ADHD: utilisation analysis

Drug utilisation sub-committee (DUSC)

June 2015

Abstract

Purpose

To review the utilisation of PBS-listed medicines used in the management of attention deficit hyperactivity disorder (ADHD).

Data Source / methodology

This analysis used three data sources: DUSC database, Medicare pharmacy claim data and Medicare Australia authority approvals data.

Key Findings

Over the five year period 2010-2014:

- The number of patients treated with PBS medicines for ADHD has risen steadily, with an annual increase of 5-8%, and 5 year growth of 31%.
- Similarly the number of prescriptions and PBS expenditure has also increased steadily.
- The most commonly used medicine is methylphenidate. The majority of prescriptions supplied for methylphenidate are as the modified release forms.
- Adults represent a slightly higher proportion of people treated over time, but do not constitute a higher proportion of people new to treatment.
- More males than females are treated, although the ratio is decreasing over time.

A snapshot of medicine use in 2014 shows that:

- The majority of prescriptions are written by a specialist, usually a paediatrician or psychiatrist. Most Australian states and territories restrict the prescribing of methylphenidate and dexamphetamine for the treatment of ADHD to specialist medical prescribers.
- Over 875,000 prescriptions were dispensed at a cost to the PBS of approximately $30 million.
- Rates of prescribing vary across states and territories. The rates of treatment in school-aged children are highest in the ACT, NSW and Queensland. Rates of treatment in adults are highest in Western Australia.
- 117,403 people were granted authority approval for a PBS medicine for ADHD. Of these:

- 32% were adults, 22% were adolescents, 43% were children aged 6-12 years and 2% were children under the age of 6.
- 24,232 started an ADHD medicine for the first time. The majority of people commence treatment with an immediate release product, most commonly methylphenidate.

Purpose of analysis

To review the utilisation of PBS-listed medicines used in the management of attention deficit hyperactivity disorder (ADHD).

The ADHD medicines considered in this analysis are:

- dexamphetamine sulphate
- methylphenidate hydrochloride (immediate release (IR) and modified release (MR) forms)
- atomoxetine

Background

ADHD

ADHD is characterised by inattentiveness and/or hyperactivity and impulsivity that is developmentally inappropriate and causes significant impairment in functioning across multiple settings, such as school/work, social and family settings. There are three subtypes: inattentive, hyperactive-impulsive, and combined.

The reported prevalence of ADHD is variable and may be influenced by the diagnostic criteria used. In the UK, the prevalence of ADHD in school aged children and adolescents is around 3-9% and in adults around 2%.[1] The prevalence of ADHD is higher in boys than girls, at around 9:1 to 6:1 in clinical populations, and around 3:1 in community-based population studies.[2] Many children with ADHD continue to have symptoms as adults with women more likely to have ongoing symptoms.[3]

In 2012, the National Health and Medical Research Council (NHMRC) developed 'Clinical Practice Points on the Diagnosis, Assessment and Management of Attention Deficit Hyperactivity Disorder in Children and Adolescents' (Clinical Practice Points).[3] The Clinical Practice Points recommend that ADHD be diagnosed using the DSM or International Statistical Classification of Diseases, 10th revision (ICD-10) criteria by a specialist clinician, such as a paediatrician or psychiatrist. Following diagnosis, an individualised management plan would be developed by the specialist clinician after considering the severity of symptoms, comorbid disorders, and the family's resources and ability to adhere to the plan.

Behavioural and educational interventions may be used, either alone or in combination with medicines, for the management of ADHD symptoms. This report only examines use of medicines.

Other conditions frequently coexist with ADHD including anxiety disorders, mood disorders or conduct or specific developmental disorders.[4;5] There is limited evidence for efficacy of psychotropic medicine combinations in this population.[6]

Pharmacology

The exact mechanism of action of dexamphetamine and methylphenidate in the treatment of ADHD is not known.[7;8] Dexamphetamine and methylphenidate hydrochloride are central nervous system stimulants. Atomoxetine is a selective noradrenaline reuptake inhibitor.[9]

Therapeutic Goods Administration (TGA) approved indications

Table 1 shows the TGA indications and PBS restricted uses of medicines used to treat ADHD.

Table 1: TGA indications and PBS restricted uses for ADHD medicines

Drug	TGA indications	Abbreviated PBS restricted uses
Dexamphetamine	• Hyperkinetic behaviour disorders in children • Narcolepsy	• ADHD • Narcolepsy
Methylphenidate IR	• ADHD • Narcolepsy	• ADHD
Methylphenidate MR	• ADHD	• ADHD in a patient diagnosed between ages 6 to 18
Atomoxetine	• ADHD as defined by the DSM-IV criteria for people aged ≥6 years	• ADHD as defined by the DSM-V criteria, in a patient diagnosed between ages 6 to 18, who is contraindicated to or intolerant of stimulant treatment.

Sources: Therapeutic Goods Administration (2015), Australian Register of Therapeutic Goods. Accessed: May 2015. Department of Health (2015), Schedule of Pharmaceutical Benefits. Effective 1 May 2015. Accessed May 2015.

Black box warnings

Dexamphetamine and methylphenidate have black box warnings regarding drug dependence. They should be used cautiously in people with a history of drug or alcohol dependence. Chronic abuse may lead to tolerance, psychological dependence and abnormal behaviour.[7;8]

Atomoxetine has a black box warning to monitor patients for suicidal thoughts and behaviours. Short-term placebo-controlled studies showed a positive signal for suicidal thoughts and behaviours in children aged 12 years and under.[9]

Safety alerts

The TGA issued a safety alert for atomoxetine in November 2011, advising that the drug can cause clinically significant increases in heart rate and blood pressure in some patients and that its use is contraindicated in patients with symptomatic cardiovascular diseases, moderate to severe hypertension, or severe cardiovascular disorders, whose condition would be expected to deteriorate if they experienced increases in blood pressure or in heart rate.[10]

The TGA issued another safety alert for atomoxetine in October 2013 in relation to the risk of suicidal ideation and behaviour in children and adolescents.[11] The advice reinforced that while the risks of suicidal ideation and behaviour are well known, it is important that health professionals adequately inform parents and caregivers of the risks of suicidal ideation and behaviour in children and adolescents taking atomoxetine.

In October 2014, the TGA issued a safety alert advising health professionals that in very rare cases treatment with methylphenidate may potentially lead to prolonged and sometimes painful erections.[12]

Dosage and administration

Treatment is usually commenced on dexamphetamine or the short acting presentation of methylphenidate. Dexamphetamine and methylphenidate IR are usually given 2-3 times a day. Doses are started low and then up-titrated weekly to optimal doses. The usual dose of dexamphetamine is in the range of 0.5 – 1 mg/kg up to a maximum of 40 mg per day. The maximum dose of methylphenidate in children is 40 mg and in adults is 60 mg daily.[13] Patients frequently move to long acting methylphenidate once responding.

Some patients require both short and long acting preparations to manage symptoms.[14] In some patients, psychostimulant dose may be altered at times of high cognitive demand.[13]

If the maximum stimulant dose has been reached, and significant improvement in symptoms has not occurred after a month or unacceptable side effects have developed, alternative treatments should be trialled.[3]

There are no established guidelines for the length of time a child should be maintained on stimulants.[15]

Full details on dosing and titration schedules can be found in the Product Information. The current Product Information (PI) and Consumer Medicine Information (CMI) are available from the TGA (Product Information) and the TGA (Consumer Medicines Information).

Clinical situation

In Australia, psychostimulants (dexamphetamine and methylphenidate) are considered the first-line pharmacological treatment for ADHD for all age groups.[14] The NHMRC Clinical Practice Points focus on use of psychostimulants and do not include atomoxetine. Atomoxetine should be considered for children, adolescents and adults with severe ADHD who are contraindicated to, do not respond to, or are intolerant of, stimulants.[14]

The Therapeutic Guidelines recommend that, with rare exceptions, stimulants should not be used in children aged younger than 4 years.[15] State and territory laws also contain specific regulation regarding the treatment of very young children (see Appendix A). Best practice is to start with non-pharmacological interventions, such as parent training or educational programs supported by behavioural intervention in the preschool setting. If preschool children are prescribed ADHD medicines, small doses should be used to account for differences in pharmacokinetics in this age group.

Methylphenidate and dexamphetamine are Schedule 8 controlled drugs. Additional prescribing restrictions for these drugs apply in most states and territories (refer to Appendix A).

There is some evidence of benefit for the following medicines in the treatment of ADHD:

- clonidine in primary school aged children
- modafinil in adults
- bupropion in adults.[14]

These medicines could be considered for the treatment of ADHD in the specified patient populations, in patients who do not respond to stimulants or atomoxetine.[14]

This utilisation analysis does not consider use of buproprion, modafinil or clonidine as these medicines are not TGA-indicated for the treatment of ADHD. PBS subsidised use of modafinil is restricted to the treatment of narcolepsy, while subsidised use of buproprion is restricted to its use as an aid in smoking cessation. Use of clonidine is unrestricted on the PBS; however, its use in the treatment of ADHD would be difficult to distinguish from use to treat other conditions as clonidine may also be used to treat sleep disturbance resulting from treatment with psychostimulants.[16]

PBS listing details (as at 1 May 2015)

Table 2: PBS listings of medicines used in the treatment of ADHD.

Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
1165H	DEXAMPHETAMINE SULFATE Tablet 5 mg, 100	1	5	$18.53	Aspen Pharma Pty Ltd
8839F	METHYLPHENIDATE HYDROCHLORIDE Tablet 10 mg, 100	1	5	$17.23	Ritalin 10 Novartis
2387P	METHYLPHENIDATE HYDROCHLORIDE Tablet 18 mg (modified release) , 30	1	5	$51.66	Concerta Janssen-Cilag Pty Ltd
2172H	METHYLPHENIDATE HYDROCHLORIDE Tablet 27 mg (modified release), 30	1	5	$55.80	Concerta Janssen-Cilag Pty Ltd
2388Q	METHYLPHENIDATE HYDROCHLORIDE Tablet 36 mg (modified release) , 30	1	5	$60.03	Concerta Janssen-Cilag Pty Ltd
2432B	METHYLPHENIDATE HYDROCHLORIDE Tablet 54 mg (modified release) , 30	1	5	$70.09	Concerta Janssen-Cilag Pty Ltd
3440C	METHYLPHENIDATE HYDROCHLORIDE Capsule 10 mg (modified release), 30	1	5	$34.39	Ritalin LA Novartis

2276T	METHYLPHENIDATE HYDROCHLORIDE Capsule 20 mg (modified release), 30	1	5	$44.91	Ritalin LA Novartis
2280B	METHYLPHENIDATE HYDROCHLORIDE Capsule 30 mg (modified release), 30	1	5	$52.37	Ritalin LA Novartis
2283E	METHYLPHENIDATE HYDROCHLORIDE Capsule 40 mg (modified release), 30	1	5	$54.90	Ritalin LA Novartis
9092M	ATOMOXETINE Capsule 10 mg, 28	2	5	$221.52	Strattera Eli Lilly Pty Ltd
9093N	ATOMOXETINE Capsule 18 mg, 28	2	5	$221.52	Strattera Eli Lilly Pty Ltd
9094P	ATOMOXETINE Capsule 25 mg, 28	2	5	$221.52	Strattera Eli Lilly Pty Ltd
9095Q	ATOMOXETINE Capsule 40 mg, 28	2	5	$221.52	Strattera Eli Lilly Pty Ltd
9096R	ATOMOXETINE Capsule 60 mg, 28	2	5	$221.52	Strattera Eli Lilly Pty Ltd
9289X	ATOMOXETINE Capsule 80 mg, 28	1	5	$147.45	Strattera Eli Lilly Pty Ltd
9290Y	ATOMOXETINE Capsule 100 mg, 28	1	5	$147.45	Strattera Eli Lilly Pty Ltd

Source: Department of Health (2015), *Schedule of Pharmaceutical Benefits Effective 1 May 2015*, Canberra.
Notes: Novartis = Novartis Pharmaceuticals Australia Pty Limited.

Restrictions

Dexamphetamine

Authority required

Use in attention deficit hyperactivity disorder, in accordance with State/Territory law

Authority required

Narcolepsy

Note: Care must be taken to comply with the provisions of State/Territory law when prescribing dexamphetamine.

Note: Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.

Methylphenidate IR

Authority required

Use in attention deficit hyperactivity disorder, in accordance with State/Territory law.

Note: Care must be taken to comply with the provisions of State/Territory law when prescribing methylphenidate hydrochloride.

Note: Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.

Methylphenidate MR (Ritalin LA®)

Authority Required

Treatment of attention deficit hyperactivity disorder (ADHD) in a patient diagnosed between the ages of 6 and 18 years inclusive, who has demonstrated a response to immediate release methylphenidate hydrochloride with no emergence of serious adverse events, and who requires continuous coverage over 8 hours.

Note: Care must be taken to comply with the provisions of State/Territory law when prescribing methylphenidate hydrochloride.

Note: Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.

Methylphenidate MR (Concerta®)

Authority Required

Treatment of attention deficit hyperactivity disorder (ADHD) in a patient diagnosed between the ages of 6 and 18 years inclusive, who has demonstrated a response to immediate release methylphenidate hydrochloride with no emergence of serious adverse events, and who requires continuous coverage over 12 hours.

Note: Care must be taken to comply with the provisions of State/Territory law when prescribing methylphenidate hydrochloride.

Note: Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.

Atomoxetine

Authority required (STREAMLINED)

4591

Attention deficit hyperactivity disorder

Treatment Phase: Initial treatment

Clinical criteria: The condition must be or have been diagnosed by a paediatrician or psychiatrist according to the DSM-5 criteria, AND

Patient must have a contraindication to dexamphetamine or methylphenidate as specified in TGA-approved product information; OR

Patient must have a comorbid mood disorder that has developed or worsened as a result of dexamphetamine or methylphenidate treatment and is of a severity necessitating treatment withdrawal; OR

Patient must be at an unacceptable medical risk of a severity necessitating permanent stimulant treatment withdrawal if given a stimulant treatment with another agent; OR

Patient must have experienced adverse reactions of a severity necessitating permanent treatment withdrawal following treatment with dexamphetamine and treatment with methylphenidate (not simultaneously).

Population criteria: Patient must be or have been diagnosed between the ages of 6 and 18 years inclusive.

Authority required (STREAMLINED)

4578

Attention deficit hyperactivity disorder

Treatment Phase: Continuing treatment

Clinical criteria: Patient must have previously been issued with an authority prescription for this drug.

Note: No increase in the maximum quantity or number of units may be authorised.

Note: No increase in the maximum number of repeats may be authorised.

Current PBS listing details are available from the PBS website.

Date of listing on PBS

The dates of listing and changes to listing for these medicines are available in Appendix B.

Current PBS listing details are available from the PBS website.

Relevant aspects of the PBAC consideration

Methylphenidate IR

At the March 2005 meeting, the PBAC recommended listing on a cost-minimisation basis compared to dexamphetamine sulfate, with the equi-effective doses being methylphenidate hydrochloride 10 mg and dexamphetamine sulfate 5 mg.[17] The PBAC was concerned over the possible extent of use of the product and requested that the DUSC monitor this.

Methylphenidate MR (Concerta®)

At the November 2006 meeting the PBAC recommended listing of methylphenidate MR (Concerta®) as an authority required benefit on a cost effectiveness basis over methylphenidate IR. Although the extent of any clinical benefit over methylphenidate IR remained uncertain, the Committee agreed that the likely improvements in compliance and in ease of administration, particularly in relation to the removal of the need for a dose of medication at school, were sufficient to justify listing.[18]

In July 2012 the PBAC rejected a submission to extend the listing to include patients diagnosed with ADHD after the age of 18 years, on the basis of uncertain efficacy and safety in the proposed population, and high and highly uncertain cost to the PBS.[19]

Methylphenidate MR (Ritalin LA®)

In November 2007, the PBAC recommended listing of methylphenidate hydrochloride modified release (Ritalin LA®) capsules on the PBS on a cost-minimisation basis compared with methylphenidate hydrochloride modified release tablets (Concerta®) at the same price per day, as reflected by the equi-effective doses.[20]

Atomoxetine (Strattera®)

The PBAC recommended the listing of atomoxetine (Strattera®) 10 mg, 18mg, 25 mg, 40 mg and 60 mg in November 2006, on a cost-effectiveness basis over placebo. The PBAC considered that there was a clinical need for the product and that the proposed restriction targeted the appropriate population.[21]

In July 2008, the PBAC recommended the listing of two additional strengths of atomoxetine (Strattera®), 80 mg and 100 mg, but rejected a submission to extend the use of atomoxetine to patients diagnosed with ADHD as adults due to insufficient evidence of clinical and cost-effectiveness. The submission claimed that the new strengths were unlikely to increase atomoxetine use or cost to the PBS.[22]

In March 2014, the PBAC recommended that the current Authority Required restriction for atomoxetine be changed to Authority Required (STREAMLINED).

Copies of the PBAC Meeting Outcomes and Public Summary Documents are available on the PBAC Meetings website.

Previous reviews by the DUSC

The DUSC reviewed this therapeutic area in October 2010, as part of the 24 month Predicted versus Actual (PvA) review of atomoxetine. The DUSC noted that there was lower than expected utilisation of atomoxetine, which may have been influenced by the listing of Concerta® three months before the listing of atomoxetine and possible over-estimation of the number of patients with the required contraindications to stimulants to meet the restriction.[23]

The DUSC reviewed ADHD medicines again in June 2012, with further analyses requested by the DUSC considered in October 2012.[24] Key findings were:

- Overall, the analyses suggested steady growth in the utilisation of ADHD medicines between January 2005 and October 2011.
- PBS benefits paid for ADHD medicines in November 2010–October 2011 totalled around $24.6 million, up 4.2% from the previous year. The highest cost medicine to the PBS was Concerta® at $11.2 million, followed by atomoxetine at $6.2 million, despite its low utilisation.
- Initiation to ADHD medicines is highest in patients aged 5–10 years, peaking at 7 years of age. Methylphenidate IR is the most commonly initiated medicine in children, while adults and late teens most commonly initiate dexamphetamine. Of concessional patients initiating ADHD medicines in 2011, 63% were male. Inclusion of

general patients by analysis of authority approvals data did not significantly affect the distribution of initiating ADHD drug by patient age.

- When considering all people treated with ADHD medicines, highest use was in children aged 10 years.
- ADHD drug utilisation rates and trends vary significantly by state/territory. In the years 2006 to 2011, the approvals per 1000 population for dexamphetamine in WA were at least 4 times that of other states or territories, with the exception of the ACT. The difference was primarily due a high rate of use of dexamphetamine in adults in WA. PBS authority approvals for ADHD drugs in the ACT were also comparatively high, but this was driven by approvals for dexamphetamine, atomoxetine and Concerta®. Differences in state/territory regulations did not appear to be driving differences in utilisation.
- Around 9.6% of all prescriptions for ADHD medicines were private prescriptions. The proportion of private prescriptions was not higher for drugs with age restrictions on the PBS.

Methods

This analysis used three data sources: DUSC database, Medicare pharmacy claim database and Medicare authority approvals database. All data are de-identified.

Prior to April 2012, the Medicare pharmacy claim database only included data for PBS prescriptions where a subsidy was paid. From April 2012, all PBS prescriptions are captured, including those priced below the general patient co-payment where a subsidy was not paid. The ADHD medicines priced below the general patient co-payment are dexamphetamine, short acting methylphenidate (Ritalin 10) and the 10mg strength of modified release methylphenidate (Ritalin LA).

The DUSC database includes an estimate of under co-payment prescriptions until April 2012 and an estimate of private prescriptions until August 2012.[25]

The Medicare authority approvals database includes information on medicines that require approval to prescribe through the PBS. All medicines for ADHD are authority required, including those priced below the general patient co-payment, allowing longitudinal analysis to be conducted that covers the complete PBS population.[i] A limitation of these data is that there may be some authorities granted where the prescription is never dispensed; however an analysis of the number of patients receiving an authority approval and supplied a medicine in 2014 showed that this is of minor consequence (see Appendix C).

The analyses undertaken included prescription volume, PBS expenditure, number of patients treated and commencing treatment, age, sex, length of treatment, same day supply of multiple ADHD medicines or other psychotropic medicines, state/territory of residence, and prescriber type. Further details are provided in Appendix C. Sources are also provided at the bottom of each table/graph in the Results section.

[i] Atomoxetine ceased to require prior approval when its listing was changed to Authority Required (STREAMLINED) in August 2014.

The PBS data presented in this report includes use for repatriation patients. This constitutes a very small proportion of overall use (<0.2%).

Results

Analysis of drug utilisation

Number of patients by age and gender

The numbers of patients who have been treated with PBS medicines for ADHD in 2010 to 2014 inclusive are shown in Table 3 and 4. The data are presented as the number of new patients starting treatment for the first time (Table 3) and all patients treated (new and continuing) by age and gender (Table 4).

Table 3: Number of new patients treated with ADHD medicines by age and gender.

	2010	2011	2012	2013	2014
<6 years male	1,208	1,355	1,538	1,599	1,697
<6 years female	260	285	359	388	383
6-12 years male	7,481	8,278	8,931	9,476	9,732
6-12 years female	2,042	2,382	2,466	2,806	2,863
13-17 years male	1,977	1,953	1,893	1,922	1,810
13-17 years female	844	840	889	884	952
18+ years male	3,340	3,550	3,882	4,060	4,013
18+ years female	1,901	2,224	2,207	2,474	2,476
Unknown	324	335	189	173	306
Total New patients	19,377	21,202	22,354	23,782	24,232

Source: DHS Authority approval data, extracted May 2015. Unknown denotes age or sex not available in data.

Table 4: Number of people treated with ADHD medicines by age and gender.

	2010	2011	2012	2013	2014
<6 years male	1,675	1,869	2,106	2,212	2,266
<6 years female	374	388	452	507	518
6-12 years male	30,378	32,532	35,075	38,013	40,298
6-12 years female	7,200	8,011	8,712	9,635	10,317
13-17 years male	17,167	18,071	18,778	19,321	19,660
13-17 years female	4,586	4,826	5,154	5,416	5,663
18+ years male	16,035	18,121	20,560	22,841	23,965
18+ years female	9,592	10,815	11,966	13,318	14,105
Unknown	2,335	1,485	648	449	611
Total All patients	89,342	96,118	103,451	111,712	117,403

Source: DHS Authority approval data, extracted May 2015. Unknown denotes age or sex not available in data.

The number of people prescribed ADHD medicine is increasing over time in every age bracket. While the number of people new to treatment increases over time, the pattern

varies across the age groups, with increases in each year for children, but not in every year for adolescents and adults.

Tables 5 and 6 present the same data as percentage of use.

Table 5: Percentage of new patients prescribed ADHD medicine by age and gender.

	2010	2011	2012	2013	2014
<6 years male	6%	6%	7%	7%	7%
<6 years female	1%	1%	2%	2%	2%
6-12 years male	39%	39%	40%	40%	40%
6-12 years female	11%	11%	11%	12%	12%
13-17 years male	10%	9%	8%	8%	7%
13-17 years female	4%	4%	4%	4%	4%
18+ years male	17%	17%	17%	17%	17%
18+ years female	10%	10%	10%	10%	10%
Unknown	2%	2%	1%	1%	1%
Total New patients	**100%**	**100%**	**100%**	**100%**	**100%**

Source: DHS Authority approval data, extracted May 2015. Unknown denotes age or sex not available in data.

Table 6: Percentage of all patients prescribed ADHD medicine by age and gender.

	2010	2011	2012	2013	2014
<6 years male	2%	2%	2%	2%	2%
<6 years female	0%	0%	0%	0%	0%
6-12 years male	34%	34%	34%	34%	34%
6-12 years female	8%	8%	8%	9%	9%
13-17 years male	19%	19%	18%	17%	17%
13-17 years female	5%	5%	5%	5%	5%
18+ years male	18%	19%	20%	20%	20%
18+ years female	11%	11%	12%	12%	12%
Unknown	3%	2%	1%	0%	1%
Total All patients	**100%**	**100%**	**100%**	**100%**	**100%**

Source: DHS Authority approval data, extracted May 2015. Unknown denotes age or sex not available in data.

For people new to ADHD treatment, the demographic mix has altered slightly over the five year period, with a slight increase in the contribution of male and female children, offset by a decrease in the contribution of adolescent males.

While the demographic mix of all people prescribed ADHD medicine was similar over time, there has been a slight decrease in the contribution of adolescent males, and a slight increase in the contribution of 6-12 year old females and adult males and females.

Adults represent a slightly higher proportion of people treated over time, but do not constitute a higher proportion of people new to treatment.

In 2014, around two thirds of people supplied a PBS ADHD medicine were less than 18 years of age.

The age distribution of all patients supplied with an ADHD medicine in 2014 is shown in Figure 1.

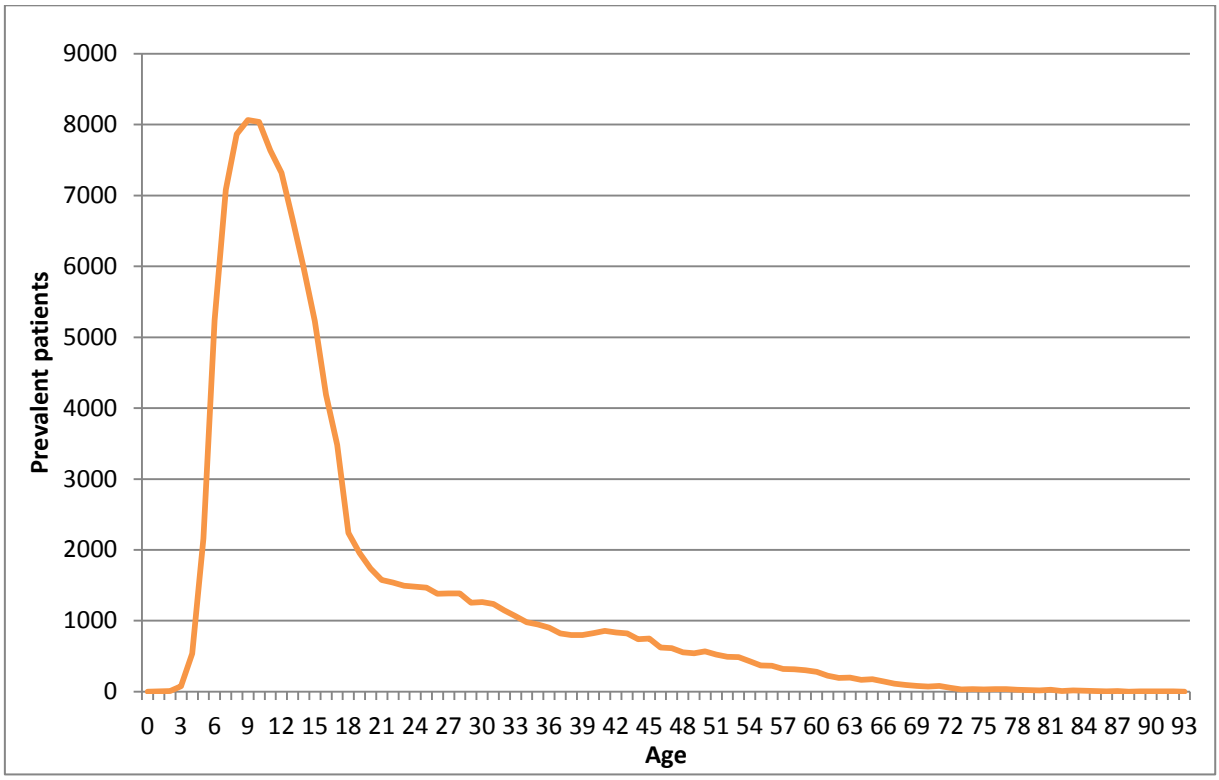

Figure 1: People supplied PBS ADHD medicine in 2014 by age

Source: Medicare pharmacy claims database; extracted 1 April 2015.

The ratio of males to females who received an authority approval for ADHD medicine by year is shown in Figure 2.

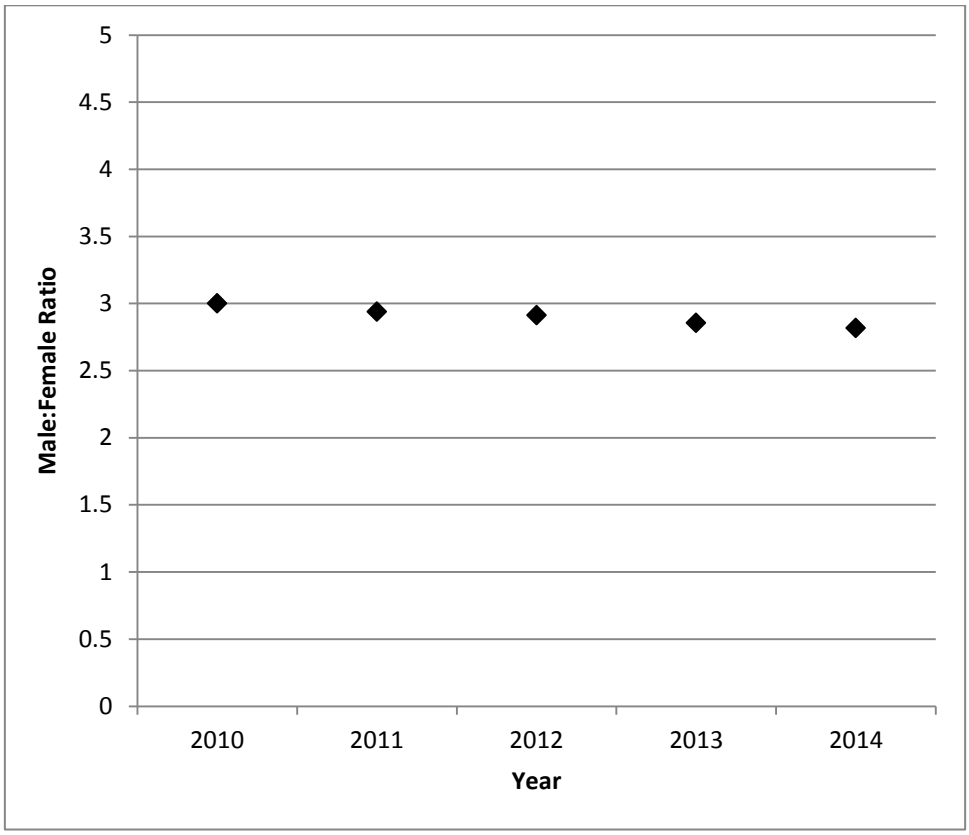

Figure 2: Ratio of males to females granted authority approval for ADHD medicine by year

Source: Medicare authority approvals database; extracted May 2015.

The ratio of males to females who received an authority approval for ADHD medicine decreased from 3.00:1 in 2010 to 2.82:1 in 2014 (Figure 2). As discussed in the background section (page 3) women are more likely to have ongoing symptoms of ADHD into adulthood.[3] This can be seen in the 2014 data presented below (Figure 3).

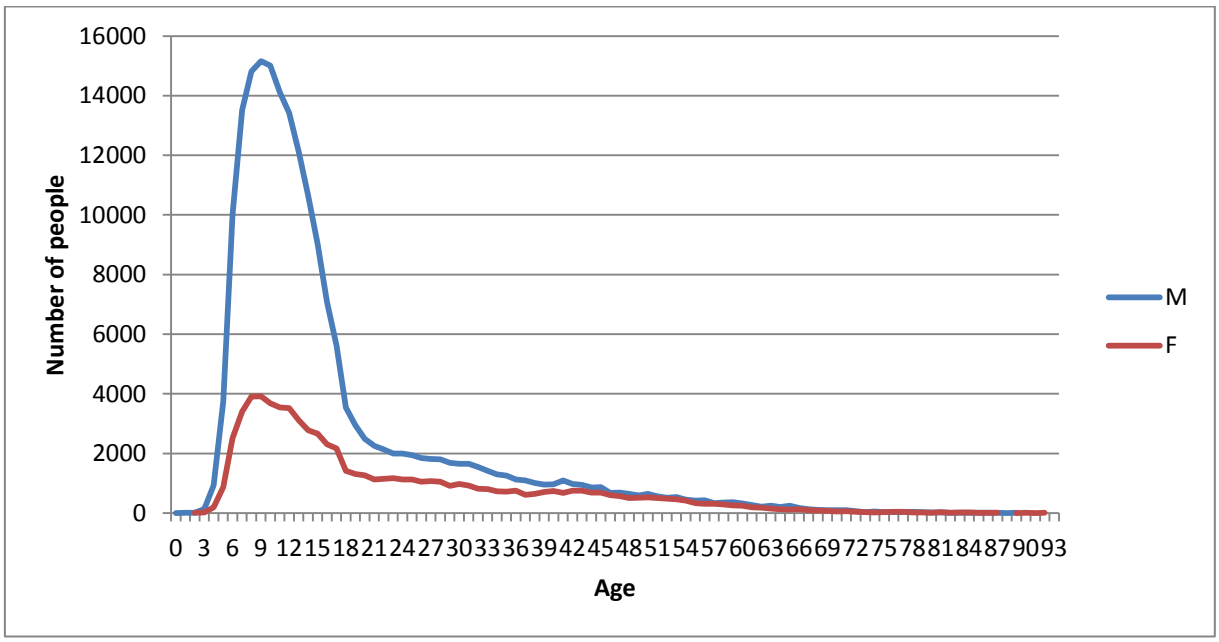

Figure 3: Number of people supplied an ADHD medicine in 2014 by age and sex

Source: Medicare pharmacy claims database; extracted 29 April 2015.

ADHD medicines used

Figure 4 shows the number of prescriptions for each medicine by the quarter and year of supply, between quarter 1 2010 and quarter 4 2014.

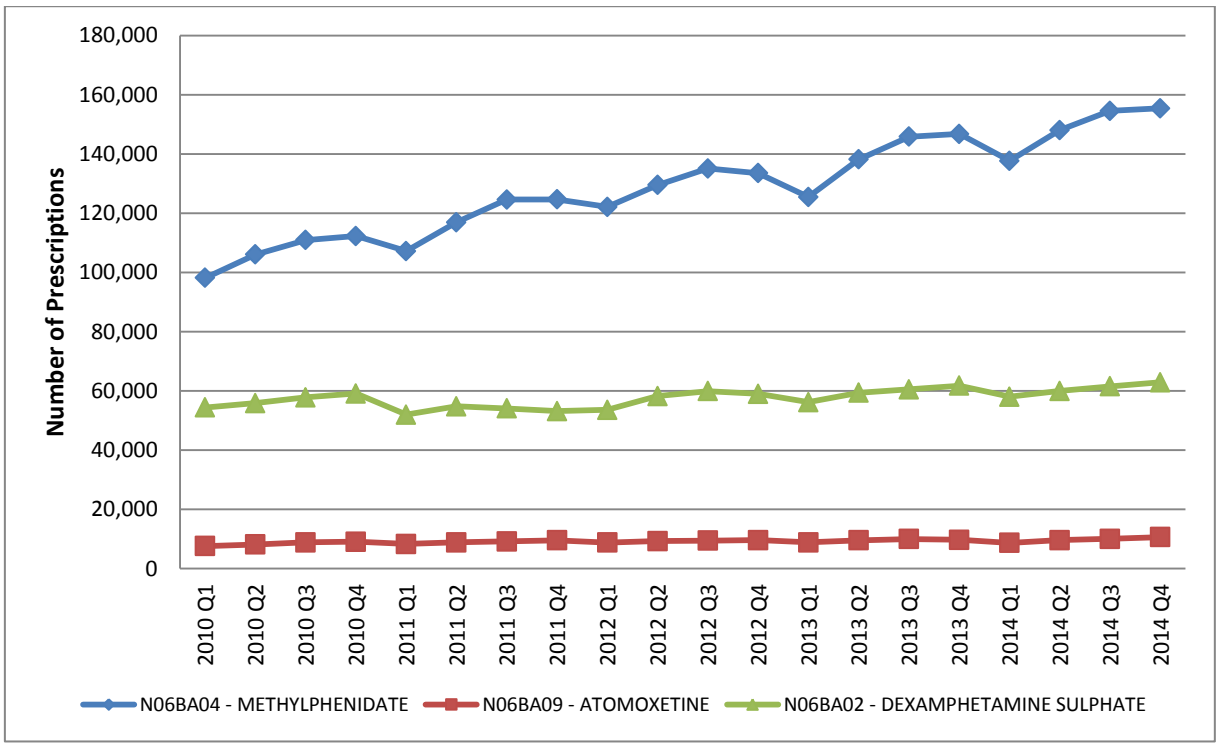

Figure 4: Prescriptions for ADHD medicines

Source: DUSC drug utilisation database; extracted 2 April 2015. Includes private and under co-payment estimate, and under co-payment actual.

Figure 5 presents the number of prescriptions for methylphenidate (the blue line in Figure 4) as immediate release and modified release forms.

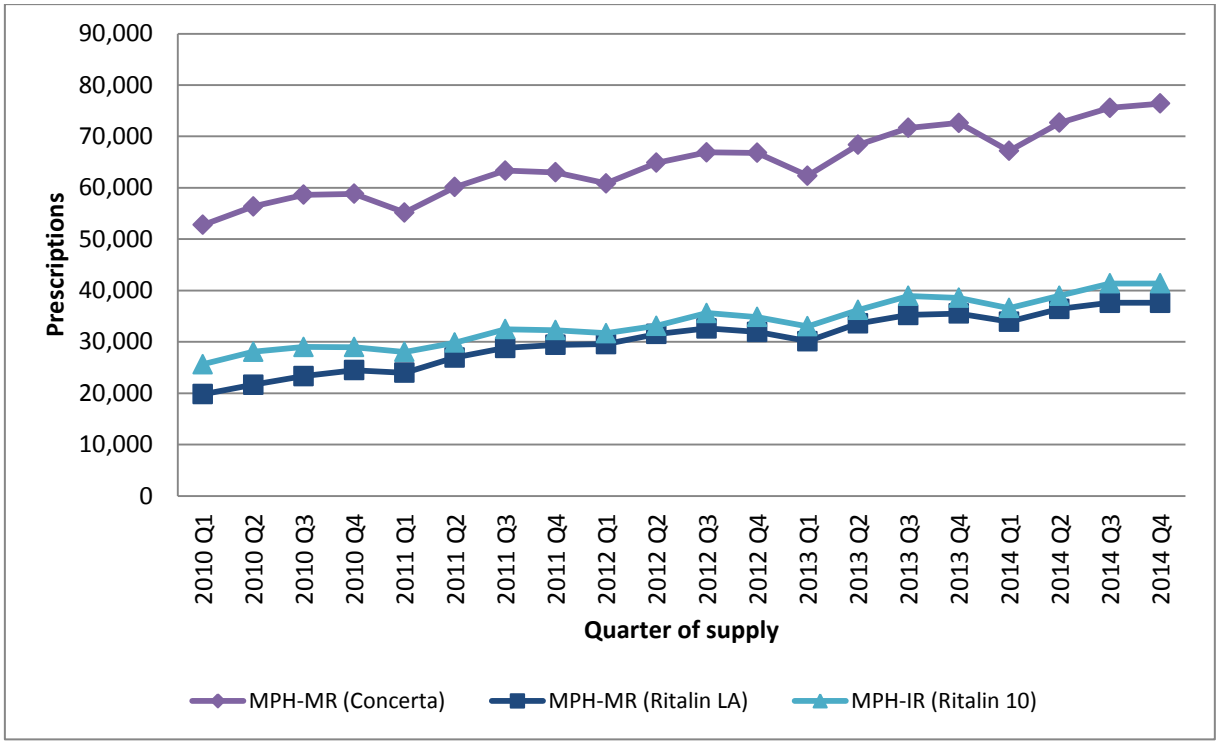

Figure 5: Prescriptions for methylphenidate

Source: DUSC drug utilisation database; extracted 2 April 2015. Includes private and under co-payment estimate, and under co-payment actual.

Almost all of the growth in the number of prescriptions dispensed is accounted for by increasing use of methylphenidate immediate release and modified release. The annual number of prescriptions is summarised in Table 7.

Table 7: Prescriptions of ADHD medicines

ADHD Medicines	2010	2011	2012	2013	2014
Dexamphetamine	227,264	214,109	230,794	237,852	242,474
Methylphenidate IR (Ritalin 10)	111,660	122,615	135,198	146,758	158,327
Methylphenidate MR (Ritalin LA)	89,259	109,134	125,654	134,483	145,560
Methylphenidate MR (Concerta)	226,573	241,634	259,399	274,994	291,771
Atomoxetine	33,837	36,023	37,242	38,175	39,074
Total	688,593	723,515	788,287	832,262	877,206
% growth from previous year		5.1%	9.0%	5.6%	5.4%

Source: DUSC drug utilisation database; extracted 2 April 2015

The number of prescriptions gives an overall measure of the utilisation of ADHD medicines. The relative use of medicines is not directly comparable because one prescription does not provide an equal number of days of therapy for all medicines. This is because the pack sizes

vary, doses are titrated to optimal doses, and children generally use lower doses than adults. In the 2012 consideration of the utilisation of ADHD medicines, DUSC noted that DDD/1000population/day is also not an ideal measure of utilisation because the DDD specified by the WHO is based on average dose used for adults, while the ADHD population is predominantly children where doses used are lower. The current report focuses on the number of patients treated and the medicines used.

The higher growth in prescriptions in 2012 (9.0%) is likely due to the introduction of actual under co-payment data from April 2012, as the number of under co-payment prescriptions prior to this date may have been under-estimated.

Table 8 shows the medicines used in new patients. Table 9 shows the medicines used in all patients. In table 9 the total number of people is fewer than the sum of the number of people for each drug, as people may be supplied with more than one medicine over the calendar year.

Table 8: Number of new patients treated with each ADHD medicine.

ADHD Medicine Name	2010	2011	2012	2013	2014
Dexamphetamine	4,397	4,508	4,355	4,452	4,636
Methylphenidate IR	11,498	13,497	14,937	16,346	16,970
Methylphenidate MR (8 hour coverage)	1,030	977	993	946	932
Methylphenidate MR (12 hour coverage)	1,257	1,096	1,104	1,041	1,022
Atomoxetine	1,195	1,124	965	997	672
Total New patients	19,377	21,202	22,354	23,782	24,232

Source: Medicare authority approval data, extracted May 2015
*For 2014 only, Medicare pharmacy claims data was used for atomoxetine, due to its listing being streamlined in August 2014.

Table 9: Total number of patients treated with each ADHD medicine.

ADHD Medicine Name	2010	2011	2012	2013	2014
Dexamphetamine	28,250	28,969	29,882	31,416	32,295
Methylphenidate IR	30,250	34,076	38,452	42,572	45,446
Methylphenidate MR (8 hour coverage)	14,184	16,805	19,089	21,073	22,934
Methylphenidate MR (12 hour coverage)	29,076	30,460	33,014	35,429	37,691
Atomoxetine	6,739	6,884	7,003	7,295	7,493*
Total All patients	89,342	96,118	103,451	111,712	117,403

Source: Medicare authority approval data, extracted May 2015
*For 2014 only, Medicare pharmacy claims data was used for atomoxetine, due to its listing being streamlined in August 2014.

Most people start PBS therapy with the short acting medicines, dexamphetamine and methylphenidate IR, which is consistent with clinical guidelines.[15] A small proportion of people initiated PBS therapy on modified release forms of methylphenidate. Initiating therapy on modified release forms of methylphenidate is inconsistent with both guidelines and the PBS restriction.

When considering all patients, methylphenidate MR is used by most people. The number of individuals prescribed methylphenidate IR is much higher than the number of people starting ADHD therapy on methylphenidate IR, indicating that methylphenidate IR and MR forms are likely to be used together in some people.

Atomoxetine is used in a very small proportion of patients. Use is stable and in the short time since the Authority Required restriction was simplified and changed to streamlined (August 2014) use does not appear to have increased at a higher rate.

The choice of medicine may vary by age. Figures 6 and 7 show the age distribution of medicines used for new and all patients in 2014.

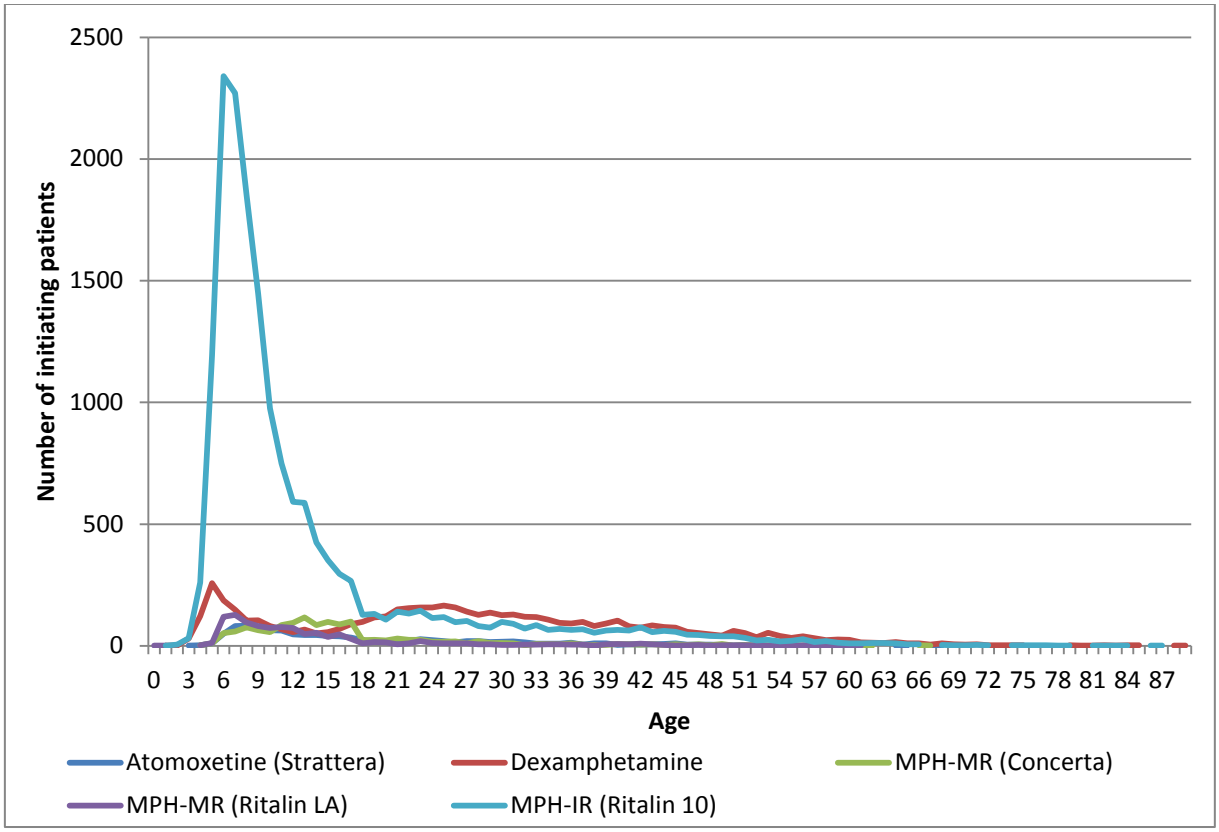

Figure 6: Medicines used to initiate PBS ADHD therapy by patient age in 2014

Source: Medicare pharmacy claims database; extracted 1 April 2015.

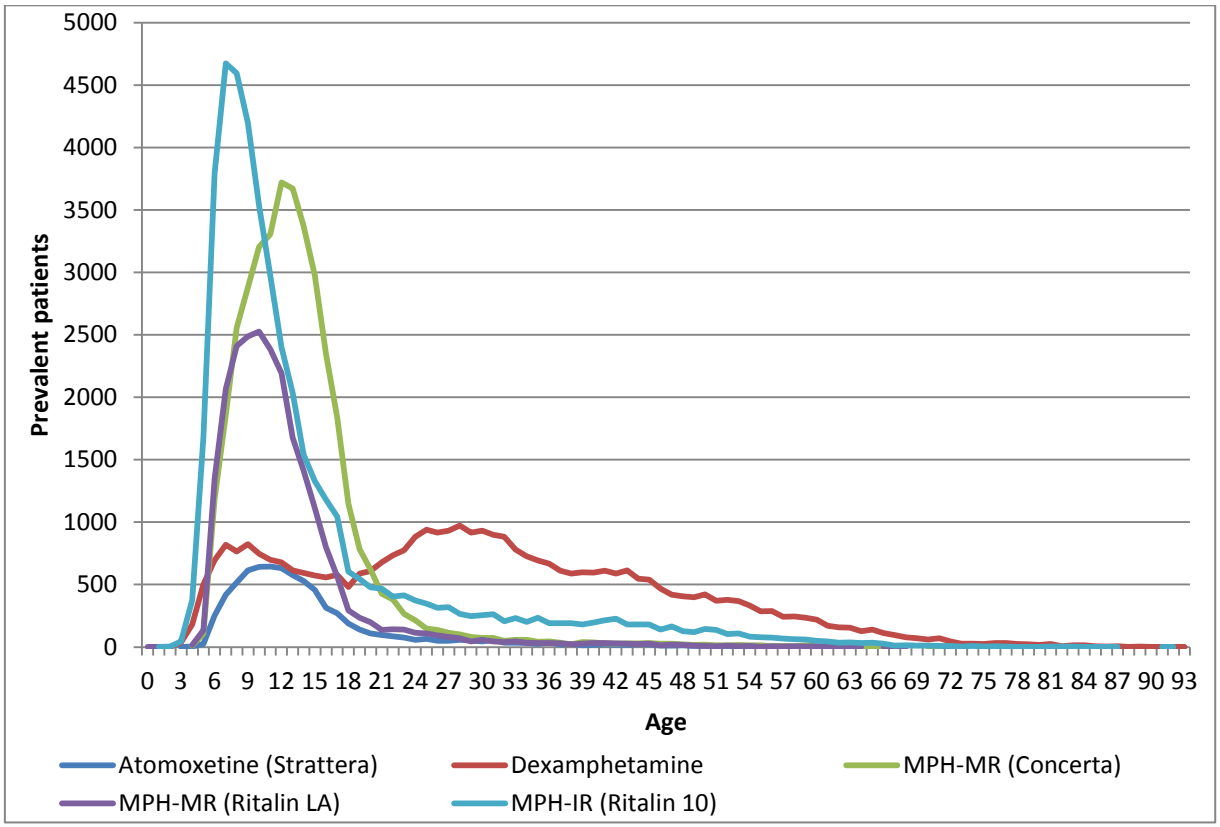

Figure 7: People supplied PBS ADHD medicine in 2014 by age and medicine

Source: Medicare pharmacy claims database; extracted 1 April 2015.

In adults commencing PBS subsidised therapy for the first time, dexamphetamine is the most common medicine, followed by short acting methylphenidate (Figure 6).

In children and adolescents, the most common first prescribed medicine for ADHD is short acting methylphenidate (Figure 6). While short acting methylphenidate is the most used product in school-aged children, long acting methylphenidate formulations also have large market share in this age group (Figure 7). This indicates that children either switch therapy from immediate release to modified release formulations or that modified release formulations are added to immediate release therapy; consistent with guidelines and PBS listings.

When considering all patients (Figure 7), the number of people supplied MPH-IR peaks at 7 years of age, MPH-MR (Ritalin LA) at 10 years of age, MPH-MR (Concerta) at 12 years of age and atomoxetine at 11 years of age. The age of people supplied dexamphetamine has a bimodal distribution, with a peak at 28 years and a secondary peak at 9 years.

Duration on PBS therapy

A Kaplan-Meier analysis was used to show the length of time people remain on treatment. The overall median length of treatment on ADHD medicine was 4.2 years, and the mean was 5.0 years (Figure 8).

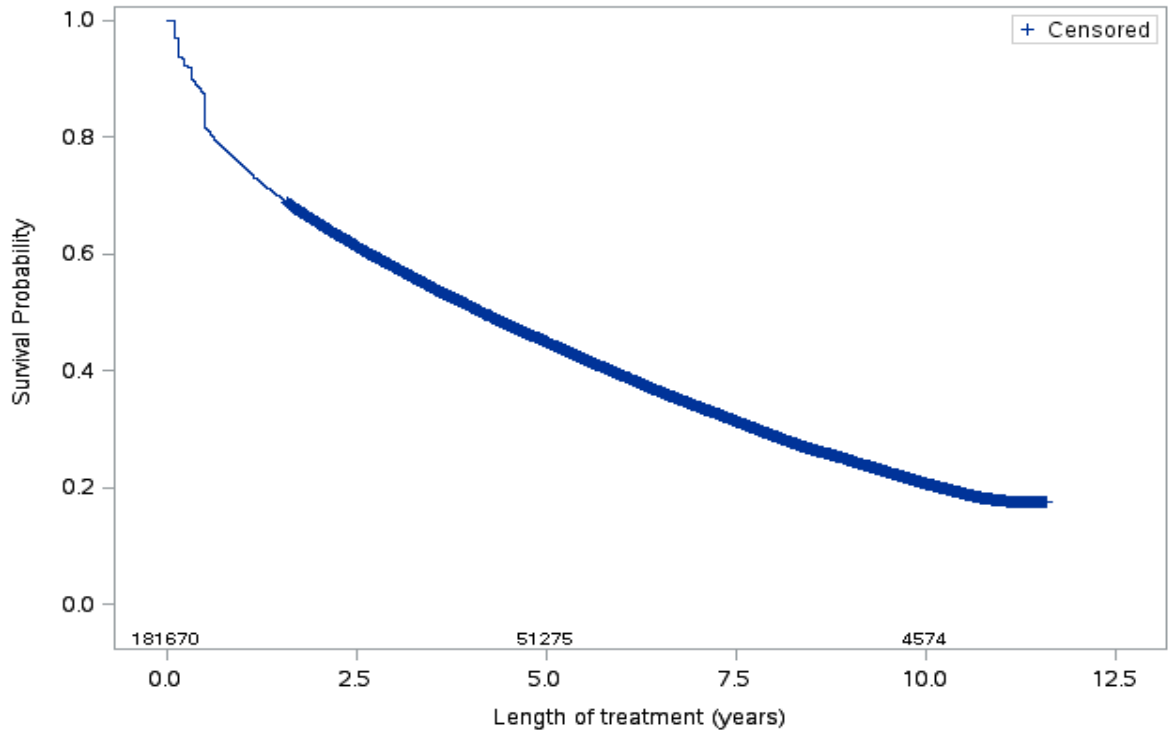

Figure 8: Kaplan-Meier length of treatment analysis

Median = 4.2 years, Mean = 5.0 years

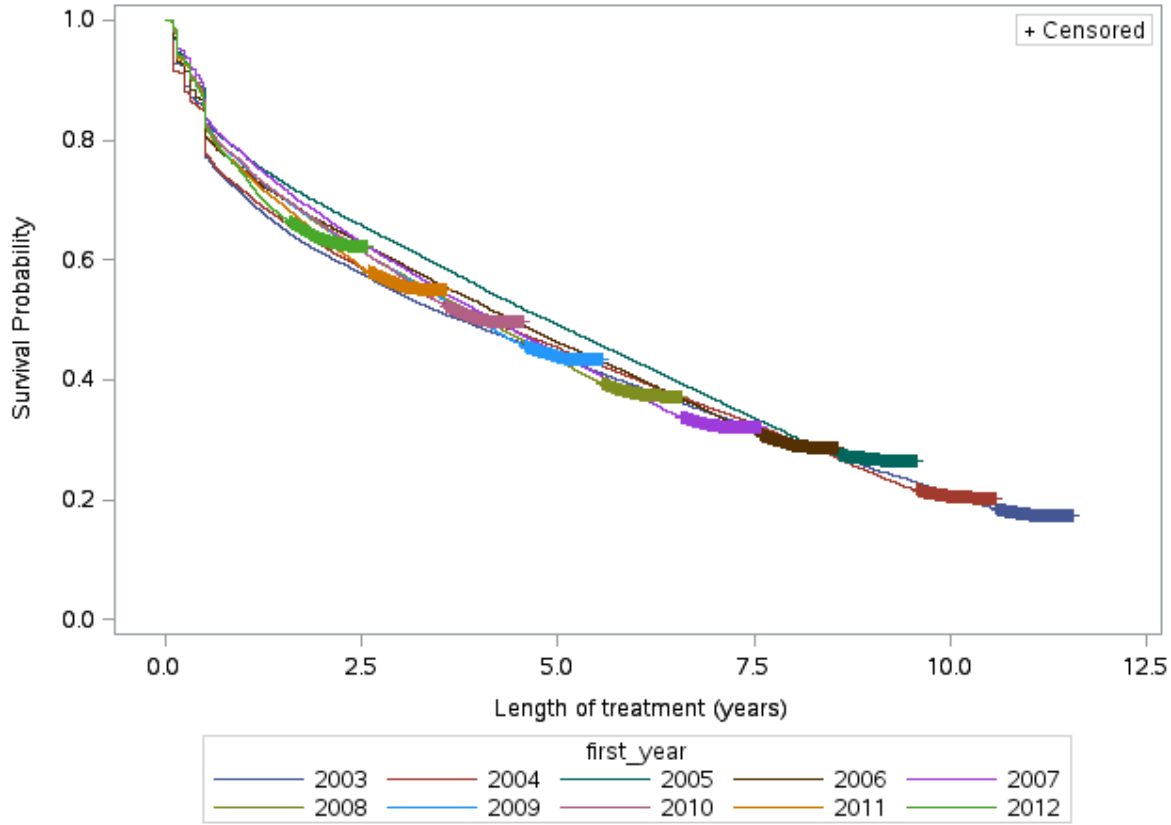

Figure 9: Length of treatment – initiators by calendar year from 2003 to 2012

Table 10: Length of treatment – initiators by calendar year from 2003 to 2012

Year of Initiation	Median (years)	Mean (years)
2003	3.76	4.89
2004	4.10	4.79
2005	4.88	4.96
2006	4.41	4.44
2007	4.18	4.15
2008	4.06	3.72
2009	3.98	3.35
2010	4.05	2.92
2011	NA	2.41
2012	NA	1.81

Excluding initiators in 2013 & 2014 because of short follow up period

The median lengths of treatment for the cohorts by year of initiation to ADHD therapy were between 3.76 years and 4.88 years (Table 10).

Co-administered PBS medicines

An estimate of co-administration based on medicines being supplied on the same day in 2013 is presented in Table 11. Table 12 shows an estimate for 2014.

Table 11: proportion of people with same day dispensing in 2013 by age group

Same day dispensing	0-5 years	6-12 years	13-17 years	18+ years	Total
Multiple ADHD medications	0.1%	0.4%	0.4%	0.3%	0.3%
Multiple forms of MPH	1.0%	8.0%	9.3%	2.6%	6.3%
ADHD with antipsychotic	2.3%	5.3%	6.5%	6.7%	6.0%
ADHD with anxiolytic	0.0%	0.1%	0.2%	5.9%	2.1%
ADHD with sedative	0.0%	0.0%	0.2%	2.3%	0.8%
ADHD with antidepressant	1.4%	5.1%	12.1%	26.6%	13.9%

Source: Medicare pharmacy claims database, extracted May 2015; MPH = methylphenidate

Table 12: proportion of people with same day dispensing in 2014 by age group

Same day dispensing	0-5 years	6-12 years	13-17 years	18+ years	Total
Multiple ADHD medications	0.1%	0.3%	0.3%	0.3%	0.3%
Multiple forms of MPH	0.7%	7.9%	9.8%	2.8%	6.4%
ADHD with antipsychotic	3.8%	5.3%	6.7%	6.7%	6.0%
ADHD with anxiolytic	0.0%	0.1%	0.2%	6.1%	2.2%
ADHD with sedative	0.0%	0.0%	0.1%	2.4%	0.8%
ADHD with antidepressant	2.0%	5.4%	13.0%	27.1%	14.4%

Source: Medicare pharmacy claims database, extracted May 2015; MPH = methylphenidate

A very small proportion of people were supplied multiple ADHD medicines (two or more of dexamphetamine, methylphenidate or atomoxetine) on the same day. Multiple forms of methylphenidate were more commonly supplied on the same day to adolescents compared with other age groups.

Rates of co-supply of an ADHD medicine with an antidepressant were higher than rates of co-supply of an ADHD medicine with anxiolytics, sedatives or antipsychotics. The proportion

of people who received a same day supply of ADHD medicine with antidepressant increased with increasing age, being highest in adults.

Prescribers

The diagnosis and management of ADHD may involve multidisciplinary care. The NHMRC Clinical Practice Points recommend diagnosis (and management) by a specialist paediatrician, child/adolescent psychiatrist or clinical or neuro-psychologist; supported when necessary by other allied health clinicians.[3] The role of the general practitioner is providing ongoing surveillance and support, which may involve overseeing the mental health care plan.[3;5]

Any medical practitioner can prescribe PBS ADHD medicines, as long as prescribing is also in accordance with State/territory law. Nurse practitioners can prescribe continuing therapy for all ADHD medicines except atomoxetine providing they also comply with State/territory law.

The PBS restriction for atomoxetine requires that the diagnosis by a paediatrician or psychiatrist according to the DSM-5 criteria.

Table 13 and 14 show the proportion of first ever prescriptions (new patients), first prescription for a particular medicine, and all prescriptions supplied by medicine and prescriber type in 2014.

Table 13: Use of ADHD medicine by prescriber type (%) for new patients (first prescription for any ADHD medicine)

Prescriber Type	Paediatrician	Psychiatrist	GP	Nurse practitioner	Other
Dexamphetamine	22%	59%	10%	0%	9%
Methylphenidate IR	69%	23%	5%	0%	3%
Methylphenidate MR (8 hour coverage)	66%	19%	12%	0%	3%
Methylphenidate MR (12 hour coverage)	57%	27%	12%	0%	3%
Atomoxetine	45%	38%	12%	0%	4%

Source: Medicare pharmacy claims database, extracted May 2015

Table 14: Use of ADHD medicine by prescriber type (%)

Prescriber Type	Paediatrician	Psychiatrist	GP	Nurse practitioner	Other
Dexamphetamine	19%	49%	25%	0%	7%
Methylphenidate IR	60%	21%	15%	0%	3%
Methylphenidate MR (8 hour coverage)	70%	11%	16%	0%	3%
Methylphenidate MR (12 hour coverage)	65%	13%	18%	0%	3%
Atomoxetine	50%	22%	25%	0%	3%

Source: Medicare pharmacy claims database, extracted May 2015

The initial and continuing prescriber is most likely influenced by state and territory regulations, described in detail in Appendix A.

Utilisation by State/Territory

Figure 10 shows the number of people supplied ADHD medicine per 1000 population by patient state/territory.

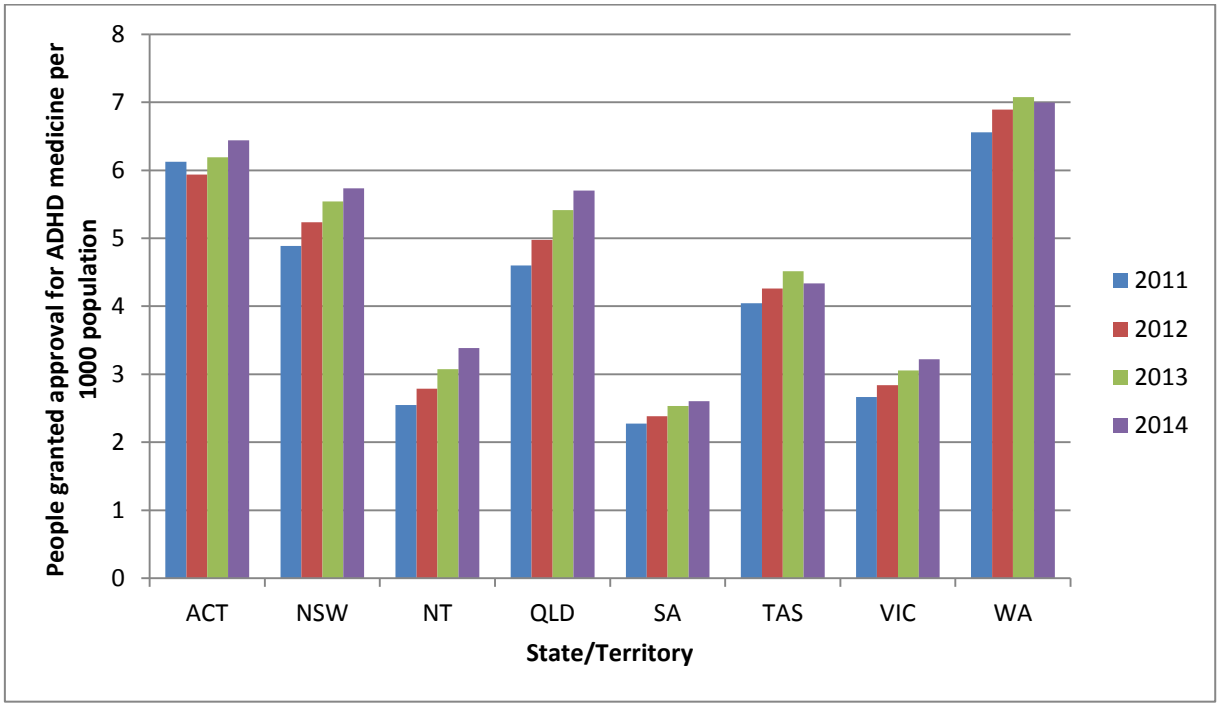

Figure 10: Number of people granted authority approval for an ADHD medicine per 1000 population by patient state/territory and year

Source: Medicare authority approvals database; extracted 5 May 2015. These data are not age standardised.

The analysis in Figure 10 was not adjusted to account for differences in the age distribution across states and territories. Rates of prescribing by age group in 2014, adjusted for the age and size of the population of each state and territory, are shown in Figure 11.

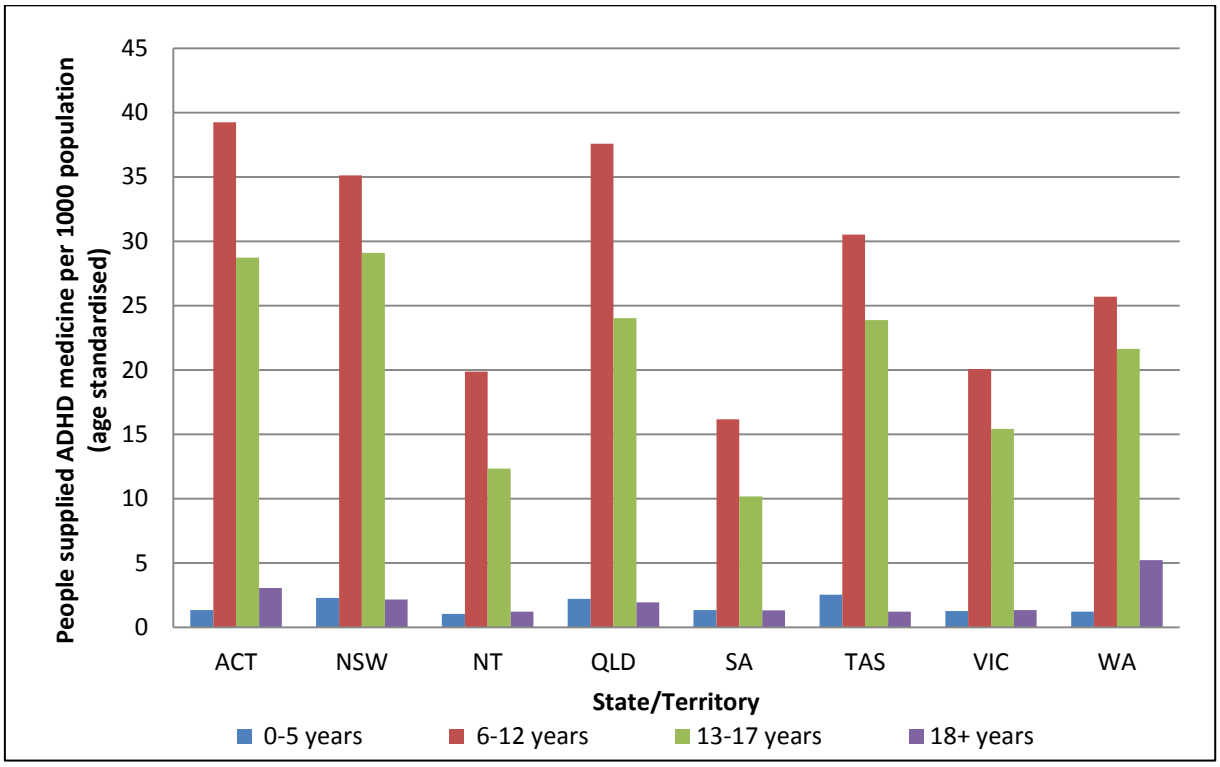

Figure 11: Number of people supplied an ADHD medicine per 1000 population (age standardised) in 2014 by patient state/territory and age group

Source: Medicare pharmacy claims database; extracted 5 May 2015.

When the size and age distribution of the states and territories is taken into account, the rates of ADHD medicine supply differ. The rate of ADHD medicine supply to 6-12 year olds was highest in the ACT (39.26 per 1000 population), followed by Queensland (37.59/1000 population) and NSW (35.13/1000 population). The rate of ADHD medicine supply in adolescents was highest in NSW (29.11/1000 population), followed by the ACT (28.72/1000 population). For children under 6, the rate of ADHD medicine supply was low, ranging from 1.05/1000 population in the Northern Territory to 2.53/1000 population in Tasmania. For adults, the rate of supply of ADHD medicine was highest in Western Australia (5.23 per 1000 population), with the next highest being the ACT (3.06/1000 population).

Figure 12 shows the number of people supplied ADHD medicine per 1000 population in 2014 by patient state/territory and medicine. There are differences in the pattern of use of ADHD medicines across the states and territories; for example, the number of patients supplied dexamphetamine in WA is higher per 1000 population compared with the other states and territories. A previous DUSC analysis (October 2012) showed that use of dexamphetamine in WA was predominantly in 20-30 year olds.

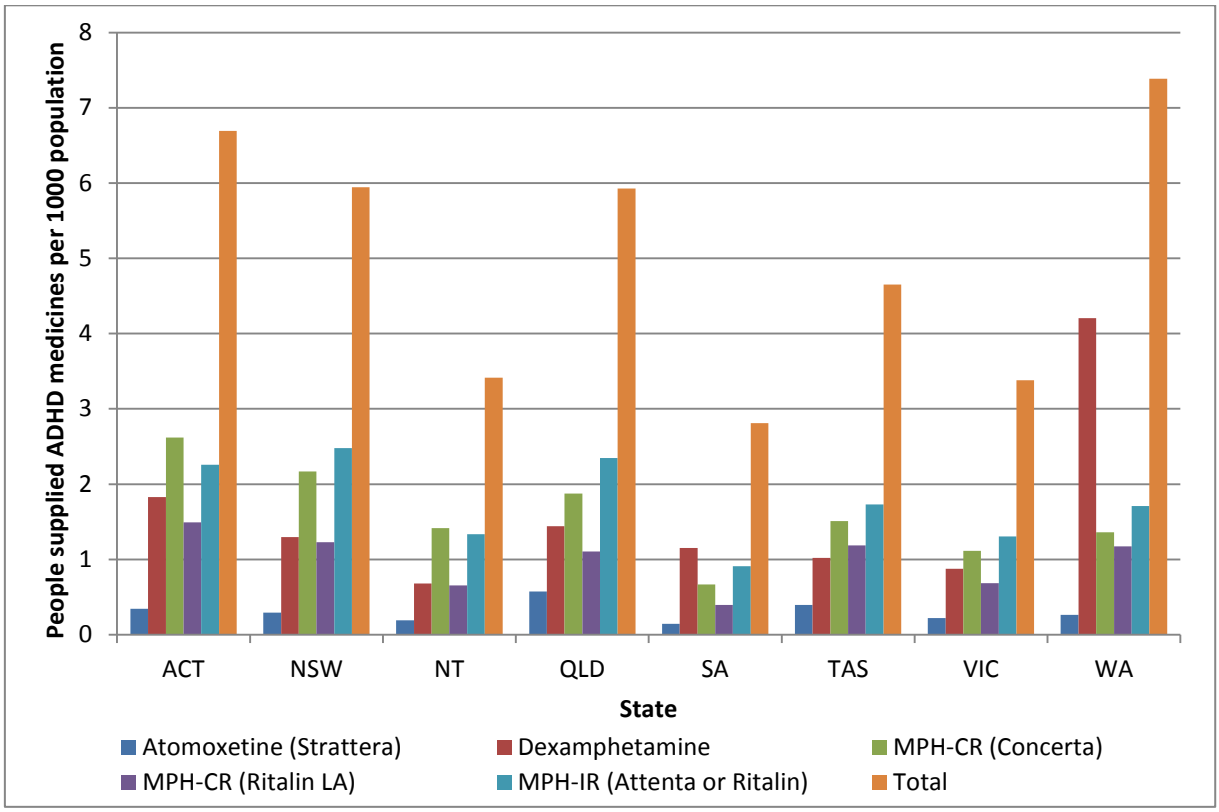

Figure 12: Number of people supplied an ADHD medicine per 1000 population in 2014 by patient state/territory and medicine.

Source: Medicare pharmacy claims database; extracted 29 April 2015. These data are not age standardised.

Analysis of expenditure

Table 15 shows the benefits paid by Government for PBS subsidised prescriptions for each ADHD medicine by the year of supply, between 2010 and 2014, and the percentage growth form the previous year. Benefits paid for ADHD medicines grew between 4-7% in each year of this period. In 2014, just over $30 million in benefits was paid for ADHD medicines. The highest cost medicine in 2014 was methylphenidate-MR (Concerta®) at $13.9 million.

Table 15: PBS benefits paid for ADHD medicines

	2010	2011	2012	2013	2014
Dexamphetamine	$2,298,508	$2,245,767	$2,256,961	$2,337,024	$2,423,152
Methylphenidate IR (Ritalin 10)	$949,241	$986,006	$1,081,447	$1,183,084	$1,273,698
Methylphenidate MR (Ritalin LA)	$3,193,694	$3,655,083	$4,166,122	$4,630,933	$4,976,765
Methylphenidate MR (Concerta)	$11,248,598	$11,328,786	$12,192,958	$13,175,447	$13,944,768
Atomoxetine	$6,415,585	$6,845,118	$7,043,246	$7,341,801	$7,382,266
Total	$24,105,627	$25,060,759	$26,740,733	$28,668,289	$30,000,649
% growth from previous year	n/a	4%	7%	7%	5%

Source: DUSC drug utilisation database; extracted 2 April 2015

Discussion and DUSC consideration

The DUSC considered that the pattern of use in relation to age and gender has not changed substantially over time. The DUSC noted the ratio of males to females is decreasing slowly over time, and considered that this change may be due to diagnostic changes. In the past ADHD tended to be diagnosed based on external behaviour more often evident in boys whereas there is now increasing recognition of internalising features that may increase diagnosis in girls.

The DUSC noted that almost all the growth in the number of prescriptions dispensed is accounted for by increasing use of methylphenidate. The DUSC considered atomoxetine use to be low and stable.

The DUSC noted that the positive recommendation for PBS listing of lisdexamfetamine had not been implemented at the time the report was prepared. When recommending listing, the PBAC accepted that a modest clinical need exists for alternative treatments for ADHD in children and adolescents as patient response to one treatment over another appears to be highly individualised.

With respect to duration of therapy, the DUSC noted there is no clear guidance on how long people should remain on therapy and acknowledged that treatment would need to be withdrawn to determine whether treatment is necessary. Interpretation of measures of duration of therapy is further complicated by drug holidays (periods of intended cessation), which are often taken in children as the therapies can diminish growth velocity and cause weight loss.

The DUSC noted the methodology for co-administration relied on same day dispensing; and is therefore an underestimate of the true extent of co-administration. The DUSC acknowledged that some of the co-administration of ADHD medicines might be appropriate; for example, co-prescription of ADHD medicine with an antipsychotic (risperidone) in children with Conduct Disorder or Oppositional Defiance Disorder. The DUSC considered that some use of antidepressants in children 5 years and under might be accounted for by use of

tricyclic antidepressants for bed-wetting, but some may be inappropriate. However, DUSC was concerned that there are children aged 5 years and under receiving prescriptions for an ADHD medicine and an antipsychotic medicine on the same day.

DUSC actions

The DUSC requested the report be provided to PBAC for information.

Context for analysis

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

Sponsors' comments

Aspen Pharma Pty Ltd
Eli Lilly Pty Ltd
Janssen-Cilag Pty Ltd
Novartis Pharmaceuticals Pty Ltd

The sponsors have no comment.

Disclaimer

The information provided in this report does not constitute medical advice and is not intended to take the place of professional medical advice or care. It is not intended to define what constitutes reasonable, appropriate or best care for any individual for any given health issue. The information should not be used as a substitute for the judgement and skill of a medical practitioner.

The Department of Health (DoH) has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

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Appendix A: Summary of state and territory regulations for the prescribing of psychostimulants

Under the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP), dexamphetamine and methylphenidate are Schedule 8 drugs or poisons, also known as controlled drugs. Schedule 8 drugs have high potential for abuse and addiction. Their prescribing is tightly regulated and monitored, but regulations vary between the states and territories. A summary of these regulations is presented below, with more detailed information by state/territory in Table A.1.

Most Australian states and territories restrict the prescribing of methylphenidate and dexamphetamine for the treatment of ADHD to specialist medical practitioners, including psychiatrists, neurologists and paediatricians. These specialist prescribers are generally required to obtain prior authorisation from the relevant state or territory regulatory body for each patient. Prescribing of psychostimulants to patients under the age of 2 years is generally prohibited, and there are usually additional regulatory requirements to prescribe psychostimulants to patients aged 2 or 3 years, such as requiring a second specialist opinion and/or review by an expert committee.

There are some variations and exceptions to the regulatory requirements between states and territories. For example, some jurisdictions:

- Allow GPs to continue prescribing psychostimulants where treatment was initiated by an appropriate specialist and there is periodic review by a specialist.
- Allow authorised specialists to prescribe psychostimulants without making an application for each patient, but they may be required to provide notifications of treatment and monthly data on prescribing.
- Limit the number of patients a practitioner may treat with psychostimulants, without an additional authorisation.
- Allow treatment on a short term basis without an authority, usually only for 1–2 months.

Guidelines are also provided at the state and territory level with respect to the dosing of methylphenidate and dexamphetamine, with some jurisdictions restricting the maximum dose that can be prescribed (see Table A.2). Regulations and guidelines usually stipulate that patients should be initiated on the lowest practicable dose, with doses titrated according to the patient's needs. State regulations may also limit the number of prescriptions for psychostimulants that may be dispensed to a patient at any one time, or the number of months' supply that may be prescribed, or the period of validity of prescriptions.

Table A.1. Summary of state and territory regulations for prescribing stimulant medications

State	Summary of Regulations
ACT[26;27]	A prescriber must have either an approval from the Chief Health Officer (CHO) for each patient, or a standing approval to prescribe a controlled medicine such as methylphenidate. CHO Approval: With regard to ADHD medicines, a prescriber must obtain a CHO approval when they intend to prescribe a controlled medicine for >2 months to a patient, or where the patient has been prescribed a controlled medicine in the last 2 months. Prescriptions must be annotated with the details of the CHO approval number. Another doctor at the same clinic may prescribe under the relevant CHO approval for a patient. Certain criteria must be met for a CHO approval to be issued for the prescription of amphetamines for the treatment of ADHD: • Patients under 4 years: Initial applications must be submitted by a paediatrician, appropriate psychiatrist or neurologist, and supported by a second clinician from these specialities. Continuing applications should be submitted by the initiating specialist. • Patients aged 4–19 years: Initial applications must be submitted by a paediatrician, appropriate psychiatrist or neurologist. Continuing applications may be submitted by a GP if the treatment has been reviewed by an appropriate specialist within 2 years. • Patients over 19 years: Initial applications must be submitted by a neurologist or psychiatrist. Continuing applications may be submitted by a GP if the treatment has been reviewed by an appropriate specialist within 3 years, and there is no increase in dosage. Standing Approval: A standing approval means that a prescriber is automatically authorised to prescribe a controlled substance and applies where the patient is an in-patient at a hospital or hospice, or a CHO approval is not required (see requirements above). The Standing approval process allows timely initiation of treatment and dose titration prior to seeking CHO approval for a patient. Except for in-patients, prescriptions must be annotated, e.g. with the words 'Standing short term approval'. Legislation: *Medicines, Poisons and Therapeutic Goods Act 2008* and the Medicines, Poisons and Therapeutic Goods Regulation 2008.
NSW[28;29;30;31]	Dexamphetamine, methylphenidate and lisdexamphetamine may be prescribed only with the prior written authority of the NSW Ministry of Health. Authorities for individual patients: Authorities for individual patients are only issued to relevant specialists, usually paediatricians, psychiatrists and neurologists for the treatment of ADHD, but some GPs may also apply. Authorities to prescribe psychostimulants for the treatment of ADHD are only issued in accordance with the TG 181 'Criteria for the Diagnosis and Management of Attention Deficit Hyperactivity Disorder in Children and Adolescents'[30] and TG 190 'Criteria for the Diagnosis and Management of Attention Deficit Hyperactivity Disorder in Adults'.[31] Authorities are not granted for children under 2 years of age and there are additional regulatory requirements for children aged 2–3 years. General authorities for specialists: Psychiatrists, neurologists and paediatricians may apply for a general authority number (S28c number) to prescribe psychostimulant medication for the treatment of ADHD. These prescribers must notify the Ministry of their psychostimulant prescribing on a monthly basis. Individual patient applications must still be made for patients who do not meet the routine prescribing criteria (e.g. age under 4 years, higher dosage than the specified range, history of substance abuse, or significant co-morbidities or side-effects). Legislation: *Poisons and Therapeutic Goods Act 1966* and the Poisons and Therapeutic Goods Regulation 2008.

NT[32;33]	Authorisation from the CHO is required for each patient before dexamphetamine, lisdexamphetamine or methylphenidate is prescribed. Treatment must be initiated by a paediatrician, psychiatrist, physician, neurologist, or registrar in training in one of these disciplines. Other medical practitioners and nurse practitioners (NP) may continue the supply of these medicines, but the patient must see an appropriate specialist or registrar every 2 years. If the specialist is based interstate or overseas, a medical practitioner or NP may continue to supply the relevant medicine for up to 6 months, before review by an appropriate NT based specialist or registrar. Paediatricians may initiate supply without an authorisation if the supply is for less than 30 days. If the patient is under 4 years old, it is recommended that a second specialist opinion is obtained. The authority to supply for a specific patient must be renewed every 2 years where the patient is being managed by a neurologist, psychiatrist, physician or a registrar in these disciplines, or being co-managed by a medical practitioner or NP. Where the patient is being managed by a paediatrician or their registrar, the authority is valid until the patient turns 18 years old. Generally, no more than one months' supply is to be dispensed at any one time. Changes between medications and cessation of treatment must be notified to the CHO. Legislation: *Medicines, Poisons and Therapeutic Goods Act 2012* and Medicines, Poisons and Therapeutic Goods Regulations.
QLD[34]	Doctors may only prescribe methylphenidate, dexamphetamine and lisdexamphetamine for the treatment of narcolepsy, brain damage in a child at least 4 years old, or attention deficit disorder. Paediatricians and psychiatrists may only prescribe these drugs for the treatment of brain damage or attention deficit disorder in a child. Legislation: *Health (Drugs and Poisons) Regulation 1996* and the Health (Drugs and Poisons) Regulation
SA[35]	An authority from the Minister for Health is required to prescribe psychostimulants to a patient for a period exceeding 2 months, which includes periods of treatment provided by other prescribers. The authority will stipulate the conditions under which the drug may be supplied, including dosage and quantity. Treatment should generally be initiated by a relevant specialist, such as a neurologist, paediatrician or psychiatrist for a child, or a psychiatrist for an adult. Authorities may be granted to GPs to continue prescribing stimulants to a patient with ADHD, conditional on support and annual review by a relevant specialist. Prescriptions should be limited to no more than three months' supply. Legislation: *Controlled Substances Act 1984* and Controlled Substances (Poisons) Regulations 2011.
TAS[36;37]	Before issuing a prescription for a psychostimulant, authority must be obtained from the Secretary of the Department of Health and Human Services. For children and adolescent patients, authorities are only issued to child psychiatrists, paediatricians, and specialist physicians. The specialist may request that the authority list a GP as a co-prescriber under their direction. Applications for patients outside the routine authorisation criteria (e.g. higher than recommended dosage, and patients with significant side-effects or severe psychiatric co-morbidity) are referred to the Psychostimulant Advisory Panel, which may request additional reports or opinions. Prescribing these medicines for children under 2 years of age is not permitted. For children aged 2 years, a second specialist opinion is required and the maximum authority length is 3 months. Both the prescriber and second specialist must provide reports indicating that the treatment is appropriate on all authority applications until the child reaches age 3. An authority for a child aged 3 years also requires a second specialist opinion. For children aged over 3 years, authorisations remain in effect until the patient reaches 18 years of age or has completed secondary school.

	For adults, initial authorisations are for 3 months, to facilitate appropriate reassessment, and continuing authorisations are for 12–24 months. In general, only psychiatrists may initiate psychostimulant treatment of adults with ADHD. However, the psychiatrist may request that a patient's GP take over prescribing following the initial application. Legislation: *Poisons Act 1971* and Poisons Regulations 2008.
VIC[38]	A medical practitioner must hold a permit for each patient from the Drugs and Poisons Regulation Group, Victorian Department of Health, before prescribing psychostimulants. However, there is an exemption from this requirement for paediatricians and psychiatrists where: • the patient is being treated for ADHD and the treatment is not expected to be for greater than 8 weeks (including a preceding period of treatment) – no permit or notification is required. • the patient is under the age of 18 years and being treated for ADHD for a period greater than 8 weeks – the specialist must provide notification of the treatment (section 34D notification). Adult patients being treated for ADHD for greater than 8 weeks require a permit. GPs may be issued with a permit to prescribe psychostimulants for a patient where the application indicates that diagnosis was undertaken by a specialist and there are at least yearly reviews by a specialist. Other clinicians at the same clinic may prescribe under the same permit. Permits are not required for patients in prison or a residential aged care service, or hospital in-patients. Legislation: *Drugs, Poisons and Controlled Substances Act 1981* and Drugs, Poisons and Controlled Substances regulations 2006.
WA[39]	Authorised specialists may prescribe psychostimulants to patients who meet the clinical criteria in the Stimulant Prescribing Code (the Code). These specialists are issued a Stimulant Prescriber Number by the Department of Health. Treatment of ADHD with stimulants may only be initiated by a neurologist, paediatric neurologist, paediatrician, psychiatrist, a child and adolescent psychiatrist or a medical practitioner approved by the Department of Health. Psychostimulants may not be prescribed for patients with a history of psychosis or drug abuse, or a diagnosis of bi-polar disorder. Annual drug screening of patients aged over 13 years is required. To prescribe outside the clinical criteria in the Code, special authorisation must be obtained by an authorised specialist from the Department of Health. Psychostimulants must not be prescribed to patients under 2 years of age, and prescribing for patients aged 2-3 years requires a special authorisation. Patients under 6 years must not be treated with lisdexamphetamine. Legislation: *Poisons Act 1964* and Poisons Regulations 1965.

Abbreviations: ADHD = Attention Deficit Hyperactivity Disorder; CHO = Chief Health Officer.

Table A.2. Summary of state and territory regulations for maximum quantities of dexamphetamine and methylphenidate that may be prescribed for the treatment of ADHD, with comparison to the maximum recommended doses in the Product Information.[a]

	Max daily dose of dexamphetamine		Max daily dose of methylphenidate	
	Children and adolescents	**Adults**	**Children and adolescents**	**Adults**
NSW[30;31; b]	1 mg/kg up to 50 mg	30 mg	2 mg/kg up to 108 mg	60 mg
SA[35; b]	-	30 mg	-	IR: 60 mg MR: 75 mg
TAS[36;37; b]	0.9 mg/kg	30 mg	1.8 mg/kg	60 mg
WA[39; c; d]	1 mg/kg up to 60 mg	60 mg	2 mg/kg up to 120 mg	120 mg
Product Information[7;8;9]	40 mg	-	IR: - MR: 54–60 mg	IR: - MR: 72–80 mg

Abbreviations: IR: immediate release methylphenidate; MR: modified release methylphenidate

Notes: [a] ACT, Victoria, Queensland and the NT do not have specific regulations on maximum doses of psychostimulants that can be prescribed.

[b] NSW, SA and Tasmania allow applications for increased doses of psychostimluants beyond the maximums listed, but there are additional regulatory requirements.

[c] The maximum dose of lisdexamphetamine that may be prescribed in WA is 70 mg/day.

[d] Where both dexamphetamine and methylphenidate are prescribed, the maximum dexamphetamine equivalent dose must not exceed 1 mg/kg/day or a maximum of 60 mg/day for children and adolescents, or 60 mg/day for adults. The maximum dexamphetamine equivalent dose is determined by dividing the methylphenidate dose (in mg) by two and adding to the dexamphetamine dose (in mg).

Appendix B: PBS listing dates and changes to listings for ADHD medicines

Table B.1. Date of listing of PBS medicines used in the treatment of ADHD.

Date	Drug name	Brand name	Strength	Item
Dec 1973	Dexamphetamine	-	5 mg	1165H
Aug 2005	Methylphenidate IR	Ritalin 10	10 mg	8839F
Dec 2005	Methylphenidate IR	Attenta*	10 mg	8829F
April 2007	Methylphenidate MR	Concerta	18 mg	2387P
			36 mg	2388Q
			54 mg	2432B
July 2007	Atomoxetine	Strattera	10 mg	9092M
			18 mg	9093N
			25 mg	9094P
			40 mg	9095Q
			60 mg	9096R
Aug 2007	Methylphenidate MR	Concerta	27 mg	2172H
April 2008	Methylphenidate MR	Ritalin LA	20 mg	2276T
			30 mg	2280B
			40 mg	2283E
Dec 2008	Atomoxetine	Strattera	80mg	9289X
			100 mg	9290Y
Aug 2010	Methylphenidate MR	Ritalin LA	10mg	3440C

Notes: * The Attenta® brand of methylphenidate IR was delisted in March 2009.

Table B.2. Changes to PBS restrictions of medicines used in the treatment of ADHD.

Date	Drug name	Change to the restriction/s
Aug 2007	Methylphenidate MR (Concerta®)	Replacement of "…child or adolescent aged 6 to 18 years inclusive" with "…patient aged 6 to 18 years inclusive".
Nov 2008	Atomoxetine (all items)	The restrictions were changed to remind prescribers that atomoxetine is not PBS subsidised for use with other ADHD medicines. "Initial treatment…" was replaced by "Initial sole PBS-subsidised treatment…", and "Continuing treatment…" was replaced by "Continuing sole PBS-subsidised treatment…". A note was also added, "No applications for increased maximum quantities and/or repeats will be authorised", as the listing of the 80 mg and 100 mg doses was considered to negate the need for increased maximum quantities.
Oct 2009	Methylphenidate (modified release) (all items)	The restrictions were modified to extend the listing to the treatment of patients aged over 18 years who were diagnosed between ages 6–18. "Treatment of attention deficit hyperactivity disorder (ADHD) in a patient between the ages of 6 and 18 years inclusive" was changed to "'Treatment of attention deficit hyperactivity disorder (ADHD) in a patient *diagnosed* between the ages of 6 and 18 years inclusive".
Aug 2014	Atomoxetine (all items)	The restriction was simplified and changed from Authority Required to Authority Required (STREAMLINED). The requirement for diagnosis using the DSM-IV criteria was updated to the DSM-V. The emphasis on "sole PBS-subsidised treatment" use was removed. References in the previous restriction to specific contraindications and adverse events were generally removed.

Appendix C: Methodology

Authority approvals data

To consider if the number of people receiving ADHD medicine is changing over time, the Medicare Authority approvals database was used, as this eliminates the effect of individuals being missed prior to the full capture of under co-payment data in April 2012.

Data were extracted from the Medicare authority approvals database. The number of individual people who received an authority approval was determined for each of the calendar years 2010 to 2014 by a count of unique patient identifiers. New patients were defined as people who had no previous prescription for an ADHD medicine since January 2007. The age and sex of these people was determined by cross-matching patient identification numbers with the Medicare pharmacy claim database. Age was determined to be the age at first approval in that calendar year.

These data are presented as:

- number of people treated by age group and sex (Table 3)
- number of people new to therapy by age group and sex (Table 3)
- number of people in each age/sex category as a percentage of the total number of new/all patients (Table 4)
- ratio of males to females (Figure 2)
- number of people treated by medicine prescribed (Table 6)
- number of people new to therapy by first medicine prescribed (Table 6)
- length of treatment (Figures 8 and 9, Table 7) - for full methods see Appendix D
- (for 2011-2014) number of people per 1000 population by patient state, standardised by total state population from ABS population statistics[2] (Figure 10)

Atomoxetine is not included in the Medicare authority approvals data after 1 August 2014. Medicare pharmacy claims data for atomoxetine in 2014 was used in Table 6.

[2] ABS pub 3101 spreadsheet 4

Counting patients from Authority approvals data as a proxy for patients supplied

In 2014 there were 117,403 people granted authority approvals for ADHD medicines. For comparison, PBS subsidised ADHD medicines were supplied to 122,036 people.

This demonstrates that people supplied authority approvals are a reasonable proxy for people dispensed ADHD medicines. The differences could be due to narcolepsy being excluded from analysis of authority data but not supply data, exclusion of atomoxetine from authorities data after August 2014, and medicines being dispensed more frequently than authority approvals granted.

Medicare pharmacy claims data

Where a snapshot of data from 2013 or 2014 is presented, the Medicare pharmacy claims line-by-line data were used. This database includes actual under co-payment data collection from April 2012. Age was determined to be the age at first supply in 2014.

These data are presented as:

- number of people supplied at least one PBS ADHD medicine by age (Figure 1)
- number of people supplied an ADHD medicine in 2014 by age and sex (Figure 3)
- medicines used to initiate PBS ADHD therapy by patient age (Figure 6). Initiators were defined as having no prior ADHD prescription since January 2011.
- number of people supplied each PBS ADHD medicine by age (Figure 7). People can be counted in more than one category if supplied multiple medicines within a calendar year.
- number of people supplied an ADHD medicine by 1000 population (age and state population standardised)[3] by state/territory of residence and age group (Figure 11)
- number of people supplied an ADHD medicine per 1000 population (state population standardised) by state/territory of residence and medicine (Figure 12)

Same day supply of medicines (Table 8)

Data were extracted from the Medicare pharmacy claims database for each of the calendar years 2013 and 2014. The data were analysed to determine how many people were supplied with certain combinations of psychotropic medicines on the same day. The medicine combinations were:

- Multiple ADHD medicine (i.e. dexamphetamine, methylphenidate, atomoxetine)
- Multiple forms of methylphenidate (i.e. IR, either brand of MR)
- Any ADHD medicine with any (non-ADHD N06BA) psychotropic medicine, by type of psychotropic medicine [i.e. ATC N05A (antipsychotics); N05B (anxiolytics); N05C (hypnotics and sedatives); N06A (antidepressants)].

[3] ABS pub 3101 data cube, population by age and sex tables, Table 8

These data were presented as the proportion of people with same day supply by age group: under 6 years, 6-12 years, 13-17 years and 18+ years.

This method provides a lower estimate of use of multiple psychotropic medicines. Using a co-administration analysis other than same day supply is difficult, as it relies on estimating the amount of coverage provided by each medicine, which is especially difficult where children receive lower dosing or weight based dosing; and where pack sizes are variable.

Prescriber type analysis (Table 9)

The prescriber type for ADHD medicines supplied in 2014 was determined from the Medicare pharmacy claims database. New patients were defined as no prescription for an ADHD medicine supplied after January 2011. However, the full ADHD medicine history including under copayment medicines (dexamphetamine, methylphenidate-IR and methylphenidate-MR 10 mg) was not available until April 2012.

DUSC database

Prescription data were extracted from the DUSC database for all prescriptions for medicines used in the treatment of ADHD between quarter 1 2010 and quarter 4 2014. Actual under co-payment data is available in the DUSC database from April 2012; prior to this an estimate of under co-payment prescriptions was included. An estimate of private prescriptions was included until August 2012. Analysis was by prescription counts by quarter.

Analysis was based on the date of supply, which may result in small differences if compared with published Medicare data that is based on the date of processing.

These data are presented as:

- number of prescriptions for ADHD drugs (Figure 4; Table 5)
- number of prescriptions for methylphenidate IR and MR forms (Figure 5; Table 5)
- PBS benefits paid for ADHD medicines (Table 10)

Data handling for dexamphetamine regarding the treatment of narcolepsy

People receiving dexamphetamine for the treatment of narcolepsy were excluded from analyses using the Medicare authority approvals database. Where data were obtained from the Medicare pharmacy claim database or the DUSC database, patients receiving dexamphetamine for the treatment of narcolepsy were included. However, the 2012 DUSC review of ADHD medicines utilisation found that there was comparatively little use of dexamphetamine for the treatment of narcolepsy. The prevalence of narcolepsy is estimated around 0.03–0.16%, and narcolepsy with cataplexy at 0.00025–0.0005%.[xl]

Appendix D: Analysis of length of treatment

Approvals data from January 2002 to July 2014 inclusive were used, with initiation defined as a first approval after 1 January 2003 (i.e. no prior approval for at least one year). Initiators to therapy in 2013 and 2014 were excluded due to insufficient follow-up. Overall length of treatment was defined as the time from initiating approval to last approval plus the median time between approvals (calculated at the form and number of repeats level, see table E.1 below). A person was deemed to be continuing treatment (i.e. censored) at the end of the data period if the last approval was within 2 x "median time between approvals" of the end of the data period (i.e. 31 July 2014). Otherwise the person was deemed to have finished treatment.

The median number of days between approvals is shown below.

Table E.1. Median days between Authority approvals by form and number of repeats

Form	Number of repeats	median days between approvals
Atomoxetine (Strattera)	0	47
Atomoxetine (Strattera)	1	88
Atomoxetine (Strattera)	2	162
Atomoxetine (Strattera)	3	121
Atomoxetine (Strattera)	4	155
Atomoxetine (Strattera)	5	165
Atomoxetine (Strattera)	> 5	105
Dexamphetamine	0	39
Dexamphetamine	1	86
Dexamphetamine	2	116
Dexamphetamine	3	182
Dexamphetamine	4	182
Dexamphetamine	5	183
Dexamphetamine	> 5	182
MPH-CR (Concerta)	0	30
MPH-CR (Concerta)	1	58
MPH-CR (Concerta)	2	91
MPH-CR (Concerta)	3	120
MPH-CR (Concerta)	4	156
MPH-CR (Concerta)	5	180
MPH-CR (Concerta)	> 5	212
MPH-CR (Ritalin LA)	0	31
MPH-CR (Ritalin LA)	1	59

Form	Number of repeats	median days between approvals
MPH-CR (Ritalin LA)	2	91
MPH-CR (Ritalin LA)	3	120
MPH-CR (Ritalin LA)	4	157
MPH-CR (Ritalin LA)	5	178
MPH-CR (Ritalin LA)	> 5	223
MPH-IR (Attenta or Ritalin)	0	56
MPH-IR (Attenta or Ritalin)	1	118
MPH-IR (Attenta or Ritalin)	2	141
MPH-IR (Attenta or Ritalin)	3	182
MPH-IR (Attenta or Ritalin)	4	181
MPH-IR (Attenta or Ritalin)	5	182
MPH-IR (Attenta or Ritalin)	> 5	185

In calculating the median days between approvals, where more than one approval exists for the same person on the same day (e.g. if the person received approvals for two different strengths of the same medicine on the same day) these were treated as a single approval.

To avoid the bias of approvals towards the end of the data period not having sufficient time for re-approval, the ones approved within the last 400 days of the end of data period (i.e. 31 July 2014) were excluded from the median calculation. If included they introduce a slight shortening bias. The 400 days was determined by observing that approximately 95% of all ADHD approvals that have a re-approval are re-approved within 400 days.

Where the person was deemed to be continuing at the end of the data period, the length of treatment was recalculated to be the time from initiating approval to the end of the period.

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