Author/s:
Wang, Y;Koplin, JJ;Lei, S;Horne, S;Allen, KJ;Hiscock, H;Peters, RL

Title:
Time trends in adrenaline auto-injector dispensing patterns using Australian Pharmaceutical Benefits Scheme data

Date:
2022-02-01

Citation:
Wang, Y., Koplin, J. J., Lei, S., Horne, S., Allen, K. J., Hiscock, H. & Peters, R. L. (2022). Time trends in adrenaline auto-injector dispensing patterns using Australian Pharmaceutical Benefits Scheme data. Journal of Paediatrics and Child Health, 58 (2), pp.318-325. https://doi.org/10.1111/jpc.15713.

Koplin Jennifer (Orcid ID: 0000-0002-7576-5142)
Hiscock Harriet (Orcid ID: 0000-0003-3017-2770)

Journal of Paediatrics and Child Health **August 2021**

Title page

Time trends in adrenaline auto-injector dispensing patterns using Australian Pharmaceutical Benefits Scheme data

Running title: AAI dispensing patterns in Australia

Original Article

Yichao Wang[1, 2,3], Jennifer J. Koplin[1, 4], Shaoke Lei[5], Simon Horne[6], Katrina J. Allen[1, 2*], Harriet Hiscock[1, 2, 5], Rachel L. Peters[1, 2]

Affiliations:

[1] Murdoch Children's Research Institute, 50 Flemington Road, Victoria, 3052, Australia.

[2] Department of Paediatrics, University of Melbourne, Victoria, 3010, Australia.

[3] Centre for Social and Early Emotional Development, School of Psychology, Deakin University, Burwood, Melbourne, Victoria, 3125, Australia.

[4] The School of Population and Global Health, University of Melbourne, Victoria, 3010, Australia.

[5] Health Services Research Unit, the Royal Children's Hospital, Victoria, 3052, Australia.

[6] Point Lonsdale Medical Group, Victoria, 3225, Australia.

*Former affiliations when this work was undertaken. No current affiliations.

Corresponding author:

Dr Jennifer J. Koplin

Murdoch Children's Research Institute

50 Flemington Road,

Melbourne, Victoria, 3052, Australia.

E-mail: jennifer.koplin@mcri.edu.au

Phone: +61 3 8341 6236

Acknowledgements

Yichao Wang's PhD research is funded by The University of Melbourne's Melbourne International Research Scholarship (MIRS) and Melbourne International Fee Remission Scholarship (MIFRS) and Murdoch Children's Research Institute's Top-up Scholarship. Research at MCRI is supported by the Victorian Government's Operation al Infrastructure Support Program. H.H. is supported by a National Health and Medical Research Council (NHMRC) Practitioner Fellowship (1136222). J.J.K., K.J.A. and R.L.P. hold or held NHMRC fellowships.

Conflicts of interest

The authors have no conflict

Journal of Paediatrics and Child Health **July 2021**

Title

Time trends in adrenaline auto-injector dispensing patterns using Australian Pharmaceutical Benefits Scheme data

Running title: AAI dispensing patterns in Australia

Main Text File

Abstract (word count: 249)

Aim

Adrenaline auto-injector (AAI) dispensing data, a community-based proxy for number of individuals at risk of anaphylaxis, provides complementary information on time trends of anaphylaxis risk in addition to hospital admission data. We examined trends of AAI dispensing over a 10-year period (from January 2005 to December 2014) in Australia.

Methods

Individuals with dispensed AAI were identified from a 10% random sample of Australian Pharmaceutical Benefits Scheme (PBS) data. PBS is the Australian national drug subsidy

program covering all Australians. Cumulative incidence and incidence rates of individuals with AAI were calculated. We assessed difference by age, sex, state and time trends.

Results

The cumulative incidence of individuals with AAI in 2005-2014 was 75.43/ 100, 000 (95%CI 75.07-75.80/100,000). Incidence rate of individuals with AAI increased from 2005 to 2014 (from 71.47 to 82.07 per 100,000 person-years) although this varied by state. Over the time assessed, there was a shift to more prescriptions being provided by general practitioners (GP) rather than specialists. Children (0-19 years) were more likely to have been prescribed an AAI from a specialist and adults from a GP.

Conclusion

Overall, an increase in dispensed AAI mirrored other evidence for a rising prevalence of allergy. This increase could also reflect changes in prescribing practices or increased awareness and education of healthcare professionals on anaphylaxis and indications for prescribing AAI. The rising rate of AAI prescribed by GPs compared to decreasing rates by specialists suggests a changing response of the Australian healthcare system to the increased burden of anaphylaxis.

Keywords
Anaphylaxis, epidemiology, allergy treatment

Abbreviations
AAI: adrenaline auto-injector, ACT: Australian Capital Territory, GP: general practitioners, NT: Northern Territory, NSW: New South Wales, PBS: Pharmaceutical Benefits Scheme, QLD: Queensland, SA: South Australia, TAS: Tasmania, VIC: Victoria, WA: Western Australia

Brief Points: Authors are to provide up to 3 separate points for each Brief Point:

What is already known on this topic?

- Hospital admissions for anaphylaxis in Australia have increased significantly over the last 2 decades
- Anaphylaxis management and treatment guidelines in Australia and internationally recommend the prescription of adrenaline auto-injectors (AAI) for all patients at risk of anaphylaxis

- International studies have reported increasing AAI prescribing trends

What this paper adds?

- Between 2005-2014, the incidence rate of individuals with AAI dispensed increased from 71.47 to 82.07 per 100,000 person-years, although this varied by state
- There was a shift to more prescriptions being provided by general practitioners (GP) rather than specialists; children (0-19 years) were more likely to have been prescribed an AAI from a specialist and adults from a GP

Introduction

Hospital admissions for anaphylaxis in Australia increased significantly between 1998 and 2012[1]. However, a rise in hospital admissions does not necessarily indicate a rise in the number of patients at risk of anaphylaxis, since these trends could also be explained by an increase in the number or severity of reactions among at-risk patients, or better recognition and coding of anaphylaxis by hospital emergency departments[2].

Anaphylaxis management and treatment guidelines in Australia and internationally recommend the prescription of adrenaline auto-injectors (AAI) for all patients at risk of anaphylaxis[3, 4]. AAI dispensing and prescription data could, therefore, be a community-based proxy for the number of individuals at risk of anaphylaxis[5], and provide complementary information on time trends of anaphylaxis risk, including patients at risk of anaphylaxis who do not experience anaphylactic reactions (e.g. due to adequate avoidance of triggers) and those who experience anaphylactic reactions but do not present to hospital[6].

Internationally, studies from United States of America (USA) and United Kingdom (UK) have reported increasing AAI prescribing trends in 2000-2012, and a study from Canada reported the increasing prescription patterns of all epinephrine formulations during 1995-2000 [5, 7, 8].

In Australia, AAI prescription and dispensing have only been reported using sales data. Kemp et al. reported a 193% increase in the total number of units provided to retail pharmacies and hospitals from 1998 to 2002[9] and a further 650% increase by 2006[10]. Mullins et al. examined prescription sales between November 2005 and October 2007[11], reporting that prescriptions were more common in younger patients and southern latitudes. There is little information on the time trends of AAI prescription or dispensing in Australia in recent years using data that can inform incident rates. Additionally, the type of practitioners who prescribe AAI can provide a snapshot of the healthcare service delivery for patients at risk of anaphylaxis.

In this study, we aimed to examine the time trends of AAI dispensing over a 10-year period (January 2005-December 2014) in Australia using the national Pharmaceutical Benefits Scheme (PBS) data. Additionally, we aimed to examine whether the prescription trends of dispensed AAI differed by speciality of prescribers.

Methods

Overview of Australian Pharmaceutical Benefits Scheme (PBS)

The Australian PBS is the national drug subsidy program covering all Australian residents who hold a current Medicare card and overseas visitors from countries with a Reciprocal Health Care Agreement (RHCA) with Australia[12]. The scheme records the dispensing of prescribed medicines subsidised by the government[12, 13]. In 2011, approximately 75% of prescribed medicines in Australia were subsidised by PBS[12]. Individuals' basic information including age and sex are collected in the PBS database. For this study, we used the PBS data for a 10% random sample of individuals across Australia, which was published online on 1 August 2016 by the Department of Health[14, 15]. This PBS sample was constructed by randomly selecting 10% of all Australians who claimed payment of Pharmaceutical Benefits from 2003 to 2014, including all claiming activities for the sample of individuals[14].

AAI records

AAI dispensing records were obtained from PBS. A study using sales data reported that 87% of the AAI prescription is PBS subsidised[11]. For individuals who are diagnosed as "at risk of anaphylaxis" by health professionals, two AAIs are PBS subsidised and repeat approvals for PBS subsidised devices are not issued unless the device is used or is about to expire[16]. However, this dataset only recorded the number of AAI prescriptions for each individual rather than the number of units dispensed.

EpiPen and EpiPen Junior were available on the PBS from 1st November 2003, while Anapen and Anapen Junior were available from 1st July 2010[17]. We identified AAI dispensing using the PBS item codes for EpiPen, EpiPen Junior, Anapen and Anapen Junior ("8698T", "8697R", "3409K" and "3408J", respectively) from 1st January 2003 to 31st December 2014. In the 10% PBS dataset, data are divided into 5 geographic regions based on locations including New South Wales and Australian Capital Territory (NSW+ACT), Queensland (QLD), Victoria and Tasmania (VCT+TAS), Western Australia (WA), South Australia and Northern Territory (SA+NT). Information on date of supply (date on which the individual received AAI from pharmacies), total cost, age, gender, geographic location and speciality of the prescriber were obtained. The permissible values for the speciality of prescriber include general practitioner (GP), specialist, allied health professional and dental practitioner. Specialists with the ability to prescribe AAI in Australia include general paediatricians, respiratory physicians, emergency department (ED) physicians and

immunologist/allergists (categorised as "specialist" in this study). GPs and other allied health professionals (where allowed) can only initiate AAI prescription under authority in "discussion with" a specialist authorised prescriber in Australia.

Definition

Incidence rate of individuals with AAI: the number of individuals who had an AAI dispensed for each year through 2005-2014 was the numerator, and the state-, age- and sex-specific population for the corresponding year as the denominator.

Cumulative incidence of individuals with AAI: between 2005 and 2014: the total number of individuals who had an AAI dispensed at any time during the whole study period was the numerator, and the total state-, age- and sex-specific population from 2005 to 2014 was the denominator.

For both the incidence rate and cumulative incidence, each individual was only counted once (in the year that they received their first AAI between 2005 and 2014); the incidence rate was reported as per 100,000 person-years and the cumulative incidence was reported as per 100,000. All numerators were multiplied by 10 since this dataset was a 10% random sample of individuals with PBS data.

Australian population

Data on the Australian population during the study period by state, age and sex were obtained from Australian Bureau of Statistics (http://www.abs.gov.au/ausstats/abs).

Statistical analysis

AAI was only available on the PBS from November 2003. The incidence rate of individuals with AAI is reported from 1st January 2005 to avoid incomplete data in 2003 and allow a one-year wash-out period.

The comparison of incidence rates of AAI dispensing for different strata of the population (e.g. male, female, various age groups and different Australian states) over the study period (2005-2014) were assessed by estimating incidence rate ratios (IRR), 95% confidence intervals (CI) and p-value for trends using a Poisson regression model. For cumulative incidence comparisons, chi-squared tests (χ^2) were used. Statistical analyses were performed in Stata version 15.1 (StataCorp, College Station, Texas).

Ethics approval

This project was determined by the ×× Human Research Ethics Committee to be exempt from organisation ethics review according to the Australian Health Records Act. No individual identifiable information was provided or used for this project.

Results

Number of AAI prescriptions dispensed and characteristics of individuals with AAI

Between 2005 and 2014, 618,260 AAI prescriptions were dispensed to 164,560 individuals in Australia, and 393,390 (63.6%) of them were dispensed to 85,890 children and young adults under 19 years of age. The total financial expenditure (including government cost and patient contribution) on AAIs during the study period estimated was $106,817,165 AUD in the total population.

The number of dispensed AAI for first prescription and total prescription (including repeats) in the study period are shown in Figure 1. The number of first AAI prescription was 34% higher in 2014 than in 2005, while the number of total AAI prescription (including repeats) was 195% higher in 2014 compared with 2005.

The demographic characteristics of individuals when they obtained their first dispensed AAI during 2005-2014 are summarized in Table 1. The median age was 16 years old (interquartile range (IQR): 5-41; range: 0-94). Approximately half of the sample obtained their first AAI prescription from GPs (n=87,770, 53.34%), while 46.26% (n=76,120) were prescribed by specialists and 0.02% (n=40) from allied health professionals. Nearly all individuals (n=163,030, 99.08%) received EpiPen and EpiPen Junior as their first AAI devices. One third (n= 54,140, 32.90%) were prescribed a junior dose of AAI (EpiPen Junior or Anapen Junior).

Time trends of AAI dispensing and variation by sex, age, state

Overall, the incidence rate of individuals with AAI increased from 71.47 to 82.07 per 100,000 person-years in Australia with a 2% increase (IRR 1.02, 95%CI 1.02-1.03) between 2005 and 2014 (Figure 2, P<0.001). Increasing trends were found in both males and females (P<0.001). A crossover was observed between 2012 and 2013 where the incidence rate in females exceeded that in males. Increasing trends were observed in 0-4, 15-19 and >19 year age groups. A rising trend for 5-9 years and a decreasing trend for 10-14 years were also observed but with weak evidence. In contrast to the increasing patterns of incidence rate of individuals with AAI in other states, a relatively stable trend in VIC+TAS was observed (Figure 2). There was a dip in AAI dispensing in 2009 in all states.

Time trends of dispensed AAI by state stratified by speciality of prescriber

The time trends of incidence rate of individuals with AAI by state stratified by speciality of prescribers during 2005-2014 are shown in Figure 3. WA had the highest cumulative

incidence of individuals with AAI prescribed by GPs, followed by SA+NT and QLD. Increasing trends of incidence rate of individuals with AAI prescribed by GPs were observed in all regions (P<0.001) except for VIC+TAS (P=0.676). In contrast, decreasing trends for the incidence rate of individuals with AAI prescribed by specialists were found in QLD and VIC+TAS (P<0.05). The cumulative incidence of individuals with AAI prescribed by specialists was also highest in WA, then VIC+TAS and NSW+ACT.

Cumulative incidence by sex, age and state

The cumulative incidence of individuals with AAI between 2005 and 2014 was 75.43/100,000 (95%CI: 75.07-75.80/100,000). Males had a higher cumulative incidence than females (76.65, 95%CI: 76.13-77.17 and 74.23, 95%CI: 73.72-74.74 /100,000, respectively, P=0.04) and children (0-19 years) had a higher cumulative incidence than adults (>19 years) (152.64, 95%CI: 151.62-153.66 and 48.59, 95%CI: 48.26-48.94/100,000, respectively, P<0.001). The highest cumulative incidence of individuals with AAI was found in WA, followed by SA and NT, and VIC+TAS (Figure 4) (P<0.001).

Discussion

Using Australian PBS data, we found the incidence rate of individuals with dispensed AAI increased during 2005-2014. Half of the individuals with AAI were under 16 years of age when they obtained their first subsidised AAI. Cumulative incidence of individuals with AAI was higher in males compared to females and children (0-19 years) compared to adults. There was a shift to more prescriptions being provided by GPs rather than specialists in most regions in Australia, which may suggest that some health services for allergy care in Australia have shifted from specialist providers to GPs, or alternatively may reflect improved communication between specialist and GPs for shared care of patients at risk of anaphylaxis.

The utilisation of Australian PBS database strengthens the reliability and representativeness of this study because it captures all subsidised AAI that were dispensed in the study period and provides reliable and objective AAI dispensing trends across the varying socio-economic levels of Australians. We reported a lower cumulative incidence (153/100,000) in children compared with that of studies from the USA and UK ranging from about 325 to 467 per 100,000 person-years, which may reflect different prescribing practices rather than anaphylaxis risk[5, 7]. Increasing trends of incidence rate were consistently reported in our study and previous studies[5, 7].

There are also some limitations. Although we propose that AAI dispensations may be a community-based proxy for anaphylaxis risk, the increases we observed could also be explained by changes in prescribing practices or increased awareness and education of healthcare professionals on anaphylaxis and indications for prescribing AAI. As the PBS database was not designed for research purposes, data on whether dispensed AAI devices were activated was not available, so we cannot determine whether the refilled AAI was to replace an activated AAI or an expired AAI. Additionally, AAI can be purchased at full retail price from pharmacies without a prescription in Australia and these purchases would not have been captured in the present study which may underestimate the true incidence rate. A previous study reported that 13% of AAI prescriptions were not government subsidised[11]. Other data that would have allowed us to address additional research questions could not be obtained such as data on the indication for AAI prescription (e.g. food, drug or insect) or patient's ethnicity which is associated with different anaphylaxis triggers[18]. We observed a dip in AAI dispensing in 2009, which could not be explained by the changes to government regulation on AAI dispensing, AAI shortages, price change or biased data from PBS. In

addition, the data used in this study was available only for 2003 to 2014 and if the PBS release newer data, further research to understand recent trends would be informative.

Consistent with other studies that EpiPen prescription rates were higher among children compared with adults[5, 8, 11], we found that higher cumulative incidence of AAI was observed among children than adults. Although the triggers of AAI dispensing were not available in our study, earlier studies reported that food-induced anaphylaxis is the main trigger for anaphylaxis in children[19, 20].

Trends of incidence rate varied by the speciality of prescribers. We found the increasing incidence rate of individuals with AAI in Australia was driven by GPs. According to the Australasian Society of Clinical Immunology and Allergy (ASCIA) report in 2007, 4.1 million Australians have at least one allergy[21]. However, the total number of clinical immunology/allergy specialist in Australia is around 210[22]. Due to the high number of individuals and low number of specialists, it may be difficult for individuals at risk of anaphylaxis to access specialist care, evident by long waiting time to see a specialist (5.4 or 10.6 months for private or public tertiary allergy services, respectively) [23], which could explain the decreasing trends of first AAI prescribed by specialists. This may have contributed to increases in AAI prescriptions by GPs. Similar increasing trends of AAI prescription by GPs in 2000-2012 was reported in the UK, with approximately four devices a year provided per high-risk child[7]. They noted that there has been little guidance of GPs on the optimal use of AAI.

The incidence of individuals with AAI varied by state. Along the east coastal area, VIC+TAS had a higher cumulative incidence compared with QLD and NSW+ACT. EpiPen prescription rates and parent-reported food allergy prevalence is also higher in southern compared northern regions of Australia[11, 24]. We also observed a higher cumulative incidence in WA and SA+NT. Geographical variation in food allergy prevalence or geographical remoteness, which is an indication for AAI prescribing in the ASICA guidelines, may contribute to the regional variation observed[4].

The uneven prescription of two types of AAI devices in our study exposed the patients at risk of anaphylaxis to a supply issue. Even though Anapen and Anapen Junior were added into PBS subsidized list since 2010, prescriptions were dominated by EpiPen and EpiPen Junior. Anapen and Anapen Junior were removed from PBS from 1st January 2017[17] which may have

exposed Australians at risk of anaphylaxis to an AAI supply issue, as evident by the shortage of EpiPens in Australia[25].

Overall, the incidence rate of dispensed AAI increased in Australia between 2005 and 2014 mirroring other evidence for a rising prevalence of allergy. The rising trends of first-dispensed AAI being prescribed by GPs while specialist prescriptions decreased in most Australian states may suggest a shift of healthcare services to GPs for patients at risk of anaphylaxis, or enhanced communication between specialists and GPs in shared care models, in response to the increasing burden of anaphylaxis. An investigation into AAI prescribing behaviour of health professionals across Australia would help to further understand the impact of these changes on healthcare provision and its cost-effectiveness. Future studies on whether all patients at risk of anaphylaxis have obtained essential AAI dispensing are also needed.

Reference

1. Mullins RJ, Dear KB, Tang ML. Time trends in Australian hospital anaphylaxis admissions in 1998-1999 to 2011-2012. J Allergy Clin Immunol. 2015;136(2):367-75.
2. Rueter K, Ta B, Bear N, Lucas M, Prescott S. Physician training programs significantly improve diagnosis in cases coded as anaphylaxis over time: A major factor compounding time-trend data? J Allergy Clin Immunol Pract. 2017;5(3):858-60.
3. Muraro A, Roberts G, Worm M, Bilo MB, Brockow K, Fernandez Rivas M, et al. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. Allergy. 2014;69(8):1026-45.
4. ASCIA, anaphylaxis emergency medication prescription guideline, https://www.allergy.org.au/health-professionals/anaphylaxis-resources/adrenaline-autoinjector-prescription, accessed by 18 Feb 2019. [
5. Lee S, Hess EP, Lohse C, Souza DL, Campbell RL. Epinephrine Autoinjector Prescribing Trends: An Outpatient Population-Based Study in Olmsted County, Minnesota. The Journal of Allergy & Clinical Immunology in Practice. 2016;4(6):1182-6.e1.
6. Wood RA, Camargo CA, Lieberman P, Sampson HA, Schwartz LB, Zitt M, et al. Anaphylaxis in America: The prevalence and characteristics of anaphylaxis in the United States. J Allergy Clin Immun. 2014;133(2):461-7.
7. Diwakar L, Cummins C, Ryan R, Marshall T, Roberts T. Prescription rates of adrenaline auto-injectors for children in UK general practice: a retrospective cohort study. Br J Gen Pract. 2017;67(657):e300-e5.
8. Simons FE, Peterson S, Black CD. Epinephrine dispensing patterns for an out-of-hospital population: a novel approach to studying the epidemiology of anaphylaxis. J Allergy Clin Immunol. 2002;110(4):647-51.
9. Kemp AS. EpiPen epidemic: suggestions for rational prescribing in childhood food allergy. J Paediatr Child Health. 2003;39(5):372-5.
10. Allen CW, Campbell DE, Kemp AS. EpiPen use in children with food allergies. Med J Australia. 2007;187(9):542-.
11. Mullins RJ, Clark S, Camargo CA, Jr. Regional variation in epinephrine autoinjector prescriptions in Australia: more evidence for the vitamin D-anaphylaxis hypothesis. Ann Allergy Asthma Immunol. 2009;103(6):488-95.
12. Department of Health, Australia Government. The Pharmaceutical Benefits Scheme. https://www.pbs.gov.au/info/about-the-pbs, accessed by 9 July 2021.
13. Page E, Kemp-Casey A, Korda R, Banks E. Using Australian Pharmaceutical Benefits Scheme data for pharmacoepidemiological research: challenges and approaches. Public Health Res Pract. 2015;25(4):e2541546.
14. Publication of MBS/PBS data, office of the Australian Information Commissioner, Australian government. https://www.oaic.gov.au/privacy/privacy-decisions/investigation-reports/mbspbs-data-publication/, accessed by 6 Feb 2021.
15. Department of Health, Australian Government. Public Release of Linkable 10% sample of Medicare Benefits Scheme (Medicare) and Pharmaceutical Benefits Scheme (PBS) Data. https://www.pbs.gov.au/pbs/news/2016/08/public-release-of-linkable-10-percent-mbs-and-pbs-data. Accessed 9 July 2021. .
16. ASCIA, Health Professionals Anaphylaxis Resources, Adrenaline autoinjectors FAQ, https://www.allergy.org.au/health-professionals/anaphylaxis-resources/adrenaline-autoinjectors-faqs, accessed by 21 May 2018.
17. PBS Publications Archive, The Pharmaceutical Benefits Scheme, Australian Government Department of Health, http://www.pbs.gov.au/info/publication/schedule/archive, accessed by 21 May 2018.

18. Wang YC, Allen KJ, Suaini NHA, Peters RL, Ponsonby AL, Koplin JJ. Asian children living in Australia have a different profile of allergy and anaphylaxis than Australian-born children: A State-wide survey. Clinical and Experimental Allergy. 2018;48(10):1317-24.
19. Sann J, Bunyavanich S, Wang J. Epinephrine autoinjector prescribing patterns in an urban pediatric population. Journal of Allergy and Clinical Immunology: In Practice. 2016;4(5):989-90.
20. Gaspar A, Santos N, Piedade S, Santa-Marta C, Pires G, Sampaio G, et al. One-year survey of paediatric anaphylaxis in an allergy department. Eur Ann Allergy Clin Immunol. 2015;47(6):197-205.
21. Mullins RJ, et al. The economic impact of allergic disease in Australia: not to be sneezed at. ASCIA/Access Economics Report, November 2007. https://www.allergy.org.au/ascia-reports/economic-impact-of-allergies, accessed by 17 July 2018.
22. ASCIA, locate a specialist, https://www.allergy.org.au/patients/locate-a-specialist, accessed by 17 July 2018.
23. Morawetz DY, Hiscock H, Allen KJ, Davies S, Danchin MH. Management of food allergy: a survey of Australian paediatricians. J Paediatr Child Health. 2014;50(6):432-7.
24. Osborne NJ, Ukoumunne OC, Wake M, Allen KJ. Prevalence of eczema and food allergy is associated with latitude in Australia. J Allergy Clin Immun. 2012;129(3):865-7.
25. Australian government department of health, therapeutic goods administration, Alerts, EpiPen adrenaline auto-injector, https://www.tga.gov.au/alert/epipen-300-mcg-adrenaline-auto-injector, accessed by 30 September 2018.

Table

Table 1. Summary and demographic characteristics of individuals with AAI in Australia between 2005 and 2014 (N=164,560).

Demographic characteristics	**N (%)**
Age	
0-4	38540 (23.42)
5-9	23370 (14.20)
10-14	13860 (8.42)
15-19	10120 (6.15)
>19	78670 (47.81)
Sex	
Female	81400 (49.47)
Male	83160 (50.53)
State	
NSW+ACT	50080 (30.43)
QLD	29730 (18.07)
SA+NT	15520(9.43)
VIC+TAS	46820 (28.45)
WA	22380 (13.60)
Unknown state	30 (0.02)
Specialty of prescriber	
General practitioner (GP)	87770 (53.34)
Specialist	76120 (46.26)
Allied health professional	40 (0.02)
NA	630 (0.38)

AAI devices	
Epipen	109770 (66.71)
Epipen Junior	53260 (32.37)
Anapen	650 (0.39)
Anapen Junior	880 (0.53)

Note: Characteristics of individuals are summarized when they obtained their first dispensed AAI.

Figure legends

Figure 1. Number of prescriptions dispensed for AAI per year from 2005 to 2014 in Australia for first prescription (1A) and total prescriptions including repeats (1B).

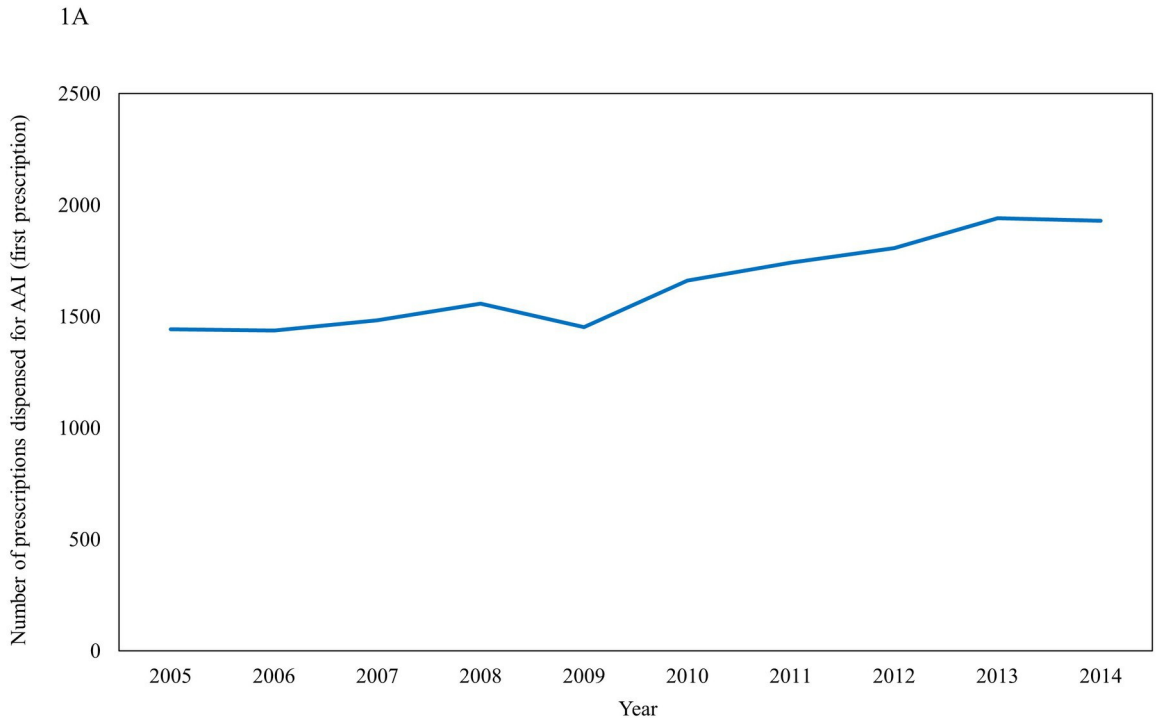
Figure 2. Trends of incidence rate of individuals with AAI by sex (2A), age (2B) and state (2C) from 2005 to 2014

*These results are estimated by Poisson regression models.

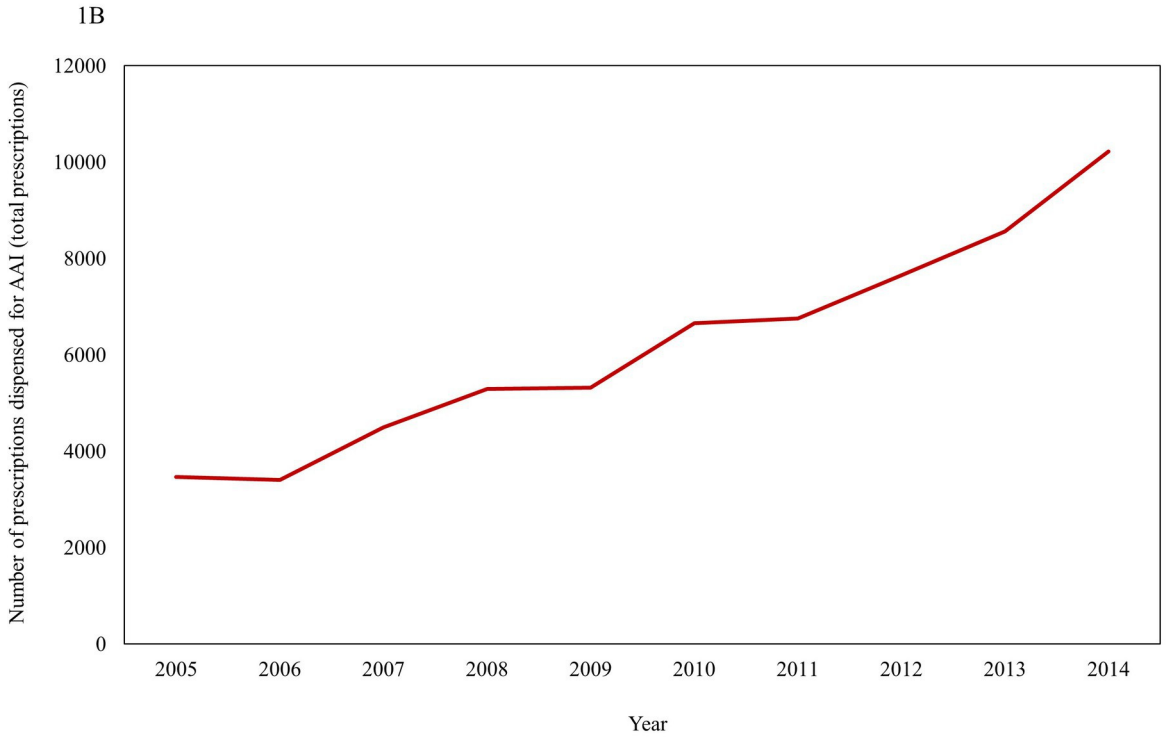
Figure 3. Trends of incidence rate of individuals with AAI by state prescribed by general practice (3A) and specialist (3B) from 2005 to 2014

*These results are estimated by Poisson regression models.

Figure 4. Cumulative incidence of individuals with AAI during 2005-2014 by state.

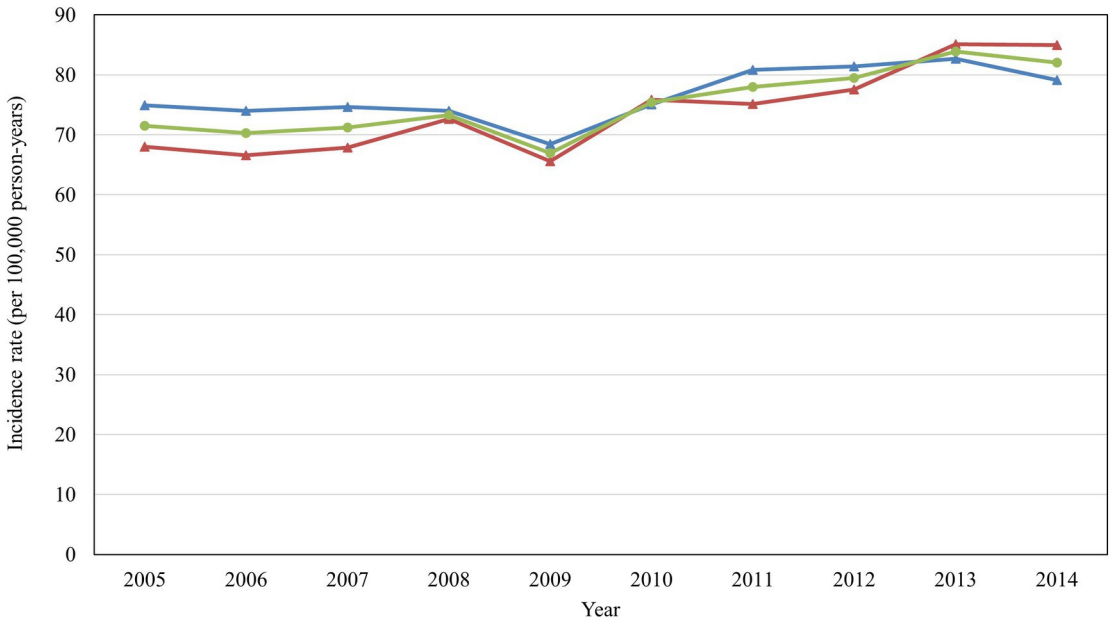


JPC_15713_Figure 1A.JPG



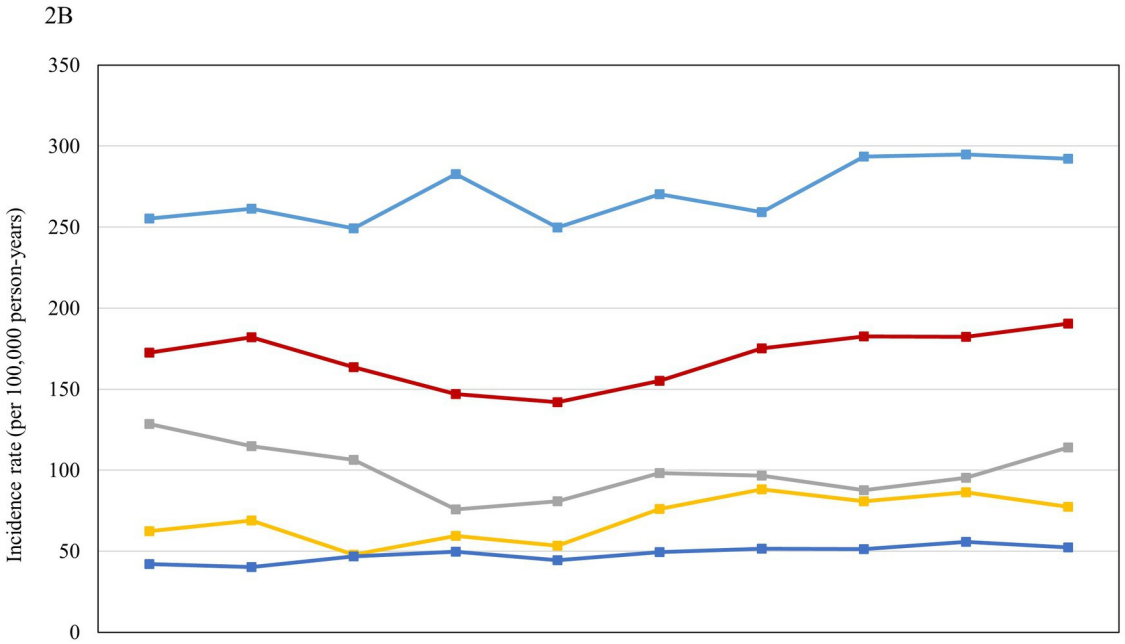
JPC_15713_Figure 1B.JPG

2A



	Male	Female	Total population
Cumulative incidence (per 100,000)	76.65	74.23	75.43
IRR 95%CI*	1.01 (1.01, 1.02)	1.03 (1.02, 1.04)	1.02 (1.02, 1.03)
P value*	**0.001**	**<0.001**	**<0.001**

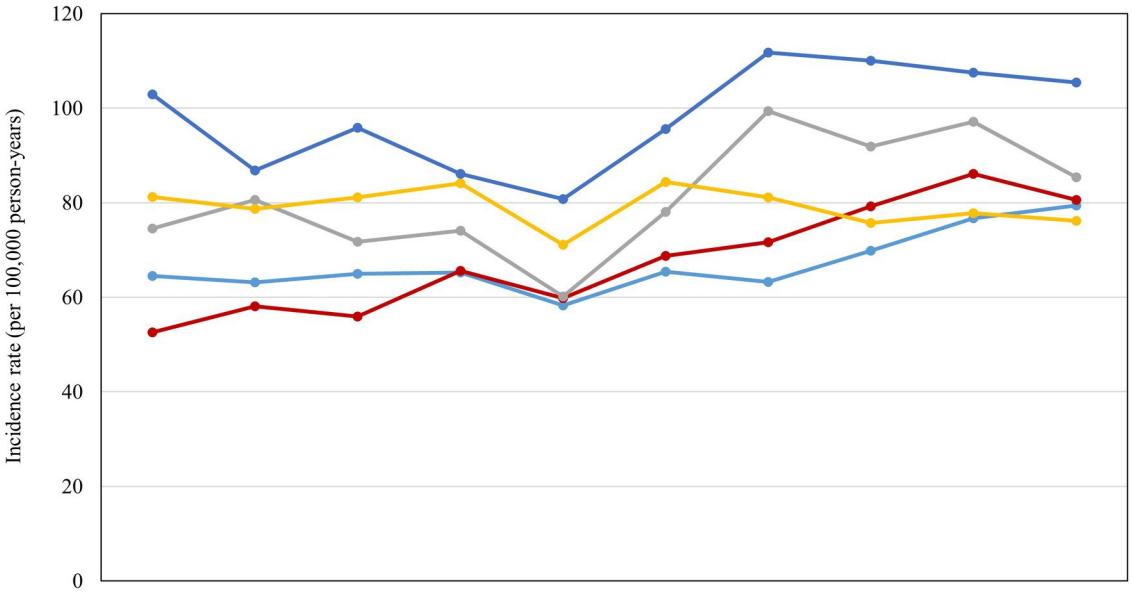
JPC_15713_Figure 2A.JPG



	0-4 Y	5-9 Y	10-14 Y	15-19 Y	>19 Y
Cumulative incidence (per 100,000)	271.53	169.64	99.86	70.18	48.59
IRR 95%CI*	1.02 (1.01, 1.03)	1.01 (1.00, 1.03)	0.98 (0.97, 1.00)	1.05 (1.03, 1.07)	1.03 (1.02, 1.04)
P value*	**0.003**	0.060	0.071	**<0.001**	**<0.001**

JPC_15713_Figure 2B.JPG

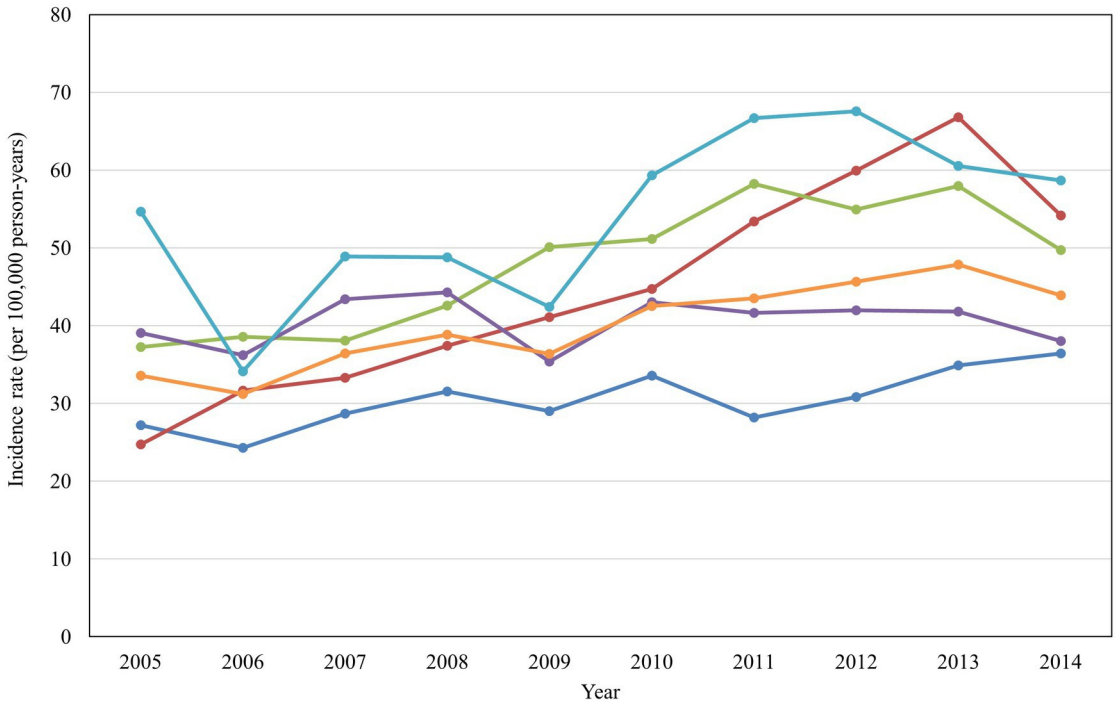
2C



	NSW+ ACT	QLD	SA+ NT	VIC+TAS	WA
Cumulative incidence (per 100,000)	67.26	68.48	84.35	79.10	98.73
IRR 95%CI*	1.02 (1.01, 1.03)	1.05 (1.04, 1.07)	1.03 (1.01, 1.05)	0.99 (0.98, 1.00)	1.02 (1.01, 1.04)
P value*	**<0.001**	**<0.001**	**0.002**	0.254	**0.004**

JPC_15713_Figure 2C.JPG

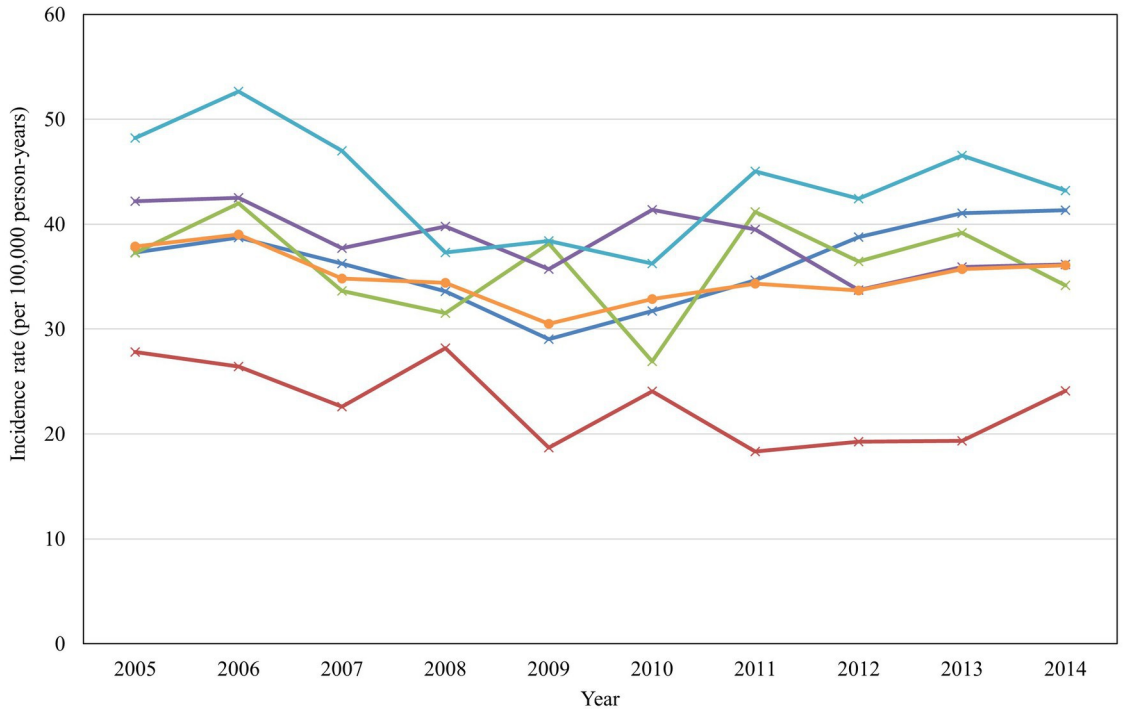
3A



	NSW+ACT	QLD	SA+NT	VIC+TAS	WA	Total
Cumulative incidence (per 100,000)	30.58	45.47	48.10	40.51	54.71	40.23
IRR 95%CI*	1.03 (1.02, 1.05)	1.10 (1.08, 1.12)	1.05 (1.02, 1.07)	1.00 (0.99, 1.02)	1.04 (1.02, 1.06)	1.04 (1.03, 1.05)
P value*	**<0.001**	**<0.001**	**<0.001**	0.676	**<0.001**	**<0.001**

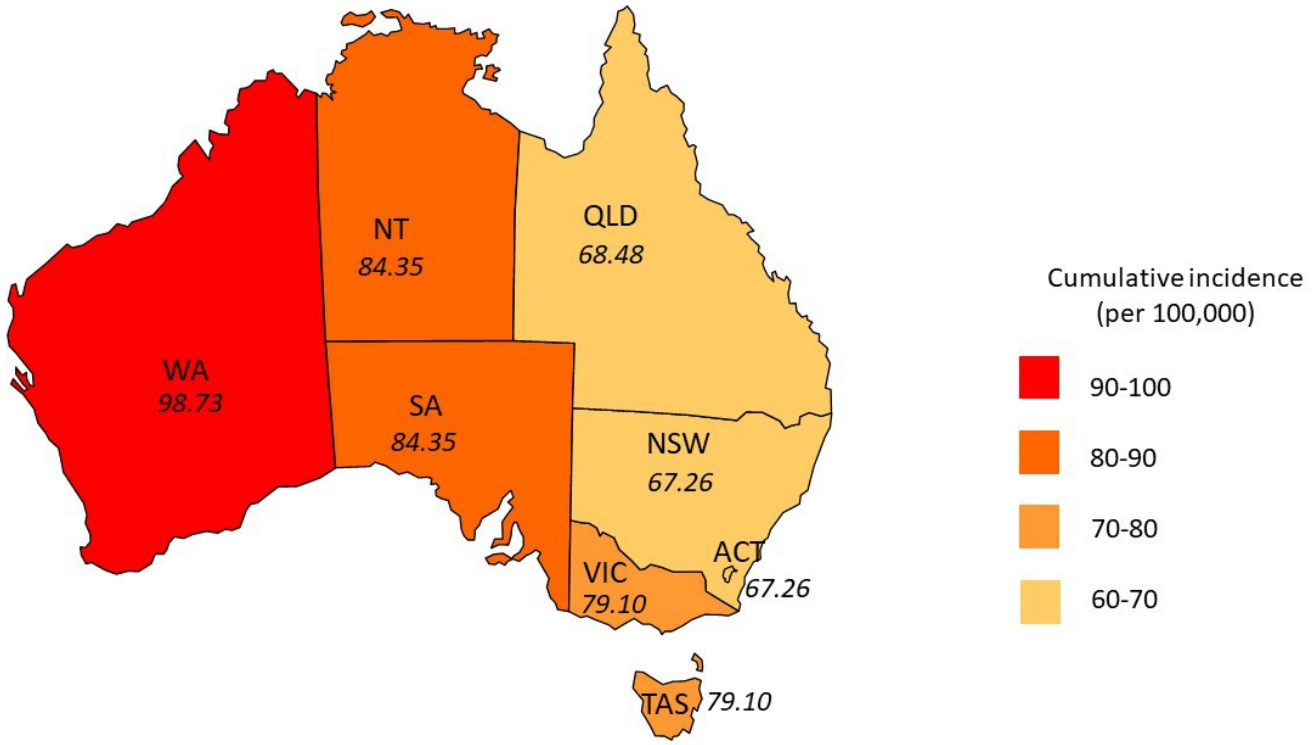
JPC_15713_Figure 3A.JPG

3B



	NSW+ACT	QLD	SA+NT	VIC+TAS	WA	Total
Cumulative incidence (per 100,000)	36.29	22.76	36.03	38.37	43.59	34.89
IRR 95%CI*	1.01 (1.00, 1.03)	0.97 (0.95, 0.99)	1.00 (0.97, 1.02)	0.98 (0.97, 1.00)	0.99 (0.97, 1.01)	0.99 (0.99, 1.00)
P value*	0.053	**0.004**	0.865	**0.013**	0.329	0.098

JPC_15713_Figure 3B.JPG



JPC_15713_Figure 4.jpg

Journal of Paediatrics and Child Health **August 2021**

Title page

Time trends in adrenaline auto-injector dispensing patterns using Australian Pharmaceutical Benefits Scheme data

Running title: AAI dispensing patterns in Australia

Original Article

Yichao Wang[1, 2,3], Jennifer J. Koplin[1, 4], Shaoke Lei[5], Simon Horne[6], Katrina J. Allen[1, 2*], Harriet Hiscock[1, 2, 5], Rachel L. Peters[1, 2]

Affiliations:

[1] Murdoch Children's Research Institute, 50 Flemington Road, Victoria, 3052, Australia.

[2] Department of Paediatrics, University of Melbourne, Victoria, 3010, Australia.

[3] Centre for Social and Early Emotional Development, School of Psychology, Deakin University, Burwood, Melbourne, Victoria, 3125, Australia.

[4] The School of Population and Global Health, University of Melbourne, Victoria, 3010, Australia.

[5] Health Services Research Unit, the Royal Children's Hospital, Victoria, 3052, Australia.

[6] Point Lonsdale Medical Group, Victoria, 3225, Australia.

*Former affiliations when this work was undertaken. No current affiliations.

Corresponding author:

Dr Jennifer J. Koplin

Murdoch Children's Research Institute

50 Flemington Road,

Melbourne, Victoria, 3052, Australia.

E-mail: jennifer.koplin@mcri.edu.au

Phone: +61 3 8341 6236

Acknowledgements

Yichao Wang's PhD research is funded by The University of Melbourne's Melbourne International Research Scholarship (MIRS) and Melbourne International Fee Remission Scholarship (MIFRS) and Murdoch Children's Research Institute's Top-up Scholarship. Research at MCRI is supported by the Victorian Government's Operation al Infrastructure Support Program. H.H. is supported by a National Health and Medical Research Council (NHMRC) Practitioner Fellowship (1136222). J.J.K., K.J.A. and R.L.P. hold or held NHMRC fellowships.

Conflicts of interest

The authors have no conflict