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1 Non-linear longitudinal associations between moderate-to-vigorous physical activity and adiposity
2 across the adiposity distribution during childhood and adolescence: Gateshead Millennium Study

3

4 Xanne, Janssen^{1*} PhD, Laura Basterfield^{2,3} PhD, Kathryn N Parkinson^{2,3} PhD, Mark S Pearce² PhD,
5 Jessica K Reilly^{2,3} BSc, Ashley J Adamson^{2,3} PhD, John J Reilly¹ PhD

6 1. University of Strathclyde, School of Psychological Science and Health, Glasgow, Scotland,
7 UK

8 2. Newcastle University, Institute of Health & Society, Newcastle upon Tyne, England, UK

9 3. Newcastle University, Human Nutrition Research Centre, Newcastle upon Tyne, England,
10 UK

11

12 *Corresponding Author

13 Dr Xanne Janssen

14 School of Psychological Sciences and Health,

15 University of Strathclyde

16 Glasgow, Scotland, G1 1QN

17 Email: xanne.janssen@strath.ac.uk

18 Tel: +44 (0)141 548 4324

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20

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22

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36

37 **ABSTRACT**

38 **Objective:** Insufficient moderate-to-vigorous intensity physical activity (MVPA) is harmful for
39 youth; however, the evidence for differential effects by weight status is limited. The study aimed to
40 examine associations between MVPA and adiposity by weight status across childhood and
41 adolescence.

42 **Methods:** Participants were from the Gateshead Millennium Study. Physical activity and body
43 composition measures were taken at age 7y (n=502; measures taken between October 2006-December
44 2007), 9y (n=506; October 2008-September 2009), 12y (n=420; October 2011-September 2012) and
45 15y (n=306; September 2014-September 2015). Participants wore an ActiGraph GT1M and epochs
46 were classified as MVPA when accelerometer counts were ≥ 574 counts/15s. Weight and height were
47 measured using standardised methods and fat mass using bioelectrical impedance. Associations
48 between MVPA and changes in BMI and FMI were examined by weight status using quantile
49 regression.

50 **Results:** Higher MVPA was associated with lower FMI for the 25th, 50th, 75th and 90th percentile and
51 lower BMI at the 50th, 75th and 90th percentile, independent of accelerometer wear time, sex and
52 sedentary time. The association between MVPA and change in adiposity was stronger in the higher
53 than lower FMI and BMI percentiles (e.g. 1hr/day more MVPA was associated with a 1.5 kg/m² and
54 2.7 kg/m² lower FMI at the 50th and 90th FMI percentiles, respectively).

55 **Conclusion:** The effect of MVPA on adiposity in the higher adiposity percentiles is stronger than
56 reported to date. Given overweight and obese children are the highest risk group for later obesity,
57 targeting MVPA might be a particularly effective obesity prevention strategy.

58

59

60 INTRODUCTION

61 Recent studies have shown low levels of physical activity (PA) in children which decrease even
62 further during both childhood and adolescence (1-3). In addition, the prevalence of obesity among
63 children and adolescents has increased to alarming levels in countries all around the world (4). It is
64 believed that one way to counteract this rise in obesity is via promotion of PA. However, while cross-
65 sectional studies have shown relatively consistent positive associations between PA and adiposity, the
66 evidence is less clear when looking at the longitudinal associations (5).

67

68 Poitras et al. (2016) showed only half of the longitudinal studies included in their review reported
69 higher levels of moderate-to-vigorous physical activity (MVPA) were associated with lower levels of
70 adiposity. In addition, the quality of the studies included in the review was low and most of the
71 longitudinal studies covered a period of 2 years or less. Since then several studies examining the
72 longitudinal association between objectively measured MVPA and adiposity have been published
73 showing a positive association of baseline MVPA and adiposity later on (6-8). However, two of these
74 studies were of a relatively short duration (i.e. 2 years) and included only one follow-up time point
75 (6,8).

76

77 To the authors' knowledge to date only two studies have examined changes in MVPA and adiposity
78 over childhood and adolescence including several follow-up time points (7, 9). Kwon et al. (2015)
79 examined changes in PA and adiposity from age 5 to 19 years. The authors reported that those who
80 decreased their MVPA from age 5 to 19 were at higher risk of becoming obese in adulthood compared
81 to participants who remained active throughout. The second study looking at changes in adiposity
82 over childhood and adolescence was conducted by Mitchell et al. (2013). Mitchell et al. (2013)
83 reported that time spent in MVPA at age 9 was associated with a change in adiposity from age 9 to 15,
84 with a stronger association being present in participants who were at the higher end of the BMI
85 distribution at age 9 years. This finding is especially interesting as the higher end of the BMI
86 distribution includes participants who are often the focus in clinical practice and public health
87 interventions. In addition to this, a more recent cross-sectional study using a quantile regression

88 approach, supported the results by Mitchell et al. (2013) (10). However, to the authors' knowledge, no
89 other longitudinal studies have used an approach which considers the possibility of associations which
90 differ in strength, and linear regression analysis may underestimate the effect of MVPA in the higher
91 percentiles of the adiposity distribution. Therefore, the current study will examine if MVPA is
92 associated with changes in adiposity by weight status and compare this to whole sample linear
93 regression analysis. We hypothesized that MVPA is associated more strongly with adiposity at the
94 higher end of the adiposity distribution and the impact of MVPA on adiposity is underestimated using
95 linear regression that models the mean of adiposity outcome variables.

96

97 **METHODS**

98 *Cohort*

99 This study was conducted as part of the Gateshead Millennium Study (GMS; 11). The GMS is a
100 longitudinal cohort study set in Gateshead, England. For the present study measurements taken at age
101 7y, 9y, 12y and 15y were included. Baseline measures for this study were taken between October
102 2006 and December 2007 (7y); follow-up was conducted between October 2008 and September 2009
103 (9y); between October 2011 and September 2012 (12y), and between September 2014 and September
104 2015 (15y). Child's date of birth, sex and parental socio-economic position, measured by Townsend
105 score (an area-based measure derived from the UK census in 1991) were recorded at birth, all other
106 measured used in this study were recorded at baseline and each of the follow-up time points. Written
107 parental consent was obtained during each data collection period and the study was approved by the
108 Gateshead and South Tyneside Local National Health Service Research Ethics Committee for data
109 collection at 7y and by the Newcastle University Faculty of Medical Sciences Ethics Committee for
110 the 9y, 12y and 15y data collections.

111

112 *Body measurements*

113 Height and weight were measured during baseline (7y) and follow-up (9y, 12y and 15y) using
114 standardized methods. Height was measured to the nearest 0.1 cm using a Leicester portable height

115 measure (Chasmors, London, UK). Weight (kg) was measured and fat mass was estimated using bio-
116 impedance while children wore light clothing using a Tanita TBF300MA. Bio-impedance data was
117 used to first calculate age and sex specific total body water using validated prediction equations (12)
118 after which lean mass was calculated using age and sex specific hydration factors as described by
119 Lohman (13). Fat mass was then calculated from weight (kg) minus lean mass. Body mass index
120 (BMI) was calculated as weight (kg) divided by height (m) squared. Fat mass index (FMI) was
121 calculated as fat mass (kg) divided by height (m) squared.

122

123 *Accelerometry – objective measurement of physical activity*

124 Physical activity was measured using Actigraph GT1M accelerometers (ActiGraph Corporation;
125 Pensacola USA) worn for 7 days during baseline and follow-up data collection points. Participants
126 were asked to wear the accelerometer on their right hip during all waking hours, except during water
127 based activities. Participants recorded times the monitor was worn using a wear time diary and non-
128 wear time and sleep time were removed based on the wear time diaries and visual inspection by a
129 trained researcher. This method has been used in several previous studies (2, 14-16). In addition, the
130 consecutive zeros method to remove non-wear time was not used as it has been shown to affect the
131 outcome significantly, especially in longitudinal studies in children and adolescence (17). Data were
132 collected in 15-second epochs and included in the analyses if participants had at least three days with
133 ≥ 6 hours per day of accelerometer data (18). Epochs were defined as sedentary behavior (SB), light
134 physical activity (LPA) and MVPA when recorded counts were ≤ 25 counts/15s, between 25-573
135 counts/15 seconds and ≥ 574 counts/15s, respectively (19).

136

137 *Statistical analysis*

138 For descriptive purposes, the means and standard deviations for anthropometric and physical activity
139 outcomes were calculated at each time point. Associations of time spent in MVPA with changes in
140 BMI and FMI were examined by weight status using quantile regression analyses. A first order
141 autoregressive correlation structure was used to account for repeated measures. The 95% confidence
142 intervals (95% CIs) were estimated using 500 cluster bootstrap samples to account for the dependence

143 between repeated measures (20). The interpretation of quantile regression is similar to that of linear
144 regression with the benefit of examining different quantiles of the distribution separately. First, the
145 effect of the independent variable (i.e. MVPA) was modeled for the 10th, 25th, 50th, 75th and 90th BMI
146 or FMI percentile (model 1). Second wear time, sex, socio-economic status (i.e. Townsend score) and
147 SB were added as co-variates to model 1 (model 2). Time was coded as 0, 2, 5 and 8 for age 7, 9, 12
148 and 15 years, respectively, to enable easy interpretation of the coefficients (i.e. change in BMI/FMI
149 per year). In addition to quantile regression, mixed effects linear regression analyses were conducted
150 so that the impact of choice of regression approach could be compared. Mixed effects linear
151 regression account for the correlation between repeated measures of the same participants over time.
152 All analyses were performed using STATA 12 (StataCorp, College Station, Texas, USA).

153

154

155 **RESULTS**

156 Descriptive results of each data collection point are shown in Table 1. Briefly, 502, 506, 420 and 306
157 participants provided valid data at age 7y, 9y, 12y and 15y, respectively. The sample included an
158 almost equal split of girls and boys. At age 7y participants participated on average 69.8 min/day in
159 MVPA. By the time participants were 15y old this had decreased to 46.4 min/day in MVPA. On
160 average, time in MVPA decreased by -1.1% (SD \pm 3.0) for 7y to 9y (equivalent to -6.1 min/day), -
161 1.8% (\pm 3.6) for 9y to 12y (-9.4 min/day), -1.1% (\pm 3.2) for 12y to 15y (-8.5 min/day).

162

163 *MVPA and adiposity using quantile regression*

164 The results of the quantile regression analysis for MVPA and FMI and BMI are shown in Tables 2
165 and 3. Higher MVPA was associated with a lower FMI for all but the 10th percentiles ($p < 0.05$). Every
166 additional hour of daily MVPA was associated with a lower FMI of -0.56 kg/m² (95%CI: -1.04, -0.07)
167 at the 25th percentile, -1.46 kg/m² (-2.04, -0.88) at the 50th percentile, -2.11 kg/m² (-3.00, -1.20) at the
168 75th percentile and -2.69 kg/m² (-3.92, -1.46) at 90th percentile, independent of accelerometer wear
169 time, sex and SB. Higher MVPA was associated with a lower BMI for the 50th, 75th and 90th BMI

170 percentiles only. Every additional hour of daily MVPA was associated with a lower BMI of -1.22
171 kg/m² (-1.94, -0.51), -2.43 kg/m² (-3.47, -1.38) at the 75th, and -3.37 kg/m² (-4.90, -1.83) at the 90th
172 percentile, independent of accelerometer wear time, sex and SB. The association between change in
173 MVPA and change in BMI and FMI was stronger in the higher BMI and FMI percentiles compared to
174 the lower BMI and FMI percentiles. In addition, analysis showed that the effect of MVPA was
175 overestimated in the lower percentiles and underestimated in the higher percentiles of both BMI and
176 FMI when using linear regression analysis (Figure 1 and Appendix Table 1).

177

178 **DISCUSSION**

179 **Main study findings and implications**

180 The present study is one of the first to provide longitudinal evidence that higher levels of MVPA are
181 associated with lower levels of adiposity during childhood and adolescence, and that the strength of
182 these associations differs along the BMI and FMI distribution. In the present study, higher MVPA was
183 associated with a lower FMI for all FMI percentiles but the 10th FMI percentile. However, higher
184 MVPA was only associated with a lower BMI at the 50th, 75th and 90th percentile. In addition, the
185 association between MVPA and changes in adiposity were stronger at the higher quantiles of the FMI
186 and BMI distribution. This may indicate that even small changes in MVPA can result in significant
187 changes in BMI and FMI in those at the higher end of the FMI and BMI distribution. In addition, the
188 results show that when using standard linear regression analysis the strength of the association
189 between MVPA and adiposity can be either overestimated (lower quantiles of adiposity distribution)
190 or underestimated (higher quantiles of the adiposity distribution).

191

192 There are several factors which may explain the associations between the difference in strength of the
193 association between MVPA and changes in adiposity observed in the present study. It may be that the
194 difference is simply due to the fact that those overweight and obese have more fat reserves and
195 therefore are more likely to lose fat mass when engaging in physical activity. Alternatively, genetic
196 differences could play a role. A meta-analysis conducted by Silventoinen et al. (2010) reported

197 genetics play had a strong effect on the variation of BMI across childhood and adolescence (21). This
198 could indicate that those in the lower end of the adiposity spectrum are less likely to gain weight due
199 to genetic reasons and therefore limited participation in PA does not necessarily lead to an increase in
200 weight. Quantile regression evidence on the genetics of childhood obesity also suggests that the
201 influence of genetic risk factors is stronger at the upper end of the distribution of adiposity (22), and
202 there is evidence that higher levels of MVPA blunt the impact of adverse genetic risk factors (23).
203 Taken together with the present study, this emerging body of evidence suggests that MVPA is
204 important for healthier energy balance regulation, particularly for those at high genetic risk of obesity
205 and/or those at the upper end of the adiposity distribution. Last, the energy cost of physical activity
206 has been shown to be higher in those who are obese compared to those who are normal weight
207 indicating that an increase in MVPA in those in the higher adiposity percentiles results in a larger
208 increase in energy expenditure and therefore will have a bigger effect on the energy balance (24).

209

210 **Comparisons with other studies**

211 Recent systematic reviews have provided conflicting evidence on associations between objectively
212 measured PA and adiposity, and have called for more studies with stronger designs, including more
213 longitudinal studies (5). While previous studies have been inconclusive, on balance the available
214 evidence has suggested that an association between MVPA and adiposity was likely. The current
215 study confirmed these results. However, the current study also indicated the strength of the
216 association between MVPA and adiposity may be underestimated in most studies using whole sample
217 linear regression analysis.

218

219 As mentioned previously, to date only two studies have included multiple follow-up points across
220 childhood and adolescence. Due to differences in analysis, results between Kwon et al. (2015) and the
221 current study are difficult to compare. However, similar to the current study, Kwon et al. did show an
222 association between change in physical activity and adiposity. Kwon et al. reported an increased risk
223 of becoming obese in those who decreased their physical activity from age 5 to 19 compared to those
224 who remained stable. The results of studies using quantile regression to examine the association

225 between MVPA and adiposity are very similar to those of the current study (9, 10) Both studies by
226 Mitchell et al. (2013 and 2017) reported significant associations between MVPA and adiposity with
227 the strength of the association increasing for each quantile of the adiposity distribution. In addition,
228 when using linear regression the association in both the current study and the study by Mitchell et al.
229 (2013) showed an underestimation of the strength of the association in the higher adiposity
230 percentiles. Consequently, if a study sample includes relatively few overweight and/or obese
231 participants the strength of the association may be reduced or not be significant at all. However, the
232 current study also showed that it is likely that many of the previous studies have underestimated the
233 effect of MVPA on adiposity in populations of particular interest for intervention studies (i.e. those in
234 the higher BMI and FMI percentiles). The present study also suggests that the influence of MVPA on
235 adiposity may increase over time in populations where there is a secular trend to increased adiposity.

236

237 **Study strengths and weaknesses**

238 The strengths of this study are the use of a contemporary cohort, the longitudinal design with multiple
239 follow-up data collection points throughout childhood and adolescence and the use of quantile
240 regression to expand analyses beyond linear regression analyses restricted to the mean of adiposity
241 phenotypes. In addition, the study used high quality measures for both exposure (accelerometry) and
242 outcome (body composition) variables. The quantile regression analysis made it possible to highlight
243 the different strengths in associations between adiposity and MVPA longitudinally, something that
244 has only been done once previously. The study also had some limitations, families' socio-economic
245 status was measured at birth and this may have changed between birth and our baseline measures.
246 Parental lifestyle may influence child's behavior, however, unfortunately we did not capture this and
247 could not include this as a covariate in our analysis. In addition, we did not control for diet which may
248 be a confounder. The sample size of the study has decreased by 40% over the 8 years of data
249 collection; however a slightly higher attrition rate is not abnormal during longitudinal data analysis (7,
250 9). The reduction in sample size may also have impacted generalizability of study findings. However,
251 the current cohort remains contemporary (born in 1999-2000), and socio-economically representative
252 of North-East England (11), and both of these characteristics should enhance generalizability.

253

254 **CONCLUSIONS**

255 In this study MVPA declined from age 7y to 15y and lower levels of MVPA were associated with
256 higher levels of adiposity throughout childhood and adolescence. The association between adiposity
257 and MVPA was stronger at higher percentiles. This study indicates that the effect of MVPA on
258 adiposity in the higher adiposity percentiles is stronger than reported to date. Consequently, given
259 overweight and obese children are the highest risk group for later obesity, using MVPA interventions
260 with overweight and obese children might be an even more effective obesity prevention strategy than
261 initially thought.

262

263

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282

283 **Conflict of Interest**

284 The authors declare no conflicts of interest

285

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369 **Figure titles and legend**

370 Figure 1. Quantile regression association between MVPA and FMI and BMI

371 Footnote figure 1: The plots are based on model 3 which controlled for sedentary time and sex. The

372 dotted line represents the linear regression coefficient for the change in FMI and BMI per hour

373 MVPA.

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