

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

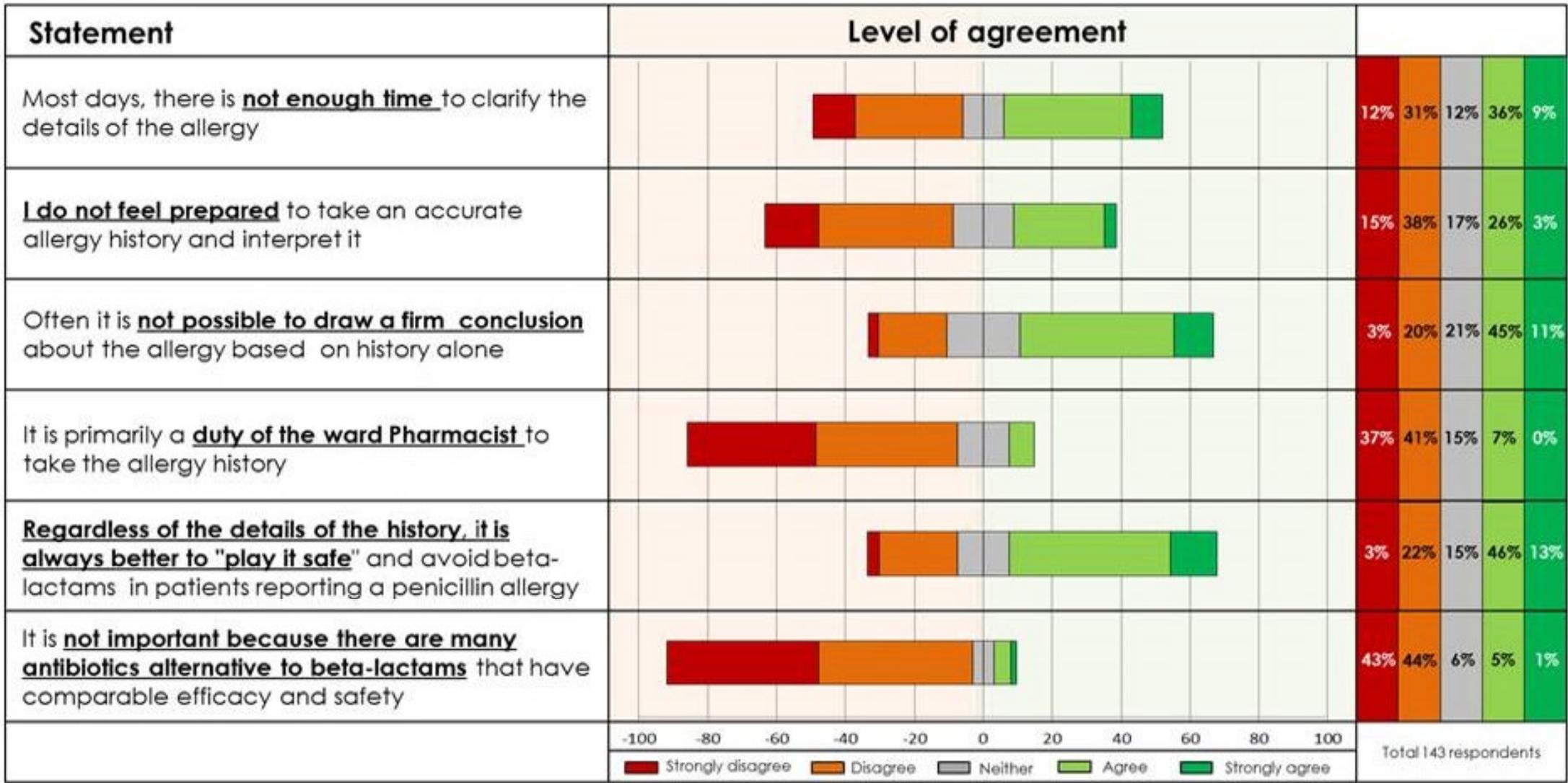


Figure 2 shows a Use Case diagram, which is a representation of a user's interaction with the system.

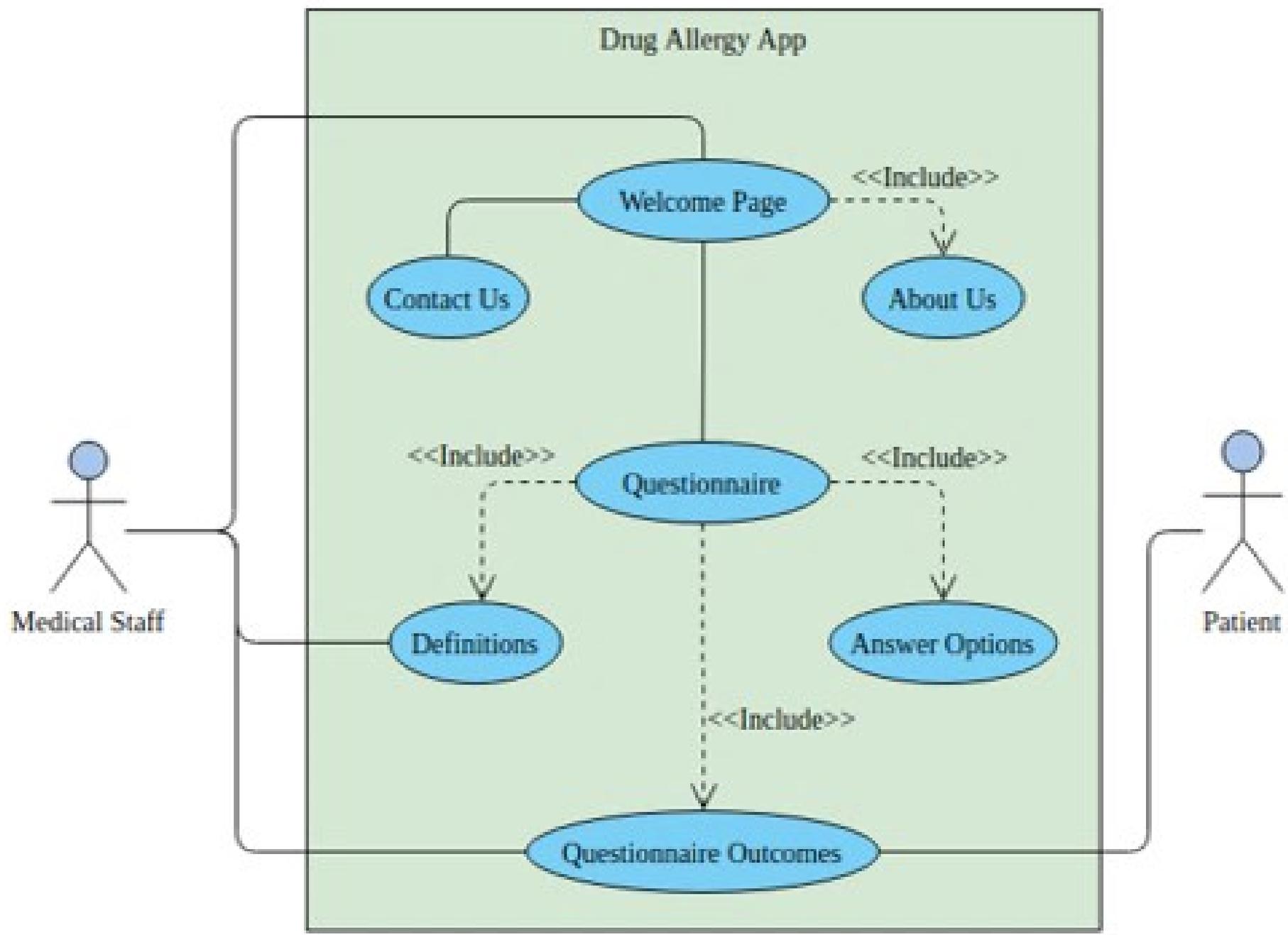


Figure 3a shows an example of wireframe, Figure 3b shows an example of a visual design creating during the System design stages.



Figure 3a

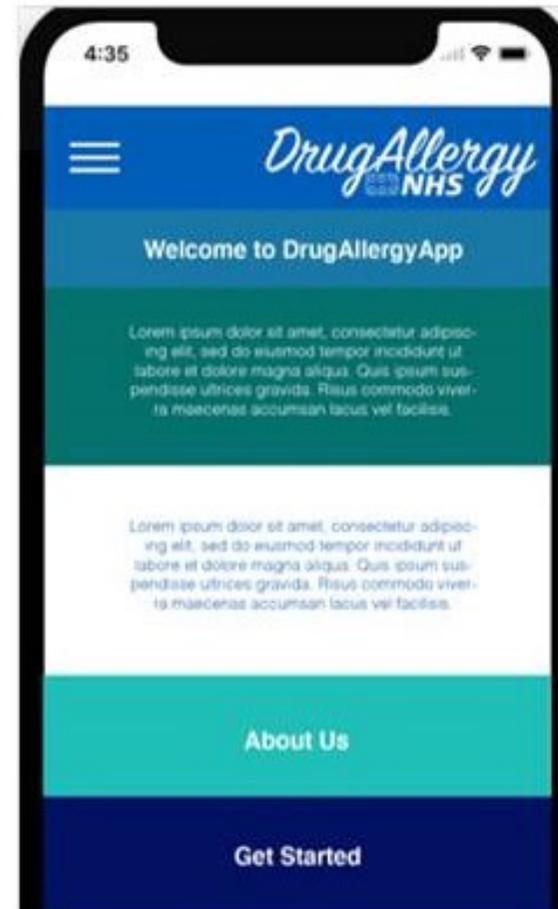


Figure 3b

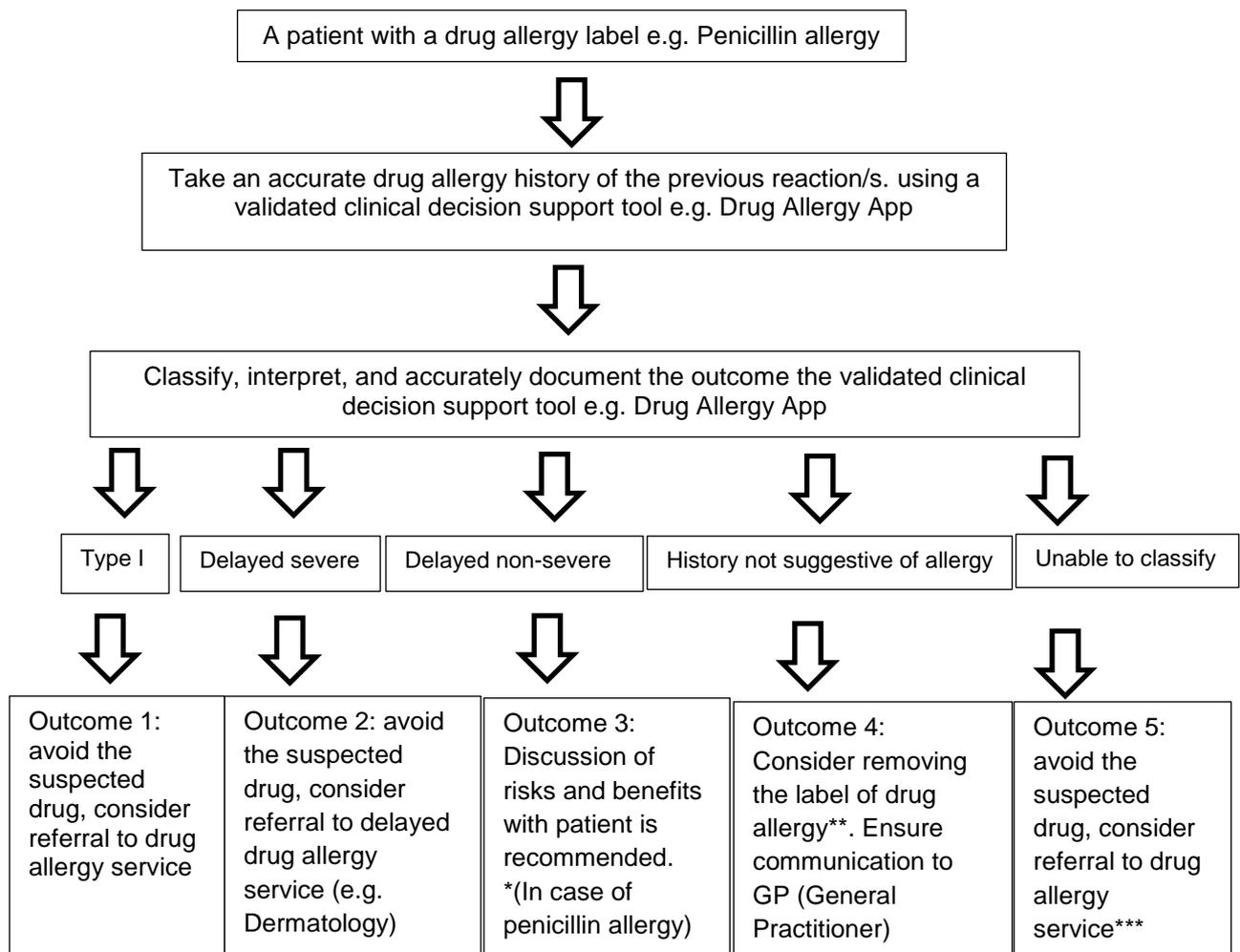


Figure 4. A proposed clinical flow chart incorporating the Drug Allergy App as a clinical decision support tool for non-allergists to accurately diagnose drug allergy and encourage referrals as appropriate.

\* In case of penicillin allergy, use of 2<sup>nd</sup> or 3<sup>rd</sup> generation cephalosporins with low risk of cross reactivity (e.g. cefuroxime & ceftriaxone) or carbapenems is unlikely to result in serious allergic reactions.

\*\* Examples included, gastrointestinal intolerance, such as diarrhoea or nausea. If the suspected drug is indicated the same medication can be given following discussion with patient. Delabelling of drug allergy can take place at this stage of clinical consultation.

\*\*\* In case of penicillin allergy, use of alternative  $\beta$ -lactam antibiotics should be discussed with drug allergy or infection specialists on a case by case basis. Discussing the risks and benefits with patient is recommended

# Supplemental online repository [A]

**Table [i].** A summary of some of the recent published studies and reports that have established the impact of penicillin allergy label vs de-labelling upon patients, clinicians, hospitals and communities. *MSSA\** *Methicillin Sensitive Staphylococcus aureus*; *C diff\*\**: *Clostridium difficile*; *MRSA\*\*\**: *Methicillin Resistant Staphylococcus aureus*; *VRE\*\*\*\**: *Vancomycin-resistant Enterococcus*

Reference	Description	Summary and recommendations
Powell et al 2020, UK <sup>2</sup>	Multi-variable log-linear modelling was used to determine associations between patients labelled as penicillin allergic and total antibiotic costs and length of stay in 750-bed NHS Hospital.	Patients with a penicillin allergy record accounted for an excess antibiotic spend of £10,637 (2.61% of annual antibiotic drug spend) and 3522 excess bed-days (3.87% of annual bed-days). Delabelling 50% of patients with a self-reported penicillin allergy record would save an estimated £5501 in antibiotic costs and £503,932 through reduced excess bed-days.
Sousa-Pinto et al 2020, Portugal <sup>22</sup>	An economic evaluation study. Models were built to project the economic impact of (1) Perform diagnostic testing (drug challenges, with or without skin tests) and (2) Do not perform diagnostic testing.	Penicillin allergy testing was found to be cost-saving in all decision models built. Allergy testing resulted in average savings of \$657 for inpatients (United States of America: \$1444, Europe: \$489) and \$2746 for outpatients (United States of America: \$256, Europe: \$6045). 75% of simulations obtained through probabilistic sensitivity analysis identified testing as the less costly option. Hence, supporting the adoption of policies promoting widespread testing of patients with a penicillin allergy label.
Blumenthal et al 2020, USA <sup>23</sup>	The prevalence and impact of a reported penicillin allergy in high-cost, high-need (HCHN) patients using multivariable logistic regression models.	20% (383) out of 1870 patients have reported penicillin allergy which has resulted in 4-fold increased odds of beta-lactam alternative antibiotic use with all the potential associated complications. A detailed drug allergy evaluation to optimize antibiotic use in these high risk patients is recommended to reduce cost and improve quality of life.
Blumenthal et al 2020, USA <sup>24</sup>	a multisite prospective study of patients seen for drug allergy at the first sites of the United States Drug Allergy Registry (USDAR)	Patients with a label of drug or antibiotic allergy were concerned about their options for receiving medical treatment, new medications, developing an allergic reaction; addressing these concerns may have great impact on patient journey and engagement with drug allergy testing.
Chan et al 2020, Hong Kong <sup>25</sup>	A total of 6081 Rheumatology patients were recruited. Prevalence and clinical outcomes of reported Drug Allergies were calculated and compared to control cohort.	The prevalence of reported Drug Allergies was found to be significantly higher in rheumatology patients, which was found to be associated with increased rate of infection-related admissions.
Vyles et al, 2020, USA <sup>26</sup>	The Public Health Impact and Safety of De-labelling	Prescription costs are 30 to 40% higher in Children with suspected Penicillin allergy. Estimated savings of prescribing amoxicillin instead of cefdinir for 50%

	Children with Reported Penicillin Allergy.	of children with otitis media would result in annual savings exceeding \$34 million.
Shenoy ES et al, 2019, USA <sup>7</sup>	Literature review of the current practice of evaluation and management of penicillin allergy	Consequences of penicillin allergy label were concluded as: Less effective agent chosen e.g. vancomycin for MSSA*, More surgical site infections when non-Penicillins used for peri-operative prophylaxis, More susceptibility to develop multi-resistant organisms and increased healthcare costs.
Moran R et, 2019, Australia <sup>3</sup>	A literature review of the current impacts of inaccurate antibiotic allergy labelling in hospitalised and critically ill adults.	15-25% inpatients have an antibiotic allergy label, even higher in immunocompromised; 30-40% did not receive first line antibiotics and resultant significant delay in time to first antibiotic (50 minutes). For critically ill patients the problem magnified; often time-critical decisions delayed whilst detailed allergy history was not available.
Blumenthal et al. 2018, USA <sup>15</sup>	Estimated cost of penicillin allergy evaluation using time-driven activity-based costing.	Lower cost estimates were achieved when only a graded drug challenge was performed in comparison to the detailed penicillin evaluation. For drug test with direct challenge only by nurse the cost was \$40. For consultant led challenge with skin testing beforehand cost was \$220. Estimated cost of penicillin allergy label during acute admission with inaccurate antibiotics allergy label and subsequent adverse events, treatment failure, health care associated infection \$3023 - \$14269 per patient
Macy E et al. 2014, USA <sup>12</sup>	Retrospective matched cohort study of subjects admitted to Kaiser Foundation hospitals in Southern California, in the period of 2010-2012.	Cases with penicillin allergy resulted in: 0.59 more total hospital days, significantly more treatments with fluoroquinolones, clindamycin and vancomycin, 23% more C diff**, 14.1% more MRSA***, 30.1% more VRE****.
Li M et al 2014 UK <sup>17</sup>	Pharmaco-economic analysis of prescribing alternative antibiotics in patients with a diagnostic label of 'penicillin allergy'.	102 patients were assessed. Total cost of antibiotics prescribed for patients with penicillin allergy was 1.82-2.58-fold higher than for first-line antibiotics. Estimated saving on antimicrobials for 41 patients if penicillin allergy label removed £5851 to £14472. Extrapolating data for Heart of England Foundation Trust translates to annual cost saving of £225 056 to £556 640 for antibiotic acquisition alone (for estimated 1577 patients)
Charneski L et al, 2011, USA <sup>5</sup>	Logistic/multiple regression models used to assess the association of allergy label with length of stay; admission to ICU; number of antimicrobials received; readmission within 4 weeks; death during hospitalisation adjusting for covariates	A total of 11,872 adults admitted to nonsurgical patient care wards who received at least one antimicrobial. On average; Length of stay was 1.21 days longer in patients with allergy label. Odd ratio of ICU admission was 1.4, 95% confidence interval [CI] (1.21-1.67). Odds ratio of needing more than one antimicrobial 1.6, 95% CI (1.43-1.81). And a 1.6-fold higher risk of dying during the hospitalization (crude OR 1.56, 95% CI 1.20-2.04).