

Title: Prevalence of drug allergy in South Australia**Authors:**

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Abstract**Introduction**

Drug allergy is commonly reported in patient notes and electronic health records. The prevalence of self-reported drug allergy in the general Australian population has not previously been studied.

Methods

We surveyed a representative sample of the South Australian adult population regarding their own perception of drug allergy, including drug type and severity as well as the use of medical alert devices. Data were weighted to correspond to age and sex of the South Australian population.

Results

22.2% of adults in South Australia consider themselves allergic to one or more drugs, 9.3% declared themselves to be allergic to penicillin, 5% to an antibiotic other than penicillin, and 13% to one or more antibiotics. Drug allergy and penicillin allergy was significantly more prevalent in females, and increased with age. Thirteen percent of those with an antibiotic allergy reported a severe reaction, of whom 27% wore a medical notification device. Of those allergic to penicillin, 75% had their index reaction more than 10 years ago and did not report severe features.

Discussion

Self-reported drug allergy is common in the general population, as it is in medical clinic and hospital populations. The majority of those reporting penicillin allergy would be considered low-risk and suitable for delabelling procedures.

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Key words: Drug allergy, Penicillin allergy, Self-reported, Population prevalence, Medical alert, Australia

Introduction

People may perceive themselves to be allergic to medications based on previous experience of adverse reactions, or other reasons. It has been demonstrated that penicillin allergy is vastly over-diagnosed, with many adverse consequences (1). The drug allergy diagnosis may be communicated through the medical record including the electronic health record (EHR), the patient's self-reported history, or a medical alerting device. In many cases, the entry of a drug allergy alert into the medical record is based on the patient's own self-reported perception of their allergic status. It is therefore important to understand the prevalence of self-reported drug allergy in the population.

A meta-analysis of studies of the prevalence of self-reported drug allergy concluded that 10% of adults perceive themselves to be allergic to one or more drugs, but this figure varied widely in different countries, and was higher in surveys of hospital inpatients or outpatients than in the general population (2). Sampling methods and survey methods also varied widely. Two recent Australian surveys of the medication charts of hospitalized patients receiving antibiotics documented antibiotic allergy rates of 25% (Melbourne (3)) and 18% (Perth (4)) with penicillin allergy rates of 13 and 9% respectively. A recent South Australian Electronic Health Record (EHR) survey of nearly 100,000 patient records documented a penicillin allergy label in 5.2% (5). An earlier Australian survey of patients attending an anaesthetic assessment pre-admission clinic documented 33% of patients reporting drug allergy, with 21% allergic to antibiotics and 11.6% to penicillin (6).

We report the first Australian epidemiological study of self-reported drug allergy in an unbiased general adult population. This was undertaken as part of the Health Omnibus Survey (Harrison Research), a population interview survey of households in South Australia focusing on health and wellbeing issues.

Aims

We sought to examine the prevalence of self-reported drug allergy in the general adult population in South Australia. We also looked at penicillin or other antibiotic allergy reporting as a sub group, at severity markers, and the use of medical alert devices in the context of drug allergy.

Methods

We performed a cross sectional study by way of a community face-to-face survey conducted between September to December 2017 (Health Omnibus Survey [HOS], Harrison Research). Subject selection was through randomized stratified sampling of households. Demographic data included age, sex, socioeconomic level (household income), education level, indigenous status, marital status, and area of residence. Information was also elicited on self-rated general health (SF-12). Subjects were questioned (yes/no answer) regarding allergy to any drug, allergy to penicillin specifically, or to antibiotics other than penicillin; whether the antibiotic reaction occurred within the last 10 years; severity of reaction as indicated by hospital attendance or urgent medical care; and usage of drug allergy notification devices (**supplementary figure 1**). The data was analysed in SPSS (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp) for significance, which was set at $p < 0.05$. Weighted data, adjusting for sex and age balance of survey respondents compared with the general population, was used to derive population prevalence figures.

Results

From an initial sample of 5,300 households across metropolitan and rural areas in South Australia, a total of 2,977 (57%) subjects participated in the survey (**table 1**). The majority of respondents were female (1,744; 58.6%). Subjects who responded positively regarding allergy to medications or penicillin or other antibiotics were considered allergic to drugs (**table 2**); some subjects reported being allergic specifically to penicillin, and/or to antibiotics other than penicillin.

The proportion of female respondents reporting drug allergy was significantly greater than male respondents for all drugs, penicillin specifically, and for all antibiotics (**table 3**). The percentage of those with drug allergy rose with age, but the rise was noticeably steeper for all drug allergies whereas penicillin allergy rose only slightly with age (**figure 1**). Drug allergy was more prevalent in those with poor self-rated health but this was less evident for penicillin allergy (**supplementary figure 1**). Reporting of drug allergy was not related to socioeconomic status, marital status, educational attainment or indigenous status (data not shown).

In those who report themselves to be allergic to antibiotics or other drugs, the severity or risk stratification of the allergy was in this survey determined by a history of hospitalization or urgent medical attention for the reaction, as well as recency of reaction (within the last 10 years). Those who had a severe reaction less than 10 years ago can be considered in the highest risk category, whereas those with a reaction that did not require hospitalization or urgent care, occurring more than 10 years ago, are in the lowest risk category (**table 4**).

Of the 418 respondents with reported antibiotic allergy, 53 (12.7%) reported requiring urgent medical attention or presenting to hospital because of their reaction; 14 (27%) of these reported wearing a drug allergy notification device. Of 29 with reactions both recent and severe, 9 (31%) had a notification device. Of those with non-severe distant reactions, 9.7% wore a medical notification device. Fifty-four subjects wore a medical alerting device because of antibiotic allergy, 26% of whom had severe and 17% recent severe reactions, and 57% had distant non-severe reactions. The odds of wearing a notification device were higher after having a more recent and severe allergic reaction versus a remote and non-severe reaction (OR 4.17, 95% CI 1.75-9.94, $p=0.0013$).

Discussion

The purpose of the drug allergy alert in the medical record is to prevent administration of drugs which carry a high risk of causing an adverse reaction. Whilst ideally a drug allergy alert would be based on a contemporaneously recorded or verified adverse drug reaction with an established basis for carrying that risk forward over time, in practice the patient history is usually the basis of the record entry. A recent study has demonstrated that a majority of the drug allergy entries in the South Australian public health service electronic health record (EPAS) were made by nurses, presumably based on the patient report (7). Given the inconsistency in the usage of the term 'drug allergy' in different settings (5,8) there remains a risk of over reporting if the drug allergy history is not critically evaluated.

Over the last 20 years, studies have demonstrated that more than 90% of those who have reported or recorded penicillin allergy have been able to tolerate penicillins following further assessment (9–11). This places the reliability of a drug allergy label, especially when referring to penicillins, into question.

The impact of an inaccurate drug allergy label is significant. Pharmaco-economic studies have demonstrated that an erroneous label can lead to greater medical expenses (12), by way of longer hospital stays (13), multiple hospital readmissions (4), as well as use of more expensive second-line agents (14). Additionally, studies have also demonstrated that a drug allergy label can result into poorer clinical outcomes and in certain populations, a greater mortality rate (15). As such, there has been growing interest in developing drug allergy assessment pathways that can better identify and correct inaccurate drug allergy labels (16).

One of the main reasons for the overestimation of the prevalence rates of drug allergy rests on the inaccuracy of self-reporting, which varies greatly across different populations. The discrepancy found in current literature may be due to the differing methods of data collection, as well as the population from which the data was collected. A recent systematic review of 53 international studies demonstrated the frequency of self-reported drug allergy at 11.4% (range 1.1 - 38.5%) in outpatients, 15.9% (range 7.5 - 23.5%) in hospital inpatients, and 5.9% (range 0.7% - 23.4%) in a general population (2). Notably, the majority of the studies were done through hospital populations, as participants were more readily accessible and could be approached and reviewed in a controlled setting.

The impact of self-reported drug allergy in the community can be expected to increase as programs such as the national electronic health record, My Health Record, requires individuals to enter their own allergies into the official database.

In this study of the South Australian general population, the rate of self-reported drug allergy of 22.2% and penicillin allergy of 9.3% is high when compared to other general (non-hospital) populations studied, and indeed is similar to reported hospital rates of penicillin allergy of approximately 10%. We found a female predominance of both self-reported drug allergy and self-reported penicillin allergy, in line with other studies (2) including similar findings in skin-test confirmed penicillin allergy (17). Drug allergy prevalence by self-report increased by 3.4-fold in the elderly compared with young adults, presumably reflecting a cumulative and absolute increase in drug exposure with age. This increase was only 1.8-fold for penicillin allergy, in keeping with the frequent reporting of penicillin allergy in children (18).

It has been shown that antibiotic allergy risk wanes over time since the index event (19) (with the probable exception of severe cutaneous reactions). A majority of those with reported antibiotic allergy (81.8%) had index reactions more than 10 years previously. Furthermore, of those with penicillin allergy, 75% had a distant, non-severe reaction history. This group would be considered at low risk for having a significant allergic reaction, if any, on repeat penicillin exposure (20) and would be considered suitable for a simple delabelling procedure such as direct oral challenge under medical supervision (21). Recent studies have demonstrated the benefits of adapting a drug allergy delabelling strategy in a hospital setting (22,23) including a clear cost benefit (24), and improved clinical outcomes (25).

In those who have a serious allergy with significant risk, communication of the allergic status should be optimized to avoid re-exposure. One method is with a personal medical alerting device which confers a literal drug allergy label. We have previously shown that of those Australians who subscribe to the MedicAlert foundation, 17% use their MedicAlert to declare a penicillin allergy (26) (or 21% for any antibiotic, 32% for any drug allergy) and 60% of these reported features potentially consistent with a severe reaction (27). In this study, only 27% of those with potentially severe antibiotic allergy wore a medical alerting device, whilst of those who did wear one, only a quarter had a history consistent with a severe allergy, suggesting that there is potential for optimizing the utility of such devices.

Whilst this survey had the advantage of encompassing a substantial number of randomly selected adult Australian subjects with rigorous statistical methods, potential limitations were the lack of detail in the drug allergy reporting, with an inability to distinguish allergy from side-effect or intolerance, and a lack of verification of drug allergy by testing or challenge. However, as we have indicated, in the majority of cases, such evaluation is not undertaken when the self-reported drug allergy is entered into the medical record.

Conclusion

This study demonstrates that the prevalence of self-reported drug allergy in South Australian adults is higher than some other populations previously studied, and the frequency of penicillin allergy in the community is comparable to that in the hospital setting. However, the risk profile of those reporting drug allergy is predominantly low. This study underscores the need for critical evaluation of patient-reported drug allergies at the medical interface including detailed history, investigation and likely delabelling in many people, whilst those with likely severe allergy should be advised to communicate this through avenues such as the hospital EHR, the My Health Record and/or a medical alerting device.

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Tables and Figures

Table 1 Respondent demographics

	N (%)
Female	1744 (58.6)
Age	
15 - 29	351 (11.8)
30 - 44	688 (23.1)
45 - 59	658 (22.1)
60 - 74	819 (27.5)
75 and over	461 (15.5)
Educational Attainment	
Still at school	41 (1.4)
Left school at 15 years or less	392 (13.2)
Left school after age 15	710 (23.8)
Trade qualification/apprenticeship	332 (11.2)
Certificate/diploma - one year full time or less	783 (26.3)
Bachelor degree or higher	715 (24.0)
Household Income (in Australian Dollars)	
Up to \$20,000	332 (11.2)
\$20,001 - \$60,000	1014 (34.0)
\$60,001 - \$140,000	792 (26.6)
\$140,000 or more	839 (28.2)

Table 2 Reported medication allergy

	Questionnaire responses (percent)	Population prevalence*(95% confidence interval)
Allergic to any medication	764 (25.7%)	22.2% (20.7%-23.7%)
Allergic to penicillin	292 (9.8%)	9.3% (8.3%-10.4%)
Allergic to other antibiotic	173 (5.8%)	5.0% (4.3% -5.8%)
Allergic to any antibiotic	418 (14.0%)	13% (11.8%-14.3%)

* The data was weighted to account for sex and age balance of subjects as compared with the population, as the respondents were more often female and slightly older than the population.

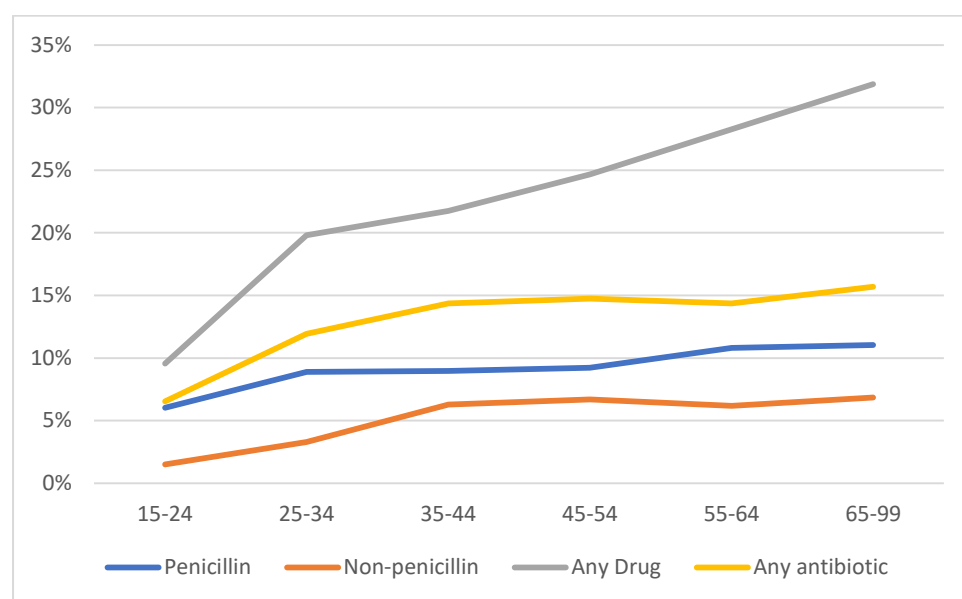
Table 3 Sex distribution of self-reported drug allergy

	Female	Male	Significance
Allergic to any medication	546 (27.7%)	218 (16.4%)	P<0.001
Allergic to penicillin	195 (10.9%)	97 (7.7%)	P=0.003
Allergic to any antibiotic	289 (15.7%)	129 (10.0%)	P<0.001

Table 4 Antibiotic allergy severity/risk stratification

	Reaction recent, <10 years	Reaction severe, emergency care	Recent and Severe	Not Recent and not Severe
Allergic to penicillin, n=292	56 (19.2%)	42 (14.4%)	25 (8.6%)	219 (75.0%)
Allergic to non-penicillin antibiotic, n=173	42 (24.3%)	27 (15.6%)	16 (9.2%)	120 (69.4%)
Allergic to any antibiotic, n=418	76 (18.2%)	53 (12.7%)	29 (6.9%)	318 (76.1%)

Figure 1. Age distribution of self-reported drug allergy



Age was significantly associated with allergy to drugs but not to penicillin- any drug, $p < 0.001$, non-penicillin antibiotic $p < 0.05$, any antibiotic $p < 0.05$, penicillin NS (t-test, comparing mean age of allergic/non-allergic groups).

Supplementary Figure 1 Questionnaire

P. ALLERGIES

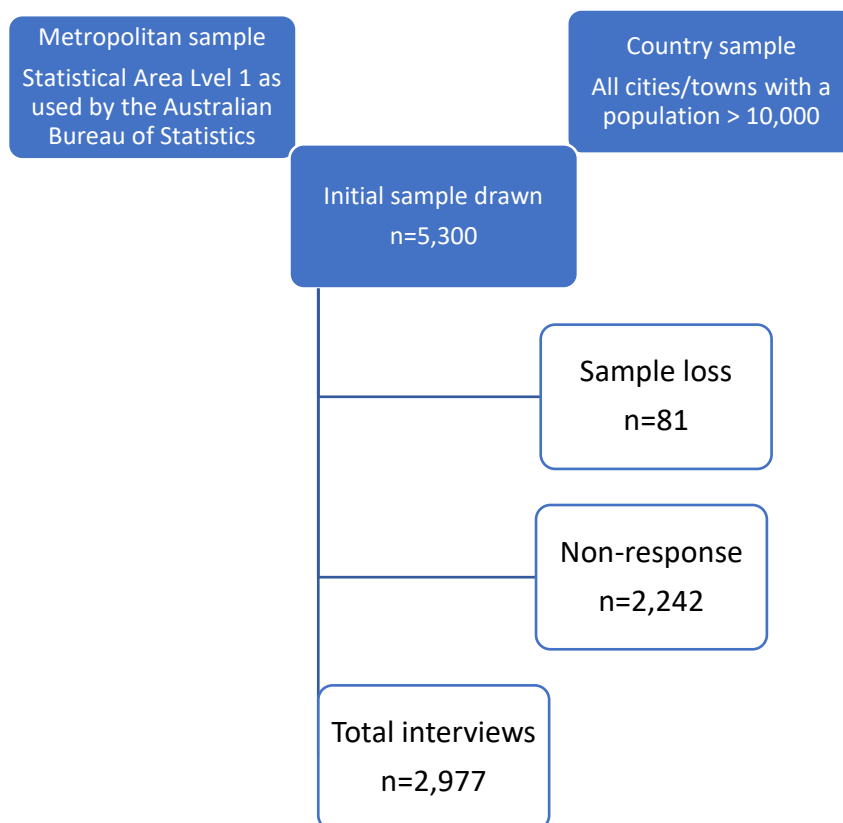
Changing the subject. The following questions are about allergies to medications and insect stings.

P1 Please indicate which of the following apply to you regarding allergy to medications.

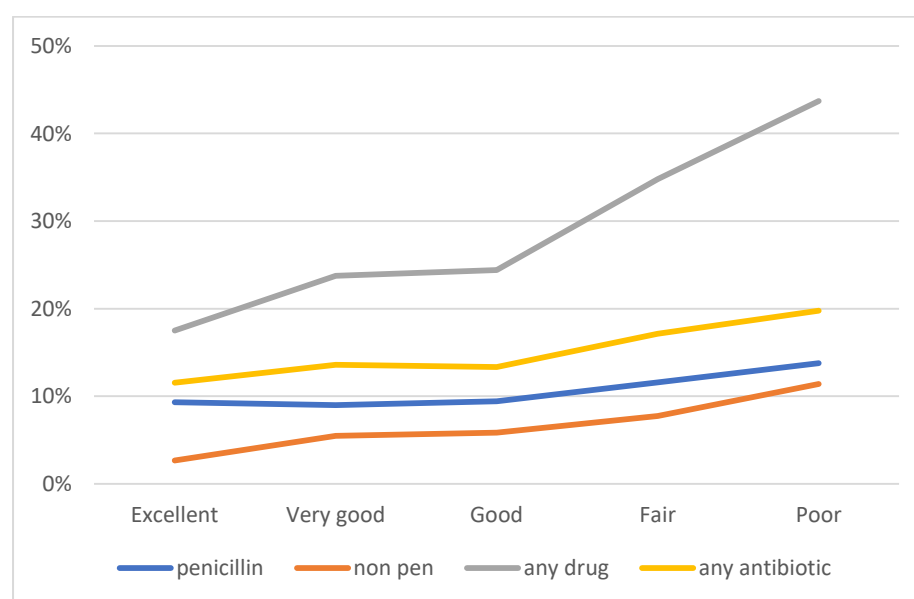
Show prompt card P1 **Multiple response**

- 1 I am allergic to one or more medications
- 2 I am allergic to penicillin
- 3 I am allergic to one or more antibiotics other than penicillin
- 4 I have experienced an allergic reaction to penicillin or other antibiotics within the last 10 years
- 5 An allergic reaction to penicillin or other antibiotics caused me to go to hospital or seek medical care urgently
- 6 I wear a MedicAlert or other type of medical notification device regarding my allergy
- 7 I am not allergic to any medications that I am aware of
- 8 Refused

Supplementary Figure 2 Sample selection



Supplementary Figure 3. Self-reported drug allergy according to self-reported general health



Supplementary Figure 1 Questionnaire

P. ALLERGIES

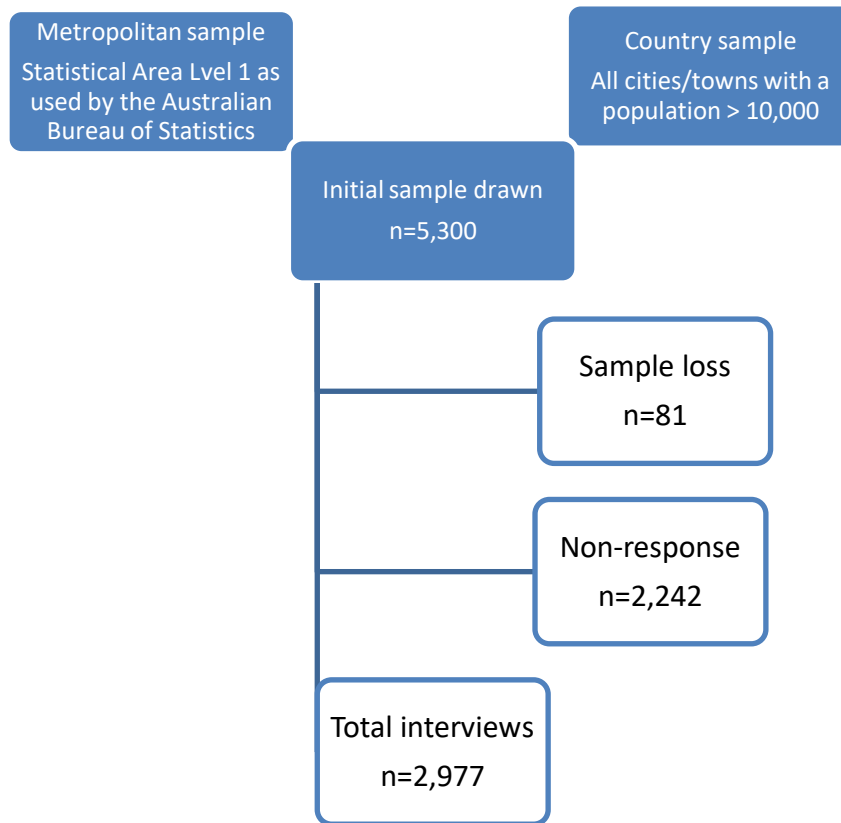
Changing the subject. The following questions are about allergies to medications and insect stings.

P1 Please indicate which of the following apply to you regarding allergy to medications.

Show prompt card P1 Multiple response

- 1 I am allergic to one or more medications
- 2 I am allergic to penicillin
- 3 I am allergic to one or more antibiotics other than penicillin
- 4 I have experienced an allergic reaction to penicillin or other antibiotics within the last 10 years
- 5 An allergic reaction to penicillin or other antibiotics caused me to go to hospital or seek medical care urgently
- 6 I wear a MedicAlert or other type of medical notification device regarding my allergy
- 7 I am not allergic to any medications that I am aware of
- 8 Refused

Supplementary Figure 2 Sample selection



Supplementary Figure 3. Self-reported drug allergy according to self-reported general health

