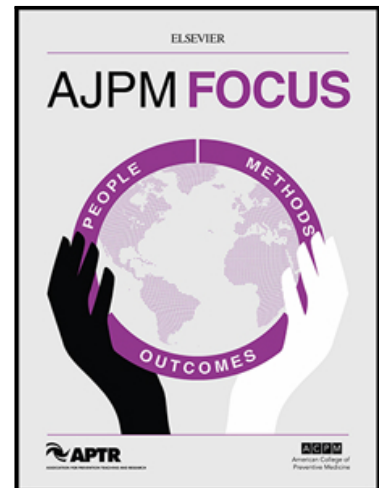


## Journal Pre-proof

Physical activity and depression and anxiety disorders in Australia: a lifetable analysis

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## Physical activity and depression and anxiety disorders in Australia: a lifetable analysis

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## Highlights

- We used lifetable modelling for the Australian population.
- Adherence to physical activity guidelines reduces anxiety and depression by 4%–7%.
- This reduces lifetime burden by gains of >0.5 million health-adjusted life years for each outcome.
- This reduces lifetime health care costs by >\$5 billion for each outcome (anxiety and depression).

## ABSTRACT

**Introduction** Mental disorders, in particular depressive and anxiety disorders are a leading cause of disability in Australia and globally. Physical activity (PA) may reduce the incidence of anxiety and depression, and this supports the inclusion of physical activity in strategies for the prevention of mental ill health. Policy makers need to know the potential impact and cost savings of such strategies. We aimed to quantify the impact of changes in PA on the burden of anxiety and depression and health care costs in Australia.

**Methods** We used a proportional multistate lifetable model to estimate the impact of changes in PA levels on anxiety and depression burdens for the 2019 Australian population (numbering 24.6 million) over their remaining lifetime. The changes in PA were modelled through three counterfactual scenarios informed by policy targets: attainment of the Australian PA guidelines, and achievement of the WHO Global Action Plan on PA targets of a 10% relative reduction in the prevalence of insufficient PA by 2025 and a 15% relative reduction by 2030.

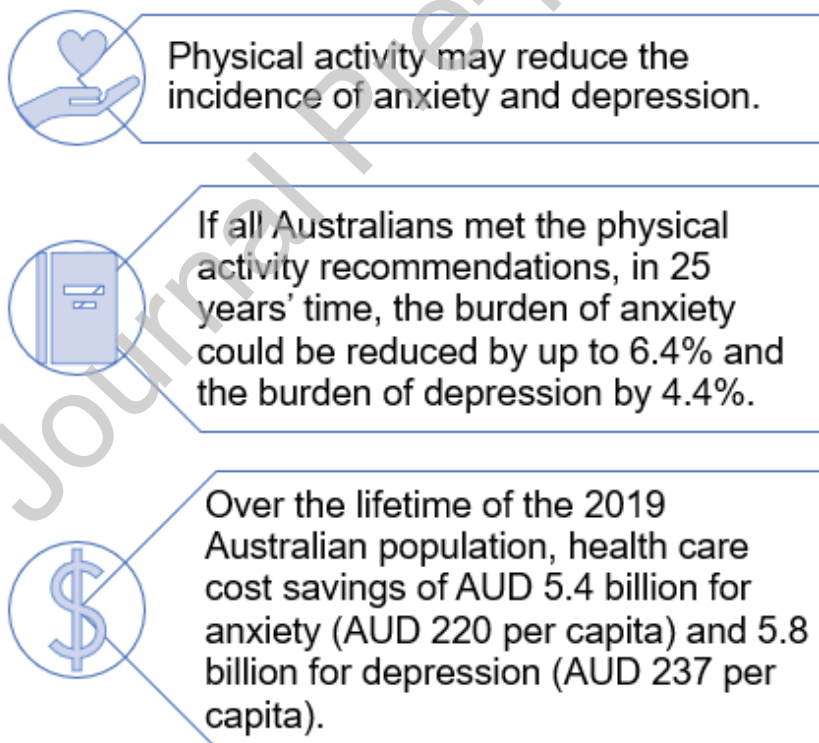
**Results** If all Australians adhered to the recommended minimum PA levels, in 25 years' time, the burden of anxiety could be reduced by up to 6.4% (95% uncertainty intervals [UIs] 2.5 to 10.6) and depression by 4.4% (95% UIs 2.3 to 6.5). Over the lifetime of the 2019 Australian population, the gains could add up to 640,592 health-adjusted life years for

anxiety (26 HALYs per 1,000 persons), 523,717 HALYs for depression (21 HALYs per 1,000 persons) and health care cost savings of AUD 5.4 billion for anxiety (AUD 220 per capita) and 5.8 billion for depression (AUD 237 per capita).

**Discussion** Adherence to the Australian PA guidelines and achievement of the 2025 and 2030 global PA targets could lead to a substantial reduction of the burden of anxiety and depression. This study provides empirical support for the inclusion of physical activity in strategies for the prevention of mental ill health. Future studies should also assess the size and distribution of the benefits for different socio-economic and ethnic groups.

### Graphical Abstract

#### Physical activity and depression and anxiety disorders in Australia: a lifetable analysis



**Keywords:** Physical activity, anxiety, depression, mental health, Australia.

## INTRODUCTION

Mental disorders, in particular depressive and anxiety disorders are a leading cause of disability worldwide.<sup>1</sup> In Australia, mental disorders were the fourth leading cause of disability in 2019 with 4.3 million prevalent cases.<sup>1</sup> Depressive and anxiety disorders constituted 57% of this burden, which further increased due to the COVID-19 pandemic-induced impairment in work and social functioning.<sup>2,3</sup> People experiencing severe mental health conditions also die up to two decades prematurely due to preventable physical conditions.<sup>4,5</sup>

Staying active regularly has been identified as essential for good mental health.<sup>6-8</sup> Prospective studies suggest that physical activity (PA) may reduce the incidence of depression and anxiety.<sup>9,10</sup> More than half (55%) of adults in Australia do not meet the recommended PA guidelines<sup>11,12</sup> and people living in socioeconomically disadvantaged communities tend to be less active.<sup>13</sup>

The Australian national mental health policy and the mental health plan emphasize the need for efforts that prevent the onset of mental ill health.<sup>14,15</sup> In a companion paper,<sup>16</sup> we systematically reviewed available epidemiological evidence to establish the relationship between PA and incident cases of anxiety and depression. We found that PA may reduce the incidence of anxiety and depression by up to 17% and 26%, respectively, and judged the relationship to probably be causal. In this current paper, we use these findings in a proportional multistate lifetable (pMSLT) modelling study to quantify the impacts of an increase in PA levels on the burden of anxiety and depression and healthcare costs in Australia. The pMSLT modelling is an established approach that has been used previously in Australia to estimate health and economic impacts of various preventive health strategies.<sup>17-20</sup> Specifically, several studies have applied this method to investigate the health and economic

impact of strategies that increase PA such as PA intervention programs in various settings and strategies that increase the use of active transport.<sup>21-25</sup> In New Zealand, Mizdrak and colleagues used the pMSLT to estimate the health and economic gains that would be if the 2018 Global Action Plan for Physical Activity target was met.<sup>26</sup> Our study expands research in this area and introduces a novel aspect where we estimate the health and economic impact of PA on anxiety, depression, outcomes not included in the previous studies.

Our study was part of a broader project commissioned by the New South Wales (NSW) Ministry of Health to value the health benefits of active transport. We developed the NSW Active Transport Health model and sought to include all relevant health outcomes that have sufficiently strong epidemiological evidence of an association with active transport. Based on our findings in our companion paper,<sup>16</sup> anxiety and depression were included as health outcomes within the NSW Active Transport Health model.<sup>27</sup>

## **METHODS**

### **Overview**

We applied epidemiological modelling to estimate the impact of changes in the Australian population's PA levels on anxiety and depression burdens. We used a proportional multi-state lifetable (pMSLT) model<sup>28</sup> to simulate the 2019 Australian population in 5-year age groups over their remaining lifetime (Supplementary File [SF] figure 1). The pMSLT method copes with multiple diseases and allows for comorbidity. The two conditions were modelled independently as two separate mental health outcomes<sup>28-30</sup> We used the Guidelines for Accurate and Transparent Health estimates Reporting (GATHER) checklist to guide the documenting of our modelling data and methods.<sup>31</sup>

### **Physical activity levels in Australia**

We used PA data from the Australia National Health survey (NHS) 2017-2018 (SF table 1).<sup>11</sup> We calculated weekly PA levels by multiplying the minutes of total weekly PA by the

average metabolic equivalent of task (MET).<sup>32</sup> To convert the weekly PA levels to METs, we used the activity categories of walking, moderate PA, and vigorous PA that were reported in the NHS microdata (walking=3.5 METs, moderate PA=5 METs, vigorous PA=7.5 METs). PA was modelled as a categorical approximation of a Dirichlet distribution, a generalization of the Beta distribution to multiple categories.<sup>33</sup> For the model, PA was categorized into four levels: inactive (0 MET), low active (>0 & <600 MET-minutes per week), moderately active (>=600 & <1600 MET- minutes per week) and highly active (>=1600 MET- minutes per week). The average MET-minutes for each PA category except inactive were assigned a lognormal distribution.

### **Association between physical activity and anxiety, depression**

In this study, we used the measures of association from our systematic review of review study whose findings are reported in a companion paper.<sup>16</sup> In summary, we found sufficient evidence to support an association between PA and incident cases of anxiety and depression. The association was graded as a probable causal relationship based on the Bradford Hill criteria<sup>34,35</sup> and the World Cancer Research Fund grading system.<sup>36</sup> To model the association between PA and depression, we used the adjusted relative risk=0.83, 95% CI=0.76, 0.90<sup>37</sup> and for the association between PA and anxiety we used the adjusted odds ratio 0.74 (95% CI = 0.62, 0.88).<sup>38</sup> The resulting risk chart is shown in Figure 1. We assumed that the lowest and highest PA categories reported for the measures of association<sup>37,38</sup> refer to the inactive and highly active categories in our model respectively. To derive the measures of association for all four modelled PA categories, scaling was done to interpolate values between ‘lowest’ and ‘highest’ PA level categories, using the findings from the meta-analysis by Ekelund and colleagues<sup>39</sup> because PA is measured relatively precisely using accelerometry. In their review, studies with good quality PA exposure measures showed diminishing returns with increasing PA levels. We assume that this also applies to the outcomes of our study. This



means that the greatest reduction in risk per unit of PA is seen in the lowest PA category and the health gains diminish at higher levels of physical activity (Figure 1). We modelled the risk measures as lognormally distributed.<sup>40</sup>

### Disease epidemiology and healthcare costs

We used age- and sex-specific incidence and prevalence data, prevalent years of life lived with disability (YLD) rates and population data from the Global Burden of Disease (GBD) 2019 study.<sup>1,41</sup> GBD was the preferred source as it provides the latest disease estimates for Australia. We used DisMod II<sup>42</sup> to enforce internal consistency in the epidemiological estimates obtained from the GBD 2019 study, while deriving remission parameters that are not provided in the GBD data (SF figure 2, SF tables 2 and 3). To determine the loss of quality of life we used disability weights, which were calculated based on disease specific prevalence and YLD estimates (SF table 4).<sup>1</sup>

Healthcare costs were calculated using data from the *Disease Expenditure in Australia 2018-19* report prepared by the Australian Institute of Health and Welfare (AIHW) (SF table 7).<sup>43</sup>

Costs per prevalent case of anxiety and depression were calculated based on GBD 2019 disease prevalence and population numbers.<sup>1</sup> Overall health care costs for all other health conditions were also included in our model (SF table 8). This is necessary because as interventions prolong life, health care costs will be incurred, 'health care costs in added years of life'.<sup>44</sup> A summary of the model input parameters is presented in Table 1.

**Table 1: Model input parameters**

Input data	Uncertainty	Source
Disease incidence	N/A	Global Burden of Disease (GBD) 2019 study. <sup>1,41</sup> ( SF tables 2-6)
Disease prevalence		
Disease remission <sup>a</sup>		
All-cause mortality rates		
Disability weights <sup>b</sup>		
Years lived with disability (YLD) (all causes and disease specific YLDs)		

Population numbers		
Relative risks <sup>c</sup>	Normal (Ln RR) <sup>d</sup>	Schuch et al. <sup>37</sup> and Schuch et al. <sup>38</sup> (Figure 1)
Scaling the 'lowest' and 'highest' PA categories reported in RRs to the four modelled PA categories	N/A	Ekelund and colleagues <sup>39</sup>
MET-minutes (walking = 3.5, moderate PA =5, vigorous PA = 7.5)	N/A	Ainsworth et al. <sup>32</sup>
PA categories defining PA levels in the population	Dirichlet	Australia National Health survey (NHS) 2017-2018. <sup>11</sup>
Modelled PA categories derived from MET minutes	Lognormal	(SF table 1).
Health care costs	N/A	<i>Disease Expenditure in Australia 2018-19</i> report prepared by the Australian Institute of Health and Welfare (AIHW) <sup>43</sup> (SF tables 7 and 8)
Discount rates applied in the sensitivity analysis	N/A	Australian Government Best Practice Regulation Guidance. <sup>45,46</sup>

<sup>a</sup> We used DisMod II<sup>42</sup> to enforce internal consistency in the epidemiological estimates obtained from the GBD 2019 study, while deriving remission parameters that are not provided in the GBD data (SF figure 2, SF tables 2 and 3)

<sup>b</sup> Disability weights were calculated based on disease specific prevalence and YLD estimates (SF table 4).

<sup>c</sup> Adjusted relative risk measures for outcome, depression and adjusted odds ratio for outcome, anxiety

<sup>d</sup> We used a modified version of the log of the relative risk function was used to avoid a skewed lognormal distribution<sup>40</sup> N/A: Uncertainty not applied in our model.

### Modelled scenarios

First, we simulated 'business as usual' scenario where the current PA levels (by age and sex) continue in the reference population, and in parallel, comparator counterfactual scenarios in which the entire population achieves changes in PA levels. The changes in PA were modelled through three counterfactual scenarios: attainment of the Australian PA guidelines,<sup>7</sup> and achievement of the 2025<sup>6</sup> and 2030 global PA targets.<sup>8</sup> We used the 'proportions shift' method<sup>47</sup> to model changes in PA levels by changing the proportion of the population in each PA category.

For the first counterfactual scenario where the entire population meets the Australian PA targets, we used the updated PA guidelines for Australians.<sup>7</sup> For 18 to 64 years, the

recommendation is to be active on most (preferably all) days, to a weekly total of 2.5 to 5 hours of moderate activity (150 to 300 minutes) or 1.25 to 2.5 hours (75 to 150 minutes) of vigorous activity, or an equivalent combination of both. For those aged 65 years and over, at least 30 minutes of moderate activity on most (preferably all) days is recommended. In the model, we implemented this scenario by moving the proportions of people in the inactive (METs = 0) and low active (>0 & <600 MET-minutes per week) PA categories to the moderately active level (>=600 & <1600 MET-min/week). For the second and third counterfactual scenarios where the entire population achieves the set global targets, we modelled two targets: a) a 10% relative reduction in the prevalence of insufficient PA by 2025, one of the nine voluntary global targets set in the WHO Global Action Plan for the Prevention and Control of Non communicable diseases (NCDs) 2013-2020<sup>6</sup>. In the model, 10% of people in the inactive and low active PA categories were moved to the moderately active level. b) a 15% relative reduction in the global prevalence of physical inactivity in adults and in adolescents by 2030 as set in the WHO Global Action Plan on PA 2018-2030,<sup>8</sup> modelled as 15% of people in the inactive and low active PA categories moved to the moderately active level. The resulting proportions of people in the four PA categories for each modelled scenario are presented in the SF table 9. This analysis was restricted to adults aged 15 and above. To reflect the attainment of the target by 2025 and 2030, we phased in the intervention effect with linear increases from 2019 to 2025 and from 2019 to 2030 towards achieving the respective targets.

### **Lifetable analysis**

We used the proportional multi-state lifetable model<sup>28</sup> to simulate changes in the PA levels on anxiety and depression for the 2019 population (numbering 24.6 million [SF table 6]) over their remaining lifetime. The lifetables were populated with a closed cohort disaggregated by sex and 5-year age groups.

The proportional multi state life table is divided into sections: a standard cause elimination life table (main life table) and a section for each disease with an independent illness death process (which we refer to as disease specific sections in this paper) (SF figure 1).<sup>28</sup>

Two disease specific sections were generated in our model. We created a switch that allowed each disease to be switched on or off and hence model one outcome at a time. The proportion of the Australian population assigned to each disease section was determined by the disease incidence (inflow) and case-fatality (outflow) rates. We assumed no mortality (case fatality) from anxiety and depression. The two included diseases were modelled applying a set of differential equations to describe the transition between four states: healthy, diseased, dead from the disease, and dead from all other causes (SF figure 2).<sup>42</sup> Transition probabilities among the four states reflected rates of incidence, remission, case fatality, and mortality from all other causes (SF table 2 and 3). For each age-sex group, a change in exposure to the risk factor, insufficient PA modified the ‘post-intervention’ incidence via potential impact fraction (PIF) calculations.<sup>47</sup> For every modelled disease, the PIF calculates the proportional change in incidence after a change in exposure to PA (SF p. 10).<sup>47</sup> We used the disease-specific sections to report changes in incidence and prevalence. Over time, reduced incidence of disease in the ‘intervention’ population results in reductions in prevalence, compared with the reference population. Changes in disease-related quality of life at every age were calculated using disease-specific disability weights (SF table 4). These disease specific changes feed into a life table. The life tables were populated with a closed cohort of the entire 2019 Australia population disaggregated by sex and five-year age group (SF table 6). The life tables integrated all-cause mortality rates and years of life lived in poor health due to disease (SF tables 3 and 5) and changes in disease specific quality of life to calculate the number of health adjusted life years (HALYs) for the Australian population. These calculations for the stratified cohorts are simulated with 1-year cycle lengths until everyone

dies or reaches the age of 100 years for both the reference and intervention populations.

Where exposure to risk factor insufficient PA is reduced in the intervention population, there is an increase in the number of HALYs when compared against the reference population (business as usual scenario).

Since the national survey only provides PA information for persons aged 15 years and over, we restricted our analysis to these age groups. However, we ran the model from age 0 so that the avoidable burden in younger cohorts is included in the outputs once they reach 15 years of age. For the main analyses, we applied no discounting of health outcomes and healthcare costs.

### **Uncertainty analyses**

We quantified the simultaneous and combined effect of the uncertainty in model inputs on our outcomes. We implemented this using a Monte Carlo simulation with bootstrapping (2,000 iterations) while incorporating probabilistic uncertainty from risk measures and PA input parameters. The 95% uncertainty intervals were calculated, reflecting parameter uncertainty in the model (2.5 and 97.5 percentiles capturing sampling error with input data).

### **Sensitivity analyses**

Sensitivity analyses were carried out to quantify the impact of change in discount rates applied on costs and health effects (HALYs). In line with Australian Government Best Practice Regulation Guidance, we applied a discount rate of 3% for the health outcomes and 7% for the healthcare costs to all modelled scenarios.<sup>45,46</sup>

We used Microsoft Excel 365 and two software Add-ins. The EpiGearXL 5.0 add-in was used for the calculation of the potential impact fraction and Ersatz (Version 1.35) was used for the uncertainty analysis.<sup>48</sup> Ethics approval was not required for the lifetable analysis.

## **RESULTS**

### **The potential impact of an increase in PA levels on anxiety and depression**

For the HALYs and healthcare costs outcomes, we report outputs estimated for the remaining lifetime of the 2019 population of Australia. For the changes in incidence, we report outputs estimated for the next 25 years (between year 2019 and 2044) and changes in prevalence for the year 2044. In the SF results table, we give additional results for all outcomes for different time periods such as the global and national NCD policy cycles, year 2025 and 2030 respectively. Additionally, in this manuscript, we present results only for the modelled scenario where all people adhered to the PA guidelines in Australia. Over the lifetime of the 2019 population of Australia, gains from a 10% relative reduction in prevalence of insufficient PA by 2025 could add up to 60,016 HALYs for anxiety (95% uncertainty intervals [UIs] 24,103 to 98,457), 50,333 for depression (95% UIs 25,954 to 75,379), (SF table 13) and health care cost savings of AUD 508 million for anxiety and 561 million for depression (SF table 15). A 15% relative reduction in prevalence of insufficient PA by 2030 could yield a gain of 85,983 HALYs for anxiety (95% UIs 34,852 to 140,789), 72,399 for depression (95% UIs 38,099 to 106,895) (SF table 13) and health care cost savings mean estimates of 732 million for anxiety and 810 million for depression (SF table 15), over the lifetime of the 2019 population of Australia.

### **Changes in disease specific incidence**

Between 2019 and 2044 (25 years), our model projects that if all people adhered to the PA guidelines in Australia, there would be a reduction in the cumulative number of new cases of anxiety by 187,266 (95% uncertainty intervals [UIs] 73,802-309,167) and of depression by over 1.1 million (95% UIs 582,556-1,681,544) (Table 2). The reduction in new cases was greater for females than males. A reduction in total incident cases of anxiety and depression over different time periods is shown in SF tables 10 and 11.

**Table 2: Reduction in disease incidence and prevalence**

	Incident and prevalence count			Proportional reduction in year 25		
	Male, mean (95% UI)	Female, mean (95% UI)	Total, mean (95% UI)	Male, % (95% UI)	Female, % (95% UI)	Total, % (95% UI)
	Incidence count in years 0-25 (2019 to 2044)					
Anxiety	81,078	106,188	187,266	5.96	6.86	6.42
	(31,817-134,310)	(41,985-174,857)	(73,802-309,167)	(2.35-9.86)	(2.72-11.27)	(2.54-10.59)
Depression	418,718	704,103	1,122,821	3.91	4.69	4.36
	(216,508-628,825)	(366,048-1,052,719)	(582,556-1,681,544)	(2.02-5.86)	(2.45-6.99)	(2.27-6.52)
	Prevalence count in year 25 (2044)					
Anxiety	21,297	38,756	60,053	4.89	5.21	5.09
	(8,356-35,308)	(15,318-63,875)	(23,673-99,183)	(1.92-8.10)	(2.06-8.58)	(2.01-8.40)
Depression	16,109	26,850	42,959	3.82	4.55	4.24
	(8,345-24,164)	(13,996-40,086)	(22,342-64,250)	(1.98-5.73)	(2.37-6.79)	(2.21-6.35)

Results for the modelled scenario: All people adhered to the physical activity guidelines in Australia  
95% uncertainty interval (UI)

**Changes in disease specific prevalence**

If all people adhered to the PA guidelines in Australia, our model projected a reduction in prevalent cases of anxiety by 60,053 (95% UIs 23,673-99,183) and of depression by 42,959 (95% UIs 22,342-64,250) in 2044, an estimated 5.1% proportional reduction in prevalent cases of anxiety and 4.2% of depression (Table 2). The estimated reduction in number and proportions over different time periods are shown in SF table 12.

**Health adjusted life years gained**

Table 3 shows that if all people adhered to the PA guidelines in Australia, over the lifetime of the 2019 population, almost twice as many HALYs would be gained in females (~400,000) compared to males (~200,000) for each health outcome. Additional results for the total HALYs gained in the lifetime for the additional two modelled scenarios and, over different time periods are shown in SF tables 13 and 14.



**Table 3: Total HALYs gained and reductions in healthcare expenditure**

	<b>Total HALYs gained over the lifetime</b>	<b>Reduction in health care expenditure over the lifetime (in AUD)</b>
	<b>Mean (95% UIs)</b>	<b>Mean (95% UIs)</b>
<b>Anxiety</b>		
Female	416,256 (165,494-683,306)	3,498,614,451 (1,395,653,298-5,728,440,670)
Male	224,336 (88,530-370,372)	1,907,269,567 (754,908,697-3,141,478,744)
Both	640,592 (254,024-1,053,678)	5,405,884,018 (2,150,561,995-8,869,919,414)
<b>Depression</b>		
Female	330,758 (173,193-491,919)	3,875,838,612 (2,029,465,286-5,764,237,082)
Male	192,958 (100,242-288,740)	1,955,792,166 (1,016,788,020-2,924,800,592)
Both	523,717 (273,435-780,658)	5,831,630,778 (3,046,253,306-8,689,037,674)

Results for the modelled scenario: All people adhered to the physical activity guidelines in Australia

95% uncertainty interval (UI), HALYs: Health adjusted life years, AUD: Australian Dollar

### **Changes in healthcare expenditure**

Over the lifetime of the 2019 Australian population, if all people adhered to the PA guidelines, the estimated savings are AUD 5.41 billion for anxiety and AUD 5.83 billion for depression (Table 3). (Additional results in SF tables 15 and 16.)

### **Sensitivity analyses**

#### *Impact of discounting on HALYs gained*

Compared to the base case (no discounting applied), for all three modelled scenarios, applying 3% discounting for the health outcomes reduced the total number of HALYs gained over the lifetime of the 2019 Australian population for both anxiety and depression by about 60% (Table 4 and SF table 17). The total HALYs gained increased with time (SF table 18).

**Table 4: Total HALYs gained and reductions in healthcare expenditure with discounting**

	<b>Total HALYs gained in the lifetime with discounting <sup>a</sup></b>	<b>Reduction in health care expenditure over the lifetime (in AUD) with discounting <sup>b</sup></b>
	<b>Mean (95% UIs)</b>	<b>Mean (95% UIs)</b>
<b>Anxiety</b>		
Female	170,588 (66,175-279,175)	567,991,909 (220,647,903-929,106,644)
Male	95,675 (36,828-157,478)	341,693,061 (131,663,556-562,377,354)
Both	266,262 (103,003-436,653)	909,684,970 (352,311,459-1,491,483,998)
<b>Depression</b>		
Female	142,633 (72,327-215,802)	812,131,892 (411,002,153-1,230,863,543)
Male	83,433 (42,031-126,868)	403,147,404 (202,928,419-613,472,778)
Both	226,065 (114,357-342,670)	1,215,279,296 (613,930,572-1,844,336,322)

Results for the modelled scenario: All people adhered to the physical activity guidelines in Australia

95% uncertainty interval (UI), HALYs: Health adjusted life years, AUD: Australian Dollar

<sup>a</sup>3% discount rate on health effects applied

<sup>b</sup>7% discount rate on healthcare costs applied

*Impact of discounting on changes in healthcare expenditure*

Compared to the base case (no discounting applied), applying 7% discounting to the healthcare costs reduced the total cost offsets in the lifetime of the 2019 Australian population for all three modelled scenarios, for both anxiety and depression by over 80% (Table 4 and SF table 19). For the scenario where all people adhered to the PA guidelines in Australia, 7% discounting reduced the total cost offsets by ~4.5 billion AUD for each health outcome (anxiety and depression).

Additional results for the additional two modelled scenarios and, over different time periods are shown in SF tables 19 and 20.

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## DISCUSSION

We found that if all Australians adhered to the recommended minimum PA levels, in 25 years' time, the burden of these two conditions could be reduced substantially - by 6.4% (95% UIs 2.5 to 10.6) for anxiety and 4.4% (95% UIs 2.3 to 6.5) for depression. Over the lifetime of the 2019 Australian population, the gains could add up to 640,592 years in perfect health (HALYs) for anxiety and 523,717 HALYs for depression, and health care cost savings of AUD 5.4 billion for anxiety and AUD 5.8 billion for depression. The health and economic impacts are larger for females than males. This is largely because, compared to males across all ages, a greater percentage of females were in the inactive and low active PA categories at baseline (SF table 1).<sup>11</sup> Also, women had a higher starting prevalence of anxiety and depression (SF table 2).<sup>1</sup> To our knowledge, this is the first study to quantify the impact of PA on the burden of anxiety and depression over the life course in Australia or any other country. Specifically, we assessed the impact of achieving three policy targets: attainment of the Australian PA guidelines, a 10% relative reduction in the prevalence of insufficient PA is achieved by 2025, and a 15% relative reduction in the prevalence of physical inactivity by 2030.<sup>6-8</sup> We report estimates on changes in incidence, prevalence, HALYs, and healthcare costs. Given that we model across the lifetime of the population, our study provides a comprehensive picture of the potential health gains due to increased PA levels, as opposed to other study types with shorter time horizons. This is valuable information for health planning and prevention policy.

Our work complements earlier studies that have applied the proportional multi state life table method to investigate the health impact of strategies that increase PA.<sup>21-26</sup> Findings from these previous studies confirm the health and economic benefits of increasing PA at the population level. Our study expands this research by investigating the health and economic impact of PA on the outcomes anxiety and depression. These outcomes have not previously been included in

health and economic assessments of PA. Our study complements the Global Burden of Disease study 2019 and the Australian Burden of Disease study 2015<sup>49,50</sup> that have estimated the disease burden attributable to physical inactivity for Australia. Neither of the two studies included mental health outcomes. Our findings show that the inclusion of mental health benefits of physical activity into burden of disease estimates could have substantial policy impacts. The findings from our review add to the recently published criticism of the estimation of the latest version of the Global Burden of Disease study using “outdated” and “incomplete” evidence on the health risks attributable to physical activity.<sup>51</sup>

### **Limitations of the study**

One of our study limitations is that for the strength of the associations between PA and depression and anxiety we rely on the evidence from previous studies – primary cohort studies summarised in systematic reviews<sup>37,38</sup> with pooled estimates. In their main analysis, the primary studies included by the review authors had varying definitions of high and low PA. Efforts to get additional information included contacting the corresponding author of the systematic reviews<sup>37,38</sup> and our review of their included primary cohort studies. Due to the variations presented, we could not establish homogenous PA categories. We applied the assumption that the lowest and highest PA categories reported in the review studies<sup>37,38</sup> refer to the inactive and highly active categories in our model respectively. Additional limitations of this evidence are discussed in our companion review study.<sup>16</sup> Another limitation is that the pMSLT model has an assumption that modelled diseases are independent.<sup>28-30</sup> This might lead to a slight overestimation of impact, since with the disability weight formula used to combine the impact of two conditions, the impact is smaller if both are in the same individuals. However, this would have a limited impact on overall estimates.<sup>29</sup> Additionally, our model did not incorporate migration, but the life table approach does include the effects of population aging. The

uncertainty intervals reflect only uncertainty in relative risks and PA input parameters and not all uncertainty in the analysis particularly, disease rates. The ‘proportions shift’ method that we used to model changes in PA has been found to introduce non-linearities where there should be none.<sup>47</sup> However, for our case, the ‘proportions shift’ method was the most intuitive for our model scenarios where we simplify and redistribute people to different PA categories.

Use of self-reported data for in the estimate of the Australian physical activity levels was limiting, but this is appropriate, given that the risk measures were also based on studies that used self-report.

The reduction of prevalent cases due to increased PA levels might happen faster than reported here because in our model, an increase in PA levels modifies only incidence and does not include established beneficial effects in people living with anxiety or depression.<sup>52-55</sup> As such our estimates are conservative and the true benefit of measures that increase PA are likely to be even greater.

### **Implications of the results for policy and practice**

Our findings are relevant to policy makers, clinicians, epidemiologists and public health researchers. Our study provides empirical support for the adoption of physical activity in strategies for the prevention of mental ill health. Efforts to increase PA levels can make significant contributions to improving mental health.

At an individual level, our findings show that even a modest increase of PA for individuals with less-than-optimal PA levels (i.e., inactive or insufficient PA) could result in a significant benefit to mental health. The potential impact of PA on the burden of anxiety and depression may also encourage clinicians to emphasize PA as a key aspect of prevention of mental ill health for their clients, in particular, clients who currently have low levels of PA.

At a population level, tackling broader social and environmental determinants that support active lives such as secure walkable neighbourhoods, access to green and blue spaces, and safe roads for pedestrians, cyclists and other active transport users, can improve uptake of physical activity at the population level.<sup>8,56,57</sup> Evidence shows that strategies that seek to create healthier environments that encourage physical activity are more effective than those that only target individuals.<sup>8</sup> Further, our research supports prioritising PA interventions for populations who experience relatively higher levels of physical inactivity such as people living in socioeconomically disadvantaged communities.<sup>13</sup> These findings are particularly important for informing policy making in light of evidence that suggests that, without targeted approaches, place based infrastructure investments tend to benefit those already socio-economically advantaged therefore missing opportunities to both address health equity and allocate limited resources where they will achieve the best outcomes.<sup>58-60</sup>

Our findings make a strong case for the inclusion of PA in potential strategies for the prevention of mental ill health. For example, they could be used in economic appraisals for business cases of such prevention strategies. The true benefits of measures that increase PA levels are likely to be even much greater, because the mental health benefits would be additional to those accrued from reduction of other disease associated with PA such as cardiovascular disease, diabetes, several types of cancer, and other chronic health conditions.<sup>61,62</sup>

### **Unanswered questions and future research**

For the strength of the associations between PA and depression and anxiety, further research could strengthen the evidence base for gender and age specific measures of association. This is important because with low prevalence of optimal physical activity levels in Australia and globally,<sup>11,12</sup> even a modest effect of PA on anxiety and depression could result in a significant benefit to mental health from interventions that improve levels of PA.



Future studies should also assess the size and distribution of the benefits for different socio-economic and ethnic groups and could be expanded to include children and adolescents (below 15 years of age).

When people are being physically inactive, they often spend a lot of their time in sedentary behaviour such as sitting. Emerging evidence suggests that high levels of sedentary behaviour may also be unfavourably associated with depression and anxiety.<sup>63-65</sup> Further research is needed to quantify the impact that sedentary behaviour has on mental health among both children and adults.

## **CONCLUSION**

Adherence to the Australian PA guidelines<sup>7</sup> and achievement of the 2025<sup>6</sup> and 2030 global PA targets<sup>6,8</sup> could lead to a substantial reduction of the burden of anxiety and depression. Over the lifetime of the 2019 Australian population, if all adhered to the recommended minimum PA levels, the gains could add up to 640,592 years in perfect health (HALYs) for anxiety, 523,717 HALYs for depression and health care cost savings of AUD 5.4 billion for anxiety and AUD 5.8 billion for depression.

This study provides empirical support for the inclusion of physical activity in strategies for the prevention of mental ill health.

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study. MNW did the modelling analysis and wrote the first version of the manuscript. JLV contributed to analysis and interpretation of findings, reviewed the first manuscript, provided critical feedback and reviewed successive versions of the manuscript. HM and FH reviewed several versions of the manuscript. RH, AM, PL contributed to the review of manuscript. All authors critically reviewed the manuscript and approved the final version for publication. No financial disclosures were reported by the authors of this paper.

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### **CONFLICT OF INTEREST STATEMENT**

All authors declare no conflict of interest.

### **FINANCIAL DISCLOSURE**

No financial disclosures were reported by the authors of this paper.

### **Credit Author Statement**

Mary Njeri Wanjau: Methodology, Investigation, Formal analysis, Data curation, Writing - Original draft preparation. Holger Möller: Investigation, Writing - Reviewing and Editing. Fiona Haigh: Investigation, Writing - Reviewing and Editing. Andrew Milat: Writing - Reviewing and Editing. Rema Hayek: Writing - Reviewing and Editing. Peta Lucas: Writing - Reviewing and Editing. J. Lennert Veerman: Conceptualization, Methodology, Validation, Investigation, Formal analysis, Resources, Writing - Reviewing and Editing, Supervision, Funding acquisition.

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**FIGURE TITLES AND FOOTNOTES**

Figure 1: Relative risk of incident anxiety, depression by level of physical activity

PA categories: Inactive (0 MET), low active (>0 & <600 MET-minutes per week), moderately active (>=600 & <1600 MET- minutes per week) and highly active (>=1600 MET- minutes per week). Source of risk measures: Adjusted odds ratios (anxiety)<sup>38</sup> and adjusted relative risks (depression).<sup>37</sup>

