# Trends in medication use for asthma in school-entry children in the Australian Capital Territory, 2000–2005

Christine B Phillips, Helen Toyne, Karen Ciszek, Robyn G Attewell and Marjan Kljakovic

sthma is common among Australian children, with an estimated prevalence of 14%–16%.¹ Over the past decade, hospitalisations and deaths related to asthma have decreased significantly.¹ Although the use of potent inhaled corticosteroids has increased in Australia,¹ as well as in New Zealand² and Scotland,³ little is known of the changing profile of medication use among children with asthma.

Published studies of the pharmacoepidemiology of childhood asthma generally explore overall trends by collating state and national data on pharmacy prescriptions. Those that have examined children's medication use have been cross-sectional studies relying on general practice data, or telephone surveys. These may permit more detailed analysis of medication use by children with asthma but do not allow us to examine time trends.

Here, we report trends in the use of asthma medications in a population-based health assessment of all school-entrant children in the Australian Capital Territory from 2000 to 2005.

# **METHODS**

All school-entry children in the ACT undergo health screening in kindergarten, which includes a survey completed by parents (delivery and structure described elsewhere<sup>7</sup>). Since 1998, this survey has comprised a general health questionnaire and an 18-item questionnaire for children with respiratory symptoms. The respiratory questionnaire includes an item asking parents to identify (from a checklist of proprietary names of asthma drugs) medications taken by their child in the last year. Parents report the average frequency of use per week for each class of medication (preventers, relievers, symptom con-

## **ABSTRACT**

**Objective:** To analyse trends in asthma medications used by school-entry children whose parents report they have asthma.

**Design and setting:** Annual cross-sectional study of all school-entry children (about 4400 each year) in the Australian Capital Territory in 2000–2005, by means of a questionnaire for parents on child health status and medication use; and a cross-sectional study of asthma prescriptions for children aged 5 years obtained from the Medicare Australia database for 2002–2005.

**Participants:** All school-entry children in the ACT with parent-reported asthma (numbers in the years 2000–2005 ranged between 435 and 589).

**Main outcome measures:** Changes in the use of different medications; changes in delivery devices for asthma; changes in the potency of inhaled fluticasone.

**Results:** Response rates to kindergarten health screening were in the range 85%–89% for 2000–2005. Parent-reported asthma prevalence ranged from 11% to 15%. Each year, around 35% of children with asthma (age range, 4–6 years) used inhaled corticosteroids. An increase in the use of fluticasone (from 11% to 33% of children with asthma) was offset by decreases in beclomethasone use (from 14% to 3%) and budesonide (from 14% to 4%). Use of cromoglycate and nedocromil fell from 46% to 16%. Nebuliser use decreased (from 45% to 20%), while the use of spacer devices increased (from 70% to 83%). Use of combined salmeterol/fluticasone increased from 8% (in 2002) to 20% (in 2005) of children with parent-reported asthma. These trends were mirrored in Medicare Australia data for 5-year-old children in the ACT.

**Conclusions:** There was marked volatility in the types of asthma medication used over the 6 years. Reciprocal trends leading to increased use of spacers and decreased use of nebulisers are in accord with national guidelines for better asthma management. The increasing use of products containing a combination of salmeterol and fluticasone requires ongoing monitoring.

MJA 2007; 187: 10-13

trollers, combination products and oral corticosteroids).

We analysed data on asthma medication use for children with parent-reported asthma for the years 2000–2005. Data from 1998 and 1999 were excluded because of inconsistencies in data collection instruments in those years. International Study of Asthma and Allergies in Childhood questions were used to determine the severity and pattern of asthma (infrequent, frequent or persistent). We assessed statistical significance by means of  $\chi^2$  tests for trend.

To validate our findings, we examined Medicare Australia data on prescriptions for fluticasone-containing products, salbutamol nebules and cromoglycate in the ACT for children who turned 5 years of age before 1 May for the years 2002–2005. Medicare Australia withheld data on prescriptions for a medication if fewer than five were dispensed per year. Using mid-year age-specific population estimates as the denominator, we calculated defined daily doses per thousand 5-year-old children for these medications. For combination products, the principles out-

# 1 Study and sample population response rates, Australian Capital Territory kindergarten health screening data, 2000–2005

	2000	2001	2002	2003	2004	2005
ACT school-entry population	4548	4411	4447	4317	4382	4314
Participated in survey	3884 (85%)	3858 (87%)	3794 (85%)	3700 (86%)	3826 (87%)	3851 (89%)
Parent-reported asthma	589 (15%)	499 (13%)	531 (14%)	466 (13%)	452 (12%)	435 (11%)
Respondents to medication question	561 (95%)	476 (95%)	517 (97%)	443 (95%)	415 (92%)	394 (91%)

2 Trends in reported medication use in the preceding 12 months for Australian Capital Territory school-entry children with parent-reported asthma, 2000–2005 (ACT kindergarten health screening data)

	2000	2001	2002	2003	2004	2005	P*
Number of children	561	476	517	443	415	394	
Medication							
Relievers	520 (93%)	432 (91%)	471 (91%)	382 (86%)	369 (89%)	355 (90%)	0.03
Salbutamol	499 (89%)	421 (88%)	456 (88%)	372 (84%)	367 (88%)	353 (90%)	8.0
Terbutaline	69 (12%)	34 (7%)	43 (8%)	19 (4%)	16 (4%)	12 (3%)	< 0.001
Anticholinergics <sup>†</sup>	158 (28%)	108 (23%)	102 (20%)	58 (13%)	41 (10%)	25 (6%)	< 0.001
Mast cell stabilisers	258 (46%)	193 (41%)	158 (31%)	112 (25%)	83 (20%)	64 (16%)	< 0.001
Sodium cromoglycate	228 (41%)	179 (38%)	146 (28%)	103 (23%)	79 (19%)	56 (14%)	< 0.001
Nedocromil sodium	46 (8%)	18 (4%)	18 (3%)	11 (2%)	7 (2%)	9 (2%)	< 0.001
Inhaled corticosteroids	199 (35%)	170 (36%)	161 (31%)	149 (34%)	161 (39%)	150 (38%)	0.2
Beclomethasone	81 (14%)	57 (12%)	12 (2%)	7 (2%)	13 (3%)	11 (3%)	< 0.001
Fluticasone	61 (11%)	71 (15%)	110 (21%)	115 (26%)	139 (33%)	129 (33%)	< 0.001
Budesonide	78 (14%)	63 (13%)	47 (9%)	34 (8%)	13 (3%)	14 (4%)	< 0.001
Long-acting $\beta_2$ agonists $^{\ddagger}$	24 (4%)	25 (5%)	27 (5%)	16 (4%)	10 (2%)	13 (3%)	0.06
Combination products <sup>§</sup>	0	0	40 (8%)	62 (13%)	75 (18%)	79 (20%)	< 0.001
Oral prednisolone	78 (14%)	72 (15%)	117 (23%)	93 (21%)	87 (21%)	106 (27%)	< 0.001
Leucotrienes <sup>1</sup>	0	3 (1%)	9 (2%)	12 (3%)	19 (5%)	30 (8%)	< 0.001

<sup>\*</sup> P value for test for trend with year. † Ipratropium bromide was the only medication mentioned. \$ Salmeterol/fluticasone was the only medication mentioned. ¶ Montelukast was the only medication mentioned.

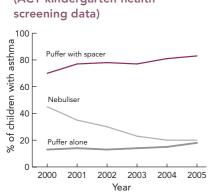
lined by the World Health Organization Collaborating Centre for Drug Statistics Methodology were followed to develop an overall defined daily dose per thousand 5-year-old children for fluticasone. <sup>10</sup>

The ACT Department of Health and Community Care Institutional Ethics Committee approved this study.

# **RESULTS**

Response rates (shown in Box 1) to the general health questionnaire ranged from 85% to

3 Trends in the use of delivery devices for asthma medication among Australian Capital Territory school-entry children, 2000–2005 (ACT kindergarten health screening data)



89%. For children with parent-reported asthma, response rates to the question on asthma medications ranged from 91% to 97%.

The prevalence of parent-reported asthma ranged from 11% to 15% (Box 1), affecting at least 430 children annually. The children's ages ranged from 4 to 6 years (median, 5 years). Sixty per cent were boys. A third of children with asthma were classified as having mild asthma, and 30% were classified as having severe asthma. Twelve per cent of children were reported to have needed admission to intensive care or a high dependency unit because of their asthma.

Overall, 94% of children with asthma were reported as using at least one asthma medication in the preceding year.

Box 2 shows that inhaled corticosteroid use remained stable, despite decreases in the use of budesonide and beclomethasone, and a threefold increase in fluticasone use. Use of all fluticasone-containing products increased from 11% to 46% of all children with asthma ( $\chi^2$  for trend, 112; P < 0.001).

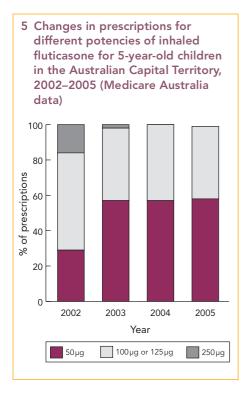
Over the study period, kindergarten health survey data showed that salbutamol use among children without parent-reported asthma increased; children without asthma accounted for 19% of all children receiving salbutamol in 2000, but 35% of all children receiving salbutamol in 2005

Box 3 shows that reported use of spacers increased over the study period from 70% to

4 Trends in defined daily doses\* of selected asthma medications for 5-year-old Australian Capital Territory children, 2002–2005 (Medicare Australia data)

	2002	2003	2004	2005
Population of 5-year-olds in the ACT	4244	4060	4154	4094
Prescriptions for fluticasone	368	384	439	486
Defined daily dose	5.19	4.13	4.49	4.62
Prescriptions for salbutamol nebules	119	81	22	21
Defined daily dose	0.61	0.44	0.11	0.10
Prescriptions for cromoglycate	241	138	131	62
Defined daily dose	2.48	1.47	1.21	0.58

<sup>\*</sup> Number of defined doses/1000 5-year-old children/day.



83% of children with asthma ( $\chi^2$  for trend, 23; P < 0.001), while reported nebuliser use fell from 45% to 20% of children with asthma ( $\chi^2$  for trend, 106; P < 0.001). The frequency of medication use remained stable over the 6 years, with 53% of children taking preventer medications (inhaled corticosteroids, mast cell stabilisers, montelukast) at least 4 days per week.

Medicare Australia data (Box 4) showed increases in the total number of prescriptions dispensed for fluticasone-containing products from 2002 to 2005, but a decrease in the number of defined daily doses per thousand 5-year-old children. Over the same period, numbers of prescriptions for salbutamol nebules and cromoglycate decreased. Medicare Australia data also showed a shift to less potent forms of fluticasone from 2003 (Box 5).

## **DISCUSSION**

Here, we report the largest study to date of trends in asthma medication use among Australian children with asthma. The trends we identified were validated against Medicare Australia data for the general population.

Our study period coincides with an important event in asthma management in Australia — the Asthma Management Program, which was announced in the 2001–02 federal budget, and emphasised evi-

dence-based asthma management.1 Some of the volatility in the use of asthma medications and delivery devices may reflect improved awareness among doctors and patients of best practice. The decline in nebuliser use may indicate improved confidence among parents in the use of spacer devices, reflecting changes in emergency department and specialist practice, and instruction in these techniques by community asthma educators. The fall in the use of ipratropium bromide probably reflects the decline in nebuliser use, as this drug is sold in nebules as well as in a metered aerosol. Declines in the use of cromoglycate and nedocromil are part of an international trend, with heightened emphasis on the use of inhaled corticosteroids, and doubts about the effectiveness of sodium cromoglycate.11

Although corticosteroid use remained largely unchanged, there was a marked increase in the use of fluticasone. Use of inhaled corticosteroids is generally held to be a marker of good asthma management (a recent meta-analysis found that, at recommended doses, they pose no risk to long-term statural growth, cortisol levels, and bone mineral density, 12 although inhaled budesonide and, to a lesser extent, fluticasone do slow growth velocity<sup>13</sup>). Nevertheless, potent corticosteroids like fluticasone may be unsafe in children if effective back-titration is not undertaken when appropriate. In New Zealand, the introduction of fluticasone led to a near doubling of the equipotent dose of inhaled corticosteroid given to children aged under 5 years, because of its increased potency.<sup>3</sup> In Australia, the Pharmaceutical Benefits Scheme moved to contain the use of highdose fluticasone by limiting the number of repeat prescriptions for preparations containing 250 µg or 500 µg of fluticasone. Our analysis of Medicare data indicated that, since 2003, more ACT children who use fluticasone have been prescribed lower doses.

The number of children using puffers alone increased slightly. Salbutamol was available over the counter during the study period. Interestingly, the number of children in our study who had used salbutamol in the preceding year, and whose parents did not report they had asthma, increased. Possible reasons may be underdiagnosis of asthma, overtreatment of respiratory symptoms which are not asthma, or parents contesting the diagnosis of asthma. All of these indicate the need for enhanced roles

for pharmacists in triage and education about asthma.

Although reported use of salmeterol was stable across the study period, there was a significant increase in use of the medication containing a combination of salmeterol and fluticasone, with a fifth of children with asthma using this product in 2005. Combination products have a role in managing children who require at least one dose of  $\beta_2$  agonist per day, <sup>14</sup> although the evidence supporting the efficacy of fixeddose combinations for children is not substantial.15 Because of concerns about an increased risk of unexplained death with salmeterol, 16 the Therapeutic Goods Administration has recommended that long-acting  $\beta_2$  agonists only be used in combination with inhaled corticosteroids.17 However, recent reports suggest that, even in combination with corticosteroids, long-acting  $\beta_2$  agonists may pose an increased risk of asthma death, particularly in genetically predisposed subpopulations. 18

Our study has some limitations. We may have missed some children with asthma who were symptom-free during their assessments. Our methods relied on parents' recall, which may have been unreliable in regard to some medications. We do not have details of the medication dosages, or the period over which children took various medications. We are unable to comment on the use of oral corticosteroids to control asthma, as these drugs are also used for children who have had treatment for croup and other steroid-responsive conditions. Our estimates of trends from Medicare Australia data are also an underestimate, as low-use medications (fewer than five prescriptions per year) were excluded from the analysis.

Our findings indicate the volatility of reported usage patterns for asthma medication among children over time. Our study raises the possibility of overuse of potent inhaled corticosteroids, and found high rates of use of combination products containing long-acting  $\beta_2$  agonists. Studies such as ours offer important windows into the pharmacological everyday life of children with asthma. There is a need for ongoing study of medication use, particularly as the recommendations for pharmacotherapy for asthma have changed quite rapidly in the past 5 years. In 2005, montelukast was introduced onto the Schedule of Pharmaceutical Benefits. Further studies should track the impact of this preparation

#### RESEARCH

on inhaled corticosteroid and bronchodilator use.

#### **ACKNOWLEDGEMENTS**

We are grateful to the maternal and child nurses from ACT Health who undertook the kindergarten health screening, Dr Clare McGuiness for advice, and Ms Maxine Robinson and staff of the Drug Utilisation Sub-Committee of the Pharmaceutical Benefits Advisory Committee, Australian Government Department of Health and Ageing for assistance with accessing Medicare Australia data.

## **COMPETING INTERESTS**

Covance Pty Ltd has ongoing consulting agreements with Boehringer Ingelheim, AstraZeneca and GlaxoSmithKline Australia. Robyn Attewell has been involved in research in primary care and clinical settings under these contracts. Her contribution to this article was not related to these contracts, and was under a separate consulting contract with ACT Health and Community Care.

#### **AUTHOR DETAILS**

**Christine B Phillips,** MBBS, MPH, FRACGP, Senior Lecturer<sup>1</sup>

Helen Toyne, BM BS, FRACGP, Lecturer<sup>1</sup> Karen Ciszek, RN, RM, Research Nurse<sup>1</sup> Robyn G Attewell, BSc, MSc, AStat, Statistician<sup>2</sup>

Marjan Kljakovic, MB ChB, FRACGP, PhD, Professor<sup>1</sup>

- 1 Academic Unit of General Practice and Community Health, Australian National University, Canberra, ACT.
- 2 Covance Pty Ltd, Canberra, ACT. *Correspondence:*

christine.phillips@anu.edu.au

#### **REFERENCES**

- 1 Australian Institute of Health and Welfare Australian Centre for Asthma Monitoring. Asthma in Australia 2005. AIHW Asthma series No. 2. Canberra: AIHW, 2005. (AIHW Cat. No. ACM 6.) http://www.aihw.gov.au/publications/index.cfm/title/10158 (accessed May 2007).
- 2 Johansson M, Hall J, Reith D, et al. Trends in the use of inhaled corticosteroids for childhood asthma in New Zealand. Eur J Clin Pharmacol 2003; 59: 483-487.
- 3 Boyter AC, Steinke DT. Changes in prescribing of inhaled corticosteroids (1999–2002) in Scotland. *Pharmacoepidemiol Drug Saf* 2005; 14: 203-209.
- 4 Robertson J, Fryer JL, O'Connell DL, et al. Limitations of Health Insurance Commission (HIC) data for deriving prescribing indicators. *Med J Aust* 2002; 176: 419-424.
- 5 Britt H, Miller GC, Knox S, et al. General practice activity in Australia 2004–05. General Practice Series No. 18. Canberra: Australian Institute of Health and Welfare, 2005. (AIHW Cat. No. GEP 18.) http://www.aihw.gov.au/publications/index.cfm/title/10189 (accessed Jun 2007).
- 6 Mommers M, Swaen GM, Weishoff-Houben M, et al. Differences in asthma diagnosis and medication use in children living in Germany and the Netherlands. *Prim Care Respir J* 2005; 14: 31-37.
- 7 Phillips CB, Yates R, Glasgow NJ, et al. Improving response rates to primary and supplementary questionnaires by changing response and instruction burden: cluster randomised trial. Aust N Z J Public Health 2005; 29: 457-460.
- 8 Ellwood P, Asher MI, Beasley R, on behalf of the International Study of Asthma and Allergies in Childhood Steering Committee and the ISAAC Phase Three Study Group. ISAAC phase three manual. Auckland: ISAAC, 2000. http://isaac.auckland.ac.nz/Phasethr/Manual.pdf (accessed May 2007).
- Australian Bureau of Statistics. Population by age and sex, Australian states and territories, 2006. Canberra: ABS, 2006. (ABS Cat. No.

- 3201.0.) http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3201.0Jun%202006? OpenDocument (accessed May 2007).
- 10 World Health Organization Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment. Oslo: WHOCC for Drug Statistics Methodology, January 2006.
- 11 Van der Wouden JC, Tasche MJA, Bernsen RMD, et al. Sodium cromoglycate for asthma in children. *Cochrane Database Syst Rev* 2003; (3): CD002173. DOI: 10.1002/14651858.CD002173 http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD002173/frame.html (accessed Jun 2007).
- 12 Pedersen S. Clinical safety of inhaled corticosteroids for asthma in children: an update of long-term trials. *Drug Saf* 2006; 29: 599-612.
- 13 Ferguson AC, Van Bever HP, Teper AM, et al. A comparison of the relative growth velocities with budesonide and fluticasone propionate in children with asthma. Respir Med 2007; 101: 118-129
- 14 Asthma management handbook 2006. Melbourne: National Asthma Council Australia, 2006. http://www.NationalAsthma.org.au/publications/amh/amhcont.htm (accessed May 2007).
- 15 Bisgaard H, Le Roux P, Bjamer D, et al. Budesonide/formoterol maintenance plus reliever therapy: a new strategy in pediatric asthma. Chest 2006; 130: 1733-1744.
- 16 Nelson HS, Weiss SC, Bleecker ER, et al; SMART Study Group. The Salmeterol Multicenter Asthma Research Trial: a comparison of usual pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol. Chest 2006; 129: 15-26. [Erratum: Chest 2006; 129: 1393.]
- 17 Janson C, de Marco R, Accordini S, et al. Changes in the use of anti-asthmatic medication in an international cohort. Eur Respir J 2005; 26: 1047-1055.
- 18 Martinez FD. Safety of long-acting beta-agonists an urgent need to clear the air. N Engl J Med 2005; 353: 2637-2639.

(Received 14 Nov 2006, accepted 19 Apr 2007)