The impact of an prescriber awareness campaign on persistent high average daily doses of inhaled steroids in New Zealand primary care.

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Aim: To assess the effectiveness of the PHARMAC Asthma Management Campaign in reducing inappropriately high average daily doses of inhaled corticosteroids.

Methods: Data on inhaled corticosteroid (ICS) prescriptions written between 1 April 2002 and 29 September 2004 were downloaded from the computerised prescribing records of a random sample of 339 general practices and beclomethasone equivalent average daily doses (ADD) of prescribed inhaled corticosteroids calculated. Monthly trends were examined and ADDs in the three months July – September for 2002 compared with the same months in 2004.

Results: Between June – September 2002 and June – September 2004 there was a statistically significant reduction in inhaled corticosteroid average daily doses for people aged over 20. The reduction was however clinically insignificant. Across all ages the reduction was 70 mcg (age adjusted), which is also clinically insignificant. There were reductions in ICS ADDs across all ethnic groups. The distribution of dosages revealed persistent inappropriately high prescribing, although the number of very high dose prescriptions decreased for all inhaled steroid types. The largest reductions were recorded for budesonide and fluticasone prescriptions, but these were highest to begin with. The highest ADDs in adults after the campaign were still for fluticasone and budesonide.

Conclusion: Despite a concerted effort from multiple parties the inappropriate prescribing of high dose inhaled corticosteroids remains a significant problem that warrants further investigation.

Key words: Health promotion, asthma, prescribing.

Introduction

Average Daily Doses (ADD) of inhaled corticosteroids (ICS) have increased appreciably since the late 1990s when high potency medications such as fluticasone and very high dose preparations (e.g. Pulmicort® 400 mcg, Flixotide® 250 mcg, Flixotide® 500 mcg) became available. In 2001 national dispensing claims data indicated that about one quarter of patients in New Zealand were prescribed ICS beyond recommended maximum daily doses. It is likely that significant numbers of clinicians had substituted fluticasone for other inhaler steroids on a similar dosage without allowing for its increased potency per microgram, as suggested in earlier research: [1]

> "The average prescribed dose of fluticasone was 80% of that for beclomethasone, even though fluticasone is at least twice as potent as beclomethasone. Similar findings were observed when the general practitioners responded to the case histories. The high doses of fluticasone prescribed may be due to a failure to appreciate that fluticasone is twice as potent as beclomethasone and to the availability of high strength preparations of fluticasone, i.e. 250 micrograms per actuation."

In addition to prescribers probably not reducing physical doses to account for increased potency, the ICS market shifted increasingly towards fluticasone rather than beclomethasone (BDP) and budesonide, particularly after a direct-to-consumer advertising campaign undertaken by the supplier in April-October 2002.[2] Industry sponsored product prescribing information advocated excessively high fluticasone daily dose, with the widely-used prescribing information contained in the "New Ethicals Catalogue" presented dose ranges far in excess those recommended by New Zealand national and most international guidelines .

The best evidence was that doses of 1000 µg/day beclomethasone-equivalents in adults are sufficient, with negligible added benefits beyond that level. [3 4 5] Concerns about the high ICS ADDs had been increasingly expressed by a number of clinicians in New Zealand [1 6] (as in Australia [7]).

The problem was recognised and a number of initiatives were implemented to reduce inappropriately high prescribing, by individual practices, by Independent Practitioner Associations (IPAs) and by Primary Health Organisations (PHOs). PHARMAC developed an intensive health professional and patient education programme, the Asthma Management Campaign, which was launched in February 2003. The campaign included GP, practice nurse and pharmacist education (materials, prescribing reports, audit tools, case studies), information packs for patients and GPs, and a patient education visual aid for use by asthma educators with patients and their families/whanua aimed specifically at Maori and Pacific Island people. The campaign involved the Asthma and Respiratory Foundation of New Zealand, the Best Practice Advocacy Centre (bpac^{nz}), PreMeC, professional colleges, pharmacy facilitators and PHOs. Details of the campaign can be found in the Appendix to this paper. This paper investigates the changes in inhaled steroid dosages over the period before and after this campaign.

Methods

A random sample of general practices were invited to take part in the study, stratified by District Health Board area (to ensure regional variations could be examined). The research was restricted to practices running the MedTech32 practice management system, which at the time was 75% of all practices. Recruitment continued until 350 practices had agreed to participate. The response rate was 73% (350/479). Recruitment commenced on 20th September 2004 and finished 29th October 2004.

Data were collected using a computerised query supplied by email or disk, which was run by the staff of the practice, while being guided by CBG staff over the telephone, if necessary. Data was returned by post or email. Data collection commenced on February 7th 2005 and was completed on March 11th. Data were collected from 339 practices. Six practices decided to no longer participate and in five practices data could not be successfully sent by floppy disk. Hence data were available from 71% of those practices initially invited (339/479).

Data were collected on 347496 prescriptions for inhaled corticosteroids – defined as metered dose inhalers and breath activated devices for the chemical entities beclomethasone dipropionate (BDP), budesonide and fluticasone propionate. Budesonide in turn was differentiated according to sole inhaled corticosteroid inhalers (Pulmicort®) and budesonide/eformoterol fixed dose combination inhaled corticosteroid/long-acting beta agonist inhalers (Symbicort®). Reporting for budesonide

inhalers in this report refers to the aggregate of Pulmicort® and Symbicort® prescriptions, described simply as the chemical entity “budesonide”.

The data collected included demographic data (age, gender, and ethnicity) and prescribing data for prescriptions for the above inhaled corticosteroids written between 01/04/2002 and 20/09/2004, a . The prescribing data included drug name, presentation, dose, frequency, any written instructions, and date of prescription. For 1246 prescriptions there was no recorded information on dose of steroid to be taken. These prescriptions were excluded from the dataset, leaving 346250 prescriptions.

Ethnicity was reported using 318 different codes. These were mapped to Statistics NZ “level 0” codes of Maori, Pacific and Other. Ethnicity data was missing for 18076 prescriptions (5.2%).

Prescriptions were written in 21946 different ways, including variations in dose, frequency, spelling and punctuation. Every way of writing a prescription that occurred more than once in the dataset of 346250 prescriptions was examined to determine a maximum and a minimum dose per day that could be taken if the instructions were followed. If the dose was not specified as a range the minimum dose and the maximum dose were the same. There were 9051 unique ways of writing a prescription that occurred only once. Because of the large clerical effort involved in coding these prescriptions for no significant gain in precision of ADD calculations these 3% of prescriptions were excluded from the analysis. In 1853 prescriptions the instructions could not be used to determine a daily dose. When these prescriptions were excluded the final dataset for ADD analyses consisted of 335346 prescriptions (96.5% of the original prescriptions).

The Average Daily Dose (ADD) of prescribed inhaled steroid was determined by calculating the number of doses per day that would be taken by the patient if they followed the instructions printed on the prescription, and multiplying this by the amount of steroid per dose for the stated presentation of the prescribed product. Where doses were expressed as a range the high value was used for the ADD calculation. There were no adjustments for outlying doses (that is, obvious keying errors providing unrealistic values in dose and/or strength fields) – all dosage regimes were included (except those prescriptions above where daily doses could not be determined). Doses were expressed as beclomethasone equivalents (“BDPE”). The BDPE dose of fluticasone was considered to be twice the dose of fluticasone, eg 250mcg of fluticasone was recorded as 500 mcg BDPE. Confidence intervals for estimates were calculated assuming the prescriptions represented a random sample of all prescriptions.

To control for any changes in the age distribution of ICS users of time (affecting daily dose requirements – see below) and to compare with previous work on inhaled corticosteroid ADD the Beclomethasone Age Equivalent Daily Dose (BAEDD) was also calculated. The BAEDD allows data for all age groups to be considered together. This measure assumes that children aged less than 12 years old require half the steroid dose that children over 12 require, for similar severity of disease.[1] Because age data (in years) were not reliably available in national data sources, the BAEDD was calculated by doubling the ADD expressed in BDPEs for scripts for patients in the “Y” (0-5) age group and multiplying the ADD for “J” (6-18) patients by 1.55, to reflect the approximate age distribution within this group. Although we had access to patients’ actual ages, we have calculated BAEDD using this approximation to maintain comparability with previous analyses.

The impact of the Asthma Management Campaign was evaluated using two methods. The first was to plot ADD or BAEDD by month, to present the trend in ADD for visual inspection. The second was to undertake a comparison of the latest 4 months data that were available (June – September 2004) with the same seasonal period before the Campaign started (June – September 2002). This approach provided control for known seasonal variations in inhaled corticosteroid ADDs.[2] Statistical significance was measured using t-tests for independent samples.

To control for the impact of differences in the age and ethnic structures of DHB populations on changes in BAEDDs, age-and-ethnicity standardised BAEDDs were calculated. Age standardisation was based on the Segi age modelled to the 2001 NZ population census ethnicity by age distribution. We did not undertake formal statistical testing for the significance of differences between DHBs' age/ethnicity standardised ADDs.

[1] When recommending daily dose maxima for ICSs for adults and children the Pharmac Therapeutics Advisory Committee respiratory subcommittee defined “children” as being aged less than 12 years.

Results

The age and ethnicity distribution of the prescription sample is shown in Table 1.

For each steroid type the proportion of all doses at each dosage was calculated before and after the campaign (June – September 2002 / 2004). The heavy skew of the data and the very low frequency of outliers makes graphical presentation problematic. Figure 1 shows the change in the distribution of BAEDD doses for all steroid types before and after the Asthma Management Campaign. Note that the x-axis is non-linear in this graph. The sum of all bars for each period (before / after) is 100%, thus the histogram shows the change in the distribution of doses within each period. There was a small overall reduction in higher doses, particularly evident in the reduction of doses of 2000 mcg BAEDD over the two years.

The greatest shift in the BAEDD distribution (decrease in high doses) was observed in fluticasone prescriptions, with budesonide next. BDP showed the smallest shift in dose distribution. The changes in mean BAEDD values are analysed by steroid type in a later section.

Figure 2 shows the ADD of inhaled steroid prescribed for “Adults/older children” (persons aged 12 or older) and for younger children aged 0-5 and 6-11, plotted by month. The Asthma Management Campaign started in February 2003. Lower ADDs for younger children reflected prescribing at lower age-appropriate nominal doses.

There was a small reduction in ADD for Adults from a high of 1015 mcg / day in September 2002. The greatest reduction occurred in the first three months of 2003. Note however that seasonal effects confound the analysis by month, making interpretation more difficult.

Table 2 compares the latest BAEDD available, in the four month period June – September 2004 in comparison with the corresponding period before the Asthma Management Campaign started, June – September 2002, by age group.

The reductions in ADD were observed in adults aged 20 and over, with larger reductions observed in older age groups. There was a statistically significance increase in ADD for children aged 6-11, although because of the large numbers of prescriptions analysed in this study, even small effects (27 mcg BAEDD in this case) may be statistically significant. At the end of the data collection period adults aged over 60 still had the highest ADD. The average change in ADD for adults over 20 was -96 mcg BDPE. Across all age groups the change in ADD was -70 mcg BAEDD.

Numbers of patients recorded as using an ICS increased for all age-groups. This was due to a number of possible reasons, including [to complete – attrition/pts moving out of practices, de novo starting on ICSs, etc.]

Figure 3 shows the adult/older children ADD series broken down by ethnicity. The reduction in adult/older children ADD was across all ethnic groups equally. The ADD prescribed for Pacific patients was lower than that of other ethnic groups, and for most months the ADD prescribed for Maori patients was lower than that of Other patients.

Table 3 compares the four month period June – September 2004 with the corresponding period before the Asthma Management Campaign started, June – September 2002. To control for the impact on these data of differences in the age structure of inhaled corticosteroid users by ethnic group, the table reports ADD expressed as BAEDDs. There were statistically significant reductions in BAEDD for all ethnic groups.

Changes in BAEDD were also examined by District Health Board (DHB) catchments, shown in Table 4. Changes in BAEDD across DHBs ranged from -11.1% to + 4.8%. The greatest absolute and percentage reduction was achieved by Northland (120 BAEDD, -11.1%). South Canterbury experienced the greatest increase (40 BAEDD, +4.8%). The highest BAEDDs are on the West Coast, both before and after the Campaign. Interestingly, Wairarapa tied with Northland in having the largest reduction in percentage terms, yet had the second lowest BAEDD before the Campaign, and the lowest BAEDD after the Campaign.

BAEDD was also examined by ICS chemical entity, shown in Table 5. The highest doses prescribed were for fluticasone (8000 mcg). In the “before” period 29% of prescriptions for budesonide and 28% of prescriptions for fluticasone were for an ADD greater than 1000 mcg BAEDD, compared with 6% for beclomethasone. The greatest decline in both mean BAEDD and in percentage terms was observed in

the 12+ age group taking budesonide (-112 mcg BAEDD, -12.1%) The next highest reductions were seen in fluticasone doses.

Discussion

Between June – September 2002 and June – September 2004 there were statistically significant reductions in inhaled corticosteroid average daily doses. However the reductions were not clinically significant. There were reductions in ICS daily doses across all ethnic groups. The distribution of dosages revealed persistent inappropriately high prescribing, although the number of very high dose prescriptions decreased for all inhaled steroid types. The largest reductions were recorded for budesonide and fluticasone prescriptions, but these were highest to begin with. The highest ADDs in adults after the campaign were still for fluticasone and budesonide. The BAEDD for younger people (aged less than 12) showed no significant change over the study period.

Pacific people had the highest BAEDD in both the "before" and "after" periods; they also had the greatest reductions in BAEDD. When examined by age group the greatest changes were observed in the 60+ group. It is likely that this group included a large number of COPD patients, a condition that is relatively insensitive to inhaled steroids.[8 9]

There were significant variations in the doses of inhaled steroids prescribed in different DHBs, after age and ethnicity standardisation. These might be explained by environmental factors resulting in differences in disease severity, but the most likely explanation is genuine differences in prescribing behaviour. Age-standardised rates of asthma hospitalisations were highest in Northland, Taranaki, Tairawhiti and Hawke's Bay DHBs during 2002 (2002 hospitalisation data, http://www.nzpho.govt.nz/website/nzpho/viewer.htm). The pattern of hospitalisations is quite different from the patterns of BAEDDs seen above. One would expect that titration of inhaled steroid dose to match clinical severity would result in an association between asthma discharges and BAEDD. The absence of this association supports the suggestion that non-clinical factors may underlie the variation in BAEDDs, both before and after the Campaign.

The analyses presented in this report have been based upon the high ADD values in any prescription where a range was stated. The sensitivity of conclusions to this decision was explored. The difference between high and low ADDs was the same (5.9%) in each of the two time periods ("before" and "after"). The analysis of BAEDD over time may be marginally confounded for children aged under 12 as the difference between high and low ADDs increased slightly between the two periods.

Examination of the pattern of ADD by month and age cohorts shows that the reduction in inhaled steroid doses started in late 2002. By January 2003 ADD had become significantly less than the highest values recorded (in September 2002). ADD continued to decline after the Asthma Management Campaign started formally, on 12 February 2003, but there was no further decline after August 2003.

In the presence of a pre-existing trend to reduced steroid doses it would not be justifiable to attribute falls in ADD solely to the PHARMAC campaign. It is certainly possible that the continued declines may have been facilitated by the Campaign. It is also possible that there was some impact from the Campaign prior to its formal launch. These possibilities cannot be examined with the available data, but could be explored qualitatively.

The major finding of this study is the relative resistance of high inhaled corticosteroid ADDs to quite concerted specific campaigns, from PHARMAC, IPAs and PHOs, and individual practices. Further research is required to understand the prescribing decision in cases where high doses are persistently prescribed. It may be possible that repeat prescription orders are filled in by nurses without doctor review, as often happens with chronic conditions, so that the impact upon prescribing of improved awareness of the risks and costs of high inhaled corticosteroid ADDs is delayed until a patient is actually seen by a doctor. However the lack of movement of BAEDDs over the last six months of data collection suggests this is unlikely to be a sufficient explanation.

The most likely explanation is that back titration of well controlled patients to lower doses of inhaled steroids is not occurring. The apparent failure of education campaigns to reduce inappropriate prescribing (and persistent variation between DHBs) suggests other strategies for reducing doses of inhaled steroids should be explored. For example, the continued availability of government subsidies for inhaled steroids presentations that facilitate exceeding recommended maximum doses (eg fluticasone 250 mcg) could be reviewed. It is clear that, in view of the significant over-prescribing that is still occurring, further monitoring is maybe indicated.

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Table 1 Demographics

	0-5 yrs	6-11 yrs	12+ yrs	Total	% of known ethnicity
Maori	5841	7391	41747	54979	**17%**
Pacific	1836	2535	14439	18810	**6%**
Other	11054	21554	221777	254385	**77%**
Missing	743	2050	15283	18076	
Total	19474	33530	293246	346250	
percent	**6%**	**10%**	**85%**		

Note: The unit of analysis is the prescription, not individuals, where prescriptions typically cover 3 months' duration.

Table 2 Change in BAEDD by age group, 2002 versus 2004

Age Group	Before	n	After	n	Diff	% change	p
0-5	547	1609	550	3651	3	0.6%	0.7788
6-11	584	4130	611	4364	27	4.7%	0.0038
12-19	956	4121	978	4563	22	2.3%	0.1015
20-34	963	5972	903	7429	-60	-6.3%	<.0001
35-59	1044	10680	947	14894	-97	-9.3%	<.0001
60+	1105	10219	990	13631	-115	-10.4%	<.0001
ALL	965	36731	895	48532	-70	-7.2%	<.0001

Table 3 Change in BAEDD by ethnicity, 2002 versus 2004

Ethnic Group	Before	n	After	n	Diff	% change	p
Other	952	26339	886	35947	-66	-7.0%	<.0001
Maori	998	5818	929	7938	-68	-6.9%	<.0001
Pacific	1055	1977	943	2754	-112	-10.6%	<.0001
ALL	965	34134	895	46639	-70	-7.2%	<.0001

Table 4 Asthma discharges versus BAEDD by DHB

DHB	Age standardised Asthma discharges*	Age standardised BAEDD Before	Age standardised BAEDD After	% change in BAEDD
Auckland	197	904	839	-7.3%
Bay of Plenty	255	925	903	-2.3%
Canterbury	200	757	769	1.6%
Capital and Coast	255	906	884	-2.4%
Counties Manukau	253	972	935	-3.8%
Hawke's Bay	299	830	754	-9.1%
Hutt	212	873	897	2.8%
Lakes	281	855	811	-5.2%
MidCentral	245	956	932	-2.5%
Nelson-Marlborough	118	1010	900	-10.9%
Northland	302	1082	962	-11.1%
Otago	171	851	858	0.8%
South Canterbury	164	822	861	4.8%
Southland	218	828	827	-0.2%
Tairawhiti	316	891	884	-0.7%
Taranaki	329	858	789	-8.0%

Waikato	196	972	892	-8.2%
Wairarapa	289	792	704	-11.1%
Waitemata	179	956	852	-10.9%
West Coast	208	1199	1108	-7.6%
Whanganui	263	842	758	-10.0%

*2002 hospitalisation data, http://www.nzpho.govt.nz/website/nzpho/viewer.htm.

Figure 1 Change in BAEDD distribution

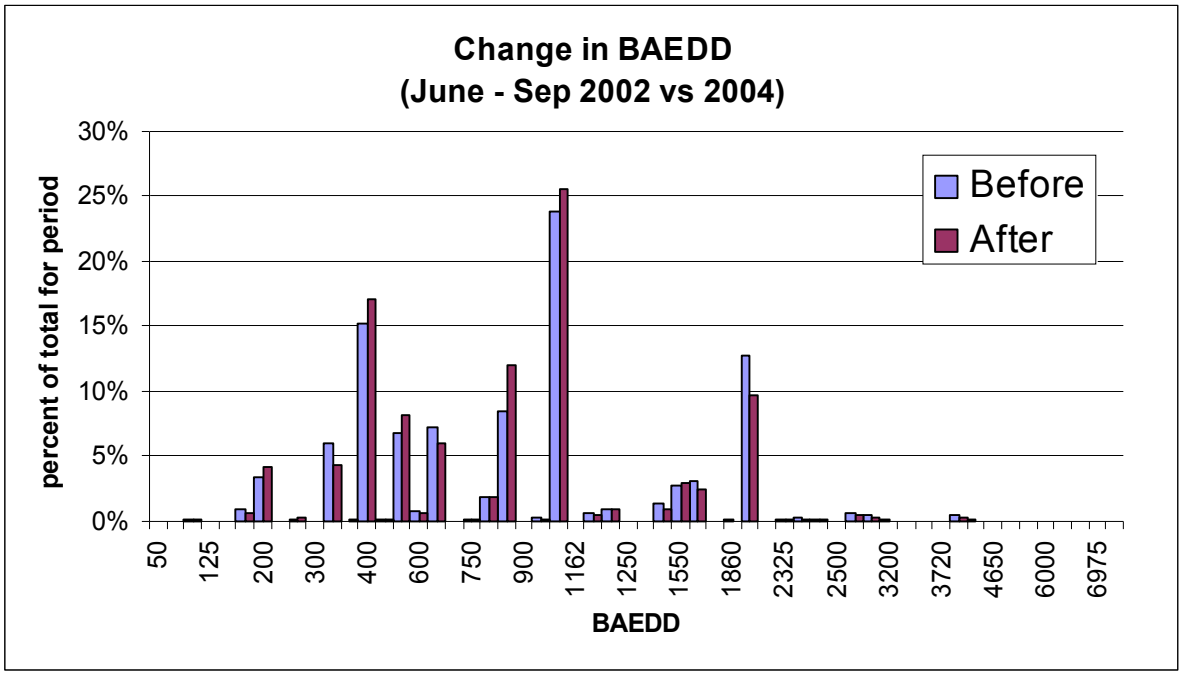

Figure 2 ADD by age group by month

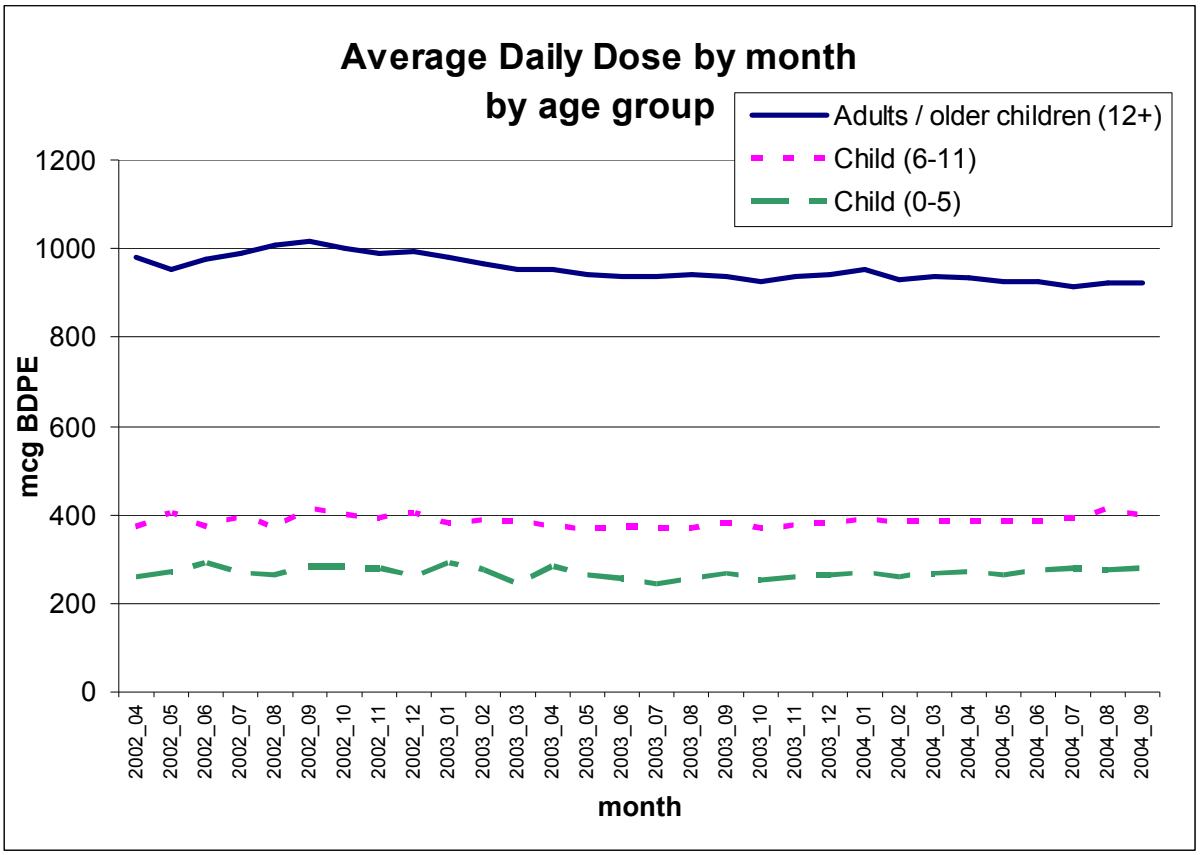

Figure 3 Adult ADD by ethnicity by month