Deloitte.
Access Economics

# Cost effectiveness of continuous positive airway pressure for obstructive sleep apnoea

Sleep Health Foundation

October 2018

Deloitte.
Access Economics

Deloitte Access Economics Pty Ltd
ACN 149 633 116
8 Brindabella Circuit
Brindabella Business Park
Canberra Airport
Canberra, ACT, 2609
Australia

Phone: +61 2 6263 7000
Fax: +61 2 6263 7004
www.deloitte.com.au

31 October 2018

Professor David Hillman
Deputy Chair
Sleep Health Foundation
Suite 114, 30 Campbell Street,
Blacktown NSW 2148

Dear Professor Hillman

**Cost effectiveness of continuous positive airway pressure for OSA**

Following our earlier work to estimate the costs of inadequate sleep in Australia, this report estimates the cost effectiveness of continuous positive airway pressure (CPAP) as a treatment for OSA in adults. The report aims to inform the evidence base for cost effective interventions to treat the large economic cost and reduce the burden of disease due to inadequate sleep stemming from sleep disorders in Australia.

We hope this report continues to aid your efforts to promote sleep health in Australia and ensure available resources are directed towards the most effective interventions.

If you would like to discuss any elements of the report, please do not hesitate to contact me.

Yours sincerely

**Lynne Pezzullo**
Lead Partner, Health Economics and Social Policy, Deloitte Access Economics Pty Ltd
Office Managing Partner, Canberra, Deloitte Touche Tohmatsu

# Contents

# Charts



# Tables



# Figures

# Glossary

| | |
|---|---|
| ABS | Australian Bureau of Statistics |
| AHI | apnoea-hypopnoea index |
| AIHW | Australian Institute of Health and Welfare |
| ASA | Australasian Sleep Association |
| CEA | cost effectiveness analysis |
| CPAP | continuous positive airway pressure |
| DALY | disability adjusted life year |
| ESS | Epworth sleepiness scale |
| GP | general practitioner |
| ICER | incremental cost effectiveness ratio |
| MBS | Medicare Benefits Schedule |
| MVA | motor vehicle accident |
| NHMRC | National Health and Medical Research Council |
| OSA | obstructive sleep apnoea |
| PAF | population attributable fraction |
| PICO | population, intervention, comparator, outcomes |
| PSG | polysomnography |
| QALY | quality adjusted life year |
| UK | United Kingdom |
| US | United States |

# Executive summary

## Introduction

Obstructive sleep apnoea (OSA) is common in Australia. Deloitte Access Economics (2011) estimated that the financial and burden of disease impacts of moderate-severe OSA and its associated impacts cost Australians $21.2 billion per year.[1]

Continuous positive airway pressure (CPAP) is a safe and effective treatment for OSA. CPAP not only reduces the symptoms of OSA, it also has demonstrable effects on outcomes for cardiovascular disease, depression, type 2 diabetes, accidents and quality of life.

In 2011, as part of an analysis of the economic costs of sleep disorders in Australia (total = $36.4 billion per year), Deloitte Access Economics conducted a cost effectiveness analysis (CEA) of CPAP for OSA and found that it was cost effective from a health system perspective, and dominant – cost saving with a gain in wellbeing – from a societal viewpoint.

More recently, Deloitte Access Economics (2017) estimated the total cost of inadequate sleep in Australia at $66.3 billion per year. However, that report did not contain a CEA of CPAP. This report updates that exercise from 2011 with the new data from the 2017 report and recent literature, using a population, intervention, comparator and outcome ("PICO") approach.

The PICO developed for this study is summarised in Table i.

Table i: Summary of the PICO

| |
|---|
| **Population:**<br>People with diagnosed OSA. |
| **Intervention:**<br>CPAP therapy – either manual or automatic titration – initiated by either a sleep specialist or a suitably credentialed general practitioner (GP) with long term follow up. |
| **Comparator:**<br>No treatment. |
| **Outcomes:**<br>• OSA severity (measured through the apnoea-hypopnoea index - AHI);<br>• non-fatal outcomes due to coronary artery disease, stroke, congestive heart failure, depression, motor vehicle accidents (MVAs), workplace accidents, and type 2 diabetes;<br>• fatal outcomes due to coronary artery disease, stroke, congestive heart failure, depression, MVAs, workplace accidents, and type 2 diabetes;<br>• health system resource utilisation;<br>• productivity improvements, including the effect on informal care;<br>• changes in other financial costs, including aids and modifications, other costs to government and to society; and<br>• change in wellbeing (measured using DALYs). |

Source: Deloitte Access Economics.

## Methodology

To model the cost effectiveness of CPAP as a management strategy for people with OSA, a two arm cost effectiveness model was developed based on the work of Hillman et al (2018). The objective was to design a clinically and economically appropriate model that could estimate not only costs directly due to OSA, but also

[1] Moderate-severe OSA is defined as an AHI>15.

costs that are associated with OSA through conditions such as cardiovascular disease, diabetes, depression, MVAs and workplace accidents[2].

Earlier work by Deloitte Access Economics (2017) and Hillman et al (2018) has established the evidence base to estimate the costs of sleep disorders, and the conditions associated with sleep disorders, through measures of inadequate sleep.

Hillman et al (2018) used a cost of illness framework to estimate the costs. In the cost of illness framework, a population attributable fraction (PAF) approach was used to estimate the prevalence and costs of conditions that are associated with OSA, including:

- coronary artery disease;
- stroke;
- congestive heart failure;
- depression;
- MVAs;
- workplace accidents; and
- type 2 diabetes.

To determine the effectiveness of CPAP therapy for people with OSA, the model links the number of AHI events per hour to secondary outcomes – non-fatal conditions that are attributed to OSA, and fatal outcomes due to the attributed conditions – by adjusting the relative risk for people who adhere to CPAP therapy. It was assumed that there would be no benefits for people who do not adhere to CPAP therapy, as there was limited evidence to assess the extent of non-adherence and the likely diminished effect size.

The rate at which CPAP was assumed to prevent conditions attributed to OSA was based on the PAFs before and after treatment (section 2.2). It was assumed that people needed to adhere to treatment for a period of five years before benefits occur (in the fifth year), with the exception of MVAs and workplace accidents as an observable reduction in accident risk occurs within days of commencing CPAP therapy (Rodenstein, 2009). The model considers the annual costs and benefits of CPAP therapy, so a discount rate has been used to bring benefits forward where they are expected to occur after a period of time. Benefits and costs were discounted using a discount rate of 3%.

Cost effectiveness was assessed from two perspectives, including:

- a health care system perspective, where costs of the intervention and associated health care resource utilisation are compared with the change in quality of life for people with OSA; and
- a societal perspective, where the net cost of the intervention incorporates health care resource utilisation, productivity losses, informal care costs and other financial costs, which is then compared to the change in quality of life for people with OSA.

### Results

The results of the CEA are shown in Table ii. The net cost of CPAP therapy from the perspective of the health care system was estimated to be $550 dollars per person per year. From the perspective of society (including other financial costs avoided) the intervention was estimated to save $470 per person per year.

It was estimated that CPAP therapy would avoid 0.0305 DALYs per person per year. From the perspective of the health care system, the incremental cost effectiveness ratio (ICER) was estimated to be $18,043 per DALY averted. From the perspective of society, the ICER was estimated to be dominant – meaning the intervention both saves money and improves wellbeing.

[2] The analysis has been limited to workplace accidents that result in an injury occurring.

Table ii: Results of the CEA

| | Health care system perspective | Societal perspective |
|---|---|---|
| Cost of treatment ($ per person per year) | 660 | 660 |
| Total costs avoided due to OSA ($ per person per year) | -110 | -1,130 |
| Net cost ($ per person per year) | 550 | -470 |
| DALYs averted (per person per year) | 0.0305 | 0.0305 |
| **ICER ($/DALY averted)** | **18,043** | **Dominant** |

Source: Deloitte Access Economics' calculations. Note: results derived based on the components in table may differ due to rounding. Dominant indicates that the intervention both saves money and improves wellbeing.

From the perspective of the health care system, the ICER ranged from $12,949 per DALY averted to $25,708 per DALY averted. From the perspective of society, the ICER ranged from $-21,186 per DALY averted (dominant) to -$8,538 per DALY averted (dominant).

## Conclusion

Given the substantial burden of OSA in Australia, cost effective interventions to treat OSA are essential to improve wellbeing and reduce the burden on the health care system and society more broadly.

CPAP therapy is a safe and effective treatment for OSA. CPAP not only reduces the symptoms of OSA, it also has demonstrable effects on outcomes for cardiovascular disease, depression, type 2 diabetes, accidents and wellbeing for people with OSA.

However, the efficacy of CPAP depends critically on adherence – CPAP is a treatment for OSA but not a cure. Some authorities suggest that CPAP should be used for a minimum of 4 hours per night for 7 nights out of every 10. Based on a literature review (Appendix A), it was assumed that close to half (56.7%) of people with OSA who are initiated on CPAP therapy will still be adherent after 5 years, and therefore receive benefits from CPAP. However, the risk of accidents is reduced immediately.

CPAP was estimated to be cost effective from the perspective of the health care system - using CPAP for OSA costs $18,043 per DALY avoided. Including societal costs such as lost productivity and carer costs, it was estimated that CPAP would be dominant – saving money for each DALY averted. These results are particularly important for funding bodies who are tasked with identifying cost effective interventions to reduce the costs of conditions with high burden in Australia.

Where relevant, strategies should be considered to improve adherence levels to maximise the benefits from CPAP therapy. It has been shown that supportive and educational interventions can have an impact on compliance, with a study finding the share of patients using CPAP for at least 4 hours per night to be 59% without supportive interventions compared to 75% with them (Wozniak et al 2014). More work is warranted in this area.

# 1 Introduction

## 1.1 Background

Deloitte Access Economics (2011) estimated the economic costs – including financial impacts and loss of wellbeing - of sleep disorders in Australia at $36.4 billion per year. The majority of these costs ($21.2 billion) were due to OSA – a sleep disorder characterised by sleep-related intermittent upper airway obstruction.

OSA is associated with episodes of oxygen desaturation and sleep fragmentation. OSA is commonly quantified by the AHI, which measures the number of obstructive and central apnoea or hypopnoea episodes per hour of sleep.

CPAP is a common form of treatment for people with OSA, although it is a method of managing OSA and not a cure. CPAP can reduce symptoms of OSA and has the potential for long term reductions in associated risks for people who comply with the recommended treatment (CADTH, 2017). CPAP therapy is delivered using a CPAP device, which consists of a mask worn over the nose, or nose and mouth, while sleeping. The device is connected by a tube to a small electric pump that provides a flow of positively pressurised air. The air acts as a 'splint' holding the upper airway open thereby preventing the occurrence of obstructive events (McDaid et al 2009).

Deloitte Access Economics (2011) previously estimated the cost effectiveness of using CPAP to treat OSA as part of their evaluation of the economic costs and sleep disorders, drawing upon health system expenditure, loss of employment and other financial impacts established in other sections of that report.

Deloitte Access Economics (2017) subsequently estimated the costs of all forms of inadequate sleep in Australia – $66.3 billion per year – noting that the majority of inadequate sleep is due to lifestyle factors rather than sleep disorders. Financial costs such as health system expenditure and lost jobs accounted for $26.2 billion of this, and loss of wellbeing was $40.1 billion. However, that report did not analyse the cost effectiveness of potential interventions to reduce the burden of inadequate sleep or sleep disorders in Australia.

A number of international studies have assessed the cost effectiveness of CPAP as a treatment for OSA. More recent studies have found that CPAP is a cost effective intervention for OSA. For example, CPAP was found to be a cost effective therapy in the United Kingdom (UK), United States (US), Canada, and France, with ICERs ranging from £3,899 per quality adjusted life year (QALY) gained to about €35,664 per QALY gained depending on severity (McDaid et al, 2009; CADTH, 2017; Poullie et al, 2016; Pietzch et al (2011)). CPAP is less cost effective for mild OSA (results not shown). Table 1.1 presents a brief summary of some recent CEAs.

To our knowledge, there are no CEAs conducted from the perspective of the Australian health care system in peer reviewed literature. Furthermore, there are very few CEAs that considered the cost effectiveness of CPAP from a societal perspective. The purpose of this report is to provide recent estimates for both perspectives in the Australian setting, recognising that the findings are likely to be generalisable to similar Organisation for Economic Co-operation and Development (OECD) economies around the world.

This current report draws upon the financial and burden of disease parameters from OSA in Deloitte Access Economics (2017) and efficacy parameters from published literature. The report uses a PICO approach to estimate the cost effectiveness of CPAP.

Table 1.1: Brief summary of cost effectiveness literature

| Source/description | Findings |
|---|---|
| Pietzch et al (2011) adopted a 10-year and lifetime Markov approach to estimate the cost effectiveness of CPAP therapy for OSA in the US. | ICER = $15,915/QALY. |
| Poullie et al (2016) conducted a CEA of CPAP therapy for OSA in France. They utilised a Markov model with two representative cohorts stratified by cardiovascular risk to model the impact of CPAP on cardiovascular risk and health system costs. | For those with high cardiovascular risk, ICER = €10,128/QALY. |
| CADTH (2017) developed a decision-analytic Markov model to assess the effectiveness and cost of CPAP treatment for OSA, compared against a baseline of no treatment, in Canada from the health care system perspective. This modelled the impact of CPAP on AHI and hypertension, MVAs, myocardial infarction, stroke, and mortality. | For moderate and severe OSA, ICER = $8,058/QALY and $7,420/QALY, respectively. |
| McDaid et al (2009) used a cost utility analysis to compare CPAP with the use of dental devices and conservative management in the treatment of OSA in the UK. Cost utility was modelled using a Markov state transition cohort model, where outcomes included heart disease, MVAs, stroke, and mortality. | For females and males with moderate OSA, ICER = £4,335/QALY and £3,899/QALY, respectively. |

Source: as noted in table.

## 1.2 PICO

Table 1.2 summarises the PICO developed for this study. The PICO approach is described in more detail in the following sections.

Table 1.2: Summary of the PICO

**Population:**
People diagnosed with OSA.

**Intervention:**
CPAP therapy – either manual or automatic titration – initiated by either a sleep specialist or a suitably credentialed GP with long term follow up.

**Comparator:**
No treatment.

**Outcomes:**

- OSA severity (measured through AHI);
- non-fatal outcomes due to coronary artery disease, stroke, congestive heart failure, depression, motor vehicle accidents (MVAs), workplace accidents and type 2 diabetes;
- fatal outcomes due to coronary artery disease, stroke, congestive heart failure, depression, MVAs, workplace accidents, and type 2 diabetes;
- health care resource utilisation;
- productivity improvements, including the effect on informal care;
- changes in other financial costs, including aids and modifications, other costs to government and to society; and
- change in wellbeing (measured using DALYs).

Source: Deloitte Access Economics.

**Population**
Treatment with CPAP should be based on a prior diagnosis of OSA (ASA[3], 2009). Diagnosis consists of an initial consultation, a sleep study – laboratory polysomnography (PSG) (level 1), home PSG (level 2) or limited channel sleep studies[4] (level 3 or level 4) – a follow-up consultation and a treatment prescription.

Therefore, the eligible population includes Australian adults aged 20 and over with diagnosed OSA.

**Intervention**
The pathway for the analysis has been developed based on consultation with experts (in July 2018) and a review of existing guidelines for Australia and the US (ASA, 2009; Epstein et al, 2009).

PSG or home testing with portable monitors are both accepted methods of establishing an initial diagnosis of OSA. To determine the optimal positive airway pressure titration, in-laboratory full-night PSG is the preferred approach (Epstein et al, 2009). Follow-up PSG is recommended in patients with substantial weight loss or weight gain, when clinical response is insufficient or symptoms return, but it is not required if CPAP treatment resolves symptoms (Epstein et al, 2009).

Close follow-up of problems and usage by suitable personnel is recommended to address problems and establish effective usage patterns (Epstein et al, 2009; ASA, 2009), with appointment on a yearly basis (ASA, 2009). In managing treatment, a multidisciplinary care team consisting of the referring physician, a sleep specialist, nurses, respiratory therapist and sleep technologist is ideal (Epstein et al, 2009; ASA, 2009).

The following two sleep studies are relevant to the care pathway:

- a person with OSA receives a laboratory (level 1) sleep study (MBS[5] item number 12203) and has follow-up consultations with a sleep specialist (MBS item numbers 110 and 116); or
- a person with OSA receives a home based (level 2) sleep study (MBS item number 12250) and has follow-up consultations with a sleep specialist or suitably credentialed GP (MBS item numbers 23 and 36).

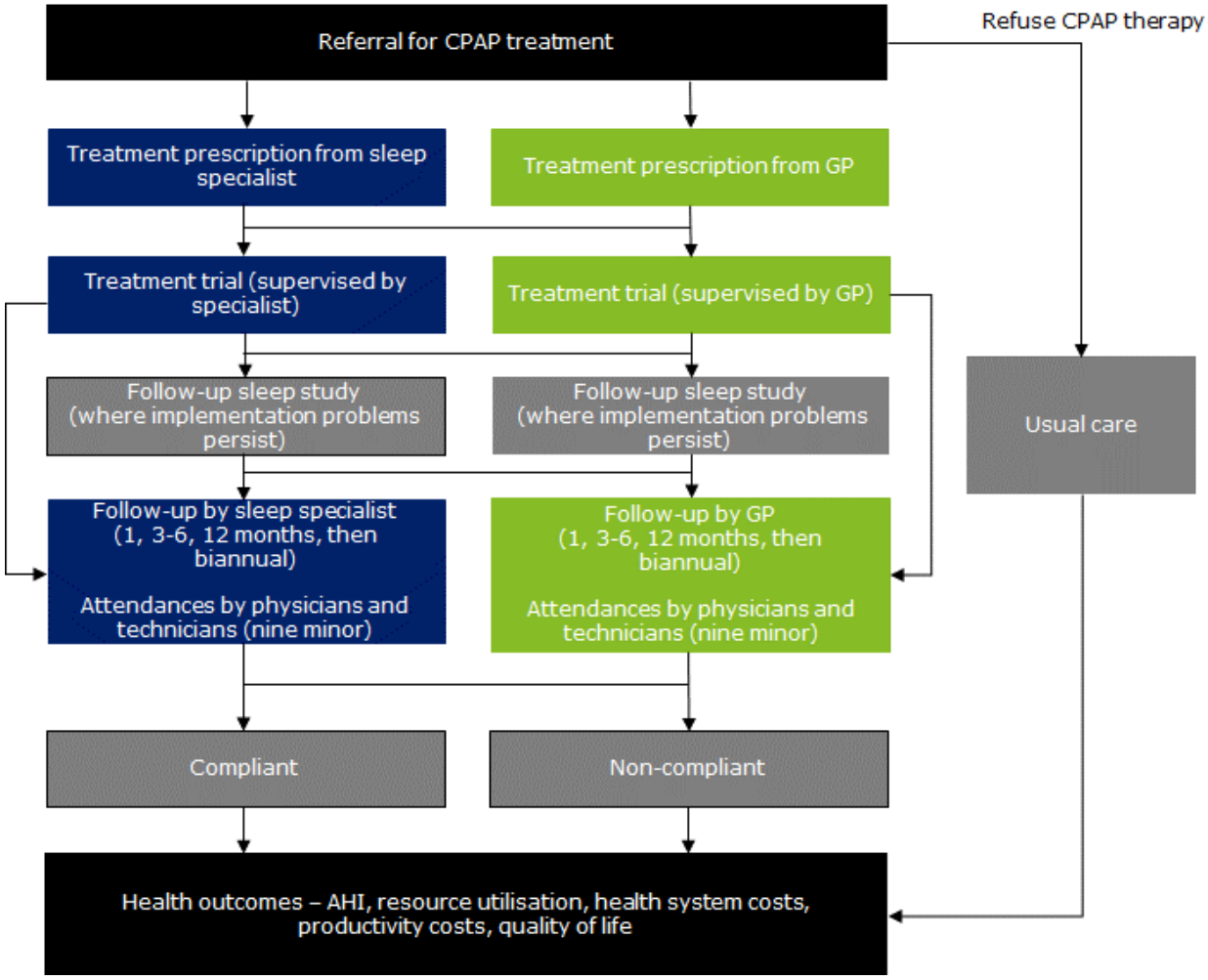
The patient receives a follow-up consultation after the initial trial CPAP period, and then annual appointments (starting in the first year) thereafter. Additionally, both pathways include the same 6 minor attendances by technicians (based on NHMRC[6], 2000) and 3 minor attendances by a GP (MBS item number 23). Patients in both pathways were assumed to receive the same CPAP device.

In summary, the intervention includes:

- an initial trial and supply of equipment to initiate CPAP therapy:
  - trial of treatment supervised by a sleep technologist or service provider for a minimum of 1 week and maximum 3 months (ASA, 2009);
  - follow up with a sleep physician/GP during and/or at end of supervised trial of treatment;
  - equipment issued or purchased;
  - a follow up sleep study where problems occur[7] with implementation that are unable to be solved by simpler means;
- long term follow up by a sleep physician/GP at 3-6 months, 12 months and then biannually thereafter with minor attendances (approximately 9) by technologists or nurses and any maintenance of equipment (e.g. new masks, straps, tubing, filters) as required.

[3] Australasian Sleep Association.
[4] In limited channel sleep studies, a restricted number of parameters are measured, which usually includes a combination of respiratory variables such as arterial oxygen saturation, respiratory effort and airflow. Sleep staging is usually omitted from limited channel sleep studies (Chai-Coetzer et al, 2014).
[5] Medicare Benefits Schedule.
[6] National Health and Medical Research Council.
[7] Approximately 1 in 10 cases.

Figure 1.1: Care pathway for CPAP treatment




Source: Deloitte Access Economics.

The intervention is restricted to people receiving care from sleep specialists or in primary care. Thus, people who bypass the medical model by going to pharmacies or other corporate providers are excluded from the analysis.

**Comparator**
The comparator for the analysis is no treatment. Other therapies such as behavioural modification, oral appliances, surgical or adjunctive therapies (Epstein et al, 2009) have not been considered.

**Outcomes**
Outcomes in the model framework comprise:

- OSA severity (measured through AHI);
- non-fatal outcomes due to coronary artery disease, stroke, congestive heart failure, depression, MVAs, workplace accidents, and type 2 diabetes;
- fatal outcomes due to coronary artery disease, stroke, congestive heart failure, depression, MVAs, workplace accidents, and type 2 diabetes;
- health care resource utilisation;
- productivity improvements, including the effect on informal care;
- changes in other financial costs, including aids and modifications, other costs to government and to society; and
- change in wellbeing (measured using DALYs).

# 2 Methods

The following sections provide an overview of the model structure and methodology (section 2.1) and inputs used to populate the model (section 2.2). The model inputs include assumptions and evidence to inform the population (severity), adherence to CPAP therapy, efficacy parameters given compliance thresholds, costs due to OSA, and costs associated with CPAP therapy.

## 2.1 Model structure

To model the cost effectiveness of CPAP as a management strategy for people with OSA, a two arm cost effectiveness model was developed based on the work of Hillman et al (2018). The objective was to design a clinically and economically appropriate model that could estimate not only costs directly due to OSA, but also costs that are associated with OSA through conditions such as cardiovascular disease, diabetes, depression, MVAs and workplace accidents.

Earlier work by Deloitte Access Economics (2017) and Hillman et al (2018) has established the evidence base to estimate the costs of sleep disorders, and the conditions associated with sleep disorders, through measures of inadequate sleep.

Hillman et al (2018) used a cost of illness framework to estimate the costs. In the cost of illness framework, a PAF approach was used to estimate the prevalence and costs of conditions that are associated with OSA, including:

- coronary artery disease;
- stroke;
- congestive heart failure;
- depression;
- MVAs;
- workplace accidents; and
- type 2 diabetes.

Costs of treating OSA were also included in the framework. Largely, the cost of treating OSA was considered to be associated with usual care, as evidence suggests that few people who are eligible and would receive benefits from CPAP therapy have a machine – approximately 11% in the UK (McDaid et al, 2009). However, an adjustment to the cost of OSA in the model have been removed where the costs were clearly associated with CPAP therapy or diagnostic sleep studies and the likes.

The cost of illness framework also includes:

- productivity costs, which include reduced workforce participation, absenteeism, presenteeism (reduced productivity at work), loss of future earnings due to premature mortality, and the value of informal care (lost income of carers);
- transfer costs, which comprise the deadweight losses, or reduced economic efficiency, associated with the need to raise additional taxation to fund provision of government services;
- other financial costs such as aids and modification costs, legal costs and insurance costs attributed to MVAs and workplace accidents, and the brought forward funeral costs due to premature mortality; and
- wellbeing effects, which includes associated years of healthy life lost due to morbidity and years of life lost due to premature mortality that occur from OSA or conditions associated with OSA.

The costs of OSA, which were estimated as part of the Deloitte Access Economics (2017) analysis, but not published then, have been summarised in section 2.2.4.

To determine the effectiveness of CPAP therapy for people with OSA, the model links the number of AHI events per hour to secondary outcomes – non-fatal conditions that are attributed to OSA, and fatal outcomes due to the attributed conditions – by adjusting the relative risk for people who adhere to CPAP therapy. It was

assumed that there would be no benefits for people who do not adhere to CPAP therapy, as there was limited evidence to assess the extent of non-adherence and the likely diminished effect size.

The rate at which CPAP was assumed to prevent conditions attributed to OSA was based on the PAFs before and after treatment (section 2.2). It was assumed that people needed to adhere to treatment for a period of five years before benefits occur (in the fifth year), with the exception of MVAs and workplace accidents as an observable reduction in accident risk occurs within days of commencing CPAP therapy (Rodenstein, 2009). The model considers the annual costs and benefits of CPAP therapy, so a discount rate has been used to bring benefits forward where they are expected to occur after a period of time. Benefits and costs were discounted using a discount rate of 3%.

Cost effectiveness was assessed from two perspectives, including:

- a health care system perspective, where costs of the intervention and associated health care resource utilisation are compared with the change in quality of life for people with OSA; and
- a societal perspective, where the net cost of the intervention incorporates health care resource utilisation, productivity losses, informal care costs and other financial costs, which is then compared to the change in quality of life for people with OSA.

The model structure is diagrammatically explained in Figure 2.1. The model structure also summarises the probabilities of certain outcomes, which are derived in section 2.2.

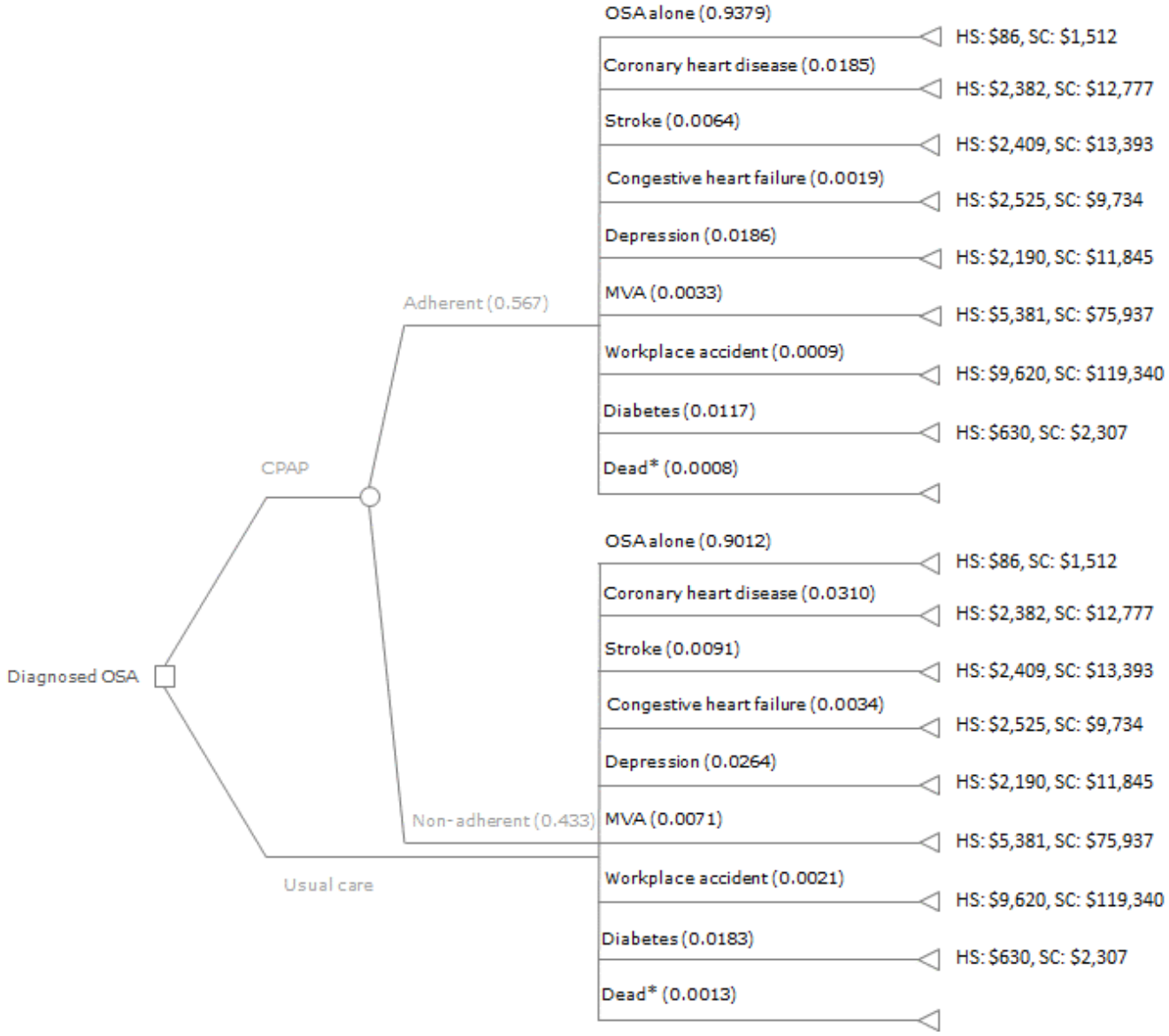
Figure 2.1 provides an overview of the two arm analysis undertaken (CPAP treatment versus no treatment). The figure shows the proportion of people who have OSA-related outcomes for people who are adherent (56.7%) relative to those who are non-adherent (43.3%).

For example, the probability of a person having stroke due to OSA for someone who is initiated on CPAP therapy and adheres to treatment was estimated to be 0.64% compared to 0.91% for a person who is non-adherent – i.e. CPAP mitigates the risk of associated health related conditions occurring. Thus at any given time, a lower proportion of people with OSA who are on CPAP would have associated conditions due to their OSA.

The change in proportions of people with OSA and associated conditions is then used to estimate the number of cases that are avoided due to CPAP. The number of cases avoided is then combined with the cost outcomes (either HS or SC in the figure) to estimate the expected savings due to CPAP relative to no CPAP.

The non-adherent group was assumed to have the same OSA-related outcomes as part of the Deloitte Access Economics (2017) analysis, but not published then. The probabilities and cost outcomes are described in section 2.2.4.

Figure 2.1: Model structure




Source: Deloitte Access Economics. Note: HS = health care system perspective. SC = societal perspective. * the probability only includes the chance of death due to conditions attributed to OSA. No costs were assigned to the outcome death. Cost outcomes do not include the cost of treatment which is different for people who are adherent or not, and for those who receive specialist care versus primary care.

## 2.2 Model inputs

This section outlines the evidence used in the cost effectiveness model. A more detailed consideration of the literature – particularly to review the evidence for compliance and adherence and to establish the effectiveness of CPAP – has been included in Appendix A.

### 2.2.1 Population

Population data were sourced from Adams et al (2017) and Cadby et al (2015) – two Australian studies. Cadby et al (2015) studied patients attending a sleep clinic referred for in-laboratory PSG for possible OSA between 1989 and 2001 in Western Australia to determine incident atrial fibrillation hospitalisation. The analysis has been used to inform the baseline severity in the model. In the OSA cohort with follow up data,

1,914 (44%) had mild OSA, 1,106 (25%) had moderate OSA and 1,332 (31%) had severe OSA. The distribution is similar to that reported in Switzerland (Heinzer et al, 2015).[8]

The prevalence of OSA used by Hillman et al (2018) was based on an Australian study by Adams et al (2017). Adams et al (2017) reported a prevalence rate of 8.3%, which appears to closely align with moderate or worse OSA as a systematic review by Senaratna et al (2017) observed a prevalence rate of 9.3% in adults over 20 where OSA was defined as AHI>15. For consistency with Hillman et al (2018), the prevalence of OSA in this study was also based on Adams et al (2017) for the aggregate results in section 3.3.

### 2.2.2 Adherence

For this analysis, relative risk of associated conditions occurring has usually been derived based on survival curves (Kaplan-Meier estimates) over a period of 10 to 15 years. Therefore, adherence, which comprises both compliance and persistence, is an important measure to determine the effectiveness of CPAP therapy for people with OSA. McArdle et al (1999) and Schoch et al (2014) both observe substantial declines in adherence over long follow up periods.

Schoch et al (2014) report that 51% of people were adherent after 10 years. Schoch et al (2014) comment that the adherence rates are substantially lower than McArdle et al (1999) due to differences in clinical algorithms. Schoch et al (2014) noted that they allowed people with low Epworth sleepiness scale (ESS) scores to receive CPAP treatment. Other studies that assess adherence over a shorter time period generally have a much higher rate of adherence – for example, Cistulli et al (2018) reported that 75% of patients adhered to CPAP over a period of 3 months. A weighted average (56.7%) across studies with a follow up period of approximately 5 years of adherence rates was selected for the modelling (Appendix A).

It should be noted that the selected adherence rate is likely very conservative relative to the real world. In reality, specialists are likely to recommend people continue CPAP therapy based on their response during the initial trial. Alternate therapies (e.g. dental therapy, weight loss or surgery) may be more appropriate in certain circumstances. In this report, CPAP is offered to all people with OSA, regardless of whether they are indicated for CPAP therapy.

In the sensitivity analysis, the minimum and maximum values were defined to be 45% and 65% respectively. Adherence was modelled using a PERT distribution. A scenario where adherence was 70% after ten years has also been reported separately.

### 2.2.3 Effectiveness and safety of CPAP

CPAP has been shown to be efficacious in reducing various metrics used to identify OSA in people of all ages. The typical outcomes used to assess efficacy are a reduction in the AHI and ESS. CPAP is effective, not only for reducing symptoms of OSA, but it also has demonstrable effects on outcomes for cardiovascular disease, depression, type 2 diabetes, accidents and wellbeing (see Appendix A).

The average reduction in AHI index events per hour was estimated to be 24.21. Based on CADTH (2017), the effect differs for people with mild, moderate and severe OSA, where the expected reduction increases with the severity of condition. CADTH (2017) estimated that the expected reduction was 2.4, 13.67, and 33.04 events per hour relative to controls – noting that the subgroup analysis was based on one systematic review where the mean difference was estimated to be -25.37 AHI events per hour (Sharples et al, 2016).

The severity distribution from section 2.2.1 was used in two ways: (1) to derive an average effect size based on the systematic review discussed by CADTH (2017) – the average reduction in AHI events per hour in an Australian setting was estimated to be 14.64 events per hour – and (2) to estimate the average severity of OSA in an Australian setting – the average severity was estimated to be approximately 25 AHI events per

[8] Heinzer et al (2015) conducted a population health study in Switzerland (n= 6,733). There were 1,525 people with OSA aged between 40 and 75 (the upper age of the study). Using the severity definitions in this report, there were 1,525 people with OSA, of which 759 (49.8%) had mild OSA; 450 had moderate OSA (29.5%); and 316 had severe OSA (20.7%). Out of the 766 people with moderate or worse OSA, 316 (41.3%) had severe OSA. This is close to the 33% of people with moderate or worse OSA who also have excessive daytime sleepiness (Deloitte Access Economics, 2017), which implies that excessive daytime sleepiness is found among those with severe OSA. The corresponding figure in those aged 40 to 65 – i.e. incident cases of OSA – is exactly 33%.

hour[9]. Thus, **when CPAP therapy is provided to people with OSA, it was expected that their severity would be reduced to mild OSA**, on average. The treatment effect occurs within days; however, CPAP therapy needs to be sustained over a long period of time for associated reductions in other conditions, apart from accident risk.

Table 2.1 represents evidence from Deloitte Access Economics (2011; 2017) and Hillman et al (2018) for ease of reading. The table shows the expected risk of associated conditions in the base case (no treatment – as per Hillman et al, 2018) and for a change in symptoms of OSA for people treated with CPAP therapy (mild OSA). The methodology to estimate the PAF – as described in Appendix I of Hillman et al (2018) – was combined with the prevalence rates outlined in Table 1 of Hillman et al (2018) to estimate the PAF for people who receive CPAP therapy.

While the above approach was suitable to model effectiveness for coronary heart disease, stroke, congestive heart failure, depression and type 2 diabetes, there was insufficient evidence in the references used by Hillman et al (2018) to estimate the PAF associated with mild OSA for MVAs and workplace accidents.

To derive the effectiveness input for accidents, the incident rate ratio from Antonopoulos et al (2011) – 0.44 - was applied to the rate estimates for OSA from Deloitte Access Economics (2017). Deloitte Access Economics (2017) estimated that the rate of MVAs and workplace accidents was 3.1% and 2.1% for people with OSA, respectively. The accident rates for the general population (excluding OSA) were 1.3% and 1.4%, respectively (Deloitte Access Economics, 2017). The rate with OSA and CPAP would be 1.4% and 0.9%[10], respectively. Using the methods outlined in the Appendix of Hillman et al (2018), the PAF for MVAs and workplace accidents was estimated to be 0.2% and 0.0%[11], respectively.

Finally, for OSA alone, wellbeing was assumed to improve in line with Chakravorty et al (2002) – an incremental gain of 0.04 DALYs averted for people who adhere to CPAP therapy. Given the relatively short follow up period (8 weeks) in Chakravorty et al (2002), it was assumed that 0.04 DALYs were averted after five years (in line with the assumptions about associated conditions) so that the results of the modelling were conservative.

The assumed improvement in wellbeing agrees with the work undertaken by CADTH (2017) and is likely to be conservative compared with a recent systematic review that observed an effect size of 0.435[12] (Gupta et al, 2016). Relative to the average DALYs incurred due to OSA in Deloitte Access Economics (2017), the incremental gain represents an improvement of 54.4% - an improvement from 0.074 DALYs per person to 0.034 DALYs per person.

[9] For mild, moderate and severe OSA respectively, the average within group number of events per hour were assumed to be 10, 22.5 and 50. The weighted average was then derived as 44% * 10 + 25% * 22.5 + 31% * 50.
[10] 3.1% * 0.44 = 1.4%. 2.1% * 0.44 = 0.9%. For workplace accidents, the estimate indicates that OSA with CPAP therapy would reduce the number of accidents relative to the general population – 0.9% compared with 1.4%. However, as the baseline rate in Antonopoulos et al (2011) was not clear, it was assumed that the rate of workplace accidents would be comparable with the general population to be conservative – i.e. that it would reduce the rate from 2.1% to 1.4% - and the PAF would be 0.0%.
[11] In cases where the condition is rare, the odds ratio and risk ratio are approximately equal. Thus, the odds ratio for MVAs and workplace accidents was defined as 1.4%/1.3% = 1.08 and 0.9%/1.4% = 0.66, respectively. The odds ratio for workplace accidents was then assumed to be 1.00 – that is, there is no reduction in the risk relative to the general population, which implies that the PAF is 0%. The revised odds ratios were used to determine the new PAF.
[12] The effect size is reported as Hedge's *g*, a standardised measure of effect that indicates that wellbeing improves by 0.435 standard deviations relative to comparison group, which was post-treatment compared with pre-treatment. The standard deviation in Chakravorty et al (2002) was 0.18, so the absolute difference in the means would be greater than 0.04.

Table 2.1: Measures of effectiveness used in the model

| Condition | Source | Measure | Mild OSA/ CPAP | Parameter in Hillman (2018) | Intervention PAF (%) | No treatment PAF (%) | Efficacy | Dist. Inputs# |
|---|---|---|---|---|---|---|---|---|
| OSA* | Chakravorty (2002) | Change in DALYs | 0.034 | 0.074 | - | - | 54.4% | 0.435, 0.544, 0.653 |
| Coronary heart disease | Gottlieb (2010) | Hazard ratio | 1.13^ | 1.58 | 1.4 | 4.8 | 70.8% | 0.57, 0.71, 0.85 |
| Stroke | Redline (2010) | Hazard ratio | 1.86 | 2.86 | 2.3 | 4.8 | 51.7% | 0.41, 0.52, 0.62 |
| Congestive heart failure | Marin (2005) | Odds ratio | 1.57 | 3.17 | 0.3 | 1.5 | 80.4% | 0.64, 0.80, 0.97 |
| Depression | Peppard (2006) | Odds ratio | 1.70 | 2.60 | 1.7 | 3.6 | 52.2% | 0.42, 0.52, 0.63 |
| MVAs | Antonopoulos (2011); Hillman (2018) | Incident rate ratio | - | - | 3.8 | 0.2 | 94.7% | 0.76, 0.95, 1.00 |
| Workplace accidents | Antonopoulos (2011); Hillman (2018) | Incident rate ratio | - | - | 1.3 | 0.0 | 100.0% | 0.80, 1.00, 1.00 |
| Diabetes | Wang (2013) | Relative risk | 1.22 | 1.63 | 0.6 | 1.7 | 63.9% | 0.51, 0.64, 0.77 |

Source: as noted in table. Note: Marin et al (2005) reported combined results for mild and moderate OSA. Peppard et al (2006) reported combined results for moderate and severe OSA. Wang et al (2013) report combined results for moderate and severe OSA. * The effectiveness for OSA applies to both morbidity and costs. ^ mild OSA was not found to significantly reduce the hazard ratio for incident heart failure, so the hazard ratio for moderate OSA was used to derive the effect size of CPAP therapy for incident heart failure. # Distributions were modelled using a PERT distribution.[13] The distribution inputs represent the minimum, mode and maximum value respectively. The efficacy applies after 5 years for OSA and associated conditions, with the exception of accidents (benefits accrue immediately).

Potential adverse events from the use of CPAP include nasal congestion, skin irritation, pharyngeal dryness, conjunctivitis, epistaxis, interface-related issues such as claustrophobia and sore eyes, abdominal bloating, anxiety, mask discomfort, and chest discomfort (Catala et al, 2016; McMillan et al, 2014; NHMRC, 2000).

Consistent with CADTH (2017), there was no evidence of severe adverse events that would not resolve quickly upon discontinuing CPAP or that could not be avoided through other treatments such as humidification. Consequently, adverse events have not been included in the modelling.

### 2.2.4 Cost and wellbeing losses due to OSA

There are a range of costs due to OSA including health system costs, productivity losses and other financial costs such as aids and modifications costs and deadweight losses that result from increased taxation rates. OSA also imposes substantial wellbeing losses both independently and due to conditions attributed to OSA. The cost and wellbeing inputs used in the economic model are based on work by Deloitte Access Economics (2017) and Hillman et al (2018). The inputs are described in the following sections.

These inputs inform the baseline costs and wellbeing losses in the no treatment arm of the cost effectiveness model.

[13] See https://en.wikipedia.org/wiki/PERT_distribution

**Health system costs**
For the purpose of the CEA, the health system costs of OSA, or more specifically, the health system costs avoided as a result of treatment with CPAP comprise the costs of the attributed conditions.

The health system costs of other conditions that are attributed to OSA were calculated as part of the Deloitte Access Economics (2017) analysis, but not published then. Deloitte Access Economics (2017) derived PAFs that were then applied to top down health system expenditure for each of the conditions that were attributed to sleep disorders. The average health system costs are shown in Table 2.2.

These represent costs attributable to OSA. For example, the cost of coronary heart disease attributed to OSA was estimated to be $2,382 per case. The average health system cost to care for untreated OSA without any attributed conditions was estimated to be $86 per person by Deloitte Access Economics (2017).

Table 2.2: Average annual health system costs per case affected, $ 2017-18

| Condition | Cost ($) | Model inputs |
|---|---|---|
| OSA | 86 | PERT dist., min = 69.00, mode = 86.25, max = 103.50 |
| Coronary heart disease | 2,382 | PERT dist., min = 1,905.34, mode = 2,381.68, max = 2,858.01 |
| Stroke | 2,409 | PERT dist., min = 1,927.36, mode = 2,409.20, max = 2,891.04 |
| Congestive heart failure | 2,525 | PERT dist., min = 2,019.85, mode = 2,524.81, max = 3,029.78 |
| Depression | 2,190 | PERT dist., min = 1,751.96, mode = 2,189.94, max = 2,627.93 |
| MVA | 5,381 | PERT dist., min = 4,304.84, mode = 5,381.05, max = 6,457.27 |
| Workplace accidents | 9,620 | PERT dist., min = 7,696.21, mode = 9,620.26, max = 11,544.32 |
| Diabetes | 630 | PERT dist., min = 504.26, mode = 630.32, max = 756.39 |

Source: Deloitte Access Economics (2017) and Hillman et al (2018).

As the data in Deloitte Access Economics (2017) were in 2016-17 dollars, health system expenditure was inflated to 2017-18 using the health price index (AIHW[14], 2016a), which was estimated for 2017-18 using 10-year average historical growth in the index. Historical expenditure was also adjusted for population growth between the year of the data point and 2017-18 (ABS[15], 2013).

**Productivity losses and other financial costs**
Financial costs of OSA other than health system expenditures include productivity losses, informal care costs, costs such as aids and modifications costs, legal costs and insurance costs attributed to MVAs and workplace accidents, as well as less obvious efficiency losses that result from increased taxation rates.

OSA can have a substantial impact on an individual's ability to engage in and attend work. Primary impacts on work include a reduced chance of employment, early retirement, or exit from the workforce due to premature mortality. As such, OSA may impose a range of productivity costs, which affect not only individuals, but also their employers and government. To estimate the potential cost savings due to CPAP for OSA, the methods and costs are based on those used for Deloitte Access Economics (2017) and Hillman et al (2018).

In some cases, there were insufficient data available to estimate average costs for conditions or cost items. For example, there were insufficient data to estimate informal care costs associated with depression. Similarly, Deloitte Access Economics (2017) did not estimate costs associated with aids and modifications for attributed conditions, except for MVAs or workplace accidents. To ensure consistency with the Hillman et al (2018), these costs have been excluded again.

[14] Australian Institute of Health and Welfare.
[15] Australian Bureau of Statistics.

As the data in Deloitte Access Economics were in 2016-17 dollars, cost inputs were inflated to 2017-18 dollars using either the consumer price index or wage price index. The average productivity and other financial costs per person are shown in Table 2.3.

Table 2.3: Average annual productivity and other financial costs per case affected, $ 2017-18

| Condition | Productivity cost | Informal care cost | Other financial cost | Deadweight loss | Total | PERT distribution (min, mode, max) |
|---|---|---|---|---|---|---|
| OSA | 1,274 | - | - | 152 | 1,426 | 1,140.56, 1,425.70, 1,710.84 |
| Coronary heart disease | 8,014 | 1,071 | - | 1,310 | 10,395 | 8,316.08, 10,395.10, 12,474.12 |
| Stroke | 8,550 | 1,071 | - | 1,363 | 10,984 | 8,787.17, 10,983.96, 13,180.75 |
| Congestive heart failure | 5,059 | 1,071 | - | 1,080 | 7,210 | 5,767.69, 7,209.61, 8,651.53 |
| Depression | 8,385 | - | - | 1,270 | 9,655 | 7,724.40, 9,655.50, 11,586.61 |
| MVA | 14,570 | 4,339 | 48,838 | 2,808 | 70,555 | 56,444.37, 70,555.46, 84,666.55 |
| Workplace accidents | 89,751 | 3,602 | 6,534 | 9,831 | 109,719 | 87,775.67, 109,719.59, 131,663.51 |
| Diabetes | 1,310 | 97 | - | 269 | 1,677 | 1,341.27, 1,676.58, 2,011.90 |

Source: Deloitte Access Economics (2017) and Hillman et al (2018). Note: components may not sum to totals due to rounding.

**Wellbeing losses**

For this analysis, wellbeing was measured using DALYs. DALYs are a measurement unit that quantify the morbidity and premature death associated with various diseases and injuries. Under the DALY framework, the total burden of disease for an individual with a condition is the sum of the years of healthy life lost due to disability (YLDs) and the years of life lost due to premature death (YLLs). DALYs are measured on a scale of zero to one, where a zero represents a year of perfect health and a one represents death.

DALYs were calculated for both the individuals with OSA and for cases of other conditions attributable to OSA (including deaths due to attributable conditions) based on PAFs. The approach used follows Deloitte Access Economics (2017) and Hillman et al (2018). Table 2.4 shows the average YLDs, YLLs and DALYs per case that inform the base case for people with OSA who are not receiving CPAP therapy. The incremental effectiveness (adjusted for adherence) is applied to the base case DALY inputs to estimate the proportion of DALYs that may be avoided through CPAP therapy.

Table 2.4: Average YLDs, YLLs and DALYs per case, no treatment

| Condition | YLDs | YLLs | DALYs | DALY model input |
|---|---|---|---|---|
| OSA | 0.07 | - | 0.07 | PERT dist., min = 0.06, mode = 0.07, max = 0.09 |
| Coronary heart disease | 0.18 | 0.36 | 0.53 | PERT dist., min = 0.43, mode = 0.53, max = 0.64 |
| Stroke | 0.24 | 0.42 | 0.66 | PERT dist., min = 0.53, mode = 0.66, max = 0.79 |
| Congestive heart failure | 0.16 | 0.15 | 0.31 | PERT dist., min = 0.25, mode = 0.31, max = 0.37 |
| Depression | 0.26 | 0.03 | 0.29 | PERT dist., min = 0.23, mode = 0.29, max = 0.35 |
| MVAs | 0.15 | 0.10 | 0.25 | PERT dist., min = 0.20, mode = 0.25, max = 0.30 |
| Workplace accidents | 0.18 | 0.03 | 0.21 | PERT dist., min = 0.17, mode = 0.21, max = 0.25 |
| Diabetes | 0.17 | 0.03 | 0.19 | PERT dist., min = 0.15, mode = 0.19, max = 0.23 |

Source: Deloitte Access Economics (2017) and Hillman et al (2018).

**Probability of associated conditions**

The proportion of other health conditions attributed to OSA was derived by Deloitte Access Economics (2017) and Hillman et al (2018). The proportion is a key component of the cost effectiveness model as it informs how many cases of other health conditions are due to OSA in the no treatment arm of the model.

Table 2.5 shows the estimated proportion of people with OSA and other health conditions due to their OSA based on the work of Deloitte Access Economics (2017) and Hillman et al (2018). The attributed cases were largely attributed to lack of sleep due to OSA. It was assumed that lack of sleep would still provide a reasonable proxy for the number of cases that can be attributed to OSA when broadening the definition of OSA – meaning that no additional cases were assigned to OSA despite including prevalence of diagnosed OSA as in Adams et al (2017). This assumption appears consistent with the literature that does not find a large difference in the relative risks for mild and moderate OSA (e.g. see Deloitte Access Economics, 2011).

Thus, the proportion of people with OSA and an associated health condition due to OSA is the number of attributed cases from Hillman et al (2018) (adjusted for population growth) divided by 1.576 million (prevalence of 8.3% in 2018). Table 2.5 also presents the proportion of people with OSA and an associated health condition given effective treatment.

Table 2.5: Proportion of people with OSA and an associated health condition

| Condition | Proportion, no treatment (%) | Proportion, treatment (%)* | Model inputs, no treatment |
|---|---|---|---|
| Coronary heart disease | 3.10 | 1.85 | PERT dist., min = 0.0248, mode = 0.0310, max = 0.0372 |
| Stroke | 0.91 | 0.64 | PERT dist., min = 0.0073, mode = 0.0091, max = 0.0109 |
| Congestive heart failure | 0.34 | 0.19 | PERT dist., min = 0.0027, mode = 0.0034, max = 0.0041 |
| Depression | 2.64 | 1.86 | PERT dist., min = 0.0211, mode = 0.0264, max = 0.0317 |
| MVA | 0.71 | 0.33 | PERT dist., min = 0.0057, mode = 0.0071, max = 0.0085 |
| Workplace accidents | 0.21 | 0.09 | PERT dist., min = 0.0017, mode = 0.0021, max = 0.0026 |
| Diabetes | 1.83 | 1.17 | PERT dist., min = 0.0147, mode = 0.0183, max = 0.0220 |

Source: Deloitte Access Economics (2017), Hillman et al (2018) and Deloitte Access Economics analysis. * The proportion of people with OSA and an associated health condition with treatment is derived using the effectiveness (Table 2.1), adherence rate and the proportion of people with OSA and an associated health condition without treatment. Therefore, the underlying distribution for no treatment will also apply to the treated group.

Taking into account the Australian population aged 20 years or older of 18.98 million in 2017-18, the estimated prevalence of OSA of (8.3%) (as in section 2.2.1), the PAFs for the various comorbidities and the per person costs and weightings, as outlined in Table 2.2 to Table 2.5, the total financial cost of OSA was $5.06 billion. This comprised direct health costs of $0.50 billion, productivity losses of $3.40 billion, informal care costs of $0.14 billion, non-medical accident costs of $0.57 billion, and deadweight losses of $0.45 billion. OSA also caused 174,204 DALYs in 2017-18, which represents a non-financial cost of $34.11 billion.

### 2.2.5 Costs of treatment

The cost of CPAP therapy was based on the care pathway outlined in section 1. Briefly:

- all individuals undertaking CPAP are assumed to fall into one of two care pathway options – primary care and sleep specialist;
- patients managed through primary care undertake a level 2 sleep study (using portable monitors) and are managed by a primary care physician, with two consultations occurring in the first year and one consultation every year thereafter; and
- patients managed by a sleep specialist undertake an in-laboratory, level 1 sleep study, with the same frequency of consultations as the primary care group.

A minor attendance by a technician was based on the cost used in NHMRC (2000) inflated to 2018 dollars. The cost was inflated using wage growth from 1998 to 2018 as it relates to wages paid to the technician (ABS, 2018).

CPAP machines available for purchase on theCPAPclinic.com.au on 17 August 2017 range in price from $485 to $6,500. A simple average of all 58 machines listed, $1,745, was used as the average device cost. The life of a CPAP device is typically assumed to be five to seven years for the purpose of calculating the cost of treatment (e.g. McMillan et al, 2014; McDaid et al, 2009; Trakada et al, 2015; Tan et al, 2008). It was assumed that the machine would last for six years.

The cost of masks, tubing, humidifiers and filters are also based on an average of each type of item listed on theCPAPclinic.com.au on 17 August 2017. It has been assumed that masks, tubing and filters would need to be replaced each year. As some devices have humidifiers built in, only half of patients were assumed to purchase a humidifier. These assumptions are consistent with other CEA studies in the literature (McMillan et al, 2014; McDaid et al, 2009; Trakada et al, 2015; Tan et al, 2008).

The total cost of treatment over five years was determined based on the number of times each component of treatment would be required. However, this total is the net present value of the costs based on the years in which the costs take place (based on a 3% discount rate). For instance, the five annual follow-up consultations occur once every year, and the expected cost of a follow-up sleep study (based on a 10% probability) takes place in the second year. All other costs are conservatively assumed to be incurred during the first year of treatment. Table 2.6 and Table 2.7 present the costs used in the analysis for the specialist and primary care pathways.

The share of patients that are expected to take each pathway is based on the volume of MBS item numbers 12203 (53%) and 122250 (47%) – that is, it was assumed that GPs would be responsible for managing people who have a level 2 sleep study and specialists for people who have a level 1 sleep study.

Table 2.6: Estimated CPAP treatment costs in specialist pathway, over 5 years in Australia, 2017-18 dollars

| Treatment protocol | Unit cost | Net present value over 5 years | Annual cost[(a)] |
|---|---|---|---|
| Overnight sleep study (level 1) | 588 | 645 | 129 |
| First follow-up consultation with physician | 153 | 153 | 31 |
| Five annual follow-up consultations | 77 | 362 | 72 |
| Three minor attendances by physicians | 38 | 105 | 21 |
| Six minor attendances by technicians | 28 | 170 | 34 |
| Purchase of CPAP machine | 1,745 | 1,745 | 291 |
| CPAP machine accessories/ spare parts | | 1,293 | 215 |
| **Total cost (adherent)** | | **4,472** | **836** |
| **Total cost (non-adherent)** | | **3,069** | **561** |

Source: Deloitte Access Economics' calculations. Note: components may not sum to totals due to rounding.

Table 2.7: Estimated CPAP treatment costs in primary care pathway, over 5 years in Australia, 2017-18 dollars

| Treatment protocol | Unit cost | Net present value over 5 years | Annual cost[(a)] |
|---|---|---|---|
| Overnight sleep study (level 2) | 335 | 368 | 74 |
| First follow-up consultation | 153 | 73 | 15 |
| Five annual follow-up consultations | 77 | 177 | 35 |
| Three minor attendances by GPs | 38 | 105 | 21 |
| Six minor attendances by technicians | 28 | 170 | 34 |
| Purchase of CPAP machine | 1,745 | 1,745 | 291 |
| CPAP machine accessories/ spare parts | | 1,293 | 259 |
| **Total cost (adherent)** | | **3,930** | **728** |
| **Total cost (non-adherent)** | | **2,349** | **418** |

Source: Deloitte Access Economics' calculations. Note: components may not sum to totals due to rounding.

Non-adherence increases the probability of avoiding health system and other financial (non-health system) costs proportional to the rate of non-adherence (Table 2.5). A non-adherent person still incurs treatment costs for the initial sleep studies, follow up consultations with a physician in the first year and the purchase of a CPAP machine, accessories and spare parts in the first year. However, it is likely that some people will trial a CPAP machine rather purchasing the machine outright. It was assumed that the CPAP machine was purchased by 90% of people who do not adhere to treatment, with the remaining 10%[16] incurring 1 month of rental costs, which was estimated to be $176.74 – or 1/12 of the total cost incurred by people who are non-adherent and purchase the device.

Table 2.8: Treatment cost inputs, $ 2017-18

| Cost | Unit cost | Model inputs |
|---|---|---|
| Specialist care – adherent | 836.17 | PERT dist., min = 668.93, mode = 836.17, max = 1,003.4 |
| Specialist care – non-adherent | 561.38 | PERT dist., min = 449.11, mode = 561.38, max = 673.66 |
| Primary care – adherent | 727.81 | PERT dist., min = 582.25, mode = 727.81, max = 873.37 |
| Primary care – non-adherent | 417.55 | PERT dist., min = 334.04, mode = 417.55, max = 501.07 |

Source: Deloitte Access Economics' calculations.

It should be noted that any reduction in consultation costs by substituting specialist with non-specialist consultations may be offset by reduced adherence rates (Pamidi et al, 2012). The effectiveness of specialist care relative to suitably credentialed GPs has not been explored in this analysis.

### 2.2.6 Estimating the cost effectiveness of CPAP

To estimate the cost effectiveness of CPAP, inputs from section 2.2.1 through section 2.2.5 were combined as follows.

- The adherence rate was multiplied by the efficacy parameters in Table 2.1 to estimate the proportion of each associated condition that would be avoided using CPAP therapy. For example, the probability of a person having stroke due to OSA for someone who is initiated on CPAP therapy and adheres to treatment was estimated to be 0.64% compared to 0.91% for a person who is non-adherent – i.e. CPAP mitigates the risk of associated health related conditions occurring.

[16] In Schoch et al (2010), it appears that approximately 10% of people discontinue CPAP therapy within one month.

- The change in the proportion of people with associated health conditions is then multiplied by the average cost outcomes in Table 2.2 and Table 2.3 – either health system only, or health system and other financial costs – to determine the average incremental cost saving for each person who adheres to CPAP therapy.
- The change in wellbeing was estimated by applying the adherence rate and efficacy parameters for each condition to the average number of DALYs per person (Table 2.4), which is then multiplied by the proportion of people with OSA with each condition (e.g. 3.10% for coronary heart disease) to derive the average DALYs avoided per person. OSA alone was further adjusted to remove the proportion of people with OSA and a related health condition, so that people were not double counted. For attributed conditions apart from MVAs and workplace accidents, the wellbeing benefits occur in the fifth year so these are discounted appropriately. The average DALYs avoided across all attributed conditions was then calculated as the sum of the discounted wellbeing benefits, noting again that the benefits for MVAs and workplace accidents occur immediately.
- The net cost of treatment was then derived as the cost of treatment (section 2.2.5) minus any cost savings from a reduction in associated conditions or health resource utilisation by people with OSA alone (step 2). The ICER can then be calculated using the net cost of treatment divided by the change in wellbeing.

The results of the analysis are described in section 3.

### 2.2.7 Sensitivity analysis

A probabilistic sensitivity analysis was conducted by assuming the distribution for the model inputs outlined in the previous sections. Probabilistic sensitivity analysis was conducted with regard to:

- the adherence rate;
- effectiveness of CPAP therapy;
- health system costs and other financial costs due to OSA or its attributed conditions;
- change in wellbeing;
- the probability of an associated event occurring; and
- the cost of treatment.

Each input was allowed to vary according to a PERT distribution. Largely, the minimum and maximum values for each distribution were assumed to be 20% lower and higher than the base value respectively. However, where the effect size is 100%, the maximum value for the distribution is also 100%.

The sensitivity analysis was then undertaken using a Monte Carlo simulation with 1,000 trials. The Monte Carlo simulation simultaneously draws a random number for each input according to its distribution. The ICER is then recalculated for each individual trial to provide an estimate of the sensitivity of the results to each individual parameter.

# 3 Results

This section outlines the results of the CEA (section 3.1) and models a hypothetical scenario that reports the potential costs and benefits had CPAP been used effectively across all Australians with OSA historically (section 3.2).

## 3.1 Cost effectiveness of CPAP

Cost effectiveness is assessed through the ICER. To calculate the ICER, the net cost of CPAP treatment is divided by the estimated DALYs avoided per person. The net cost of treatment is calculated as the cost of CPAP treatment minus the avoided health system costs of other associated conditions from the perspective of the health care system.

For the societal perspective, the net cost of treatment also incorporates savings through other financial costs such as productivity, informal care and deadweight losses. DALYs avoided per person is calculated as total DALYs attributed to OSA (due to both morbidity and mortality, from OSA and cases of other conditions caused by OSA) divided by the total individuals with OSA.

The results of the CEA are shown in Table 3.1. The net cost of CPAP therapy from the perspective of the health care system was estimated to be $550 dollars per person per year. From the perspective of society (including other financial costs avoided) the intervention was estimated to save $470 per person per year.

It was estimated that CPAP therapy would avoid 0.0305 DALYs per person per year, which represents the average across all people with OSA. From the perspective of the health care system, the incremental cost effectiveness ratio (ICER) was estimated to be $18,043 per DALY averted. From the perspective of society, the ICER was estimated to be dominant – saving money for each DALY averted. Thus, based on a benchmark of $50,000 – as typically used in health technology assessments (CADTH, 2017) – CPAP was estimated to be a cost effective intervention for OSA.

Table 3.1: Results of the CEA

| | Health care system perspective | Societal perspective |
|---|---|---|
| Cost of treatment ($ per person per year) | 660 | 660 |
| Total costs avoided due to OSA ($ per person per year) | -110 | -1,130 |
| Net cost ($ per person per year) | 550 | -470 |
| DALYs averted (per person per year) | 0.0305 | 0.0305 |
| **ICER ($/DALY averted)** | **18,043** | **Dominant** |

Source: Deloitte Access Economics' calculations. Note: results derived based on the components in table may differ due to rounding. Dominant indicates the intervention both saves money and improves wellbeing.

If the adherence with CPAP therapy were 70% on average, instead of the conservative 56.7% estimate used for this analysis, the ICER from the perspective of the health care system would improve to $14,969 per DALY averted. The ICER from the perspective of society would remain dominant – meaning that CPAP would both save money and improve wellbeing.

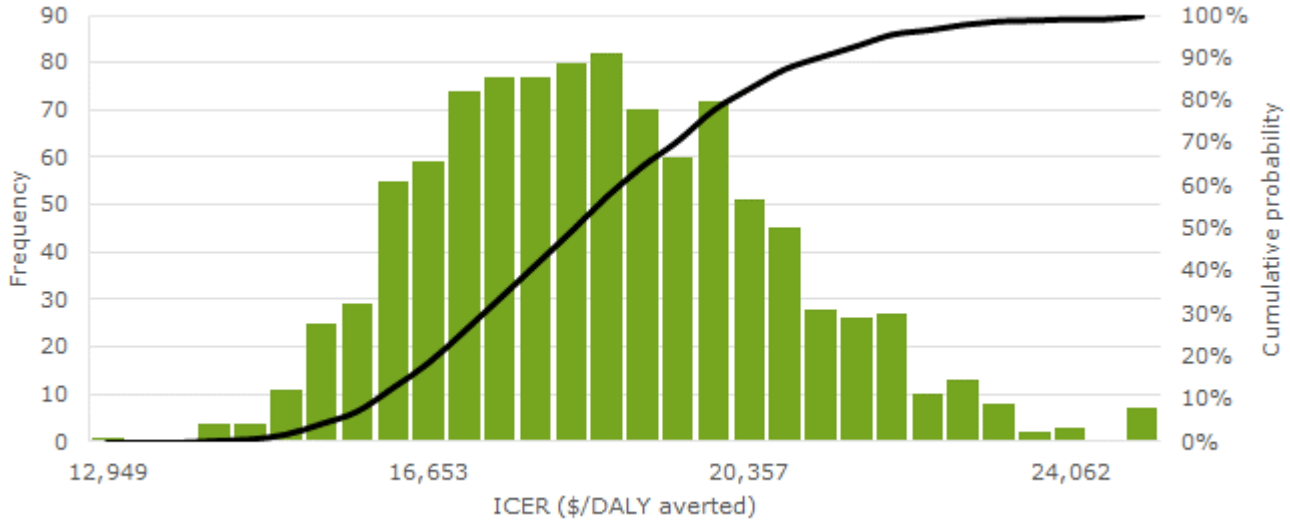
## 3.2 Sensitivity analysis

From the perspective of the health care system, the ICER ranged from $12,949 per DALY averted to $25,708 per DALY averted. From the perspective of society, the ICER ranged from $-21,186 per DALY averted (dominant) to -$8,538 per DALY averted (dominant).

The ICER was most sensitive to changes in the adherence rate, the effect of CPAP on morbidity for OSA alone (no associated conditions), the average DALY per person with OSA (no associated conditions), and the costs of the specialist and primary care pathways.

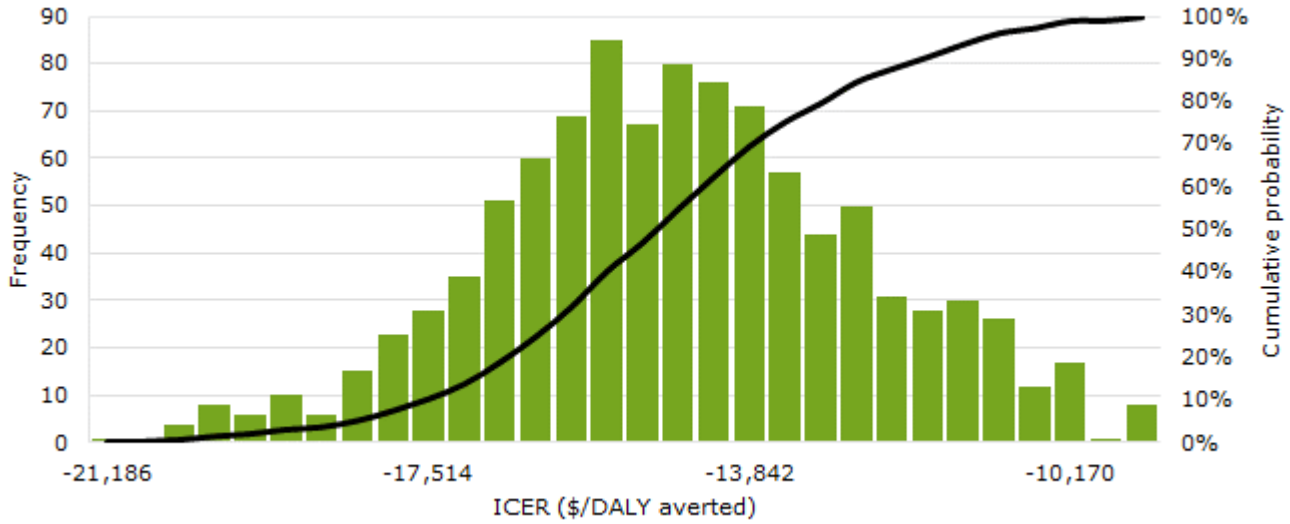
Chart 3.1 and Chart 3.2 show the distribution of ICER results from the perspective of the health care system and society, respectively.

Chart 3.1: Sensitivity analysis from the perspective of the health care system




Source: Deloitte Access Economics.

Chart 3.2: Sensitivity analysis from the perspective of society




Source: Deloitte Access Economics.

## 3.3 Scenario analysis

It was estimated that 1,575,735 Australians have OSA in 2017-18, of whom there were 1,188,669 males and 387,066 females who have OSA. Given the inputs from Hillman et al (2018) and Deloitte Access Economics (2017), the total number of DALYs due to OSA was estimated to be 162,911 in 2017-18, of which 58,314 were due to conditions attributed to OSA.

A hypothetical what-if scenario was modelled to estimate the potential savings to Australian society if all people with OSA were to receive CPAP or an (as yet un-invented) equally efficacious therapy. The what-if scenario assumes that people on CPAP therapy would have been using the therapy for a number of years already – i.e. that the benefits are accrued today, rather than in 5 years' time. The scenario is calculated based on the findings of the CEA.

Relative to no treatment, it was estimated that 53,777 DALYs could be avoided by CPAP. Similarly, it was estimated that CPAP therapy would reduce health system health expenditure by $189.2 million and reduce productivity and other financial costs by $1.7 billion. The total costs avoided were estimated to be $1.92 billion – noting this is not net of the cost of treatment. The results are shown in Table 3.2.

Table 3.2: Total cases avoided and associated costs

| Condition | Total cases avoided | DALYs avoided | Health system costs ($m) | Productivity and other financial costs ($m) | Total costs avoided ($m) |
|---|---|---|---|---|---|
| OSA | - | 32,280 | 41.9 | 693.3 | 735.2 |
| Coronary heart disease | 19,635 | 10,465 | 46.8 | 204.1 | 250.9 |
| Stroke | 4,197 | 2,768 | 10.1 | 46.1 | 56.2 |
| Congestive heart failure | 2,469 | 764 | 6.2 | 17.8 | 24.0 |
| Depression | 12,319 | 3,583 | 27.0 | 118.9 | 145.9 |
| MVA | 5,984 | 1,490 | 32.2 | 422.2 | 454.4 |
| Workplace accidents | 1,904 | 397 | 18.3 | 208.9 | 227.2 |
| Diabetes | 10,483 | 2,029 | 6.6 | 17.6 | 24.2 |
| **Total** | **-** | **53,777** | **189.2** | **1,729.0** | **1,918.1** |

Source: Deloitte Access Economics' calculations. Note: components may not sum to totals due to rounding.

The total cost of treatment for such a theoretical undertaking was estimated to be $1.04 billion, so there were estimated to be savings from CPAP relative to no treatment from the perspective of society, although not from the perspective of the health care system.

# 4 Conclusion

Given the substantial burden of OSA in Australia, cost effective interventions to treat OSA are essential to improve wellbeing and reduce the burden on the health system and society more broadly.

CPAP therapy is a safe and effective treatment for OSA. CPAP not only reduces the symptoms of OSA, it also has demonstrable effects on outcomes for cardiovascular disease, depression, type 2 diabetes, accidents and wellbeing for people with OSA.

However, the efficacy of CPAP depends critically on adherence – CPAP is a treatment for OSA but not a cure. Some authorities suggest that CPAP should be used for 4 hours per night for 7 nights out of every 10. Based on a literature review (Appendix A), it was assumed that close to half (56.7%) of people with OSA who are initiated on CPAP therapy will still be adherent after 5 years, and therefore receive benefits from CPAP. However, the risk of accidents is reduced immediately.

CPAP was estimated to be cost effective from the perspective of the health care system - using CPAP for OSA costs $18,043 per DALY avoided. Including societal costs such as lost productivity and carer costs, it was estimated that CPAP would be dominant – saving money for each DALY averted. These results are particularly important for funding bodies who are tasked with identifying cost effective interventions to reduce the costs of conditions with high burden in Australia.

Where relevant, strategies should be considered to improve adherence levels to maximise the benefits from CPAP therapy. It has been shown that supportive and educational interventions can have an impact on adherence, with a study finding the share of patients using CPAP for at least 4 hours per night to be 59% without supportive interventions compared to 75% with them (Wozniak et al 2014). More work is warranted in this area.

# References


ABS. (2013). 3222.0- Population projections, Australia, 2012 (base) to 2101. Retrieved from: http://www.abs.gov.au/ausstats/abs@.nsf/lookup/3222.0Media%20Release12012%20(base)%20to%202101

ABS. (2018). 6302.0 – Average Weekly Earnings, Australia, May 2018. Retrieved from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/6302.0Main+Features1May%202018?OpenDocument

Adams, R. J., Appleton, S. L., Taylor, A. W., Gill, T. K., Lang, C., McEvoy, R. D., & Antic, N. A. (2017). Sleep health of Australian adults in 2016: results of the 2016 Sleep Health Foundation national survey. *Sleep health*, *3*(1), 35-42.

AIHW. (2017), Health expenditure Australia 2015-16. Health and welfare expenditure series, Cat. No. HWE 67. Canberra: AIHW.

Antic, N. A., Catcheside, P., Buchan, C., Hensley, M., Naughton, M. T., Rowland, S., … McEvoy, R. D. (2011). The Effect of CPAP in Normalizing Daytime Sleepiness, Quality of Life, and Neurocognitive Function in Patients with Moderate to Severe OSA. *Sleep*, *34*(1), 111–119. JOUR. Retrieved from http://dx.doi.org/10.1093/sleep/34.1.111

Antonopoulos, C. N., Sergentanis, T. N., Daskalopoulou, S. S., & Petridou, E. T. (2011). Nasal continuous positive airway pressure (nCPAP) treatment for obstructive sleep apnea, road traffic accidents and driving simulator performance: a meta-analysis. *Sleep medicine reviews*, *15*(5), 301-310.

ASA. (2009). Position paper: Best practice guidelines for provision of CPAP therapy. Retrieved from: https://www.sleep.org.au/documents/item/66

Avlonitou, E., Kapsimalis, F., Varouchakis, G., Vardavas, C. I., & Behrakis, P. (2012). Adherence to CPAP therapy improves quality of life and reduces symptoms among obstructive sleep apnea syndrome patients. *Sleep and Breathing*, *16*(2), 563–569. JOUR. https://doi.org/10.1007/s11325-011-0543-8

Barbé, F., Durán-Cantolla, J., Sánchez-de-la-Torre, M., Martínez-Alonso, M., Carmona, C., Barceló, A., ... & Garcia-Rio, F. (2012). Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. *Jama*, *307*(20), 2161-2168.

Batool-Anwar, S., Goodwin, J. L., Kushida, C. A., Walsh, J. A., Simon, R. D., Nichols, D. A., & Quan, S. F. (2016). Impact of continuous positive airway pressure (CPAP) on quality of life in patients with obstructive sleep apnea (OSA). *Journal of Sleep Research*, *25*(6), 731–738. JOUR. https://doi.org/10.1111/jsr.12430

Cadby, G., McArdle, N., Briffa, T., Hillman, D. R., Simpson, L., Knuiman, M., & Hung, J. (2015). Severity of OSA is an independent predictor of incident atrial fibrillation hospitalization in a large sleep-clinic cohort. *Chest*, *148*(4), 945-952.

CADTH. (2017). Interventions for the Treatment of Obstructive Sleep Apnea in Adults: A Health Technology Assessment. Retrieved 28th August 2018, from https://www.cadth.ca/dv/interventions-treatment-obstructive-sleep-apnea-adults-health-technology-assessment.

Català, R., Ferré, R., Cabré, A., Girona, J., Porto, M., Texidó, A., & Masana, L. (2016). Long-term effects of continuous positive airway pressure treatment on subclinical atherosclerosis in obstructive sleep apnoea syndrome. *Medicina Clínica (English Edition)*, *147*(1), 1-6.

Chai-Coetzer, C. L., Douglas, J., McEvoy, D., Naughton, M., Neill, A., Rochford, P., ... & Worsnop, C. (2014). Guidelines for sleep studies in adults. *Prepared for the Australasian Sleep Association*.

Chakravorty, I., Cayton, R. M., & Szczepura, A. (2002). Health utilities in evaluating intervention in the sleep apnoea/hypopnoea syndrome. *European Respiratory Journal*, *20*(5), 1233-1238.

Cistulli, P. A., Armitstead, J. P., Liu, D., Yan, Y., Pepin, J. L., Woehrle, H., ... & Malhotra, A. (2018). Real World PAP Adherence: Results from a Big Data Approach in More than Two Million Patients. In *B109. Treatment Options in Sleep Disordered Breathing: Adherence and Health Outcomes* (pp. A4391-A4391). American Thoracic Society.

Deloitte Access Economics. (2011). Re-awakening Australia: the economic cost of sleep disorders in Australia, 2010. Report for the Sleep Health Foundation. Canberra.

Deloitte Access Economics. (2017). Asleep on the job: costs of inadequate sleep in Australia. Report for the Sleep Health Foundation. Canberra.

Durán-Cantolla, J., Aizpuru, F., Montserrat, J. M., Ballester, E., Terán-Santos, J., Aguirregomoscorta, J. I., ... & Carrizo, S. (2010). Continuous positive airway pressure as treatment for systemic hypertension in people with obstructive sleep apnoea: randomised controlled trial. *Bmj*, *341*, c5991.

Epstein, L. J., Kristo, D., Strollo, P. J., Friedman, N., Malhotra, A., Patil, S. P., ... & Weinstein, M. D. (2009). Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *Journal of clinical sleep medicine*, *5*(03), 263-276.

Giles, T. L., Lasserson, T. J., Smith, B., White, J., Wright, J. J., & Cates, C. J. (2006). Continuous positive airways pressure for obstructive sleep apnoea in adults. *Cochrane Database of Systematic Reviews*, (1).

Gooneratne, N. S., Gehrman, P., Gurubhagavatula, I., Al-Shehabi, E., Marie, E., & Schwab, R. (2010). Effectiveness of ramelteon for insomnia symptoms in older adults with obstructive sleep apnea: a randomized placebo-controlled pilot study. *Journal of Clinical Sleep Medicine*, *6*(06), 572-580.

Gottlieb, D. J., Yenokyan, G., Newman, A. B., O'connor, G. T., Punjabi, N. M., Quan, S. F., ... & Shahar, E. (2010). Prospective study of obstructive sleep apnea and incident coronary heart disease and heart failure: the sleep heart health study. *Circulation*, *122*(4), 352-360.

Guest, J. F., Panca, M., Sladkevicius, E., Taheri, S., & Stradling, J. (2014). Clinical outcomes and cost-effectiveness of continuous positive airway pressure to manage obstructive sleep apnea in patients with type 2 diabetes in the UK. *Diabetes care*, DC_132539.

Gupta, M. A., Simpson, F. C., & Lyons, D. C. (2016). The effect of treating obstructive sleep apnea with positive airway pressure on depression and other subjective symptoms: A systematic review and meta-analysis. *Sleep medicine reviews*, *28*, 55-68.

Heinzer, R., Vat, S., Marques-Vidal, P., Marti-Soler, H., Andries, D., Tobback, N., ... & Vollenweider, P. (2015). 'Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study'. The Lancet Respiratory Medicine, 3(4), 310-318.

Hiensch, R., Nandedkar, D. S., & Feinsilver, S. H. (2016). Optimizing CPAP Treatment for Obstructive Sleep Apnea. *Current Sleep Medicine Reports*, *2*(2), 120-125.

Hillman, D., Mitchell, S., Streatfeild, J., Burns, C., Bruck, D., & Pezzullo, L. (2018). The economic cost of inadequate sleep. *Sleep*.Hillman et al. (2018).

Khan, S. U., Duran, C. A., Rahman, H., Lekkala, M., Saleem, M. A., & Kaluski, E. (2018). A meta-analysis of continuous positive airway pressure therapy in prevention of cardiovascular events in patients with

obstructive sleep apnoea. *European Heart Journal*, *39*(24), 2291–2297. JOUR. Retrieved from http://dx.doi.org/10.1093/eurheartj/ehx597

Kim, Y., Koo, Y. S., Lee, H. Y., & Lee, S. Y. (2016). Can continuous positive airway pressure reduce the risk of stroke in obstructive sleep apnea patients? A systematic review and meta-analysis. *PLoS One*, *11*(1), e0146317.

Kohler, M., Smith, D., Tippett, V., & Stradling, J. R. (2010). Predictors of long-term compliance with continuous positive airway pressure. *Thorax*, *65*(9), 829-832.Kohler et al. 2011

Kushida, C. A., Littner, M. R., Hirshkowitz, M., Morgenthaler, T. I., Alessi, C. A., Bailey, D., ... & Kapen, S. (2006). Practice parameters for the use of continuous and bilevel positive airway pressure devices to treat adult patients with sleep-related breathing disorders. *Sleep*, *29*(3), 375-380.

Lee, M. C., Shen, Y. C., Wang, J. H., Li, Y. Y., Li, T. H., Chang, E. T., & Wang, H. M. (2017). Effects of continuous positive airway pressure on anxiety, depression, and major cardiac and cerebro-vascular events in obstructive sleep apnea patients with and without coronary artery disease. *Tzu-Chi Medical Journal*, *29*(4), 218.

Marin, J. M., Carrizo, S. J., Vicente, E., & Agusti, A. G. (2005). Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *The Lancet*, *365*(9464), 1046-1053.

Martínez-García, M. A., Capote, F., Campos-Rodríguez, F., Lloberes, P., de Atauri, M. J. D., Somoza, M., ... & Durán-Cantolla, J. (2013). Effect of CPAP on blood pressure in patients with obstructive sleep apnea and resistant hypertension: the HIPARCO randomized clinical trial. *Jama*, *310*(22), 2407-2415.

McArdle, N., Devereux, G., Heidarnejad, H., Engleman, H. M., Mackay, T. W., & Douglas, N. J. (1999). Long-term use of CPAP therapy for sleep apnea/hypopnea syndrome. *American Journal of Respiratory and Critical Care Medicine*, *159*(4), 1108-1114.

McDaid, C., Griffin, S., Weatherly, H., Durée, K., Van der Burgt, M., Van Hout, S., ... & Westwood, M. (2009). Continuous positive airway pressure devices for the treatment of obstructive sleep apnoea–hypopnoea syndrome: a systematic review and economic analysis.

McEvoy, R. D., Antic, N. A., Heeley, E., Luo, Y., Ou, Q., Zhang, X., ... & Chen, G. (2016). CPAP for prevention of cardiovascular events in obstructive sleep apnea. *New England Journal of Medicine*, *375*(10), 919-931.

McMillan, A., Bratton, D. J., Faria, R., Laskawiec-Szkonter, M., Griffin, S., Davies, R. J., ... & PREDICT Investigators. (2014). Continuous positive airway pressure in older people with obstructive sleep apnoea syndrome (PREDICT): a 12-month, multicentre, randomised trial. *The Lancet Respiratory Medicine*, *2*(10), 804-812.

Muraki, I., Wada, H., & Tanigawa, T. (2018). Sleep apnea and type 2 diabetes. *Journal of Diabetes Investigation*, *0*(0). JOUR. https://doi.org/10.1111/jdi.12823

National Health and Medical Research Council. (2000). Effectiveness of nasal continuous positive airway pressure (nCPAP) in obstructive sleep apnoea in adults. Canberra. Australian Government.

Ning, Y., Zhang, T. S., Wen, W. W., Li, K., Yang, Y. X., Qin, Y. W., ... & Yang, Y. Y. (2018). Effects of continuous positive airway pressure on cardiovascular biomarkers in patients with obstructive sleep apnea: a meta-analysis of randomized controlled trials. *Sleep and Breathing*, 1-10.

Pamidi, S., Knutson, K. L., Ghods, F., & Mokhlesi, B. (2012). The impact of sleep consultation prior to a diagnostic polysomnogram on continuous positive airway pressure adherence. *Chest, 141*(1), 51-57.

Peker, Y., Glantz, H., Eulenburg, C., Wegscheider, K., Herlitz, J., & Thunström, E. (2016). Effect of positive airway pressure on cardiovascular outcomes in coronary artery disease patients with nonsleepy obstructive sleep apnea. The RICCADSA randomized controlled trial. *American journal of respiratory and critical care medicine*, *194*(5), 613-620.

Peppard, P. E., Szklo-Coxe, M., Hla, K. M., & Young, T. (2006). Longitudinal association of sleep-related breathing disorder and depression. *Archives of internal medicine*, *166*(16), 1709-1715.

Pietzsch, J. B., Garner, A., Cipriano, L. E., & Linehan, J. H. (2011). An integrated health-economic analysis of diagnostic and therapeutic strategies in the treatment of moderate-to-severe obstructive sleep apnea. *Sleep*, *34*(6), 695-709.

Poullié, A. I., Cognet, M., Gauthier, A., Clementz, M., Druais, S., Späth, H. M., ... & Harousseau, J. L. (2016). Cost-effectiveness of treatments for mild-to-moderate obstructive sleep apnea in France. *International journal of technology assessment in health care*, *32*(1-2), 37-45.

Povitz, M., Bolo, C. E., Heitman, S. J., Tsai, W. H., Wang, J., & James, M. T. (2014). Effect of Treatment of Obstructive Sleep Apnea on Depressive Symptoms: Systematic Review and Meta-Analysis. *PLOS Medicine*, *11*(11), e1001762. JOUR. Retrieved from https://doi.org/10.1371/journal.pmed.1001762

Redline, S., Yenokyan, G., Gottlieb, D. J., Shahar, E., O'connor, G. T., Resnick, H. E., ... & Ali, T. (2010). Obstructive sleep apnea–hypopnea and incident stroke: the sleep heart health study. *American journal of respiratory and critical care medicine*, *182*(2), 269-277.

Rodenstein, D. (2009). Sleep apnea: traffic and occupational accidents–individual risks, socioeconomic and legal implications. *Respiration, 78*(3), 241-248.

Rotenberg, B. W., Murariu, D., & Pang, K. P. (2016). Trends in CPAP adherence over twenty years of data collection: a flattened curve. *Journal of Otolaryngology-Head & Neck Surgery*, *45*(1), 43.

Salepci, B., Caglayan, B., Kiral, N., Parmaksiz, E. T., Comert, S. S., Sarac, G., … Gungor, G. A. (2013). CPAP Adherence of Patients With Obstructive Sleep Apnea. *Respiratory Care*, *58*(9), 1467 LP-1473. JOUR. Retrieved from http://rc.rcjournal.com/content/58/9/1467.abstract

Sawyer, A. M., King, T. S., Hanlon, A., Richards, K. C., Sweer, L., Rizzo, A., & Weaver, T. E. (2014). Risk assessment for CPAP nonadherence in adults with newly diagnosed obstructive sleep apnea: preliminary testing of the Index for Nonadherence to PAP (I-NAP). *Sleep and Breathing*, *18*(4), 875-883.

Schoch, O. D., Baty, F., Niedermann, J., Rüdiger, J. J., & Brutsche, M. H. (2014). Baseline predictors of adherence to positive airway pressure therapy for sleep apnea: a 10-year single-center observational cohort study. *Respiration*, *87*(2), 121-128.

Senaratna, C. V., Perret, J. L., Lodge, C. J., Lowe, A. J., Campbell, B. E., Matheson, M. C., ... & Dharmage, S. C. (2017). Prevalence of obstructive sleep apnea in the general population: a systematic review. *Sleep Medicine Reviews*, *34*, 70-81.

Sharples, L. D., Clutterbuck-James, A. L., Glover, M. J., Bennett, M. S., Chadwick, R., Pittman, M. A., & Quinnell, T. G. (2016). Meta-analysis of randomised controlled trials of oral mandibular advancement devices and continuous positive airway pressure for obstructive sleep apnoea-hypopnoea. *Sleep medicine reviews*, *27*, 108-124.

Somiah, M., Taxin, Z., Keating, J., Mooney, A. M., Norman, R. G., Rapoport, D. M., & Ayappa, I. (2012). Sleep quality, short-term and long-term CPAP adherence. *Journal of Clinical Sleep Medicine*, *8*(05), 489-500.

Tan, M. C. Y., Ayas, N. T., Mulgrew, A., Cortes, L., FitzGerald, J. M., Fleetham, J. A., ... & Marra, C. A. (2008). Cost-effectiveness of continuous positive airway pressure therapy in patients with obstructive sleep apnea-hypopnea in British Columbia. *Canadian respiratory journal*, *15*(3), 159-165.

Trakada, G., Economou, N. T., Nena, E., Trakada, A., Zarogoulidis, P., & Steiropoulos, P. (2015). A health-economic analysis of diagnosis and treatment of obstructive sleep apnea with continuous positive airway pressure in relation to cardiovascular disease. The Greek experience. *Sleep and Breathing*, *19*(2), 467-472.

Tregear, S., Reston, J., Schoelles, K., & Phillips, B. (2010). Continuous Positive Airway Pressure Reduces Risk of Motor Vehicle Crash among Drivers with Obstructive Sleep Apnea: Systematic Review and Meta-analysis. *Sleep*, *33*(10), 1373–1380. JOUR. Retrieved from http://dx.doi.org/10.1093/sleep/33.10.1373

Wang, X. I. A., Bi, Y., Zhang, Q., & Pan, F. (2013). Obstructive sleep apnoea and the risk of type 2 diabetes: a meta-analysis of prospective cohort studies. *Respirology*, *18*(1), 140-146.

Weaver, T. E., & Sawyer, A. M. (2010). Adherence to Continuous Positive Airway Pressure Treatment for Obstructive Sleep Apnea: Implications for Future Interventions. *The Indian Journal of Medical Research*, *131*, 245–258. JOUR. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2972705/

Wozniak, D. R., Lasserson, T. J., & Smith, I. (2014). Educational, supportive and behavioural interventions to improve usage of continuous positive airway pressure machines in adults with obstructive sleep apnoea. *Cochrane Database of Systematic Reviews*, (1).

# Appendix A

This appendix provides additional supporting information for compliance and adherence, and for the relationships between the risk of disease for people with OSA who receive CPAP therapy.

### Evidence for compliance and adherence

While CPAP continues to be the gold standard treatment for OSA, compliance has been and continues to be an issue (Weaver et al 2013). Low adherence (which comprises compliance and persistence with therapy) limits the effectiveness of the treatment, increases the risk of comorbid conditions and impairs quality of life (Weaver et al 2010).

The definition of compliance varies across studies, and there is some uncertainty over the effectiveness of CPAP given the varying levels of compliance. A widely used definition of compliance is that used by the Centers for Medicare and Medicaid Services in the US, which specifies CPAP should be used for at least 4 hours per night on 70% of nights (Hiensch et al 2016).

A targeted literature review was conducted to identify the average level of compliance and persistence with CPAP therapy for use in the economic evaluation. The results of the targeted review are outlined in the following paragraphs. Table A.1 then summarises the findings of the review.

Salepci et al (2013) conducted a prospective cohort analysis of subjects diagnosed with OSA by PSG at two clinical sleep centres in the US. Data was collected between 2005 and 2011, and CPAP adherence was defined as use for at least 4 hours per night for at least 70% of days monitored. Follow-up was conducted at 1, 3, 6 and 12 months, and every 6 months thereafter. In the patients who attended follow-ups (38.3%), adherence was 64.5% after an average of 16.5 months. For the adherent group, the average usage was reported to be 5.7±1.2 hours per night for seven nights per week.

Cistulli et al (2018) utilised a cloud-based approach to estimate real-world adherence rates with CPAP treatment for OSA. This approach collected de-identified data from the AirView database for 2,237,700 US patients to investigate adherence over 90 days. Compliance was defined as at least four hours of use in more than 70% of nights during 30 consecutive days. Compliance in the first 90-days was estimated at 75%, with mean daily usage of 5.2-hours per night. Given that the modelling required evidence for long term adherence rates, the relatively short follow-up was considered to be a limitation of the article and it was not included in the summary table.

McArdle et al (1999) conducted a cohort-based study into the determinants of CPAP compliance among patients referred to the Scottish National Sleep Centre and prescribed CPAP between 1986 and 1997. McArdle et al (1999) found that 84% and 68% of patients were still using their CPAP machine at 12 months and 4 years, respectively. At 5 years, compliance with CPAP therapy was estimated to be 76% using a definition of >3.7 hours per night. Continued use was positively associated with severity of OSA and daytime sleepiness. The median nightly use of CPAP among those continuing treatment was 5.7 hours, and 76% of those continuing use recorded average nightly use of 3.7 hours or more per night.

Schoch et al (2014) sought to determine long-term adherence CPAP through a 10-year retrospective observational study. Participants were selected from all patients referred to a single sleep centre in Switzerland that were diagnosed with OSA between 2006 and 2011. The sample comprised 1,756 patients, and the median follow-up time was 36 months. The observed adherence in patients was 73% at one year, 55% at five years, and 51% at 10 years. At the last follow-up (1,113 participants), 21.3% of participants reported use of less than 4.3-hours per night, 22.7% of participants recorded use of between 4.3 and 6.0 hours per night, 20.2% between 6.0 and 7.1-hours per night, and 20.8% for greater than 7.1-hours per night. ESS and AHI were both positive predictors of continued compliance with CPAP therapy over time.

Kohler et al (2010) also assessed predictors of long-term compliance with CPAP. Their sample included 3,900 patients who were started on CPAP therapy between 1994 and 2005 at a single centre. Kohler et al (2010) found that 81% and 70% of patients were using CPAP after 5 and 10 years, respectively, and that 83% of the patients used CPAP for at least 3.5 hours per night. The adherence to CPAP therapy was therefore 67.2%.

Table A.1: Average adherence rates

| Author | Definition of compliance | Follow up period | Sample | Adherence |
|---|---|---|---|---|
| McArdle et al (1999) | ≥ 3.7 hours per night | 5 years | 1,103 | 51.7% |
| Schoch et al (2014) | Not stated | 5 years | 1,756 | 55.0% |
| Salepci et al (2013) | ≥ 4 hours per night, 70% of nights | 6.5 years | 248 | 64.5% |
| Kohler et al (2010) | ≥ 3.5 hours per night | 5 years | 639 | 67.2% |
| **Weighted average** | | | | **56.7%** |

Source: as noted in table.

### Effect of CPAP on conditions associated with OSA

The following sections provide an overview of literature discussing the effect of CPAP on conditions associated with OSA. The article summaries described in the following do not directly influence the modelling; however, the purpose of these sections is to provide supporting evidence that there are demonstrable improvements in outcomes given adherence to CPAP therapy.

Evidence was considered for the risk of:

- cardiovascular disease;
- depression;
- type 2 diabetes;
- MVAs; and
- workplace accidents.

**Cardiovascular disease**

The impact of CPAP on the risk of cardiovascular disease is mixed. CPAP has been shown to reduce blood pressure (Duran-Cantolla et al 2010; Martinez-Garcia 2013; McDaid et al 2009, Giles et al 2006) in the short term, and improve CVD biomarkers (Ning et al 2018).

CADTH (2017) reviewed evidence for cardiovascular events. Three of four systematic reviews that were identified reported significantly reduced risk for cardiovascular events, cardiac disease (including recurrent cardiac disease), or recurrent atrial fibrillation with CPAP compared with no treatment or no CPAP. The relative risk of the events ranged from 0.46 to 0.57. Two of the four systematic reviews reported no significant differences in the risk of major adverse cardiac events, hypertension and cardiovascular events or myocardial infarction with CPAP compared with controls or no treatment. For cerebrovascular events, two systematic reviews were identified. One of the reviews reported significantly reduced risk of stroke (not ischaemic stroke) with a relative risk of 0.27. The other systematic review did not find a significant different in the risk of stroke.

Based on the results of a meta-analysis, Khan et al (2018) concluded that CPAP therapy might reduce major adverse cardiovascular events and stroke among subjects with CPAP, where compliance exceeded 4 hours per night. Khan et al (2018) observed that increased CPAP usage time can significantly reduce the risk of major cardiovascular events. When CPAP compliance was greater than four hours per night, the risk of cardiovascular events was reduced by 57% (relative risk 0.43, 95% confidence interval 0.23-0.80), although a non-significant risk reduction was observed when studies with lower average compliance were included.

While finding that CPAP reduced the number of AHI events in patients with CVD as well as health related quality of life and mood, McEvoy et al (2016) did not find any association between CPAP and cardiovascular outcomes in patients with established cardiovascular disease. The participants had moderate to severe OSA and coronary or cerebrovascular disease, and mean adherence to treatment was 3.3 hours per night. McEvoy et al (2016) followed patients for 3.7 years on average.

In summary, it appears that CPAP can effectively reduce the number of cardiovascular outcomes that occur, although the evidence suggests that CPAP may be effective to prevent cardiovascular outcomes, rather than improving outcomes in people with established cardiovascular disease.

**Depression**
There is recent evidence that CPAP can reduce depression among people with OSA.

A systematic review of the effect of CPAP on depressive symptoms found that while improving symptoms compared to the control, there was considerable heterogeneity between trials (Povitz et al 2014). The effect of CPAP was higher in populations where the baseline depression rate was above the cut-off for depression.

Lee et al (2017) conducted a prospective study that followed patients over a period of 6 months and measured depression based on the Beck Depression Inventory-II. Lee et al (2017) found that CPAP improved anxiety and depression in people with OSA who complied with CPAP therapy (greater than 4 hours/night on 70% of days).

McDaid et al (2009) concluded from their meta-analysis of five studies reporting on the hospital anxiety depression scale that there was no statistically significant difference between CPAP and placebo for depression. There was only one study that reported the profile of mood scale, finding a statistically significant improvement. However, Giles et al (2006) – an earlier Cochrane library systematic review – found a statistically significant improvement in hospital anxiety depression scale.

**Diabetes**
The impact of CPAP on patients with diabetes and OSA has not been established (Muraki et al, 2018).

CADTH (2017) found two systematic reviews discussing the effect of CPAP on diabetes in adults. Both of the systematic reviews reported no significant differences in glycated haemoglobin (A1c) with CPAP compared with controls or pre-treatment. However, the duration of the included studies ranged from four weeks to four months.

However, it is considered likely that effective treatment of OSA will prevent some cases of type 2 diabetes from developing (Wang et al, 2013; Muraki et al, 2018). Moreover, Muraki et al (2018) notes that CPAP can improve insulin resistance.

**Accident risk**
CPAP has been shown to reduce the risk of MVA in people with OSA. For workplace accidents there has been less research directly comparing CPAP use and reduced risk of incidents. However, it is reasonable to interpret that, since CPAP is effective in treating OSA and a proportion of workplace incidents are attributable to OSA, the effective compliance with CPAP therapy could also reduce the risk of accidents. This hypothesis is supported by the literature and modelling studies – for example, see CADTH (2017).

In a systematic review and meta-analysis of 9 observational studies covering 1,976 individuals, Tregear et al (2010) found a significant risk reduction following treatment with CPAP (risk ratio = 0.278). The authors also found that daytime sleepiness improves significantly following a single night of treatment, and that simulated driving performance improved significantly within 2 to 7 days of CPAP therapy. Tregear et al (2010) concluded that treatment with CPAP reduces crash risk among drivers with moderate to severe OSA, and that it relieves symptoms of excessive daytime sleepiness associated with OSA.

CADTH (2017) supported using evidence from Antonopoulos et al (2011) to estimate the effect of CPAP therapy on the risk of accidents in patients with OSA. Antonopoulos et al (2011) found ten studies with outcomes for road traffic accidents, with a pooled sample size of 1,221 people. Antonopoulos et al (2011) estimated that CPAP would result in a statistically significant reduction in accidents, with an observed odds ratio of 0.21 and an incident rate ratio of 0.45. The authors concluded that CPAP demonstrates a sizeable protective effect on accidents.

# Limitation of our work

### General use restriction

This report is prepared solely for the use of the Sleep Health Foundation. This report is not intended to and should not be used or relied upon by anyone else and we accept no duty of care to any other person or entity. The report has been prepared for the purpose of estimating the cost effectiveness of continuous positive airway pressure to help inform the evidence-based treatment of sleep deficiencies. You should not refer to or use our name or the advice for any other purpose.

Deloitte.
Access Economics

**Deloitte Access Economics**
ACN: 149 633 116
8 Brindabella Circuit
Brindabella Business Park
Canberra Airport ACT 2609
Tel: +61 2 6263 7000
Fax: +61 2 6263 7004

Deloitte Access Economics is Australia's pre-eminent economics advisory practice and a member of Deloitte's global economics group. For more information, please visit our website

www.deloitte.com/au/deloitte-access-economics