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Anaphylaxis and Ethnicity: Higher Incidence in British South Asians

Short Title - Anaphylaxis: Higher Incidence in British South Asians

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Abstract

Background: The incidence of anaphylaxis in South Asians (Indian, Pakistani and Bangladeshi ethnicity) is unknown. Birmingham is a British city with a disproportionately large population of South Asians (22.5%) compared with the rest of the UK (4.9%). The main aims of this study were to determine the incidence and severity of anaphylaxis in this population and to investigate the differences between the South Asian and white populations.

Methods: A retrospective electronic search of emergency department attendances at three hospitals in Birmingham during 2012 was carried out. Wide search terms were used, medical notes were scrutinised, and the World Allergy Organization diagnostic criteria for anaphylaxis applied. Patients' age, sex, ethnicity, and home postal code were collected, reactions were graded by severity, and other relevant details including specialist assessment were extracted. Multivariate analysis was undertaken using 2011 UK census data.

Results: Age, sex and ethnicity standardised incidence rate of anaphylaxis was 34.5 per 100,000 person years. Multivariate logistic regression which controlled for the confounders of age, sex, and level of socioeconomic deprivation showed that incidence was higher in the South Asian population (OR 1.48, $p=0.005$). Incidence rate in the South Asian population was 58.3 cases per 100,000 person years compared to 31.5 in the white population. South Asian children were more likely to present with severe anaphylaxis (OR 5.31, $p=0.002$).

Conclusions: Incidence of anaphylaxis is significantly higher in British South Asians compared to the white population. British South Asian children are at a greater risk of severe anaphylaxis than white children.

Keywords

Anaphylaxis; ethnicity; South Asian; incidence; epidemiology.

Conflicts of interest

None

Introduction

The International Study of Asthma and Allergy in Children (ISAAC)(1–4) has shown that atopy and allergic conditions are uncommon in South Asian countries compared to their high incidence in English speaking western countries, the UK in particular. However, anecdotal observations by the authors in one of the largest National Health Service (NHS) organizations in the UK suggested that the burden of allergic conditions and anaphylaxis is high amongst the South Asian community in the local catchment area. The populations of India, Pakistan and Bangladesh comprise 22.6% of the world population(5) in addition to those of South Asian ethnicity domiciled abroad. People from these ethnicities constitute 4.85% of the overall British population(6). Birmingham is the second largest city in the UK and has a relatively high proportion of people of South Asian origin (22.5%)(6). This provides an excellent opportunity to compare the incidence rate of anaphylaxis between the white and South Asian populations living in the same environment.

There are currently no data on the incidence of anaphylaxis amongst South Asians, either in their respective countries or in those living in the western world. The incidence rates reported in previous studies in predominant white populations from the UK and other countries have shown varying estimates, likely to be attributable to the differences in definition of anaphylaxis, methodology, and search criteria employed(7–11).

In order to conduct this study we used data from the 2011 UK population census to provide us with detailed information about the population of our local area. The census is conducted every decade and it is required by law that every household completes an in-depth questionnaire about those living at an address. This information is used to build up a picture of the demographics of small areas which are then amalgamated to generate data about larger areas. There are some reports from the UK, USA and

Australia suggesting that affluence may be a risk factor for anaphylaxis(7,12,13) and as our study population has a wide range of people with varying socioeconomic status, we incorporated this variable into our analysis. The census gives a validated quantitative measure for the UK, known as the Indices of Multiple Deprivation Score (IMD score)(14) of each household's level of deprivation using information from seven domains including income, employment, health and disability, education and skills, living environment, barriers to housing and services, and crime statistics from the immediate area. The average score for each postcode is a surrogate for each individual's level of deprivation. The scores can be used to rank small geographical areas in order, from most deprived (higher numbers), to the most affluent (lower numbers).

The main aim of this study was to determine the incidence and severity of anaphylaxis in our local population and perform a comparative analysis between South Asians and white population after controlling for confounding variables including age, gender and deprivation. We also characterised clinical presentation and report etiology following thorough allergological assessment.

Methods

This is a retrospective, observational study of patients attending the emergency department with anaphylaxis carried out in one of the largest National Health Service (NHS) organizations in the UK (Heart of England NHS Foundation Trust [HoEFT]) comprising three acute care hospitals (Birmingham Heartlands Hospital, Solihull Hospital and Good Hope Hospital) covering a catchment population of 891,159 in East Birmingham, Solihull, North Birmingham and South Staffordshire.

Patients

An electronic database search was carried out using wide search terms that were routinely used by the organization for coding attendances with allergic presentations with an aim to maximise the data capture of patients admitted with anaphylaxis. The search terms used were: 'Anaphylaxis', 'Anaphylactic Shock', 'Angioedema', 'Allergic Reaction', 'Skin - Allergic Reaction', 'Bite - Insect

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Venom', 'Bite - Insect Non Venom', 'Skin - Rash, Other'. The same clinician carefully identified the presenting signs, symptoms and laboratory investigations through scrutiny of the emergency department records, ambulance crew records and identified cases meeting the World Allergy Organization (WAO) diagnostic criteria for anaphylaxis(15). Cases of allergic reactions with only single system involvement such as isolated mucocutaneous, respiratory or gastrointestinal signs or symptoms were excluded as they did not meet the WAO diagnostic criteria for anaphylaxis. Where clinically evident, cases of anaphylaxis mimics such as asthma, vasovagal syncope, vocal cord dysfunction, gastroenteritis, hereditary angioedema and hypotension from non-anaphylactic causes were excluded.

A number of steps were taken to ensure reliability of the dataset. At the outset, two operators scrutinised the World Allergy Organization diagnostic criteria for anaphylaxis and jointly examined a number of case notes to ensure consistency of inclusion and exclusion of cases. One operator then continued to examine case notes. Cases where there was uncertainty about inclusion or exclusion were jointly reviewed with the second operator at weekly meetings. At the halfway point, all previously examined case notes were re-assessed. No cases that were initially included were excluded on the basis of this re-examination although several were subsequently included as details had been missed on the initial examination. Furthermore, allergy clinic records were also reviewed for cases that attended clinic to further establish inclusion and exclusion of cases. Allergy clinic records allowed validation of symptomatology as well as identification of aetiology.

There are no private emergency departments in the UK offering a full range of open access emergency care. Patients in our area have no alternative for emergency care other than to attend one of our three hospitals. All patients admitted to NHS hospitals in the UK complete a standardised demographic pro forma which is available electronically on the hospital database. A standardised pro forma and spreadsheet (Microsoft Excel [2007]) for this study were created and data relating to age, sex, ethnicity, postal code, IMD score (level of deprivation), signs, symptoms, precipitants (established at allergological assessment) and co-morbidity (specifically asthma) were extracted. Free-text entries into spreadsheets were checked, coded and then re-checked by one operator. Spreadsheets

were then reviewed by a medical statistician for data quality and consistency.

In this study, patients of Indian, Pakistani and Bangladeshi origin were categorised as ‘South Asian’. Each case was labelled as ‘non-severe’ or ‘severe’ anaphylaxis using the ‘Brown grading system’[(16)]. For the purposes of this study, Brown grade II reactions were labelled as ‘non-severe’ and Brown grade III reactions were labelled as ‘severe’. Brown grade I reactions do not fulfil the WAO diagnostic criteria for anaphylaxis and thus were not included in the study.

Statistical analysis

Univariate and multivariate analysis

In order to investigate the association between patients’ characteristics and the incidence of anaphylaxis, univariate and multivariate logistic regression models were constructed using the generalised linear model function in R i387 v3.1.0 (The R Foundation for Statistical Computing). Demographic data from the *local catchment area* taken from the 2011 UK national census (using the local population as a control group) were used to calculate the odds ratios for developing anaphylaxis according to age, sex and ethnic group, controlling for level of deprivation. Sub-analyses were performed separately on adults (16 years and over) and children (under 16 years). We also used the generalised linear model function in R i387 to investigate the predictors of presenting to hospital with ‘severe anaphylaxis’ as defined by the Brown grading system(16). Here, in addition to age, sex, ethnicity and level of deprivation, we included history of asthma as a covariate. In this model the two groups of patients- those with ‘severe’ and ‘non-severe’ cases, were compared, rather than using the local catchment population as the control group. Again sub-analyses were performed separately on adults and children. P-values were calculated in R i386, generated from multivariate logistic regression.

Incidence Rates

Incidence rates were calculated by dividing the number of cases by the total population of the catchment area and multiplying by 100,000 to give a figure of ‘n’ cases per 100,000 person years. As our population is not representative of the population of England as a whole, we also calculated

projected national incidence rates which were standardised according to the age, sex and ethnic group make-up of the entirety of England using the 2011 census data. Standardised incidence rates were calculated as follows. First, the study population was broken into subgroups defined by age, sex and ethnicity. National data(6) was then used to express the proportion of the English population that each of these groups represent. The standardised rate for each group was then found by multiplying the incidence rate for each group by the proportion of the national population that the group represented. Summing these values gave the standardised incidence rate. Similarly, ethnicity specific rates were standardised for age and sex. Incidence rates for ethnic groups including black, East Asian, mixed ethnicity and others are not reported due to low patient numbers.

Data was stored on a secure hospital computer, in an encrypted Microsoft Excel document. Data was analysed on an anonymised version to maintain patient confidentiality. Missing data was treated as 'missing at random'. The project proposal was reviewed by the HoEFT Research and Development department and confirmation was obtained that formal ethical committee approval was not required. The study was registered with the HoEFT clinical governance unit. The study had no external funding source.

Results

The electronic search of the emergency department database revealed 3516 patients of which 426 patient episodes met the WAO criteria for anaphylaxis (figure 1: study algorithm). Demographics are summarised in table 1. There were peaks in incidence rate between the ages of 0-4 and 19-24 (figure 2).

Multivariate logistic regression analysis

In order to use local population statistics to determine whether demographic variables including age, sex, and ethnicity affected the incidence rate of anaphylaxis, we needed to exclude from the analysis patients with an address from outside of the area. Of the 395 unique patients with anaphylaxis, 332

were included in the multivariate analysis. Of those excluded, 55 patients were from outside the catchment area and eight patients had missing data. Of the 322 patients inside the catchment area with complete data, 108 patients had a severe reaction (30.5%). The study flow is summarised in figure 1.

Overall, South Asian people had a higher odds ratio of being admitted with anaphylaxis (OR 1.49, $p<0.001$) and this association remained significant both in children (OR 2.37 $p=0.001$) and in adults (OR 1.47 $p<0.001$). Findings are summarised in table 2. Amongst the group of South Asian children, a significantly higher proportion of attendances were with severe anaphylaxis than in children who were white (47.1% [27/51] vs. 17.1% [7/41] {OR 5.31 $p=0.002$ }). History of asthma was explored as a confounder in this analysis and rates of asthma were similar in both groups (34% and 35% in white, and South Asian children respectively) and we did not see history of asthma as a significant predictor of severity likely due to low numbers. In adults, although incidence of anaphylaxis was higher in South Asians, there was no association between ethnicity and the severity of the episode. Anaphylaxis was more common in adult females (OR 1.80 $p<0.001$) but there was no such association with gender in children (tables 1 and 2)

Incidence rates

The multivariate regression analysis produced relative measures of the incidence of anaphylaxis in our population. However, to put these findings into context we have gone on to provide incidence rates. One in 590 emergency department attendances were with anaphylaxis (0.17%). In our population, the incidence rate is 47.8 cases per 100,000 person years. However, as there is a higher proportion of South Asians in the study population as compared with the national population, we have used our findings in conjunction with the local and national population statistics to calculate standardised incidence rates. Our standardised incidence rate for England is 34.5 (95% CI 30.4, 38.9) per 100,000 person years and for severe anaphylaxis, the incidence rate is 12.0 (95% CI 9.62, 14.7). A further breakdown of standardised incidence rates according to age, ethnicity and severity is given in table 3. Figures compliment the multivariate regression analysis.

Level of deprivation

As a secondary outcome measure, we looked at whether there was a relationship between incidence of anaphylaxis and level of deprivation (IMD score) but did not observe an independent effect. Further analysis is provided as supplementary data.

Presenting features and precipitants

Of the 426 cases, 105 involved children and 321 involved adults. In adults 313 (97.5%) cases had mucocutaneous involvement such as urticaria, facial swelling and tongue swelling. 276 (86%) cases had respiratory involvement such as dyspnoea, bronchospasm, and hypoxia. 89 (27.8%) cases had gastrointestinal involvement such as nausea, vomiting, diarrhoea, and abdominal pain. 79 (24.6%) cases had cardiovascular involvement such as feeling lightheaded, collapse, and hypotension. In children 104 (99%) cases had mucocutaneous involvement, 75 (71.4%) had respiratory involvement, 50 (47.6%) had gastrointestinal involvement, and 14 (13.3%) had cardiovascular involvement. There were no significant differences between the ethnic groups. There were 13 (12.3%) children and 48 (15%) adults who had one or more of the following severe symptoms: stridor, respiratory arrest, hypoxia, hypotension, loss of consciousness, and chest pain.

Of 395 individual patients, 148 [37.5%] (44 [46.0%] children and 104 [35.1%] adults) were reviewed in the specialist allergology clinic so we were able to accurately determine the etiology in these patients. The most common cause of anaphylaxis in children was food (90%), and in adults the most common cause was idiopathic (54.8%) followed by food (23.1%) and medications (15%). There was a proven history of venom induced anaphylaxis in only one patient. There were no significant differences in precipitants between the two ethnic groups (table 4).

Discussion

This is the first report on the incidence of anaphylaxis in a South Asian population living in a western country and our data suggests that the incidence is significantly higher in this ethnic group in comparison to the white population. We have also shown that South Asian children are more likely to

present with severe anaphylaxis than white children. These observations highlighting marked differences between ethnic groups raise further research questions relating to gene-environment interaction in the pathogenesis of allergic conditions and are useful for policy makers in devising robust strategies for delivery of specialised health care services in areas comprising an ethnically diverse population.

Some of our other findings in this study concur with previous reports regarding epidemiology of anaphylaxis including the peaks in incidence seen in early childhood and early adulthood, higher rates in adult females and male children(11,17) as well as causative triggers. We found relatively high rates of mucocutaneous involvement in our study sample (97.5% and 99% in adults and children respectively); previous studies have reported rates of about 90%(16,18–20). The high rates seen in this study may be at least in part explained by cases of anaphylaxis with mucocutaneous involvement being more readily identified. European guidelines on food allergy emphasise the importance of clinical history as well as determining sensitisation to food(21,22). Only a third of our patients were reviewed in clinic, contrary to British national guidelines(23), either because they not referred from the emergency department or they did not attend their appointments.

In agreement with previous data, we found high rates of food-induced anaphylaxis in children(11). The breakdown of etiology in the adult patients of our cohort shows higher rates of idiopathic anaphylaxis than has been previously observed but in concordance with previous findings(11,18,24) we have still observed food and drugs to be important precipitants. The finding of a high proportion of idiopathic anaphylaxis may be a true observation but may also be influenced by a possible increased likelihood of being referred for specialist assessment and attending the appointment if the cause is uncertain. Venom-induced anaphylaxis was uncommon in this cohort and this may be due to several reasons. First, the prevalence of venom-induced anaphylaxis is known to be dependent on the geographical area(25). We studied a predominantly an urban population and although parts of the city are open and green, the areas concentrated around particularly Heartlands Hospital (the 'hub' centre) is among the most densely populated in the city and exposure to venomous insects is likely to be low. Second, the warm late-winter and cold wet spring of 2012 meant that the wild bee and wasp population was likely

to have been low for the duration of the summer(26). Finally, there are likely to be few beekeepers in this urban area and our group has previously reported that just under half of British beekeepers attended an emergency department on development of a systemic allergic reaction to a bee sting and only 16.6% were reviewed in the allergy clinic(27).

A recent review estimates incidence of anaphylaxis to be between 50 to 112 episodes per 100,000 person years(25) and our figure of 34.5 cases per 100,000 person years is slightly below this estimate. Previously published UK incidence rates based on database searches restricted to the primary diagnostic code of ‘anaphylaxis’ have given significantly lower estimates (7,28) as have studies from the U.S.A(29,30), although these are comparable with our incidence rates for ‘severe anaphylaxis’, the latter of which are more likely to be coded as ‘anaphylaxis’. Studies comparable with ours that have employed wide search term strategies and careful examination of case notes have shown incidence rates similar to those reported in this study(8–11,31).

The WAO diagnostic criteria have standardised the definition of anaphylaxis and would also include cases with relatively mild cardio-respiratory compromise. Therefore, we analysed our data as ‘severe’ and ‘non-severe’ based on previously described ‘Brown grading system’(16). Drawing this distinction allowed us to put the burden of anaphylaxis in our population and the WAO diagnostic criteria into an epidemiological perspective. This further categorization of cases means we can give a possible explanation (above) for the discrepancy between our data and the low rates of anaphylaxis reported in the previous studies from UK(7,28) which were based on database searches *per se*.

Our data supports the role of gene-environment interaction in the pathogenesis of allergic diseases. The ISAAC study reported low prevalence of allergic conditions including rhinitis, asthma and eczema in children living in South Asian countries(1–4) although it has been suggested by one Canadian study that children of South Asian ethnicity living in economically developed countries may have a similar burden of asthma as white children(32). Whilst there are no recent data on the prevalence of allergic conditions in South Asian British children, our study suggests that food allergy may be a significant problem in this ethnic group and the prevalence of food allergy seems to vary with geographical location, even within Europe(33). The higher incidence of severe anaphylaxis in

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this ethnic group is difficult to explain; the proportions of asthmatics in both groups were similar. It is plausible that these differences could be related to multiple factors including time taken to seek medical attention and administration of adrenaline, access to self-injectable adrenaline injector/s, severity of asthma, level of asthma control, presence/absence of other cofactors, and compliance to specialist advice (in cases previously reviewed) given previously. Varying exposure to a wide range of food allergens is likely to differ according to culture and ethnicity, and a recent study in British children reported that early life exposure to peanut can influence sensitization and development of immune tolerance(34). Additionally micro-environmental factors and effects at a cellular level relating to mast cell mediator release and their subsequent effects on end organs may also play a role but are not within the remit of this study.

In this study patient selection was determined by retrospective scrutiny of emergency department medical notes and ambulance records. Despite the obvious limitations of a retrospective approach using contemporaneous notes written by non-specialists, great care was taken to scrutinise every document available. Additionally, we were not depending on the clinicians' diagnostic acumen, instead, retrospectively determining whether each case fulfilled the WAO criteria. The study is of course limited by its relatively small sample size and failure to capture episodes of anaphylaxis that were either self-treated (and did not attend emergency department) or in cases where patients attended other community services or hospitals. Furthermore, we were unable to capture cases of 'in-hospital' anaphylaxis, although this is a rare occurrence(35).

In this urban, ethnically diverse population living in Birmingham, UK, the incidence of anaphylaxis is significantly higher in the South Asian population compared to the white population and South Asian children are at greater risk of developing severe anaphylaxis. A larger, multi-centre, prospective study is needed to confirm these observations and to gain further insight into factors contributing to allergen sensitization and anaphylaxis in the South Asian ethnic group living in the UK.

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Table 1: Demographics of the study population.

Number of cases of anaphylaxis	426
Number of individual patients (<i>there were patients with >1 attendance</i>)	395
<i>Of total attendances (n= 426)</i>	
Number of severe cases (according to Brown severity grading)(16)	145 (34.0%)
Median age	26.5 (range 0-90)
Sex	
Males	171 (40.1%)
Females	255 (59.9%)
Children (<16)	105 (24.7%)
Male	59 (56.2%)
Female	46 (43.8%)
Adults (≥16)	321 (75.4%)
Male	112 (34.9%)
Female	209 (65.1%)
Ethnicity	
White	239 (56.6%)
South Asian	134 (31.8%)
Black	24 (5.7%)
Mixed	4 (0.9%)
Other	11 (2.6%)
Unknown	15 (3.3%)
Deprivation (IMD score compared to population of England)	
<1% (87.8 - 67.8) <i>Most deprived</i>	9 (2.3%)
1-5% (67.8 - 53.5)	72 (18.2%)
5-25% (53.5 - 30.2)	135 (34.2%)
25-50% (30.2 - 17.3)	67 (17.0%)
50-75% (17.2 - 9.8)	55 (13.9%)
75-100% (9.8 - 0.5) <i>Least deprived</i>	56 (14.2%)

Table 2: Odds ratios. Results of multivariate logistic regression analysis showing odds of presenting with anaphylaxis according to female sex and South Asian ethnicity.

	Odds Ratio (95% CI*)	p-value
All patients		
Female	1.49 (1.27 - 1.71)	<0.001
Asian	1.64 (1.36 - 1.91)	<0.001
Children (<16y)		
Female	1.14 (0.71 - 1.58)	0.55
Asian	2.37 (1.83 - 2.90)	0.001
Adults		
Female	1.80 (1.53 - 2.06)	<0.001
Asian	1.47 (1.15 - 1.79)	<0.001

*95% CI: 95% Confidence Interval

Table 3: Standardized incidence rates of anaphylaxis. Incidence rates were first calculated using the number of attendances in the local population and then using the population structure of the whole of England to give estimates of the national incidence rates for the population overall, adults, children, the white population and the South Asian population. Figures were standardised for age, sex and ethnicity except the separate figures for each ethnic group which were standardised for age and sex only. P-values are not given as the significance of differences between groups were explored in multivariate logistic regression analysis (table 2).

	Age standardised incidence rates: Cases of anaphylaxis per 100,000 person years	
Adults and children	All cases (95% CI*)	Severe (95% CI*)
All persons	34.5 (30.4, 38.9)	12.0 (9.6, 14.7)
South Asian ethnicity	58.3 (42.8, 76.3)	20.4 (10.6, 33.1)
White ethnicity	31.5 (27.2, 36.3)	10.7 (8.3, 13.6)
Adults (≥16)		
All adults	34.1 (29.6, 39.1)	12.7 (10.0, 15.9)
South Asian ethnicity	57.5 (38.7, 80.0)	18.7 (7.0, 35.1)
White ethnicity	32.0 (27.3, 37.4)	12.2 (9.3, 15.6)
Children (<16)		
All children	35.9 (27.0, 46.3)	9.15 (5.0, 14.7)
South Asian ethnicity	61.3 (42.9, 84.9)	26.9 (15.4, 43.7)
White ethnicity	29.5 (20.1, 41.6)	4.30 (1.4, 10.0)

*95% CI: 95% Confidence Interval

Table 4: Precipitants of anaphylaxis in patients who were reviewed in the specialist allergy clinic. The total number seen was 148 (37.5% of 395 unique patients). There were no statistically significant differences between the precipitants of anaphylaxis seen in the different ethnic groups. In children the most common precipitant was food (86.4%) and in adults, anaphylaxis was most commonly attributed to no identifiable cause - idiopathic - (54.8%), followed by food (23.1%) and medications (17.3%).

Children (<16y)				
	White	South Asian	Other ethnicity	Total
<i>Number seen in clinic (% of total in group)</i>	23	16	5	44
<i>% of each group reviewed in clinic</i>	62.2%	38.1%	25%	41.9%
Medication	0	1 (6.3%)	0	1 (2.3%)
<i>of which antibiotic</i>	0	0	0	0
Food	20 (87%)	14 (87.5%)	4 (80%)	38 (86.4%)
<i>of which nuts</i>	13 (56.5%)	6 (37.5%)	1 (20%)	20 (45.5%)
Venom	1 (4.3%)	0	0	1 (2.3%)
Idiopathic	1 (4.3%)	1 (6.3%)	1 (20%)	3 (6.8%)
Other	1 (4.3%)	0	0	1 (2.3%)
Adults (≥16y)				
	White	South Asian	Other ethnicity	Total
<i>Number seen in clinic (% of total in group)</i>	70	28	6	104
<i>% of each group reviewed in clinic</i>	36.8%	36.8%	20%	35.1%
Medication	12 (17.1%)	6 (21.4%)	1 (16.7%)	18 (17.3%)
<i>of which antibiotic</i>	5 (7.1%)	1 (3.6%)	0	6 (5.8%)
Food	15 (21.4%)	5 (17.9%)	4 (66.7%)	24 (23.1%)
<i>of which nuts</i>	11 (15.7%)	3 (10.7%)	4 (66.7%)	18 (17.3%)
Venom	1 (1.4%)	0	0	2 (1.9%)
Idiopathic	40 (57.1%)	16 (57.1%)	1 (16.7%)	57 (54.8%)
Other	2 (2.9%)	1 (3.6%)	0	3 (2.9%)

Figures

Figure 1: Study algorithm. 3516 attendances to the emergency department during 2012 were identified using an electronic search of the attendances database using wide search terms. 426 attendances fulfilled the WAO diagnostic criteria for anaphylaxis. Of these, 20 patients had >1 attendance so there were 395 individual patients. 63 patients were excluded from the multivariate analysis predominantly as they were from outside the catchment area leaving 322 patients to be included in the multivariate analysis and subsequent subgroup analysis.

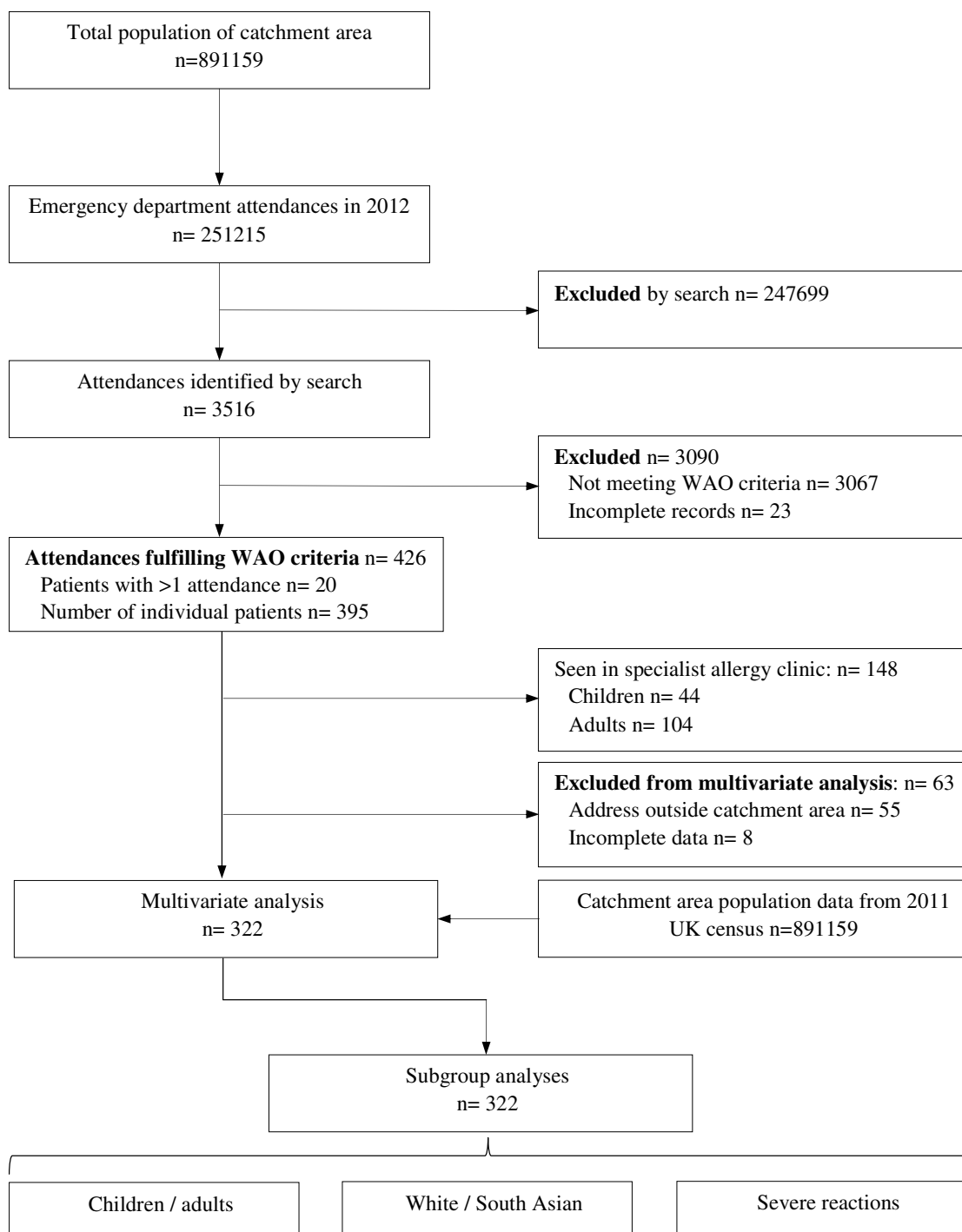
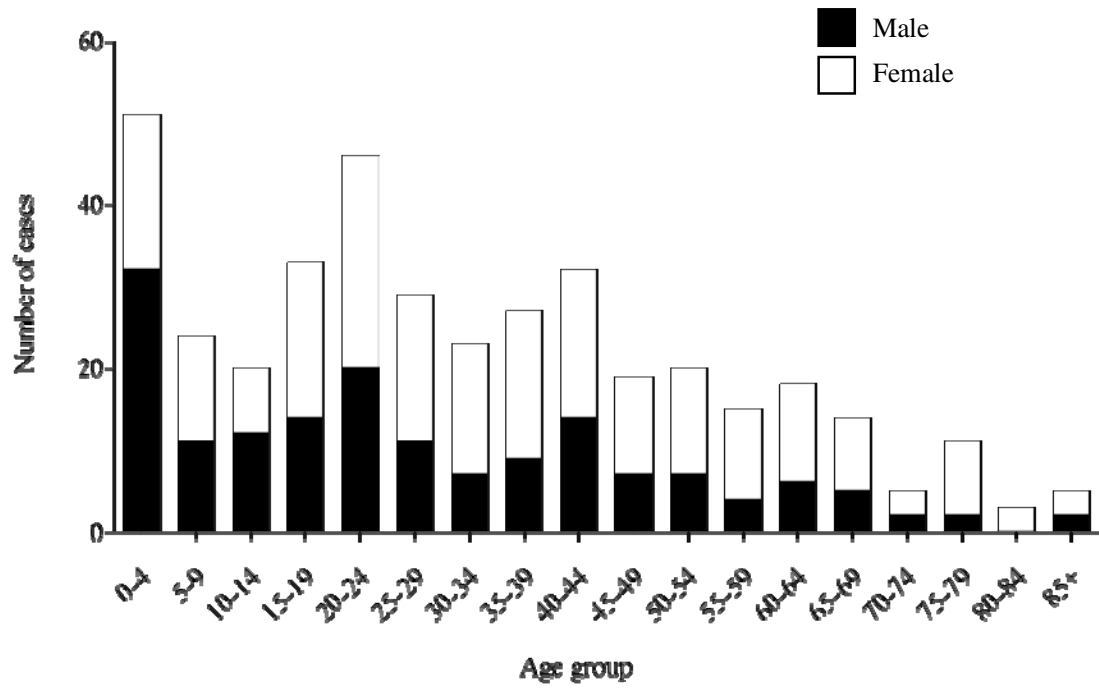


Figure 2: Number of cases by age group and sex. There are peaks in the 0-4 and 20-24 years age groups.



Supplementary

Deprivation analysis

To explore the effect of deprivation, average IMD score for each council ward was plotted against incidence of anaphylaxis per ward (figure S1). To determine the best model to demonstrate the relationship between IMD score and incidence rate per council ward (the key unit of UK administrative geography used to elect local government councillors), the Akaike Information Criteria were used. This rewards goodness of fit but contains a penalty function which increases with the number of parameters to be estimated. The most plausible relationship was linear but weak, suggesting that more deprived areas had lower incidence of anaphylaxis (Pearson correlation coefficient -0.28 [p=0.047]). However, this model does not take into account other confounding factors particularly ethnicity. In multivariate logistic regression that controlled for age, sex and ethnicity, a single point increase in IMD score was not associated with a statistically significant change in odds of presenting to hospital with anaphylaxis (OR 1.001 p=0.696).

Supplementary figure

Supplementary figure S1: Incident rate of anaphylaxis against deprivation by council ward.

Incidence rate by area (council wards) within the study population plotted against average IMD score for each ward. The English IMD give a quantitative measure of deprivation for each household according to results from the population census as described in the methods section. The higher the IMD score, the higher the level of deprivation. There is a very weak negative correlation showing decreasing incidence with as level of deprivation increases (-0.28 [$p=0.047$]) but this effect is not reflected in multivariate analysis.

