This is the peer reviewed author accepted manuscript (post print) version of a published work that appeared in final form in:

Laba, Tracey Lea, Jan, Stephen, Zwar, Nicholas A, Roughead, Elizabeth, Marks, Guy B, Flynn, Anthony W, Goldman, Michele D, Heaney, Aine, Lembke, Kirsty A & Reddel, Helen K 2019 'Cost-related underuse of medicines for asthma-opportunities for improving Adherence', *Journal of allergy and clinical immunology: in practice* vol. 7, no. 7, pp. 2298-2306.e12

This output may not exactly replicate the final published authoritative version for which the publisher owns copyright. It is not the copy of record. This output may be used for non-commercial purposes. This version is licensed under a Creative Commons CC-BY-NC-ND 4.0 license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

The final definitive published version (version of record) is available at:
https://doi.org/10.1016/j.jaip.2019.03.024

Persistent link to the Research Outputs Repository:
http://researchoutputs.unisa.edu.au/11541.2/137298

General Rights
Copyright and moral rights for the publications made accessible in the Research Outputs Repository are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the persistent link identifying the publication in the Research Outputs Repository

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

COST-RELATED UNDERUSE OF MEDICINES FOR ASTHMA – OPPORTUNITIES FOR IMPROVING ADHERENCE

Tracey-Lea Laba[1,2] BSc. (Hons) App Chem (Forensic Science), BPharm (Hons) PhD (Corresponding author: tracey.laba@sydney.edu.au); Stephen Jan[2] BEc, MEc, PhD (sjan@georgeinstitute.org.au); Nicholas A. Zwar[3, 4] MBBS, MPH, PhD (nzwar@uow.edu.au); Elizabeth Roughead[5] B.Pharm, G.Dip Health Prom, M.App.Sc., PhD (libby.roughead@unisa.edu.au); Guy B. Marks[6, 7] BMedSc, MBBS, PhD (guy.marks@sydney.edu.au) PhD; Anthony W. Flynn[8] (BHSc (Nursing), Post GradDip (Crit.Care. Nurs), MSocSci, (aflynn@asthmafoundation.org.au); Michele D Goldman[8] BBus (Marketing & Advertising) (mgoldman@asthma.org.au); Aine Heaney[9] BSc (Pharmacy) (aheaney@nps.org.au); Kirsty A. Lembke[9] BMedSc, MPharm, MPH (klembke@nps.org.au); Helen K. Reddel[6] (helen.reddel@sydney.edu.au) MBBS PhD

[1.] The University of Sydney, Menzies Centre for Health Policy, School of Public Health, Faculty of Medicine and Health, Australia.

[2.] The George Institute for Global Health, University of New South Wales, Camperdown, Australia

[3.] School of Public Health and Community Medicine, University of New South Wales, Randwick, Australia

[4.] Faculty of Health Sciences and Medicine, Bond University, Robina, Australia

[5.] Quality Use of Medicines and Pharmacy Research Centre, School of Pharmacy and Medical Sciences, University of South Australia, Australia

[6.] Woolcock Institute of Medical Research, University of Sydney, Sydney, Australia

[7.] South Western Sydney Clinical School, University of New South Wales, Sydney, Australia

[8.] Asthma Foundation Queensland and New South Wales, now part of Asthma Australia Limited

[9.] NPS MedicineWise, Sydney, Australia

Authors contributions: All authors have contributed to the conception or design of the work; acquisition, analysis or interpretation of data for the work; drafting or critical revision for intellectual content; final approval of submitted version and are accountable for all aspects of the work.

Financial support: This study was funded by a National Health and Medical Research Council (NHMRC) partnership grant (GNT1077204) with matching funding (including in-kind in the form of staff time) from Asthma Foundation NSW and Asthma Australia Inc. (both now part of the new merged Asthma Australia Limited) and from NPS MedicineWise. TL is supported by a NHMRC Early Career (Sidney Sax) Fellowship (APP 1110230). SJ is supported by an NHMRC Principal Research Fellowship (APP111943). ER is supported by an NHMRC Senior Principal Research Fellowship (APP1110139)

Conflict of Interest Statement: HKR reports receiving independent research grants and study inhalers from GlaxoSmithKline and AstraZeneca, honoraria from AstraZeneca, GlaxoSmithKline, Merck and Novartis for participation on a data safety monitoring board, and honoraria for providing independent medical advice on advisory boards or steering committees from AstraZeneca, GlaxoSmithKline, Novartis and Boehringer Ingelheim, and for providing independent medical education at symposia funded by AstraZeneca, GlaxoSmithKline, Novartis, Teva, Boehringer Ingelheim and Mundipharma. HKR is Chair of the Global Initiative for Asthma (GINA) Scientific Committee and a member of the Australian Asthma Handbook Guidelines Committee.

GBM reports non-financial support from GlaxoSmithKline PLC, grants from AstraZeneca, outside the submitted work.

MG reports from Multiple pharmaceutical and device manufacturers outside the submitted work, specifically: non-financial support from Bird Healthcare, non-financial support from GSK, non-financial support from Astra Zeneca, grants from GSK, grants from Astra Zeneca, grants from Sanofi, grants from Bayer, and grants from Cipla.

TLL, AJ, NAZ, ER, AF, AH, and KL do not have any conflict of interest disclosures to report

Short running head: Cost-related underuse of asthma medicines

Abstract word count: 249

Total word count: 2739

Abstract

Background

In asthma, underuse of cost-effective preventive treatments increases morbidity and mortality. The cost of medicines contributes to underuse ('non-adherence'), but the extent to which people with asthma skip or reduce doses or let prescriptions go unfilled when faced with cost pressures is unknown.

Aims

To estimate the extent of cost-related underuse behaviors and associated factors

Methods

Using previously validated summary indicators, we conducted an online cross-sectional survey of adults and parents of children 5-17 years with asthma in Australia (a high income country) and developed logistic regression models for adults and children with asthma, controlling for key clinical and demographic factors.

Results

The survey was completed by n=792 adults (mean age 47 [SD 17] years, male 47%, concession 60%) and n=609 parents of children (5-10 years 51%, male 60%, concession 59%) with asthma. Cost-related underuse was reported by 52.9% adults and 34.3% parents, predominantly decreasing or skipping doses to make medicines last longer. Higher odds of cost-related underuse were observed with: younger adults (adults: OR 1.19 95%CI 1.12, 1.27), males (adults: OR 1.49 95%CI 1.06, 2.08), having concerns about medicines (adults: OR 3.12 95%CI 2.17, 4.35; parents: OR 2.63 95%CI 1.56, 4.55) , less comfortable talking to prescribers about cost (parents: OR 1.22 95%CI 1.12, 1.33) or changing medicines (adults:

OR 1.12 95%CI 1.03, 1.22), feeling less engaged with prescribers about medicine decisions (parents: OR 1.11 95%CI 1.01, 1.23), and with poorer asthma control (adults, poor control OR 1.87 95%CI 1.13, 3.09; parents, poor control: OR 3.87 95%CI 1.99, 7.54) and requiring specialist (parents: OR 1.83 95%CI 1.16, 2.87) or urgent healthcare visits (adults: OR 1.54 95%CI 1.06, 2.23). Income and concession card status were not associated with cost-related underuse.

Conclusions

Adults and parents of children with asthma indicate high rates of cost-related underuse of asthma medicines, even in the context of national medicines subsidies. Urgent targeting of interventions to promote discussion of medicines and costs between doctor and patients, particularly young adult males, is needed.

Highlights box

What is already known about this topic?

Non-adherence with asthma medicines is a global, avoidable problem exacerbated in the presence of financial barriers. In the United States, evidence has shown cost-related under-use of asthma medicines to be common amongst older patients.

What does this article add to our knowledge?

Despite universal medicine access, cost-related underuse behaviour rates (e.g. reducing doses, skipping medicines, not (re)-filling prescriptions) were high across all age groups, impervious to concession beneficiary status and household income, but influenced by doctor-patient relationships.

How does this study impact current management guidelines?

Targeting of interventions by physicians involved in respiratory care to promote the discussion of medicine costs with patients is urgently needed to address the unmet needs of nonadherence in asthma.

Keywords: Medication adherence, asthma, drug therapy,

Abbreviations:

ICS Inhaled corticosteroid;

LABA long-acting beta agonist;

CPI consumer price index

INTRODUCTION

Asthma, a common chronic disease in children and adults, is one of the world's leading causes of death and disability and a substantial economic strain on health systems.(1) Inhaled corticosteroids (ICS) are cost-effective controller treatments which, if taken regularly, reduce the risk of serious exacerbations(2, 3) and asthma-related death.(4) However, underuse of ICS limits clinical effectiveness and thus likely reduces the potential health-related and economic benefits on offer from such therapies.(5)

Adherence with ICS-containing medications is poor, averaging as little as 25% of the prescribed dose.(6) Many factors, including lack of belief about the necessity of treatment and concerns about risks, are known to contribute.(5, 7) Out-of-pocket costs to patients also impact on the use of medicines for asthma among both adults and children.(8-10) Higher out-of-pocket costs not only lead to significant lower supply of long-term medicines(9) but also to more asthma-related hospitalisations, outpatient and emergency departments visits.(8, 10) Evidence from the US shows asthma to be associated with the some of the highest rates of cost-related underuse behaviors (i.e. reducing doses, skipping medicines, or not (re)-filling prescriptions because of cost). This behavior is not related to income (11) and occurs to a greater extent for asthma than for medications prescribed for other conditions such as cardiovascular diseases and diabetes.(12) In one of the only studies that has specifically compared cost-related underuse of medicines among those with and without asthma, people with asthma (and other chronic pulmonary diseases) who were prescribed inhalers had 43% higher odds of reporting cost-related underuse behaviors compared to those without such diseases.(13)

In Australia, while residents benefit from federally-funded universal health coverage,(14) and all inhaled asthma controller medications are government-subsidized, individuals pay a co-payment for each medicine dispensed. For concessional patients (those receiving government benefits (aged, unemployed, single parents and long term disability)) this is currently USD4.75 per prescription, whilst general (non-concessional) patients pay up to USD29.23 per prescription. A 'safety net' caps total annual co-payments at the family level at USD284.16 (concession) and USD1126.13 (general). Co-payments and safety nets increase annually with the consumer price index (CPI).

When the value of co-payments for medicines rose in real terms (i.e, more than the CPI increase) in 2005, dispensing data showed marked decreases in medicine use particularly for asthma and COPD, especially among vulnerable groups.(15) This reinforced earlier evidence suggesting cost as a barrier to the purchase of ICS inhalers,(16) but efforts to address cost as a barrier to the use of asthma medicines have yet to emerge. Recent qualitative evidence shows that whilst such costs are acknowledged as a major issue by people with asthma, awareness of this by general practitioners is low.(17, 18)

Despite such evidence, the extent to which people with asthma skip or reduce doses or let prescriptions go unfilled when faced with cost pressures is unknown. This study sought to determine the extent of underuse of asthma medicines due to cost and identify factors that may be associated with such behaviour, across a broad range of people with asthma. Some of the results of this study have been previously reported in the form of an abstract.(19, 20)

METHODS

Population

This study included a cross-section of Australian adults and parents of children aged 5-17 years with asthma. A nationally representative sample, based on Australian Bureau of Statistics for people with asthma stratified by age, gender and location, was recruited through an online panel provider (Survey Sampling International, Melbourne, Australia), using a methodology that has been previously reported in detail.(21) Panel members were selected via a three stage random selection process. First, a random sample of panel members was asked to participate in a survey (topic unspecified). Those who responded were asked one of several randomly-selected profiling questions, including "Which of the following ailments have you ever suffered from?"; those who selected "Asthma" were then filtered to identify those with current asthma and parents of children with current asthma aged 5-17 years, using standardized screening questions (see Table E1 in the online repository).

Study recruitment was stratified by age, gender and state of residence according to Australian Bureau of Statistics data for people with asthma.(22) For completing the survey, participants received 'points' to a value of approximately USD1.11 from the panel provider.

The study was approved by University of New South Wales Australia Human Research Ethics Advisory Panel Committee (Approval number # HREAP 2014-7-34), and all participants provided informed consent.

The survey was conducted between December 2015 and March 2016. Details about the survey, including the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) can be

found in the methods in the online repository and the full survey is available from the corresponding author upon request.

Outcome

A previously validated and extensively used summary indicator for medication underuse behaviors due to cost was used.(23, 24) It was based on participants responding “yes, sometimes” or “yes, often” on any of the following questions specific to asthma medicines during the previous 12 months: “skipped doses to make the medicine last longer”; “taken smaller doses of a medicine to make the medicine last longer”; or, “decide not to fill or refill a prescription because it was too costly”. These questions have shown high test-retest reliability and construct validity.(23, 24)

Statistical analysis

Survey questions were used to determine the extent of cost-related underuse and two logistic regression models were developed to determine the factors associated with cost-related underuse separately in i) adults and ii) children with asthma. Given the large numbers of potential factors, a purposeful selection procedure was used(25) controlling for key clinical and demographic factors (age, gender, income, concession status, household composition, number of medicines, ICS inhaler experience) (see Table 3 and Methods in the online repository). Factors that approached significance at the univariable level ($P<0.25$) were retained and the model was sequentially reduced to a preliminary main effects model by eliminating factors at the $p>0.05$ level and comparing model fit and changes to co-efficient sizes (>20% indicating potential confounding and retention of the candidate factor). Factors initially excluded based on the univariable analysis were sequentially added back into the preliminary main effects model and retained if significant at the $P<0.05$ level. Pre-

196 specified interaction terms (i.e. income and concession care status; ICS inhaler experience
197 and concerns about medications) were then added sequentially and if significant retained in
198 the model. Statistical analyses were performed using Stata v14.

199

200 **RESULTS**

201 The flow-chart of study participation is shown in Figure E1 in the online repository. Of the
202 1944 participants eligible to complete the survey, 395 were excluded because their
203 stratification quota were full; 1401 of the remaining 1549 participants completed the survey
204 (90.4% completion rate).

205 The descriptive characteristics of the participants overall and for those reporting cost-
206 related underuse behaviors are shown for adults and children in Table 1 and Table E2 in the
207 online repository. Participants were similar in terms of age and gender compared to the
208 broader asthma population, however there was an over-representation of participants from
209 inner regional Australia and an under-representation from outer regional/remote areas (see
210 Table E3 of the online repository). Of the adults with asthma (n=792, 47.3% male, mean age
211 47.0 years (SD 17.0)), the majority (77.5%) had partly or poorly controlled asthma
212 symptoms. Overall, 58.8% had used any ICS-containing medication in the previous year
213 (80.2% of these as ICS/LABA). Of the children with asthma (n=609, 59.8% male), 50.7% were
214 aged 5-10 years and 49.3% 11-17 years; 75.6% had partly or poorly-controlled asthma
215 symptoms. Overall, 47.1% of children had used any ICS-containing medication in the
216 previous year (50.9% as ICS/LABA). A high proportion of both adults (44.6%) and children
217 (64.0%) reported urgent health care for asthma in the previous 12 months.

Overall, one quarter of adults and parents reported not filling one or more asthma prescriptions (either new or refill) in the previous 12 months (Table 2), with the most common reasons given being due to cost.

Figure 1 shows that cost-related underuse of asthma medications was reported by 52.9% of adults and 34.3% parents of children with asthma. This primarily comprised modifying or skipping the dose of asthma medicines to make them last longer (as opposed to delaying or not filling prescriptions because of cost). The multivariable models presented in Table 3 and Figure 2 demonstrate a number of factors associated with higher odds of cost-related underuse (see Tables E4 and E5 in the online repository for univariable associations). For adults, significant demographic factors were younger age and being male. Adults who reported any concerns about medicines or lower comfort talking to the prescriber about changing their medicines had higher odds of cost-related underuse. Having less well-controlled asthma symptoms, any urgent utilization of health services for asthma and use of an ICS-containing medication in the previous 12 months were also significantly associated with cost-related underuse.

For children with asthma, after controlling for the age and gender of the parent responding to the survey, higher odds of cost-related underuse were associated with having more than 1 medication for a chronic disease (in addition to asthma), and visiting a specialist for asthma in the previous 12 months. In addition, parents having concerns about asthma medications, reporting less comfort discussing the cost of medicines with the prescriber, and less involved in making decisions about medicines had higher odds of cost-related underuse. For children, as for adults, having poorer asthma symptom control was significantly associated with cost-related underuse.

241 For both adults and children, neither concession card status (reflecting the co-payment
242 faced by respondents for each medicine), income (reflecting the potential ability to pay) nor
243 their interaction were statistically significantly associated with cost-related underuse. The
244 exception was that parents of children in a mid-range income household (USD38,480 to
245 53,871) were at a higher odds of indicating cost-related underuse than those in the highest
246 income bands (OR 1.83 95%CI 1.03-3.26, P<0.05).

247 Table E6 in the online repository includes the model for cost-related underuse amongst
248 adults and children with asthma who had used an ICS-containing medication in the previous
249 12 months.

250

251

252

DISCUSSION

In spite of Australia's universal health care system, with government subsidy of all asthma controller inhalers, cost-related underuse of asthma medicines was reported by over half of adults and almost a third of parents of children 5-17 years with asthma in this study. In this cross-sectional survey of a nationally-representative asthma population, younger male adults, people who had any concerns about asthma medicines or were less comfortable talking to prescribers about cost or changing their medicines, those with poorer asthma control and people requiring either specialist or urgent health care visits for their asthma were more likely to report underuse of medicines because of cost. Parents who felt less engaged with prescribers about decisions regarding their child's asthma medications were also at higher odds of reporting cost-related underuse. Cost-related underuse of asthma medicines was not associated with concession card status and only associated with income when comparing children with asthma in a mid-range income band household to those in the highest income band.

The rates of cost-related underuse of medicines reported in this study appear substantially higher than US studies that found 20-31% of adults with asthma indicating these behaviors. For example, amongst 450 people aged ≥50 years using prescription medication for asthma, Piette et al(12) reported that 20% had under-used asthma medication in the previous year, 12% at least monthly; asthma was one of the chronic conditions with the highest rates of cost-related underuse. In another study of 1726 patients aged ≥65 years using inhaled medication for asthma or COPD, Castaldi et al(13) found that 31% reported cost-related underuse in the previous year. In our study the rate of cost-related underuse among people ≥65 years was 32% and similar to the US study. But for people ≥50years, the rate of cost-

related underuse was 39.2%, almost double that reported (i.e. 20%) in the US study by Piette et al.(12) While both studies used a similar summary indicator, the older age-group in the two US studies accounts for some of the observed differences. In our study, older age was associated with significantly lower cost-related underuse. Nevertheless, the figures indicating cost-related underuse are high when comparing features of the US and Australian health systems. These findings reinforce the hidden problem of costs in the access to health care in Australia.(26) The findings also highlight a potentially perverse structural problem in pricing medicines for asthma. For example, regular use of ICS-containing medications is associated with a substantial reduction in the risk of asthma-related hospitalisation or death, but out-of-pocket costs in Australia for commonly-prescribed ICS/LABA inhalers are five times that for reliever inhalers (e.g. USD29.08 for fluticasone/salmeterol compared to USD5.55 for albuterol) which provide only short-term symptom relief.

Of particular importance, therefore, was our finding of a high level of uncontrolled symptoms (three-quarters of adults and children) and need for urgent asthma healthcare (45% adults, 64% children). Significant associations were found between cost-related underuse of asthma medications and worse asthma symptom control, and, in adults, with a greater need for urgent health care for asthma in the previous 12 months. Children with poor asthma symptom control, which in other studies has been associated with obesity, learning disabilities, and poor mental health, were nearly four times as likely to have cost-related underuse; and adults needing urgent asthma care in the previous 12 months were 50% more likely to have cost-related under-use. Cause and effect cannot be disentangled in a cross-sectional study, but prospective studies have shown a clear relationship between poor adherence and risk of uncontrolled asthma and exacerbations.(27)

From a clinical standpoint, the study findings highlight the importance of out-of-pocket cost to adherence behavior by patients with asthma in Australia and the need for practitioners involved in their care to be open to and initiate discussions about medicine costs and concerns. Multifaceted interventions to improve medication use primarily address factors such as the role of the patient, their beliefs and self-management proficiency, and treatment-related factors such as dosing, inhaler technique and adverse consequences. In more recent studies the interaction between patients and their health care providers has been addressed.(28) However, in a recent qualitative study, we found that few GPs were aware of cost as a potential contributor to medication under-use, none were aware of the levels of out-of-pocket costs for asthma medications, and few asked their patients if cost was an issue.(17) This lack of communication about medication costs was confirmed in qualitative interviews with patients and parents of children with asthma.(18) The present findings should prompt an enquiry about cost as a potential problem rather than dose escalation, which would simply worsen cost pressures. Furthermore, educating clinicians and patients about the availability of lower cost and effective treatment options is needed. This is especially important in Australia where most adults and half of children are prescribed ICS as ICS/LABA, despite substantial, but little known, cost savings for both general and concessional patients through prescribing of low-dose ICS-alone.(29) Additionally, better involvement of parents of children with asthma in medication decisions appears important, and there is some evidence that shared decision-making leads to better adherence.(30, 31)

The lack of association with concession card status and income on cost-related underuse may be due to the substantial discounts (of up to 84%) on co-payments available to low-income concession card holders. The increased odds of cost-related underuse for children in

middle income households compared to higher income households potentially reflects the inclusion of a subgroup that could be classified as the working poor, that is people who are just above the income thresholds to qualify for concession card status. This idea has been raised previously,(32) and our results suggest that further work is needed in this area to ensure necessary access to medicines.

Limitations

Although a validated indicator for cost-related underuse has been used, and robust methodology was used to avoid selection bias and response bias, this study has limitations. First, this was a cross sectional study involving members of a large online panel and self-reporting medication-taking behavior over a 12-month look-back period. Although representative of the broader Australian asthma population in terms of gender, age and location, it may not be representative for other factors that are important to cost-related underuse. Furthermore, self-reporting bias and recall bias cannot be excluded, though in this case we would expect our results to understate estimates. Additionally, the indicator for cost-related underuse has not been validated in the Australian context, including against more objective measures of medicine use such as prescription claims data or pill count. Second, non-validated measures of shared decision-making and comfort talking to doctors were used. Third, we have not adjusted our models for annual household out-of-pocket costs; although this question was asked, participant responses were incomplete or not answered for 38% of participants (38% adults, 34% parents of children with asthma). Additionally, whether a lower out-of-pocket cost reflects fewer treatments because of better health or cost-related underuse could not be disentangled. Finally, causative

345 associations with clinical outcomes cannot be ascertained. Further prospective
346 investigations are needed to better understand the clinical impact of cost-related underuse.

347 *Conclusions*

348 Adults and parents of children with asthma indicate high rates of cost-related underuse of
349 asthma medicines in this Australian cohort. These behaviors were unrelated to concession
350 card status and household income but were particularly prominent amongst males and
351 younger participants and in high need patients. Interventions that promote the discussion of
352 medicines and costs between doctor and patients or parents, including the initiation of
353 discussion around the availability of lower cost options, appear warranted.

354

REFERENCES

1. Papi A, Brightling C, Pedersen SE, Reddel HK. Asthma. The Lancet.391(10122):783-800.

2. Pauwels RA, Pedersen S, Busse WW, Tan WC, Chen YZ, Ohlsson SV, et al. Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial. Lancet (London, England). 2003;361(9363):1071-6.

3. Suissa S, Ernst P, Kezouh A. Regular use of inhaled corticosteroids and the long term prevention of hospitalisation for asthma. Thorax. 2002;57(10):880-4.

4. Suissa S, Ernst P, Benayoun S, Baltzan M, Cai B. Low-Dose Inhaled Corticosteroids and the Prevention of Death from Asthma. New England Journal of Medicine. 2000;343(5):332-6.

5. Dekhuijzen R, Lavorini F, Usmani OS, van Boven JFM. Addressing the Impact and Unmet Needs of Nonadherence in Asthma and Chronic Obstructive Pulmonary Disease: Where Do We Go From Here? The Journal of Allergy and Clinical Immunology: In Practice. 2018;6(3):785-93.

6. Boulet LP, Vervloet D, Magar Y, Foster JM. Adherence: the goal to control asthma. Clinics in chest medicine. 2012;33(3):405-17.

7. Horne R. Compliance, adherence, and concordance: implications for asthma treatment. Chest. 2006;130(1 Suppl):65s-72s.

8. Campbell JD, Allen-Ramey F, Sajjan SG, Maiese EM, Sullivan SD. Increasing pharmaceutical copayments: impact on asthma medication utilization and outcomes. The American journal of managed care. 2011;17(10):703-10.

9. Karaca-Mandic P, Jena AB, Joyce GF, Goldman DP. Out-of-pocket medication costs and use of medications and health care services among children with asthma. JAMA. 2012;307(12):1284-91.

10. Ungar WJ, Paterson JM, Gomes T, Bikangaga P, Gold M, To T, et al. Relationship of asthma management, socioeconomic status, and medication insurance characteristics to exacerbation frequency in children with asthma. Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology. 2011;106(1):17-23.

11. Piette JD, Beard A, Rosland AM, McHorney CA. Beliefs that influence cost-related medication non-adherence among the “haves” and “have nots” with chronic diseases. Patient preference and adherence. 2011;5:389-96.

12. Piette JD, Heisler M, Wagner TH. Cost-related medication underuse among chronically ill adults: the treatments people forgo, how often, and who is at risk. American journal of public health. 2004;94(10):1782-7.

13. Castaldi PJ, Rogers WH, Safran DG, Wilson IB. Inhaler costs and medication nonadherence among seniors with chronic pulmonary disease. Chest. 2010;138(3):614-20.

14. Australian Government Department of Health. Pharmaceutical Benefits Scheme (PBS) | About the PBS.

15. Hynd A, Roughead EE, Preen DB, Glover J, Bulsara M, Semmens J. The impact of co-payment increases on dispensings of government-subsidised medicines in Australia. Pharmacoepidemiology and Drug Safety. 2008;17(11):1091-9.

16. Ampon RD, Reddel HK, Correll PK, Poulos LM, Marks GB. Cost is a major barrier to the use of inhaled corticosteroids for obstructive lung disease. Med J Aust. 2009;191(6):319-23.

17. Tudball J, Reddel HK, Laba T-L, Jan S, Flynn A, Goldman M, et al. General practitioners’ views on the influence of cost on prescribing of asthma preventer medicines: a qualitative study. Australian Health Review. 2018;In press (accepted 01/19/18) doi: 10.1071/AH17030.

18. Davis SR, Tudball J, Flynn A, Lembke K, Zwar N, Reddel HKR. “You’ve got to breathe, you know” – asthma patients and carers’ perceptions around purchase and use of asthma preventer medicines. Aust NZ J Public Health, 2019. Online; doi: 10.1111/1753-6405.12865

19. Reddel HK, Laba T-L, Jan S, Marks GB, Flynn A, Roughead E, et al. Effects of Out-of-Pocket Costs on Patient Adherence with Asthma Medicines. American Thoracic Society 2018 International Conference; San Diego: ATS Journals; 2018. p. A1083.

20. Zwar N, Laba T-L, Reddel HK, Lembke K, Flynn A, Roughead E, et al. Cost-related non-adherence and extreme compensatory behaviour in an Australian cohort of adults and children with asthma. NAPCRG; Montreal: North American Primary Care Research Group; 2017.

21. Reddel HK, Sawyer SM, Everett PW, Flood PV, Peters MJ. Asthma control in Australia: a cross-sectional web-based survey in a nationally representative population. Med J Aust. 2015;202(9):492-7.

22. National Health Survey: First Results, 2014-15 - Australia [Internet]. Commonwealth of Australia. 2015. Available from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/4364.0.55.0012014-15?OpenDocument.

23. Pierre-Jacques M, Safran DG, Zhang F, Ross-Degnan D, Adams AS, Gurwitz J, et al. Reliability of new measures of cost-related medication nonadherence. Med Care. 2008;46(4):444-8.

24. Burcu M, Alexander GC, Ng X, Harrington D. Construct Validity and Factor Structure of Survey-based Assessment of Cost-related Medication Burden. Medical Care. 2015;53(2):199-206.

25. Hosmer D, Lemeshow S, Sturdivant R. Model building strategies and methods for logistic regression. Applied logistic regression. 3rd ed: John Wiley and Sons, Inc.; 2013.

26. Jan S, Essue BM, Leeder SR. Falling through the cracks: the hidden economic burden of chronic illness and disability on Australian households. Med J Aust. 2012;196(1):29-31.

27. Williams LK, Peterson EL, Wells K, Ahmedani BK, Kumar R, Burchard EG, et al. Quantifying the proportion of severe asthma exacerbations attributable to inhaled corticosteroid nonadherence. The Journal of allergy and clinical immunology. 2011;128(6):1185-91.e2.

28. van Boven JFM, Ryan D, Eakin MN, Canonica GW, Barot A, Foster JM. Enhancing Respiratory Medication Adherence: The Role of Health Care Professionals and Cost-Effectiveness Considerations. The Journal of Allergy and Clinical Immunology: In Practice. 2016;4(5):835-46.

29. Reddel HK, Lembke K, Zwar N. The cost of asthma medicines. Australian Prescriber. 2018;41:34-6.

30. Fiks AG, Mayne SL, Karavite DJ, Suh A, O'Hara R, Localio AR, et al. Parent-reported outcomes of a shared decision-making portal in asthma: a practice-based RCT. Pediatrics. 2015;135(4):e965-73.

31. Wilson SR, Strub P, Buist AS, Knowles SB, Lavori PW, Lapidus J, et al. Shared treatment decision making improves adherence and outcomes in poorly controlled asthma. American journal of respiratory and critical care medicine. 2010;181(6):566-77.

32. Kemp-Casey A, B Preen D, Glover J, Semmens J, Roughead E. Impact of cost of medicines for chronic conditions on low income households in Australia. Journal of Health Services Research & Policy. 2013;18(1):21-7.

FIGURE LEGENDS

Figure 1: Proportion of cost-related underuse behaviors reported by adults (n=792) and parents of children with asthma (n=609) in the last 12 months.

Figure 2: Multivariable logistic regression of cost-related underuse of asthma medications.

A: Adults with asthma. Variables controlled for in this model were: annual household income, concession beneficiary status, private health insurance, household composition, and the number of other chronic medications.

B: Children with asthma. Variables controlled for in this model were: age and sex of child with asthma, concession card status, household composition, and inhaled corticosteroid use in the previous 12 months.

TABLES

Table 1: Characteristics of 1401 respondents with asthma (792 adults and 609 children), overall and by self-reported cost-related medication underuse (see Figure 1)

		Adult		Children	
		Overall (n=792)	**Any cost-related underuse (n=419, 52.9%)**	**Overall (n=609)**	**Any cost-related underuse (n=209, 34.3%)**
Age (mean, SD)*		47.0 (17.0)	42.3 (16.2)	40 (10.3)	36.9 (9.8)
Age, child with asthma	5-10 years	-	-	309 (50.7)	130 (62.2)
	11-17 years	-	-	300 (49.3)	79 (37.8)
Male gender (of person with asthma)		375 (47.3)	203 (48.4)	364 (59.8)	135 (64.6)
Annual Household income, pre-tax (USD)	less than $38,480	298 (37.6%)	141 (33.7%)	149 (24.5%)	47 (22.5%)
	$38,480 to $53,871	137 (17.3%)	85 (20.3%)	102 (16.7%)	44 (21.1%)
	>$53,871	269 (34.0%)	163 (38.9%)	301 (49.4%)	100 (47.8%)
Concession beneficiary	Yes	478 (60.4)	252 (60.1)	322 (52.9)	132 (63.2)
Self/parent-rated health of person with asthma	Excellent	34 (4.3)	19 (4.5)	86 (14.1)	35 (16.7)
	Very Good	209 (26.4)	103 (24.6)	312 (51.2)	103 (49.3)
	Good	314 (39.6)	173 (41.3)	174 (28.6)	53 (25.4)
	Fair	182 (23.0)	96 (22.9)	33 (5.4)	15 (7.2)
	Poor	53 (6.7)	28 (6.7)	4 (0.7)	3 (1.4)
GINA symptom control, previous 4 weeks	Well controlled	178 (22.5)	57 (13.6)	149 (24.5)	18 (8.6)
	Partly controlled	362 (45.7)	197 (47)	244 (40.1)	79 (37.8)
	Poorly controlled	252 (31.8)	165 (39.4)	216 (35.5)	112 (53.6)

		Adult		Children	
		Overall (n=792)	**Any cost-related underuse (n=419, 52.9%)**	**Overall (n=609)**	**Any cost-related underuse (n=209, 34.3%)**
Urgent health service utilization for asthma, previous 12 months	1 or more ED or hospital visit for worsening asthma	170 (21.5)	125 (29.8)	251 (41.2)	131 (62.7)
	1 or more urgent GP visit for asthma	337 (42.6)	228 (54.4)	366 (60.1)	165 (78.9)
	Any urgent health service utilization for asthma	353 (44.6)	236 (56.3)	390 (64)	170 (81.3)
ICS containing medications in last 12 months	No ICS	326 (41.2)	165 (39.4)	322 (52.9)	96 (45.9)
	ICS-alone only	92 (11.6)	59 (14.1)	141 (23.2)	54 (25.8)
	ICS/LABA +/- ICS-alone	374 (47.2)	195 (46.5)	146 (24.0)	59 (28.2)
Concerns with asthma medications[†]	Possible side effects of medications	241 (30.4)	154 (36.8)	214 (35.1)	84 (40.2)
	Overuse of medication	148 (18.7)	103 (24.6)	180 (29.6)	89 (42.6)
	The cost of medication	231 (29.2)	181 (43.2)	176 (28.9)	104 (49.8)
	Forgetting the medication	144 (18.2)	100 (23.9)	183 (30)	71 (34)
	There are no issues that concern med	325 (41.0)	105 (25.1)	190 (31.2)	26 (12.4)
Shared decision-making[‡]	Mean (SD)	4.3 (2.7)	4.6 (2.5)	4.4 (2.2)	4.9 (2.2)
Comfort discussing with doctor[§]	Changing medications (mean, SD)	7.0 (2.4)	6.6 (2.4)	6.7 (2.2)	6.1 (2.0)
	Cost of medications (mean, SD)	6.6 (2.7)	6.1 (2.7)	6.4 (2.5)	5.5 (2.4)

ED: emergency department, GINA: Global Initiative for Asthma, GP: general practitioner, ICS: inhaled corticosteroid, LABA: long-acting beta agonist, SD: standard deviation, ;[*] For children, of parent responding to survey; [†] "In your use of asthma medication, do any of the following issues concern you?" This was a multiple item response [‡] Respondents were asked to indicate on a scale of 0 to 10, "Who usually makes the decision about what your asthma treatment will be?" with 0 = me only, 10 = doctor only [§] Respondents were asked to indicate on a scale of 0 to 10 "How comfortable do you feel talking to your doctor about a) asking to change your medications b) the cost of your medications?", with 0 =not comfortable at all, 10= very

Table 2: Reasons for not filling asthma prescriptions reported by adults and parents of children with asthma (n, %)

	Overall (n=1401)	Adult (n=792)	Children (n=609)
During the last 12 months, were any asthma medicines prescribed that you did not get?*			
Yes	355 (25.34)	198 (25.00)	157 (25.78)
If yes: which of these reasons explains why you did not get your asthma medicine?†			
Thought it would cost too much	105 (29.58)	56 (28.28)	49 (31.21)
Felt better, didn't need medicine	101 (28.45)	55 (27.78)	46 (29.30)
Didn't think it was necessary for my asthma	69 (19.44)	47 (23.74)	22 (14.01)
Didn't have time	67 (18.87)	27 (13.64)	40 (25.48)
Couldn't get the medicine soon enough	48 (13.52)	27 (13.64)	21 (13.38)
Was afraid of / was experiencing side effects	46 (12.98)	29 (14.65)	17 (10.83)
No pharmacy convenient	38 (10.70)	13 (6.57)	25 (15.92)
Didn't have a way to get the medicine	27 (7.61)	9 (4.55)	18 (11.46)
Didn't think the medicine would help my asthma	25 (7.04)	12 (6.06)	13 (8.28)
Don't like taking medicine	22 (6.20)	19 (9.60)	3 (1.91)

* During the last 12 months, were any asthma controller medications prescribed for you that you did not get filled (dispensed from a pharmacy)? Please think about refills as well as new prescriptions; † Respondents could select more than one reason

Table 3: Relation between respondent demographic, treatment and health variables and cost-related underuse of asthma medicines, as measured by odds ratio (OR, 95% confidence interval) derived from multivariable logistic regression (For unadjusted OR, see Table E3 and E4 in the online repository)[*]

Variable		Adults (n=792)		Children (n=609)	
		Adjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Age respondent, per 5 year increase		0.84 (0.79-0.89)	<0.001	0.86 (0.77-0.97)	0.012
Age of child with asthma	5-10 years	*Not applicable*		1.37 (0.89-2.11)	0.155
	11-17 years	*Not applicable*			
Gender (of person with asthma)	Male	1.00		1.00	
	Female	0.67 (0.48-0.94)	0.021	0.75 (0.49-1.16)	0.195
Gender (parent respondent)	Male	*Not applicable*		1.00	
	Female			0.61 (0.39-0.96)	0.031
Annual Household income, pre-tax (USD)	$53,872 or more	1.00		1.00	
	$38,480 to $53,871	0.89 (0.54-1.48)	0.659	1.83 (1.03-3.26)	0.039
	$38,479 or less	0.70 (0.42-1.14)	0.148	1.31 (0.72-2.40)	0.376
	Prefer not to say	0.35 (0.19-0.64)	0.001	0.95 (0.46-1.98)	0.895
Concession beneficiary	No	1.00		1.00	
	Yes	1.22 (0.81-1.85)	0.347	1.27 (0.80-2.03)	0.309
Private Health insurance	No	1.00			
	Yes	0.70 (0.49-1.00)	0.052		
Household composition	Single living without dependents	1.00		1.65 (0.73-3.69)[‖]	0.226
	Couple living without dependents	1.09 (0.71-1.68)	0.870		
	Single living with dependents	0.97 (0.63-1.47)[§]	0.705	1.00	
	Couple living with dependents			1.17 (0.62- 2.21)	0.634
Number of other chronic medications	None	1.00		1.00	
	1-4	1.33 (0.91-1.95)	0.145	2.39 (1.48-3.87)[**]	<0.001
	5 or more	1.03 (0.61-1.75)	0.913		
GINA symptom control, previous 4 weeks	Well controlled	1.00		1.00	
	Partly controlled	1.59 (1.03-2.45)	0.038	2.65 (1.39-5.05)	0.003
	Poorly controlled	1.87 (1.13-3.09)	0.015	3.87 (1.99-7.54)	<0.001
Any urgent health service utilization for asthma	No	1.00			
	Yes	1.54 (1.06-2.23)	0.024		
Specialist visit for asthma, previous 12 months	No			1.00	
	Yes			1.83 (1.16-2.87)	0.009
Inhaled corticosteroid (ICS) containing medications	No ICS	1.00		1.00	
	ICS experienced	1.59 (1.11-2.28)	0.011	1.07 (0.70-1.63)	0.756

Concerns with asthma medications					
There are no issues that concern me	No	1.00		1.00	
	Yes	0.32 (0.23-0.46)	<0.001	0.38 (0.22-0.64)	<0.001
Shared decision-making				1.11 (1.01-1.23)	0.036
Comfort discussing changing medications with doctor	0-2‡	1.10 (0.73-1.65)	0.659		
	3-10‡	0.89 (0.82-0.97)	0.007		
Comfort discussing medication costs with doctor	Mean			0.82 (0.75-0.89)	<0.001
Model Fit Statistics	Hosmer-Lemeshow Goodness of Fit (Prob > chi2)	0.5182		0.3579	
	AIC	892.6		606.9	
	McFadden R2, adj	0.166		0.216	
	Observations	773†		603†	

AIC: Akaike Information Criterion, GINA: Global Initiative for Asthma, ICS: inhaled corticosteroid, OR: Odds Ratio, Prob: probability, *Both multivariable models adjusted for age, gender, income, concession status, household composition, number of medicines, ICS inhaler experience; † Household composition=other omitted from analysis (n=19 adults and n=6 children); ‡Linear spline with knot at score=3 as determined from Lowess smoothing plot of Probability of cost-related underuse against variable; § Single or couple living with dependents; ‖ Single or couple living without dependents; ** 1 or more other chronic medications