European Journal of Pharmaceutical Sciences 213 (2025) 107240

Contents lists available at ScienceDirect

European Journal of Pharmaceutical Sciences

journal homepage: www.elsevier.com/locate/ejps

Prevalence and risk assessment of drug allergies in hospitalized patients: Potential for allergy delabeling

Robert Nacsa [a,b], Maria Matuz [a,b], Erika Papfalvi [a,c], Helga Hambalek [a,b], Roxana Ruzsa [a,b], Ni Made Amelia Ratnata Dewi [a], Edit Hajdu [d], Fruzsina Reka Ambrus [a,b], Zsoka Szikora [a,b], Ria Benko [a,b,c,*]

[a] Institute of Clinical Pharmacy, Faculty of Pharmacy, University of Szeged Szikra Street 8, Szeged, Hungary
[b] Institute of Clinical Pharmacy, Albert Szent-Györgyi Health Center, University of Szeged Semmelweis Street 6-8, Szeged, Hungary
[c] Emergency Patient Care Unit, Albert Szent-Györgyi Health Center, University of Szeged Semmelweis Street 6, Szeged, Hungary
[d] Infectology Ward, Department of Internal Medicine, Albert Szent-Györgyi Health Center, University of Szeged Állomás Street 8, Szeged, Hungary

ARTICLE INFO

Keywords:
Drug allergy
Risk assessment
Inpatient
Delabeling
Antibiotic stewardship

ABSTRACT

Background: Drug allergy prevalence is high and predicted to rise in the future. Although allergy labels are essential for patient safety, evidence supports the fact that incorrectly recorded drug allergy labels might lead to suboptimal treatments, increased healthcare costs, prolonged hospital stays, and the emergence of antimicrobial resistance (AMR). Drug allergy risk assessment and subsequent delabeling could be **a** solution for this problem. Despite the importance of this subject, the number of studies on the prevalence of drug allergies or delabeling is low, especially from Eastern European countries.

Aims: This study aimed to determine the prevalence and characteristics of drug allergies in hospitalized patients and assess the associated risk of future exposure to the reported culprit drugs to evaluate the potential for allergy delabeling.

Methods: A cross-sectional study was conducted at the tertiary care teaching hospital of University of Szeged in Hungary, involving adult inpatients across multiple surgical wards. Data collection included patient interviews using a structured questionnaire and subsequent risk assessment. Adverse drug reactions were categorized as high or low risk based on the history of the reported reaction.

Results: Of the 1522 study participants, 242 (15.90 %, 95 % CI: 14.14 - 17.82 %) patients reported at least one drug allergy, resulting in a total of 384 reported allergy cases. Among these, 277 cases were included in the risk assessment, with 252 (90.97 %) classified as low risk and eligible for potential allergy delabeling. Antibiotics were the most frequently reported culprit drug, followed by analgesics and anti-inflammatory drugs. Skin manifestations were the most common symptoms.

Conclusion: This study highlights the high prevalence of self-reported drug allergies and the significant proportion of low-risk cases suitable for delabeling. Systematic allergy evaluation and delabeling should be a key element of (antibiotic) stewardship programs.

1. Introduction

Adverse drug reactions (ADRs) are defined by the World Health Organization (WHO) as any noxious and unintended response to a drug that occurs in doses used for prevention, diagnosis, or treatment (Khan and Solensky, 2010). ADRs may be predictable type A reactions based on the known pharmacological properties of a drug, or unpredictable type B reactions (e.g. drug allergies) that are related to the individuals immunologic response or genetic heterogeneity. ("WAO White Book on Allergy | World Allergy Organization," 2012).

Abbreviations: ADR, Adverse drug reaction; WHO, World Health Organization; DA, Drug allergy; NSAID, Non-steroidal and anti-inflammatory drugs; SCAR, severe cutaneous adverse reactions; ATC, Anatomical Therapeutic Chemical; ECDC, European Center for Disease Prevention and Control.

* Corresponding author at: Szikra utca 8, Szeged, 6725, Hungary.
E-mail addresses: nacsa.robert@szte.hu (R. Nacsa), matuz.maria@szte.hu (M. Matuz), papfalvi.erika.piroska@med.u-szeged.hu (E. Papfalvi), hambalek.helga@med.u-szeged.hu (H. Hambalek), ruzsa.roxana@med.u-szeged.hu (R. Ruzsa), ni.made.amelia.ratnata.dewi@szte.hu (N.M.A.R. Dewi), horvathne.hajdu.edit@med.u-szeged.hu (E. Hajdu), ambrus.reka.fruzsina@szte.hu (F.R. Ambrus), szikora.zsoka@szte.hu (Z. Szikora), benko.ria@med.u-szeged.hu (R. Benko).

https://doi.org/10.1016/j.ejps.2025.107240
Received 16 May 2025; Received in revised form 18 August 2025; Accepted 20 August 2025
Available online 21 August 2025

ADRs may account for up to 6 % of all hospital admissions and occur in 10 to 15 % of hospitalized patients. Eighty percent of all ADRs are considered type A reactions, while the remaining 20 % are type B reactions (Thong and Tan, 2011).

Drug allergies (DA) are frequent and are expected to increase further in the future due to the increased availability of new drugs (Doña et al., 2024). The prevalence rates of patient-reported DAs are highly variable in the literature, partly due to differences in the study population: A multicenter study showed that 30 % of elective surgical patients in the United Kingdoms had a history of drug allergies (Thomas et al., 2021). Another systematic review that included not only hospitalized patients, but also outpatients and the general population showed that in average 8.3 % of the study population reported a drug allergy (Sousa-Pinto et al., 2017). Furthermore, data on the prevalence of DA may differ according to geographical regions (Doña et al., 2024).

Although drug allergy is frequently reported by patients, the consequently recorded drug allergy labels are commonly incorrect (Hierro Santurino et al., 2016; Thong et al., 2003). While properly recorded drug allergy labels are essential for patient safety, incorrect allergy labels have several negative consequences, one of which being their direct impact on patient health. Patients who are allergic to standard medications will receive an alternative second-line treatment, which may generally have lower efficacy and/or increased side effects. Furthermore, as part of their social-economic impact, allergy labels can lead to an increase in the cost of treatment, can prolong hospital stay, and in the case of antibiotics, contribute to the emergence of antimicrobial resistance (AMR) (Jones et al., 2021).

As a solution to the problem, the procedure called allergy delabeling (the removal of allergy labels) is becoming an increasingly relevant practice in the case of antibiotic allergies. This is also supported by the fact that the WHO has defined antibiotic allergy delabeling as a key point for antimicrobial stewardship (AMS) programs ("The WHO AWaRe (Access, Watch, Reserve) antibiotic book," 2022).

Determining drug allergy prevalence and identifying patients who are candidate for drug allergy delabeling is generally important in all hospitalized patients. It is especially important in surgical patients, due to the frequent use of antibiotics in terms of e.g. surgical antibacterial prophylaxis where beta-lactam antibiotics are common first choice agents.

Despite the importance of the topic, the number of studies in eastern European countries on the prevalence of drug allergies or delabeling is scarce and limited to Poland (Balińska–Miśkiewicz et al., 2006; Sztormowska et al., 2016), Macedonia (Stoleski et al., 2010) and Serbia (Velicković et al., 2015).

2. Aims

As a primary analysis, we sought to determine the prevalence of drug allergies reported by patients and the characteristics of the reported reactions. We also conducted a risk assessment as a secondary analysis, to determine the associated risks of future exposure to culprit drugs and the possibility of allergy delabeling.

3. Methods

3.1. Study design and setting

An observational, cross-sectional study was conducted in the Orthopedic, Surgical, Traumatological, and Neurosurgical Clinics of the Albert Szent-Györgyi Health Centre of the University of Szeged. Data was collected on 19 study days. We included all adult (18 years or older) patients present in the hospital on study days who had sufficient mental alertness or cognitive ability to reliably answer questions. Our main exclusion criteria were the eligibility of the allergy case for the study (e.g. we excluded the cases if the culprit agent was not a drug). Data collection was carried out in the form of patient interviews, using a preconstructed questionnaire.

3.2. Construction of the questionnaire

The questionnaire had two main domains. The first domain included general characteristics of the patient (e.g. age, sex, level of education) and regular medications. The second domain included questions on the perceived adverse drug reaction that resulted in the drug allergy label: e.g. culprit drug related information, reported symptoms, severity of the adverse reactions (including the necessity of hospital admission), timing of the reaction in relation to drug exposure, and medications used to counteract the symptoms.

The second domain was only filled out if the patient reported a DA. For every individual patient who reported an allergic reaction with a different drug, a new questionnaire was filled out.

3.3. Evaluation of the questionnaire

As part of the risk assessment, ADRs were divided into two categories (for reference, see Table 1): First, if the reported reaction occurred within 10 years and the symptoms were consistent with those of a potential immediate severe allergy (i.e. anaphylaxis), the case was classified as high risk. In the case of SCAR (severe cutaneous adverse reactions, e.g. Stephen-Johnson syndrome), we also classified the case as high risk, regardless of the time passed since the reaction. In these cases, the allergy label of patients was not considered removable, since the risk of developing a severe allergic reaction in the future is high. A second category was created for cases with a low risk of developing a future allergic reaction after exposure to the culprit drug. We classified every case as low risk in the following cases: If the ADR happened more than 10 years ago (Li et al., 2019; Shenoy et al., 2019), or the patient was not seen by a physician in relation to the reaction or did not receive any pharmacological treatment after the ADR, regardless of the symptoms.

Table 1
Risk assessment of adverse drug reactions.

	High risk	**Low risk**
Severity of the symptoms	• Symptoms of anaphylaxis (e.g.: angioedema, dyspnea, fainting / shock) within 6 h after drug exposure and less than 10 years after the reaction • Symptoms of SCAR (Even more than 10 years after the reaction) (Blisters, skin/ mucosal erosion, rash after first dose) • Other organ involvement (Even more than 10 years after the reaction) (e.g.: Hepatitis, nephritis, thrombocytopenia, hemolytic anemia)	• Typical, dose-dependent „Type A" side effects of the medication (e.g.: diarrhea after the use of antibiotics, dizziness after taking antihypertensive drugs) • Mild allergic symptoms (e.g.: rash, erythema, pruritus) more than 6 h after drug exposure • Symptoms of anaphylaxis more than 10 years after the reaction
Necessity of hospital admission and systemic DRUG treatment	• Admitted to a hospital AND received systemic DRUG treatment	• Admitted and OBSERVED/ not admitted to hospital AND did not receive systemic DRUG treatment
	Allergy label not removable	**Allergy label MIGHT BE removable after further investigation**

Patients were also classified as low risk if, based on reported symptoms or other details of the event, it was a typical mild allergic reaction symptom (e.g. morbilliform rash, without any other symptoms) or it was uncertain if the reaction was an allergic ADR. Also, if the symptoms were possible side effects of the culprit drug (type A ADR) (e.g. diarrhea developing during antibiotic treatment), the case was seen as low risk. If the allergy case was classified as low risk, the allergy label could be removed from the patient, but only after further investigation of the allergy case (e.g. skin prick test or direct oral challenge) (Copaescu et al., 2024).

Lastly, if the information provided by the patient was not enough to include the allergy case in our risk assessment, we classified the case as non-determinable.

Ethical permission (IV/3071- 1 /2021/EKU) for the study was obtained from the Scientific and Research Ethics Committee of the Medical Research Council of Hungary.

3.4. Statistical analysis

Descriptive data were presented as mean, standard deviation, minimum, maximum or proportions. For analyses of categorical variables, chi-squared test or Fischer exact test was used, as appropriate. A p-value <0.05 was considered significant. Statistical analyses were performed with IBM SPSS statistics (version 29). Sample size calculation was based on previous estimations on drug allergy prevalence and was done using an online, reliable sample size calculation tool. The optimal sample size should be between 200–400 based on our calculations (expected drug allergy prevalence of 10 %), which corresponds to the simple size of this work (error rate: 5 %, absolute error: 3 %) (Wang and Ji, 2020).

4. Results

4.1. Patient characteristics

In total, 242 patients reported to be allergic to at least one drug, this result was obtained in the following manner. A total of 1522 patients were hospitalized on study days in the included surgical wards, among them there were 28 (1.84 %) non-contactable patients. Of the remaining 1494 (98.16 %) patients, 244 reported at least one 'allergic' reaction, with a total of 401 'allergic' events. Allergy cases were excluded from analysis if the reported culprit agent was not a drug (2 patients, 5 allergy cases), or the case was a duplicate (12 allergy cases) (when patients reported the same culprit agent more than once). Finally, reported allergy cases were not included in our risk assessment if the information provided by the patients was incomplete.

Therefore, in total, 242 (15.90 %, 95 % CI: 14.14 - 17.82 %) patients reported to be allergic to at least one drug and the total number of drug allergy cases was 384. Of these, 277 allergy cases, reported by 163 patients, were included in our risk assessment analysis.

Data in the following paragraphs are from level D of Fig. 1 (Flowchart). Regarding the age distribution, the majority of our study population was above the age of 60 years (187 patients, 77.27 %). The main age was 66.36 $\pm$ 13.43 years, and a female dominance could be observed (see Table 2).

In terms of patient education, most patients' highest level of education was secondary (134 patients, 55.37 %).

The number of patients with polypharmacy (taking 5 or more medications per day) was above 50 % (124 patients, 51.24 %). More than 30 % (75 patients) of the study population took 6–10 medications and nearly 15 % (30 patients) of the patients took 10 or more different medications every day.

Most frequently, patients reported one (164 patients, 67.77 %), two (44 patients, 18.18 %), three (19 patients, 7.85 %), or even more than three (15 patients, 6.20 %) DAs. The maximum number of DAs reported by a patient was eight.

4.2. Risk assessment

Data in the following paragraphs are from level E of Fig. 1 (Flowchart). During the risk assessment process, the reported DAs were classified into high or low risk groups. Twenty-five cases (9.03 %) proved to be high risk for further drug reactions on exposure with the same active agent. More than 90 % of the patients reported cases of DA (252 cases, 90.97 %) were considered low risk, amongst which were also type A ADRs (e.g.: possible side effects of the culprit drug (61 cases, 22.02 %).

Finally, the information provided by the patients was insufficient for risk assessment in almost a third of all reported allergic cases (107 cases, 27.9 %). The most frequent reason for excluding drug allergy cases from our risk assessment was patients not remembering important details about the reaction (e.g. timeliness and/or symptoms of the reaction, the need for medical care). In total 54 allergy cases (14.1 %) were excluded from the risk assessment due to lack of information provided by the patient. Allergy cases were also excluded from the risk assessment if the symptoms of the reported reaction were similar to the symptoms of the original treated problem (53 reported allergy cases, 13.8 %) (e.g. mild skin symptoms after using iodine solution for a skin condition).

4.3. Characteristics of the culprit drugs

The most common pharmacological group reported as 'allergy inducer' was systemic antibacterial agents (ATC: J01) (102 cases, 36.82 %). The second and third most common groups were analgesics (ATC: N02) (65 cases, 23.47 %) and anti-inflammatory and anti-rheumatic products (ATC: M01) (28 cases, 10.11 %). The fourth most reported pharmacological group was anesthetics (ATC: N01) (13 cases, 4.69 %). A list of the active substances reported the most frequently can be found in Table 3. A Sankey plot of culprit agent groups and their risk assessment can be found in Fig. 2. For the full list of ATC categories with corresponding risk assessment, see Supplementary material 1.

4.4. Perceived symptoms

Regarding the symptoms experienced by the patients, skin manifestations were the most frequent (151 cases). Other typical allergy symptoms, such as itching (pruritus) (128 cases), angioedema (78 cases) and dyspnea (67 cases) were also frequently reported. Time passed since the reported reaction was a major characteristic of our risk assessment (Li et al., 2019; Shenoy et al., 2019), serious symptoms, such as angioedema, were classified as low risk if more than 10 years passed since the reaction. For prevalence of symptoms in the high/low risk categories, see Table 4.

The need for hospitalization and pharmacological treatment was also recorded. Hospital admission was required in 38 (13.72 %) cases due to the reported DA experienced by the patient, while in 76 cases (27.44 %), the reaction occurred during hospital stay. In the remaining 163 (58.84 %) cases, hospitalization was not necessary.

Time passed since the reported adverse drug reaction was a major determinant during the risk assessment. In a total of 96 reported DAs (34.66 %), no more than 10 years have passed since the reaction, of which 10 allergic events (3.61 %) occurred during the current hospital stay of the patient. In the remaining 181 cases (65.34 %), the reaction occurred more than 10 years ago.

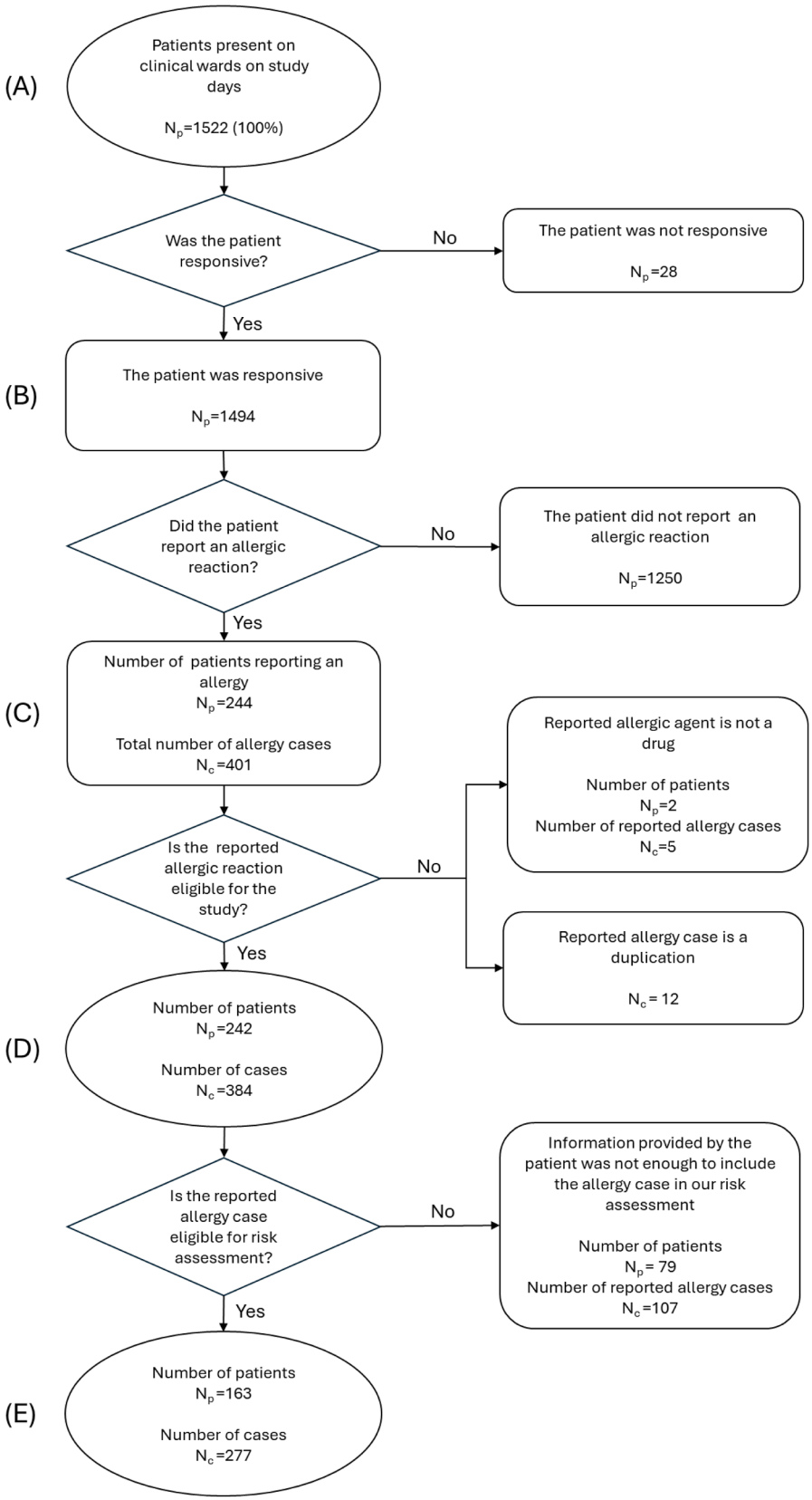

Fig. 1. Flowchart of patient inclusion.

Table 2
Main patient characteristics.

		N_p (242)	%	Mean ± SD	Min-max
Age [Years]	18–40	14	5.79		
	40–60	41	16.94		
	60+	187	77.27		
	Total	242	100	66.36 ± 13.43	19–94
Sex	Female	189	78.10		
	Male	53	21.90		
Education	Primary	76	31.40		
	Secondary	134	55.37		
	Tertiary	32	13.22		
Number of medications	0	27	11.16		
	1–2	48	19.83		
	3–5	62	25.62		
	6–10	75	30.99		
	10+	30	12.40		0–20
Number of drug allergies (DAs)	1	164	67.77		
	2	44	18.18		
	3	19	7.85		
	3+	15	6.20		1–8

Table 3
Top 10 most frequent culprit active substances.

Active substance	Low risk	High risk	Total
Penicillin (Not specified)	36	2	38
Metamizole sodium	31	1	32
Sulfamethoxazole + trimethoprim	15	0	15
Diclofenac	14	1	15
Lidocaine	14	0	14
Amoxicillin + clavulanic acid	7	4	11
Penamecillin	8	1	9
Oxytetracycline	8	0	8
Aminophenazone	7	0	7
Tolperisone	7	0	7

5. Discussion

In this study, our goal was to identify the prevalence of drug allergy (DA) in an inpatient population and conduct a risk assessment of reported DA cases. This is one of the few studies done in the Eastern European region on the prevalence of DAs (Balińska–Miśkiewicz et al., 2006; Stoleski et al., 2010; Sztormowska et al., 2016; Velicković et al., 2015). In addition, it is one of the few drug allergy risk assessment studies (Li et al., 2021; Lim et al., 2022; Vyles et al., 2017).

The prevalence of drug allergies (242 patients, 15.90 %) is in line with a review showing the results of four similar studies done in inpatient populations (Ranged between 7.5 - 23.5 %;) (Sousa-Pinto et al., 2017). Another study, similarly done in a surgical population in Serbia showed much higher rate of DAs (38.5 % versus 15.90 %) (Velicković et al., 2015).

Despite the scarcity of similar studies, some correlations can be established. In this study, the majority of the patients with reported DAs were elderly (>60 years, 77.27 %). A study done on Japanese hospitalized patients admitted to an acute general medical ward found that 69.3 % of all patients with a DA label were above the age of 65 years (Li et al., 2021). The dominance of the elderly and the corresponding high incidence of drug allergy in elderly patients have a few possible reasons behind it. One of them is the higher rate of exposure to frequently reported allergizing agents, such as antibiotics and NSAIDs (Blumenthal et al., 2017). Polypharmacy is also common among older patients, which further contributes to the increased prevalence of drug allergies (Sheikh-Taha and Asmar, 2021). In addition, allergy labels are rarely removed and thus accumulate over a lifetime (Jones et al., 2021; Lucas et al., 2019).

We also observed a female dominance among patients with reported DAs (189 patients, 78.10 %). Other studies also describe a definitive female dominance in drug allergies, regardless of the study population. A study done in the population of Lower Silesia (Poland) shows a significant female predominance for drug allergy (12.6 % in females vs. 4.9 % in males) in the total study population (Balińska–Miśkiewicz et al., 2006). In another study, which investigated the prevalence of documented drug allergies in a large healthcare system found the proportion of women to be 58 % in the study population (Zhou et al., 2016), while another study found the prevalence to be 60 % amongst patients presenting at an American emergency department (Kiechle et al., 2018) . While the exact reason behind female predominance is currently unknown some factors can be attributed to this phenomenon. For example, hormonal influences, particularly the effects of estrogens, may play a crucial role in the increased susceptibility of women to drug allergies (Triambodo et al., 2021). Furthermore, genetic factors associated with sex chromosomes may contribute to this phenomenon, as differential

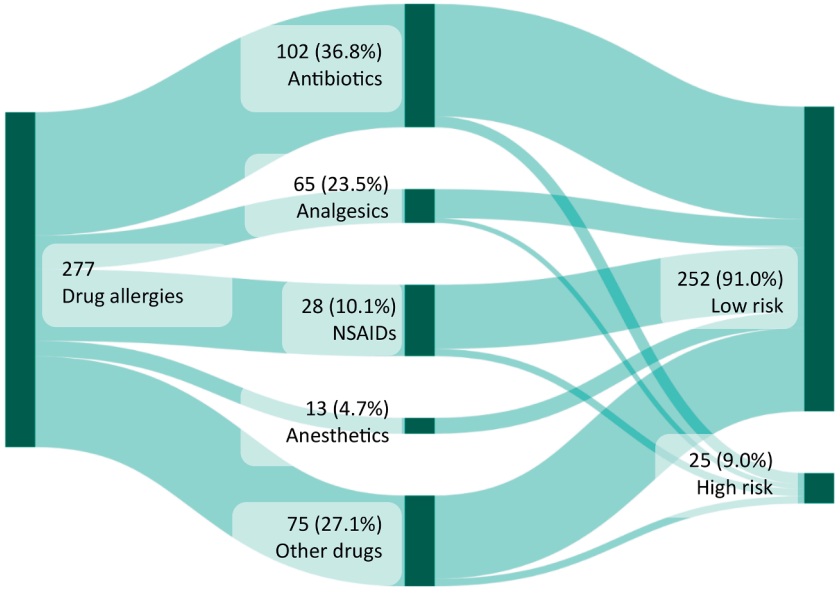

Fig. 2. Sankey plot of culprit agent groups and risk assessment.

Table 4
Reported reaction characteristics.

		High risk	Low risk	Total	
Number of allergy cases		**25 (100 %)**	**252 (100 %)**	**277**	**p**
Symptoms reported by patients	Loss of consciousness	3 (12 %)	16 (6.35 %)	19	0.394[1]
	Angioedema (e.g. swelling around the mouth or eye)	13 (52 %)	65 (25.79 %)	78	0.009[1]
	Choking, dyspnea (e.g. shortness of breath)	12 (48 %)	55 (21.83 %)	67	0.006[1]
	Spasmodic abdominal complaints	4 (16 %)	33 (13.1 %)	37	0.756[1]
	Nausea, vomiting, diarrhea	6 (24 %)	45 (17.86 %)	51	0.425[1]
	Tachycardia, hypotension (e.g. dizziness, feel of palpitation)	5 (20 %)	18 (7.14 %)	23	0.043[1]
	Skin symptoms (e.g. rash)	15 (60 %)	136 (53.97 %)	151	0.675[1]
	Itching	9 (36 %)	119 (47.22 %)	128	0.302[1]
	Oedema (limb)	3 (12 %)	21 (8.33 %)	24	0.464[1]
	Other (headache, runny nose, sneezing, fever, conjunctivitis, sweating, weakness)	3 (12 %)	40 (15.87 %)	43	0.777[1]
Age of the patients at the time of allergic reaction	0 - 14 years	1 (4 %)	33 (13.1 %)	34	$P<.001$[2]
	14 - 64 years	14 (56 %)	199 (78.97 %)	213	
	65+ years	10 (40 %)	20 (7.94 %)	30	
Time passed since the adverse drug reaction	$\leq$ 1 year	8 (32 %)	17 (6.75 %)	25	$P<.001$[2]
	1 year - 10 years	17 (68 %)	54 (21.43 %)	71	
	> 10 years	0 (0 %)	181 (71.83 %)	181	
Hospital admission was necessary due to adverse drug reaction	Yes	7 (28 %)	31 (12.3 %)	38	0.13[2]
	Allergic reaction occurred in a hospital	8 (32 %)	68 (26.98 %)	76	
	No	10 (40 %)	153 (60.71 %)	163	
Received medication to treat the adverse drug reaction	Yes	16 (64 %)	109 (43.25 %)	125	0.16[1]
	No	9 (36 %)	143 (56,75 %)	152	

[1] Fisher test.
[2] Chi-square test.

gene expression linked to sex can influence immune responses (Shah, 2012).

In all reported drug allergy cases excluded from the risk assessment analysis, either the patient did not remember important information on the reported reaction (54 patients, 14.1 %) (e.g. timeliness and/or symptoms of the reaction, the need for medical care) or the symptoms of the reported reaction were similar to the symptoms of the original treated problem (53 reported cases, 13.8 %) (e.g. mild skin symptoms after using iodine solution for a skin condition). Other studies chose to include reported drug allergy cases with missing data in their risk assessment. Rozłucka et al. included patients with remote (>10 y) unknown reactions without features of immunoglobulin E in their low risk group (Rozłucka et al., 2024) and Arikoglu et al. considered patients who provided a vague or inconclusive report and whose reaction was not observed by health care staff was considered to have a weak history (similar category to low risk) (Arikoglu et al., 2015). This strategy acknowledges the inclusion of poorly documented – but nominally low risk – cases in the risk assessment, which may improve the sensitivity for identifying allergy cases available for delabeling, but also may compromise the safety and reliability of the conducted risk assessment (Copaescu et al., 2024). Our more defensive approach might reduce the misclassification of the included allergy cases but also might underestimate the number of cases with the potential of allergy delabeling.

The most frequently reported suspected causes of allergic reactions were antibiotics (ATC3: J01,102 cases, 36.82 %), analgesics (ATC3: N02, 65 cases, 25.47 %) and anti-inflammatory and anti-rheumatic products (ATC3: M01, 28 cases, 10.11 %). This finding is consistent with other studies that identified antibiotics and analgesics as major contributors to drug allergies, although data on inpatient populations is missing. For example, among inhabitants with reported DA, the frequency of penicillin allergy was 31.9 % while analgesics allergy was 16.3 % (Balińska−Miśkiewicz et al., 2006). Another study found that among recorded drug allergies in patients presenting at an emergency department, the relative share was 47 % for antibiotics, and 17 % for analgesics. (Kiechle et al., 2018) One of the reasons behind the difference in the share of antibiotics as culprit agents (47 % in the study of Kiechle et al. vs. 34.38 % in this study) could be the differences in the study population. While our study population included inpatients requiring surgical care, an emergency department functions as a transition between outpatient and inpatient care, with a significantly more diverse patient population.

Among all antibiotic allergies, penicillins were the most frequently reported culprit agents in this study (22.38 %). Other studies also show a high prevalence of penicillin allergy. For example, in the study of Thomas et al., more than 40 % of patients with reported DAs had mentioned penicillins as the culprit drug (Thomas et al., 2021). Another study done in a surgical population in Serbia also showed that in nearly 50 % (47.6 %) of all reported DA, penicillins were named as the culprit drug (Velicković et al., 2015).

The frequent use and high penicillin exposure are partially responsible for the high prevalence of penicillin allergies and consequently explain why penicillin allergies are frequently studied. In total, 30 % of all antimicrobials for systemic use in acute care hospitals were penicillins according to the latest ECDC point prevalence survey (European Centre for Disease Prevention and Control., 2024) and recent studies in Hungarian ambulatory and hospital care sectors also highlighted that penicillins were frequently used in Hungary (Hambalek et al., 2024; Ruzsa et al., 2024). Another reason for considering penicillin and beta-lactam allergy is their important clinical implications. Patients who did not receive the preferred beta-lactam therapy due to their reported beta-lactam allergy proved to be more likely to have an adverse event, compared to those who did not report a beta-lactam allergy (unadjusted odds ratio [uOR], 3.43; 95 % confidence interval [CI], 1.48–7.96) (MacFadden et al., 2016)).

Almost 91 % (252 cases, 90.97 %) of the allergic cases included in our study proved to be low risk after risk assessment, making the removal of these 'low risk' allergy labels a possibility. Other drug allergy risk assessment studies done in inpatient populations are few in number, and the existing ones use different risk assessment tools. Because of this and differences in patient populations and study designs comparison should be done with caution. For example, a recent study conducted on the elective surgical population of the United Kingdom (Thomas et al., 2021) found that 69.3 % of all reported drug allergies are low risk. One of the reasons behind the significant difference between these findings could be that the British study did not consider the time passed since the reaction among their risk stratification criteria, while the present study considered the case "low risk" if 10 or more years passed since the allergic reaction. The approach of Thomas et al. leads to a higher

number of high-risk allergy cases, as it did not consider the importance of a temporal factor as a well-established critical determinant (Li et al., 2019; Shenoy et al., 2019). Other notable differences in the risk assessment criteria are that the British study did not include details on patient history in the survey such as the necessity of hospital admission and drug treatment for the reported reaction.

Studies that conduct risk assessment and consecutive delabeling on penicillin allergy cases show that carefully conducted delabeling is an excellent way of not only increasing patient safety, but also reducing the use of alternative medications and reducing healthcare associated costs (Alvarez-Cuesta et al., 2022; Anstey et al., 2022; Powell et al., 2023). For example, a recent meta-analysis evaluated the beneficial effects of penicillin allergy delabeling: 36 % of the included studies reported increased penicillin use after delabeling (Powell et al., 2023). The annual projected savings associated with penicillin allergy delabeling were reported between $12.400 (Beth Israel Deaconess Medical Center,) and $26.000 (UMMC) according to the same meta-analysis (Powell et al., 2023). Anstey et al. also conducted a systematic review of studies examining antibiotic allergy delabeling programs (Anstey et al., 2022) and some of their most important findings were the decreased use of vancomycin, aztreonam, aminoglycosides and fluoroquinolones (Blumenthal et al., 2015) and a significant decrease in prescribing of restricted antibiotics (3rd-/4th-generation cephalosporins, carbapenems, fluoroquinolones, glycopeptides, piperacillin/tazobactam, lincosamides, linezolid, daptomycin) (Devchand et al., 2019). Despite these benefits, studies on risk assessment of drug allergies, apart from penicillin allergies, are missing.

The negative effects of the use of alternative medications can be various in case of penicillin allergy and risk assessment matters a lot. If risk assessment is conducted, usually other beta-lactam antibiotics (e.g. cephalosporins or carbapenems) can be used as alternative medications, or in some special cases, even the culprit drug can be used again, however strategies might differ by publishing organizations ("Choice of antibiotics in penicillin-allergic hospitalized patients - UpToDate," 2024; Wijnakker et al., 2023). If risk assessment is not conducted, the use of second- or third-line antibiotic groups, such as macrolides or fluoroquinolones, may be necessary in bacterial respiratory tract infections such as tonsillopharyngitis, acute otitis media, rhinosinusitis, pneumonia, etc. where penicillins are first-line antibiotics ("The WHO AWaRe (Access, Watch, Reserve) antibiotic book," 2022). The disadvantage of fluoroquinolone use is their association with severe side effects: tendinitis, tendon rupture, peripheral neuropathy, central nervous system related reactions (e.g. seizures), and QT prolongation (Gorelik et al., 2019; Research, 2019). Macrolides can also cause serious side effects, such as cardiotoxicity and hepatotoxicity (Albert et al., 2014; Zhang et al., 2022). Another negative aspect of these antibiotics is their interaction potential. Both macrolides and fluoroquinolones have clinically relevant drug-drug interactions, primarily manifesting through the CYP 450 enzyme system. Macrolides primarily inhibit both CYP 3A4 and CYP 1A2 isoenzymes, while fluoroquinolones have inhibitory effect on CYP 1A2. Through the inhibition of these enzymes, macrolides and fluoroquinolones may alter the metabolism of other drugs but the inhibitory capacity of different active ingredients from these two antibiotic groups may differ (Fish, 2001; Pai et al., 2000). Additionally, it is important to mention the high resistance inducing potential of fluoroquinolones (Ortega et al., 2009). For example, *Escherichia coli*, the most common causative organism of urinary tract infections, shows significant resistance to fluoroquinolones, both in urine (24.7 %, Hungary's National Bacteriological Survey ("Nemzeti Bakteriológiai Surveillance (NBS)," 2023) and in invasive samples (22.0 %, (European Centre for Disease Prevention and Control., 2022)) due to the overuse of fluoroquinolones. Streptococcus pneumoniae, common causative agent of respiratory tract infections also shows high resistance to macrolides in both non-invasive (28.3 %, Hungary's National Bacteriological Survey ("Nemzeti Bakteriológiai Surveillance (NBS)," 2023) and invasive samples (17.9 % (European Centre for Disease Prevention and Control., 2022)). By contrary, the resistance data of Streptococcus pneumoniae to penicillins is low both in national (3.0 %, ("Nemzeti Bakteriológiai Surveillance (NBS)," 2023) and international reports (Between 5–10 % (European Centre for Disease Prevention and Control., 2022)). This data further underlines the use of penicillins as first line antibiotics in common infections. As there is a known correlation between the rate of antibiotic utilization and the development of antibiotic resistance (AMR), it is desirable to reduce the use of fluoroquinolones and macrolides to avoid escalation of the AMR problem, which is facilitated by DA delabeling.

Beside the described positive effects of drug allergy delabeling, the process is not without its negative effects, which, in some cases may endanger patient safety. One of the most notable risks of delabeling is the misclassification of true allergy labels, although it is an unlikely possibility in this study. The prevalence of true drug allergies is estimated to be much lower than previously thought (Hierro Santurino et al., 2016; Thong et al., 2003), but the attempted removal of these true allergy labels may have serious clinical consequences. However, it is important to mention, that the prevalence of adverse events during direct oral challenges and skin testing is low and most frequently these patients experience mild reactions (Blumenthal et al., 2024; Stul et al., 2024). Another risk of delabeling lies in the lack of validated guidelines. Even in institutions where delabeling protocols exist, such protocols are highly variable and rarely validated. This lack of standardization poses a significant complication on the implementation of delabeling protocols (Stone et al., 2020). The most commonly used validated tool is PEN-FAST, a risk assessment criterion usable in the case of penicillin allergies (Foran et al., 2024; Piotin et al., 2022), but its implementation in clinical setting is limited to pilot studies and single-center initiatives.

5.1. Limitations

One of the most important limitations of this study was the typical drawbacks of patient-reported data, such as memory distortion, that might limit accurate culprit drug identification or symptom recall in some cases. We excluded patients with insufficient information on the perceived reaction, which might cause slight underestimation of low risk patients who are candidate for drug allergy delabeling. However, this limitation does not affect the main conclusion of this work and the opposite approach has been criticized, because it compromises the safety and reliability of the conducted risk assessment (Kiechle et al., 2018). The patient population in this study can also be considered as a limitation. As our study population consists of surgical patients, direct comparison with other risk assessment studies with different patient populations or direct extrapolation to general patient population might not be possible. However, due to the frequent use of antibiotics, especially first line beta-lactam antibiotics in this patient population, potential drug allergy label removal is of special importance.

6. Conclusion

This study highlights the high prevalence of self-reported drug allergies and identifies a considerable number of low-risk cases eligible for drug allergy delabeling. Systematically re-evaluating allergy labels are essential to optimize patient care.

Funding

This work was implemented with support provided by the Ministry of Innovation and Technology of Hungary from the National Research, Development and Innovation Fund, financed by ITM NKFIA TKP2021-EGA-32.

Author declaration

We affirm that this manuscript is original, has not been published elsewhere, and is not under consideration for publication in another journal. All authors have approved the final manuscript and declared no conflicts of interest.

CRediT authorship contribution statement

Robert Nacsa: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Maria Matuz:** Writing – review & editing, Visualization, Validation, Supervision, Software, Resources, Methodology, Investigation, Data curation, Conceptualization. **Erika Papfalvi:** Writing – review & editing, Validation. **Helga Hambalek:** Writing – review & editing. **Roxana Ruzsa:** Writing – review & editing. **Ni Made Amelia Ratnata Dewi:** Writing – review & editing. **Edit Hajdu:** Writing – review & editing, Validation. **Fruzsina Reka Ambrus:** Writing – review & editing. **Zsoka Szikora:** Writing – review & editing. **Ria Benko:** Writing – review & editing, Validation, Supervision, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ejps.2025.107240.

Data availability

Data will be made available on request.

References

Albert, R.K., Schuller, J.L., COPD Clinical Research Network, 2014. Macrolide antibiotics and the risk of cardiac arrhythmias. Am. J. Respir. Crit. Care Med. 189, 1173–1180. https://doi.org/10.1164/rccm.201402-0385CI.

Alvarez-Cuesta, E., Madrigal-Burgaleta, R., Broyles, A.D., Cuesta-Herranz, J., Guzman-Melendez, M.A., Maciag, M.C., Phillips, E.J., Trubiano, J.A., Wong, J.T., Ansotegui, I., Ali, F.R., Angel-Pereira, D., Banerji, A., Berges-Gimeno, M.P., Bernal-Rubio, L., Brockow, K., Villa, R.C., Castells, M.C., Caubet, J.-C., Chang, Y.-S., Ensina, L.F., Chikhladze, M., Chiriac, A.M., Chung, W.-H., Ebisawa, M., Fernandes, B., Garvey, L.H., Gomez, M., Vera, J.G., Diaz, S.G., Hong, D.I., Ivancevich, J.C., Kang, H.-R., Khan, D.A., Kuruvilla, M., Sousa, J.I.L., Latour-Staffeld, P., Liu, A.Y., Macy, E., Malling, H.J., Maspero, J., May, S.M., Mayorga, C., Park, M.A., Peter, J., Picard, M., Rodriguez-Bouza, T., Romano, A., Sanchez-Borges, M., Tanno, L.K., Torres, M.J., Ureña-Tavera, A., Valluzzi, R.L., Volcheck, G. W., Yamaguchi, M., 2022. Standards for practical intravenous rapid drug desensitization & delabeling: a WAO committee statement. World Allergy Organization Journal 15. https://doi.org/10.1016/j.waojou.2022.100640.

Anstey, K.M., Tsao, L., Otani, I.M., 2022. Drug allergy delabeling programs: recent strategies and targeted populations. Clinic Rev Allerg Immunol 62, 484–504. https://doi.org/10.1007/s12016-021-08913-x.

Arikoglu, T., Aslan, G., Batmaz, S.B., Eskandari, G., Helvaci, I., Kuyucu, S., 2015. Diagnostic evaluation and risk factors for drug allergies in children: from clinical history to skin and challenge tests. Int. J. Clin. Pharm. 37, 583–591. https://doi.org/10.1007/s11096-015-0100-9.

Balińska−Miśkiewicz, W., Boznański, A., Liebhart, J., Małolepszy, J., Grabowski, M., Konieczny, A., 2006. Drug hypersensitivity of inhabitants in chosen Lower Silesia regions. Advances in Clinical and Experimental Medicine 15, 81–87.

Blumenthal, K.G., Lai, K.H., Huang, M., Wallace, Z.S., Wickner, P.G., Zhou, L., 2017. Adverse and hypersensitivity reactions to prescription nonsteroidal anti-inflammatory agents in a large health care system. J. Allergy Clin. Immunol.: In Practice 5, 737–743. https://doi.org/10.1016/j.jaip.2016.12.006 e3.

Blumenthal, K.G., Shenoy, E.S., Varughese, C.A., Hurwitz, S., Hooper, D.C., Banerji, A., 2015. Impact of a clinical guideline for prescribing antibiotics to inpatients reporting penicillin or cephalosporin allergy. Annals Allergy, Asthma & Immunol. 115, 294–300. https://doi.org/10.1016/j.anai.2015.05.011 e2.

Blumenthal, K.G., Smith, L.R., Mann, J.T.S., Salciccioli, I., Accarino, J.J.O., Shah, R.J., Alvi, F.I., Cardoso-Fernandes, A., Ferreira-da-Silva, R., Schunemann, H.J., Sousa-Pinto, B., 2024. Reaction risk to direct penicillin challenges: a systematic review and meta-analysis. JAMa Intern. Med. 184, 1374–1383. https://doi.org/10.1001/jamainternmed.2024.4606.

Choice of antibiotics in penicillin-allergic hospitalized patients - UpToDate [WWW Document], 2024, URL https://www.uptodate.com/contents/choice-of-antibiotics-in-penicillin-allergic-hospitalized-patients/print?search=penicillin%20allergy&source=search_result&selectedTitle=2%7E150&usage_type=default&display_rank=2 (Last update: 2024) (accessed 4.22.25).

Copaescu, A.M., Li, L., Blumenthal, K.G., Trubiano, J.A., 2024. How to define and manage low-risk drug allergy labels. J. Allergy Clin. Immunol.: In Practice 12, 1095–1106. https://doi.org/10.1016/j.jaip.2024.03.021.

Devchand, M., Kirkpatrick, C.M.J., Stevenson, W., Garrett, K., Perera, D., Khumra, S., Urbancic, K., Grayson, M.L., Trubiano, J.A., 2019. Evaluation of a pharmacist-led penicillin allergy de-labelling ward round: a novel antimicrobial stewardship intervention. J. Antimicrobial Chemotherapy 74, 1725–1730. https://doi.org/10.1093/jac/dkz082.

Doña, I., Torres, M.J., Celik, G., Phillips, E., Tanno, L.K., Castells, M., 2024. Changing patterns in the epidemiology of drug allergy. Allergy 79, 613–628. https://doi.org/10.1111/all.15970.

European Centre for Disease Prevention and Control., 2024. Point Prevalence Survey of Healthcare-Associated Infections and Antimicrobial Use in European Acute Care hospitals, 2022-2023. Publications Office, LU.

European Centre for Disease Prevention and Control, 2022. Antimicrobial Resistance in the EU/EEA (EARS-Net) - Annual Epidemiological Report for 2020. European Centre for Disease Prevention and Control., Stockholm.

Fish, D.N., 2001. Fluoroquinolone adverse effects and drug interactions. Pharmacotherapy: J. Human Pharmacol. Drug Therapy 21, 253S–272S. https://doi.org/10.1592/phco.21.16.253S.33993.

Foran, M.B., Brown, A., Thompson, J.A., Schwob, T., Padilla, B.I., Bush, M.A., 2024. Evaluation of current practice for penicillin allergy labeling using the PEN-FAST tool. Antimicrobial Stewardship Healthcare Epidemiol. 4, e161. https://doi.org/10.1017/ash.2024.382.

Gorelik, E., Masarwa, R., Perlman, A., Rotshild, V., Abbasi, M., Muszkat, M., Matok, I., 2019. Fluoroquinolones and cardiovascular risk: a Systematic review, Meta-analysis and network meta-analysis. Drug Saf. 42, 529–538. https://doi.org/10.1007/s40264-018-0751-2.

Hambalek, H., Matuz, M., Ruzsa, R., Papfalvi, E., Nacsa, R., Engi, Z., Csatordai, M., Soós, G., Hajdú, E., Csupor, D., Benkő, R., 2024. Returned rate and changed patterns of systemic antibiotic use in ambulatory care in Hungary after the pandemic—A longitudinal ecological study. Antibiotics 13, 848. https://doi.org/10.3390/antibiotics13090848.

Hierro Santurino, B., Mateos Conde, J., Cabero Morán, M.T., Mirón Canelo, J.A., Armentia Medina, A., 2016. A predictive model for the diagnosis of allergic drug reactions according to the medical history. J. Allergy Clin. Immunol.: In Practice 4, 292–300. https://doi.org/10.1016/j.jaip.2015.11.003 e3.

Jones, T.W., Fino, N., Olson, J., Hersh, A.L., 2021. The impact of beta-lactam allergy labels on hospitalized children. Infection Control Hospital Epidemiol. 42, 318–324. https://doi.org/10.1017/ice.2020.424.

Khan, D.A., Solensky, R., 2010. Drug allergy. J. Allergy Clin. Immunol. 125, S126–S137. https://doi.org/10.1016/j.jaci.2009.10.028 e1.

Kiechle, E.S., McKenna, C.M., Carter, H., Zeymo, A., Gelfand, B.W., DeGeorge, L.M., Sauter, D.A., Mazer-Amirshahi, M., 2018. Medication allergy and adverse drug reaction documentation discrepancies in an urban, academic emergency department. J. Med. Toxicol. 14, 272–277. https://doi.org/10.1007/s13181-018-0671-7.

Li, J., Cvetanovski, V., Fernando, S., 2021a. Single-step direct drug provocation testing is safe for delabelling selected non-low-risk penicillin allergy labels. Ann. Allergy Asthma Immunol. 127, 232–235. https://doi.org/10.1016/j.anai.2021.04.008.

Li, P.H., Chung, H.Y., Lau, C.S., 2021b. Epidemiology and outcomes of geriatric and non-geriatric patients with drug allergy labels in Hong Kong. Hong. Kong. Med. J. 27, 192–197. https://doi.org/10.12809/hkmj208716.

Li, P.H., Siew, L.Q.C., Thomas, I., Watts, T.J., Ue, K.L., Rutkowski, K., Lau, C.-S., 2019. Beta-lactam allergy in Chinese patients and factors predicting genuine allergy. World Allergy Organizat. J. 12. https://doi.org/10.1016/j.waojou.2019.100048.

Lim, P.P., Desai, A.P., Wessell, K.R., Moore, L., Minich, N.M., 2022. Inpatient allergy delabeling of pediatric patients with low-risk penicillin allergy status through direct graded oral amoxicillin challenge. Open. Forum. Infect. Dis. 9. https://doi.org/10.1093/ofid/ofac492.612 ofac492.612.

Lucas, M., Arnold, A., Sommerfield, A., Trevenen, M., Braconnier, L., Schilling, A., Abass, F., Slevin, L., Knezevic, B., Blyth, C., Murray, K., von Ungern-Sternberg, B., Rueter, K., 2019. Antibiotic allergy labels in children are associated with adverse clinical outcomes. J. Allergy Clin. Immunol. Pract. 7, 975–982. https://doi.org/10.1016/j.jaip.2018.09.003.

MacFadden, D.R., LaDelfa, A., Leen, J., Gold, W.L., Daneman, N., Weber, E., Al-Busaidi, I., Petrescu, D., Saltzman, I., Devlin, M., Andany, N., Leis, J.A., 2016. Impact of reported beta-lactam allergy on inpatient outcomes: a multicenter prospective cohort study. Clinical Infectious Diseases 63, 904–910. https://doi.org/10.1093/cid/ciw462.

Nemzeti Bakteriológiai Surveillance (NBS) [WWW Document], 2023, URL https://www.nnk.gov.hu/index.php/mikrobiologi/nemzeti-bakteriologiai-surveillance-nbs/category/397-escherichia-coli.html (Publication year: 2023) (accessed 1.29.25a).

Nemzeti Bakteriológiai Surveillance (NBS) [WWW Document], 2023, URL https://www.nnk.gov.hu/index.php/mikrobiologi/nemzeti-bakteriologiai-surveillance-nbs/category/394-streptococcus-pneumoniae.html (Publication year: 2023) (accessed 1.31.25b).

Nemzeti Bakteriológiai Surveillance (NBS) [WWW Document], 2023, URL https://www.nnk.gov.hu/index.php/mikrobiologia/nemzeti-bakteriologiai-surveillance-nbs/category/394-streptococcus-pneumoniae.html (Publication year: 2023) (accessed 4.13.25c).

Ortega, M., Marco, F., Soriano, A., Almela, M., Martínez, J.A., Muñoz, A., Mensa, J., 2009. Analysis of 4758 *Escherichia coli* bacteraemia episodes: predictive factors for isolation of an antibiotic-resistant strain and their impact on the outcome. J. Antimicrob. Chemotherapy 63, 568–574. https://doi.org/10.1093/jac/dkn514.

Pai, M.P., Graci, D.M., Amsden, G.W., 2000. Macrolide drug interactions: an update. Ann. Pharmacother 34, 495–513. https://doi.org/10.1345/aph.19138.

Piotin, A., Godet, J., Trubiano, J.A., Grandbastien, M., Guénard-Bilbault, L., de Blay, F., Metz-Favre, C., 2022. Predictive factors of amoxicillin immediate hypersensitivity and validation of PEN-FAST clinical decision rule. Ann. Allergy Asthma Immunol. 128, 27–32. https://doi.org/10.1016/j.anai.2021.07.005.

Powell, N., Stephens, J., Kohl, D., Owens, R., Ahmed, S., Musicha, C., Upton, M., Kent, B., Tonkin-Crine, S., Sandoe, J., 2023. The effectiveness of interventions that support penicillin allergy assessment and delabeling of adult and pediatric patients by nonallergy specialists: a systematic review and meta-analysis. Int. J. Infect. Dis. 129, 152–161. https://doi.org/10.1016/j.ijid.2022.11.026.

Research, C. for D.E. and, 2019. FDA Drug Safety Communication: FDA Updates Warnings for Oral and Injectable Fluoroquinolone Antibiotics Due to Disabling Side Effects. FDA.

Rozłucka, L., Rymarczyk, B., Gawlik, R., Glück, J., 2024. Is the anamnesis enough to de-label patients with reported beta-lactam allergy? J. Clin. Med. 13, 7267. https://doi.org/10.3390/jcm13237267.

Ruzsa, R., Benkő, R., Hambalek, H., Papfalvi, E., Csupor, D., Nacsa, R., Csatordai, M., Soós, G., Hajdú, E., Matuz, M., 2024. Hospital antibiotic consumption before and during the COVID-19 Pandemic in Hungary. Antibiotics 13, 102. https://doi.org/10.3390/antibiotics13010102.

Shah, S., 2012. Hormonal link to autoimmune allergies. ISRN. Allergy 2012, 910437. https://doi.org/10.5402/2012/910437.

Sheikh-Taha, M., Asmar, M., 2021. Polypharmacy and severe potential drug-drug interactions among older adults with cardiovascular disease in the United States. BMC. Geriatr. 21, 233. https://doi.org/10.1186/s12877-021-02183-0.

Shenoy, E.S., Macy, E., Rowe, T., Blumenthal, K.G., 2019. Evaluation and management of penicillin allergy: a review. JAMa 321, 188–199. https://doi.org/10.1001/jama.2018.19283.

Sousa-Pinto, B., Fonseca, J.A., Gomes, E.R., 2017. Frequency of self-reported drug allergy: a systematic review and meta-analysis with meta-regression. Annals of Allergy, Asthma & Immunology 119, 362–373. https://doi.org/10.1016/j.anai.2017.07.009 e2.

Stoleski, S., Bislimovska, J., Minov, J., Mijakoski, D., Risteska-Kuc, S., Marsenic, M., Milovska, S., 2010. Self-reported drug hypersensitivity among adults in the Republic of Macedonia.

Stone, C.A., Trubiano, J., Coleman, D.T., Rukasin, C.R.F., Phillips, E.J., 2020. The challenge of de-labeling penicillin allergy. Allergy 75, 273–288. https://doi.org/10.1111/all.13848.

Stul, F., Heytens, S., Ebo, D.G., Sabato, V., Piessens, V., 2024. Safe penicillin allergy delabeling in primary care: a systematic review and meta-analysis. The Journal of Allergy and Clinical Immunology: In Practice 12, 2415–2426. https://doi.org/10.1016/j.jaip.2024.06.017 e1.

Sztormowska, M., Skonieczny, P., Niedoszytko, M., Chelminska, M., Jassem, E., 2016. Comparison of the prevalence of allergic diseases and risk factors of asthma development in urban and rural Pomeranian region. Alergologia Polska - Polish J. Allergol. 3. https://doi.org/10.1016/j.alergo.2016.06.003.

The WHO AWaRe (Access, Watch, Reserve) antibiotic book [WWW Document], 2022, URL https://www.who.int/publications/i/item/9789240062382 (Publication year: 2022) (accessed 9.16.24).

Thomas, C., Clark, S., Fallaha, D., Wilson, M., Hopkins, P.M., Savic, S., Savic, L., 2021. DALES, Drug Allergy Labels in Elective Surgical patients: a prospective, multicentre cross-sectional study of prevalence, nature and anaesthetists' approach to management. Br. J. Anaesth. 127, 897–904. https://doi.org/10.1016/j.bja.2021.05.026.

Thong, B.Y.-H., Leong, K.-P., Tang, C.-Y., Chng, H.-H., 2003. Drug allergy in a general hospital: results of a novel prospective inpatient reporting system. Ann. Allergy Asthma Immunol. 90, 342–347. https://doi.org/10.1016/S1081-1206(10)61804-2.

Thong, B.Y.-H., Tan, T.-C., 2011. Epidemiology and risk factors for drug allergy. Br. J. Clin. Pharmacol. 71, 684–700. https://doi.org/10.1111/j.1365-2125.2010.03774.x.

Triambodo, B., Putera, A.M., Hermanto, B., 2021. Profile of determinant factors on drug allergy severity in Indonesian children at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. Indian J. Forensic Medic. Toxicol. 15, 2083–2088. https://doi.org/10.37506/ijfmt.v15i2.14671.

Velicković, J., Palibrk, I., Miljković, B., Velicković, D., Jovanović, B., Bumbasirević, V., Djukanović, M., Sljukić, V., 2015. Self-reported drug allergies in surgical population in Serbia. Acta Clin. Croat. 54, 492–499.

Vyles, D., Adams, J., Chiu, A., Simpson, P., Nimmer, M., Brousseau, D.C., 2017. Allergy testing in children with low-risk penicillin Allergy symptoms. Pediatrics. 140, e20170471. https://doi.org/10.1542/peds.2017-0471.

Wang, X., Ji, X., 2020. Sample size estimation in clinical research. Chest 158, S12–S20. https://doi.org/10.1016/j.chest.2020.03.010.

WAO White Book on Allergy | World Allergy Organization [WWW Document], 2012 URL https://www.researchgate.net/publication/285855670_The_WAO_white_book_on_allergy_2011-2012 (Publication year: 2012) (accessed 11.14.23).

Wijnakker, R., Van Maaren, M.S., Bode, L.G.M., Bulatovic, M., Hendriks, B.J.C., Loogman, M.C.M., Lutgens, S.P.M., Middel, A., Nieuwhof, C.M.G., Roelofsen, E.E., Schoones, J.W., Sigaloff, K.C.E., Sprikkelman, A.B., De Vrankrijker, L.M.M., De Boer, M.G.J., 2023. The Dutch Working Party on Antibiotic Policy (SWAB) guideline for the approach to suspected antibiotic allergy. Clin. Microbiol. Infect. 29, 863–875. https://doi.org/10.1016/j.cmi.2023.04.008.

Zhang, M.-Q., Zhang, J.-P., Hu, C.-Q., 2022. A rapid assessment model for liver toxicity of macrolides and an integrative evaluation for azithromycin impurities. Front. Pharmacol. 13. https://doi.org/10.3389/fphar.2022.860702.

Zhou, L., Dhopeshwarkar, N., Blumenthal, K.G., Goss, F., Topaz, M., Slight, S.P., Bates, D. W., 2016. Drug allergies documented in electronic health records of a large healthcare system. Allergy 71, 1305–1313. https://doi.org/10.1111/all.12881.