MEDICINES Australia

BETTER HEALTH THROUGH RESEARCH AND INNOVATION

# Medicines Australia
# Submission
# to the
# Senate Select Committee on Mental Health

Role of medicines and the pharmaceutical industry in the management of mental illness in Australia

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## Executive Summary

- Innovative medicines play a key role in managing mental illness like depression and schizophrenia.
- Without medication, in many cases patients would be less able to benefit from other non-medication based treatments.
- Use of newer medications to treat mental illness has grown in Australia over the last 15 years and has provided a number of advantages to patients and the Government.
- The pharmaceutical industry has an important role in supporting a range of collaborative research efforts in mental health.
- Quality use of medicines is especially important to treating mental health.
- There is a potential role for new technologies, such as the Internet, to help in managing mental illness.

## Recommendations

- More resources need to be devoted to treat mental illness, given the disease burden placed on the Australian community.
- Greater focus should be put on the quality use of medicines and educational efforts by stakeholders to enhance outcomes in treating mental illness.
- There is a need for greater research and analysis to identify and quantify the impacts of mental disorders on productivity in the community and the economy.
- Initiatives such as the Better Outcomes in Mental Health and ongoing support for consumer and carer organisations and networks deserve greater resources and funding given their important role in treating mental illness.
- There is a need for government to play more of a role in encouraging industry's role in research.
- More progress needs to be made in developing innovative support networks, such as web-based patient support and greater community awareness and support.

## 1. Introduction

Australia has excellent data on the prevalence and impact of mental illness across the whole spectrum of disorders, from the so-called low prevalence disorders of schizophrenia and bipolar disorder (formerly known as manic depressive disorder) to the high prevalence disorders, depression and anxiety. Following the landmark work by Murray and Lopez in 1996 on the Global Burden of Disease[1] it has been accepted in most developed countries that mental illness is a leading cause of disability. It is increasing rapidly and likely to surpass the widely recognised physical illnesses such as heart disease and cancer as the single greatest cause of disability in developed countries. Recent work in Australia by Mathers et al[2] confirmed this applies in this country also.

The considerable individual disability and economic impact of mental illness has significant implications for Australia. The high prevalence disorders such as depression affect somewhere between 5 and 10% of the adult population in any one year[3] (this equates to approximately 1 million people). Whereas the relatively lower prevalence disorders such as schizophrenia and bipolar disorder have a severe impact on the individual in terms of suicide (50% will try and 10% will successfully suicide) and functioning. Because many of these disorders appear at a relatively early age and impact individuals in the "prime" of their life, there are considerable consequences, not only for the individual, but also for society, which must manage the social and economic sequelae. All three of these disorders (depression, bipolar disorder and schizophrenia) are accompanied by a significantly increased risk of suicide.

Australia has for some time recognised the importance of mental health and mental illness, as reflected in the National Health Priority Areas and the subsequent development of the National Mental Health Strategy (now in its third iteration for 2003 -2008)[4]. Creation of innovative approaches such as the *beyondblue* depression initiative has also been a significant advance.

However, there has been much criticism in recent years that in spite of this recognition of the growing problem and the development of national strategy, actual delivery of care on the ground continues to be inadequate in many ways and in many areas, to the extent that the burden experienced by consumers and carers in Australia continues at a level greater than that expected as a result of the national strategy and available evidence-based interventions.

In the area of research, Australia has great expertise in the basic neurosciences, neurology and neuropsychiatry. There are centres of excellence in a range of neuroscience research throughout Australia. Although they may have different research foci, some of these centres have international reputations and the expertise to contribute significantly to the reduction of the burden of mental illness in Australia.

In this submission, MA highlights the importance of the role of evidence-based interventions in managing mental illnesses and the important role of innovative medicines and the pharmaceutical industry itself. We demonstrate this by highlighting contributions of the pharmaceutical industry to advances in treatment, neuroscience research, advocacy and patient care.

When levels of funding for mental health are criticised, it is often pointed out that significant increases in Commonwealth funding have occurred in recent years, partly due to increased in funding of medicines via the PBS. While this is true, medicines are but one piece of the overall management strategy, albeit a key piece. This is because in many cases, without the benefits of medicines, patients would be less able to participate in and benefit from the multitude of other, non-medication based interventions (such as psychological and vocational therapies) and support. This aspect (the interdependence of medicines and other support and non-medication based interventions) goes in both directions i.e. adherence to medication to the extent required to produce real functional improvement may require other non-medication support and services.

## 2. Expenditure on medicines for mental illness via the Pharmaceutical Benefits Scheme: a cost-effective investment in mental health

Two major changes have impacted the understanding and amelioration of mental illness in recent decades. The first was the development of improved systems of classification of mental illnesses, along with improved clarity and specificity of diagnosis.

The second major change, which is still continuing, has been the growth in understanding of biological psychiatry. This has included enormous progress in understanding the structure and function of the regions of the brain along with similar progress in identifying and understanding the roles of an increasing number of neurotransmitters. The pharmaceutical industry has spearheaded the research effort with a number of major advances in the past two decades.

While the level of expenditure on pharmacological treatments for mental health has increased with the above advances, Australian health expenditure data confirms that this remains a modest component of total cost of mental disorders (16.5% of total mental health costs spent on pharmaceuticals versus 41.7% of total cost spent on hospitalisation).

**Table 1: Total health system cost of mental disorders, Australia, 2000-01**

| | Hospital and aged care homes | Medical and other health professionals | Pharmaceuticals (prescription and OTC) | Research | Community and Public Health | Total |
|---|---|---|---|---|---|---|
| $m | 1,561 | 633 | 616 | 109 | 821 | 3,741 |
| % | 41.7 | 16.9 | 16.5 | 2.9 | 21.9 | 100 |

Source: AIHW[5].

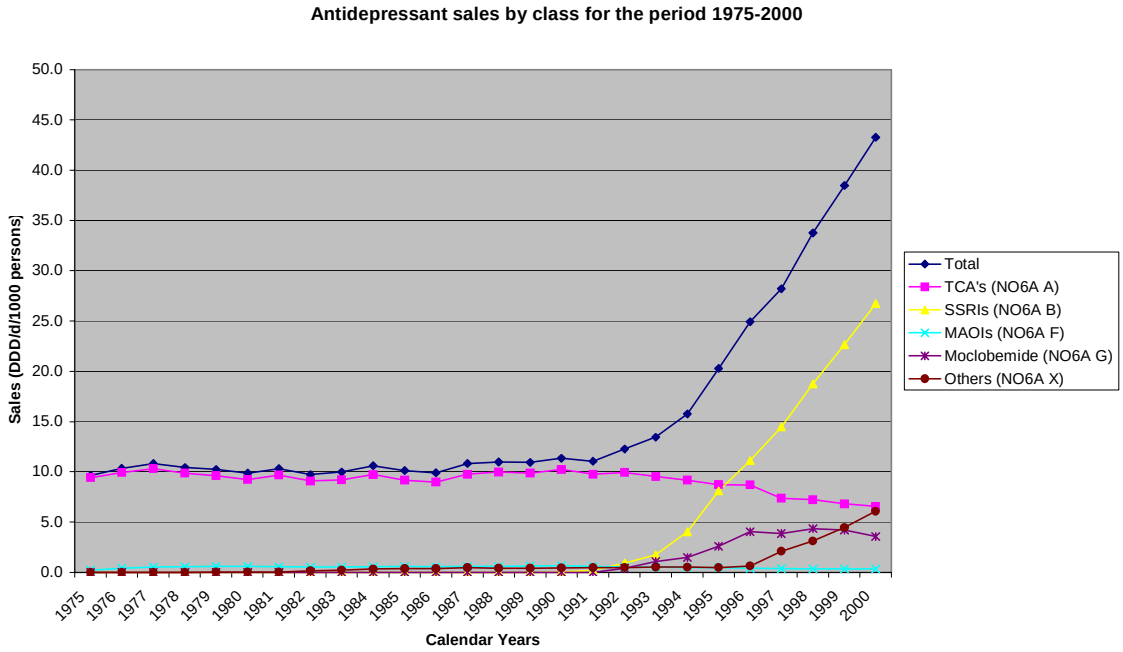
## 2.1 Depression

*Innovative Medicines*
The industry research effort produced a quantum leap in treating mental illness: the first Selective Serotonin Receptor Inhibitor (SSRI) for the treatment of depression with the development of fluoxetine. Fluoxetine, or Prozac by its brand name, changed the treatment of depression, largely due to the fact that SSRIs are better tolerated than the older tricyclic antidepressants and can be given at an effective dose from the start of treatment. This combination of features means that a patient is more likely to achieve a therapeutic response within a reasonable time frame (2 to 6 weeks) and to remain on an effective dose for the time required to achieve remission of the depressive episode (3 to 6 months). As other medications from the same class followed, educational activities undertaken by the industry, especially in general practice, have contributed to the increased awareness, diagnosis and treated prevalence of depression and other affective disorders.

The SSRI antidepressants have been used as a positive example of medical technology development in the recently released Productivity Commission progress report on *Impacts of Medical Technology in Australia* [6]. The Productivity Commission noted that SSRIs are better because they have less side-effects, save money in the hospital system, and provide patients with a better quality of life. They have also been the subject of academic study by experts in the area of drug utilisation and quality use of medicines in Australia. The rapid adoption of the SSRIs and similar medicines is clearly shown in the research done by McManus et al [7],

*Dispensing of antidepressant prescriptions through community pharmacies in Australia increased from an estimated 12.4 DDDs/1000 population per day in 1990 (5.1 million prescriptions) to 35.7 DDDs/1000 population/day in 1998 (8.2 million prescriptions). There has been a rapid market uptake of the selective serotonin reuptake inhibitors (SSRIs), accompanied by a decrease of only 25% in the use of tricyclic antidepressants (TCAs). In 1998, the level of antidepressant use in Australia was similar to that of the United States, while the rate of increase in use between 1993 and 1998 was second only to that of Sweden. In Australia, depression has risen from the tenth most common problem managed in general practice in 1990-91 to the fourth in 1998-99, and the number of people reporting depression in the National Health Surveys (1995 v 1989-90) has almost doubled. Of the prescriptions dispensed in 1998 for antidepressant drugs subsidised by the Pharmaceutical Benefits Scheme, 85% were written by general practitioners, and 11.2% by psychiatrists.*

## Figure 1




Source: IMS Health.

Randomised controlled clinical trials and associated analyses have convincingly demonstrated the clinical advantages and comparative cost effectiveness of SSRIs compared to the older tricyclic antidepressants. Under Australia's PBS scheme and associated PBAC processes, this is a prerequisite for PBS listing.

However, from the perspective of government outlays for health programs in mental health, a more relevant question is whether or not this increased expenditure on antidepressant medication has been accompanied by commensurate gains in health outcomes, such as reduction in symptoms, reduced burden of illness, improved remission rates, decreased relapse rates and less attempted or completed suicides.

These outcomes can be considered separately in terms of evidence, while clearly they are interrelated clinically and in terms of lived experience.

a) Remission rates: The short term goal in treating depression is to reduce the symptoms which are at best debilitating, leading to functional impairment and at worst fatal. Clinical trials of antidepressant medications have for many years utilised symptom rating scales to measure these effects. Reductions in symptoms to a level regarded as "remission" (over a period of 3-6 weeks) is becoming the initial aim, followed by efforts to ensure this is maintained for a longer period during which relapse prevention strategies can be employed, including non-drug interventions such as increased exercise.

b) Relapse rates: There is now strong evidence to support the view that medication should be maintained for a period of at least 6 months following initial improvement. Less than that tends to be associated with increased relapses where the acute symptoms of depression reappear. There is also evidence to suggest repeated relapse has a worse longer term prognosis.

c) Suicide rates: Suicide is clearly the most tragic outcome of depression. Until recently there has been no clear evidence that the increase in awareness, treatment rates and utilisation of antidepressants have actually impacted on suicide rates.

   However, recent studies from Sweden and Hungary have shown a strong association between the introduction and increased use of the SSRIs and a decline in suicide rates. Hall et al [8] undertook a similar analysis using Australian data and demonstrated a trend across the population of decreased suicide rates over the same period of increased prescribing of SSRIs. This association was seen most strongly in older adults, who were more likely to be prescribed an antidepressant. The overall findings led them to conclude:

   "*Thus, even if some antidepressant prescribing is unnecessary or ineffective, increased exposure to these agents through prescribing in general practice may have produced a measurable reduction in the burden of depression in the population".*

A further major consideration when assessing the value for money associated with expenditure on newer antidepressants is the impact on absenteeism and workplace productivity. This significant economic impact occurs via both routes – frank absenteeism as well as reduced productivity when on the job[9].

Several academic studies in the United Stated have looked at the economic impact of depression. Recent papers in the Journal of the American Medical Association report that In that country depression cost US employers approximately US$35 billion a year[10]. This area is the subject of a major research program here in Australia involving academic researchers and major employers.

## 2.2 Schizophrenia

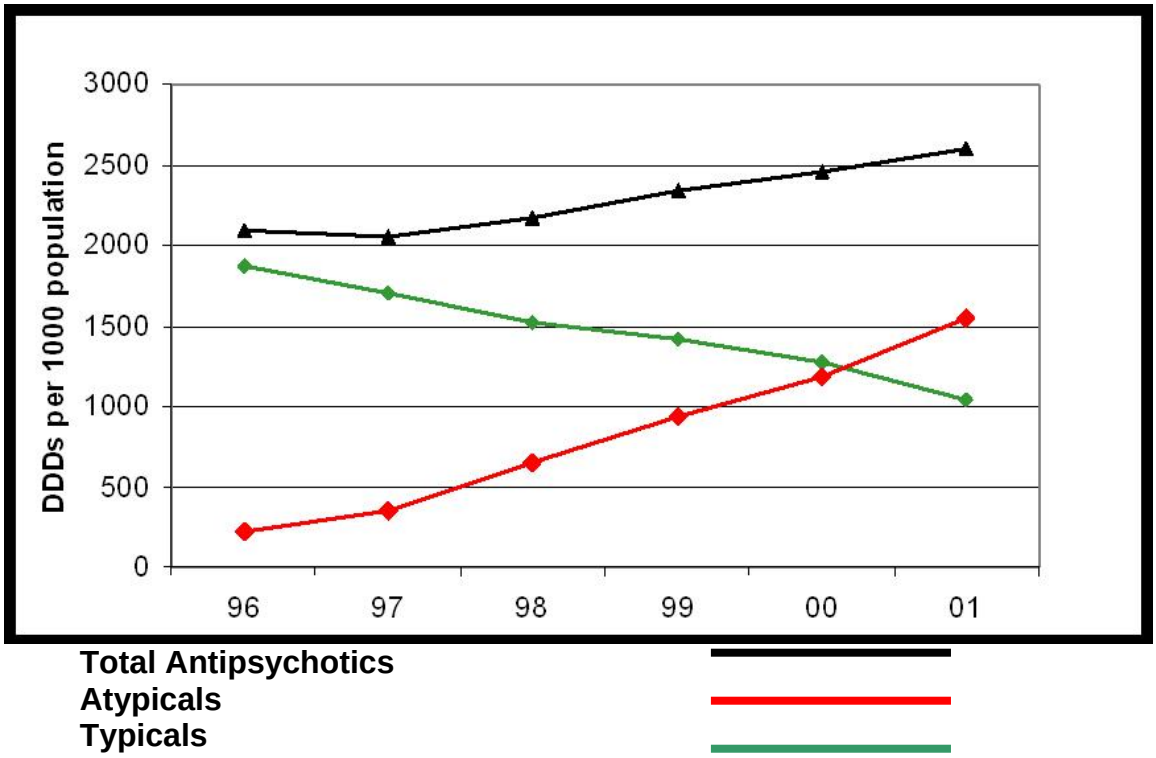
A second major area of contribution to the understanding and amelioration of mental illness has been in the area of antipsychotic medication. There had been little change in the type of medication for psychoses since their discovery in the 1950s, with the mainstay up until the early 1990s being the so-called typical antipsychotic drugs. There are many drugs within this general class, but all to some extent or other have the disadvantage of producing a range of side effects from being unpleasant to being debilitating. These include extrapyramidal symptoms (or EPS), cardiovascular changes, and hormonal changes and on occasions, permanent muscular spasm termed tardive dyskinesia. For patients whose illness causes lack of insight and changed perceptions of reality, anything that detracts from adherence to medication instructions is likely to result in poor compliance and relapse of the disease.

Treatment with antipsychotic medication is an important part of the overall management of schizophrenia. If antipsychotics are not used 60% of patients will relapse within 12 months. With appropriate medication this decreases to 20%[11]. Adherence to medication is a critical factor in maintaining symptom control, and long-

term tolerability is possibly the most important predictor of good adherence to prescribed medications in this patient population.

The introduction of the newer atypical antipsychotics has seen these agents replace to a large extent the older typical agents (Figure 2). This has been driven by patient and clinician dissatisfaction with the efficacy and safety profile of the typical antipsychotics.

**Figure 2: Patterns of use of antipsychotic medications in Australia, 1996-2001[12].**



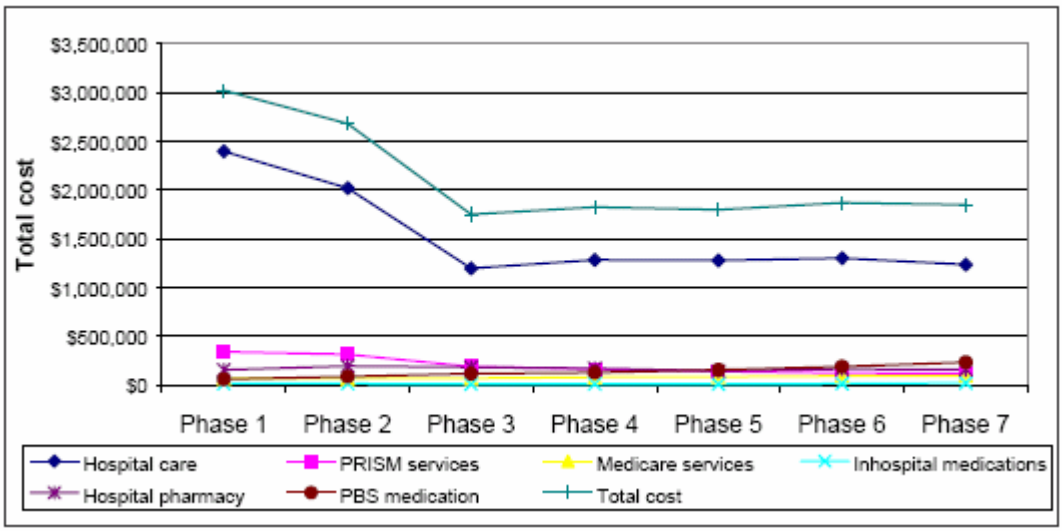

Increased understanding of the complex roles of various neurotransmitters has lead to the development of a number of new antipsychotic medications during the 1990s and into this decade. As a class they have been termed atypical antipsychotics to differentiate them from the older drugs. They differ from older typical drugs both in terms of increased efficacy and reduced adverse side effects. This combination of benefits has been proven to be very beneficial in terms of increased insight, reduced symptoms and increased compliance, all of which contribute to increased engagement in essential psychosocial rehabilitation.

As with many pharmacological interventions, an important question is whether or not the benefits demonstrated in randomised trials are in fact obtained in real world situations. In the case of the newer, atypical antipsychotic medications, these benefits have been demonstrated in a number of large observational (or "real world") studies. While many of these studies have been conducted in the USA, one such study has been completed in Australia, the ***Schizophrenia Care and Assessment Program*** (SCAP)[13]. This is a large, naturalistic study investigating the outcomes of care provided to patients with schizophrenia. The overall objective of SCAP is to

document the costs and outcomes of mental health care for schizophrenia. These data inform the effectiveness and efficiency of such care in Australia.

This intensive research project was the result of collaboration between Australian psychiatric researchers and the pharmaceutical industry. It spanned over three years and provided key information into the outcomes of care for persons with schizophrenia, the use and costs of new technology for care in schizophrenia, and detailed schizophrenia treatment. This research approach is currently being applied in the investigation of bipolar disorder, in a large group of patients in Melbourne and Geelong.

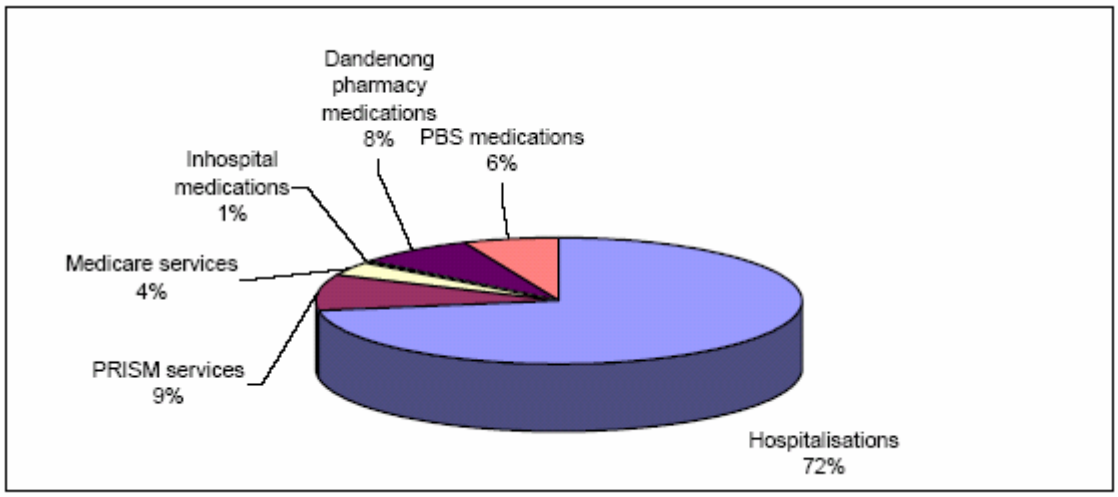
**Figure 3: Total treatment costs of patients with schizophrenia over a 3 year period (Australian SCAP study)**




*PRISM services – refer to hospital based outpatient psychiatric care.*

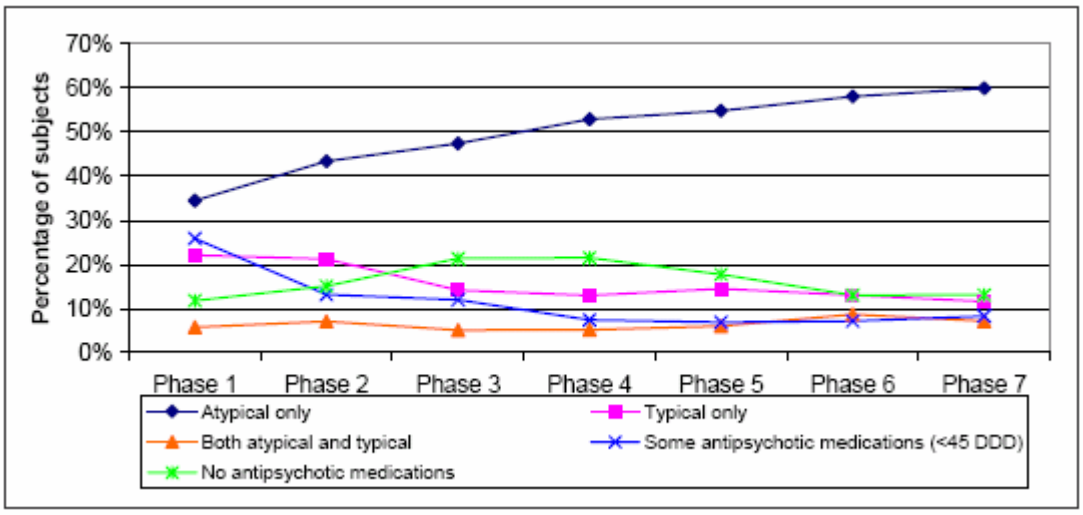
The total cost of health care services and medications used by the SCAP subjects over the study period was $14,787,283 (Figure 3). This corresponds to an approximate annual cost of $15,000 per person. Each phase in the study represents six months of treatment. Twenty percent of the total costs were incurred in phase 1, 18% in phase 2, and approximately 12% in each of the phases 3 to 7. Medical services were by far the most expensive treatment component. They accounted for an average of 85% of the total treatment costs. Overall, medication treatment was consistently much less expensive and accounted for only 15% of the total treatment costs.

**Figure 4: Breakdown of service costs for patients (Australian SCAP study)**




The predominant cost to the health care system for the treatment of people with schizophrenia is admission to hospital (Figure 4). This accounts for 72 % of the total health care costs. During the study period, total treatment costs decreased by over 60%, driven mainly by a substantial reduction in service costs of 51%.

**Figure 5: Proportion of subjects by medication over a 3 year period (Australian SCAP study)**




On the other hand, medication costs nearly doubled over the study period. The fastest increasing costs were those of medications dispensed from community pharmacies which increased nearly five-fold during the study period. The gradual transition of treatment from the older typical antipsychotics to the atypical agents is clearly shown in Figure 5.

Importantly the Australian SCAP study clearly shows that the more atypical antipsychotic agents were used, medication costs increased, however this was offset by an even larger decrease in hospitalisation costs, with the net effect of a decrease in total costs. The larger decreases in hospital costs were largely as a result of fewer and shorter hospital admissions.

## 3. Other areas of mental illness and pharmaceutical industry commitment to Australian neuroscience and psychiatry research:

The pharmaceutical industry's excellence in neuroscience research continues with recent introductions of other medication classes to treat disorders such as depression, bipolar disorder, Attention Deficit Hyperactivity Disorder (ADHD), anxiety and Alzheimer's Disease.

Data from the US pharmaceutical industry indicates that as at November 2004, there are 46 new medicines for mental illnesses in the various phases of research that make up the industry pipeline[14].

In terms of overall health and medical research, mental disorders are under funded in Australia. Only 3% of total health expenditure is related to research. The research-based pharmaceutical industry in Australia can and does provide significant support for basic and applied research into mental illness in a range of ways, such as supporting:

- Clinical trials of new medicines
- basic laboratory research e.g. the Neurosciences Victoria research collaboration includes significant industry funding.
- academic research groups engaged in a variety of research from basic to clinical, imaging, health outcomes and economics and psychosocial e.g. the Lilly Melbourne Academic Psychiatry collaboration with the University of Melbourne
- unconditional grants from various companies to assist the work of major mental health research groups such as the Black Dog Institute (University of NSW), the Brain and Mind Institute (University of Sydney) and the Mental Health Research Institute (Melbourne).
- the world-leading ORYGEN Youth Mental Health Research Centre in Melbourne
- Australian researchers via several grants and awards programs. This includes basic science research, investigator-initiated clinical trials, health outcomes research and psychosocial rehabilitation research.

It is also noted that in the past 12 months there has been a consultation through a task force on the potential in Australia for some form of national neuroscience research collaboration. The Minister for Health and Ageing established this task force as a result of recommendations from the Prime Minister's Science, Engineering and Innovation Committee. However, the task force findings and recommendations have not yet been released.

## 4. Quality Use of Medicines and non-pharmacological interventions

The concept of Quality of Medicines is a key element of Australia's National Medicines Policy. The concept includes recognition that:

- when diagnosing any illness, a medicine is not necessarily the most appropriate intervention
- once a decision is made to prescribe a medicine, the most appropriate one should be selected on the basis of the patient's condition and the risk / benefit of each option
- once an option is selected it should be prescribed in the right dose for the appropriate length of time

While the above concepts apply to any prescribing situation they are especially relevant to the treatment of mental illness. In many instances, the presenting condition may respond well to non-pharmacological interventions, for example mild depression. In this instance psychological treatments such as Cognitive Behavioural Therapy should be available and may be the first line treatment. However, for more severe disorders (both depression and psychotic disorders) the need is for effective intervention to bring about symptom relief as soon as possible. Very often overall improvement (ideally to the point of recovery) will require concomitant psychosocial support and intervention.

With regard to serious mental illness (psychosis and bipolar disorder) there is another important example of the need for a QUM approach. There is increasing recognition of the need to attend to physical health of consumers with these conditions at the same time as managing their mental health. There has been considerable effort applied to highlighting the physical health issues (smoking, weight gain, increased risk of diabetes) and collaborations between industry and health professionals are assisting this.

When considering outlays associated with PBS expenditure on antidepressants and antipsychotics, it is important to remember that general practitioners require appropriate training and support if they are to be effective in their management of mental illness. The current Commonwealth Government program "Better Outcomes in Mental Health Initiative" is to be commended for its comprehensive approach to up-skilling GPs, providing incentives for increased consultations and referrals to relevant allied health professionals such as psychologists, as well as assisting linkages with specialist psychiatric advice and consultation. Increasingly, industry educational programs are being aligned with such initiatives to ensure the optimal gains are made from increased expenditure on pharmaceutical interventions.

## 5. Role of new web-based technologies

People with depression may benefit from support in the form of reassurance that their illness is neither unusual nor incurable. Support in the early stages following awareness of a problem and/or diagnosis may be critical in ensuring that the individual seeks appropriate professional help. Once treatment is initiated (whether pharmacological or non-pharmacological) encouragement to continue to the necessary length of time may also be critical. While there a number of ways individuals can access such support, the role of the Internet and web-based services is increasing. Organisations such as Depression Net and beyondblue provide essential web based support and access to additional information and services. These services deserve adequate funding to enable continuity of delivery plus further

development of additional services in new formats and via new networks (e.g. Depression Net is exploring the provision of such consumer support services to the work place).

Within Australia there are also experiments ongoing in web-based consumer tools and data collection. Projects in this area are exploring the use of the Internet to enable consumers undergoing treatment to complete measurement tools and questionnaires, record their improvements and adverse experiences, or to engage in web-based interaction with the treatment team.

In all of the above cases the pharmaceutical industry is a potential partner to support pilot funding and programs. Provided care is taken to avoid any suggestion of direct to consumer promotion or influence, industry support is a legitimate option for innovation in patient care and research.

## 6. Conclusions and recommendations:

a) *Burden of mental illness:*
All available data support the view that mental disorders represent a significant burden in Australia. Resources need to be made available across the spectrum of health care expenditure in order to combat this problem.

b) *Value of expenditure on pharmacological interventions:*
While expenditure has increased significantly on pharmacological interventions there is good evidence these are effective and cost-effective. Such expenditure should not be viewed in isolation. Rather, increased collaboration between stakeholders should focus on Quality Use of Medicines and on aligned educational efforts to optimise return on this investment. Additional efforts to research and quantify the impacts of mental disorders on productivity should be supported.

c) *Importance of sustaining and increasing Commonwealth funding of other non drug areas:*
Programs such as the Better Outcomes in Mental Health initiative are critical if treatment is to be accessed in a holistic and optimal fashion. For example, GPs must be equipped to decide when non-drug interventions are the first choice (such as Cognitive Behavioural Therapy) and to access such interventions when needed. Ongoing support for consumer and carer organisations and networks are also critical for grass roots support of patients, as these are often preferred by consumers as the means of accessing additional services.

d) *Industry role in psych and neuroscience research:*
This is considerable and should be fostered. Opportunities exist for increased collaboration among research stakeholders and governments need to recognise the important and catalytic role that can be played by industry.

e) *Future opportunities:*
Additional progress can be made in innovative areas, such as web based

patient support and web based consumer and health care professional interaction. Additional gains can be made also in the area of workplace awareness and support for depression as well as increased efforts to support vocational reintegration for those recovering from serious mental illness.

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