Development and Validation of a Mobile Clinical Decision Support Tool for the Diagnosis of Drug Allergy in Adults: The Drug Allergy App

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Abstract (248 words)

Background:

Penicillin allergy overdiagnosis has been associated with inappropriate antibiotic prescribing, increased antimicrobial resistance, worse clinical outcomes, and increased healthcare costs.

Objective:

The aim of this project was to develop and validate a questionnaire-based algorithm built in a mobile application to support clinicians in collecting accurate history of previous reactions and diagnosing drug allergy appropriately.

Methods:

A survey was completed by 164 medical and nonmedical prescribers to understand barriers to best practice. Based upon the survey recommendations; we created a 10-item questionnaire-based algorithm to allow classification of drug allergy history in line with the National Institute for Health and Care Excellence guidelines on drug allergy. The algorithm was incorporated into a mobile application and retrospectively validated using anonymised clinical databases at a regional Immunology and Dermatology Centres in Manchester, UK.

Results:

The important findings from our survey: 55.2% of prescribers (95%CI 47-63.4%) thought that it is not possible to draw a firm conclusion based on history alone and 59.4% (95%CI 51.4-67.5%) felt that, regardless of the details of the penicillin allergy history, they will avoid all beta-lactams. A Drug Allergy mobile application was

developed and retrospectively validated revealing a low risk for misclassification of outcomes compared to gold standard drug allergy investigations in the allergy and dermatology clinics.

Conclusion:

Perceived lack of time and preparedness to collect an accurate drug allergy history appear to be important barriers to appropriate antimicrobial prescribing. The Drug Allergy App may represent a useful clinical decision support tool to diagnose drug allergy correctly and support appropriate antibiotic prescribing.

What is already known about this topic?

The burden and impact of penicillin and antibiotic allergies have been established by many studies. However, the main problem is how to implement a safe clinical decision support tool to de-label patients with inaccurate penicillin allergy.

What does this article add to our knowledge?

This article summarises the development and retrospective validation of a mobile clinical decision support tool for the diagnosis of drug allergy to be used by clinicians to de-label individuals with inaccurate penicillin allergy label.

How does this study impact current management guidelines?

The Drug Allergy App may represent a useful clinical decision support tool for non-allergists to diagnose drug allergy correctly and support appropriate antibiotic prescribing as an attempt to address antimicrobial stewardship.

Key words

Algorithm, Drug Allergy Application, Drug Allergy App, Drug allergy, decision support tool, gold standard allergy test, inaccurate penicillin allergy, NICE, Prescribers, Survey, Retrospective Validation

Abbreviations

AGEP: Acute Generalised Exanthematous Pustulosis

AR: Augmented Reality

BCU: Birmingham City University

C diff: Clostridium difficile

DevOps: Development Operations

DRESS: Drug Rash Eosinophilia and Systemic Symptoms syndrome

EAAC: European Academy of Allergy and Clinical Immunology

FRCPath: Fellowship of the Royal College of Pathologists

HEE: Health Education England

IgE: Immunoglobulin E

iOS: Apple Operating System

IRAS: Integrated Research Application System

MBBS: Bachelor of medicine & surgery

MFT: Manchester University NHS Foundation Trust

MRCP: Membership of the Royal College of Physician

MRSA: Methicillin Resistant Staphylococcus aureus

MSSA: Methicillin Sensitive Staphylococcous aureus

NHS: National Health Service

NICE: The National Institute for Health and Care Excellence

NPV: Negative Predictive Value

PenA: Penicillin allergy

PPV: Positive Predictive Value

SDLC: Software Development Lifecycle

SJS: Stevens-Johnson syndrome

TEN: Toxic Epidermal Necrolysis

VR: Virtual reality

VRE: Vancomycin-resistant Enterococcus

Introduction

Drug allergies are commonly reported, especially penicillin allergy (PenA)[1,2]. Many patients are inaccurately labelled as being penicillin allergic[1,2]. Penicillins are the preferred option for treatment of many common and serious infections[3,4]. From previous studies and our work in this project ~10% of the general population and ~15% of inpatients carry a PenA label[2-7], however, following specialist allergy tests,[7-9] 90-99% of people with such a label are proven to tolerate penicillin[8]. Many factors have been found to be associated to inaccurate PenA, including knowledge gaps, lack of training in allergy medicine amongst healthcare professionals[9,10] and errors in documentation[11,12]. Inaccurate PenA limits treatment options, can lead to medication errors, suboptimal management and result in increased morbidity, mortality, prolonged hospitalisation, increased costs and the risk of multi-resistant microorganisms such as Methicillin Resistant Staphylococcus aureus (MRSA) and Clostridium difficile (C diff).[13-15]

Antimicrobial resistance is currently on the UK national risk register and is a high priority area for the European Commission and United Nations. It is, however, not

possible to exclude allergy in everyone with inaccurate PenA as the required investigations are labour intensive, require specialist allergy input and there is a high demand for Immunology and Allergy services in the UK and world wide[16-18]. Consequently, current standard of care involves administration of second line antibiotics with all the cost and complications associated with them.[17,18]

The impact of penicillin allergy label and evidence of strategic thinking:

A large body of evidence demonstrated the negative clinical and economic impact of inaccurate PenA labelling (see table [i], supplemental online repository [A]).

Our intervention is in line with one of the key priorities for implementation identified in the NICE clinical guidance [183][18]. In addition, based upon our work on this project and the emerging evidence from other studies (table [i], supplemental online repository [A]); we estimated that 25 -30% of patients with an PenA allergy label can be de-labelled on the basis of clinical history alone, i.e. without the need for the drug allergy investigations in the allergy and dermatology clinics. We started a quality improvement project with the aim of improving the accuracy of drug allergy diagnosis and antimicrobial prescribing in patients with a label of PenA. As part of this quality improvement project we carried out a survey of medical and non-medical prescribers to identify barriers to best practice and possible solutions. Based on the results of the survey we developed a diagnostic algorithm and incorporated the algorithm into a mobile application that we named ‘The Drug Allergy App’ as a decision support tool.

Objectives:

Primary Objectives:

1. To explore practical aspects of developing a mobile clinical decision support tool (Drug Allergy Application) for the diagnosis of drug allergy to be used by clinicians (non-allergists) to de-label individuals with inaccurate penicillin allergy label
2. To retrospectively validate the Drug Allergy Application algorithm using anonymised clinical databases of drug allergy challenges and delayed hypersensitivity reactions at the regional Immunology and Dermatology Centres at Salford Royal NHS Foundation Trust.

Secondary Objectives:

1. The Drug Allergy Application will guide drug allergy history taking and documentation. It will also serve as an educational platform that encourages safe medical practice and reinforce good behaviour.
2. The classification generated by the Drug Allergy Application will assist in de-labelling patients with inaccurate penicillin allergy history

Methods & Results

Trust wide survey of medical and non-medical prescribers on management of patients with a history of penicillin allergy

A 20-item online survey was developed using SurveyMonkey.com and was sent via email to ‘1511’medical and non-medical prescribers at Manchester University NHS Foundation Trust (MFT). The survey investigated prescriber’s knowledge of penicillin allergy diagnosis and management, their views about the barriers to correct

management and the improvement interventions that we are planning to implement in the Trust. Summary of the results is included in Figure 1.

A total 164 prescribers responded to the survey (11% uptake rate):

- Doctors in training 47.6%
- Consultants 44.5%
- Non-medical prescribers 7.9%

Questions on cross-reactivity rates with other beta-lactams in patients reporting a previous history of penicillin allergy, the median estimates from the survey report were: 10% for ceftriaxone and 5% for meropenem.

Most respondents 56.1% (95%CI 47.9-64.3%) were not aware of the availability of penicillin allergy testing in the hospital. Among those that were aware of it, 63.9% (95%CI 51.9-76%) had not referred any penicillin-allergic patient to Immunology during the past year.

Barriers to accurate allergy history collection

- 55.2% (95%CI 47-63.4%) thought that it is not possible to draw a firm conclusion based on history alone

- 59.4% (95%CI 51.4-67.5%) agreed with the statement saying that, regardless of the details of the allergy history, it is always better to “play it safe” and to avoid all beta-lactams in patients labelled as being penicillin-allergic.

Among the interventions proposed; practical educational sessions, an interactive questionnaire to guide allergy history taking and classification and a modified antibiotic policy to guide prescribing based on the allergy classification, were all rated as useful (average score >7 on a scale from 1 - not useful at all - to 10 – very useful)

Figure 1. Summary of the trust wide survey of medical and non-medical prescribers on management of patients with a history of penicillin allergy

Development of a clinical algorithm based on the NICE Clinical Guidance [183][18]:

We designed a clinical algorithm based on The National Institute for Health and Care Excellence (NICE) clinical guidance [183][19] for drug allergy: diagnosis and management. The clinical algorithm was written in a simple format for prescribers to ask their patients a few questions that allow classification of a previous drug reaction into one of five outcomes (Appendix A &B):

1) Type I (IgE mediated, immediate onset) allergic reactions, e.g. Anaphylaxis.
2) Delayed severe allergic reaction, e.g. Stevens-Johnson syndrome.
3) Delayed non-severe allergic reaction, e.g. benign delayed drug eruption.
4) History not suggestive of an allergic reaction, e.g. gastrointestinal intolerance.
5) Unable to classify, allergic reaction cannot be excluded.

Development of the Drug Allergy Application (The App)

Overall description

User's workshops were conducted to collect prescribers' views to improve the algorithm. Based on the feedback collected, the algorithm was updated, and the mobile application was developed to facilitate efficient drug allergy recognition and learning. The application starts with a welcome page, from where the user can go to 'The Questionnaire' or 'About Us' page. The other pages in the application are: Definitions, Outcomes, Settings, Terms and Conditions, Questionnaire, Questionnaire Outcomes. The algorithm analyses the responses to each question and provides and outcome.

User's workshops and feedback

Four user's workshops were undertaken to obtain constructive and tailored feedback to optimise the Drug Allergy Application questions before development of the mobile application. Two hundred participants took part at these workshops; participants included pharmacists, foundation trainee doctors, core medical trainee doctors, speciality trainee doctors, specialist immunology and allergy nurses, immunology and allergy specialist registrars and immunology and allergy consultants.

Motivation for development

The evolution of digital technologies, leading to development of collaborative systems to empower and engage the communities to experiment and learn the innovative solutions of real-world problems[27] have inspired this project by bringing healthcare, technology and innovation together to develop a digital decision support tool, the Drug Allergy App. We chose to develop a mobile application as opposed to an interactive website to allow remote and easy access/use of the algorithm. For developing this application, the following steps[27,28] were undertaken:

- Requirements' assessment
- Application design & development
- Usability study.

Requirements' assessment

The requirements of the system were gathered as follows (Figure 2):

- Cross-platform: application should run on both iOS and Android.
- User friendly design: the application should be easy to use by non-technical users.
- High usability to enhance learning and drug allergy recognition.

- Option for visual impairments and users with special requirements.

Figure 2 shows a Use Case diagram, which is a representation of a user's interaction with the system.

System Design

The first stage for developing the application with a good user experience was working on wireframes before starting the development stage. Wireframes (Figure 3a) were used to present information that will be displayed on the page and give an outline of the structure and layout of each page in the application as well as convey the overall direction and description of the user interface. Visual designs (Figure 3b) were then created based on these wireframes to work on the appearance of the application, colour choices, fonts, and graphics. An example of these can be seen in Figures 3a and 3b.

Figure 3a shows an example of wireframe, Figure 3b shows an example of a visual design creating during the System design stages.

Development methods

The algorithm was implemented to be used in a mobile application, with the usage scenario of rapidly changing hospital setting in mind. Considering this, the application was written similarly to web application which allows it to be transformed into a fully formed website with minimal changes required.[29]

Data structure

Data structures in computing are a way of organising information to enable its storage and retrieval within software artefacts. Once the data types are decided upon, the ways of storing and retrieval data can be investigated. The data flow in the

program needs to be considered (Figure [i] - Supplemental online repository [B]). For the Drug Allergy App, a stateful application was chosen, which allows saving data from one session to be used in the next session, hence allowing further data analysis for research purposes. All answers provided whist using the questionnaire along with outcomes were recorded anonymously.

Deployment

Currently there are three primary platforms; as reviewed by Tsai et al[31], the largest portion of mobile operating system market share is taken by Google's Android (88.1%), followed by Apple's iOS (12.7%), and Microsoft's Windows Mobile platform (0.8%). This application was designed and developed to be deployed on Google's Android and Apple's iOS, as they cover most of the today's market.

We chose a framework called Flutter which allows simultaneous deployment to both platforms. This was a strategic choice because developing an application for both platforms separately means duplicating the workload, hence doubling the development time, which was avoided using this framework. Deployment portals are Android Store and Apple App Store, both of which come with a layer of guidelines to help assure the quality for end-user. All requirements for deployment were satisfied and met.

Retrospective validation of the drug allergy Application's algorithm

Recruitment procedure

Anonymised clinical databases of drug allergy challenges at the regional Immunology Centre and delayed hypersensitivity reactions at the regional dermatology Centre at Salford Royal NHS Foundation Trust in the period December 2015 to December 2020 were reviewed and analysed.

All outcome measures were recorded electronically and stored in a secure area. The electronic database was completely anonymised, and password protected. The medical records (clinical notes during inpatient admission and outpatient clinic letters) of all patients with a confirmed diagnosis of drug hypersensitivity reactions (including immediate and delayed severe or non-severe) by dermatologists, allergists or immunologists were reviewed.

Study protocol

Inclusion Criteria:

• All Adult patients who have undertaken drug allergy challenges at the regional Immunology Centre at Salford Royal NHS Foundation Trust during the period December 2015 to December 2020.

• All Adult patients who have been treated for delayed hypersensitivity reactions at the regional Dermatology Centre at Salford Royal NHS Foundation Trust during the period December 2015 to December 2020.

Exclusion Criteria:

• All patients younger than 18 years old.

• Patients who have not completed their investigations either at the regional Immunology centre (Skin and/or intradermal and allergy challenges) or Dermatology centre (diagnosis confirmed by consultant dermatologist) at Salford Royal NHS Foundation Trust to reach their final diagnoses.

• Patients who were diagnosed with drug hypersensitivities by non-specialists (i.e. not immunologists, allergists nor dermatologists).

Equality

This validation study is limited to patients treated at the regional Immunology & Dermatology Centres at one NHS Trust which may limit the generalisability of the study findings to other settings. However, a prospective multicentre validation study is proposed to be conducted in the future.

Consent procedure

This is a retrospective study involved analysis of data previously collected as part of normal routine care. The anonymised data was used to retrospectively validate the Drug Allergy Application algorithm. Consent from individual patients is therefore not required as the data was collected retrospectively by clinicians working within the same hospital (Salford Royal Foundation Trust).

Regulatory and Ethical Considerations

Study conduct

The study was conducted in accordance with the UK Policy Framework for Health and Social Care Research and other applicable guidance.

The study was approved by Health Research Authority (HRA) – [IRAS Project ID (287385), protocol number S21HSR01-S, REC reference 20/HRA/6378].

Statistical analyses and data handling

Descriptive analysis was undertaken as follows:

- Sensitivity (proportion of patients, with a confirmed diagnosis of type I or delayed severe allergic reactions correctly identified by the algorithm)
- Specificity (proportion of patients with negative drug allergy testing and no history of delayed severe allergic reactions) identified by the algorithm as

having either history not suggestive of drug allergy or allergic reaction cannot be excluded based on history alone.

- Negative predictive value (NPV – proportion of algorithm-negative cases, i.e. Negative drug allergy testing and no history of delayed severe allergic reactions
- Positive predictive value (PPV – proportion of algorithm- positive cases, i.e. Confirmed diagnosis of type I or delayed severe allergic reactions.

The Drug Allergy Application algorithm was validated using the anonymised clinical databases as stated above. The outcomes have been compared to the gold standard testing to calculate the sensitivity, specificity, NPV and PPV.

To diagnose type I (Immediate -IgE mediated) allergic reactions, gold standard testing include skin and/or intradermal drug allergy testing followed by drug challenges)

To diagnose delayed severe allergic reactions, gold standard testing is skin biopsy and/or confirmation of the diagnosis by consultant dermatologist.

Demographics:

Positive control: n=100. This group include all patients with a confirmed diagnosis of drug allergy by specialist (Drug Allergy App Outcomes 1 and 2).

Males (n=46/100) and females (n=54/100)

Mean age = 47 years old, (20 to 75 years old)

Ethnicity:

Asian = 7 patients, Black = 15 patients, White = 64 patients, Others = 14 patients

(others: include all the rest of ethnic minority groups who classify themselves as not black or Asian)

Negative control: n=100. This group include all patients for whom the diagnosis of drug allergy was confidently excluded by specialists (Drug Allergy App Outcomes 4 and 5)

Males (n=47/100) and females (n=53/100)

Mean age = 50 years old, (20 to 75 years old)

Ethnicity:

Asian = 17 patients, Black = 17 patients, White = 50 patients, Others = 16 patients

(others: include all the rest of ethnic minority groups who classify themselves as not black or Asian)

Descriptive analysis:

Summary of all the outcomes generated by the Drug Allergy App were included in table1.

Table 1. Summary of the outcomes generated by the Drug Allergy App

Table 2. Drug allergy App – outcome 1 (History suggestive of a type I (Immediate) Allergic reaction:

Sensitivity = True Positives / (True Positives + False Negatives)

= TP / (TP + FN)

= 67/67+17

= 79.7% (~ 80%)

Specificity = True Negatives / (True Negatives + False Positives)

= TN / (TN + FP)

= 100/100+17

= 85 %

PPV = True Positives / (True Positives + False Positives)

= TP / (TP + FP)

= 67/84

= 79.7% (~ 80%)

NPV = True Negatives / (True Negatives + False Negatives)

= TN / (TN + FN)

= 100/(100+0)

= 100%

Table 3. Drug allergy App – outcome 2 (History suggestive of a delayed severe Allergic reaction):

Sensitivity = True Positives / (True Positives + False Negatives)

= TP / (TP + FN)

= 33/33+0

= 100%

Specificity = True Negatives / (True Negatives + False Positives)

= TN / (TN + FP)

= 100/100+0

= 100%

PPV = True Positives / (True Positives + False Positives)

= TP / (TP + FP)

= 33/33+0

= 100%

NPV = True Negatives / (True Negatives + False Negatives)

= TN / (TN + FN)

= 100/(100+0)

= 100%

There were no available data on delayed non-severe allergic reaction (Outcome 3) to record at this retrospective validation. This outcome will be further validated at the next stage of the prospective validation.

Table 4. Drug allergy App – outcome 4 & 5 (Patients with negative drug allergy testing and no history of delayed severe allergic reactions)

Sensitivity = True Positives / (True Positives + False Negatives)

= TP / (TP + FN)

= 100/100+17

= 85%

Specificity = True Negatives / (True Negatives + False Positives)

= TN / (TN + FP)

= 67/67+0

= 100%

PPV = True Positives / (True Positives + False Positives)

= TP / (TP + FP)

= 100/100+0

= 100%

NPV = True Negatives / (True Negatives + False Negatives)

= TN / (TN + FN) = 67/(67+17) = 79.7% (~ 80%)

Due to the selection bias, there were only 4 patients with outcome (4) where the history was not suggestive of an allergic reaction. We recognise that all the patients included in this retrospective study were referred to regional immunology and dermatology centres, majority of patients with “history not suggestive of an allergic reaction” would not make it to drug challenges; as the de-labelling process will take place at the first clinical consultation. Hence none of these patients will require the gold standard testing at the allergy clinics i.e. skin and/or intradermal drug allergy

testing followed by drug challenges. At the next stage of the prospective validation of the Drug Allergy App by clinicians on the “shop floor” i.e. acute medical and surgical settings, higher percentage of outcome (4) will be expected where the delabelling process can take place at the first clinical consultation. Outcome (5) is when allergic reactions cannot be excluded based on history alone is included in this control group as the final diagnosis of drug allergy was confidently excluded by specialists (immunology, dermatology or allergy consultants) implementing the gold standard testing.

Discussion:

The burden and impact of penicillin and antibiotic allergies have been established by many studies (table [i], supplemental online repository [A]). However, the main challenge is how to implement a safe clinical decision support tool to de-label patients with inaccurate PenA; moreover, given the limited numbers of allergy and immunology services in the United Kingdom[18]. This huge task cannot be undertaken by immunologists and allergists across the United Kingdom; hence the way forward is to empower non-immunologists & non-allergists to champion this process.

Attempts by non-immunologists & non-allergists to de-label penicillin allergy across the Globe:

There have been many successful attempts to establish a risk stratification pathways (table [i], supplemental online repository [A]); approximately 25 to 30% of patients with penicillin allergy label could have been delabelled[32] on the basis of clinical history alone, without the need for allergy tests; several studies[33,34] have explored models of non-specialist PenA delabelling. Studies have taken place in emergency department, inpatient (pharmacy led), preoperative and in the outpatient settings.

The risk stratification processes, inclusion and exclusion criteria have varied[33,35]. Delabelling has been based on history alone in some cases, and others have included skin testing and / or direct oral challenge testing. The outcomes have overall been positive with very few adverse reactions, all of which would be classified as mild without any cases of anaphylaxis or delayed severe hypersensitivity occurring[33]. A recent systematic review[33] confirms the safety of direct oral provocation, after risk assessment, in low risk non-specialist cohorts. The global experience is strongly supportive of non-specialist delabelling using risk assessment and/or decision support tools such as our proposed Drug Allergy App. The British Society for Allergy and Clinical Immunology (BSACI) is encouraging such practice and there are current plans of setting up a national working group to address this issue of inaccurate PenA by empowering non-immunologists and non-allergists to champion these initiatives[36].

A validated Drug Allergy App – what is next?

In addition to improved patient safety, this intervention might lead to future cost savings. According to NICE guidance costing statement 183[18], correct identification of drug allergy may reduce costs by preventing further reactions, some of which could be severe or fatal. In addition, fewer people would be prescribed inappropriate treatments that are sometimes at higher cost due to a false recording of drug allergy (see table [i], supplemental online repository [A]).

By empowering non-immunologists & non-allergists to correctly identify patients with drug allergies via using the drug allergy App; a subsequent increase in referrals to Immunology and allergy services would be inevitable; the capacity within such services would need to be increased. The increase in referrals would result in

increased costs in the short-term; however, there are future benefits and costs avoided in the medium/long-term that may offset these temporary pressures.
For example, in a patient with inaccurate PenA and frequent requirement for antibiotic therapy (e.g. due to diabetic foot infection), the cost of a specialist allergy outpatient appointment to undertake the gold standard testing (skin and/or intradermal drug allergy testing followed by drug challenges) might be lower than the cost of alternative more expensive and less effective antimicrobial options, that can result in increased toxicity and prolonged hospitalisation.
We are proposing a clinical flow chart incorporating the Drug Allergy App as a useful clinical decision support tool for non-allergists to diagnose drug allergy correctly and encourage referrals to drug allergy services as appropriate in order to support appropriate antibiotic prescribing as an attempt to address antimicrobial stewardship.

Figure 4. A proposed clinical flow chart incorporating the Drug Allergy App as a clinical decision support tool for non-allergists to accurately diagnose drug allergy and encourage referrals as appropriate.

Moreover, this drug Allergy App can be a platform that enhances visual presentation and user interaction which could be further improved by including VR/AR technology (Virtual reality/Augmented reality). This would not only facilitate learning through 3D representations of potential allergy symptoms, but also improve accuracy for intuitively recognising allergies and various skin manifestations in such patients.
Recent work in innovative research is using machine learning algorithms to automate and improve medical investigation and diagnosis such as histological images of

human colorectal cancer, digital mammograms[37] and COVID19 chest X-ray images[38].

Limitation of the retrospective validation of the drug allergy Application algorithm:

The retrospective validation of the algorithm has some limitations. Data may be subject to error due to low quality or missing information; however, we have excluded all patients who have not completed the gold standard investigations to reach final diagnoses such as the graded oral challenge to penicillins, and in case of delayed hypersensitivity reactions; all cases should have been diagnosed by consultant dermatologist. All obtained data was of high quality and adequate for the purpose of this project.

This validation study is limited to patients treated at a regional Immunology & Dermatology centres at one large NHS hospital; due to selection bias; generalisability of the study findings to other settings might be limited. However, a prospective multicentre validation study is proposed to be conducted in the near future.

Conclusion

From our survey of prescribers, there was an obvious tendency to adopt an over-cautious approach to prescribing alternative beta-lactams in patients with reported penicillin allergy.

Because of all the issues that may result from inaccurate PenA label such as suboptimal management and increase in morbidity, mortality, prolongation of hospital admissions and increased costs on one hand and the inabilities to do allergy tests on everyone with inaccurate PenA; we designed a clinical algorithm based upon NICE

classification of drug allergy to make the de-labelling process easier and safer to non-immunologists and non-allergists via the drug allergy App. The algorithm has the lowest risk for misclassification of outcomes compared to gold standard drug allergy investigations in the allergy and dermatology clinics. The Drug Allergy App may represent a useful clinical decision support tool for clinicians to diagnose drug allergy correctly and support appropriate antibiotic prescribing. Further work is required to confirm the utility of this tool in clinical practice.

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Table 1. Summary of the outcomes generated by the Drug Allergy App

Study group	Outcomes generated by the mobile application algorithm					
	Type I (immediate) Allergy	Delayed Severe Allergic reaction	Delayed NON- Severe Allergic reaction	History not suggestive of allergy	Unable to classify based on History alone	
Confirmed Type 1 (immediate) allergic reactions	67	0	0	0	0	67
Confirmed Delayed severe allergic reactions	0	33	0	0	0	33
Patients with negative drug allergy testing and no history of delayed severe allergic reactions	17	0	0	4	79	100
	84	33	0	4	79	200

Table 2. Drug allergy App – outcome 1 (History suggestive of a type I (Immediate) Allergic reaction:

	Type I (immediate) Allergy confirmed	**Type I (immediate) Allergy excluded**	**Total**
Application outcome 1	67 (TP)	17 (FP)	84
Application outcome 4,5	0 (FN)	100 (TN)	100
Total	67	117	184

Table 3. Drug allergy App – outcome 2 (History suggestive of a delayed severe Allergic reaction):

	Delayed Severe Allergic reaction confirmed	Delayed Severe Allergic reaction excluded	Total
Application outcome 2	33 (TP)	0 (FP)	33
Application outcome 4,5	0 (FN)	100 (TN)	100
Total	33	100	133

Table 4. Drug allergy App – outcome 4 & 5 (Patients with negative drug allergy testing and no history of delayed severe allergic reactions)

	Patients with negative drug allergy testing and no history of delayed severe allergic reactions	Patients with positive drug allergy testing	Total
Application outcome 4,5	100 (TP)	0 (FP)	100
Application outcome 1	17(FN)	67 (TN)	84
Total	117	67	184