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Fewer colds, less asthma? A hypothesis to explain the fall in childhood asthma in the UK

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ABSTRACT

UK asthma prevalence fell significantly between 1993 and 2000. In children aged <5 years hospital admissions for asthma fell by 52% and primary care presentations in children under 14 years by over 40%. From 1994 to 2000, primary care consultations for acute respiratory infections in all age groups fell by 36%, and for the common cold by 46%. Isolates for respiratory syncytial virus notified to the Health Protection Agency voluntary reporting scheme fell by 56% between 1993 and 2003. Falls in UK birth rate and improvements in living conditions were reported by the Office of National Statistics over this time. The authors hypothesise that the fall in asthma reflects a fall in respiratory infections, the most important proximal trigger for asthma exacerbations, and that this in turn may be related to a fall in household members to a number too low for effective virus transmission. Future research into the prevalence of asthma must consider the effect of changing respiratory virus burden on populations.

Asthma prevalence appears to have fallen in the UK over the last 10 years.¹ New cases,² asthma hospitalisations³ and acute asthma exacerbations in the community^{4 5} are all reported to be down. Between 1993 and 2000, hospital admission rates decreased by 52% in children less than 5 years of age, and by 45% in children aged 5–14.² The decline in new cases is most notable in preschool children, down by two thirds.⁶ Explanations considered elsewhere^{1 4 5 7} include changes in population atopic status, changes in aeroallergen exposure, atmospheric pollution, diet, increased inhaled corticosteroid (ICS) prescribing and diagnostic transfer.

However, the number of patients presenting to primary care with acute respiratory infections (ARIs) has also fallen,^{8 9} and a reduction in respiratory syncytial virus (RSV) isolates is reported.¹⁰ ARI is the commonest precipitant of both asthma and wheeze,¹¹ and respiratory viruses are present in up to 85% of asthma exacerbations in schoolchildren.¹² Rhinovirus and RSV infection in children are both important.^{13–15} Rhinovirus-induced wheeze in infancy is the strongest predictor of third-year wheeze.¹³ Thus, a reduced burden of respiratory virus infection may provide a plausible explanation for the observed reduction in preschool asthma. Infection depends on infectivity, which in turn reflects close living and overcrowding. Changes in living conditions could explain a change in respiratory virus infectivity and ARI prevalence.

HYPOTHESIS

The purpose of this study is to collate data to inform the hypothesis that a fall in respiratory

virus infections may be causally related to the fall in asthma prevalence over a similar time.

METHODS

UK prevalence data on childhood hospital admissions with acute asthma, and presentations to primary care with asthma between 1993 and 2000,¹⁶ were reviewed, along with the published results of two nationally representative general practice databases^{8 9} for presentations to primary care with respiratory infections, covering the period 1994–2000. For 1993–2003, primary source data for RSV, parainfluenza, and influenza A and B isolates notified to the Health Protection Agency (HPA), a voluntary reporting scheme involving the majority of microbiology laboratories in England and Wales, were reviewed.¹⁷ Office of National Statistics data on living conditions and family size were also reviewed.^{2 18} UK hospital episode statistics (www.hesonline.nhs.uk) data for all causes of acute wheeze were obtained for the period 1998–2006,¹⁹ and were extrapolated from published results for the period 1990–2001.³

Statistical analyses were carried out using the Statistical Package for Social Sciences (SPSS) version 13.0 to assess associations between variables using Pearson correlation statistics.

RESULTS

Hospital admissions and new asthma diagnoses

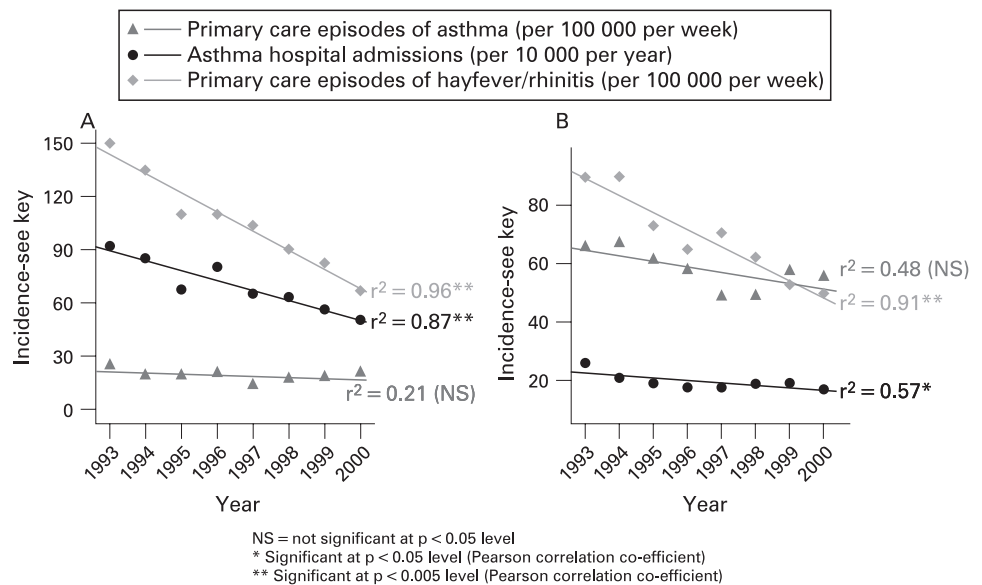
UK prevalence data on hospital admissions (per 10 000 per year) with acute asthma, and presentations to primary care (per 100 000 per week) with asthma between 1993 and 2000,¹⁶ for children under 5 and for schoolchildren are presented in figure 1. Admissions fell by 43% in those under 5 and by 27% in 5–14-year-olds, whilst primary care presentations fell by 43% and 46% respectively. Data for hayfever and allergic rhinitis are also presented as markers for atopy. These data show that while asthma has fallen significantly, hayfever and allergic rhinitis have not.

ARIs in primary care

Two primary care databases—the weekly returns service (WRS) of the Royal College of General Practitioners,⁸ and the general practice research database (GPRD)⁹ each covering approximately 600 000 patients—list a fall of 36% in ARIs across all ages presenting to primary care (consultations per 1000 patients per year) between the years 1994 and 2000 (fig 2A). ARI was classified by ICD-9 codes 460–466 by WRS,⁸ and by database-specific codes for respiratory infections in the GPRD.⁹ Subsection analysis of ARI⁹ shows a similar fall of

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Figure 1 Hospital admission rates and primary care episodes for asthma and hayfever/allergic rhinitis in children 1993–2000.¹⁶ (A) Children aged <5 years; (B) children aged 5–14 years.



46% in the number of consultations for the common cold (fig 2B).

RSV isolates

For 1993–2003, primary source data for RSV, parainfluenza, and influenza A and B isolates recorded in a voluntary reporting scheme involving the majority of microbiology laboratories in England and Wales were reviewed.¹⁷ Although isolates of RSV in 0–4-year-olds fell by 56% (fig 3), neither parainfluenza ($r^2 = 0.2$) nor influenza A ($r^2 = 0.02$) and B ($r^2 = 0.07$) isolates fell, although these were 20-fold fewer than for RSV.

In 5–14-year-olds, viral isolates totalled <100/annum.¹⁷ Hospital admissions (www.hesonline.nhs.uk)¹⁹ for acute bronchiolitis due to RSV in 0–14-year-olds fell significantly by about 25% between 1999 and 2006 (International Classification of Diseases (ICD) 10 code J21.0—fig 4). Data before this are not freely available. Overall, bronchiolitis admissions (J21), and acute bronchitis admissions (J20—data not shown) were unchanged.

Living conditions

Meanwhile, the UK birth rate fell by 11% between 1993 and 2003,² overcrowding (as defined by the bedroom standard, which compares the number of bedrooms available to a household against the number required) fell from 3% in 1991

to 2% in 2004,² and numbers living per household fell by 4% between 1991 (2.5 per household) and 2001 (2.4 per household).¹⁸ Furthermore, the number of non-decent homes (homes without thermal comfort and not in a reasonable state of repair) in the UK fell from 45% of homes in 1996 to 31% by 2003.¹⁸

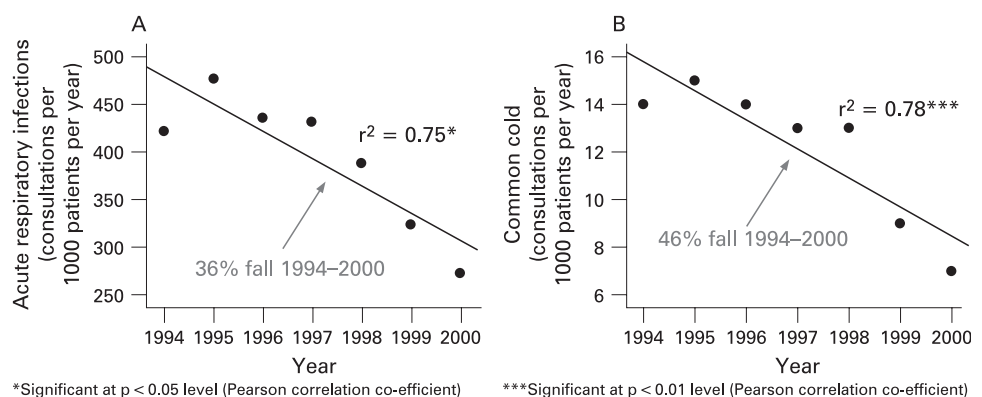
In summary, reported childhood asthma prevalence, acute respiratory infections reported in primary care across all age groups, total RSV isolates and reported RSV bronchiolitis have all fallen significantly over the last decade. Over a similar period, overcrowding and living conditions have improved.

DISCUSSION

We propose that the substantial fall in ARI presentations to primary care reflects a true fall in respiratory virus infections, and that this may in turn be causally related to the fall in asthma prevalence over a similar time.

The fall of 36% in reported ARI in primary care between 1994 and 2000,^{9–9} occurred at the same time as admissions to hospital and presentations to general practice with asthma fell in both school-age and preschool children by similar magnitudes. UK figures before this showed an increase in asthma admissions in 0–14-year-olds between 1981 and 1992.²⁰ The ARI data have not been stratified for age but it would be surprising if these falls did not reflect falls of ARI in the childhood population.

Figure 2 Acute respiratory infections and the common cold in primary care, 1994–2000 (all ages). Data source: extrapolated from published results of the GPRD.⁹ (A) Acute respiratory infections in primary care: consultations per 1000 patients per year; (B) the common cold in primary care: consultations per 1000 patients per year.



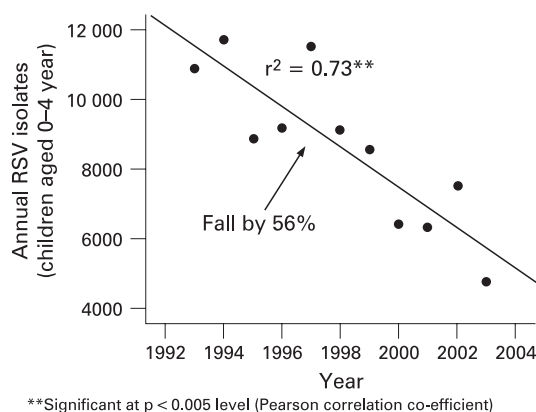


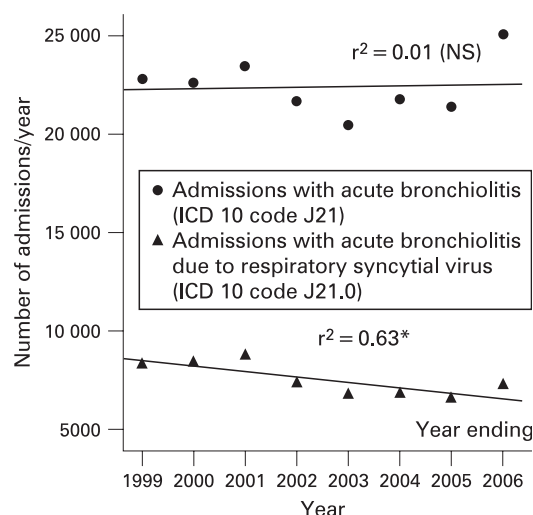
Figure 3 Annual RSV isolates in children aged 0–4 years (England and Wales), 1993–2003.¹⁷

From 1993–2003, RSV isolates in preschool children fell by 56%,¹⁷ and between 1999 and 2006, admissions for RSV bronchiolitis also fell, although the numbers of admission for unspecified bronchiolitis did not change.¹⁸ The total number of nasopharyngeal aspirates (NPAs) sent to the reference laboratory is unknown as only positive results are notified to the HPA's voluntary reporting scheme (M Cooke, HPA, personal communication). Although a reduction in the number of NPAs sent might explain this fall in RSV numbers, falls in influenza and parainfluenza isolates might also have been expected. This was not the case in this age group. It is unlikely that the total number of NPAs sent fell, as children's departments in hospitals, the most likely source for NPAs, are encouraged to screen for viruses to facilitate cohorting of patients.

For any future epidemiological studies examining the prevalence of respiratory virus infection, it is imperative that the total number of NPAs examined be recorded. The 46% reduction in presentations with "common colds" to primary care reported between 1994 and 2000⁹ suggests a fall in rhinovirus infections, the commonest cause of the common cold. In preschool children, rhinovirus is 20 times more likely to be associated with wheeze than RSV¹⁴ although the mechanism for rhinovirus-induced wheeze remains poorly understood.²¹ Thus, a reduction in respiratory virus infection appears a plausible explanation for falling asthma prevalence.

If ARIs have truly fallen, what could be the reason? A favourable hypothesis is that reductions in both overcrowding² and family size¹⁸ are related to a reduction in virus transmission. It is also true that improvements in living conditions in the 1970s and 1980s were at a time when asthma prevalence appeared to be increasing. However, evidence suggests that this was mediated by a change in population atopic status, possibly because of a reduction in childhood infections.²² It may be that residents per household have reached a critical number so that virus transmission is less successful. Our data are representative of trends in childhood asthma in the UK. Longitudinal data for asthma and ARIs are not available for countries where living conditions remain poor. It is possible that unknown factors, such as a change in immune status, could affect both viral transmission and asthma prevalence. Future prospective studies of viral infection and asthma would need to consider household conditions as well as other socioeconomic factors, such as urban or rural living, known to affect asthma prevalence.

Whilst preschool asthma exacerbations in general practice fell by 56% between 1993 and 2001, presentations with allergic rhinitis and hayfever were similar throughout,¹⁶ suggesting

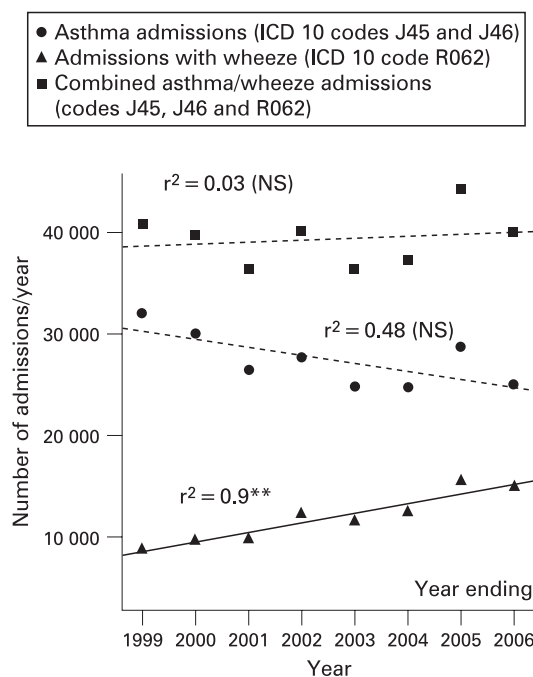


NS = not significant at $p < 0.05$ level

* Significant at $p < 0.05$ level (Pearson correlation co-efficient)

Figure 4 Bronchiolitis admissions in children aged 0–14 years between 1998/9 and 2005/6. (Source: <http://www.hesonline.nhs.uk>)¹⁹

atopy is unchanged. If the fall in presentations with the common cold is because children are less likely to be taken to primary care with a cold, then it would seem surprising if they continued to be taken with allergic rhinitis, a condition with similar symptoms. This observation suggests that the fall in the common cold is not artefactual. Furthermore, the WRS found no change in consultations for other minor illnesses such as skin infections,⁸ and there is no evidence that parents are not taking their wheezy preschool children to their family doctor.

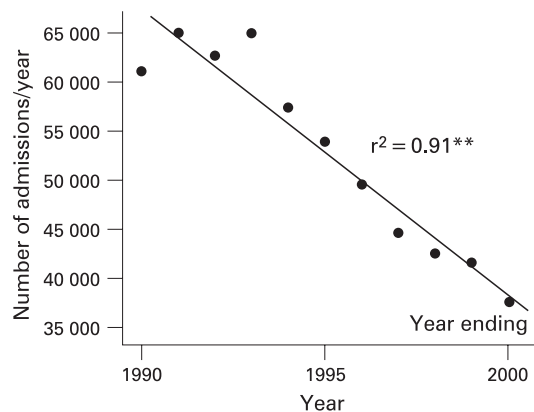


NS = not significant at $p < 0.05$ level

* Significant at $p < 0.0001$ level (Pearson correlation co-efficient)

Figure 5 Hospital admissions with asthma and non-asthmatic wheeze 1998–2006 in children aged 0–14 years. (Source: <http://www.hesonline.nhs.uk>)

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** Significant at $p < 0.0001$ level (Pearson correlation co-efficient)

Figure 6 Hospital admissions for asthma and wheeze in children aged 0–14 years (1990–2001). Data sources: extrapolated from MacFaul R, *Arch Dis Child* 2004.³

UK particulate matter atmospheric pollution (PM_{10}) fell on average by 4.4% per year between 1992 and 2003.²³ A 29% fall of PM_{10} between 1992 and 2001 in Switzerland was accompanied by a fall in respiratory symptoms, but no change in asthma prevalence,²⁴ and in the UK no link has been found between air quality and asthma.²⁵ Reduced dietary antioxidants were considered a potential explanation for previously observed asthma increases,^{26 27} although while asthma rates have fallen since the mid-1990s, diet has not been reported to have improved.^{28 29} The association between maternal smoking and preschool wheeze is well documented.³⁰ Smoking during pregnancy increased between 1995 and 2001,³¹ and a fall in passive smoking is unlikely as the proportion of adult smokers has remained unchanged for more than 10 years.³²

ICS prescribing in preschool asthmatics increased by over 40% from 1994 to 1998.³³ This could explain falling asthma episodes.³ However, in this age group, adherence with these drugs is about 50%,³⁴ evidence for their benefit is limited³⁵ and they do not prevent exacerbations.³⁵ Yet the greatest falls in asthma have been seen in the under-5s.

During the 1980s, the reasons for rising asthma prevalence were considered.³⁶ It was not until the beginning of the last decade, after the fall had begun, that a number of publications suggested that the reporting of wheeze was inaccurate, suggesting that other respiratory sounds were being mislabelled as wheeze.^{37 38} Have these observations resulted in fewer respiratory illnesses being labelled as asthma? It has been argued that diagnostic transfer explains the apparent fall in the diagnosis of preschool asthma.³⁹

This would not explain the reduction in hospital admissions with asthma, unless wheezing illnesses became less severe over the same period. The numbers of hospital admissions with non-asthmatic wheeze remained unchanged between 1990–2000.³ “The health of children and young people” report noted that falling asthma admission rates were not accompanied by an increase in admissions from other respiratory causes.¹⁶

However, more recent hospital episode data do suggest that diagnostic transfer may provide an explanation for falling asthma prevalence.¹⁹ All asthma admissions (ICD 10 code J45) for children aged 0–14 years from 1998/9 to 2005/6 are shown in fig 5 along with those admissions coded as wheeze, where no other diagnosis was suggested (Code R062). These figures

What this study adds

This paper proposes a causal link between respiratory virus infection rates and the prevalence of asthma symptoms.

Policy implications

Epidemiological investigation of childhood wheezing episodes should more carefully consider the prevalence of respiratory virus infections.

suggest that while asthma has fallen, the numbers of wheezing illnesses admitted to hospital remain unchanged.

Thus, recent trends in hospitalisation¹⁹ suggest that diagnostic transfer of asthma into ICD codes for non-asthmatic causes of wheeze may offer another explanation for the observed fall in asthma prevalence.

However, between 1990–2000,³ and 1994–8,¹⁶ there is no reported evidence for diagnostic transfer as an explanation for the reported fall in asthma prevalence.^{3 16}

Data on admissions with ICD-9 and ICD-10 (Asthma J45, Status Asthmaticus J46, Wheezing R062, Unspecified Bronchitis J40, and Chronic Bronchitis J42) codes for asthma and wheeze were considered for the period 1990–2001 (fig 6), extrapolating numbers from previously published work.³

It appears that combined wheeze and asthma admissions in children aged 0–14 years fell between 1990 and 2000 from rates above 60 000 per annum to a level of 40 000 per annum.

Falling admissions for all causes of wheeze and asthma from 1990–2001 occurred along with simultaneous witnessed falls in respiratory virus isolates (1993–2003) and primary care presentations with ARI (1994–2000), suggesting that diagnostic transfer could not explain the fall in asthma prevalence over this time period.

SUMMARY

There is strong evidence that infection with a respiratory virus is the most frequent proximal trigger for asthma.^{12 15 21 40} A fall in ARI prevalence would, therefore, be expected to be reflected in a fall in asthma prevalence. Living conditions have continued to improve in the UK in the second half of the last century. We propose that the numbers of people in households, in particular children, have reached a critical level for effective respiratory virus transmission. Future epidemiological investigation of wheezing illnesses in children should continue to evaluate the role of respiratory virus infections. This may help to confirm or refute the hypothesis that reduced respiratory virus burden is associated with a decrease in asthma prevalence.

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