extracorporeal systems must be considered as well as ventilator free days and length of ICU stay.

In conclusion, the combination of NIV and extracorporeal CO_2 elimination might be effective to prevent IMV and its potentially lethal side-effects in patients with AECOPD.

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Influence of social deprivation and air pollutants on serious asthma

To the Editors:

Asthma is an important disorder worldwide, as a major cause of hospital admissions, medical consultations, prescriptions and impaired quality of life. The precise causes of asthma, although largely unknown, are multifactorial and involve a complex interaction of genetic and environmental factors.

Although hospital admission rates are often increased for people in lower socioeconomic groups [1], little has been reported specifically for serious asthma (*i.e.* prolonged admissions and/or death within 30 days). Evidence about the effects of air pollutants on the occurrence of serious asthma is also unclear [2].

We aimed to establish the hospital admission rate and case fatality for serious asthma, and whether admissions are associated more strongly with social deprivation or air pollutants.

We used medical record linkage of inpatient data from the Patient Episode Database for Wales (PEDW) and mortality data from the National Health Service (NHS) Welsh Administrative Register. PEDW covers inpatient admissions to all NHS hospitals across 22 local health authorities in Wales, UK (population three million) and has been used as the basis of many previous published studies.

We included all emergency admissions from April 1, 1999 to March 31, 2007 where asthma (ICD-10 codes J45 and J46) was the principal diagnosis at discharge. Patients of all ages with admissions lasting $\geqslant$3 days, or who died (from any cause) within 30 days, were classified as ''serious'' cases. We included all first ''serious'' admissions during the study period, and subsequent serious admissions providing they occurred >30 days after the preceding serious admission.

We measured social deprivation and its seven domains using the Welsh Index of Multiple Deprivation 2005 [3]. Social deprivation scores were assigned to 1,896 lower super output areas (LSOAs) across Wales (average LSOA population 1,560) [3]. The LSOAs were ranked according to their social deprivation score and categorised into quintiles (I: least deprived; V: most deprived).

Data on the following eight air pollutants were provided by the AEA Energy and Environment Company (the official British air pollution monitoring agency) from 1999–2007: benzene, carbon monoxide, nitric oxide, nitrogen dioxide, ozone, particulate matter <10.0 $\mu m \cdot m^{-3}$ and <2.5 $\mu m \cdot m^{-3}$ in diameter and sulfur dioxide [4]. The air pollutants were based on annual means of hourly measurements. In 2007 (2005 for ozone), they were interpolated from 23 sites to geographical levels of 1 km^2 [4].

The main outcome measures were, first, hospitalised incidence of serious asthma per 100,000 population, standardised directly using the standard European population, and secondly, case fatality (all causes of death) at 30 days, standardised directly using the study population. Statistical methods include the Chi-square trend test, adjusted and unadjusted correlations between hospitalised incidence of serious asthma and, respectively, social deprivation and air pollutants. They were calculated at the LSOA level and derived through multiple linear regression using logged incidence rates. Correlations between serious asthma and social deprivation were adjusted for air pollutants, and *vice versa*. Although many air pollutants were quite stable over time [5], we also investigated trends by correlating monthly means of air pollutants over the 8-yr study period with corresponding monthly (logged) incidence of serious asthma to all hospitals in the local authority corresponding to each site. We also investigated correlations between the air pollutants and social deprivation at the LSOA level.

There were 12,740 admissions for serious asthma among 9,986 different patients (54.5 admissions per 100,000 population), mean$\pm$SD age 50.0$\pm$23.9 yrs. Females were older ($p<0.001$) than males (mean 52.4 *versus* 45.0 yrs). There were 183 deaths within 30 days of admission (case fatality 1.4%), mostly (72%) among people aged $\geqslant$65 yrs.

Hospitalised incidence of serious asthma was highest among infants (90.6 per 100,000) and older people aged 75–84 yrs (108) and $\geqslant$85 yrs (131). Incidence was higher ($p<0.001$) for females (72) than males (36). Age specific incidence was higher ($p<0.001$) among male infants than female infants, similar among male and female children, but significantly higher among females than males in all adult age groups.

Hospitalised incidence was 2.48-fold higher (95% CI 2.34–2.62) for the most deprived quintile V (77.0 per 100,000) compared with the least deprived quintile I (31.0). This increased risk was found across all age groups; <14 yrs (1.95 increased risk), 15–54 yrs (2.66) and $\geqslant$55 yrs (2.38). There was a significant ($p<0.001$) trend of increasing incidence across deprivation quintiles I to V.

Across LSOAs, hospitalised incidence was correlated significantly with social deprivation (0.45; $p<0.001$) and with all seven components of deprivation (all $p<0.001$; table 1). There were positive correlations with six components; ''income'' (0.45), ''employment'' (0.44), ''education'' (0.40), ''health'' (0.34), ''housing'' (0.15) and ''physical environment'' (0.14) and a negative correlation with geographical ''access to services'' (-0.29).

There were modest, significant positive correlations between hospitalised incidence and seven of the eight air pollutants ranging from 0.12 for sulfur dioxide to 0.18 for particulate matter <10.0 $\mu m \cdot m^{-3}$ and <2.5 $\mu m \cdot m^{-3}$, but no correlation with ozone (0.005; table 1). Correlations between trends in monthly air pollutant means and trends in serious asthma were also mainly quite weak (table 1). After adjusting for social deprivation, the air pollutants were correlated more weakly with asthma (table 1). However, after adjusting for the air pollutants, the correlations between social deprivation and asthma were not affected substantially (table 1).

Across LSOAs there were modest significant positive correlations between the air pollutants and social deprivation, ranging from 0.07 (ozone) to 0.19 (benzene; table 1). There was a significant reduction over time in hospitalised incidence of serious asthma from 1999/2000 to 2006/2007 ($p<0.001$) by 1.6% per year (95% CI 0.9-2.3%), but no significant trend for case fatality ($p=0.15$).

A major strength of this study is its size, covering >12,000 hospital admissions in a geographically defined population of three million. It is based on record linkage of inpatient and mortality data, which enables repeat admissions for the same patients to be identified as well as deaths following hospital discharge. Study limitations are, first, that the asthma admissions and air pollutants covered 8 yrs from 1999 to 2007, but air pollutants were measured geographically to 1 km^2 in 1 yr only (2007), and social deprivation was measured in 2005. Social deprivation measures are consistent over time, and although many air pollutants were quite stable over time [5], we also investigated monthly means of air pollutants from 1999 to 2007 to account for possible trends. Secondly, our data lacked detailed information on disease history, pathology, medical observations, treatments and deaths before admission, although this should not detract substantially from the main study conclusions on incidence. Since our study covered serious asthma hospitalisations of $\geqslant$3 days, possible misdiagnoses arising from cursory clinical judgement should be minimal. The air pollutants were based on residences, rather than workplaces, which may also impact on asthma through exposure to occupation-related dusts, gases and aeroallergens.

Our overall hospitalised incidence of serious asthma (54.5 per 100,000) compares with 138 for all asthma admissions in Wales in 2002 [6], which is among the highest in the world.

We found modest correlations between hospital admissions for serious asthma and seven of the eight air pollutants. These correlations (all <0.20) were much weaker than those for social deprivation (0.45), including ''employment'', ''income'' and ''education'' (0.40–0.45). When adjusting for deprivation, correlations for the air pollutants were substantially reduced (<0.14). Furthermore, correlations between monthly means of air pollutants and monthly admissions for ''serious asthma'' were also mostly quite modest or weak, and weaker than between social deprivation and ''serious asthma''. Our findings support a lack of constant relationship between trends in asthma exacerbations and trends in air pollutants [2].

Community studies internationally have often reported conflicting findings about the relationship between asthma prevalence and socioeconomic group, although one of the largest studies (across 15 European countries) reported higher asthma prevalence in lower socioeconomic groups [7]. Most studies of admissions for asthma report substantially higher rates among deprived groups [1], which suggests that a link between asthma and socioeconomic group is stronger in secondary care than in community settings. Possible reasons for our higher hospitalised incidence of ''serious asthma'' among deprived groups include differences in health seeking behaviour, compliance with healthcare, possible lower thresholds for hospitalisation and longer inpatient stays (of $\geqslant$3 days) resulting from lower levels of community and self support.

The much higher incidence of serious asthma among the most deprived also reflects more frequent severe exacerbations, which could reflect differences in exposure. For example, deprived

TABLE 1 Correlations between the hospitalised incidence of serious asthma and, respectively, social deprivation and air pollutants

	Correlations between hospitalised incidence of serious asthma and, respectively, social deprivation and air pollutants at LSOA level across Wales[#]	
	Unadjusted correlation[¶]	**Adjusted correlation[+]**
Social deprivation component (2005)[§]		
Income	0.45 (<0.001)	0.45 (<0.001)
Employment	0.44 (<0.001)	0.46 (<0.001)
Education	0.40 (<0.001)	0.39 (<0.001)
Health	0.34 (<0.001)	0.31 (<0.001)
Housing	0.15 (<0.001)	0.26 (<0.001)
Physical environment	0.14 (<0.001)	0.11 (<0.001)
Access to services	-0.28 (<0.001)	-0.30 (<0.001)
Overall	0.45 (<0.001)	0.45 (<0.001)
Air pollutant (annual mean, 2007)[ƒ]		
Particulate matter <10.0 $\mu m \cdot m^{-3}$ in diameter	0.18 (<0.001)	0.13 (<0.001)
Particulate matter <2.5 $\mu m \cdot m^{-3}$ in diameter	0.18 (<0.001)	0.13 (<0.001)
Benzene	0.17 (<0.001)	0.10 (<0.001)
Carbon monoxide	0.16 (<0.001)	0.10 (<0.001)
Nitrogen dioxide	0.14 (<0.001)	0.11 (<0.001)
Nitric oxide	0.13 (<0.001)	0.10 (<0.001)
Sulfur dioxide	0.12 (<0.001)	0.08 (<0.001)
Ozone	0.005 (0.839)	-0.03 (0.237)
	Correlations between monthly means of air pollutants at measurement sites and the monthly hospitalised incidence of serious asthma to hospitals in the local authority corresponding to the measurement site	
	Median correlation across sites	
Air pollutant (monthly means from 1999–2007)		
Particulate matter <10.0 $\mu m \cdot m^{-3}$ in diameter	-0.01 (-0.10–0.11)	
Particulate matter <2.5 $\mu m \cdot m^{-3}$ in diameter	-0.04 (-0.16–0.08)	
Benzene	0.08 (0.05–0.11)	
Carbon monoxide	0.25 (0.11–0.30)	
Nitrogen dioxide	0.30 (0.17–0.36)	
Nitric oxide	0.22 (0.09–0.33)	
Sulfur dioxide	0.16 (0.08–0.23)	
Ozone	-0.05 (-0.22–0.02)	

Data are presented with p-values or interquartile ranges in parentheses. [#]: correlations between the hospitalised incidence of serious asthma and, respectively, social deprivation and air pollutants are based on 1,896 lower super output areas (LSOAs) across Wales (mean population 1,560 people per LSOA). [¶]: excluding infants and older people (aged ⩾85 yrs) made little differences to these findings. Correlations for the deprivation components were, in order of listing: 0.45, 0.45, 0.42, 0.35, 0.16, 0.15, -0.28, 0.45; and for the air pollutants they were: 0.17, 0.18, 0.18, 0.17, 0.15, 0.14, 0.12, 0.030, -0.004. [+]: adjusted correlations between hospitalised incidence of serious asthma and air pollutants are adjusted for social deprivation (overall). Adjusted correlations between the hospitalised incidence of serious asthma and social deprivation are adjusted for the eight air pollutants. [§]: correlations at the LSOA level between social deprivation (overall) and the eight air pollutants (annual mean, 2007) were as follows: particulate matter <10.0 $\mu m \cdot m^{-3}$ (correlation 0.14); particulate matter <2.5 $\mu m \cdot m^{-3}$ (0.15); benzene (0.19); carbon monoxide (0.16); nitrogen dioxide (0.11); nitric oxide (0.10); sulfur dioxide (0.11); ozone (0.07); all $p<0.001$. [ƒ]: the geographical measurement of these air pollutants (to 1 km^2) was taken from 2007 as this was the best available study year, in terms of the interpolation methodology used and the number of air pollution sites used to measure each air pollutant. The annual mean for sulfur dioxide was in 2005 rather than in 2007. The 1-km^2 measures were then averaged over the corresponding LSOA.

groups smoke more, which independently accelerates lung decline and worsens symptoms [8], while asthmatic smokers have more admissions and use more healthcare resources than nonsmokers [9]. The modest associations between air pollutants and areas of social deprivation across Wales [10] further suggests that the stronger association between social deprivation and serious asthma is linked more strongly with social factors than with air pollutants. High levels of deeply inhaled pollutants from smoking are likely to overwhelm any effect of background air pollutants in causing acute asthma attacks.

Although air pollutants may provoke asthma exacerbations, their effects appear small, and less than that for social deprivation. Further investigations into social inequalities in

serious asthma should focus on the possible confounding role of cigarette smoke exposure, weather, workplace exposure and geographical variation in viral infections.

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Asthma and the regulated retrotransposon transcriptome

To the Editors:

Asthma is a complex disease characterised by inflammation and remodelling of the airways. Over the past few decades enormous progress has been made to understand which genes are associated with asthma development and several interactions between genes and environmental factors have been elucidated. Investigations into genetic and gene expression profiling, as well as single nucleotide polymorphism analyses, have helped to better understand the underlying molecular mechanisms of asthma. However, the recent identification of novel regulatory functions for transposable and transposed genetic elements (TEs) may be an important and new key to help understand the genetics that cause the heterogeneous manifestations of the asthma pathology.

Approximately 45% of the human genome is made of TEs [1]. The vast majority of TEs originate from retrotransposition of genetic elements known as short and long interspersed nuclear elements, long terminal repeat-superfamilies and direct transposition of TE-containing genomic DNA. Formerly regarded as junk DNA, it is now becoming increasingly evident that TEs often function to regulate and fine tune gene expression [2, 3]. TE-driven transcription frequently controls the expression of protein coding genes *via* alternative promoters, cis-regulatory non-protein-coding RNAs and through the formation of double stranded short RNAs. FAULKNER and CARNINCI [3] demonstrated that transcription initiation from promoters present in TEs is a general phenomenon, even when they are corrupted and not easily recognised as genuine transposons. In addition, TE insertions into gene sequences affect RNA stability and splicing variants [4, 5]. Approximately 30% of human mRNA contains at least one retrotransposon, and the mRNA levels were shown to be inversely proportional to the percentage of retrotransposons [6]. Such findings suggest that TEs are intrinsic components of