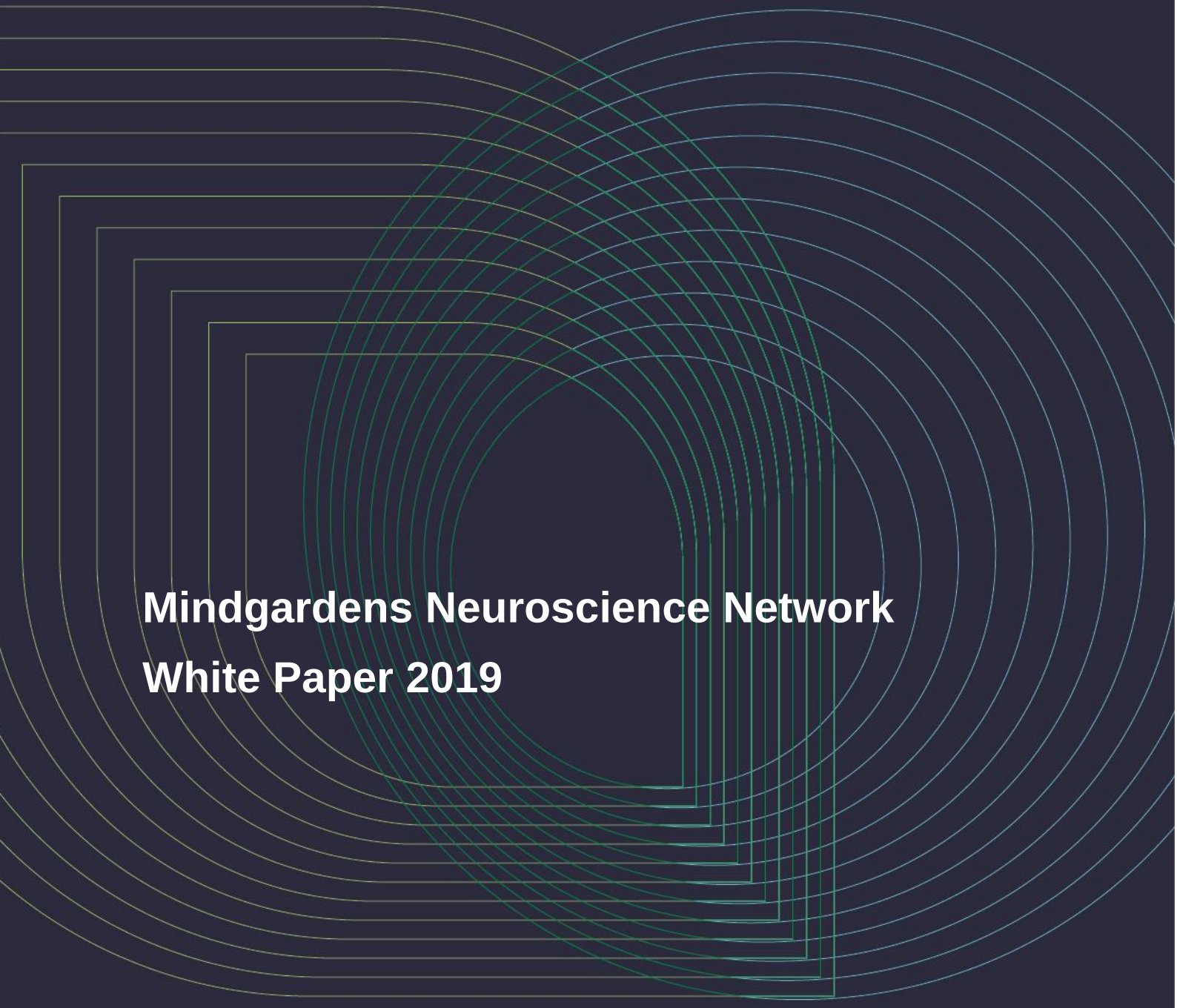
mindgardens
Neuroscience Network

Sydney | Australia

# Review of the burden of disease for neurological, mental health and substance use disorders in Australia



**Mindgardens Neuroscience Network**

**White Paper 2019**

*“Neurological, mental health and substance use disorders currently account for over 20% of the burden of disease in Australia. In the future these brain disorders will have a greater cost to the Australian economy than heart disease, cancer, and respiratory disease combined. Mindgardens Neuroscience Network commissioned KPMG to review this data and our White Paper shows the burden of disease cost in 2017 was in excess of $74 billion. We need to build new models of care to reduce this burden of disease for all Australians.*

*Let’s start this conversation today, not tomorrow.”*

Mindgardens Neuroscience Network (2019) Review of the burden of disease for neurological, mental health and substance use disorders Australia. www.mindgardens.org.au/news/whitepaper/

Released on the 14th March 2019 Sydney, Australia.



Website address for further details. www.mindgardens.org.au

‘*Mindgardens Neuroscience Network would like to acknowledge KPMG for assisting with the research into this Report*’.

# INTRODUCTION

## The economic burden associated with brain disorders in Australia topped $74 billion in 2017

With the formation of the Mindgardens Neuroscience Network in 2018, our founding partners sought to determine the current burden of disease in Australia and the associated costs that arise from the spectrum of brain disorders – neurological, mental health and substance use disorders. We also sought to determine a number of potential actions that could lead to better understanding, treatment, cure and prevention of these major disorders.

We commissioned KPMG to prepare this white paper to review the data and provide us with a clear picture of the size and scale of brain disorders in Australia. The white paper reveals the tremendous scale of burden associated with neurological, mental health and substance use disorders in Australia, the vast negative impact they have on patients, families, communities and the enormous health and productivity costs.

The burden of neurological, mental health and substance use disorders represented over 20 per cent of the total Australian burden of disease. Globally this figure is only 11 per cent. That our burden of brain disorders is almost double that of the global figures is especially concerning.

The costs are staggering. Mental health disorders and suicide cost the nation over $33.6 billion each year. Neurological disorders cost over $30.5 billion and substance use disorders almost $10 billion. Combined, this cost of over $74 billion per annum, will shortly mean that the brain disorders will have a greater cost to the Australian economy than heart disease, cancer, and respiratory disease combined.

Our white paper has clearly identified the enormity of the issue – but working together with state and federal governments, we have developed innovative and technological solutions to deliver new models of care that can be scaled and rolled out across Australia.

Mindgardens is based in Sydney, Australia. Our aim is to be an international leading precinct for innovative research and compassionate healthcare for all brain disorders. Our approach will help afford all Australians the best quality of life possible.

Prof Peter Schofield AO
Interim Joint CEO

Prof Helen Christensen AO
Interim Joint CEO

# Key points

- This new white paper illustrates the magnitude of burden associated with the neurological, mental health and substance use disorders in Australia and the vast negative impact they have on patients, families, the community, health costs and lost national productivity.

- Globally, the burden of neurological, mental health and substance abuse disorders account for 11.1 per cent of the total burden of disease, approximately half the Australian share which sits at 20.5 per cent over the overall disease burden (Figure 2.2), highlighting the relatively high burden of these disorders within Australia.

- In 2017, the burden of neurological, mental health and substance use disorders was nearly 1.2 million DALYs[1] or 20.5 per cent of Australia's total burden of disease (Figure 2.1). Compared to 2010, this figure has increased by 13.5 per cent from 1.04 million DALYs. These results reinforce the findings from earlier key studies highlighting the substantial contribution from neurological, mental health and substance disorders to the total burden of disease.

- The Australian cost of burden of disease has increased by 13.5 per cent since 2010.

- In 2017, mental health disorders accounted for the highest burden of disease (46%), followed by neurological disorders (37%) and substance disorders (16%).

- Substance use disorders have the highest growth rate between 2010 and 2017 (24.7%), followed by neurological disorders (15.6%) and mental disorders (8.6%).

- The burden by disorders is disproportionality spread across age groups. For mental health and substance abuse disorders, the burden peaks early in life (before the age of 30), is maintained through middle age before tapering in later years, contrastingly neurological disorders predominantly impact on later senior life.

Mindgardens is focused on research-led and clinically tested solutions driven by patient and community involvement. Our white paper has clearly identified the enormity of the issue – but by working together with state and federal governments, Mindgardens is developing innovative and technological solutions where new models of care can be scaled and rolled out across Australia.

[1] The World Health Organization (WHO) defines Disability-Adjusted Life Year (DALY) as lost year of "healthy life". DALYs for a disease are calculated as the sum of the Years of Life Lost (YLL) due to premature mortality and Years Lost to Disability (YLD). The sum of these components across the population represents the gap between current health status and an ideal health situation.

# Questions and Answers

### What is the Mindgardens Neuroscience Network?

A collaborative alliance of four clinical, research and education partners including, The Black Dog Institute, Neuroscience Research Australia, South Eastern Sydney Local Health District and UNSW Sydney that brings together the largest group of scientists and researchers in the southern hemisphere to create the Australian Comprehensive Brain Disorders Centre.

### What will Mindgardens do?

The vision of Mindgardens is to link outstanding patient care with world-class research and clinical trials to create new models of care that will change the way we approach, diagnose, treat, monitor, and integrate services into the community to afford all Australians the best life possible.

### Why is Mindgardens important to all Australians?

Mental health, neurological and substance use disorders currently account for over 20% of the burden of disease in Australia. Our burden of brain disorders is almost double that of the global figures which is extremely concerning and calls for immediate action.

### What is the Mindgardens model of care?

The Mindgardens model is built around an "integrated system of care" to address physical, mental health, drug and alcohol and neurological disorders concurrently. Linkage to community care hubs provides critical time sensitive patient information, to model individual support and therapeutic adjustments that deliver a complete 360-degree picture of the patient, needs and progress.

### What effective health interventions were identified in the white paper?

The white paper identified examples where high-quality evidence is available to support improved health care interventions that provide a positive return on investment (ROI). Mindgardens will implement these interventions in pilot programs to evaluate their impact in real-world clinical settings. Examples include:

- exercise therapy for neurological disorders which has an ROI of 3.9
- internet-based cognitive behavioural therapy (iCBT) which has an ROI of 2.1 for mental illness.

The positive ROIs from these interventions suggest that, in the long-term, cost savings from the investment will make a comprehensive difference to prevalence and burden of disease.

### Why Sydney, Australia? – the statistics add up.

The Southern and Eastern areas of Sydney have some of the highest rates of suicide in the country. The national suicide rate is 12.6 per hundred thousand. In Randwick, the standardised rate was 20.3 in 2016. Within this local health district area, South Sydney has a rate of 18.6 and Waverley a rate of 25.4, more than twice that of Australia.

### What are the aims of Mindgardens?

Mindgardens aims to become the Silicon Valley of brain disorder research, using innovation and technological solutions to develop new models of care that can be developed and tested and then rolled out into trials using best practice hubs across Australia.

# List of acronyms

| Acronym | Description |
|---|---|
| **ABS** | Australian Bureau of Statistics |
| **AD** | Alzheimer's Disease |
| **AIHW** | Australian Institute of Health and Welfare |
| **BI** | Brief Intervention |
| **CBA** | Cost Benefit Analysis |
| **CBT** | Cognitive Behavioural Therapy |
| **CR** | Cognitive Remediation |
| **DALYs** | Disability Adjusted Life Years |
| **DBS** | Deep Brain Stimulation |
| **DBT** | Dialectical Behaviour Therapy |
| **DSM-IV-TR** | Diagnostic and Statistical manual of Mental Disorders (4th Edition Text Revision) |
| **ED** | Emergency Department |
| **GBD** | Global Burden of Disease |
| **GHDx** | Global Health Data Exchange |
| **iCBT** | Internet-based Cognitive Behavioural Therapy |
| **ICD** | International Classification of Disease |
| **IHME** | Institute for Health Metrics and Evaluation |
| **MMT** | Methadone Maintenance Therapy |
| **NHMC** | National Mental Health Commission |
| **NHMRC** | National Health and Medical Research Council |
| **NRT** | Nicotine Replacement Therapy |
| **OECD** | Organisation for Economic Co-operation and Development |
| **PPP** | Purchasing Power Parity |
| **RCTs** | Randomised Controlled Trials |
| **ROI** | Return on Investment |
| **SBI** | Screening and Brief Intervention |
| **QALYs** | Quality Adjusted Life Years |
| **TAU** | Treatment As Usual |
| **TBI** | Traumatic Brain Injury |
| **TI** | Thrombolytic Interventions |
| **tPA** | Tissue-type Plasminogen Activator |
| **YLD** | Years Lost due to Disability |
| **YLL** | Years of Life Lost |

# Contents

# Executive Summary

## ES.1. Overview

A substantial proportion of the world's health problems in both high-income countries and low-to middle-income countries arises from neurological, mental health, and substance use disorders (Murray et al. 2012). Collectively, these disorders represent some of society's most complex, high impact health challenges. Mindgardens is committed to transforming the understanding, treatment, cure and prevention of neurological, mental health and substance use disorders. Mindgardens engaged KPMG to review the burden of disease in Australia and analyse the evidence base of a selected number of interventions; with the aim being to describe the potential impact that organisations such as Mindgardens could have, and complete return on investment (ROI) modelling on six of the interventions. The paper further illustrates the unique agenda Mindgardens is driving, through forming holistic and differential approaches to research, informing clinical practice and involving individuals with lived experiences in driving the research agenda.

## ES.2. Burden of disease and burden cost

In 2017, mental health, neurological and substance use disorders accounted for 20.5 per cent of total Australian daily adjusted life years (DALYs), making them the leading cause of disability (Whiteford et al. 2015). Within the group, mental health disorders accounted for the highest burden of disease (46%), followed by neurological disorders (37%) and substance disorders (16%). Understanding the contribution neurological, mental health and substance use disorders make to Australia's total burden of disease involved the analysis of statistical and academic literature, with the data synthesised to highlight prevalence rates, age group clusters, mortality rates and total burden cost. Evidence suggests that neurological, mental health and substance use disorders rarely exist in isolation (Hesdorffer 2016). Cross sectional studies highlighted comorbidities increase disease burden costs and effect the course an illness takes, and the use of services an individual will require. (Hesdorffer 2016). Evidence illustrates that allowing consumers to inform research discussions can have long term implications on the succession of interventions and decrease burden cost (SLHD 2017). The unique perspective of consumers highlights and moderates' inefficiencies of care. The paper illustrates the magnitude of burden associated with neurological, mental health and substance use disorders in Australia and the vast negative impact they have on patients, families, the community, health costs and lost national productivity.

## ES.3. Intervention and ROI

Slow progress, lack of commitment to funding for investigations into new treatments and poor translation of research outcomes has substantially contributed to the burden of disease and its continual growth. Flow on effects to patients, families, the community, health costs and losses in national productivity highlight major challenges requiring immediate action. The complexity of issues associated with the disorders as mentioned, calls for effective solutions and coordinated strategies to redesign integrated models of care. We analysed 17 interventions and found that 10 had strong, high-quality evidence supporting their effectiveness. The remaining interventions although not qualified as strong demonstrate efficacy any warrant future research. Research illustrated that a focus on the treatment lifecycle i.e. prevention, early intervention and treatment itself is vital to reducing overall burden. Return on investment (ROI) modelling, an economic method to measure how much benefits are derived from a program in relation to its costs, was completed for six interventions where those aligned with Mindgardens research priorities. The modelling has resulted in a range of ROIs. For neurological disorders, the intervention of exercise therapy has an ROI of 3.9, while mental health intervention of iCBT has an ROI of 2.1. For drug and alcohol disorders, programs such as brief intervention resulted in an ROI between 0.7 – 0.8 depending of risk status of participants. The positive ROIs from these interventions suggest that, in the long-term, cost savings from the investment will make a comprehensive difference to prevalence and burden of disease.

# Recommendations

1. This paper highlights the significant burden neurological, mental health and substance use disorders have and will continue to have on the Australian population. Research and return on investment evidence illustrates that action to reduce this burden can be taken both immediately and in the future.
2. The largest burden of disease is exhibited by opioid use disorders, major depressive and anxiety disorders, stroke and Alzheimer's/dementia disorders. Relative to cancer and cardiovascular disease, these disorders do not receive overall research investment commensurate with the burden they impose on the community. The national research agenda should align to better incorporate and prioritise these disorders, and build the specific research capability to address them into the future.
3. Investigation into the potential return on investment for already validated health interventions indicates a number which, if adopted, would cost-effectively improve health outcomes. These include online mental health programs which are highly effective in treating depression and anxiety. However, the infrastructure to put these treatments into action is weak. Established e-mental health infrastructure and shared industry/health models could then be used to expand these cost effective health interventions to treat and prevent neurodegenerative and substance use disorders.
4. Comorbidity in individuals suffering from neurological, mental health or substance use disorders is high. Establishing Apex clinics that examine, simultaneously, the whole health of the person - from physical health, neurological, mental health and substance use - will encourage and support collaborative care approaches to ensure quality health care outcomes. The approach to care should aim to treat complexity while decreasing the cost of traditionally 'siloed' service provision, thereby providing a better experience for patients.
5. Consumers are critical to improving health care and its research. They have priorities that can direct topics for research; they see what can be improved; they are appreciative of good clinical care; they detect inefficiencies, and they champion the importance of science and medical research. Clinical research that is led and informed by consumer perspectives will be better, more collaborative, better supported and lead to faster breakthroughs.
6. The findings from this review, combined with other recent reports (e.g. *Investing to Save*[2]*)* highlight how the national research agenda should be providing an evidence base from which new and improved interventions can be adopted. Workplace interventions, assertive support after a suicide attempt, and dementia support services, result in both economic returns on investment and positive health and wellbeing outcomes for individuals.

To summarise, urgent attention to neurological, mental health and substance use disorders conditions is needed. Our report, along with others, provides clear evidence of positive Return on Investment for current treatments, both in hospitals and in the community. Comorbidity is common, therefore healthcare is required that incorporates intensive and collaborative assessment and treatment, through Apex clinics, community centres of clinical excellence, and technology-based outreach.

[2] Mental Health Australia, and KPMG. 2018, 'Investing to Save'. Retrieved from https://mhaustralia.org/sites/default/files/docs/investing_to_save_may_2018_-_kpmg_mental_health_australia.pdf

# 1. Introduction and purpose

## 1.1. Background

Neurological, mental health and substance use disorders represent some of society's most complex, high impact health challenges and together represent the highest global burden of disease. In 2010, mental health, neurological and substance use disorders accounted for 10.4 per cent of global Disability Adjusted Life Year (DALYs), 2.3 per cent of global Years of Life Lost (YLLs) and, 28.5 per cent of global Years Lost Due to Disability (YLDs), making them the leading cause of disability (Whiteford et al. 2015). Experiencing a disorder is associated with substantial disability for the affected individual. Inability to carry out daily activities of life results in multifaceted strain on both the individual and the wider community. The economic burden associated with these disorders is also high and represented by costs linked with loss of productivity, decreased participation in the workforce, increased need for provision of treatment and support services and premature death and disability.

Understanding the burden, impact and cost of neurological, mental health and substance use disorders, as well as funding dedicated to research, is vital in advocating for policy change. Investing in evidence-based preventative programs and interventions would reduce personal, and economic burden, and potentially prevent symptom manifestation (Moodie, Tolhurt, and Martin 2016). The sheer burden and prevalence of neurological, mental health and substance use disorders in Australia illustrates the need for immediate funding allocation to research centres that will not only support individuals living with these conditions, but will also cater for the future needs of the Australian community.

Mindgardens represents innovation and leadership, cultivating clinical excellence, research and education in neurological, mental health and substance use disorders. Mindgardens draws upon the expertise of some of Australia's best researchers, clinicians and educators, from its member organisations; the Black Dog Institute, Neuroscience Research Australia, South Eastern Sydney Local Health District and University of New South Wales (UNSW), Sydney.

Recently formed, Mindgardens will provide national and international leadership, reimagining the way research, clinical services and training collaborate, in order to improve patient and community outcomes across a range of neurological, mental health and substance use disorders. Mindgardens facilitates collaborative engagement of its members to identify and leverage new and additional resources to achieve its goals and thus positively impact patients and consumers, clinicians and researchers and the broader community.

This paper discusses in an Australian context, neurological, mental health and substance use disorders in alignment with one another. The Australian data set produced in this study is one of the first of its kind. The paper illustrates the unique agenda Mindgardens is driving, forming holistic and differential approaches to research, informing clinical practice and involving individuals with lived experience in driving the research agenda.

## 1.2. Methodology

The development of the paper involved a number of steps to draw a comprehensive picture of the burden of neurological, mental health and substance use disorders, and the potential of interventions to help alleviate the burden. First, an initial literature and desktop scan was undertaken followed by data collection to provide the high-level overview of the prevalence, costs and burden of the disorders. This was followed by a review of the evidence base of the interventions designed to treat and prevent the disorders. Finally, economic modelling was undertaken for a subset of interventions, to highlight not only the health but also the economic returns from investment in improving mind health.

**Literature scan and data collection: burden of disease**

A literature scan was completed to review the prevalence, burden and cost of neurological, mental, and substance use disorders.

To align with the International Classification of Disease (ICD) and classifications provided in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR), the three disorders were further disaggregated into 21 sub-diseases (Table 2.1).

The primary data source for burden of disease data was the Global Health Data Exchange (GHDx) within the Institute for Health Metrics and Evaluation (IHME) at the University of Washington. Other key sources included the Australian Bureau of Statistics (ABS), the Australian Institute of Health and Welfare (AIHW), the National Mental Health Commission (NMHC), and research reports into individual diseases. A detailed dataset was assembled in conjunction with the literature, comprising disease classifications, prevalence, mortality, burden and cost. The information includes age group classification to analyse the onset of the disease.

The cost burden was derived by using a typical threshold valuation for each Quality Adjusted Life Year (QALY) of $50,000[3], reflecting the willingness to pay for achieving the health improvement within the healthcare system.

**Literature scan: evidence base for interventions**

A high level literature scan was also completed to review the evidence base for interventions to assist in the treatment and prevention of neurological, mental, and substance use disorders. Research questions were designed and search terms identified. The evidence was appraised by identifying its nature e.g. systematic review, meta-analysis, etc., sample size and level of validation i.e. peer review status. Low level assignment was allocated if evidence was located but the quality was low, i.e. the evidence base is still developing. Medium level assignment was allocated if strong quality evidence was located but provided mixed results, i.e. further research is required to establish consistency of results. High level assignment was allocated if numerous systematic reviews had been identified and illustrated a high-quality evidence base for the intervention. Analysis of literature was conducted to evaluate each interventions effectiveness and efficacy and inform ROI modelling. Refer to appendix B for complete methodology approach.

**Return on investment modelling**

Return on investment (ROI) modelling was then completed for six of the interventions where the evidence base was strong (or emerging) and the potential to impact the burden of disease was high.

Costs and benefits for each intervention were sourced from the literature. Benefits were confined to health service utilisation savings and productivity improvements where the evidence base was strong (meta-analyses, systematic reviews or RCTs). Costs and benefits were drawn from international studies, conversion to Australian dollars was completed using Purchasing Power Parity data from the OECD (OECD and Eurostat 2012),and inflated to 2017 dollars using the ABS CPI data (ABS cat. no. 6401).

[3] No exact threshold is used in Australia, however revealed studies tend to find figures between $40,000AUD and $80,000AUD/QALY e.g. Shiroiwa, T., Sung, Y.K., Fukuda, T., Lang, H.C., Bae, S.C. and Tsutani, K., 2010. International survey on willingness-to-pay (WTP) for one additional QALY gained: what is the threshold of cost effectiveness?' *Health economics*, 19(4), pp.422-437, and Schilling, C., Mortimer, D. and Dalziel, K., 2017. Using CART to identify thresholds and hierarchies in the determinants of funding decisions. *Medical Decision Making*, 37(2), pp.173-182.

## 1.3. Prevalence

Total prevalence for neurological disorders in 2017 accounted for 10.6 million people or 43 per cent of Australian population, followed by mental health disorders of 4 million people (16.3 %) and substance disorders of 0.8 million people (3.2%)[4].

The most common causes of neurological disorders are migraine and tension-type headache, which affected 4.5 and 7.9 million people respectively (50.4%). Alzheimer's disease and other dementias have the next largest prevalence of nearly 250,000 people. Less common causes include epilepsy, Parkinson's disease and multiple sclerosis. Stroke, which can be classified as neurological disorders and cardiovascular disease, affected closely to 300,000 people.

Major depressive disorders, dysthymia or persistent depressive disorders and anxiety disorders remain the most prevalent conditions for mental health disorders, affecting 10.4 per cent of the population or around 2.5 million people. Other major causes include schizophrenia, bipolar disorders, attention-deficit/hyperactive disorders and eating disorders. Adding to this, a total of 3,128 suicide related deaths were registered in 2017 where 75.1 per cent were males.

Substance use disorders, a sub-condition of drug use, which includes opioid, cannabis, cocaine and amphetamine disorders, affecting 1.9 per cent of the population or around 450,000 people. Alcohol use disorders affected 1.4 per cent of the population or around 337,000 people. Adults aged 18 years and over who smoked daily was 2.8 million people in 2016, approximately 11.5 per cent of the population.

## 1.4. Burden of disease

**Overall burden**

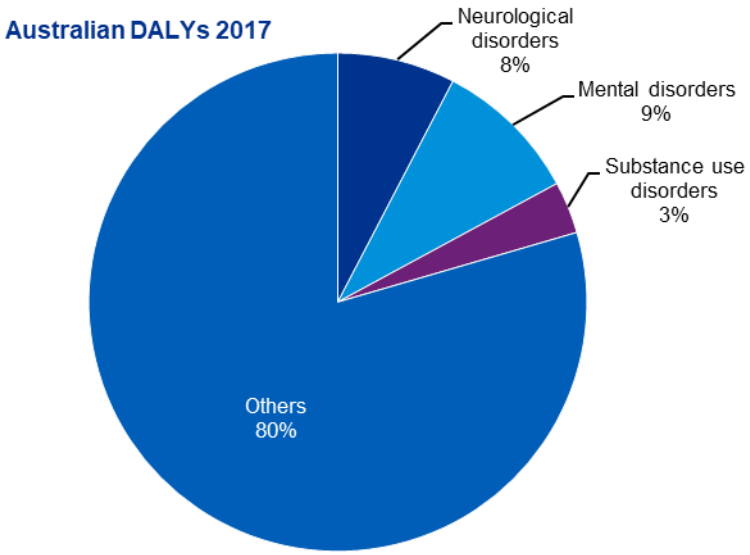
In 2017, the burden of neurological, mental health and substance use disorders was nearly 1.2 million DALYs[5] or 20.5 per cent of Australia's total burden of disease (Figure 2.1). Compared to 2010, this figure has increased by 13.5 per cent from 1.04 million DALYs. These results reinforce the findings from earlier key studies (GBD 2015; Whiteford et al 2015; GBD 2010) highlighting the substantial contribution from neurological, mental health and substance disorders to the total burden of disease.

Globally, the burden of neurological, mental health and substance abuse disorders account for 11.1 per cent of the total burden of disease, approximately half the Australian share (Figure 2.2), highlighting the relatively high burden of these disorders within Australia.

[4] The prevalence numbers for each disorder from Global Health Data Index (IHME) are subject to comorbidity from sub-diseases.

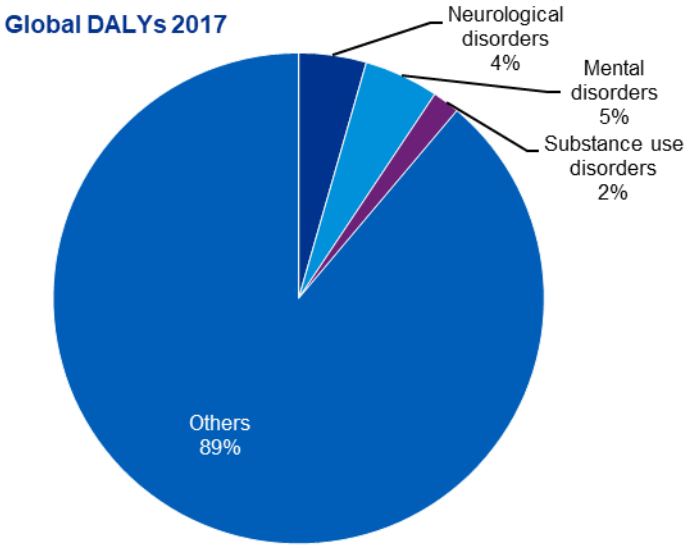
[5] The World Health Organization (WHO) defines Disability-Adjusted Life Year (DALY) as lost year of "healthy life". DALYs for a disease are calculated as the sum of the Years of Life Lost (YLL) due to premature mortality and Years Lost to Disability (YLD). The sum of these components across the population represents the gap between current health status and an ideal health situation.

**Figure 1.1. Proportion of Australian burden of disease from neurological, mental health and substance use disorders in 2017.**




Source: IHME (2018)

**Figure 1.2. Proportion of Global burden of disease from neurological, mental health and substance use disorders 2017.**




Source: IHME (2018)

**Burden by disorder**

Mental health disorders accounted for the highest burden of disease (46%), followed by neurological disorders (37%) and substance disorders (16%). While mental health disorders have the largest burden of disease, substance disorders has the highest growth rate between 2010 and 2017 at 24.7 per cent, followed by neurological disorders (15.6%) and mental disorders (8.6%).

The burden of disease from suicide in 2017 was estimated to be 118,086 DALYs. The AIHW (2016) suggests that 36 per cent of the burden of respiratory diseases, 22 per cent of lung cancer, 12 per cent of cardiovascular diseases and 3.5 per cent endocrine diseases are attributable to tobacco use. In 2016, this summed to 92,026 DALYs.

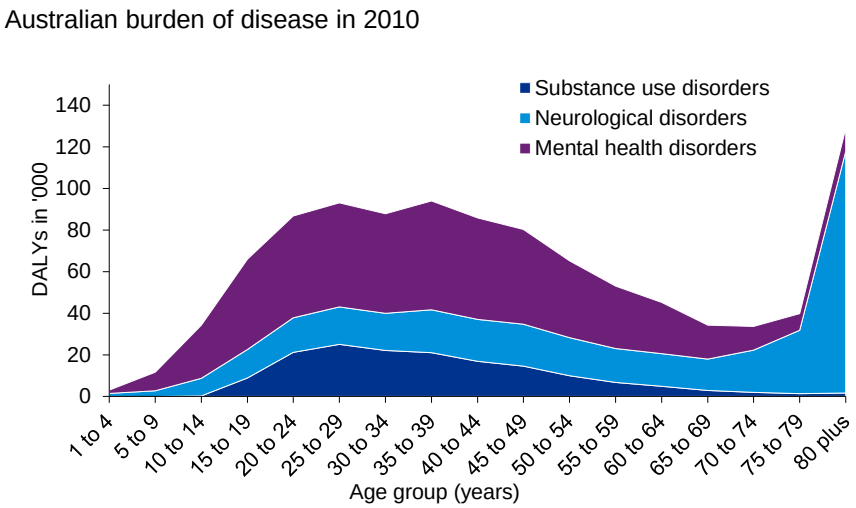
**Burden by age group**

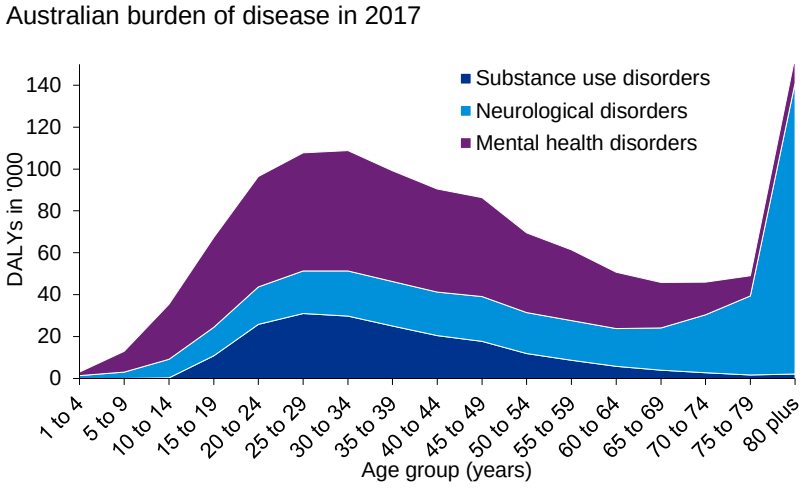
The burden of disorders is disproportionately spread across age groups. For mental health and substance abuse disorders, the burden peaks early in life (before the age of 30), is maintained through middle age before tapering in later years; contrastingly neurological disorders predominantly impact on later-life.

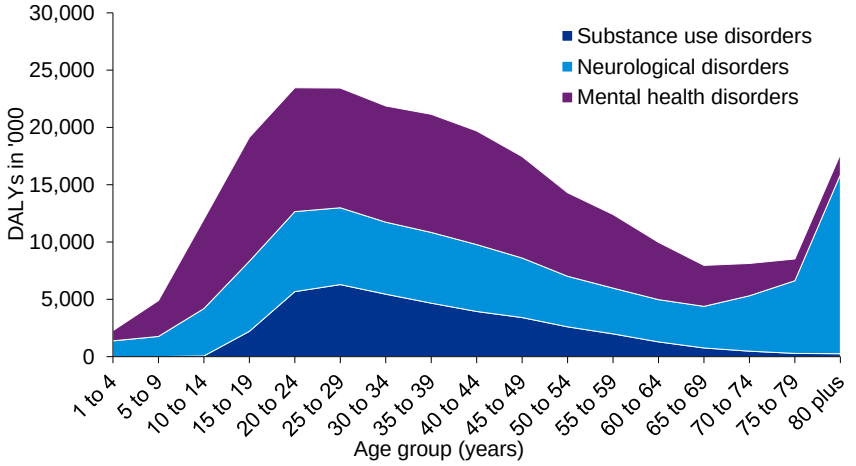
In Australia for the 15-24 year age group, neurological and mental health disorders grew by 3.5 per cent and 3.6 per cent respectively from 2010 to 2017, substance abuse disorders increased by 22.4 per cent. These figures contrast with the global results, where substance disorders and mental disorders have been decreasing at 1.7 per cent and 0.7 per cent respectively. For neurological disorders including conditions such as Alzheimer's and Parkinson's disease, the burden has continued to increase for those aged above 70 years, with a 22 per cent increase from 2010 to 2017. Combined, these statistics highlight the growing concern of these disorders within the Australian population.

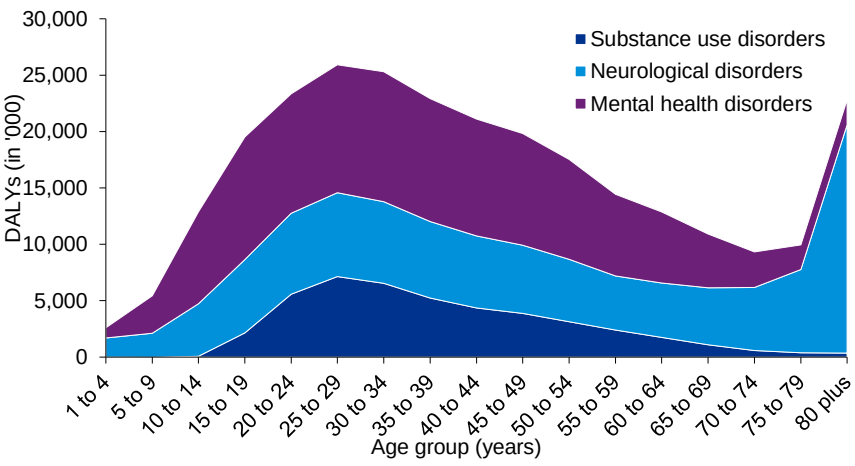
Figure 1.3 and Figure 1.4 summarise the trend of Australia and Global burden of disease in 2010 and in 2017.

**Figure 1.3. Australian and Global burden of disease by age group (in years)**



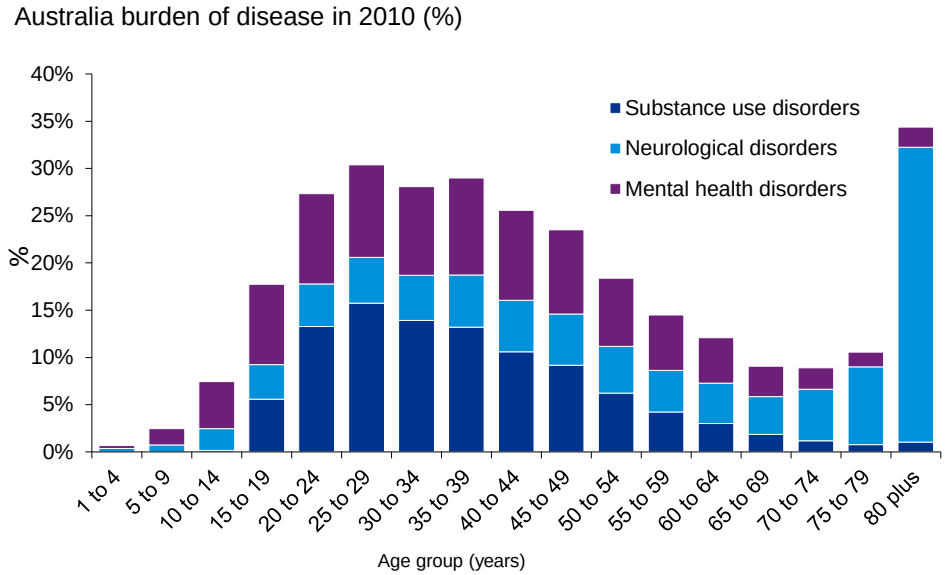



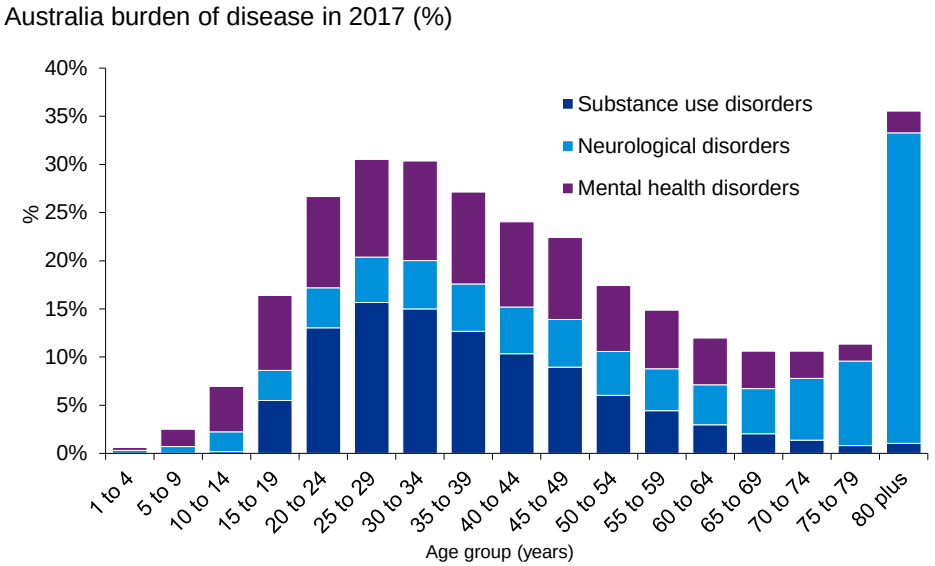



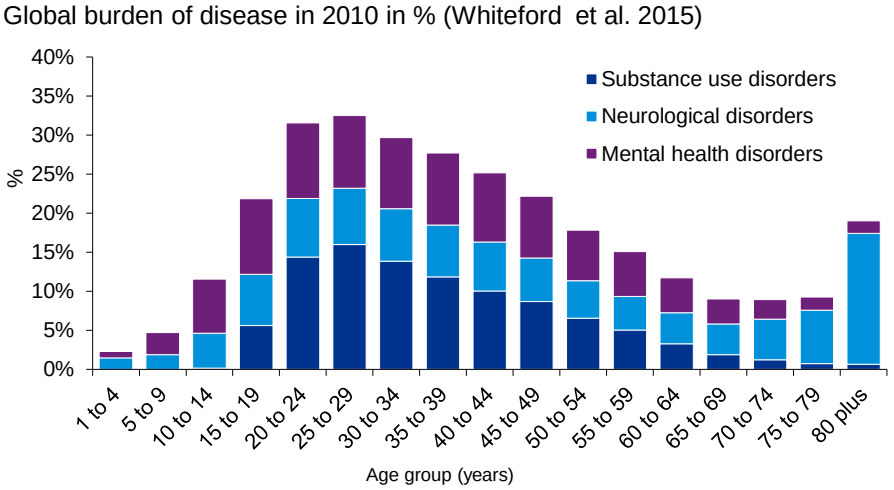



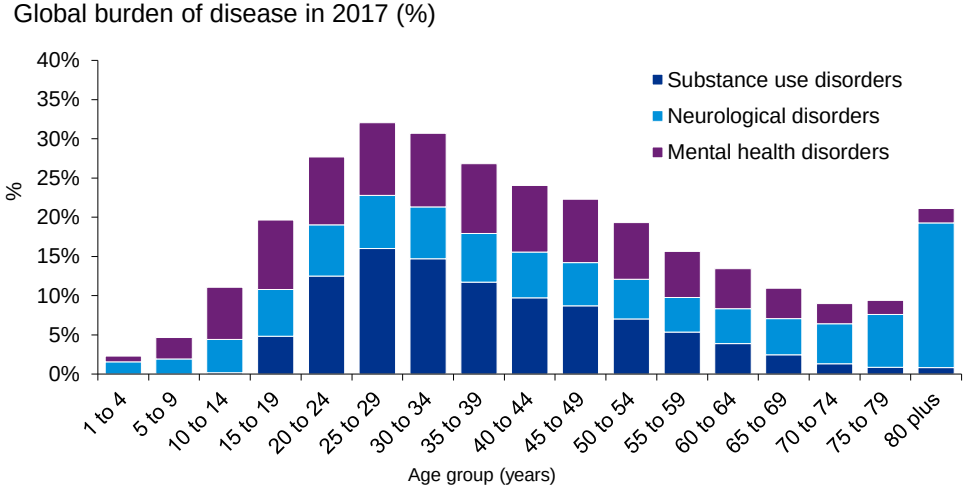

Source: IHME (2018)

**Figure 1.4. Australian and Global burden of disease by age group (in %)**




Source: IHME (2018)

**Table 1.1. Summary of neurological, mental health and substance disorders in Australia – 2017**

| Disease - 2017 | Prevalence (no.) | Mortality (no.) | Burden (year) | | | Total burden cost ($ billion) |
|---|---|---|---|---|---|---|
| | | | YLDs | YLLs | DALYs | |
| **Neurological disorders** | **10,577,762[a]** | **20,449** | **242,098** | **188,748** | **430,845** | **$21.5** |
| Alzheimer's disease and other dementias | 242,870 | 17,119 | 36,315 | 135,004 | 171,319 | $8.6 |
| Parkinson's disease | 47,209 | 2,328 | 6,658 | 26,190 | 32,848 | $1.6 |
| Epilepsy | 62,435 | 291 | 14,004 | 10,296 | 24,300 | $1.2 |
| Multiple sclerosis | 14,756 | 160 | 3,781 | 4,218 | 7,999 | $0.4 |
| Migraine | 4,522,390 | - | 154,149 | - | 154,149 | $7.7 |
| Tension-type headache | 7,866,877 | - | 23,799 | - | 23,799 | $1.2 |
| Other neurological disorders | 100 | 551 | 3,392 | 13,039 | 16,431 | $0.8 |
| **Stroke [b]** | **284,034** | **12,506** | **46,637** | **130,560** | **177,197** | **$8.9** |
| **Mental disorders** | **4,010,159[a]** | **3,131** | **554,510** | **118,271** | **672,781** | **$33.6** |
| Major depressive disorder | 730,867 | - | 147,843 | - | 147,843 | $7.4 |
| Dysthymia | 369,981 | - | 35,362 | - | 35,362 | $1.8 |
| Bipolar disorder | 255,576 | - | 51,830 | - | 51,830 | $2.6 |
| Schizophrenia | 90,636 | - | 57,420 | - | 57,420 | $2.9 |
| Anxiety disorders | 1,456,702 | - | 138,296 | - | 138,296 | $6.9 |
| Eating disorders | 186,180 | 3 | 39,152 | 185 | 39,337 | $2.0 |
| Autism spectrum disorders | 129,425 | - | 19,402 | - | 19,402 | $1.0 |
| Attention-deficit/hyperactivity disorder | 449,978 | - | 5,443 | - | 5,443 | $0.3 |
| Conduct disorder | 132,490 | - | 16,020 | - | 16,020 | $0.8 |
| Idiopathic developmental intellectual disability | 45,137 | - | 1,999 | - | 1,999 | $0.1 |
| Suicide [c] | - | 3,128 | - | 118,086 | 118,086 | $5.9 |
| Other mental disorders | 567,427 | - | 41,743 | - | 41,743 | $2.1 |
| **Substance use disorders** | **790,492[a]** | **1,827** | **125,879** | **72,291** | **198,170** | **$9.9** |
| Alcohol use disorders | 336,572 | 604 | 33,358 | 18,790 | 52,148 | $2.6 |
| Opioid use disorders | 110,629 | 649 | 45,542 | 29,004 | 74,546 | $3.7 |
| Cocaine use disorders | 37,113 | 10 | 5,015 | 508 | 5,522 | $0.3 |
| Amphetamine use disorders | 147,334 | 51 | 19,155 | 2,652 | 21,808 | $1.1 |
| Cannabis use disorders | 162,701 | - | 4,670 | - | 4,670 | $0.2 |
| Other drug use disorders | 22,519 | 513 | 18,139 | 21,336 | 39,476 | $2.0 |

Sources: IHME (2018); AIHW (2018); ABS (2018).

Notes: [a] Total prevalence is subject to comorbidities of sub-diseases within disorders.

[b] In the Global Health Data Exchange (IHME), Stroke is classified as cardiovascular disease (code B.2).

[c] Suicide and tobacco use data are from ABS and AIHW.

## 1.5. Cost of burden of disease

Table 1.1 summarises the cost of burden of disease for sub-conditions in each disorder. The aggregate cost of burden of disease from neurological (including stroke), mental health and substance disorders in Australia was estimated to be $74 billion in 2017.

Mental health disorders account for the largest burden cost of $33.6 billion (52%), depressive disorders (major depressive disorders and dysthymia) account for $9.2 billion in burden costs and $6.9 billion of the total burden cost is due to anxiety disorders. Suicide incidence is translated into the burden cost of productivity loss due to premature mortality. The estimated burden cost for suicide in 2017 was $5.9 billion.

The cost of burden of disease from neurological disorders in 2017 is also substantial, estimated to be $21.5 billion (33%). Alzheimer's disease and other dementias has the largest proportion of total burden cost in neurological disorders (40%) or $8.6 billion, followed by migraines ($7.7 billion), Parkinson's disease ($1.6 billion) and epilepsy ($1.2 billion). The burden cost from stroke, which is classified as neurological disorders and cardiovascular disease, estimated to be $8.9 billion in 2017.

The estimated cost burden of burden of disease for substance use disorders was $9.9 billion in 2017, with more than half of the amount (53%) attributed to drug use disorders ($5.3 billion). The cost burden for alcohol use disorders was estimated to be $2.6 billion or 26 per cent from total burden cost in substance use disorders.

In terms of tobacco smoking, the combined risk factors that contributed to the total DALYs of tobacco use has resulted in burden cost of $4.6 billion in 2016.

# 2. Case for action

The previous section highlighted the magnitude of the burden associated with neurological, mental health and substance abuse conditions. In this section, the evidence base for interventions that can help reduce the burden is assessed, and a ROI analysis is conducted for six specific interventions.

A positive ROI greater than one suggests that the interventions not only improve health outcomes but also deliver cost savings. However, it is important to note that most health interventions cost rather than save money: total knee replacements deliver excellent health benefits but cost around $15,000 per operation; pharmaceutical treatments subsidised by the Pharmaceutical Benefits Scheme deliver benefits to patients, but at a cost to the government. This means that most health interventions have a ROI of less than one. Such interventions are still deemed 'cost effective' if they deliver enough gain in health outcomes to warrant the extra cost. In countries such as the United Kingdom, America and Australia, health interventions are deemed 'cost effective' if they deliver an extra Quality Adjusted Life Year (an extra year of life that's been adjusted for morbidity) for a cost of around AUD$50,000. Where an intervention does deliver both health gains and cost savings, it is considered a 'dominant' intervention in health economics, because they are obvious interventions to fund.

The summary of estimated ROI from the selected interventions from neurological, mental and substance disorders is in Table 2.1.

## 2.1. Neurological disorders

Deep brain stimulation (DBS) involves the implantation of electrodes which send impulses, into targeted areas within the brain that control discrete functions (Herrington, Cheng and Eskandar, 2016). DBS has illustrated particular efficacy in producing therapeutic benefits for individuals suffering from Parkinson's and Alzheimer's disease (Chen et al. 2012). Stimulation has shown rapid improvements in the quality of life of patients, although improvements in psychosocial scores long-term don't illustrate maintenance improvements in motor functioning are maintained up to 36 months post intervention (Volkman, Albanese and Kulisevsky 2009). In Alzheimer's patients, DBS has shown to activate the brains memory circuit and in some cases illustrate improvements and/or slowing of cognitive decline (Laxton et al. 2010). The increase in cortical metabolism stimulation which is associated with positive outcomes in global cognition and memory had been increasingly observed following DBS when compared to traditional pharmacotherapy treatments (Smith, Laxton and Tang-Wai 2012).

Whilst there is currently no cure for Alzheimer's disease (AD) the use of neuroimaging, in conjunction with neuropsychological evaluation and genotyping, is contributing towards the development of therapeutic intervention. This is being achieved by facilitating the selection of appropriate patients for therapy trials, and allowing the non-invasive, invivo measurement of therapeutic efficacy on disease biomarkers (Rinne et al., 2010). This may allow more accurate and earlier treatment of AD patients, giving therapies currently under development a better chance of success at slowing or halting the disease before it has a chance to fully develop. The identification of risk factors for AD and the mechanistic process behind the relationship will aid in the development of therapeutic interventions and may highlight a population at risk of the disease.

Functional interventions, in conjunction with psychotherapy have been found to aide in adjustment to life post injury following stroke or traumatic brain injury (TBI) (Barman, Chatterjee and Bhide 2016). Other successful therapies include cognitive rehabilitation, which incorporates interventions for attention, memory, social communication skills, executive function and comprehensive-holistic neuropsychological rehabilitation after TBI and stroke (Cicerone et al. 2005). Resilience training and adjustment intervention target adjustment challenges, and emphasizes education, skill-building and psychological support.

This intervention has been found to significantly improve psychological health after TBI, with a very large effect size reported (Kreutzer et al. 2018). Whilst it is often not possible to reverse damage in more severe cases, these interventions can help individuals adapt to new lifestyle.

### 2.1.1. Exercise therapy

Exercise therapy takes a multidisciplinary approach to enhancing recovery and quality of life. It is focused on both improving biomedical physical functionality and regaining cognitive functions. Studies have illustrated that beyond improvements in impairment and activity, stroke patients engaging with exercise therapies integrate into the community more effectively and strain on carers significantly decreases (Galvin et al. 2011). Exercise therapy has shown to be highly effective for patients with Parkinson's diseases in improving cognitive and procedural functioning and aerobic capacity (Duchesne, Lungu and Nadeau 2015). When compared with treatment as usual groups exercise therapy intervention subjects illustrate increased improvements in positive mental states of mind (Gorczynski and Faulkner 2010) and optimised recovery and management rates (Stoller et al. 2012).

### 2.1.2. Thrombolytic interventions

Thrombolytic interventions (TI) involve the administration of medications that rapidly dissolve clots associated with strokes, restoring blood flow is crucial in avoiding brain damage and encouraging recovery (Wardlaw et al. 2014). Medications administered within the first three hours after an occurrence of a stroke illustrate the greatest results in the proportion of deaths and individuals that become dependent (Wardlaw et al. 2014). TI however, have been shown to result in increases in symptomatic intracranial haemorrhage, mortality at seven and ten days and death at final follow up (Wardlaw et al. 2014). Follow up studies have illustrated the ability of TI to maintain decreased in disability and when compared with a control group equality in deaths was demonstrated (Sandercock et al. 2012). Long term follow-up studies over six months and research into the optimal time at which initial administration should occur requires further investigation.

## 2.2. Mental health disorders

Dialectical behaviour therapy (DBT) is a form of psychotherapy that builds upon traditional cognitive behavioural approaches, focusing on psychosocial aspects of treatment (Soler et al. 2012). The effectiveness of DBT on non-suicidal self-injury has been examined specifically across the adolescent population and has shown to reduce both suicidal and self-injurious behaviours (Cook and Gorraiz 2016). Across the wider population including adults from inpatient and outpatient settings and among individuals both with and without suicidal/self-injurious behavioural histories, DBT has illustrated an ability to reduce self-directed violence and rates of psychiatric crisis service usage (DeCou, Comtois and Landes 2018). The effectiveness of DBT in reducing suicidal ideation among patients with borderline personality disorder and bipolar disorder has been widely researched. Reductions in self-harm behaviours and suicidality are evident, however, when compared with treatment as usual, results are similar (Canadian Agency for Drugs and Technologies in Health 2010). Further, efficacy of treatment has been demonstrated when analysing the stabilisation of behaviour and improving patient compliance (Panos et al. 2014). DBT reveals net benefits across suicidal tendencies and treatment, however, more research is needed to confirm findings.

Interventions for depression fall into three main, medically recognised categories: Medications, therapies, and medical procedures. There remains substantial interest in the debate regarding placebos versus anti-depressants. Research suggests that antidepressants do result in a significant reduction of symptoms greater than that observed in placebos (Khan et al. 2012). However, patients subjected to a placebo, experienced similar improvement in symptomology when compared with control subjects who underwent their usual treatment, which in some cases may have included antidepressants. Increases in antidepressant-placebo differences have been reported in clinical trials including higher severity of depression (Khan et al. 2012).

The use of psychotherapy, in conjunction with antidepressants, has demonstrated only a slight advantage to antidepressants or therapy alone. It has been theorised that whilst psychotherapy and psychopharmacological intervention have very different features, they may have the same mechanisms of action, resulting in reduced symptomology. This suggests that non-specific therapeutic factors exist amongst even diverse treatments, perhaps accounting for the effectiveness within depression treatment trials.

Cognitive behavioural therapy (CBT) has been well demonstrated as an effective treatment as compared with no treatment (Beltman, Oude Voshaar, and Speckens 2010 ). Whilst there are mixed results from studies comparing CBT to other therapies treatments (Beltman et al. 2010), some have reported similar reductions in depressive aetiology as those seen in the psychopharmacological interventions range (Vos et al. 2004). Studies suggest that this equality in efficacy is more common amongst those with more severe depression (Driessen et al. 2010). In these cases, CBT has been found to reduce relapse rates, with an effect of equal magnitude to that observed when patients are kept on medications (Driessen et al. 2010). Efficacy of CBT seems to be affected by patient demographic, with those who are married or who exhibit higher levels of pre-treatment functional attitude seemingly more responsive to treatment that their unmarried counterparts or those showing high levels of dysfunctional attitudes (Driessen et al. 2010).

The efficacy of a treatment is made up of four factors: client factors, therapist factors, common factors and technique specific factors. Technique specific factors contribute 10-20 per cent of the therapeutic outcome (Duncan, Miller and, Sparks 2004; Lambert 1992). Unfortunately, modern clinical trials are reportedly less effective than they were many years ago. The placebo has been blamed for this trend, suggesting that it is stronger for newer treatments, gradually waning over time, as strong initial expectations begin to fade. CBT has potentially fallen victim to this phenomenon. Initially showcased as the gold standard for treatment, this method has been reported as less effective (Baardseth et al. 2013; Wampold et al. 2002, 1997). The increasing availability of information about CBT to the public, may be the cause of this, with CBT reaching a ceiling effect in its first few years and gradually tapering off (Johnsen et al. 2015).

### 2.2.1. Internet CBT treatment

Face-to-face CBT sessions require an individual to make long-term often costly commitments, computer-based delivery illustrates a unique opportunity to increase adherence to treatment while simultaneously targeting individuals who otherwise might remain untreated (Spek et al. 2010). Self-guided programs supported by both clinicians and non-clinicians allow flexibility in communication and cater for the individual needs of a patient. Studies have gone beyond demonstrating initial benefits of programs, improvements have been shown to be maintained at various follow up points (Andrews et al. 2010). Notably computer-based sessions that are partnered with professional support highlight the greatest effect size (Anderson and Cuijpers 2009). When compared with control and placebo groups, internet-based psychological intervention participants demonstrate significant levels of satisfaction, reduced levels of both depression and anxiety and improved quality of life scores (Andrews et al., 2010; and Wright et al., 2017).

### 2.2.2. Early intervention for psychosis

Psychosis entails a significant departure from reality, resulting in false perceptions and beliefs, disordered thoughts and speech, markedly interfering with functioning. Emotional and motivational deficits, mood abnormalities and sleep disturbances often occur alongside episodes. Patients commonly experience less social contact, struggle to obtain employment, and face challenges to independent living, significantly impacting their quality of life. Subtle cognitive deficits have been identified in patients during their first psychotic episode, and have been argued as an indicator of work and social functioning (Meltzer et al. 1996, Green et al. 2000, McGurk and Meltzer 2000).

Longitudinal studies analysing early intervention (EI) for psychosis have illustrated the ability of such interventions to improve the long-term functionality of individuals cognitively, physically and in education and work settings (Santesteban-Echari et al. 2017). EI's, when compared with treatment as usual and cognitive behavioural therapy, have been shown in addition to support the delay and/or prevent an individual transitioning to a psychotic state when administered following initial onset (Stafford et al. 2013). Evidence suggests that EI's have the ability to minimise strain on healthcare services by reducing admission occurrences for individuals presenting with early stage psychotic symptoms (Randall et al. 2015).

## 2.3. Substance use disorders

Cognitive remediation (CR) targets the cognitive decline associated with drug and alcohol related disorders including attention, memory, executive functioning, social cognition or meta cognition with the ultimate aim of improving functional outcomes (Kaneko and Keshavan 2012). Remediation is split into two distinct approaches, compensatory and restorative, both built on scientific principles of learning e.g. reinforcement and errorless learning (Kaneko et al. 2012). Remediation is designed to manage or restore cognitive decline through skill acquisition and improve behavioural adaptions (Kaneko et al. 2012). Studies have illustrated that CR when delivered alongside an additional activating intervention e.g. work therapy, has efficacy in remediating verbal learning and memory deficits in patients with substance use disorders (Bell, Vissicchio, and Weinstein 2016). Further, CR has been shown to have differential improvements when compared to traditional approaches when overcoming executive dysfunction in patients with substance abuse (Gamito and Oliveira 2014). The ability to exercise self-control and monitor impulsivity following engagement with CR when compared with treatment as usual has been illustrated particularly in patients with illicit drug dependencies (Brooks et al. 2017).

Nicotine replacement therapy (NRT) involves the release of a low dose of nicotine into the body which increases plasma concentration levels while avoiding toxic exposure (Prochaska 2015). NRT has consistently illustrated effectiveness in raising succession rates of a smoking cessation attempt regardless of setting (Hartmann-Boyce et al. 2018). The long-term application of NRT although safe, fails to provide differing results beyond those illustrated in an initial 24-month period (Schnoll et al. 2015), alluding to the need for research into additional support to assist with long-term therapy adherence. Efficacy is conformed when comparing intervention groups with controlled placebo groups, prolonged abstinence and decreased levels of smoking urges is evident among subjects within intervention groups (Schnoll et al. 2015).

### 2.3.1. Brief interventions

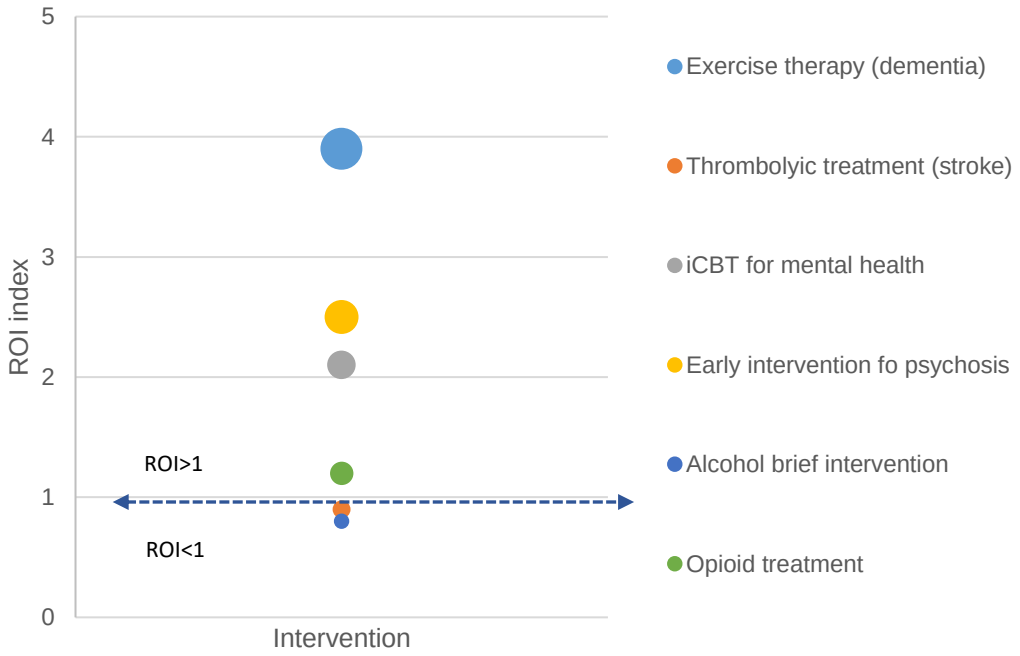
Brief interventions (BI) are time limited interventions focused on changing behaviours and involve the exchange of feedback and discussion on responsibility and self-efficacy in an attempt to elicit behavioural thought adjustments. Brief interventions can involve knowledge sharing, the provision of advice and dissemination of awareness, motivational interviewing or skill-based counselling and goal setting. Motivational interviewing has been shown to be particularly successful in minimising harm long term (Wachtel and Staniford 2010). Studies have illustrated the positive effect BI has on reducing illicit drug and alcohol consumption and a decrease in engagement with risk taking behaviours e.g. driving under the influence of illicit substances (Fischer et al. 2013). Although follow up in some cases voided the maintenance of positive effects studies illustrate when compared with controlled placebo groups fewer deaths in BI groups and self-reports of consumption reduction is evident (McQueen et al. 2011).

### 2.3.2. Opioid therapy

Management of opioid dependency through supplementary therapy involves long-term managed administration of an opioid (Fonseca and Torrens 2018). The therapy aims to create homeostasis of an individual's neurochemistry (Fonseca and Torrens, 2018).

The therapy intends to supress opioid withdrawal symptoms and minimise the effect of intoxication e.g. euphoria or sedation (Fiellin, Friedland and Gourevitch 2006). Supplementary therapy has shown to result in effects beyond the reduction of drug abuse including improved treatment retention rates and a reduction in risk related behaviours related to HIV/sexually transmitted diseases (Ferri, Davoli and Perucci 2011).
When analysing treatment retention rates and suppression of usage, methadone maintenance treatment (MMT), a widely used supplementary therapy, has been shown to be superior when compared with traditional detoxification treatments (Amato et al. 2005). A reduction in levels of crime and mortality has also been shown to be associated with opioid supplementary therapies when compared to no therapy placebo groups (Connock et al. 2007).

**Figure 2.1 ROI of six interventions**




Source: KPMG estimation

**Table 2.1 Estimated ROI for selected interventions**

| Interventions | Treatment summary | ROI | References |
|---|---|---|---|
| **Neurological disorders** | | | |
| **Exercise therapy** | Exercise therapy is a multidisciplinary approach to enhancing recovery and quality of life, focussing on both improving biomedical physical functionality and regaining cognitive functions. It is considered to be highly effective for patients with neurodegenerative diseases. | A recent randomised study of 131 people with dementia found that the exercise therapy has the potential to be cost-effective (D'Amico, F et al. 2016; Lowery, D et al. 2014). The 12-week program delivering physical exercise of walking 20-30 minutes daily and facilitated by professional exercise therapist, resulted in reduced healthcare utilisation after the program. However the intervention is highly contextual and dependent on the severity of the individual's condition, the program's setting and costs. Assuming a program size of 6 participants per therapy group, and converting costs from the aforementioned study to Australian dollars, the average intervention cost is estimated at $528. The reductions in healthcare service utilisation are estimated to save $2,042 on average, resulting return on investment (ROI) of 3.9. | D'Amico F, et al. 2016, 'Cost-effectiveness of exercise as a therapy for behavioural and psychological symptoms of dementia within the EVIDEM-E randomised controlled trial', *International Journal of Geriatric Psychiatry*, vol. 31, no.6, pp. 656-665.;<br>Lowery, D et al. 2014, 'The effect of exercise on behavioural and psychological symptoms of dementia: the EVIDEM-E randomised controlled clinical trial', I*nternational Journal of Geriatric Psychiatry,* vol. 29, no.8, pp. 819-927. |
| **Thrombolytic therapy** | Thrombolytic interventions (TI) involve a restored blood flow in avoiding brain damage. Medications administered within the first three hours after an occurrence of a stroke illustrate the greatest results in the proportion of deaths. | Recent evidence from the US has performed a micro-simulation trial between MRI-based strategy with tissue-type plasminogen activator (tPA) treatment, which is a thrombolytic treatment, and without tPA treatment. Total cost includes hospitalisation, health personnel and administrator wages. The benefit is measured after 90 days of discrepancy in cost-saving between treatment with tPA and without tPA This includes rehospitalisation cost, outpatients' services and gain from quality-adjusted life years (QALYs). The estimation resulted in an ROI of 0.9. Treatment is expected to differ by country due to different sample size and cost components. | Pandya, A et al. 2016, 'Modelling the cost effectiveness of neuroimaging-based treatment of acute wake-up stroke', *Plos One*, DOI: 10.1371; Shireman, TI et al. 2017, 'Cost-effectiveness of solitaire stent retriever thrombectomy for acute ischemic stroke', *Stroke*, DOI; 10.1161.<br>Tung, CE et al. 2011, 'Cost-effectiveness of tissue-type plasminogen activator in the 3 to 4.5 hour time window for acute ischemic stroke, *Stroke*, DOI: 10.1161/STROKEAHA.111.615682. |
| **Mental health disorders** | | | |

| | | | |
|---|---|---|---|
| **Internet-mediated cognitive behavioural therapy (iCBT)** | Self-guided programs supported by both clinicians and non-clinicians in communication and cater for the individual needs of a patient. Notably computer based sessions that are partnered with professional support. | A recent RCT compared the outcomes between internet-mediated cognitive behavioural therapy (iCBT) and treatment as usual (TAU) (Holts, A et al. 2018; Kraeplien, M et al. 2018). The 12-week iCBT program included a GP visit and therapist consultations to diagnose and validate participants during the program, and was estimated to cost an average of $747 (PPP 2017). The benefits of the program reduced health services utilisation and increased productivity, which in total saved an average of $1,589 per person over 12 months. The result is an ROI of 2.1. | Holst, A et al. 2018, 'Cost-effectiveness analysis of internet-mediated cognitive behavioural therapy for depression in the primary care setting: results based on a controlled trial', *BMJ Open*, DOI:10.1136.<br>Kraepelien, M et al. 2018, 'Cost-effectiveness of internet-based cognitive-behavioural therapy and physical exercise for depression', *BJPsych open*, 4 pp. 265-273. |
| **Psychosis early intervention** | In the early intervention, for psychosis, the treatment is mainly aimed at reducing the duration of untreated psychosis, featuring a combined of regular monitoring mental health and safety and followed by supportive counselling to improve social functioning. | A United Kingdom study highlighted the costs of early intervention include increased levels of inpatient and community care, which when valued at $1,029 per day based on psychiatric bed day costs from the AIHW sum to $8,691. The benefits of the intervention were reduced outpatient and inpatient stays totalling $21,539. This results in an ROI of 2.5. An Australian study found cost savings of almost $9,000 per annum after 8 years following the intervention, which results in benefits of $74,437 and an ROI of 8.6 over the long term. | McCrone P. et al. 2010, 'Cost-Effectiveness of an Early Intervention Service for People with Psychosis', *British Journal of Psychiatry* , vol.196, pp 377-382.<br>Australian Institute of Health and Welfare, 2015, 'Table EXP.7: Recurrent expenditure(a) ($) per patient day(b) on specialised mental health public hospital services, constant prices(c), by hospital type, states and territories, 1992–93 to 2014–15.<br>Mihalopoulos, C., et al. 2009 'Is early intervention in psychosis cost-effective over the long term?', *Schizophrenia Bulletin*, vol.35, pp 909-918. |
| **Substance use disorders** | | | |
| **Brief intervention** | Brief interventions (BI) are time limited interventions focused on changing behaviours and involve the exchange of feedback and discussion on responsibility and self-efficacy in an attempt to elicit behavioural thought adjustments. Brief interventions can involve | Based on systematic reviews of screening and brief intervention (SBI) programs, the costs of the SBI range from $118 to $257 and include screening to identify people with alcohol dependency, costs for nurse and GP consultations, and material costs (Kaner et al. 2018; Purshouse et al. 2013; Bray et al. 2012). The benefits from the SBI include a reduction in health services cost such physician visits, ED visits and nurse home visits. Translating these into benefits ranging from $81 to $202 over 12 months (Ettner et al. 2014; Kaner et al. 2018). | Kaner EFS et al. 2018, 'Effectiveness of brief alcohol interventions in primary care populations', *Cochrane Database of Systematic Reviews*, Issue 2. Art. No.: CD004148.<br>Ettnet et al. 2014, 'The effect of an educational intervention on alcohol consumption at risk drinking, and health care utilisation in older adults: the Project |

| | | | |
|---|---|---|---|
| | knowledge sharing and dissemination of awareness and skill-based counselling. | The estimation resulted in an ROI between 0.7 (low risk status) and 0.8 (high risk status). | SHARE study, *Journal of Studies on Alcohol and Drugs*, vol. 75, no. 3, pp. 447-457.<br>Purshouse et al. 2013, 'Modelling the cost-effectiveness of alcohol screening and brief interventions in primary care in England', *Alcohol and Alcoholism*, vol. 48.no. 2, pp. 180-188. |
| **Opioid supplementary treatment** | Management of opioid dependency through supplementary therapy that involves long-term managed administration of an opioid. The therapy is intends to supress opioid withdrawal symptoms and minimise the effect of intoxication. | The treatment referred to recent evidence in UK and US of 6 months methadone-maintenance therapy (MMT). Intervention costs during the treatment include drug cost for the treatment, clinic cost and services from hospital and community. Benefits of the program are calculated after 6 months. Cost-savings consist of lower inpatient cost (rehabilitation) and lower outpatient costs such as ED and physician visits. It translates the average intervention cost of $12,873 to total benefit of $15,739 after 12 months. The average ROI from program is 1.2. | Byford, S et al. 2013, 'Cost-effectiveness of injectable opioid treatment v. oral methadone for chronic heroin addiction', *The British Journal of Psychiatry,* vol. 203, pp. 341-349.<br>Baser, O et al. 2011, 'Cost and utilization outcomes of opioid-dependence treatments', *The American Journal pf Managed Care*, vol. 17, no.8. pp. 235-248. |

Note: Economic modelling for the ROI estimations relied on recent evidence that are subject to differ in intervention setting and sample size.

# 3. Discussion

Evidence suggests that neurological, mental health and substance use disorders rarely exist in isolation (Hesdorffer 2016). Cross sectional studies highlight comorbidities increase disease burden and effect the course an illness takes, and the use of services an individual will require (Hesdorffer 2016). The severity of illness experienced by an individual experiencing comorbidity is significantly greater and associated with complex health care needs and service utilisation rates including hospital admissions, primary care consultations and prescriptions (Browne, 2017). Mental health research specifically, continues to highlight the pervasive risk of comorbidity within mental disorders (Plana-Ripoll et al. 2019). Although onset is most likely within one year of initial diagnosis risks persist for up to 15 years (Plana-Ripoll et al. 2019). This paper has taken a unique approach in the identification and discussion of neurological, mental health and substance use disorders. Disorders are presented in alignment with one another and within an Australian context. Combined with the completion of return of investment models for six interventions, this paper provides Mindgardens with a strong platform to advocate for policy change, health reform and further investment in the Alliance, while reinforcing the importance of collaboration across all Mindgardens Alliance partners.

The premature mortality associated with severe neurological, mental health and substance use disorders highlights the need to invest in evidence-based interventions. The life expectancy of individuals with a severe mental health disorder is decreased by 15 to 20 years (Lawrence, Hancock and Kisely 2013). This paper provides a solid basis in the identification of key areas for future research, specifically the collection of further evidence-based research and an opportunity to conduct trials on effective interventions. It also enables a platform for multidimensional growth for the Alliance to focus on coordinating and integrating efforts and investments across research, clinical care and education of the next generation of clinicians and health professionals. Emphasis on collaboration removes abilities of the Alliance partners to operate in isolation and provides opportunities to:

- Support the delivery of world's best practice in the diagnosis, treatment and prevention of mental health, neurological and substance use disorders.
- Create a link between research partners and the Local Health District connecting clinicians to best practice research and treatment.
- Implement evidence based models of care including apex clinics and integrated community hubs.
- Create opportunities for consumers, researchers and the clinical workforce to share expertise and build awareness.

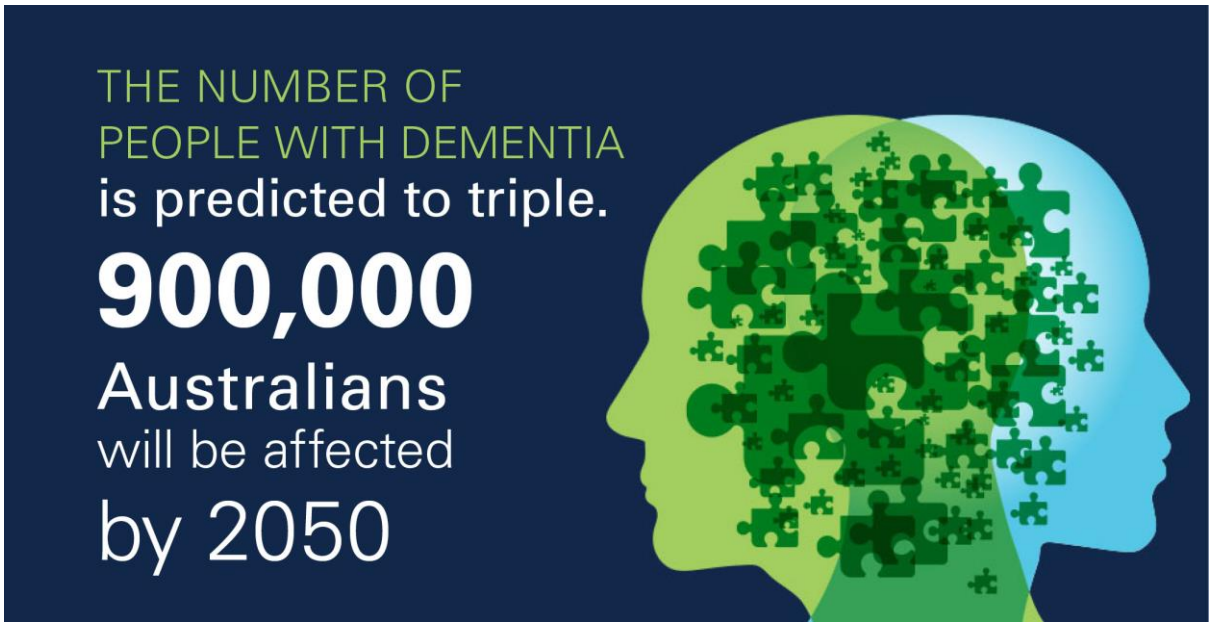
Increasing the scope of research and aligning research portfolios across Mindgardens establishes it as an international leader in all forms of research and increases the potential of private and public funders. Findings from the *Investing to Save* report prepared for Mental Health Australia revealed that workplace mental health interventions, assertive interventions after a suicide attempt and e-health early interventions are key areas to prioritise. The interventions illustrated both positive return on investment and improved health and wellbeing outcomes for individuals (Mental Health Australia and KPMG 2018). Trialling these models within Mindgardens presents significant opportunities to reduce the associated disease and cost burdens.

In 2017, $174.8 million was invested into cancer research and $103.8 into cardiovascular disease, compared with $67.3 for mental health and $50.7 for dementia (NHMRC 2018). Analysis of cost and burden accentuates the need for continual and increased focus on research in neurological, mental health and substance use disorders. Likewise, the paper illustrates merit in directing resources toward interventions e.g. dialectical behaviour therapy, cognitive remediation and deep brain stimulation that are delivering strong results, but where further research is required to attain 'gold standard status' i.e. systematic review, meta analyses and randomised control trials that possess consistent results and conclusive efficacy.

Analysis of the evidence base highlighted the effectiveness of psychosocial models of care and the benefit that can be produced from bridging the gap between traditional and progressive models of care. Future research provides an opportunity to understand the unique alignment and interrelationships between disorders and how interventions can be simultaneously delivered. Leveraging the foundation of evidence discussed in this paper and translating it into resource-intensive pilots and efficacy trials presents an ability to provide deep insight into how inclusive models of care can put downward pressure on the burden and cost of disease. Commitment across Mindgardens partners to such comprehensive research and drive toward aligned models of care therefore has the ability to reach further to those who currently experience barriers to intervention or care delivery. Failure to recognise the complex interplay between social, economic and physical factors on treatment and health service access increases the burden of disease.

Consumer lead research is a central component of Mindgardens. Determining research priority areas, influencing methodology and ensuring the voice of the consumer is apparent throughout research and its translation into practice are key objectives of Mindgardens. In light of this, consultation with individuals with lived experience guided the modelling of interventions and translation of evidence by providing insight into the complex spectrum of disease diversity. Shifting the role of consumers from participants to leaders has the ability to broaden research perspective frameworks, increasing the benefit of the end product for those most reliant upon it. Mindgardens is focused on encouraging consumer led research dissemination and translation, acknowledging the unique impact and value it can have on its intended target. Allowing consumers to inform research discussions can have long term implications on the succession of interventions, their unique perspective highlights and moderates' inefficiencies of care (SLHD 2017). Successful research requires simultaneous collaboration between academics and consumers.

Identifying effective interventions and preventative programs to the complex range of issues and challenges associated with the cost, burden and impact of neurological, mental health and substance use disorders requires innovative leadership. Poor translation of research outcomes in effective implementation of the best models of care and a lack of integration across the health sector contributes to the overall increase in the burden of disease. Strengthening approaches to research and practice translation will strengthen evidenced based models of care, which will ultimately evolve the disease burden environment. The approach of Mindgardens to coordinate and integrate efforts and investments across research, clinical care and the education of clinicians and health professionals highlights an opportunity to combat inefficiencies and reduce disease burden.



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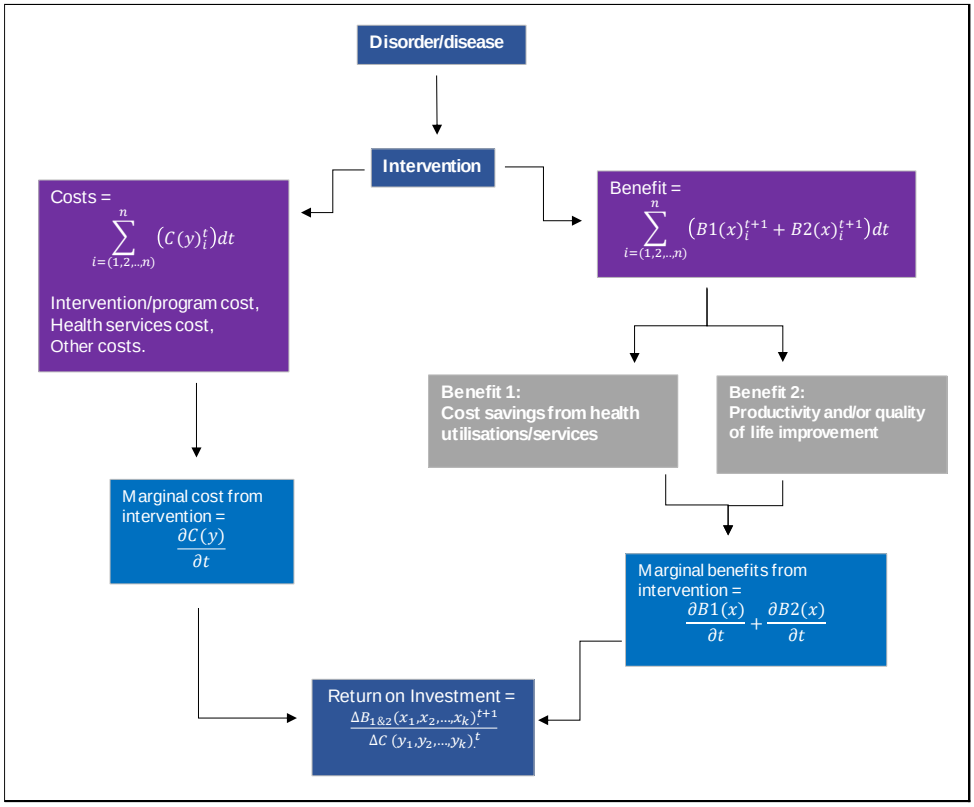
*“ Mindgardens’ vision is to enable clinicians and scientists to collaborate to develop and implement new models of care in three critical health areas: Ageing and Neurodegeneration, Mental Health, and Drug & Alcohol, based on the Comprehensive Cancer Centre Model. We need to build new models of care to reduce this burden of disease for all Australians. Let’s start this conversation today, not tomorrow. ”*

# Appendix A – Summary of ROI modelling

## A.1. Return on investment matrix and framework

| Intervention | Intervention cost and other related costs | Benefits from healthcare services utilisation | Benefit from quality of life (QALYs) |
|---|---|---|---|
| **Neurological disorders** | | | |
| Thrombolytic treatment | √ | √ | √ |
| Exercise therapy | √ | √ | |
| **Mental health disorders** | | | |
| Internet-based CBT (iCBT) | √ | √ | - |
| Early intervention for psychosis | √ | √ | - |
| **Substance use disorders** | | | |
| Brief intervention | √ | √ | - |
| Opioid treatment | √ | √ | - |




Source: KPMG

## A.2. ROI summary

### a. ROI exercise therapy (neurological disorders)

A dyadic exercise regimen for people with dementia and their carer

| Cost structure | Unit | Source |
|---|---|---|
| Duration (week) | 12 | D'Amico, F et al. 2016 and Lowery, D et al. 2014 |
| Walking program | daily | D'Amico, F et al. 2016 and Lowery, D et al. 2014 |
| Per dyad walking program (median in minute) | 25 mins | D'Amico, F et al. 2016 and Lowery, D et al. 2014 |
| Exercise therapist attendance | 6 week | D'Amico, F et al. 2016 and Lowery, D et al. 2014 |
| Professional therapist cost ($) | $87.95 | MBS 2018 item 80130 |

**Benefit from cost savings (before and after)**

| Components (in £ 2013) | Before intervention | After intervention | Benefit (after 12 weeks) | Source |
|---|---|---|---|---|
| Accommodation | € 1,300.90 | € 697.00 | € 603.90 | D'Amico, F et al. 2016 |
| Hospital services | € 577.50 | € 146.70 | € 430.80 | D'Amico, F et al. 2016 |
| Community services | € 682.40 | € 390.50 | € 291.90 | D'Amico, F et al. 2016 |
| Equipment and adaptation | € 112.00 | € 89.00 | € 23.00 | D'Amico, F et al. 2016 |
| Day services | € 259.60 | € 229.10 | € 30.50 | D'Amico, F et al. 2016 |
| Medications | € 272.80 | € 285.20 | -€ 12.40 | D'Amico, F et al. 2016 |
| **Total HSC** | **€ 3,205.20** | **€ 1,837.50** | **€ 1,367.70** | |

HSC: Health services costs

| Cost (6 weeks) | in PPP 2017 |
|---|---|
| Professional therapist attendance (weekend) | $528 |
| **Total intervention cost** | **$528** |

| Benefit | in PPP 2017 |
|---|---|
| **Total HSC** | **$2,042** |

| ROI | 3.9 |
|---|---|

## b. ROI thrombolytic treatment (neurological disorders)

**ROI model 2**

Cost is estimated for one-time treatment

| Unit cost of hospitalisation | in 2013 USD | Note | Source |
|---|---|---|---|
| Hospitalisation without treatment | $11,462 | The costs include ICU, imaging, supplies, nurse and administrator wages. | Pandya, A et al. 2016 and Tung, CE et al. 2011 |
| Hospitalisation with thrombolytic treatment (tPA) | $18,182 | The costs include ICU, imaging, supplies, nurse and administrator wages. | Pandya, A et al. 2016 and Tung, CE et al. 2011 |

mRS scale conversion to QALYs of post-stroke condition

| Scale | mRS value | QALYs range | Source |
|---|---|---|---|
| mRS 0 (no symptoms) | 0.275 | 0.8-1 | |
| mRS 1 (no significant disability) | 0.249 | 0.8-0.95 | |
| mRS 2 (minimal disability) | 0.141 | 0.68-0.9 | |
| mRS 3 (moderate disability) | 0.093 | 0.45-0.65 | Tung, CE et al. 2011 |
| mRS 4 (moderate to severe ) | 0.093 | 0.1-0.4 | |
| mRS 5 (severe disability) | 0.081 | 0-0.32 | |
| mRS 6 (death) | 0.067 | 0 | |

**ROI estimation**

| | in 2013 USD | | in PPP 2017 |
|---|---|---|---|
| **Average QALYs gained** | **0.0473** | | |
| **QALYs threshold** | **$50,000** | | $73,580 |
| **Cost and benefit analysis** | | **in PPP 2017** | |
| Benefit from QALY gained over life time | $2,367 | | $3,483 |
| Incremental benefit from treatment cost (with and without tPA) | $3,828 | | $5,633 |
| **Total benefit** | | | **$9,116** |
| Incremental cost from treatment cost (with and without tPA) | $6,720 | | $9,889 |
| **Total cost** | | | **$9,889** |
| **ROI** | **0.92** | | |

## c. ROI iCBT (mental health disorders)

Internet-mediated cognitive behavioural therapy for depression the primary care setting.

**ROI model 1**

| Cost Components | Unit in SEK 2013 | Conversion in PPP 2017 | Note | Source |
|---|---|---|---|---|
| iCBT programme | 1000 | $171.20 | Material cost, 12 weeks intervention program | Holts et al. 2018; OECD and Eurostat 2012 |
| GP visits | 782 | $133.88 | Diagnose and recruit participants: >18 years and have mild to moderate depression (MADRS). | Holts et al. 2018; OECD and Eurostat 2012 |
| Therapist (iCBT support) | 856 | $146.55 | Therapist support is required to validate the patient. | Holts et al. 2018; OECD and Eurostat 2012 |
| Phone counselling (15 min) | 1025 | $175.48 | Av. Nurse consultation per week for 8 weeks by phone or email. | Holts et al. 2018; OECD and Eurostat 2012 |
| Medication (antidepressants + sedatives) | 382 | $65.40 | Medications are part of the program. Data retrieve from questionnaires to monitor the intervention. | Holts et al. 2018; OECD and Eurostat 2012 |
| Total cost (12 weeks) | 4045 | **$692.52** | | |

| BDI-II score | Healthcare outcomes (point) | in PPP 2017 | Accumulation | Source |
|---|---|---|---|---|
| 3 months | 13.39 | $889.45 | **$889.45** | Holts et al. 2018 |
| 6 months | 12.68 | $842.29 | **$1,731.75** | Holts et a. 2018 |
| 12 months | 10.97 | $728.70 | **$2,460.45** | Holts et al. 2018 |

**ROI model 2**

| Cost Components | Unit in £ 2012 | Conversion PPP 2017 | Note | Source |
|---|---|---|---|---|
| GP visit | 192.14 | $287.53 | 12 weeks program. Participants are randomly selected. Initial diagnose and screening from GP. | Krapelian et al. 2018, OECD and Eurostat 2012 |
| Social worker | 18.97 | $28.39 | Part of the program on questionnaires validation. | Krapelian et al. 2018, OECD and Eurostat 2012 |
| Therapist | 42.57 | $63.70 | As a guide during the treatment | Krapelian et al. 2018, OECD and Eurostat 2012 |
| Psychological treatment | 56.01 | $83.82 | Treating the patient during the treatment. Average 16 mins per week. | Krapelian et al. 2018, OECD and Eurostat 2012 |
| iCBT cost | 501.08 | $749.84 | | Krapelian et al. 2018, OECD and Eurostat 2012 |
| Total cost (12 weeks) | 810.77 | **$1,213.27** | | |

| Benefit | Unit in £ 2012 | Conversion PPP 2017 | Note | Source |
|---|---|---|---|---|
| 3 months | 297.52 | $445.22 | Measuring discrepancy cost-savings between TAU and iCBT cost: healthcare, non-medical costs, productivity loss (sick leave and unemployment) | Krapelian et al. 2018, OECD and Eurostat 2012 |
| 12 months | 1061.88 | $1,589.04 | Measuring discrepancy cost-savings between TAU and iCBT cost: healthcare are, non-medical costs, productivity loss (sick leave and unemployment) | |

| | |
|---|---|
| **ROI for 12 months (average)** | **2.1** |

### d. ROI Brief Intervention (substance use disorders)

Screening and brief intervention program

| Cost component | Note | Amount | Source | Additional note |
|---|---|---|---|---|
| Screening cost | Primary care ($ 2011) | 23.99 | Navarro et al. 2011, in Bray et al. 2012 | Cost to identify individuals who are not alcohol dependent but who drink more than the guidelines recommend. |
| Brief intervention cost | Unit cost of practice nurse (per minute in £ 2007) | 0.55 | Curtis 2008 in Purshouse et al. 2013 | 12 months evaluation in 10 years |
| | Unit cost of GP (per minute in £ 2007) | 2.72 | Curtis 2008 in Purshouse et al. 2013 | 12 months evaluation in 10 years |
| Per intervention with nurse | In minute (median) | 25 | Kaner et al. 2018 | Cochrane database of systematic review |
| Per intervention with GP | In minute (median) | 10 | Kaner et al. 2018 | Cochrane database of systematic review |
| Brief intervention | Session (primary care) | 1 to 5 | Kaner et al. 2018 | Cochrane database of systematic review |
| Material cost | Per intervention (in £ 2007) | 8.84 | Lock et al. 2006 in Purshouse et al. 2013 | |

| Benefit component | Setting | Amount | Souce |
|---|---|---|---|
| Lower physician visits | Health services | 1.14 | Ettner et al. 2014, Kaner et al. 2018 |
| Reduce ED visit | Health services | from 25% to 16% | Ettner et al. 2014, Kaner et al. 2018 |
| Reduce nurse home visit | Health services | from 3% to 2% | Ettner et al. 2014, Kaner et al. 2018 |
| Reduce assistance from a non-professional caregiver | Health-related services | from 17% to 12% | Ettner et al. 2014, Kaner et al. 2018 |

**AIHW guideline (NDSHS 2016) of alcohol drinking status people aged 14 years or older**

| Status | Note |
|---|---|
| Low risk | On average, had more than 2 standard drinks per day. |
| Risky | Had more than 4 standard drinks at least once a year. |
| High risk | Had more than 4 standard drinks at least once a month. |

| | |
|---|---|
| Risky/High risk | Had more than 4 standard drinks at least once a week. |

| Conversion | Unit (coefficient/$) | Source |
|---|---|---|
| USD coef adjustment | 0.679 | OECD PPP 2017 |
| GBP coef adjustment | 2.044 | OECD PPP 2018 |
| Physician cost ($) | 153.15 | MBS (2018) item 110 |
| ED visit ($) | 285.05 | MBS (2018) item 520 |
| Nurse home visit ($) | 53.7 | MBS (2018) code 10983 |
| Professional caregiver ($) | 78.95 | MBS (2018) code 82222 |

| Valuation cost and benefit | in PPP 2017 |
|---|---|
| **Cost** | |
| Screening cost | 16.30 |
| Practice nurse per minute | 1.12 |
| Practice GP per minute | 5.56 |
| Material cost | 18.07 |
| **Benefit** | |
| 1.14 X Physician visits | 174.59 |
| 9% X ED visit | 25.65 |
| 1% X Nurse home visit | 0.54 |
| 2% X Assistance from a non-professional caregiver | 1.58 |

**Assumptions**

| Brief intervention setting | Low risk | Risky | High risk | Risky/High risk | Reference |
|---|---|---|---|---|---|
| Doctor consultation | 1 | 2 | 2 | 3 | Kaner et al. 2018 |
| Nurse consultation | 1 | 1 | 2 | 2 | Kaner et al. 2018 |
| Total brief intervention | 2 | 3 | 4 | 5 | Kaner et al. 2018 |
| Benefit weight | 40% | 60% | 80% | 100% | Ettner et al. 2014, Kaner et al. 2018 |

| Component | Low risk | Risky | High risk | Risky/High risk |
|---|---|---|---|---|
| **Cost** | | | | |
| Screening | $16.30 | $16.30 | $16.30 | $16.30 |
| Nurse consultation | $28.11 | $28.11 | $56.22 | $56.22 |
| GP consultation | $55.61 | $111.22 | $111.22 | $166.83 |
| Material cost | $18.07 | $18.07 | $18.07 | $18.07 |
| **Total cost** | **$118.09** | **$173.70** | **$201.81** | **$257.42** |
| **Benefit** | | | | |
| Reduce physician visit | $69.84 | $104.75 | $139.67 | $174.59 |
| Reduce ED visit | $10.26 | $15.39 | $20.52 | $25.65 |
| Reduce nurse visit | $0.21 | $0.32 | $0.43 | $0.54 |
| Reduce Assistance | $0.63 | $0.95 | $1.26 | $1.58 |
| **Total benefit** | **$80.94** | **$121.42** | **$161.89** | **$202.36** |

| ROI at individual level | Low risk | Risky | High risk | Risky/High risk |
|---|---|---|---|---|
| **ROI** | **0.69** | **0.70** | **0.80** | **0.79** |
| **Average ROI** | **0.74** | | | |

## e. ROI opioid supplementary treatment (substance use disorders)

| Cost | MMT (Methadone-maintenance therapy) | | | | |
|---|---|---|---|---|---|
| **Cost components (£ 2008)** | **Supervised injectable methadone** | **Optimised oral methadone** | **Note (Supervised injectable methadone)** | **Note (Optimised oral methadone)** | **Source** |
| Intervention costs | 4673 | 2568 | 26 weeks or 6 months intervention program. Once daily per individual max 200mg/day of methadone, self-administered under nursing supervision. | 26 weeks or 6 months intervention program. Prescribed, once daily per individual of >=80 mg/day - 5 days per week. Under direct nursing supervision. | Byford et al. 2013 |
| Drug costs | 720 | 205 | Taken from British National Formulary | Taken from British National Formulary | Byford et al. 2013 |
| Clinic costs | 2571 | 1047 | | | Byford et al. 2013 |
| Weekly case management | 984 | 922 | Based on annual budget for clinic costs. | Based on annual budget for clinic costs. | Byford et al. 2013 |
| Urine test | 398 | 394 | | | Byford et al. 2013 |
| Other service use | 2745 | 2274 | | | Byford et al. 2013 |
| Staffed accomodation | 660 | 783 | | | Byford et al. 2013 |
| Hospital services | 486 | 622 | | | Byford et al. 2013 |
| Community services | 719 | 618 | | | Byford et al. 2013 |
| Criminal justice services | 880 | 251 | | | Byford et al. 2013 |
| **Total cost over 26 weeks (6 months)** | **7418** | **4842** | | | Byford et al. 2013 |

| Cost | | |
|---|---|---|
| **Cost components in PPP 2017** | **Supervised injectable methadone** | **Optimised oral methadone** |
| **Intervention costs** | **$9,813** | **$5,393** |
| Drug costs | $1,512 | $431 |
| Clinic costs | $5,399 | $2,199 |
| Weekly case management | $2,066 | $1,936 |
| Urine test | $836 | $827 |
| **Other service use** | **$5,765** | **$4,775** |
| Staffed accomodation | $1,386 | $1,644 |
| Hospital services | $1,021 | $1,306 |
| Community services | $1,510 | $1,298 |
| Criminal justice services | $1,848 | $527 |
| **Crimes committed** | **$0** | **$0** |
| **Total cost over 26 weeks (6 months)** | **$15,578** | **$10,168** |
| | **Average in 12 months $12,873** | |

**Benefit**

| Healthcare services (in PPP 2017) | Baseline cost | Cost after 6 months treatment pharmacotherapy | Benefit |
|---|---|---|---|
| **Inpatient** | | | |
| Rehabilitation | $175 | $389 | -$213 |
| Opioid-related inpatient admission | $372 | $673 | -$300 |
| Non-opioid related inpatient admission | $19,666 | $11,741 | $7,925 |
| **Outpatient** | | | |
| Visits ED | $687 | $680 | $7 |
| Physician provider | $12 | $77 | -$65 |
| Psychosocial provider | $6 | $32 | -$26 |
| Non-opioid services | $71 | $9,087 | -$9,016 |
| **Other costs (pharmacy, psychiatric)** | $11,539 | $1,981 | $9,558 |
| **Total** | **$32,528** | **$24,659** | **$7,869** |
| | | **Average in 12 months** | **$15,739** |

| Intervention | Supervised injectable methadone | Optimised oral methadone | Average |
|---|---|---|---|
| **ROI** | **0.51** | **0.77** | **0.64** |
| **extrapolate in 12 months** | **1.2** | | |

# Appendix B – Methodology approach

**Purpose**

The literature scan undertaken by KPMG focused on the neurological, mental health and substance disorders.

The purpose of the initial scan was to review the impact, cost and burden of related disorders to guide the development of research into current evidence based interventions positively transforming the disorder environment.

The review syntheses relevant material sourced during a scan of publically available literature. However, it should be noted that this document is not intended to be an exhaustive review of all available literature.

**Methodology**

| Cost, burden, impact review | |
|---|---|
| **Research question** | • What are the prevalence, morbidity and mortality rates of neurological, mental health and substance related disorders?<br>• To what extent do related disorders burden and impact Australia's healthcare system?<br>• What is the economic cost related to disorder burden?<br>• What evidenced based interventions are most effective in treating disorders? |
| **Search terms** | Neurological diseases in Australia + Alzheimer in Australia + Parkinson/stroke in Australia<br>+ + +<br>Mental health/mental illness in Australia + Depression/schizophrenia/anxiety + Alcohol and drug disorders in Australia<br>Mental health/illness treatment/intervention(s) + Depressive series treatment/programs Alcohol and drugs programs/campaigns/ interventions<br>+<br>Economic cost/burden of neurological diseases Economic cost of dementia/Parkinson/ stroke/Alzheimer Economic cost/impact of alcohol and drug abuses/disorders<br>Evidence of neurological, mental health, alcohol and drug disorders Alcohol and drug programs/campaign Impact of physical health, metabolic syndrome<br>Neurological programs/campaigns/interventions Evidence based policy on mental health/alcohol and drug disorders Occurrence of associated co-morbidities<br>Economic cost/burden/impact of psychosis and suicide |
| **Search parameters** | • Peer-reviewed journal in the condition and treatment of neurological disease/mental health and alcohol and drug disorders in Australia and comparable countries (UK, Canada, New Zealand, OECD countries).<br>• Journal articles/reports/government publications of the economic cost methodology/benchmarking/best practice in mental health, neurological diseases (e.g. Dementia, Parkinson, Stroke), alcohol and drug disorders.<br>• Inpatient hospitalisation, outpatient visits and emergency room visit data.<br>• Journal articles/reports/government publications on the effectiveness of policy/programs/campaign in mental health and alcohol and drug disorders. |
| **Indicative sources, databases or search engines (indicative only)** | • ProQuest<br>• PubMed<br>• Cochrane library<br>• Wiley online library<br>• Scopus<br>• Science direct (Elsevier)<br>• JSTOR<br>• EconLit<br>• Australian Institute of Health and Welfare (AIHW) |

| | | | |
|---|---|---|---|
| | • Australian Bureau of Statistics<br>• The Institute for Health Metrics and Evaluation (IHME) and The Global Health Data Exchange (GHDx)<br>• Google Scholar | | |
| **Evidence assessment hierarchy** | Nature of research | Sample size | Validation and review |
| | 1. Panel data analysis<br>2. Cost-effectiveness method<br>3. Policy review<br>4. ROI – marginal cost and marginal benefit approach.<br>5. Literature Review<br>6. Systematic review<br>7. Meta analysis<br>8. Randomised control trial | 1. Large<br>2. Medium<br>3. Small | 1. Peer reviewed<br>2. Validated tool applied |

**Output**

Results of the literature review regarding the cost, burden and impact of neurological, mental health and substance disorders will be used to inform investigation strategy into the current evidence based interventions. The literature scan will be attached as an appendix to the final white paper and provided to Mindgardens.

# APPENDIX C – Supplementary evidence paper (Interventions)

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
|---|---|---|---|---|
| *Mental health* | | | | |
| Resilience training and stress management | Resilience is the ability of an individual to adapt and recover following the endurance of stress or adversity.<br><br>Resilience and stress management training aims to promote the well-being, mental health and productivity of an individual.<br><br>Falls within the field of prevention and promotion of mental health.<br><br>Programs drive self-efficacy beliefs and promote self-esteem and the development of emotional regulation to reduce feelings of distress, anxiety and/or depressive thoughts prior, during or following challenging situations. | • CBT-based stress management interventions produce individual benefits in terms of reduced stress and symptoms. However, this does not appear to translate to notable improvements in absenteeism. Return-to-work programs which incorporate CBT and problem-focused strategies have a positive effect on organisational and individual outcomes. (1).<br>• Stress management programs were associated with favourable medium to large effect sizes and cognitive-behavioural stress management programs consistently produced the largest effects (mainly on psychological outcomes) in occupational settings. (2).<br>• Significantly decreased depressive symptoms and intentions to retire early at seven month follow-up of the intervention group. Younger employees and employees with elevated levels of depression or exhaustion at the beginning of the intervention benefited most. (3).<br>• Meta-analytic studies found a greater effect size of individual interventions on individual outcomes. Organisational interventions showed mixed evidence of benefit. Organisational programs for physical activity showed a reduction in absenteeism. Specifically, cognitive-behavioural programs produced larger effects at the individual level compared with other interventions. Some interventions appeared to lead to deterioration in mental health and absenteeism outcomes. Individual interventions (like CBT) improve individuals' mental health. Physical activity as an organisational intervention reduces absenteeism. (4).<br>• Following emotion-focused and problem-focused worksite stress management interventions, improvements in mental health and work-related variables were found (including on: General Health Questionnaire results, Beck Depression Inventory, and Propensity to innovate). (5).<br>• Training interventions using mindfulness and CBT techniques illustrated enhancement in resilience measures. (6). | 1. Joyce, S., Modini, M., Christensen, H., Maykletun, A., Bryant, R., Mitchell, P.B., and Harvey, S.B. (2016) 'Workplace interventions for common mental disorders: A systematic review', in *Psychological Medicine* 46, pp 683-697.<br><br>2. Richardson, K.M., and Rothstein, H.R. (2008) Effects of occupational stress management intervention programs: a meta-analysis. J *Occup Health Psycho*l 13, pp 69-93.<br><br>3. Vuori, J, Toppinen-Tanner, S., and Mutanen, P. (2012) Effects of resource-building group intervention on career management and mental health in work organizations: randomized controlled field trial. J *Appl Psychol* 97:2, pp 273-86.<br><br>4. Bhui, K.S., Dinos, S., Stansfeld, S.A., and White, P.D. (2012) A synthesis of the evidence for managing stress at work: A review of the reviews reporting on anxiety, depression, and absenteeism. *Journal of Environmental and Public Health* 12.<br><br>5. Bond, F.W., and Bunce, D. (2000) Mediators of change in emotion-focused and problem-focused worksite stress management interventions. J O*ccup Health Psychol* 5, pp 156-63. | HIGH – several systematic reviews have identified a strong evidence base for this intervention |

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
|---|---|---|---|---|
| | | | 6. Joyce, S., Shand, F., Tighe, J., Laurent, S. J., Bryant, R. A., & Harvey, S. B. (2018). Road to resilience: a systematic review and meta-analysis of resilience training programmes and interventions. *BMJ open*, *8*(6), e017858. doi:10.1136/bmjopen-2017-017858. | |
| Collaborative care for people with co-morbid physical and mental illnesses | Mental illnesses are frequently comorbid with physical illnesses. One-dimensional independent treatment results in an increase in complications, less efficacious treatment and ultimately an unfavourable prognoses (Sartorius 2013).<br><br>Multi-disciplinary approach that involves collaboration of health care professionals. Central to the primary health care team, a care manager responsible for coordinating care, the provision of *evidence bases interventions* and monitoring patient progress.<br><br>Collaborative care addresses medical conditions concurrently while focusing on patient, provider and the organisation of care. | • A meta-analysis demonstrated that collaborative care interventions were significantly more effective than usual care, and depression reduction was maintained at 12 months. By comparison, short-term (up to 12 weeks), but not longer-term effectiveness was demonstrated for both pharmacological and psychological interventions. (1).<br>• It has been estimated that collaborative care depression interventions are associated with a modest increase of £613 per patient, which is cost-effective based on increases in patient-quality-adjusted life years. The overall effect size of collaborative care versus usual care for illness burden was OR 1.64 (95% CI 1.47;1.83), d=0.27 (95% CI 0.21; 0.33). The effect of collaborative care on physical outcomes, yielded an overall OR for collaborative care compared to usual care was 1.46. The highest OR was found for hypertension. (2).<br>• Collaborative care was superior to care as usual, with a small effect size for all anxiety disorders combined and a moderate effect size in a subgroup analysis (five studies) on patients with panic disorder. (3)<br>• Collaborative care that included psychological interventions predicted improvement in depression. Systematic identification of patients and the presence of a chronic physical condition predicted use of anti-depressant medication. This indicates that trials of collaborative care that included psychological treatment, with or without anti-depressant medication, appeared to improve depression more than those without psychological treatment. Compared with usual care, collaborative care was associated with improvements in depressive symptoms and increased anti-depressant use (4).<br>• Participants showed significantly improved depression and treatment intensification, sustained over 12 months of intervention and reduced 10-year cardiovascular disease risk. Mean depression scores after 6 months of intervention for patients with moderate-to-severe depression decreased by | 1. Li, M., Kennedy, E.B., Byrne, N., Gerin-Lajoie., Katz, M.R., Keshavarz, H., Sellick, S., and Green, E. (2016) 'Systematic review and meta-analysis of collaborative care interventions for depression in patients with cancer', in*Psycho-Oncology* 26, pp 573–587.<br><br>2. Van Eck van der Sluijs, J.F., Castelijns, H., Eijsbroek, V., Rijnders, GAT., van Marwijk, H.W.J., and van der Fletz-Cornelis, C.M. (2017) 'Illness burden and physical outcomes associated with collaborative care in patients with comorbid depressive disorder in chronic medical conditions: A systematic review and meta-analysis', in *General Hospital Psychiatry* 50:, pp 14.<br><br>3. Muntingh, A.D.T., van der Feltz-Cornelis, C.M., MArwijk, H.W.J., Spinhoven, P., and Balkom, A.J.L.M. (2016) 'Collaborative care for anxiety disorders in primary care: a systematic review and meta-analysis', in BMC Family Practice 17, pp 62.<br><br>4. Coventry, P.A., Hudson, J.L., Kontopantelis, E., Archer, J., Richards, D.A., Gilbody, S., Lovell, K., Dickens, C., Gask, L., Waheed, W., and Bower, P. (2014) 'Characteristics of Effective Collaborative | HIGH – several systematic reviews have identified a strong evidence base for this intervention |

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
|---|---|---|---|---|
| | | 5.7±1.3 compared with 4.3±1.2 in control, a significant difference, with a 95% confidence range. (5) | Care for Treatment of Depression: A Systematic Review and Meta-Regression of 74 Randomised Controlled Trials', in *PLoS ONE* 9:9.<br><br>5. Morgan, M.A.J., Coates, M.J., Dunbar, J.A., Prasuna, R., and Schlicht, K. (2013) 'The TrueBlue model of collaborative care using practice nurses as case managers for depression alongside diabetes or heart disease: a randomised trial', in In *BMJ Open* 3:1 | |
| Internet-based CBT programs and general e-mental health | Face-to-face CBT sessions require long-term monetary and non-monetary commitment, internet and computer based delivery highlights an opportunity to increases adherence and reduce the demands on the individual.<br><br>Self-guided programs supported by both clinicians and non-clinicians can include lessons with take away assignments, telephone communications and emails or comment posting on forums. | • The review indicated that internet-based CBT interventions, especially with therapist support, were effective. In general, effect sizes of internet-based interventions for symptoms of anxiety were larger than effect sizes for depressive symptoms; however, this might be explained by differences in the amount of therapist support. Interventions for anxiety had a large mean effect size and very low heterogeneity. When examining the second set of subgroups, based on therapist assistance, no significant heterogeneity was found. Interventions with therapist support (n=5) had a large mean effect size, while interventions without therapist support (n=6) had a small mean effect size. (1).<br>• Computerized CBT for anxiety and depressive disorders, especially via the internet, has the capacity to provide effective acceptable and practical healthcare for those who might otherwise remain untreated. The mean effect size superiority was 0.88, and the benefit was evident across all four disorders. Improvement from computerized CBT was maintained for a median of 26 weeks follow-up. Acceptability, as indicated by adherence and satisfaction, was good. Research probity was good and bias risk low. Five studies comparing computerized CBT with traditional face-to-face CBT were identified, and both modes of treatment appeared equally beneficial. (2).<br>• Although more studies were needed, internet and computerised treatments were shown to have promise as potential treatments for depression. Compared with control, internet-based psychological interventions were statistically significantly superior. Subgroup analysis indicated that professional support had a significant impact upon the | 1. Spek, V., Cuijpers, P., Nyklicek, I., Riper, H., Keyzer, J., and Pop, V. (2007) 'Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis', in *Psychological Medicine* 37:3, pp 319-328.<br><br>2. Andrews, G., Cuijpers, P., Craske, M. G., McEvoy, P., and Titov, N. (2010) 'Computer Therapy for the Anxiety and Depressive Disorders Is Effective, Acceptable and Practical Health Care: A Meta-Analysis', in *PLoS ONE*, 5:10.<br><br>3. Andersson G., and Cuijpers P. (2009) 'Internet-based and other computerized psychological treatments for adult depression: a meta-analysis', in *Cognitive Behaviour Therapy* 38:4, pp 196-205.<br><br>4. Wright, B., Tindall, L., Littlewood, E., Allgar, V., Abeles, P., Trepel, D., and Ali, S. (2017) 'Computerised cognitive–behavioural therapy for depression in adolescents: feasibility results and 4-month | HIGH – several systematic reviews have identified a strong evidence base for this intervention |

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
|---|---|---|---|---|
| | | results. Studies that had professional support alongside the intervention had a higher effect size compared with those that offered no professional support. (3).<br>• From baseline to 4 months post intervention, BDI scores and MFQ scores decreased for the Stress busters group but increased in the website group. Quality of life, as measured by the EQ-5D-Y, increased for both groups while costs at 4 months were similar to baseline. Good feasibility outcomes were found, suggesting the trial process to be feasible and acceptable for adolescents with depression. (4). | outcomes of a UK randomised controlled trial', in *BMJ Open* 7:1. | |
| Transcranial magnetic stimulation | Transcracial magnetic stimulation involves the placing of an insulated coil on the scalp and application of time-varying currents, which stimulate the prefrontal cortex of the brain. | • Subjects in study weren't responding to antidepressant medication, TMS was effective in treating major depression. Consistent results were evident across cohort. Active TMS significantly superior to 'sham' TSM. Minimal side effects. (1).<br>• Safe in patients not responding to antidepressant medication. Patients who had not responded to three or more previous antidepressant medications. Long term effect evident – stable maintenance over three months. (2). | 1. O'Reardon, J. P., Solvason, H. B., Janicak, P. G., Sampson, S., Isenberg, K. E., Nahas, Z., Sackeim, H. A. (2007). Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: A multisite randomized controlled trial. Biological Psychiatry, 62(11), 1208-1216. doi:10.1016/j.biopsych.2007.01.018<br><br>2. Levkovitz, Y., Isserles, M., Padberg, F., Lisanby, S. H., Bystritsky, A., Xia, G., Zangen, A. (2015). Efficacy and safety of deep transcranial magnetic stimulation for major depression: A prospective multicenter randomized controlled trial. World Psychiatry, 14(1), 64-73. doi:10.1002/wps.20199 | Moderate – have been undertaken in this area, but additional gold standard research is required. |
| Exercise physiology and social interventions | These interventions are provided by health and physical activity, education, advice and support, and lifestyle modification with a strong focus on achieving behavioural change. | • Exercise therapies led to a modest increase in levels of physical capabilities. No noticeable change for symptoms of mental health (depression, anxiety) or quality of life in respect to physical/mental domains. (1).<br>• Endurance exercise can quickly lead to substantial improvements of mood in patients with severe depression. Complementary treatment while awaiting for antidepressant drugs to take effect. Necessary to reach threshold of energy expenditure/intensity to achieve a clinical reduction of depression. Exercise provides a feeling of body control, distract patients from depressive thought and increases feelings of motivation → increased patient mood. (2). | 1. Pearsall, R., Smith, D. J., Pelosi, A., & Geddes, J. (2014). Exercise therapy in adults with serious mental illness: A systematic review and meta-analysis. BMC Psychiatry, 14(1), 117-117. doi:10.1186/1471-244X-14-117<br><br>2. Knubben, K., Reischies, F. M., Adli, M., Schlattmann, P., Bauer, M. & Dimeo, F. (2007). A randomised, controlled study on the effects of a short-term endurance | Moderate – studies have been undertaken in this area, but additional gold standard research is required. |

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
|---|---|---|---|---|
| | | | training programme in patients with major depression. *British Journal of Sports Medicine*, 41 (1), 29–33 | |
| Post suicide attempt follow up support | This intervention is aimed at preventing suicide by addressing the need for improved discharge planning, referral and support for people at risk of deliberate self-harm or suicide. | • Suicide prevention apps (offering acceptance-based therapy) have the ability to reduce distress and depression but fail to reduce suicide ideation or impulsivity. Specifically successful in lowering mental health symptoms of those living in remote communities. (1).<br>• Mass media campaigns when delivered in succession with multicomponent suicide prevention strategy was found to be most effective in improving behavioural outcomes e.g. suicide knowledge and help-seeking behaviour. Mass media multilevel campaigns → decrease in suicide deaths and or attempts. Standalone campaigns = moderate effect on increasing suicide literacy. Fundamental to campaign success = level of exposure, repeat exposure and community engagement. (2). | 1. Tighe, J., Shand, F., Ridani, R., Mackinnon, A., De La Mata, N., & Christensen, H. (2017). Ibobbly mobile health intervention for suicide prevention in australian indigenous youth: A pilot randomised controlled trial. BMJ Open, 7(1), e013518. doi:10.1136/bmjopen-2016-013518<br><br>2. Torok, M., Calear, A., Shand, F., & Christensen, H. (2017). A systematic review of mass media campaigns for suicide prevention: Understanding their efficacy and the mechanisms needed for successful behavioral and literacy change. Suicide and Life-Threatening Behavior, 47(6), 672-687. doi:10.1111/sltb.12324 | Moderate – studies have been undertaken in this area, but additional gold standard research is required. |
| Dialectical behaviour therapy | Dialectical behaviour therapy (DBT) is a form of psychotherapy that builds upon traditional cognitive behavioural approaches, focusing on psychosocial aspects of treatment. | • The effectiveness of DBT on non-suicidal self-injury has been examined specifically across the adolescent population and has shown to reduce both suicidal and self-injurious behaviours. (1).<br>• Across the wider population including adults from inpatient and outpatient settings and among individuals both with and without suicidal/self-injurious behavioural histories, DBT has illustrated an ability to reduce self-directed violence and rates of psychiatric crisis service usage. (2).<br>• The effectiveness of DBT in reducing suicidal ideation among patients with borderline personality disorder and bipolar has been widely researched. Reductions in self-harm behaviours and suicidality are evident however, when compared with treatment as usual results are similar. (3).<br>• Efficacy of treatment has been demonstrated when analysing the stabilisation of behaviour and improving patient compliance. (4). | 1. Cook, N. E., and Gorraiz, M. (2016). Dialectical behavior therapy for nonsuicidal self-injury and depression among adolescents: Preliminary meta-analytic evidence', *Child and Adolescent Mental Health*, vol. 21, no.2, pp. 81-89.<br><br>2. DeCou, C. R., Comtois, K. A., and Landes, S. J 2018, 'Dialectical behavior therapy is effective for the treatment of suicidal behavior: A meta-analysis', *Behavior Therapy*, doi:10.1016/j.beth.2018.03.009.<br><br>3. Canadian Agency for Drugs and Technologies in Health (CADTH) 2010, 'Dialectical behaviour therapy in adolescents for suicide prevention: | HIGH – several systematic reviews and meta-analysis's have identified a strong evidence base for this intervention |

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
|---|---|---|---|---|
| | | | Systematic review of clinical-effectiveness', *CADTH Technology Overviews*, 1(1).<br><br>4. Panos, P. T., Jackson, J. W., Hasan, O., and Panos, A. 2014, 'Meta-analysis and systematic review assessing the efficacy of dialectical behavior therapy (DBT)', *Research on Social Work Practice*, vol. 24, no.2, pp. 213-223. doi:10.1177/1049731513503047. | |
| Cognitive behavioural therapy | A psycho-social intervention that aims to improve mental health by challenging unhelpful cognitive distortions and behaviours. | • Cognitive behavioural therapy has been well demonstrated as an effective treatment as compared with no-treatment. (1).<br>• Some have reported similar reductions in depressive aetiology as those seen in psychopharmacological interventions range after 12 months of treatment. (2).<br>• Some have reported similar reductions in depressive aetiology as those seen in psychopharmacological interventions range after 12 months of treatment. Efficacy of CBT seems to be affected by patient demographic, with those who are married or who exhibit higher levels of pre-treatment functional attitude seemingly more responsive to treatment that their unmarried counterparts or those showing high levels of dysfunctional attitudes. (3),<br>• CBT is reported to be exhibiting a drop in efficacy, from when it was first introduced as treatment. Some suggest it has reached ceiling effect. (4). | 1. van Straten, A., Geraedts, A., Verdonck-de Leeuw, I., Andersson, G., & Cuijpers, P. (2010). Psychological treatment of depressive symptoms in patients with medical disorders: a meta-analysis. Journal of Psychosomatic Research, 69(1), 23-32.<br><br>2. Siddique, J., Chung, J. Y., Brown, C. H., & Miranda, J. (2012). Comparative effectiveness of medication versus cognitive-behavioral therapy in a randomized controlled trial of low-income young minority women with depression. Journal of consulting and clinical psychology, 80(6), 995.<br><br>3. Driessen, E., & Hollon, S. D. (2010). Cognitive behavioral therapy for mood disorders: efficacy, moderators and mediators. Psychiatric Clinics, 33(3), 537-555.<br><br>4. Baardseth, T. P., Goldberg, S. B., Pace, B. T., Wislocki, A. P., Frost, N. D., Siddiqui, J. R., ... & Minami, T. (2013). Cognitive-behavioral therapy versus other therapies: Redux. Clinical Psychology Review, 33(3), 395-405. | HIGH – several systematic reviews and RCT's have identified a strong evidence base for this intervention |

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
|---|---|---|---|---|
| Medications | General sentence about what they intend to do Antidepressants often result in a number of side effects, making patient compliance challenging. Antidepressants typically include SSRIs and Tricyclic Antidepressants. | • Antidepressants do result in a significant reduction of symptoms greater than that observed in placebos. However, no significant differences have been reported in symptom reduction between psychotherapy, antidepressants, alternative therapies and active intervention controls. (1).<br>• Increases in antidepressant-placebo differences have been reported in clinical trials including higher severity of depression. (2).<br>• Antidepressants have been reported to be more efficacious that psychotherapy in some depressive and anxiety disorders such as dysthymia, but not in others such as obsessive compulsive disorder. (3). | 1. Khan, A., Faucett, J., Lichtenberg, P., Kirsch, I., & Brown, W. A. (2012). A systematic review of comparative efficacy of treatments and controls for depression. PloS one, 7(7), e41778.<br><br>2. Fournier, J. C., DeRubeis, R. J., Hollon, S. D., Dimidjian, S., Amsterdam, J. D., Shelton, R. C., & Fawcett, J. (2010). Antidepressant drug effects and depression severity: a patient-level meta-analysis. Jama, 303(1), 47-53.<br><br>3. Cuijpers, P., Sijbrandij, M., Koole, S. L., Andersson, G., Beekman, A. T., & Reynolds III, C. F. (2013). The efficacy of psychotherapy and pharmacotherapy in treating depressive and anxiety disorders: a meta-analysis of direct comparisons. World Psychiatry, 12(2), 137-148. | Moderate – a number of studies have been undertaken in this area, but additional gold standard research is required. |
| Early intervention for psychosis | Early intervention is a clinical approach for individuals experiencing symptoms of psychosis for the first time. | • Longitudinal studies analysing early intervention for psychosis have illustrated the ability of such interventions to improve the long-term functionality of individuals cognitively, physically and in education and work settings. (1).<br>• Early interventions, when compared with treatment as usual and cognitive behavioural therapy, have been shown in addition to support the delay and/or prevent an individual transitioning to a psychotic state when administered following initial onset. (2).<br>• Evidence suggests that EI's have the ability to minimise strain on healthcare services by reducing admission occurrences for individuals presenting with early stage psychotic symptoms. (3). | 1. Santesteban-Echarri, O., Paino, M., Rice, S., González-Blanch, C., McGorry, P., Gleeson, J. and Alvarez-Jimenez, M 2017, 'Predictors of functional recovery in first-episode psychosis: A systematic review and meta-analysis of longitudinal studies', *Clinical Psychology Review*, vol. 58, pp. 59-75.<br><br>2. Stafford, M.R., Jackson, H., Mayo Wilson, E., Morrison, A.P. and Kendall, T 2013, 'Early interventions to prevent psychosis: systematic review and meta-analysis', *BMJ : British Medical Journal*, vol. 346, no. 7892, pp. DOI: 10.1136/bmj.f185.<br><br>3. Randall, J.R., Vokey, S., Loewen, H., | HIGH – several systematic reviews and RCT's have identified a strong evidence base for this intervention |

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
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| | | | Martens, P.J., Brownell, M., Katz, A., Nickel, N.C., Burland, E. and Chateau, D 2015, 'A Systematic Review of the Effect of Early Interventions for Psychosis on the Usage of Inpatient Services', *Schizophrenia bulletin*, vol. 41, no. 6, pp. 1379-1386. | |
| *Drug and alcohol disorders* | | | | |
| Cognitive remediation | Cognitive remediation targets the cognitive decline associated with drug and alcohol related disorders including *attention, memory, executive functioning, social cognition or meta cognition* to ultimately assist improve functional outcomes.<br><br>Compensatory and restorative approaches built on scientific principles of learning e.g. reinforcement and errorless learning. Remediation is designed to manage or restore cognitive decline through skill acquisition and improve behavioural adaptions. | • Results at 3-month follow-up revealed significant condition effects favouring cognitive training for verbal learning and verbal memory. Condition effects were sustained at 6-month follow-up. At Baseline, 55.9% of participants showed a significant deficit in verbal memory and 58.8% showed a deficit in verbal learning compared with a premorbid estimate of Verbal IQ. At 3-month follow-up there was a significant reduction in the number of participants in the cognitive training condition with clinically significant verbal memory deficits compared with the work therapy alone condition, and a trend toward significance for verbal learning deficits, which was not sustained at 6-month follow-up. The study demonstrates that cognitive training within the context of another activating intervention (work therapy) may have efficacy in remediating verbal learning and memory deficits in patients with alcohol use disorder. (1).<br>• The results of the neuropsychological assessments with the remaining 54 patients showed an overall increase of general cognitive abilities, mental flexibility, psychomotor processing speed, and attentional ability in both experimental and control groups. However, there was a more pronounced improvement specifically in frontal lobe functions from baseline to follow-up in the experimental group but not in the control group. The overall increase in general cognitive function for both experimental and control groups supports the beneficial role of existing alcohol treatment protocols aimed at minimizing withdrawal symptoms, but the differential improvements observed in frontal lobe functioning supports the use of cognitive remediation for neuropsychological stimulation to overcome executive dysfunction in patients with alcohol dependence. (2).<br>• Feelings of self-control were higher in cognitive remediation group (CR) than treatment as usual (TAU) at follow-up and also compared to CR baseline, lack of planning significantly improved in CR between baseline and follow-up, as did total impulsivity scores. Measures of self-regulation | 1. Bell MD, Vissicchio NA, Weinstein AJ. Cognitive training and work therapy for the treatment of verbal learning and memory deficits in veterans with alcohol use disorders. J Dual Diagn. (2016) 12:83–9.<br><br>2. Gamito P, Oliveira J. Executive functioning in alcoholics following an mHealth cognitive stimulation program: randomized controlled trial. J Med Internet Res. (2014) 16:e102.<br><br>3. Brooks SJ, Wiemerslage L, Burch KH, Maiorana SA, Cocolas E, Schiöth HB, et al. . The impact of cognitive training in substance use disorder: The effect of working memory training on impulse control in methamphetamine users. Psychopharmacology (2017) 234:1911–21.<br><br>4. Rezapour T, Hatami J, Farhoudian A, Sofuoglu M, Noroozi A, Daneshmand R, et al. Cognitive rehabilitation for individuals with opioid use disorder: a randomized controlled trial.<br>Neuropsychol Rehabil. (2017) 27:1–17.<br><br>5. Bell MD, Laws HB, Petrakis IB. A randomized controlled trial of cognitive | HIGH – several RCT's have identified a strong evidence base for this intervention |

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
|---|---|---|---|---|
| | | were improved in the CR group compared to TAU at follow-up, in total score, receiving score and searching score. Implementing self-regulation was higher in the CR group compared to TAU (3).<br>• Analysis illustrated that the cognitive remediation (CR) group performed significantly better in tests of learning, switching, processing speed, working memory and memory span. Moreover, the CR group had significantly lower opiate use over the control group during 3-months follow-up. Analysis including only those with a history of methamphetamine use showed that the CR group had significantly lower amphetamine use. No group differences were observed for treatment retention. Findings provide evidence that adding CR as an adjunct intervention to methadone maintenance treatment can improve cognitive performance as well as abstinence from both opiates and stimulants. (4).<br>• Mixed effects models of cognitive change over time revealed significant differences favoring CR on working memory (WM) and executive function indices. Global index of cognition showed a non-significant trend favoring CR. CR was well accepted by outpatient veterans with substance use disorders and led to significant improvements in WM and executive functions beyond that of normal cognitive recovery. (5).<br>• *Schizophrenia* - CR was associated with significant improvements in cognitive functioning, symptoms and functional outcomes. Medium effect size for cognitive performance, similar effect for psychosocial functioning and a small effect for symptoms. The effects of cognitive remediation on psychosocial functioning were significantly stronger in studies that provided adjunctive psychiatric rehabilitation than in those that provided cognitive remediation alone. (6). | remediation and work therapy in the early phase of substance use disorder recovery for older veterans: neurocognitive and substance use outcomes. Psychiatr Rehabil J. (2017) 40:94.<br><br>6. Kaneko, Y., and Keshavan, M 2012, 'Cognitive remediation in schizophrenia. Clinical psychopharmacology and neuroscience', *The scientific journal of the Korean College of Neuropsychopharmacology*, vol. 10, no.3, pp. 125-35. | |
| Brief intervention | Time limited intervention focused on changing behaviour.<br><br>Brief interventions can involve knowledge sharing, the provision of advise and dissemination of awareness, motivational interviewing or skill-based counselling and goal setting. | • Three-month follow-up assessments based on repeated measures analysis of variance techniques found a decrease in the mean number of cannabis use days in the total sample, reduced deep inhalation/breath holding use and reduced driving after cannabis use compared with controls. Feasibility and short-term impact of the BIs were demonstrated. (1).<br>• Results demonstrated that patients receiving brief interventions had a greater reduction in alcohol consumption compared to those in control groups at six month and nine months follow up. However this was not maintained at one year. Self-reports of reduction of alcohol consumption at 1 year were found in favour of brief interventions, in addition there were significantly fewer deaths in the groups receiving brief interventions than | 1. Fischer B, Dawe M, McGuire F, Shuper PA, Capler R, Bilsker D, et al. Feasibility and impact of brief interventions for frequent cannabis users in Canada. Journal of Substance Abuse Treatment. 2013;44(1):132–8.<br><br>2. McQueen J, Howe TE, Allan L, Mains D, Hardy V. Brief interventions for heavy alcohol users admitted to general hospital | HIGH – several RCT's have identified a strong evidence base for this intervention |

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
|---|---|---|---|---|
| | Involve the exchange of feedback and discussion on responsibility and self-efficacy in an attempt to elicit behavioural adjustment thoughts.<br><br>Examples:<br>- Informal discussions around drug use in a youth drop-in centre<br>- Telephone services such as Kids Helpline<br>- One-to-one counselling<br>- Self-help manuals<br>- Computer based quizzes | in control groups at 6 months and one year follow up. Screening (asking participants about their drinking patterns) may also have a positive impact on alcohol consumption levels and changes in drinking behaviour. Results of this review indicate that there are benefits to delivering brief interventions to heavy alcohol users admitted to general hospital wards in terms of reduction in alcohol consumption and death rates. (2).<br>• Motivational interviewing (a form of brief intervention) was partially successful, with the most encouraging results relating to harm minimisation. Long-term follow-up trials using motivational interviewing reported significant reductions in alcohol intake and harmful effects, however this may be partially attributed to a normal maturation trend to a steady reduction in alcohol consumption. (3).<br>• Reduction in drinking was evident one year after a brief intervention had been deployed. Both men and women reduced their drinking equally after receiving a brief intervention. The study found moderate-quality evidence that brief interventions can reduce alcohol consumption in hazardous and harmful drinkers compared to minimal or no intervention. (4). | wards. Cochrane Database of Systematic Reviews 2011, Issue 8.<br><br>3. Wachtel, T. and Staniford, M. (2010), The effectiveness of brief interventions in the clinical setting in reducing alcohol misuse and binge drinking in adolescents: a critical review of the literature. Journal of Clinical Nursing, 19: 605-620.<br><br>4. Kaner EFS, Beyer FR, Muirhead C, Campbell F, Pienaar ED, Bertholet N, et al. Effectiveness of brief alcohol interventions in primary care populations. Cochrane Database Syst Rev 2018:CD004148. | |
| Opioid supplementary therapy | Management of opioid dependency through supplementary therapy involves long-term managed administration of an opioid.<br><br>The therapy aims to create homeostasis of an individual's neurochemistry.<br><br>The therapy intends to supress opioid withdrawal symptoms and minimise the effect of intoxication e.g. euphoria or sedation. | • Supplementary therapy has shown to result in effects beyond the reduction of drug abuse including improved treatment retention rates and a reduction in risk related behaviours related to HIV/sexually transmitted diseases. (1).<br>• When analysing treatment retention rates and suppression of usage, methadone maintenance treatment, a widely used supplementary therapy, has been shown to superior when compared with traditional detoxification treatments. (2).<br>• A reduction in levels of crime and mortality has also been shown to be associated with opioid supplementary therapies when compared to no therapy placebo groups. (3). | 1. Ferri M, Davoli M, and Perucci CA 2011, 'Heroin maintenance for chronic heroin-dependent individuals', *Cochrane Database of Systematic Reviews*, Issue 12. Art. No.: CD003410. DOI: 10.1002/14651858.CD003410.pub4.<br><br>2. Amato L, Davoli M, Perucci CA, Ferri M, Faggiano F, and Mattick RP 2005, "An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research", *Journal Substance Abuse Treatment*, vol. 28, pp. 321–329.<br><br>3. Connock M, Juarez-Garcia A, Jowett S, Frew E, Liu Z, Taylor RJ, et al. Methadone and buprenorphine for the management of | |

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
|---|---|---|---|---|
| | | | opioid dependence: a systematic review and economic evaluation. Health Technol. 2007;11:1–171. | |
| *Neurological diseases* | | | | |
| Exercise therapy | Types of exercise include resistance, flexibility and coordination training.<br><br>Multidisciplinary focus, biomedical physical improvements and regaining cognitive functions.<br><br>Focus on enhancing recovery and quality of life. | • Trials assessed the effects of exercise on physical and mental health. Two trials compared exercise to standard care and both found exercise to significantly improve negative symptoms of mental state, although no absolute effects were found for positive symptoms of mental state. Physical health improved significantly in the exercise group compared to those in standard care, but no effect on peoples' weight/BMI was apparent. One trial compared exercise with yoga and found that yoga had a better outcome for mental state, the trial also found those in the yoga group had significantly better quality of life scores. Although studies included in this review are small and used various measures of physical and mental health, results indicated that regular exercise programs are possible in this population, and that they can have positive effects on both the physical and mental health and well-being of individuals with schizophrenia.(1).<br>• *Mixed* - Exercise was shown to have selective benefits for cognitive functioning by improving frontal lobe based executive function. No significant effects were demonstrated for mood or disease-specific quality of life. These results are consistent with previous research demonstrating selective benefits of exercise for executive function among normal ageing adults and PD.(2).<br>• Statistically significant differences in favor of the exercise (FAME) group were noted on all measures of impairment and activity post intervention. These improvements were persisted at the 3-month follow-up but only walking was statistically significant. Participants in the FAME group were also significantly more integrated into their community at follow-up. Family members in the FAME group reported a significant decrease in their levels of caregiver strain at the follow-up when compared with those in the control group. This evidence-based FAME intervention can serve to optimize patient recovery and family involvement after acute stroke at the same time as being mindful of available resources. (3).<br>• The meta-analysis illustrates that stroke survivors may benefit from cardiovascular exercise during sub-acute stages to improve peak oxygen | 1. Gorczynski P, Faulkner G. Exercise therapy for schizophrenia. Cochrane Database of Systematic Reviews 2010, Issue 5.<br><br>2. Cruise KE, Bucks RS, Loftus AM, Newton RU, Pegoraro R, Thomas G. Exercise and Parkinson's: benefits for cognition and quality of life. Acta Neurol Scand: 2011: 123: 13–19.<br><br>3. Galvin R., Cusack T., O'Grady E., Murphy T. B., & Stokes E. (2011). Family-mediated exercise intervention (FAME): Evaluation of a novel form of exercise delivery after stroke. Stroke, 42, 681–686.<br><br>4. Stoller, O., de Bruin, E. D., Knols, R. H., & Hunt, K. J. (2012). Effects of cardiovascular exercise early after stroke: systematic review and meta-analysis. *BMC neurology*, *12*, 45.<br><br>5. Duchesne C, Lungu O., Nadeau, A., et al. 2015, 'Enhancing both motor and cognitive functioning in Parkinson's Disease: aerobic exercise as a rehabilitative intervention', *Brain Cognition*, vol. 99, pp. 68-77. | HIGH – several systematic reviews and RCT's have identified a strong evidence base for this intervention |

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
|---|---|---|---|---|
| | | uptake and walking distance. Thus, cardiovascular exercise should be considered in sub-acute stroke rehabilitation. (4).<br>• The exercise program was effective in illustrating significant improvement in aerobic capacity in all participants. The program improved inhibition but not flexibility, and motor learning skill, in both groups. *Results* suggest that exercise programs can be a valuable non-pharmacological interventions to promote physical fitness in early Parkinson's disease, but also to improve cognitive and procedural functioning of suffers. (5). | | |
| Deep brain stimulation | Adjustable, reversible, non-destructive neurological intervention.<br><br>Electrodes are surgically implanted into specific targeted regions within the brain. The electrodes send impulses controlling discrete functions. | • Deep brain stimulation (DBS) has provided remarkable therapeutic benefits for people with a variety of neurological disorders. Despite the uncertainty of the precise mechanisms underlying its efficacy, DBS was clinically effective in improving motor function of essential tremor, Parkinson's disease and primary dystonia and in relieving obsessive-compulsive disorder. (1).<br>• *Mixed* - At 6 months significant improvements in off-period motor symptoms and activities of daily living were paralleled by significant reductions in the total, physical, and psychosocial scores in both treatment groups. At 3 years, sustained improvements were observed in the physical dimension score after DBS. All other scores approached baseline values, but were still the same or better whereas motor functioning remained stable after 36 months. DBS led to significant early improvements in quality of life. Despite sustained motor improvements many of these initial benefits were lost after 3 years, reflecting either progression of the disease or adaptive changes in the subjective perception of health-related wellbeing over time.(2).<br>• DBS drove neural activity in the memory circuit and activated the brain's default mode network. PET scans illustrated an early and striking reversal of the impaired glucose utilization in the temporal and parietal lobes that was maintained after 12 months of continuous stimulation. Evaluation of the Alzheimer's Disease Assessment Scale cognitive subscale and the Mini Mental State Examination suggested possible improvements and/or slowing in the rate of cognitive decline at 6 and 12 months in some patients. There were no serious adverse events. (3).<br>• Evidence for the use of DBS to treat dementia was preliminary. Fornix and nucleus basalis of Meynert DBS can influence activity in the pathologic neural circuits that underlie AD and Parkinson disease dementia. Further | 1. hen X, L, Xiong Y, Y, Xu G, L, Liu X, F: Deep Brain Stimulation. Intervent Neurol 2012;1: 200-212.<br><br>2. Volkmann J, Albanese A, Kulisevsky J, et al. Long-term effects of pallidal or subthalamic deep brain stimulation on quality of life in Parkinson's disease. Mov Disord. 2009;24(8):1154–1161.<br><br>3. Laxton, A. W., Tang-Wai, D. F., McAndrews, M. P., Zumsteg, D. , Wennberg, R. , Keren, R. , Wherrett, J. , Naglie, G. , Hamani, C. , Smith, G. S. and Lozano, A. M. (2010), A phase I trial of deep brain stimulation of memory circuits in Alzheimer's disease. Ann Neurol., 68: 521-534.<br><br>4. Laxton, W., Lozano, A. (2013). Deep Brain Stimulation for the Treatment of Alzheimer Disease and Dementias. World Neurosurgery, 80.<br><br>5. Smith GS, Laxton AW, Tang-Wai DF, et al. Increased Cerebral Metabolism After 1 Year of Deep Brain Stimulation in Alzheimer Disease. *Arch Neurol.* 2012;69(9):1141–1148. | Moderate – a number of studies have been undertaken in this area, but additional gold standard research is required. |

| Intervention type | Description | Effectiveness of intervention | References | Strength of evidence |
|---|---|---|---|---|
| | | investigation into the potential clinical effects of DBS for dementia is warranted. (4).<br>• After one year of DBS increased connectivity was observed in Alzheimer's patients (consistent with decreased connectivity over progression). Cortical metabolism associated with positive clinical outcomes in patients was increased post treatment are was greater than the benefits achieved by the pharmacotherapy group. Increased metabolism after one year of DBS was correlated with better outcomes in global cognition, memory, and quality of life . (5) .<br>• DBS elicited sustained (6 months) clinical / behavioral changes or remission within the subjects without alterations to medications being made. PET scans illustrated positive alterations mirroring those of antidepressants in the cerebral networks within the brain associated with depression. (6). | | |
| Thrombolytic therapy | Thrombolytic interventions (TI) involve the administration of medications that rapidly dissolve clots associated with strokes, restoring blood flow is crucial in avoiding brain damage and encouraging recovery. | • Medications administered within the first three hours after an occurrence of a stroke illustrate the greatest results in the proportion of deaths and individuals that become dependent. TI however, have been shown to result in increases in symptomatic intracranial haemorrhage, mortality at seven and ten days and death at final follow up. (1).<br>• Follow up studies have illustrated the ability of TI to maintain decreased in disability and when compared with a control group equality in deaths was demonstrated. (2). | 1. Wardlaw, JM., Murray, V., Berge, E., and del Zoppo, GJ. 2014, 'Thrombolysis for acute ischaemic stroke', *Cochrane Database of Systematic Reviews*, Issue 7. Art. No.: CD000213. DOI: 10.1002/14651858.CD000213.pub3.<br><br>2. Sandercock, P., Wardlaw, J.M., Lindley, R.I., Dennis, M., Cohen, G., Murray, G., Innes, K., Venables, G., Czlonkowska, A., Kobayashi, A., Ricci, S., Murray, V., Berge, E., Slot, K.B., Hankey, G.J., Correia, M., Peeters, A., Matz, K., Lyrer, P., Gubitz, G., Phillips, S.J., Arauz, A. & IST-3 collaborative group 2012, 'The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial', Lancet, vol. 379, no. 9834, pp. 2352-2363. | Moderate – a number of studies have been undertaken in this area, but additional gold standard research is required. |

# APPENDIX D – Supplementary evidence paper (ROI)

| Intervention/focus area | Evidence/findings | References | Strength of evidence |
|---|---|---|---|
| Exercise therapy | The intervention cost of exercise therapy is more cost-effective that treatment as usual for people with dementia. | D'Amico F, et al. 2016, 'Cost-effectiveness of exercise as a therapy for behavioural and psychological symptoms of dementia within the EVIDEM-E randomised controlled trial', *International Journal of Geriatric Psychiatry*, vol. 31, no. 6, pp. 656-665. | HIGH - The outcome also measures quality adjusted life years that has an implication for policy and health practice. |
| Thrombolytic treatment | Modelling the effectiveness of thrombolytic treatment by measuring the treatment cost and gain from QALYs. | Pandya, A et al. 2016, 'Modeling the cost effectiveness of neuroimaging-based treatment of acute wake-up stroke', *Plos One*, DOI: 10.1371 | HIGH - Simulation model includes variable of short term and long-term health and cost outcomes under different treatment and assumptions. |
| | Both thrombolytic treatment of stent retriever thrombectomy pus tissue-type plasminogen activator (SST+tPA) and tPA only are cost-effective for people with ischemic stroke. SST-tPA treatment provides higher cost-saving of hospitalization costs and substantial gains in quality-adjusted life year. | Shireman, TI et al. 2017, 'Cost-effectiveness of solitaire stent retriever thrombectomy for acute ischemic stroke', *Stroke*, DOI; 10.1161 | |
| Internet-based CBT (iCBT) | Estimate total cost per patient for the iCBT treatment, which is more cost-effective than treatment as usual (TAU). The approach estimates not only healthcare perspective but also from societal perspective. | Holst, A et al. 2018, 'Cost-effectiveness analysis of internet-mediated cognitive behavioural therapy for depression in the primary care setting: results based on a controlled trial', *BMJ Open*, 8. | HIGH – several systematic reviews have identified a strong evidence base for this intervention |
| | The iCBT and physical exercise treatment are more cost-effective compared with treatment as usual (TAU). | Kraeplien, M et al. 2018, 'Cost-effectiveness of internet-based cognitive-behavioural therapy and physical exercise for depression', *BJPsych open*, vol. 4, pp. 265-273. | |

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| Brief intervention | The study estimated the cost effectiveness and health gains from brief intervention program for people with alcohol disorders. | Purshouse et al. 2013, 'Modelling the cost-effectiveness of alcohol screening and brief interventions in primary care in England', *Alcohol and Alcoholism*, vol. 48, no. 2, pp. 180-188. | HIGH –Evidence from the RCT was from 31 primary care providers and program has been implemented for 10 years with a regular yearly assessment. |
| | The 12-month brief intervention for risk drinkers was significantly associated with reductions in alcohol consumption, physician visits and emergency department (ED) visits. | Ettner et al. 2014, 'The effect of an educational intervention on alcohol consumption at risk drinking, and health care utilisation in older adults: the Project SHARE study, *Journal of Studies on Alcohol and Drug*s, vol. 75, no. 3, pp. 447-457. | |
| Opioid treatment | Systematic review of opioid-use-disorder therapy, in particular the methadone-maintenance therapy. In general, the review confirms evidence from previous findings that the treatment is a cost-effective. | Murphy, SM, Polsky, D, 2017, 'Economic evaluations of opioid use disorder interventions: a systematic review', *Pharmacoeconomics*, vol. 34, no. 9, pp. 863-887. | HIGH -Systematic review from 98 articles (including RCTs) of economic evaluation of interventions for opioid use disorders. |
| | Estimate the cost of opioid treatment of injectable and oral methadone for 6 months programs. The study also measures QALYs gained after the treatment. | Byford, S et al. 2013, 'Cost-effectiveness of injectable opioid treatment v. oral methadone for chronic heroin addiction', *The British Journal of Psychiatry*, vol. 203, pp. 341-349. | |
| Psychosis | Determine the average annual cost of psychosis, comprising in lost productivity and cost to society. | Neil, AL et al. 2014, 'Costs of psychosis in 2010: Findings from the second Australian National Survey of Psychosis', Australian & New Zealand Journal of Psychiatry, vol.48, no. 2, pp. 169-182. | HIGH – Strong evidence from longitudinal survey of Psychosis. |
| Cost of illness method – burden of disease | Introduce a variety of methods in estimating the cost-of-illness related to mortality, morbidity and disability. | Jo, C 2014, 'Cost-of-illness studies: concepts, scopes and methods', *Clinical and Molecular Hepatology*, DOI;10.3350/cmh.2014.20.4.327 | HIGH – Methods are applicable to most disease cases. The concept and scope are |

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| | | | updated to latest studies. |