure for coronary heart disease was 1.27.⁶

As socioeconomic conditions have improved in the UK there is evidence that height is increasing and that the influence of a number of early life factors on height, such as social class, maternal education and crowding, are becoming less marked.⁷ This raises the possibility that the early life influences on the risk of developing COPD may be becoming less important.

In order to investigate this question we have used a computerised general practice database to quantify the current relationship between adult height and the risk of having COPD and have stratified our results by age group, sex and adult socioeconomic status.

Methods (600 words)

The Health Improvement Network (THIN) is a large computer database of anonymous medical records that have been collected and entered by primary care practitioners and staff as part of routine clinical care using the VISION software package (In Practice Systems) since 1987.¹⁰ The dataset includes information on participants demographic as well as their healthcare – including all diagnoses recorded by the general practitioner and also prescriptions issued. In addition general practitioners routinely code and enter data from other sectors of the health care system – particularly clinic letters and discharge summaries from secondary care. For this study the dataset used was part of a larger programme of research into COPD and this work included an assessment of the impact of the NICE guidelines.² For this reason the dataset was extracted to reflect the prevalence of COPD on 25/02/05, exactly one year after new NICE guidelines for COPD were published, and practices were excluded if they were not also providing data for THIN on 25/02/2003 - one year before the NICE guidelines. The study design for this study is therefore cross-sectional.

At the time our dataset was extracted there were about 2.3 million people alive and contributing data to THIN on 25/02/05. We excluded people under the age of 35 years because a diagnosis of COPD is discouraged in this age group.¹¹ We only included people in our analysis if they had a recorded height and for this reason our dataset was restricted to 1,025,662 participants (85% of the initial total of 1,204,110). People were defined as having COPD if they had a medical code for COPD recorded anywhere in their medical records prior to the 25/02/05. The list of medical codes we used for this were identical to those used for the Quality Outcomes Framework – which is in turn used to reimburse general practitioners for certain aspects of clinical care for people with COPD. We have previously shown that 62% of people with a clinical diagnosis of COPD in THIN have spirometry data in their records, and where present these data are strongly predictive of mortality suggesting that they are valid.²

We recorded age (in years) on 25/02/05 into the following categories: 35-49, 50-59, 60-69, 70-79, 80-89 and greater than or equal to 90 years. Townsend scores based on 2001 census output areas were used as the measure of current adult social class, and these were available in THIN as quintiles. The majority of people with missing Townsend scores were living in Scotland reflecting differences in collection of census data. Adult Height was measured to the nearest centimetre and if there were multiple measurements, the mean was taken. We then divided adult height into quintiles separately for men and women using the `xtile` command in Stata.

Initially we used linear regression to calculate the mean height difference between people with and without a diagnosis of COPD, adjusting for age group, sex and Townsend score. We then used logistic regression to calculate the odds ratios for having COPD with each increasing quintile of height, adjusting for sex, age group and Townsend score. We analysed quintile of height first as a categorical variable and then as a continuous variable. We used multiplicative interaction terms to look for evidence of effect modification by sex, age group and Townsend score and also calculated the stratum specific odds ratios for the association between COPD and increasing quintile of height. All data analysis was carried out in Stata version 10 and likelihood ratio tests were used for hypothesis tests.

The study protocol for the programme of research on COPD was reviewed and approved by Nottingham Ethics Committee 1.

Results (320 words)

Our study population consisted of 1,025,662 people, of whom 28,374 (2.77%) had a diagnosis of COPD recorded at some point in their records before 25/02/05 (Table 1). The total population had a slightly higher proportion of women than men, but a higher proportion of the people diagnosed with COPD were men (52.1%). Younger people were less likely to have been diagnosed with COPD than older people. The prevalence of COPD increased markedly with increasing social deprivation. The mean height of men in our total population was 175.8cm and that for women was 161.7cm. Overall mean height decreased with increasing age group and with increasing levels of socioeconomic disadvantage.

The results of our linear regression analysis showed that after adjusting for sex, age group and Townsend score the average height difference between people with and without COPD was 1.12cm. The size of this difference was similar when men (1.09cm) and women (1.10cm) were analysed separately. When we divided people into quintiles of height the approximate difference in height between quintile was 4cm for men and women (Table 2).

The results of our logistic regression showed that the risk of having COPD increased with being male, older age and socioeconomic disadvantage (Table 3). There was a strong dose related association between increasing height and a reduced risk of having COPD that persisted after adjusting for age group, sex and socioeconomic status. In our fully adjusted model people in the tallest quintile had a 39% reduction in the odds of having COPD compared to people in the shortest quintile. Our tests for interaction and stratified results showed that the association between height and the risk of having COPD was similar for males and females but was strongest in the youngest age groups and decreased in strength with increasing age group (Table 4). Although there was a strongly statistically significant interaction between Townsend score and height there was no clear trend across the strata.

Discussion (1377 words)

The results of our study show that men and women who are taller have a reduced risk of being diagnosed with COPD. This difference was confounded by age and adult socioeconomic status but even after allowing for the effects of these variables for every increase in quintile of height (approximately 4cm) there was a 10% reduction in the odds of having COPD. We found evidence of effect modification by age group such that the association between COPD and height was most marked in the youngest age group and decreased progressively with increasing age. Our findings add to the previous literature that a shorter adult height is a risk factor for having COPD and demonstrate that early life experience is still an important risk factor for COPD and will remain so for some time to come.

Strengths and weaknesses

The main strengths of our study are the large and contemporary nature of the dataset which allowed us to produce up to date results and to stratify our results by age and an adult marker of socioeconomic status. An additional benefit is the completeness of the data on height with a value available for more than 85% of people over the age of 35 years in THIN. The main potential weaknesses of our dataset that need consideration are the validity of the data on height and the validity of diagnoses of COPD. The average heights for men and women that we found in our study (175.8cm for men and 161.7cm for women) are remarkably similar to the figures reported from the 2005 Health Survey for England (175.3cm for men and 161.4cm for women – www.ic.nhs.uk) suggesting that overall our data are valid. It seems likely to us that information on height recorded in general practice records will come from a variety of sources and be collected in a variety of settings and this means that a degree of random error is inevitable. This means that if anything we will have underestimated the true association between COPD and decreased adult height. We were not able to validate the diagnoses of COPD recorded in THIN directly, but as we have discussed before in terms of prevalence of the condition and the age, sex, smoking habit and survival of people with the

diagnosis the data appear appropriate.² Furthermore since COPD is a diagnosis that general practitioners are very familiar with we believe that the specificity of this diagnosis will be high, in other words most of the people with a diagnosis of COPD will have that condition. It seems likely that the sensitivity of the COPD diagnoses will be less good and that there will be a significant number of people with COPD in whom the diagnosis has not been made or recorded. For example in a study using the Third National Health and Nutrition Examination Survey (NHANESIII) Coultas et al found that doctor diagnosed COPD had a prevalence of 3.1% in adults over the age of 45 years, but when using lung function criteria based on the lower limit of normal this prevalence increased to 12%.¹² In this study the people with undiagnosed COPD tended to have milder disease than those with a doctor diagnosis both in terms of lung function impairment and symptoms. The implication for our study is that the people we have defined as having COPD are likely to represent the more severe end of the disease spectrum, and that a number of people with milder undiagnosed COPD will be included with the non-COPD group. This in turns means that if adult height is a risk factor for having COPD but does not influence the severity of disease that we may have underestimated the true association between adult height and COPD. On the other had if adult height also predicts the severity of COPD we may have over-estimated the strength of its association with COPD.

Comparison to other studies and possible explanations for findings

Although the literature on adult height and COPD is much smaller than that for cardiovascular disease there have been a few previous studies. In general these studies have focused on the mortality follow-up of large cohorts. As mentioned in the introduction analyses of the Whitehall cohort and the Renfrew and Paisley cohort both found an inverse association between adult height and death from respiratory disease. In order to compare our figures directly with those from the Whitehall study we have estimated the odds ratio for having COPD for each decrease in height of 6 inches (15.24cm) and found this to be 1.43 (95% confidence interval 1.39 to 1.47) and this figure is similar to the Hazard ratio of 1.58 reported for the increased risk of dying from COPD for the same

decrease in height. Similar findings have also been reported from cohorts in Korea^{9,13} and Finland¹⁴. In general the associations between height and death from COPD and/or respiratory disease have been greater in magnitude than those seen for all cause mortality and cardiovascular disease. Our current study is that first study that we are aware of to demonstrate an association between adult height and risk of COPD in living people, and also the first of sufficient size to be able to stratify the data by age groups.

Our hypothesis is that factors related to socioeconomic disadvantage early in life lead to both decreased growth and an increased risk of COPD in later life but there are other possible explanations for our data. The first is reverse causation, i.e. that COPD leads to a decrease in height rather than the other way around. This alternative explanation was suggested by Leon et al⁶ with the development of kyphosis as a consequence of corticosteroid use being a possible mechanism. This seems unlikely to us for two reasons. Firstly the difference in height between people with and without COPD was greatest in the youngest age group and decreased progressively with age. If COPD causes “shrinkage” we would expect this association to be the other way around as in general older people have had COPD for longer. Secondly in the general practice population the use of oral corticosteroids is actually quite low as most people have mild disease.¹⁵

Another possible explanation for our findings is that people who are shorter have smaller lungs in the first place and so shorter people with COPD may be more likely to present than taller people with COPD, and may also tend to present at a younger age. This would be the case if respiratory symptoms were more closely related to absolute lung volumes rather than percent predicted values which take account of height, age and sex. The data available in this area are limited but the one study available suggests symptoms are actually more strongly related to percent predicted values than absolute values so again this alternative explanation seems unlikely to us.¹⁶

In our study the association between adult height and the risk of having COPD was most marked in the youngest age category and the reasons for this are not clear. If the relationship between height and risk of COPD simply reflected an impact of early life socioeconomic disadvantage we would have expected the difference in height to be greatest in the oldest age category because social conditions in the UK have improved progressively over the last fifty years. There are a number of potential explanations for our findings. The first is survival bias arising from the cross-sectional nature of our study design. If COPD associated with early life deprivation and reduced stature is particularly severe then these people may present and die at a younger age and so be under represented in the older categories in our cross-sectional study. The second explanation is that although the social factors such as housing have improved progressively in the UK over the last fifty years the ones most relevant to COPD have not. Further longitudinal analyses of the age categories in our dataset will be needed to determine which of these explanations is correct.^{7;17}

Clinical implications

Although there can be no doubt that social factors have improved in the UK over the last fifty years the results of our study suggest that early life socioeconomic disadvantage still has an important influence on the risk of developing COPD in the UK, particularly in younger adults.

Author Contributions

The original idea for the study came from RH. KW did all of the data management and analysis under the supervision of RH as part of her BMedSci degree at the University of Nottingham. KW led on the writing of the paper but RH was responsible for the final editing of the paper.

Table 1 – Characteristics of people in the study according to the presence or absence of COPD

	People without COPD		People with COPD	
	Number of People (%)	Mean Height /cm (SD)	Number of People (%)	Mean Height /cm (SD)
Total	997,288	168.3 (10.0)	28,374	166.2 (9.8)
Males	461,132 (46.2)	175.9 (7.2)	14,789 (52.1)	172.8 (7.1)
Females	536,156 (53.7)	161.8 (6.9)	13,585 (47.9)	159.0 (6.7)
Age group				
35 to 49.9	387,629 (38.9)	169.8 (9.9)	1,213 (4.3)	167.4 (10.0)
50 to 59.9	228,227 (22.9)	168.8 (9.8)	3,747 (13.2)	167.1 (9.9)
60 to 69.9	179,185 (18.0)	168.0 (9.6)	7,988 (28.2)	167.2 (9.5)
70 to 79.9	126,450 (12.7)	166.2 (9.6)	9,537 (33.6)	166.2 (9.6)
80 to 89.9	64,409 (6.5)	163.5 (9.5)	5,260 (18.5)	164.3 (9.6)
90 and over	11,388 (1.1)	160.0 (9.4)	629 (2.2)	161.4 (10.5)
Quintile of Townsend Score				
1	231,035 (23.2)	169.2 (9.8)	3,610 (12.7)	167.9 (9.9)
2	193,481 (19.4)	168.7 (9.8)	3,986 (14.0)	167.4 (9.6)
3	171,667 (17.2)	168.1 (9.9)	4,814 (17.0)	166.2 (9.7)
4	135,438 (13.6)	167.5 (10.0)	5,596 (19.7)	165.6 (9.7)
5 (most disadvantaged)	88,967 (8.9)	166.9 (10.1)	5,209 (18.4)	164.9 (9.6)
Missing	176,700 (17.7)	168.2 (10.1)	5,159 (18.2)	166.2 (9.9)

Table 2 – quintiles of height for men and women

Quintile of height (cm)	Females		Males	
	number	height (cm)	number	height (cm)
1	114,664	<156.0	105,787	<170.0
2	129,782	156.0 to 160.0	91,577	170.0 to 174.0
3	92,926	160.1 to 163.0	112,602	174.1 to 178.0
4	102,421	163.1 to 167.8	75,075	178.1 to 182.0
5	109,948	>167.8	90,880	>182.0

Table 3 Odds ratios for the association between COPD and height and other co-variables

	Univariate analysis		Multivariate analysis*	
	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
Female	1.00		1.00	
Male	1.27	1.24 to 1.30	1.38	1.35 to 1.42
Age				
35 to 49.9	1.00		1.00	
50 to 59.9	5.25	4.92 to 5.60	5.33	4.99 to 5.69
60 to 69.9	14.25	13.41 to 15.14	14.32	13.47 to 15.21
70 to 79.9	24.10	22.70 to 25.59	23.29	21.92 to 24.74
80 to 89.9	26.10	24.50 to 27.79	24.15	22.66 to 25.73
90 and over	17.65	16.00 to 19.47	16.09	14.57 to 17.77
Quintile of Townsend Score				
1	1.00		1.00	
2	1.32	1.26 to 1.38	1.25	1.19 to 1.31
3	1.79	1.72 to 1.87	1.76	1.68 to 1.84
4	2.64	2.53 to 2.76	2.57	2.46 to 2.68
5 (most disadvantaged)	3.75	3.59 to 3.91	3.68	3.52 to 3.85
Missing	1.87	1.79 to 1.95	1.90	1.82 to 1.99
Quintile of height				
1 (shortest)	1.00		1.00	
2	0.69	0.66 to 0.71	0.87	0.84 to 0.89
3	0.55	0.53 to 0.57	0.77	0.75 to 0.80
4	0.48	0.46 to 0.50	0.79	0.76 to 0.82
5	0.30	0.29 to 0.31	0.61	0.58 to 0.63
Odds ratio per quintile of height	0.76	0.75 to 0.76	0.90	0.89 to 0.91

**mutually adjusted for all variables in the table*

Table 4: Odds ratios for COPD per quintile of height stratified by other covariates

	Odds ratio*	95% confidence interval			Pinteraction
Female	0.89	0.88	to	0.91	
Male	0.90	0.89	to	0.91	0.06
Age					
35 to 49.9	0.86	0.82	to	0.89	
50 to 59.9	0.88	0.86	to	0.90	
60 to 69.9	0.89	0.88	to	0.91	
70 to 79.9	0.90	0.88	to	0.91	
80 to 89.9	0.94	0.92	to	0.96	
90 and over	0.95	0.88	to	1.02	<0.0001
Quintile of Townsend Score					
1	0.90	0.88	to	0.93	
2	0.91	0.88	to	0.93	
3	0.88	0.86	to	0.90	
4	0.89	0.87	to	0.91	
5 (most disadvantaged)	0.92	0.90	to	0.94	
Missing	0.89	0.87	to	0.91	<0.0001

*Mutually adjusted for the other variables in the table

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