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Dr Sam Sample
123 Sample Street
SAMPLETOWN ABC 1234

19 September 2011

Dear Dr Sample,

Please find enclosed the current issue of *Prescribing Practice Review* and confidential data on your prescribing of antipsychotics.

Antipsychotics are first-line therapy for schizophrenia, but they are also used for many other psychiatric indications, on- and off-label. This *Prescribing Practice Review* considers the implications of antipsychotic adverse effects for GP management, concentrating on schizophrenia, bipolar disorder and behavioural symptoms of dementia.

Other activities offered in the NPS program **Balancing benefits and harms of antipsychotic therapy** are:

- A clinical audit, available now. You can enrol online at www.nps.org.au/clinical_audits to receive individualised feedback against best practice guidelines.
- A case study covering antipsychotic adverse effect management. *Emily is a 28-year-old woman with schizophrenia who has come to see you about the side effects of her medication.* Completing this activity provides you with an opportunity to compare your clinical decision-making skills with those of your colleagues. See Case Study 70 at casestudy.nps.org.au.

For more information contact us on 02 8217 8700 or visit nps.org.au.

Yours sincerely,



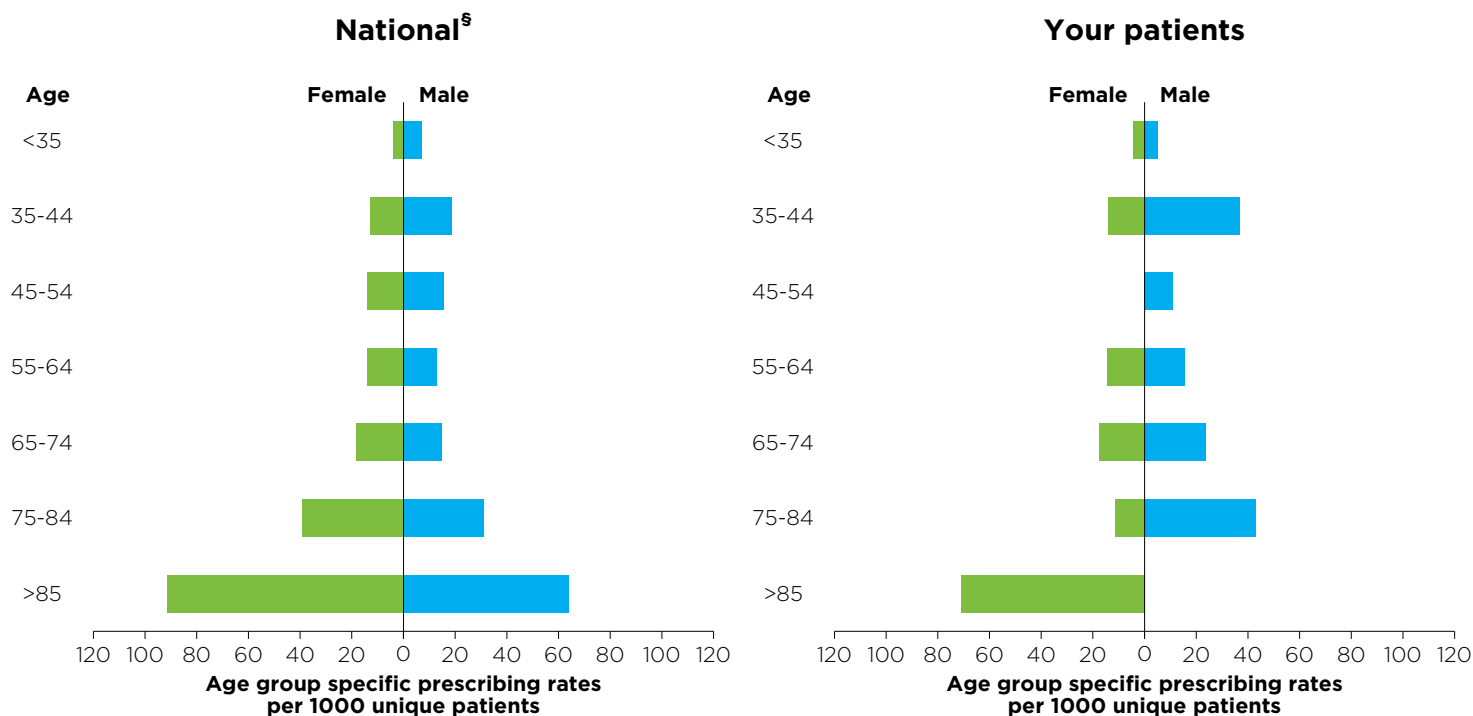
Dr Janette Randall
Chair



Your confidential prescribing data

The data presented from Medicare Australia includes PBS prescriptions dispensed for concession card holders and items above the co-payment for general patients. Depending on the cost of the drug the data shown will cover all your patients (if the drug is above the co-payment) or only concession card holders (if the drug is below co-payment). Indication for use cannot be determined.

What was the age/sex distribution of patients on antipsychotic medicines‡ in 2010?

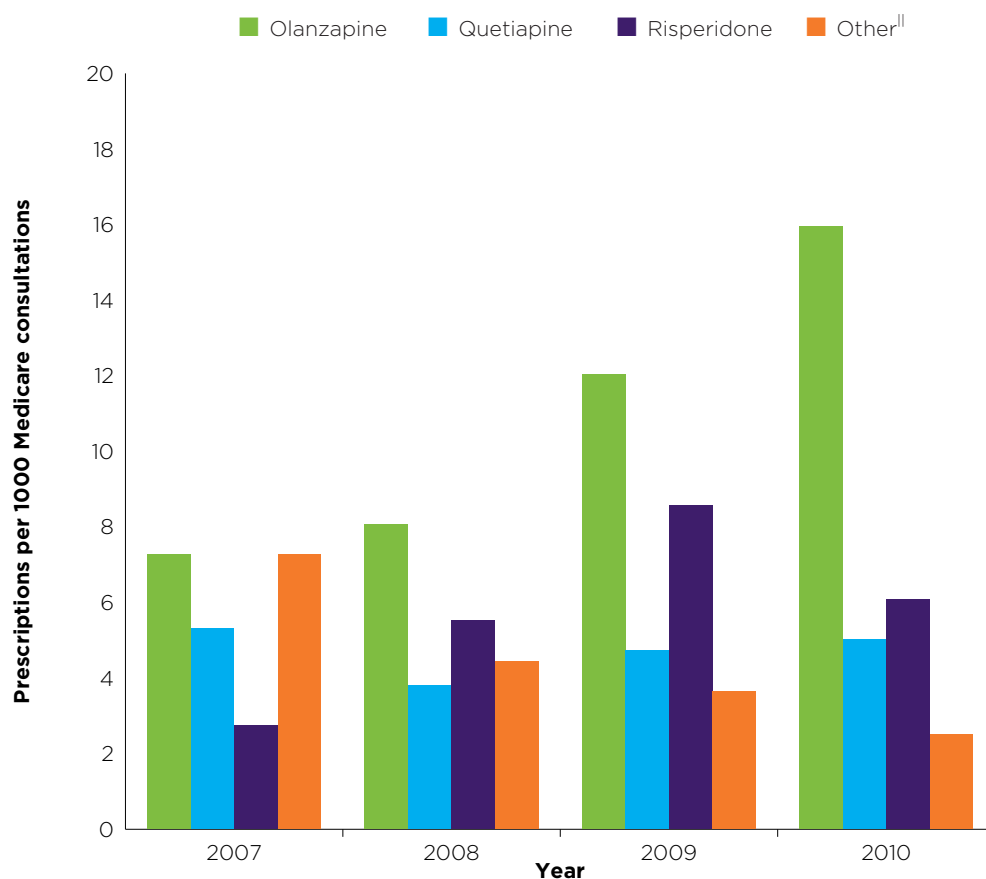


§ Includes unique patients prescribed antipsychotic medicines in the primary care setting by GPs and other medical practitioners. Does not include patients prescribed antipsychotic medicines by specialists.

Points for reflection

- Tailor the antipsychotic medicine to the individual patient. Consider symptoms, adverse effect profiles and risk factors for adverse effects, previous experience and response with the medicine, comorbid conditions and social factors (e.g. unemployment).¹ Prescribe antipsychotic medicines in combination with non-pharmacological approaches.^{2,3}
- Reinforce the importance of adherence to antipsychotic therapy, considering factors that may affect adherence (see NPS PPR 55 for more information). Poor adherence to medicines is the main cause of relapse, especially in young people with recent-onset disease.¹
- Engage the patient and/or carer in discussions about the benefits and adverse effect profile of the antipsychotic medicine prescribed.³

How has your use of antipsychotic medicines changed over time?



Points for reflection

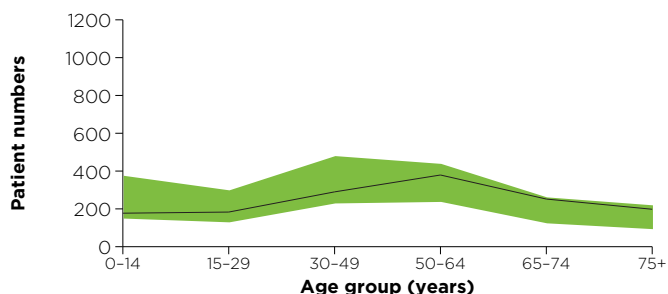
- Regularly enquire about adverse effects when reviewing patients. Consider a change in medicine if adverse effects are unacceptable or persist and when other measures (e.g. dose reduction) have failed.
- Monitor cardiometabolic risk factors, and general physical health of patients throughout treatment (see NPS *PPR 55* for more information).^{1,4,5}
- For behavioural symptoms of dementia, use antipsychotic medicines only when non-pharmacological approaches have been unsuccessful. Use the lowest possible dose and review the effect on targeted behaviour and treatment-related adverse effects every 3 months (see NPS *PPR 55* for more information).¹

Practice profile

The data below, based on Medicare claims, are provided to help you interpret your prescribing data within the profile of your practice.

Age profile of patients in your practice

(1 January 2010 to 31 December 2010)



The black line represents the age profile of patients in your practice. 25% to 75% of other GPs in your RRMA[#] fall within the shaded area. Your RRMA peer group is **5**.

Medicare patients and concession card holders in your practice

(1 April 2010 to 30 June 2010)

| Patients | You | Median other GPs in your RRMA [#] |
|---------------------------------------|-----|--------------------------------------------|
| Total Medicare | 567 | 620 |
| Concession card holders ^{##} | 305 | 238 |

^{##} Includes those reaching Safety Net

Data from a 3 month period (1 April 2010 to 30 June 2010) that best represents your patient mix have been provided.

Confidentiality

NPS has a contract with Medicare Australia to provide your prescribing feedback data directly to you. NPS does not have access to these data. The data contained in this feedback are not used for any regulatory purposes.

Discrepancies may occur between the data provided and your own prescribing practice. This may be due to either inaccurate recording of your prescriber number in the pharmacy or your prescription pad having been used by another doctor.

If you consider your individual data to be incorrect, have other data queries or general feedback, please contact NPS on 02 8217 8700 (and select option 2) or by email at info@nps.org.au

This information is derived from a critical analysis of a wide range of authoritative evidence. NPS has taken reasonable care to ensure that the information is accurate and up-to-date at the time of creation. NPS does not warrant its completeness and excludes liability where permitted by law. Healthcare professionals must continue to rely upon their own skill, care and inquiries taking into account the individual circumstances of each patient when providing medical advice.

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Notes

- † Data shown are an aggregate for all your provider locations.
- ‡ Includes antipsychotic medicines supplied on PBS and Section 100 supplied in-hospital.
- || Other includes amisulpride, aripiprazole, chlorpromazine, clozapine, flupenthixol, fluphenazine, haloperidol, paliperidone, pericyazine, thioridazine, trifluoperazine, ziprasidone, zuclopenthixol.
- # The comparator group 'other GPs in your RRMA' includes all prescribers who are currently located in a similar geographical region i.e. **1.** capital cities, **2.** other metropolitan centres, **3.** large rural centres, **4.** small rural centres, **5.** other rural centres, **6.** remote centres and **7.** other remote centres. **Your RRMA peer group is 5.**

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Balancing the benefits and harms of antipsychotic therapy

Key messages

- Assess benefits and harms of antipsychotic therapy
- Engage patients and carers in recognising and managing adverse effects
- Reinforce the importance of adherence to antipsychotics when prescribed
- Review ongoing need for antipsychotics for behavioural symptoms of dementia and trial withdrawal

Assess benefits and harms of antipsychotic therapy

Most clinical data for antipsychotics are from trials in schizophrenia and bipolar I disorder. Adverse effect data reported in these conditions are also useful for clinical decision-making in other psychotic disorders for which there is less evidence.

Antipsychotic choice in schizophrenia requires individual tailoring

Drug safety profiles and patient risk factors for adverse effects should guide antipsychotic choice. Weigh up the potential to cause metabolic side effects (e.g. weight gain), extrapyramidal side effects (including tardive dyskinesia) and other common problems such as sedation or anticholinergic effects (see Table 1, page 2).^{1,2}

On average, the trade-off between efficacy and adverse effects does not favour any particular antipsychotic.² The newer “atypical” antipsychotics are most frequently prescribed, but recent trials challenge the view that they are more effective overall than older “conventional” antipsychotics.³

Antipsychotic maintenance therapy prevents relapse of hallucinations, delusions and abnormal behaviours in schizophrenia; however, achieving an acceptable outcome involves trial and error. Lack of clinical response or poor tolerability can occur with any antipsychotic. Assess regularly and, if necessary, review choice of antipsychotic and dose.¹

Antipsychotics are one of several options in bipolar disorder

Antipsychotics, lithium, antidepressants and anticonvulsants all have a place in treating bipolar disorder.^{1,4,5} The likelihood of short- and long-term adverse effects, patient preferences and individual risk factors will influence the choice of treatment. Diagnosis and treatment selection for people with bipolar disorder requires specialist expertise and, as in schizophrenia, multiple therapeutic trials may be necessary.

Consider adjunctive psychotherapy for people who are relatively stable but have mild to moderate affective symptoms. Psychotherapy can improve symptoms and reduce relapse rates.^{4,6}

There is some evidence for using antipsychotics in all phases of bipolar disorder. However, the relative effectiveness of antipsychotics versus other drugs such as lithium is uncertain. Only a few antipsychotics have been adequately assessed in randomised controlled trials for relapse prevention or bipolar depression, and evidence supporting use of antipsychotics for people with bipolar II disorder (i.e. who do not experience full-blown mania) is limited.^{1,4,5} A table of antipsychotic approved indications and PBS listings is available on the NPS website (www.nps.org.au/antipsychotics).



Non-pharmacological approaches are first line for behavioural symptoms of dementia

Rule out physical causes of distress or delirium, medicines that can impair cognition, environmental factors and diagnoses such as depression before considering other treatment.¹

Ensure carers have access to advice and training in behaviour management techniques (see www.nps.org.au/antipsychotics for a list of resources).

A variety of psychosocial and other non-drug therapies can reduce agitation and aggression associated with dementia, with a low risk of adverse effects.⁷ An individually tailored non-pharmacological approach is first line, given that antipsychotics have limited efficacy and can cause serious or intolerable adverse effects.

Use an antipsychotic only if aggression, agitation or psychotic symptoms of dementia cause severe distress or an immediate risk of harm

Risperidone has the most evidence for efficacy in managing behavioural symptoms of dementia and is the preferred antipsychotic. Olanzapine is an alternative, but is not PBS listed for this indication. Other antipsychotics may be efficacious; however, there is less evidence to support their use. Continue non-pharmacological approaches during antipsychotic treatment.¹

Discuss the proposed treatment with the patient, family or carer. Contact the State or Territory Adult Guardian, Public Guardian or Public Advocate's office for information about the legislation on substitute consent.

With any antipsychotic, adverse effects such as parkinsonism, sedation, confusion and falls offset reductions in symptoms. In one large trial, failure to respond or intolerable adverse effects caused most patients to discontinue treatment.⁸

Other pharmacological treatments do not have established efficacy in managing behavioural symptoms.⁹

Table 1: Selected common and serious adverse effects of oral antipsychotics^{1,10}

| Adverse effect | <i>amisulpride</i> (Solian, Sulprix) | <i>aripiprazole</i> (Ablify) | <i>chlorpromazine</i> (Largactil) | <i>clozapine</i> (Clopine, Clozaril) | <i>haloperidol</i> (Seranace) | <i>olanzapine</i> (Zyprexa) | <i>paliperidone</i> (Invega) | <i>quetiapine</i> (Seroquel, Seroquel XR) | <i>risperidone</i> (Ozidal, Resdone, Rispera, Risperdal, Rixadone) | <i>ziprasidone</i> (Zeldox) |
|--------------------------------------------------------------|-------------------------------------------------------------------------------|---------------------------------|--------------------------------------|-----------------------------------------|----------------------------------|--------------------------------|---------------------------------|----------------------------------------------|-----------------------------------------------------------------------|--------------------------------|
| Weight gain | + | + | +++ | +++ | ++ | +++ | ++ | ++ | ++ | + |
| Sedation | + | + | +++ | +++ | + | +++ | ++ | +++ | ++ | ++ |
| Anticholinergic (e.g. dry mouth, dizziness, constipation) | + | + | +++ | +++ | + | +++ | + | ++ | + | + |
| Extrapyramidal | ++ | + | ++ | + | +++ | + | ++ | + | ++ | + |
| Orthostatic hypotension | + | + | +++ | ++ | + | + | ++ | ++ | ++ | ++ |
| Tardive dyskinesia | Occurs more frequently with "conventional" antipsychotics (listed in italics) | | | | | | | | | |
| QTc prolongation | Can occur with all antipsychotics; ziprasidone has a greater risk | | | | | | | | | |
| Neuroleptic malignant syndrome | Reported with all antipsychotics | | | | | | | | | |

Key: Frequencies at therapeutic oral doses in non-elderly adults: + = ≤ 10%; ++ = > 10%; +++ = > 30%.

Adapted with permission from Psychotropic Expert Group. Therapeutic guidelines: psychotropic. Melbourne: Therapeutic Guidelines Ltd; 2008. p.32-3.

Engage patients and carers in recognising and managing adverse effects

Use multiple methods to assess side effects

Ask about adverse effects as part of routine patient review; it may also help to provide written information about antipsychotics so that patients are aware of what to expect (see Box 1). Most people with a psychotic illness experience one or more troublesome adverse effects day to day.¹¹ While these effects reduce quality of life and may cause poor adherence, relatively few report them to their GP or psychiatrist without prompting.¹²

Manage according to patient needs and relapse risk

Adverse effects may subside a few weeks after starting or altering treatment, or may be manageable with non-drug approaches. When unacceptable adverse effects persist, a change in regimen is preferable to non-adherence. If symptoms are well controlled, assess if the dose can be reduced without risk of relapse.¹

Switching to an antipsychotic with a different adverse effect profile is often necessary, for example in case of rapid weight gain or metabolic abnormalities. The protocol for tapering from the old drug to the new one should be worked out with a psychiatrist. Engage patients and carers, informing them about the risk of relapse or temporary exacerbation of adverse effects during the changeover period, as well as the potential benefits.¹

Box 1: Information for patients and carers about mental health and antipsychotic treatment

Antipsychotic medicine brochure. Includes information on how to take antipsychotics, precautions to take and common side effects. www.nps.org.au/SSWAHS_antipsychotic

SANE Australia, for information on schizophrenia and bipolar disorder, as well as on antipsychotic treatment. www.sane.org

Beyond Blue www.beyondblue.org.au and the **Black Dog institute** www.blackdoginstitute.org.au for information on bipolar disorder

Alzheimer's Australia for information about behavioural symptoms of dementia and advice about non-pharmacological treatments and support for carers. www.alzheimers.org.au

Regularly monitor the physical health of people receiving antipsychotics long term

Monitor for cardiometabolic risk factors, burdensome adverse effects such as extrapyramidal symptoms or symptoms of hyperprolactinaemia (e.g. sexual disturbances, amenorrhoea or gynaecomastia).¹

Reinforce the importance of adherence to antipsychotics when prescribed

Poor adherence is strongly associated with relapse of psychotic illness

Assess adherence to antipsychotic therapy regularly and systematically.² As well as asking about side effects, ask about attitudes to and problems taking medicines.¹⁶ Simple measures can help adherence, especially addressing troublesome adverse effects (see Box 2).¹ Risk factors for non-adherence include alcohol and illicit drug use, lack of family involvement, poor clinician–patient relationship and a negative attitude towards treatment.¹⁷ In one study, people with recent-onset schizophrenia were several times more likely to relapse if they had poor adherence (odds ratio 14.6, 95% confidence interval 3.3 to 64.0).¹⁸

Australian survey data indicate a high prevalence of cardiovascular and metabolic risk factors.¹³ Prompt management can forestall serious long-term adverse effects of antipsychotic treatment. A checklist of suggested items for review along with a template for monitoring results can be downloaded from the NPS website (www.nps.org.au/antipsychotics).

Additional monitoring may need to be negotiated with other members of the mental health team, depending on risk factors or for people on particular drugs.

GPs have a leading role in managing the physical health of people taking antipsychotics and GP visits may be the only opportunity to receive lifestyle assessment and support, allied health referrals or preventive health screening. People with serious mental illness often have poor physical health, which can be a consequence of the adverse effects of antipsychotics, poor diet, a lack of physical activity, and alcohol and illicit drug use. There is also evidence that limited access to healthcare adds to the problem.¹⁴

Monitor symptoms intensively in people with dementia receiving an antipsychotic

When starting antipsychotic therapy for agitated or aggressive behaviour in dementia:

- assess the targeted behaviour weekly
- measure blood pressure at baseline and within the first 7 days of treatment
- check body weight and blood glucose at baseline
- observe closely for signs of sedation, postural hypotension, extrapyramidal symptoms (e.g. abnormal movements of the face, arms, legs or trunk) or anticholinergic effects (e.g. dry mouth, constipation, urinary hesitancy or delirium).¹⁵

Box 2: Practical measures to promote adherence¹

- Provide and discuss written information and personalised instructions
- Prescribe the simplest dosing regimen possible
- Give positive feedback for treatment adherence
- Assess and address adverse effects
- Involve family, carers or friends when appropriate
- Suggest daily routines as prompts to remind patients to take their medicines
- Monitor use, e.g. consider medication review
- Enquire about patients' preference for using any particular dosage form

Review ongoing need for antipsychotics for behavioural symptoms of dementia and trial withdrawal

Discontinue antipsychotic use if there is no improvement in the targeted behaviour

Response usually occurs in 1–2 weeks¹⁹; discontinue if there is no improvement within 12 weeks and reassess. An alternative antipsychotic may be tried. The incremental benefit of antipsychotics over placebo is small, for example in 3 randomised controlled trials of 12 weeks, an average of 46% of participants treated with risperidone responded, compared with 33% of participants treated with placebo (odds ratio 1.8, 95% confidence interval 1.4 to 2.3).¹⁹

Cease antipsychotics gradually—taper the dose by 50% every 2 weeks and continue for 2 weeks on the minimum dose before stopping.

Review at least every 3 months

If symptoms are stable, try a gradual dose reduction and withdrawal. Review the targeted behaviour, changes in function and treatment-related adverse effects every 3 months or according to clinical need.¹ Behavioural symptoms can fluctuate significantly or resolve within 12 weeks, as reflected in the high placebo response rates in clinical trials. People with dementia whose behavioural symptoms are under control often show no worsening when they stop antipsychotics.^{20–22}

Antipsychotic use in dementia is associated with serious adverse effects

Trial data show an excess of approximately 1 death for each 100 people with dementia treated with risperidone, olanzapine, quetiapine or aripiprazole for 10–12 weeks.²³ Deaths appeared to be cardiovascular or infectious (e.g. pneumonia) in nature.²⁴ This risk appears to extend to all antipsychotics.²⁵

Expert reviewers

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For online resources go to: nps.org.au/ppr_55