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1           **Physical activity, walking and quality of life in women with depressive symptoms**

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13

14 **Abstract**

15 **Background:** Physical activity (PA) has a positive association with health-related quality of life  
16 (HRQL) in the general population. The association between PA and HRQL in those with poor  
17 mental health is less clear.

18 **Purpose:** To examine the concurrent and prospective dose-response relationships between total  
19 physical activity (TPA) and walking only with HRQL in women aged 50-55 with depressive  
20 symptoms in 2001.

21 **Methods:** Participants were 1904 women born in 1946-1951 who completed mailed surveys for  
22 the Australian Longitudinal Study on Women's Health in 2001, 2004, 2007 and 2010 and who, in  
23 2001, reported depressive symptoms. At each time point, they reported their weekly minutes of  
24 walking, moderate PA, and vigorous PA. A summary TPA score was created that accounted for  
25 differences in energy expenditure among the three PA types. Mixed models were used to  
26 examine associations between TPA and HRQL (SF-36 component and subscale scores) and  
27 between walking and HRQL, for women who reported walking as their only PA. Analyses were  
28 conducted in 2013-2014.

29 **Results:** Concurrently, higher levels of TPA and walking were associated with better HRQL  
30 ( $p < 0.05$ ). The strongest associations were found for physical functioning, vitality, and social  
31 functioning subscales. In prospective models, associations were attenuated, yet compared with  
32 women doing no TPA or walking, women doing "sufficient" TPA or walking had significantly  
33 better HRQL over time for most SF-36 scales.

34 **Conclusions:** This study extends previous work by demonstrating trends between both TPA and  
35 walking and HRQL in women reporting depressive symptoms.

## 36 **Background**

37 Depression is projected to be the second-leading cause of burden of disease worldwide by 2030  
38 and the leading cause in high-income countries.<sup>1</sup> Given the high prevalence<sup>2</sup> and associated  
39 burden of disease,<sup>1,3</sup> there is an urgent need to identify modifiable factors to improve the health-  
40 related quality of life (HRQL) of those with this condition. There is good evidence from both  
41 cross-sectional<sup>4-12</sup> and prospective<sup>13-19</sup> studies that physical activity (PA) can improve health-  
42 related quality of life in the general population,<sup>20</sup> but the association between PA and HRQL has  
43 been less frequently examined in people with poor mental health, including in those with  
44 depression. Cross-sectional data have indicated a positive association for people with bipolar  
45 disorder,<sup>21</sup> and for those with affective, anxiety, or substance-dependence disorders,<sup>22</sup> although  
46 no association has been found for inpatients with a serious mental illness, including  
47 schizophrenia and psychosis.<sup>23</sup> More work is needed to examine the relationship between PA and  
48 HRQL in people with depression.

49  
50 Research is particularly needed to understand the dose-response relationship between PA and  
51 HRQL in depressed people. Cross-sectional studies in general adult populations have suggested a  
52 curvilinear relationship,<sup>11</sup> a linear trend,<sup>8,24,25</sup> stronger associations for low or high than  
53 intermediate PA levels,<sup>26</sup> and an association only for intermediate levels of PA.<sup>27</sup> A prospective  
54 study with older adults demonstrated a linear trend,<sup>28</sup> while another with young to mid-aged  
55 adults found a positive association only for higher levels of PA.<sup>16</sup> Understanding the beneficial  
56 levels of PA for HRQL in people with depression could have important management  
57 implications, as there may be thresholds below which PA offers no benefits, or above which PA  
58 provides no additional benefits for HRQL.<sup>20</sup>

59  
60 HRQL is a multidimensional construct, and the dose-response relationship with PA in depressed  
61 people may differ between physical and psychological aspects. In general populations, higher PA  
62 levels are associated more consistently with higher physical functioning and vitality than other  
63 aspects of HRQL.<sup>20</sup> Some cross-sectional data for women, however, indicate certain dimensions  
64 of PA (i.e., moderate-intensity PA,<sup>27</sup> leisure-time PA,<sup>29</sup> and sports participation<sup>26</sup>) are more  
65 strongly associated with psychological HRQL than physical HRQL. Prospective studies suggest  
66 change in PA over time is predominantly associated with improvement in psychological  
67 HRQL,<sup>13,16,24</sup> although a study in women showed greater improvements in physical HRQL.<sup>19</sup> In  
68 another study the association between PA and HRQL was mainly for physical HRQL in cross-  
69 sectional analyses, and predominantly for psychological and social HRQL in prospective  
70 analyses.<sup>24</sup> A review of five exercise training studies for people with depression indicated  
71 statistically significant changes in physical HRQL for four studies, but no changes in  
72 psychological HRQL.<sup>30</sup> There is, therefore, a need to examine in more detail the associations  
73 between PA and the different components of HRQOL, both cross-sectionally and over time.

74  
75 The primary aim of this study was to examine concurrent and 9-year prospective associations  
76 between total PA (TPA) and HRQL, and between walking only and HRQL, in community-  
77 dwelling healthy women who reported depressive symptoms (CESD10 score  $\geq 10$ )<sup>31</sup> in 2001,  
78 when they were aged 50 to 55 years. The secondary aim was to describe the nature of these dose-  
79 response relationships.

80

81 **Methods**

## 82 **Australian Longitudinal Study on Women's Health (ALSWH)**

83 ALSWH is a prospective study of health and well-being of Australian women born in 1973-  
84 1978, 1946-1951 and 1921-1926. Sampling and recruitment details have been reported  
85 elsewhere.<sup>32</sup> Surveys were first posted in 1996 and subsequently on a 3-year rolling basis. The  
86 study was approved by the Ethics Committees of The University of Queensland and the  
87 University of Newcastle. Informed consent was received from all respondents. Further study  
88 details are available on the ALSHW website at <http://www.alswh.org.au/>.

89

## 90 **Participants**

91 The analysis sample included women born in 1946-1951 who completed surveys in 2001, 2004,  
92 2007 and 2010. These surveys were chosen because PA was measured the same way in each  
93 year. The first survey in 1996 was completed by 14,100 women, who were broadly  
94 representative of the general population of mid-aged women, although Australian-born,  
95 employed and university-educated women were over-represented.<sup>32</sup> After loss to follow-up  
96 between 1996 and 2001, the baseline for these analyses, data from 11,219 women were available  
97 for analysis. Women lost to follow-up after 1996 were more likely to report poorer health, less  
98 education, and being born in a non-English-speaking country than those who continued in  
99 ALSWH.<sup>33</sup> Of these, 2323 met the inclusion criteria of reporting depressive symptoms in 2001  
100 (CESD10 score  $\geq 10$ ),<sup>31</sup> 207 of whom were excluded because they reported at one or more  
101 surveys that they were unable to walk 100 m. Another 212 were excluded because they had  
102 missing data for a predictor or outcome variable for  $\geq$ two surveys ( $<3\%$  of any variable except  
103 6% for BMI). Among women who reported depressive symptoms at baseline (n=2323), notable  
104 differences were found between those included (n=1904) and those excluded (n=405) from

105 analysis. Excluded women were more likely to have not completed high school, to find  
106 managing on their income impossible/difficult, and to be more unhealthy ( $p < 0.05$ ; Appendix A).

107

## 108 **Variables**

109 **Health-related quality of life.** HRQL was measured with the well-validated Medical Outcomes  
110 Study's Health Status Survey short form (SF-36).<sup>34</sup> Four subscales (21 items) assess physical  
111 HRQL: bodily pain, physical functioning, general health perception, and role limitations from  
112 physical problems. The remaining four subscales (14 items) measure psychological HRQL:  
113 vitality, social functioning, mental health, and role limitations from emotional problems. Each  
114 subscale was treated as a separate outcome variable. In addition, Physical and Mental HRQL  
115 Component Summary scales (PCS and MCS, respectively), with factor structures validated using  
116 the baseline ALSWH surveys,<sup>35</sup> served as summary measures of self-reported general physical  
117 and psychological HRQL. HRQL scores were standardized to range from 0-100, with the  
118 population average of each cohort set at 50.<sup>35</sup> Higher scores indicated better HRQL.

119

120 **Physical activity.** TPA and (only) walking were measured with the validated Active Australia  
121 survey.<sup>36,37</sup> The survey assesses time in the previous week (in  $\geq 10$ -minute bouts) spent walking  
122 briskly ('for recreation or exercise or to get from place to place'), in moderate-intensity PA ('like  
123 golf, social tennis, moderate exercise classes, recreational swimming, line dancing'), and in  
124 vigorous-intensity PA ('that makes you breathe harder or puff and pant, like aerobics,  
125 competitive sport, vigorous cycling, running, swimming'). A TPA MET.min/week score was  
126 computed by multiplying minutes in each activity type by an assigned metabolic equivalent  
127 (MET): (walking=3.0 METs; moderate-intensity PA=4.0 METs; vigorous-intensity PA=7.5

128 METs) and summing.<sup>38</sup> Scores were categorized as: none (<40); very low (40-<300);  
129 intermediate (300-<600); and sufficient (600+).<sup>39</sup> Participants in the sufficient category were  
130 considered meeting national PA guidelines<sup>40</sup> because the lower cut-off for this category is  
131 equivalent to 150 minutes/week of moderate-intensity PA. For women whose only PA was  
132 walking, an (only) walking score (MET.min/week) was additionally computed by multiplying  
133 walking minutes by 3.0 (METs) and using the same categorizations as for TPA.

134

135 **Confounders.** Socio-demographic and health-related variables indicated by previous work to be  
136 confounders in women without depressive symptoms<sup>18</sup> were included as potential confounders  
137 here. These included demographic variables: country of birth (proxy for ethnicity), area of  
138 residence (derived from postal codes), educational attainment, and ability to manage on one's  
139 income (proxy for income status). Social variables assessed were marital status, the number of  
140 stressful life events in the past 12 months (e.g., death of partner), provision of care for children,  
141 provision of care for adults (e.g., with a long-term illness, disability, or frailty), and social  
142 support (measured with the Medical Outcomes Study Social Support Index<sup>41</sup>). Health-related  
143 variables included body mass index (BMI; kg/m<sup>2</sup> computed from self-reported height and  
144 weight), menopausal status, number of doctor-diagnosed chronic conditions in the previous 3  
145 years (from a list that included diabetes, cancer, and heart disease), and medical diagnoses or  
146 treatment for anxiety or other psychiatric condition in the previous 3 years. Health behaviors  
147 assessed were smoking status and alcohol consumption. See Table 1 and Supplementary Table A  
148 for further details.

149

150 **Statistical Analyses**



151 Associations between TPA and (only) walking with HRQL scores were examined using random  
152 intercept multivariable mixed models in Stata (version 13.0). Separate models were computed for  
153 each HRQL variable. Logistic models (the XTLOGIT function) were used for the role limitations  
154 from physical problems subscale and the role limitations from emotional problems subscale, as  
155 these scales exhibited bimodal distributions. For all other HRQL scales, linear models (the  
156 XTREG function) were used. Individuals served as random effects. Survey year served as a  
157 covariate to account for changes in the outcome as the women aged, and area of residence at  
158 baseline served as a covariate to account for oversampling of rural and remote areas. Bootstrap  
159 corrections were applied to skewed outcome variables (physical functioning and social  
160 functioning scales). All predictor variables were treated as categorical except social support,  
161 which was continuous.

162  
163 To examine sequential cross-sectional (concurrent) relationships between TPA and each HRQL  
164 outcome, TPA and confounders measured in 2001, 2004, 2007 and 2010 served as fixed effects  
165 in models without a time lag, with HRQL at the same survey periods serving as outcome  
166 variables. These models have a longitudinal element, as they account for repeated observations  
167 from the same woman, and the overall estimates account for within-subject correlations. To  
168 examine prospective associations between TPA and each HRQL outcome, TPA and confounders  
169 measured in 2001, 2004, and 2007 served as fixed effects in prospective models with time-lag,  
170 with HRQL in 2004, 2007, and 2010, respectively, serving as outcome variables. Among the  
171 subgroup of women who reported no moderate or vigorous PA in 2001, 2004 and 2007 (walking  
172 was their only PA), the same modeling was used, except walking replaced TPA.

173

174 **Results**

175 Select characteristics of participants are presented in Table 1. Additional characteristics are  
176 reported in Supplementary Table 1.

177

178 Women's activity and HRQL scores at each survey are listed in Table 2. The percentage of  
179 participants who reported sufficient PA increased over the study's first 6 years but slightly  
180 decreased for the 9-year survey. Mean SF-36 scores were fairly consistent across surveys  
181 although the percentage of women scoring above 50.0 for role limitations from physical and  
182 from emotional problems increased substantially from the first to last survey. Significant trends  
183 for HRQL were observed across PA categories (Supplementary Table 2), indicating  
184 improvements in HRQL with greater PA levels.

185

186 The associations between both TPA and (only) walking with HRQL variables are shown in  
187 Tables 3-4. The dose-response relationships are displayed in Figure 1. In concurrent models,  
188 most coefficients were significantly higher for each activity level above the none level than for  
189 the none level. Exceptions were the low PA level and the low and intermediate (only) walking  
190 levels for role limitations from emotional problems. Overall, coefficients were higher with  
191 increasingly higher levels of TPA and walking levels, indicating better HRQL with more PA.  
192 Larger coefficients were seen for TPA than for (only) walking. The strongest associations were  
193 found for physical functioning (9.3 points higher for the highest level of TPA and 8.4 points  
194 higher for the highest walking level, than the none level), vitality (8.9 points higher for the  
195 highest level of TPA and 6.6 points higher at the highest walking level), and social functioning  
196 (8.6 points higher at the highest level of TPA and 6.8 points higher at the highest walking level).

197  
198 In prospective models, the dose-response relationships were attenuated, with the greatest point  
199 difference from the none level being 3.75 (for physical functioning at the intermediate walking  
200 level). Intermediate and sufficient levels of TPA and (only) walking were associated with  
201 improvements in general health perceptions, MCS, vitality and mental health. Sufficient levels of  
202 TPA and (only) walking were also significantly associated with improved bodily pain, and a  
203 sufficient level of TPA was associated with improved physical functioning, social functioning,  
204 and role limitations from emotional problems.

205

## 206 **Discussion**

207 As far as we are aware, this is the first study to describe the nature of the dose-response  
208 relationship between PA and the multidimensional aspects of HRQL, both concurrently and  
209 prospectively, in women reporting depressive symptoms. The current study included women  
210 who reported depressive symptoms in 2001.

211

212 Overall, associations were observed between TPA and (only) walking with HRQL. Positive  
213 concurrent associations were observed between the PA measures and all HRQL measures, and  
214 associations were stronger for TPA than for (only) walking. Although women doing the most  
215 TPA and (only) walking had the highest HRQL scores, even those doing low levels of TPA or  
216 (only) walking had better HRQL than women doing no PA. Prospectively, associations were  
217 attenuated, with greater attenuation for physical HRQL than for psychological HRQL. This may  
218 suggest that the physical and psychological benefits derived from PA are greater in the  
219 immediate context than over time.

220  
221 In concurrent modeling, clinically meaningful improvements in scores ( $\geq 3$ -points)<sup>20</sup> were  
222 observed for women doing low to sufficient levels of TPA and (only) walking, although most  
223 clinically meaningful improvements were seen for women doing *sufficient* TPA or (only)  
224 walking. The strongest relationships were for PA and physical functioning, vitality and social  
225 functioning. Compared with no TPA, low to sufficient TPA was associated with markedly  
226 higher scores for physical functioning, vitality and social functioning (3.2 to 9.1 point higher  
227 scores). The current findings are consistent with previous cross-sectional studies with people  
228 without depression, demonstrating a positive association between PA and HRQL,<sup>4-12,18</sup>  
229 vitality<sup>20,29</sup> and social wellbeing,<sup>26,27,42</sup> and stronger associations with physical HRQL at higher  
230 PA levels.<sup>12,26</sup> The results also support other research demonstrating the value of walking for  
231 HRQL in women,<sup>18,27</sup> although this may be potentially lower than for other types of PA.<sup>4</sup>  
232  
233 Prospectively, all physical HRQL subscale scores were attenuated, and overall PCS scores were  
234 no longer significantly associated with TPA or (only) walking. However, associations were  
235 observed for most physical HRQL subscale scores, including physical functioning. The  
236 associations were seen among women doing sufficient TPA or (only) walking, and were weak. In  
237 contrast, in a study of non-depressed women of the same age in ALSWH, improvements in PCS  
238 were observed for women doing at least an intermediate level of TPA although these  
239 improvements were not clinically meaningful ( $< 3.0$  point improvement).<sup>18</sup> Clinically  
240 meaningful improvements in physical functioning were observed with increasing TPA and  
241 walking levels in that study.<sup>18</sup> The current findings are consistent with other prospective research  
242 in general populations that demonstrates a positive association between PA and improvements in

243 physical functioning,<sup>13,16,19,28</sup> and add to this evidence by suggesting that PA-related  
244 improvements in physical HRQL may be limited to specific components of HRQL in women  
245 with depressive symptoms.

246  
247 In prospective models of psychological HRQL, findings were also attenuated. MCS, vitality  
248 scores and mental health scores were, however, improved for women at intermediate and  
249 sufficient TPA and (only) walking levels. These results confirm cross-sectional research  
250 demonstrating an association between walking and psychological and social HRQL,<sup>27</sup> and  
251 between recommended levels of PA and HRQL.<sup>12</sup> Results are also consistent with other  
252 prospective research indicating associations between PA and mental health, vitality, and social  
253 functioning.<sup>13,16,24</sup> As previously reported, in mid-age women in ALSWH without depression,  
254 however, MCS and mental health scores were not associated with TPA and walking  
255 prospectively except at very high levels of TPA.<sup>18</sup> Vitality was improved across all levels of TPA  
256 and most walking levels for those women, and associations at the intermediate and sufficient  
257 levels were clinically meaningful (3.0 to 5.4 point improvements).<sup>18</sup> In the current study, the  
258 remaining psychological HRQL scores (social functioning and role limitations–emotional) were  
259 improved among women doing sufficient TPA or (only) walking. Only women at a sufficient  
260 level of TPA had a clinically meaningful improvement, and this improvement (3.4 points) was in  
261 social functioning. As these two SF-36 scales were not evaluated in the previous work with  
262 ALSWH women without depression,<sup>18</sup> the current results cannot be compared with the earlier  
263 findings. Overall, it seems that PA has a greater influence on psychological HRQL in women in  
264 their 50s and 60s with depression than in those without depression. This may be because there is

265 greater capacity for improvement in psychological HRQL in those with depression than those  
266 without.

267

268 The major strength of this study was the use of data from four time points from a large  
269 population-based cohort. Important confounders were included in analysis, made possible by the  
270 large number of variables included in ALSWH. The main limitation is the reliance on self-report  
271 data, which are subject to recall and measurement bias. The strength of the associations may  
272 have been underestimated as a result, as misclassification is possible. However, the PA measures  
273 have adequate reliability and validity,<sup>36,37</sup> and HRQL is a subjective judgement. Of note is that  
274 the sample was selected on the basis of reporting depressive symptoms in 2001, and it is  
275 acknowledged that these symptoms may have changed over time. The generalizability of the  
276 findings is limited by the potential effect of study attrition. The ALSWH included reasonably  
277 representative national samples of women responding at baseline,<sup>32</sup> but as with all prospective  
278 studies, participants have withdrawn over time, with more healthy women remaining in the  
279 study.<sup>33</sup> Therefore, the findings cannot be generalized to all Australian women in their 50s to 60s  
280 who have reported depressive symptoms.

281

282 Overall, the findings indicate that most improvements in HRQL for Australian women in their  
283 50s-60s with depressive symptoms are associated with participation in levels of activity that  
284 reflect guidelines<sup>40</sup> ( $\geq 600$  MET.minutes/week of PA, equivalent to  $\geq 150$  minutes of moderate-  
285 intensity PA or  $\geq 200$  minutes of [only] walking). Smaller gains in HRQL are possible with  
286 smaller doses of TPA or (only) walking. This study adds to the literature by documenting the 9-  
287 year dose-response relationship between PA and measures of well-being in women in their 50s

288 and 60s with depressive symptoms. These findings add to the growing body of evidence  
289 indicating that PA can improve HRQL, and demonstrate that PA may provide a mechanism by  
290 which to improve the quality of life in women with depressive symptoms.

291 The implications of these findings are that encouraging walking or a mixture of different types of  
292 activity, at levels commensurate with current PA guidelines, will improve aspects of well-being,  
293 including mental health and vitality, which are important for women with depressive symptoms.

294 The findings show that higher PA levels are associated with more benefits, and, just as  
295 importantly from a clinical point of view, that even low PA levels are beneficial.

296

297

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303



304

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417 **Figure 1** Associations between both total physical activity and walking with measures of health-  
418 related quality of life, in Australian women born in 1946-1951. Each graph shows concurrent  
419 models of both TPA (solid line and filled square: —■—) and walking (solid line and filled ball: —●—)  
420 and prospective models of TPA (dotted line and open square: -□-) and walking (dotted line and  
421 open ball: -⊖-). The x-axis represents activity level, and the y-axis represents beta coefficients  
422 and 95% CIs for SF-36 scores with the first activity category serving as the reference category  
423 ( $\beta=0$ ).  
424