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DALES; Drug Allergy Labels in Elective Surgical patients; a prospective, multicentre cross-sectional study of prevalence and nature and anaesthetists' approach to management

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Short title: Drug Allergy Labels in Elective Surgical patients

Keywords

Anaesthetist attitudes, drug allergy labels, hospital wristbands, patient reported drug allergy, perioperative allergy.

Abstract

Background

We sought to define the prevalence and nature of patient-reported drug allergies, determine their impact on prescribing, and explore drug allergy knowledge and attitudes amongst anaesthetists.

Methods

Prospective cross-sectional study in 213 UK hospitals. Elective surgical patients interviewed, with a detailed allergy history taken in those self-reporting drug allergy. Self-completed questionnaire for anaesthetists.

Results

Of 21,219 patients , 6214 (29.3 %) [95% CI 28.7- 29.9] reported drug allergy. Antibiotics, non-steroidal anti-inflammatory drugs and opioids were the most frequently implicated agents. Of a total 8755 reactions, 2462 (28.1 %) [95% CI 29.2- 31.1] were categorised as high-risk for representing genuine allergy following risk stratification. A history suggestive of chronic spontaneous urticaria significantly increased the risk of reporting drug allergy (OR 2.68, 95% CI 2.4-3) p <0.01).

Of 4756 anaesthetists, 1473 (31%) [95% CI 29.7-32.3] routinely discuss perioperative allergy risk with patients. Prescribing habits in the presence of drug allergy labels differ depending on the implicated agent. Most anaesthetists (4678/4697, 99.6%) [95% CI 99.4 - 99.8] prescribe opioids when reactions are consistent with side effects, although 2269/ 4697 (48%) [95% CI 46.9 -49.7] would avoid the specific opioid reported.

Conclusions

Approximately 30% of UK elective surgical patients report drug allergies but the majority of reported reactions are likely to be non-allergic in nature. Allergy labels can impact on perioperative prescribing through avoidance of important drugs and use of less effective alternatives. We highlight important knowledge gaps about drug allergy amongst anaesthetists, and the need for improved education around allergy.

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Author contributions

Contribution to all aspects of the study: CT, LS, SC, DF.

Writing of the manuscript: PH, SS.

Statistical analysis: MW.

Background

The World Allergy Organization classifies adverse drug reactions (ADRs) as predictable reactions related to the pharmacological actions of the drug (side effects), or idiosyncratic and unpredictable reactions (such as a patient with infectious mononucleosis developing a rash with ampicillin), or drug allergy.[1,2] Idiosyncratic reactions may be severe or recur on re-exposure to the drug. Drug allergy is a specific term referring to IgE-mediated type 1 hypersensitivity or, more rarely, delayed type 4 T-cell mediated reactions such as toxic epidermal necrolysis. However, the term 'allergy' is frequently applied to reactions which lack any clinical features of allergy, and which have not been subject to specialist investigation. The consequences of an incorrect allergy diagnosis may be significant if important drugs are avoided and less effective alternatives used. The potential for harm has been demonstrated for the penicillin allergy label. [3-6]

The prevalence of patient-reported drug allergy is high. In a study of the electronic healthcare records of 1.7 million patients in the USA, 35.5% of records indicated an allergy to at least one drug [7]. Other studies suggest a prevalence ranging from 7-38%, with antibiotics, non-steroidal anti-inflammatories (NSAIDs) and opioids the most frequently reported culprits. [8-14] It is widely accepted that a significant proportion of drug allergy labels are incorrect, with side effects or other non-allergic phenomena misattributed to allergy by patients or their healthcare providers.[15-17] We aimed to determine the prevalence of patient-reported drug allergies in the UK elective surgical population and risk stratify the reported reactions for likelihood of genuine allergy. We further examined the impact of penicillin and opioid allergy labels on perioperative prescribing. The results of the penicillin sub-study have been reported previously [18] . This paper covers all reported drug allergies and opioid prescribing. We also examined the use of wristbands to denote drug allergy, to determine whether there was variation in use across the UK. We sought to understand anaesthetists' knowledge and attitudes towards perioperative drug allergy, including prescribing habits in the presence of specific allergy labels.

Methods

Study design and participants

A UK-wide cross-sectional observational study was conducted across 213 NHS hospitals (referred to below as sites). Participating sites were identified through the Research and Audit Federation of Trainees (RAFT) [19] network. Individual sites selected three data collection days between 21st March and 31st August 2018. The study comprised a semi-structured patient interview, a site survey detailing local guidelines and practices, and an anaesthetist survey. For inclusion and exclusion criteria, see Supplementary Materials 1. Study data were collected using Research Electronic Data Capture (REDCap) [20] hosted by Anaesthesia.Audit on Scotland's Health on the Web (SHOW) secure servers. The study gained ethics (REC reference 17/LO/2106) and HRA approval (IRAS ID 232512). Electronically verified informed consent was gained. The STROBE checklist for cross-sectional studies was used to guide reporting of this study. [21]

1. Patient study

A semi-structured interview was conducted using an electronic device (typically a mobile phone or tablet) held by the data collector. Questions were logic-gated and further stems presented according to the previous response. The term 'sensitivity' was taken to indicate allergy, since these terms are used interchangeably by patients and healthcare professionals. In our subsequent analysis we use the term 'allergy' to indicate type I (IgE mediated) hypersensitivity reactions. We collected data on age, sex, history of atopy, urticaria and/or angioedema, and self-reported drug allergies. For the patient interview and follow-up data collection tool, see Supplementary Materials 2 and 3.

Patients reporting an opioid allergy were followed up on the day of surgery, except those undergoing cataract surgery because opioid use is rare for this procedure. Anaesthetic charts were examined postoperatively by local investigators using a structured proforma, to determine whether opioids had been administered intraoperatively and whether any degree of significant perioperative hypersensitivity was likely to have occurred. This was defined as the use of epinephrine, steroids or antihistamines, unplanned admission to intensive care, documentation on the anaesthetic chart that an allergic reaction was suspected to have occurred, or evidence of perioperative mast cell tryptase sampling.

Drug allergy histories were subsequently risk stratified by the study team according to criteria defined *a priori* (Supplementary Materials 4). Adverse reactions were defined as being at low risk of genuine allergy where reported symptoms were consistent with known side-effects of the drug and included no clinical features of allergy. If a patient reported symptoms consistent with genuine allergy or severe delayed type IV hypersensitivity reactions such as Stevens-Johnson syndrome, they were categorised as high-risk. A third category was used for patients who described non-allergic but

nevertheless serious adverse reactions, for example, malignant hyperthermia, or avoidance of NSAIDs in the presence of renal impairment. Patients could list multiple symptoms or reasons for wishing to avoid a particular drug, but if they reported any high risk symptoms they were categorised as high risk irrespective of other adverse reactions. The options for reporting a reaction varied with the culprit drug to reflect variation in side-effects, and an expanded list of options was available for beta-lactams to allow further reporting on penicillin allergy (reported elsewhere). The option of reporting a reaction as anaphylaxis or another life threatening reaction was given consistently.

2. *Site survey*

Baseline data were collected from 213 sites on the number of patients eligible for inclusion on study days and on the use of wristbands for patients with drug allergies (Supplementary Materials 5).

3. *Anaesthetist study*

All anaesthetists working on elective surgery lists on study days were invited to complete the anaesthetist survey. See Supplementary Materials 6. Knowledge about drug allergy was explored using closed and scenario-based questions. Prescribing habits in the presence of opioid allergy labels were identified. All responses were anonymised and linkage to patient data collected during the study was not attempted.

Statistical analysis and data management

Patient characteristics were summarised and differences between groups compared using chi-squared tests. Univariable logistic regression was used to assess associations between predictor variables and binary outcomes. All statistical analyses were carried out in R [22] . Significance tests were two-sided, and p-values < 0.05 were considered significant. For information on REDCap and data handling see Supplementary Materials 7.

Results

Patient data

From 21,770 uploads, complete data were obtained from 21,219 patients. See Supplementary Materials 8 for patient characteristics and study flowchart. The age range and sex distribution of patients who reported allergies is shown in Figure 1.

Classification of reactions

Amongst 6,214 (29.3 %) patients there were 9,487 separate reports of a reaction to a drug or dressing. Reactions to penicillin, non-steroidal anti-inflammatory drugs (NSAIDSs) and opioids were the most commonly reported. For a complete list of all reported allergies, see Supplementary Materials 9. There was sufficient information to enable risk stratification of 8,755 reactions. Of these, 28.1% (2,462) reactions were high risk of genuine allergy, 69.3% (6,066/8,755) were classified as low risk of genuine allergy and 2.6 % (227/8,755) reactions were reported as serious, non-allergic reactions (or potential serious non-allergic adverse reactions). Table 1 shows the most frequently reported drugs and other drugs of specific interest to anaesthetists.

Univariable logistic regression identified that increasing age was associated with increased likelihood of reporting a reaction, with those in the 26-50 yrs (odds ratio (OR) 1.57, 95% CI 1.3-1.8), 51-75 yrs and >75 yrs age groups (OR 1.57, 95% CI 1.3-1.8 for both groups) more likely to report an allergy than those in the 18-25 yrs age group. Patients in the 51-75 yrs age group were more likely to report high risk reactions than those in the 18-25 yrs age group (OR 1.41,95% CI 1.13-1.79). Females were more likely to report an allergy than males (OR 2.31, 95% CI 2.2-2.5) and more likely to report a high-risk reaction than males (OR 2.11, 95% CI 1.92-2.33). The reporting of multiple (two or more) allergies was more common among females (OR=1.92, 95% CI 1.69-2.18, p-value <0.001), with 34% of females but only 21% of males reporting multiple allergies. The likelihood of reporting multiple allergies also increased with age; OR 1.48 (95% CI 1.05-2.13) in the 26-50 yrs age group, 1.82 (95% CI 1.30-2.59) in the 51-75 yrs age group and 1.95 (95% CI 1.38-2.81) in the > 75 yr age group.

Urticaria/angioedema and atopy

We identified patients who reported a tendency to develop urticaria (hives) and/or angioedema. This history indicates a possible underlying diagnosis of chronic spontaneous urticaria, a common condition resulting in episodes of urticaria/angioedema which are non-allergic in origin, with flares typically precipitated by infection, heat or stress. [23] It is extremely common for these symptoms to be misattributed to allergy by patients and clinicians. We found that a history consistent with chronic spontaneous urticaria was reported by 5.7% of the total study population (1215 of 21,219)

and was associated with a more than doubling of the risk of reporting drug allergy (OR 2.68, 95% CI 2.4-3) p <0.01).

We also sought to determine the incidence of self-reported drug allergy in the presence of atopy (defined as hayfever, eczema, rhinitis, asthma or dust allergy), in order to explore the widely held belief that atopy increases the likelihood of drug allergy. Of all patients, 35.0 % (7419 of 21,219) gave a history of atopy and within this group the likelihood of reporting a drug allergy was increased (OR 1.5, 95% CI 1.4-1.6).

The effect of reported reactions on perioperative prescribing

One thousand and two patients reported 1316 reactions to opioid drugs, with many reporting allergies to multiple drugs within the opioid family. The most frequently reported culprits were codeine (434, 32.9%), tramadol (291, 22.0 %), morphine (275, 20.9%) and co-codamol (147, 11.2%). A total of 37 patients reported reactions which were high-risk for genuine allergy. Of these, 29 were reports of anaphylaxis or a potentially life-threatening reaction and 10 were reports of blistering or skin peeling. See Table 2 for the nature of reported opioid reactions.

Among 916 patients eligible for follow-up, data were returned for 832 (91.0 %). Of these, 655 (78.7%) received an opioid perioperatively and within this group 76 (9.1 %) were given the specific opioid to which they had reported a previous reaction. Of the 37 patients (4.4 %) who had reported a previous life-threatening reaction, 32 (86.5%) were given an opioid perioperatively. Following structured chart review, no patient with a reported opioid allergy suffered suspected anaphylaxis perioperatively.

Terminology used to describe reactions

We recorded the terminology used by patients when describing their reactions to drugs or dressings. Of the 2462 reactions which were stratified as high risk, 2409 were reported as either allergy or sensitivity. Of the 2409, 2305 (96%) were reported as an allergy and 104 (4%) were reported as a sensitivity. Of the 6066 reactions which were stratified as low risk, 5715 were reported as either allergy or sensitivity. Of the 5715, 4459 (78%) were reported as allergy, and 1256 (22%) were reported as a sensitivity.

Site data on wristband use

The National Patient Safety Agency has issued guidance around the use of wristbands to denote patient alerts, including allergy. [24] Of 213 sites, 112 (52.6 %) used wristbands to indicate an allergy but without displaying the reported allergen on the wristband; 56 (26.3 %) used wristbands displaying a named allergen and 45 sites (21.1 %) did not use wristbands to indicate allergy. At 165/168 (98%) sites which use the wristband to indicate allergy, wristbands are red, but at 3 (1.8 %) these are white.

Anaesthetist data

Questionnaire responses were returned by 4798 anaesthetists. Not all questions were answered by all anaesthetists; where variation occurs in the denominator this represents the number answering the question. There were no additional unreported responses e.g. 'don't know'. Of 4793 returning data on seniority, 63.6 % (3051) were consultant grade, 23.6 % (1129) were in training posts, 12.3 % (590) were in non-training posts and 0.49% (23) were anaesthetic practitioners.

Variation existed in the preoperative discussion of allergy. Of 4756 anaesthetists, 31.0 % (1473) stated they routinely discuss the risk of allergy with patients, 29.6 % (1407) discuss this only if describing rare complications of anaesthesia, and 39.4 % (1876) only discuss this if a patient specifically asks about allergy.

Anaesthetists were asked how they would convey the risk of perioperative allergy. Of 4763 respondents, 42.8 % (2052) describe the risk as 'rare' and of 4752 respondents, 38.5% (1831) describe the risk as less than 1:10,000. See Figure 2.

Anaesthetists' prescribing habits in the presence of egg, soy and nut allergies were explored. There are historical reports linking these food allergies to anaesthetic drug allergies, subsequently proven to be incorrect. [25] Nevertheless, 1537/4745 (32.4 %) respondents would avoid propofol in the presence of these specific food allergies.

Anaesthetists were asked about prescribing habits in the context of patients undergoing a painful procedure who report an opioid allergy where reported symptoms are consistent with side effects (nausea, constipation, or minor itching). Of 4697 respondents, 2382 (50.7%) would prescribe opioids

but with additional prophylaxis such as an antiemetic, 48.3% (2269) would 'always' avoid the specific opioid(s) detailed but would prescribe alternative opioids, 39.4% (1850) would prescribe opioids as usual, 13.2% (619) would prescribe synthetic / semi-synthetic opioids, and 19 (0.4%) would avoid all opioids regardless of the nature of the allergy label.

Discussion

This study identifies for the first time the incidence and potential impact of patient-reported drug allergies in a large elective surgical cohort in the UK. We determined that nearly one third of elective surgical patients carry a drug allergy label and that even using a cautious risk assessment process, the majority of reported allergies are at low risk of being genuine. This supports previous work suggesting that many or most reported allergies are not found to be genuine when tested.[15-17] Drug allergies were most commonly reported to antibiotics, NSAIDs and opioids and were more common in older, female patients. These findings are in keeping with previous studies [8-14] but the reasons for them are unknown. One possibility is that older patients have had a greater number of potentially sensitising drug exposures, with antibiotics and analgesics some of the most frequently used drugs. Once a label has been applied to a patient it is unlikely to be removed and therefore drug allergy labels tend to accumulate over a patient's lifetime. In addition, older patients are more likely to be subject to polypharmacy which increases the likelihood of adverse drug reactions. We also found that reactions were more commonly described as a sensitivity rather than an allergy by patients if the reaction was subsequently stratified as being at low risk of representing genuine allergy.

We aimed to determine how drug allergy labels affect patient outcomes by examining the specific impact of opioid allergy labels on perioperative prescribing. We found that the majority of anaesthetists still administer opioids to patients with an opioid allergy label who are undergoing a painful surgical procedure, although half would avoid the specific opioid to which the patient has reported a reaction. In contrast, penicillin allergy labels are almost always upheld and alternative non-penicillin antibiotics used. [18] This might reflect the greater familiarity anaesthetists have with common opioid side effects such as nausea and transient, localised flushing at the injection site secondary to histamine release, combined with a lack of suitable alternatives for painful surgery. By comparison, there is usually a readily available alternative for penicillin and therefore few immediately obvious downsides to avoiding it.

We found that almost 6% of our study population gave a history suggestive of chronic spontaneous urticaria, in keeping with the literature. [23] Amongst this group, the likelihood of reporting drug allergy was more than doubled. In such patients, reported drug allergies typically result from non-allergic

triggers for the symptoms of their underlying condition, such as concurrent infection or stress. Chronic spontaneous urticaria is widely unrecognised by patients and their healthcare providers, with symptoms commonly misattributed to allergy. Our findings illustrate the potential impact of this diagnosis on false reporting of drug allergy and highlights the need to improve awareness of the condition. We also found increased reporting of drug allergy amongst those with a history of atopy. The reasons for this are not clear, since atopy is not a risk factor for drug allergy. [1]

Of the 213 sites, 112 (52.6 %) use wristbands to indicate the presence of allergy, but not to detail the allergen or nature of reaction. This is in line with NICE and NPSA guidance. However, we found potentially dangerous variation in practice across the UK, in particular the inconsistent use of red wristbands to denote this serious patient safety issue.

Knowledge and behaviour around drug allergy have been demonstrated to be poor amongst healthcare professionals, with deficiencies in education at all levels. [26-28] In this study, we found variation in anaesthetists' discussion of the risk of allergy with patients, with only 31% doing so routinely. The incidence of anaphylaxis is typically quoted as 1:10,000 but this is likely to be a significant underestimate.[29] We explored other key attitudes and behaviours among one third of practising anaesthetists in the UK and identified important knowledge gaps, for example, the persistent belief that particular food allergies preclude the use of propofol. This historical concern has long been proven to be unfounded, yet perpetuates within anaesthetic practice. [25] This may reflect the length of time required for knowledge to disseminate through the anaesthetic community or may indicate disproportionate concern about perioperative drug allergy. Our findings highlight the need for education around this and other aspects of perioperative drug allergy. This adds to findings from the 6th National Audit Project [30] in which knowledge gaps such as the relative risk of allergy from different drugs and various aspects of anaphylaxis management were identified.

When making prescribing decisions in the presence of a drug allergy label, there is an apparent discrepancy in the perception of risk between different drugs. Our data suggest that nearly 80% of patients with an opioid allergy label are prescribed intraoperative opioids, although often a different one to the suspected culprit. In contrast, data from this study presented elsewhere demonstrates that only 6% of patients with a penicillin allergy label received penicillin when this was the first-line prophylactic antimicrobial choice. It is of note that no patient receiving either penicillin or opioid, in the presence of an allergy label to this, suffered a suspected perioperative allergic reaction.

Limitations

The most significant limitation is the lack of long-term follow-up data to determine the impact of allergy labels on patient outcomes. Secondly, the risk stratification process was necessarily brief, lacking sufficient detail to confirm or refute any diagnosis of hypersensitivity in the participants. The options for reporting a reaction in the patient study varied to reflect varying drug-specific side effects and there is the possibility of misclassification. Only with further diagnostic evaluation by an allergist could the true incidence of allergy be determined. However, it is probable that an even greater proportion of labels would be identified as false following investigation. Thirdly, we were unable to risk stratify all reported allergic reactions since some drugs/substances were not included within the patient questionnaire.

Conclusions

The prevalence of patient-reported drug allergy in the UK elective surgical population is almost 30%, with antibiotics and analgesics the most commonly implicated drugs. The majority of labels are incorrect, but their presence may nevertheless impact negatively on perioperative prescribing in ways which have not yet been fully elucidated. Prescribing behaviour amongst anaesthetists appears to vary depending on the drug reported and the nature of the reaction, and this inconsistency has the potential to lead to unsafe prescribing. Further research is needed to understand the long term impact of drug allergy labels in the surgical population and to identify effective pathways for preoperative allergy testing.

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References

1. World Allergy Organisation. Definition and classification of adverse drug reactions. Available from http://worldallergy.org/education-and-programs/education/allergic-disease-resource-center (accessed 10 Jan 2021).

2. Demoly P, Adkinson NF, Brockow K *et al*. International Consensus on drug allergy. *Allergy.* 2014; **69**: 420–37.

3.Blumenthal KG, Ryan EE, Li Y, Lee H, Kuhlen JL, Shenoy ES. The Impact of a Reported Penicillin Allergy on Surgical Site Infection Risk. *Clin Infect Dis* 2018; **66** :329-36.

4.West RM, Smith CJ, Pavitt SH *et al*. 'Warning: allergic to penicillin': association between penicillin allergy status in 2.3 million NHS general practice electronic health records, antibiotic prescribing and health outcomes. *J Antimicrob Chemother*. 2019; **74**: 2075–82.

5.Blumenthal KG, Na L, Yuqing Z *et al*. Risk of meticillin resistant *Staphylococcus aureus* and *Clostridium difficile* in patients with a documented penicillin allergy: population based matched cohort study *BMJ.* 2018; **361** :k2400

6.Knezevic B, Sprigg D, Seet, J *et al*. The revolving door: antibiotic allergy labelling in a tertiary care centre. *Intern Med J*. 2016: **46**: 1276-83.

7. Zhou L, Dhopeshwarkar N, Blumenthal KG *et al*. Drug allergies documented in electronic health records of a large healthcare system. *Allergy*. 2016;**71**:1305-13.

8.Hung OR, Bands C, Laney G *et al*. Drug allergies in the surgical population. *Can J Anaesth.* 1994; **41**:1149-55.

9.Gomes E, Cardoso MF, Praça F, Gomes L, Mariño E, Demoly P. Self-reported drug allergy in a general adult Portuguese population. *Clin Exp Allergy*. 2004; **34**:1597-601.

10.Tamayo E, Alvarez FJ, Castrodeza J *et al*. Self-reported drug allergies and the diagnostic work-up in the surgical population. *J Eval Clin Pract*. 2010; **16**:902-4.

11. Velicković J, Palibrk I, Miljković B et al. Self-reported drug allergies in the surgical population in Serbia. *Acta Clin Croat*. 2015; **54**: 492-9.

12. Sousa-Pinto B, Fonseca J, Gomes E. Frequency of self-reported drug allergy. A systematic review with meta-analysis and meta-regression. *Ann Allergy Asthma Immunol*. 2017; **119**: 362-73

13. Blumenthal KG, Lai KH, Huang M, Wallace ZS, Wickner PG, Zhou L. Adverse and Hypersensitivity Reactions to Prescription Nonsteroidal Anti-Inflammatory Agents in a Large Health Care System. *J Allergy Clin Immunol Pract*. 2017; **5**:737-743.

14. MacPherson RD, Willcox C, Chow C, Wang A. Anaesthetist's responses to patients' self-reported drug allergies. *Br J Anaesth.* 2006; **97**: 634–39.

15.Santurino BH, Conde JM, Morán MTC, Canelo JAM, Medina AA. A Predictive Model for the Diagnosis of Allergic Drug Reactions According to the Medical History. *J Allergy Clin Imm: In Prac*. 2016; **4**: 292-300. e3

16. Thong BY, Leong KP, Tang CY, Chng HH. Drug allergy in a general hospital: Results of a novel prospective inpatient reporting system. *Ann Allergy Asthma Immunol*. 2003; **90**: 342-7.

17. Macy E, Ngor EW. Safely Diagnosing Clinically Significant Penicillin Allergy Using Only Penicilloyl-Poly-Lysine, Penicillin, and Oral Amoxicillin. *J All Clin Imm: In Prac*. 2013; **1**; 258-63.

18. Savic L, Thomas C, Fallaha D *et al*. DALES, Drug Allergy Labels in Elective Surgical patients: a prospective multicentre cross-sectional study of incidence, risks, and attitudes in penicillin de-labelling strategies. *Br J Anaesth*. 2020;**125**: 962-969.

19. Research and Audit Federation of Trainees. Available from http://www.niaa.org.uk/research-and-audit-federation-of-trainees-RAFT (accessed 10 Jan 2021).

20. Harris P, Taylor R, Thielke R et al. Research electronic data capture (REDCap) – A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009; **42**:377-81.

21. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies.
J Clin Epidemiol. 2008; **61**:344-9.

22. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. Available from https://www.r-project.org (accessed 10 Jan 2021).

23. Powell R. Leech SC, Till S, Huber PAJ, Nasser SM, Clark AT. BSACI guideline for the management of chronic urticaria and angioedema. *Clin Exp Allergy*. 2015; **45**: 547– 65.

24. National Health Service Improvement. *Safer practice notice; standardising wristbands improves safety*. National Patient Safety Agency, London, 2007.

25. Harper NJN. Propofol and food allergy. *Br J Anaesth*. 2016; **116**: 11-13.

26.Vorobeichik L, Weber E, Tarshis J. Misconceptions surrounding penicillin allergy; implications for anaesthesiologists. *Anaesth Analg*. 2018; **127**: 642-9

27. Young C. What underlies the unconscious negative attitude of healthcare professionals towards patient-reported drug allergies? *Drugs Ther Perspect*. 2017; **33**: 345-7.

28.Stukus DR, Green T, Montandon SV, Wada KJ. Deficits in allergy knowledge among physicians at academic medical centers. *Ann Allergy Asthma Immunol*. 2015;**115**:51-55.

29. Mertes PM, Ebo DG, Garcez T *et al*. Comparative epidemiology of suspected perioperative hypersensitivity reactions. *Brit J Anaesth*. 2019; **123**: e16-28.

30. Kemp HI, Cook TM, Thomas M, Harper NJN. UK anaesthetists' experiences and perspectives of severe perioperative anaphylaxis: NAP6 baseline survey. *Br J Anaesth*. 2017; **119**: 132-39.

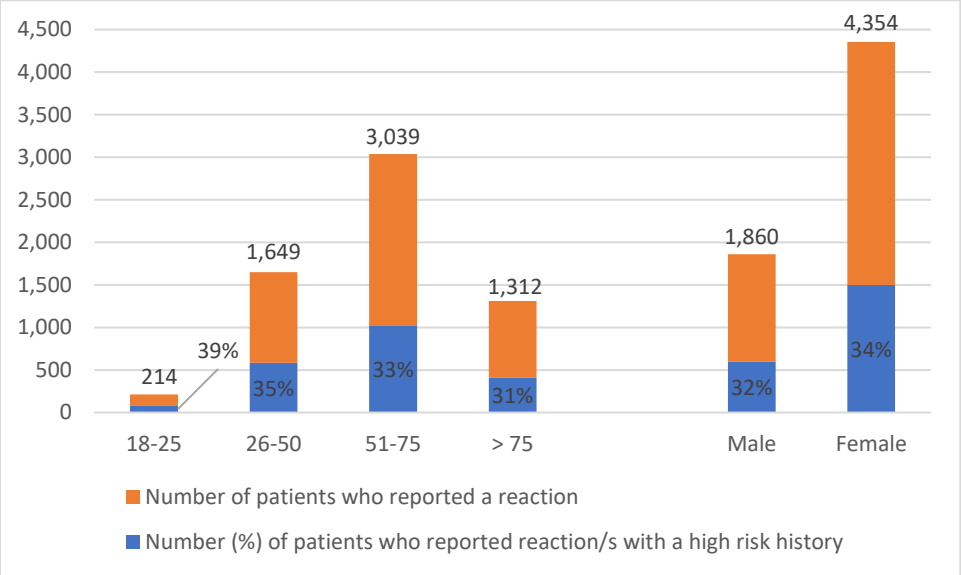


Figure 1: Age and sex distribution of patients reporting allergies to drugs or dressings

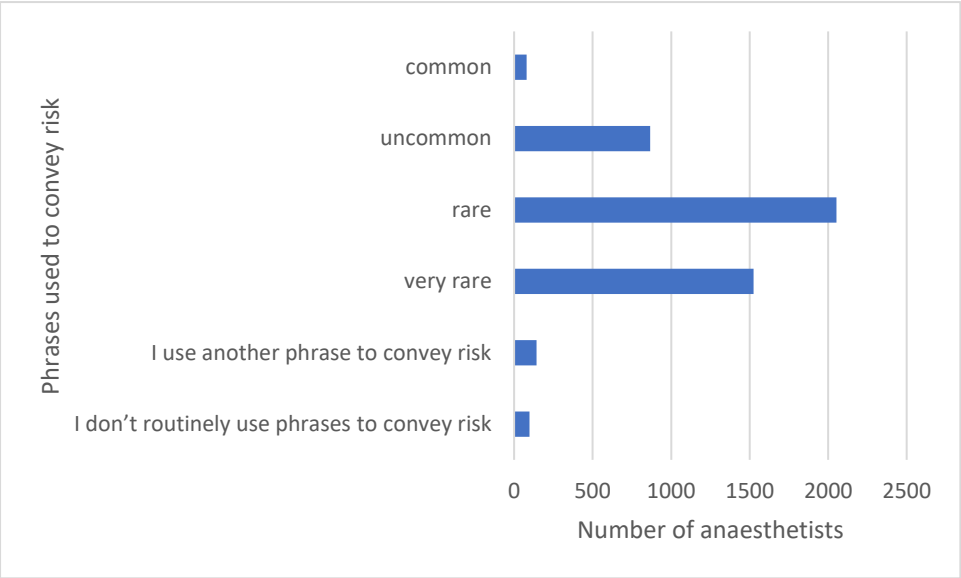
Implicated substance	**Number of patients reporting a reaction**	**Number (%) of high risk reactions**	**Number (%) of low risk reactions**	**Number (%) of serious non-allergic reactions or avoided**
Penicillin	2,626	1,418 (54)	1,208 (46)	0
Non-steroidal anti-inflammatory drugs*	1,044	389 (34)	540 (47)	211 (19)
Opioids*	1,002	70 (5)	1,244 (94)	2 (0.2)
Other antibiotics*	923	142 (13)	966 (86)	3 (0.3)
Dressings or tapes	844	3 (0.4)	841 (99.6)	0
Latex	261	116 (44)	145 (56)	0
Other analgesics*	173	42 (24)	131 (74)	3 (2)
Statins	143	4 (3)	139 (97)	0
Angiotensin converting enzyme (ACE) inhibitors	134	36 (27)	98 (73)	0
Iodine ***	101	66 (65)	35 (35)	0
Further drugs of anaesthetic interest				
Antihistamines	62	6 (10)	56 (90)	0

Contrast media	46	34 (74)	11 (24)	1 (2)
Local anaesthetics	30	18 (60)	12 (40)	0
Neuromuscular blocking agents *	21	7 (26)	16 (59)	4 (15)
Medical dyes	20	14 (70)	6 (30)	0
Chlorhexidine	15	11 (73)	4 (27)	0
Intravenous anaesthetics **	14	2 (20)	7 (70)	1 (10)
Colloids	3	0	3 (100)	0
Syntometrine	1	0	1 (100)	0
Sugammadex	0	0	0	0

Table 1: Number of reactions reported by drug or dressing categories; 10 most frequently reported agents and further drugs of anaesthetic interest. *patients reported reactions to more than one drug in this group , ** patients reported reactions which could not be reliably classified. *** iodine source was unidentified.

Nature of opioid reaction	Frequency of report
GI Symptoms	571
Confusion and hallucinations	269
Other reaction	182
Rash or itching	154
Anaphylaxis or potentially life-threatening reaction	29
Unknown reaction	22
Respiratory depression	22
Blisters or skin peeling	10
Advised to avoid	8

Table 2: The nature of reported opioid reactions



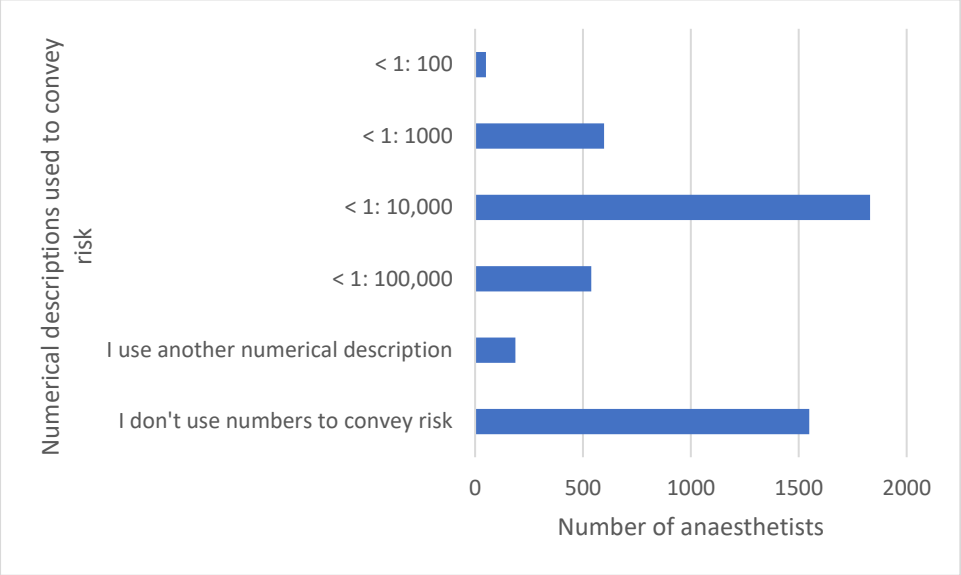


Figure 2a and b. Anaesthetist’s use of phrases (a) and numerical descriptions (b) to convey the risk of perioperative allergy.