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Early childhood obesity and subsequent asthma diagnoses: A longitudinal study using linked routinely collected data from Wales

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Abstract

Introduction

Obesity and asthma are two of the most common childhood conditions and their prevalence have increased over the last decades. Several cross-sectional studies provide strong evidence for a positive association between these two conditions. However, few longitudinal studies have examined the temporal relationship between them.

Objective

To examine the relationship between body mass index (BMI) at school starting age and the risk of developing bronchial asthma later in childhood.

Methods

We used anthropometric measurements of children aged 4 to 5 years, obtained as part of a national surveillance programme in Wales, linked to multiple population-level longitudinal administrative and clinical datasets within a trusted research environment provided by the Secure Anonymised Information Linkage (SAIL) Databank. We examined whether obesity at age 4 to 5 years was associated with increased risk of having a recorded diagnosis of asthma during a nine year follow-up period using logistic regression analysis.

Results

Out of 22,790 children included in the study, 7% had a recorded diagnosis of asthma during the nine years following their anthropometric measurement. Children with obesity (Body Mass Index [BMI] z-score $\geq$98$^{\text{th}}$ Centile) had a 41% increased risk of having a recorded diagnosis of asthma (adjusted odds ratio [aOR]: 1.41; 95% confidence interval [CI]: 1.17–1.7). Females were 26% less likely to have a recorded diagnosis of asthma after adjusting for weight status and deprivation index (aOR: 0.74; 95% CI: 0.67–0.82).

Conclusion

Obesity in children aged 4 to 5 years carries an increased risk of developing asthma. Anthropometric measurements obtained through standardised population-level surveillance programmes enable important research that would otherwise be impossible. Expanding these programs to include older age groups is recommended. Additionally, lifestyle interventions aimed at weight loss may help reduce the risk of developing asthma.

Keywords

obesity; asthma; child health; linked data; administrative data; SAIL Databank; longitudinal

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Introduction

Childhood obesity is a global health concern and its prevalence has increased over the last decades. It is estimated that 124 million children and adolescents aged 5–19 were affected by obesity worldwide in 2016 and a further 213 million were overweight [1].

Asthma is the most common chronic disease of childhood [2], affecting approximately 11.5% of children in the 6-7 year age group and 13.5% in the 13–14 year age group.

Both childhood obesity and asthma have been increasing in prevalence over the previous decades [3], and multiple cross-sectional studies show evidence of a positive association between the two conditions [4–6]. Previous research also indicates that the relationship between childhood obesity and asthma is complex and bidirectional [7, 8]. However, few longitudinal studies have examined the temporal relationship between these conditions. Many published studies had small cohort sizes and there was broad heterogeneity in terms of exposure and outcome definitions and follow-up times [9, 10]. While most published studies have shown a positive association between childhood obesity and subsequent development of asthma, the magnitude of the effect was variable across studies. Large longitudinal studies with long follow-up times are warranted.

In Wales, a national surveillance programme exists whereby anthropometric measurements of children in reception year (age 4-5 years) are obtained by trained personnel following prescribed standards and guidelines, the Child Measurement Programme (CMP) [11]. While this programme had been running in some form for many years, the academic year 2012/13 was the first year where measurements were taken using the current unified standards [11].

We examined data from the CMP linked to multiple longitudinal administrative and clinical datasets housed within the Secure Anonymised Information Linkage (SAIL) Databank [12], to assess whether obesity at the age of 4–5 is associated with an increased risk of having a recorded diagnosis of asthma during a nine year follow-up period.

Methodology

Study design and population

This was a population-level, retrospective, observational study utilising routinely collected linked data, to examine the relationship between the weight status of children aged 4-5 years and the risk of having a recorded diagnosis of asthma during the nine years following initial BMI measurement, the maximum period for which data were available.

Data sources and access

All data used in this study were accessed via the SAIL Databank, hosted at Swansea University. The SAIL Databank provides a Trusted Research Environment enabling access to a number of datasets representing routinely collected administrative and health data pertaining to the population of Wales in the United Kingdom. All data within SAIL have been anonymised by removing personally identifiable information and assigning each individual a unique identifier referred to as anonymised linkage field (ALF), which can be used to link records pertaining to the same individual across different datasets and sources. Access and utilisation of data within the SAIL Databank complies with the Data Protection Act of 2018 and with the General Data Protection Regulation of 2016. [12–14]

Several data sources were linked and used in this study:

The National Community Child Health Database (NCCHD) compiles data from Child Health System databases which are held by National Health Service (NHS) organisations and includes data on birth registrations, child health examinations and vaccinations. This dataset includes the anthropometric measures of children taken as part of the CMP programme described above.

The Welsh Longitudinal General Practice (WLGP) dataset includes data about patient encounters from 80% of GP practices in Wales, covering approximately 83% of the Welsh population [15]. Where diagnosis codes are available for an encounter, they are encoded using the Read coding system [16].

The Welsh Demographic Service Dataset (WDSD) contains demographic and address information for people accessing NHS services in Wales and registered to a Welsh address. WDSD was used to derive age, sex, and socio-economic deprivation quintile for the cohort.

The Outpatient Database for Wales (OPDW) contains data on all scheduled outpatient appointments in all Welsh hospitals. Diagnoses are coded using the International Classification of Disease (ICD), 10^{th} iteration (ICD-10) [17].

Patient Episode Dataset for Wales (PEDW) includes attendance and clinical information pertaining to all admissions to Welsh hospitals, both inpatient and day cases. Diagnoses are coded using the ICD-10 system.

The Emergency Department Dataset (EDDS) consists of administrative and clinical data for all NHS Wales Accident and Emergency department attendances. Diagnoses are coded using a dataset-specific system [18].

The Annual District Death Extract (ADDE) is a register of all deaths relating to Welsh residents, including those that died out of Wales.

Measures

BMI and standardised z-scores

CMP data included height, weight and date of measurement for all children in the cohort. Body Mass Index (BMI) was calculated as the weight in kilograms (kg) divided by height in metres (m) squared (BMI = wt.[kg]/height^2[m^2]). Each BMI value was assigned a standardised Z-score by other members of the research team as part of a previous study. These scores were available to the researchers and were used in the present study. The assignment of standardised z-scores was performed based on the work of Cole et al [19]. BMI status was categorised into 4 mutually exclusive groups based on the UK1990 clinical reference standards and using the LMS method as follows: "underweight" (BMI <second centile), "normal weight" (<second to <91^{st} centile), "overweight" (≥91^{st} to <98^{th} centile), or "obese" (≥98^{th} centile) [20].

Asthma diagnosis

All records pertaining to each member of the cohort were searched for codes denoting a diagnosis of asthma. For datasets utilising the ICD-10 coding system (OPDW and PEDW), records were searched for codes J45 for asthma or J46 for status asthmaticus [21–23]. The GP dataset (WLGP) was searched for Read codes signifying a diagnosis of asthma derived from lists used in previous studies [22] and the concept library available within SAIL Databank. Code 14A denoting asthma was used for the accident and emergency (EDDS) dataset. A full list of codes used for our study is included in the Supplementary Material. A participant was flagged as having a recorded diagnosis of asthma if they had a relevant code mentioned in any of the datasets.

Covariates

Sex of cohort participants was derived from the WDSD dataset. It was a binary variable denoting male or female.

The WDSD dataset was also the source of the Lower layer Super Output Area (LSOA) code of the address registered as the child's residence at the date of BMI measurement.

The Welsh Index of Multiple Deprivation (WIMD) is the Welsh Government's official deprivation measure for small areas in Wales. The overall WIMD is a weighted area-level aggregation of eight domains of deprivation that can be recognized and measured separately (income, employment, education, health, geographical access to services, housing, and physical environment). WIMD 2011 was used for this study as it was closest to the time of measurement. The health domain was removed from the WIMD score since this study is related to health outcomes [24]. LSOAs were ranked in order of deprivation and divided into five quintiles with one being the most deprived and five being the least deprived. WIMD quintiles were assigned to each participant according to their LSOA at the time of measurement.

Cohort preparation

Figure 1 provides a summary and outline of the steps taken to derive the study cohort. Out of 31,506 children for whom anthropometric measures were available as part of the 2012/13 CMP programme, 3,250 were excluded as their week of birth (WOB) was before 01 September 2007 or after 31 August 2008. This large number is explained by the fact that one Welsh county measured some children during school-year one rather than during the reception year in the academic year 2012/13 [11]. The report explained that these measurements were excluded from the analysis but they may however have been included in the data available in the SAIL Databank. A further 31 children were excluded as the date of measurement fell outside the academic year, that is before 01 September 2012 or after 31 August 2013. Children classified as underweight at the time of measurement (BMI <second centile) were also excluded since some previous studies suggest an independent relationship between underweight and wheezing disorders [25].

The previous steps resulted in 28,051 children for inclusion. To be included in the final study cohort, individuals needed to have nine years of follow-up data available. For the purposes of this study, this was interpreted as the individuals being alive and registered to a Welsh address for at least nine years following the date of anthropometric measurement. Nine individuals had died and 1,996 individuals did not continue to live in Wales for at least 9 years following the date of measurement. Longitudinal datasets were interrogated for all records pertaining to the remaining 26,046 individuals mentioning a diagnosis code denoting asthma, and those who had a mention of an asthma diagnosis before 01 September 2012 were excluded (i.e., before the anthropometric measurement), as was done in similar studies [10].

The final study cohort therefore included 22,790 individuals for whom anthropometric measurements as part of the CMP programme during the academic year 2012/13, whose age at measurement was at least 4 years and no more than 6 years, who continued to reside in Wales for at least nine years following the measurement date, and who did not have a recorded diagnosis of asthma before the start of the 2012/13 academic year on 01 September 2012.

Statistical analysis

All analyses were performed using R Statistical Software 4.2.1 [26]. Logistic regression was used to evaluate the association between weight status at time of measurement and the likelihood of having a recorded diagnosis of asthma at any time during the nine years following the date of measurement, while adjusting for the covariates of sex and WIMD quintile. Model coefficients were exponentiated, and the unadjusted and adjusted odds ratios (aOR) and 95% confidence intervals (95% CI) are reported.

Results

Table 1 shows the characteristics of participants who had a diagnosis of asthma recorded during the follow-up period versus those who did not. Out of 22,790 participants, 1,638 (7%) developed asthma during the nine years following anthropometric measurement. Of those who had a recorded diagnosis of asthma, 913 (57.4%) were male, while those who did not have a recorded diagnosis of asthma showed a more equal sex distribution with 49.4% males and 50.6% females.

In terms of BMI status, 79.4% of participants who developed asthma were classified as having healthy weight, 12.4% as overweight and 8.2% as obese. Of those who did not have a recorded diagnosis of asthma, 82.8% were classified as having healthy weight, 11.1% as overweight and 6.1% as obese. The breakdown of participants in terms of deprivation index (WIMD) quintiles is shown in Table 1.

Logistic regression modeling results showed children who were classified as obese (BMI z-score $\geq$ 98th Centile) date had 41% increased risk of having a recorded diagnosis of asthma over the subsequent nine years (aOR 1.41; 95% CI: 1.17–1.7). No statistically significant association was found between being overweight at measurement and the risk of having a recorded diagnosis of asthma during follow-up.

Detailed unadjusted and adjusted logistic regression analysis results are detailed in Table 2 and a graphical representation of the adjusted results is shown in Figure 2.

Figure 1: Cohort derivation and exclusions

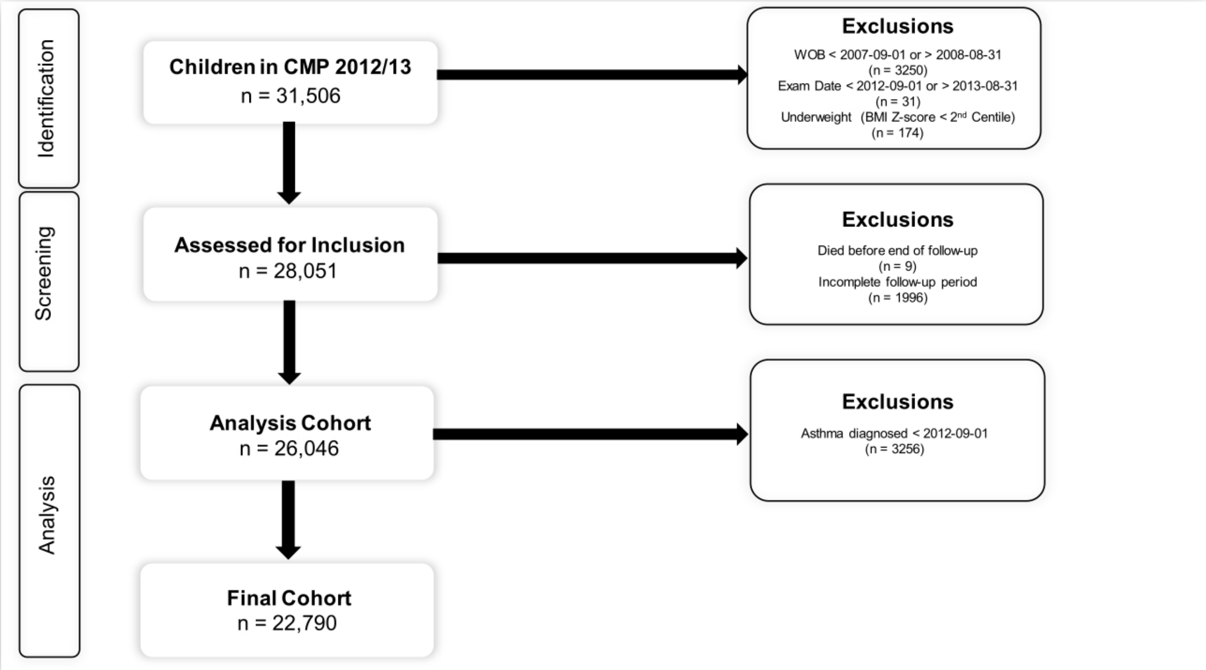


Table 1: Breakdown of participants who had a recorded diagnosis of asthma during follow-up versus those who did not in terms of sex, BMI status at time of measurement and WIMD quintile

	Asthma recorded during Follow-up period	Asthma not recorded during During follow-up period
Total	1,638 (7%)	21,152 (93%)
Sex		
Male	913 (57.4%)	10,456 (49.4%)
Female	707 (42.6%)	10,696 (50.6%)
BMI		
Healthy Weight (2nd Centile $\leq$ BMI z-score $<$ 91st Centile)	1,300 (79.4%)	17,517 (82.8%)
Overweight (91st Centile $\leq$ BMI z-score $<$ 98th Centile)	203 (12.4%)	2,348 (11.1%)
Obese (BMI z-score $\geq$ 98th Centile)	135 (8.2%)	1287 (6.1%)
Deprivation Index (WIMD Quintile)		
1st Quintile (Most Deprived)	454 (28.2%)	5,436 (25.7%)
2nd Quintile	368 (22.5%)	4,288 (20.3%)
3rd Quintile	283 (17.1%)	4,110 (19.4%)
4th Quintile	260 (15.5%)	3,566 (16.9%)
5th Quintile (Least Deprived)	273 (16.7%)	3,752 (17.7%)

Discussion

Summary of key findings

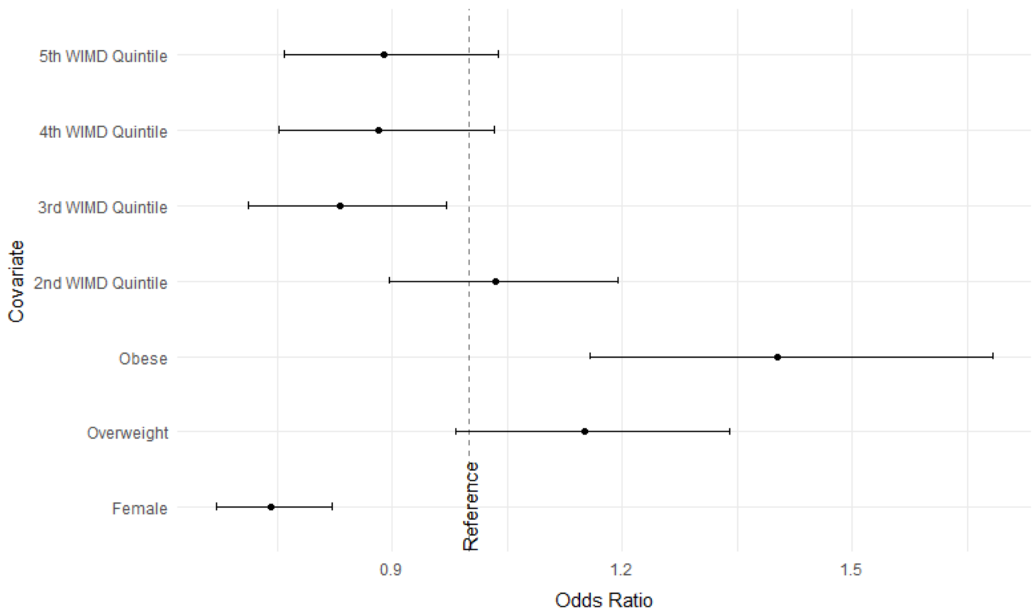
This study assessed whether 4- to 5-year-old children with obesity as measured by BMI who had anthropometric measures taken as part of a national surveillance program in Wales were more likely to have a recorded diagnosis of asthma in several primary and secondary care linked longitudinal clinical datasets during the nine years following measurement.

Seven percent of the 22,790 children who were included in this study had a recorded diagnosis of asthma in the nine years following the measurement date, 57.4% of whom were male. Of those who had a recorded diagnosis of asthma, 8.2% were classified as obese (BMI z-score $\geq$ 98th Centile) as opposed to 6.1% of those who did not. Children with obesity at the time of measurement were 41% more likely to have a recorded diagnosis of asthma during follow-up, after adjusting for sex and deprivation index quintile. Females were 26% less likely to

Table 2: Factors associated with asthma

	Unadjusted odds Ratio (95% CI)	p-value	Adjusted odds Ratio (95% CI)	p-value
Sex				
Male (baseline)	1		1	
Female	0.74 (0.67–0.82)	<0.001	0.74 (0.67–0.82)	<0.001
BMI				
Healthy weight (baseline)	1		1	
Overweight	1.15 (0.98–1.34)	0.05	1.16 (1.0 - 1.36)	0.07
Obese	1.4 (1.16–1.68)	<0.001	1.41 (1.17–1.7)	<0.001
WIMD Quintile				
1 Most deprived (baseline)	1		1	
2	1.04 (0.9–1.2)	0.71	1.03 (0.89–1.19)	0.63
3	0.83 (0.71–0.97)	0.01	0.82 (0.71–0.96)	0.02
4	0.88 (0.75–1.03)	0.09	0.87 (0.74–1.02)	0.12
5 Least Deprived	0.89 (0.76–1.04)	0.08	0.87 (0.74–1.02)	0.13

Figure 2: Adjusted logistic regression model results



have a recorded diagnosis of asthma compared to males, after adjusting for weight status and deprivation index quintile.

Comparison with existing literature

Many prior studies have explored the relationship between childhood obesity and the risk of bronchial asthma using different study designs [27]. Additionally, variations among studies in terms of participant age groups, exposure and outcome definitions, and study population size added to the challenges of comparing and/or aggregating study results [25]. Very few population-level studies examined the association between obesity and asthma and those we are aware of had a relatively short follow-up period [28]. To our knowledge, this is the first population-level study to examine the relationship between children's weight status at the relatively early age of 4-5 years and the risk of being diagnosed with bronchial asthma during a 9-year follow-up period.

Egan et al. [10] performed a meta-analysis of six prospective studies looking at the relationship between childhood BMI and subsequent physician-diagnosed asthma. Their analysis found that children who were classified as obese had an increased relative risk of having a subsequent diagnosis of asthma (combined risk ratio [RR] = 1.50; 95% CI: 1.22–1.83). Egan et al. defined obesity as BMI $>95^{\mathrm{th}}$ centile, which is slightly different from our definition, their results were similar to those of our study.

Another meta-analysis by Mebrahtu et al. [25] used data standardisation across studies in terms of the exposure variable (BMI) and outcome variable (asthma or wheeze) and so avoided some of the shortcomings of other similar studies. The included studies covered over one million children and the analysis revealed a significant increase in the risk of wheezing disorders in children with obesity (OR = 1.46; 95% CI: 1.36-1.57), again very similar to our study.

A population-based longitudinal study by Black et al. [28] included over 600,000 participants, although the median follow-up time was 3 years, quite shorter than that in our study. As in our study, their results showed that children with extremely obese status had increased adjusted risk of developing asthma (aRR: 1.37; 95% CI: 1.32-1.42).

Strengths and limitations

To our knowledge, this is the first study that linked population-level anthropometric data collected through the CMP in Wales with multiple primary and secondary care longitudinal datasets providing near-complete coverage of the Welsh population to study the association between obesity in children and the risk of developing asthma later in childhood. Measurements in the CMP programme are taken by trained personnel following specific standards and guidelines [11]. This fact, coupled with this being a nation-wide programme comprising a large number of participants, makes this anthropometric dataset especially valuable. These data could be linked with several longitudinal clinical and administrative datasets providing almost-complete coverage of the Welsh population. Also, participants were followed up for nine years following measurement, a long period compared to similar studies in the literature. Nissen et al. [29] evaluated the efficacy of using asthma-specific diagnosis codes in identifying asthma patients in a large UK primary care dataset, and concluded that a recorded asthma-specific Read code had a high predictive value and was sufficient to identify patients with asthma. This study did not therefore include asthma medications.

However, we do acknowledge a number of limitations with our study. While secondary care datasets have full coverage of the population, the primary care dataset includes only 80% of Welsh GP practices who had agreed to share data with the SAIL Databank, covering approximately 83% of Welsh population. Thus, some children who were included in the CMP 2012/13 dataset may be registered with non-participating GP practices. Also, only 84.3% of eligible children actually had their measurements taken as part of the 2012/13 CMP programme [11]. Parents can opt out of having their children's measurement taken. Also, there was a measles outbreak in Wales during the spring of 2013, which may have affected whether children were measured. So it is unclear whether the missing data was missing at random.

This study relied on whether a diagnosis code for asthma was present in the child's medical record. Asthma has a broad spectrum of symptoms and diagnostic criteria may vary across providers and settings. Finally, we were able to adjust for a limited number of confounders, namely sex and deprivation status. Other possible predictors were not corrected for such as other chronic conditions, family history of asthma and others.

Implications and further research

This study adds to the growing body of evidence supporting the association between childhood obesity and asthma. The strengths of this research in terms of cohort size, exposure measure standardisation and long follow-up period support the significance of its contribution to this area of research. We have shown the utility of data derived from national surveillance programmes such as the CMP. A follow-up measurement later in childhood will provide valuable information regarding the trajectory of weight status during childhood and open further research avenues.

While a growing body of evidence supports the relationship between obesity and asthma in childhood, few studies have examined the effectiveness of weight loss interventions and lifestyle changes on the severity of asthma symptoms and disease control [30], and further studies are needed to explore the effect of community and individual-level weight loss interventions on asthma symptoms and control. The complications of obesity are well documented in childhood and beyond, and our study suggests that further research is warranted on weight surveillance and management in children with asthma and wheezing disorders.

Conclusion

The relationship between childhood obesity and asthma is complex and nuanced. This study provides further evidence that obesity in childhood is associated with an increased risk of developing subsequent asthma. Population-level anthropometric surveillance programmes such as the CMP in Wales offer valuable opportunities for studying the association between weight status and clinically significant diseases and conditions, and expanding these programmes to include follow-up measurements at a later age will expand on their utility. Weight surveillance and management in clinical settings may play a role in decreasing the risk of developing asthma and controlling its severity.

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Statement on conflicts of interest

None to declare.

Ethics statement

This study only utilised anonymised data within the SAIL Databank. No personally identifiable data was accessed or utilised in the study, and thus ethical approval was not required. Nevertheless, this study was performed as part of a project that received approval from SAIL Information Governance Review Panel (project 1001) [13].

Data availability statement

The data sources are thoroughly detailed in the methods section and were accessed and analysed within a Trusted Research Environment (TRE). Due to the conditions of use, extracting data from the TRE is prohibited. Accredited researchers can apply to access the SAIL Databank through a governed approval process, which operates independently of the study authors.

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Abbreviations

ALF: anonymised linkage field
BMI: Body Mass Index
CMP: Child Measurement Programme
CI: Confidence Interval
EDDS: Emergency Department Dataset
GP: general practice
NHS: National Health Service
LSOA: Lower layer Super Output Area (LSOA)
NCCHD: National Community Child Health Database
OPDW: Outpatient Database for Wales
OR: odds ratioPEDW: Patient Episode Dataset for Wales
SAIL: Secure Anonymised Information Linkage
WDSD: Welsh Demographic Service Dataset
WIMD: Welsh Index of Multiple Deprivation
WLGP: Welsh Longitudinal General Practice (dataset)

Supplementary Materials

Asthma diagnosis codes

Primary care asthma diagnosis codes

Code	Description	Coding system
173A.00	Exercise induced asthma	Read codes v2
1O2..00	Asthma confirmed	Read codes v2
H312000	Chronic asthmatic bronchitis	Read codes v2
H33..00	Asthma	Read codes v2
H33..11	Bronchial asthma	Read codes v2
H330.00	Extrinsic (atopic) asthma	Read codes v2
H330.11	Allergic asthma	Read codes v2
H330.12	Childhood asthma	Read codes v2
H330.13	Hay fever with asthma	Read codes v2
H330.14	Pollen asthma	Read codes v2
H330000	Extrinsic asthma without status asthmaticus	Read codes v2
H330011	Hay fever with asthma	Read codes v2
H330100	Extrinsic asthma with status asthmaticus	Read codes v2
H330111	Extrinsic asthma with asthma attack	Read codes v2
e H330z00	Extrinsic asthma NOS	Read codes v2
H331.00	Intrinsic asthma	Read codes v2
H331.11	Late onset asthma	Read codes v2
H331000	Intrinsic asthma without status asthmaticus	Read codes v2
H331100	Intrinsic asthma with status asthmaticus	Read codes v2
H331111	Intrinsic asthma with asthma attack	Read codes v2
H331z00	Intrinsic asthma NOS	Read codes v2
H332.00	Mixed asthma	Read codes v2
H333.00	Acute exacerbation of asthma	Read codes v2
H334.00	Brittle asthma	Read codes v2
H335.00	Chronic asthma with fixed airflow obstruction	Read codes v2
H33z.00	Asthma unspecified	Read codes v2
H33z.11	Hyperreactive airways disease	Read codes v2
H33z000	Status asthmaticus NOS	Read codes v2
H33z011	Severe asthma attack	Read codes v2
H33z100	Asthma attack	Read codes v2
H33z111	Asthma attack NOS	Read codes v2
H33z200	Late-onset asthma	Read codes v2
H33zz00	Asthma NOS	Read codes v2
H33zz11	Exercise induced asthma	Read codes v2
H33zz12	Allergic asthma NEC	Read codes v2
H33zz13	Allergic bronchitis NEC	Read codes v2

Secondary care asthma diagnosis codes

Code	Description	Coding system
J45	Asthma	ICD-10
J46	Status asthmaticus	ICD-10

Emergency care asthma diagnosis codes

Code	Description	Coding system
14A	Asthma	EDDS Code