Edinburgh Research Explorer

Land cover and air pollution are associated with asthma hospitalisations

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Abstract: International evidence suggests that green space has beneficial effects on general and mental health but little is known about how lifetime exposure to green space influences cognitive ageing.
Employing a novel, longitudinal, life course approach, we examined the association between lifetime availability of public parks and cognitive ageing. Lifetime residential information was gathered from the participants of the Lothian Birth Cohort 1936 using a "life-grid" questionnaire at age 78 years. Parks information from 1949, 1969 and 2009 was used to determine a percentage of parks within a 1,500 m buffer zone surrounding residence for childhood, adulthood, and later adulthood periods. Linear regressions were undertaken to test for association with age-standardised, residualised change in cognitive function (Moray House Test score) from age 11 to 70 years, and from age 70 to 76. The most appropriate model was selected using the results of a partial F-test, and then stratified by demographic, genetic and socioeconomic factors.
The local provision of park space in childhood and adulthood were both important in explaining the change in cognitive function in later life. The association between childhood and adulthood park availability and change in the Moray House Test Score from age 70 to 76 was strongest for women, those without an APOE e4 allele (a genetic risk factor), and those in the lowest socioeconomic groups.
Greater neighbourhood provision of public parks from childhood through to adulthood may help to slow down the rate of cognitive decline in later life, recognising that such environmental associations are always sensitive to individual characteristics.

Response to Reviewers* (NO AUTHOR DETAILS)

Reviewer Comments

Reviewer 3

1. To add a copyright statement onto Figure S3 to cover the use of postcode and census data.

   We agree that copyright information should be included and have added this to Figure S3.

2. To add the sample size N into the abstract, so readers are made aware of the size of the cohort at the beginning of the manuscript.

   We agree that it is important to display the sample size in the abstract; we have added this information to pg 1 line 11.

Reviewer 4

1. "The authors have done a good job in addressing most of the comments. The manuscript looks improved now. However, I still have serious concerns regarding the interpretation of the findings. Even by ignoring that I would not agree with the authors saying that by having an interaction term in the model, the main effects are not meaningful, I still firmly believe that the findings do not support the conclusion of the manuscript. It is because from different models whose results are presented in Table 3, only one shows significant results, which could be a chance finding given the number of comparisons made (i.e. multiple comparison issue) and the inconsistent pattern of the associations for different models that show different strengths and direction of associations. Even if we believe that this is not a chance finding, still this association has lost its statistical significance after adjustment for the relevant covariates, meaning that it could be due to the confounding by these covariates rather than a genuine association between green space exposure and cognitive decline. Hence, based on these observations, it is quite unrealistic to conclude that "Greater neighbourhood provision of public parks in adulthood and particularly childhood may help to slow down the rate of cognitive decline in later life." To me, these findings do not support such an association."

   Thank you for your comments regarding the interpretation of the results. The rationale behind testing multiple combinations of parks is to provide a formal comparison of several hypotheses, this is a method that has been utilised elsewhere, without correction for multiple testing. This is useful to stimulate discussion on the merits of the relationship. We think this is the right way to approach the question: "does public park availability affect cognitive ageing over life?" because prior research is sparse for this relationship and we would be at risk of choosing the wrong exposure combination (i.e. increase in type 2-error rate). As Mishra et al., note picking a single exposure combination can "produce misleading or incomplete results that do little to help the understanding of how life course trajectories affect health".

   On the question of the loss of statistical significance, we welcome the reviewer's consideration of the effects presented in greater detail. Although we opted to present the interaction continuously, the association is mostly driven by the top end of adulthood park availability. To highlight this, we have conducted supplementary

analysis using tertiles of adulthood park availability (Figure S4, Table S3 and Table S4). In these results the interaction between childhood park availability and the highest tertile (>9.3%) of adulthood parks remains significant in each of the nested models. These results support the amended statement on Pg 1 ln 18:

"Greater neighbourhood provision of public parks from childhood through to adulthood may help to slow down the rate of cognitive decline in later life…"

On the final point of the differences in the coefficients by individual effect modifiers. We think these are important results, which do not weaken the associations presented but give them context. Public park availability throughout life is a small but important, modifiable exposure which will be more or less significant dependent on other factors that affect individual susceptibility. We have stressed this in the abstract on Pg 1 ln 19:

"…, recognising that such environmental associations are always sensitive to individual characteristics."

2. "Moreover, I am missing an answer on the issue that I raised on the credibility of Google maps and Open Street Maps (which are quite recent maps) to geocode addresses 70-80 years ago. This can have serious implications on the precision of exposure assessment during childhood (i.e. higher exposure measurement error for the childhood period), especially by considering the fact that this study has only found an association in relation with childhood exposure."

    This is a valid point on the credibility of using google maps and open street maps to geocode historical addresses. We have utilised the strengths of three sources: Open street map (contemporary Edinburgh accuracy), google maps API (fuzzy string matching) and historic repositories (temporal coverage). As we were geocoding a relatively small number of addresses we were able to manually check the difference between the geocoded addresses and those supplied by the participant. This could have been explained more clearly so we have re-written the section on the geocoding method on Pg 7 ln 157-171:

    "We have utilised contemporary sources to geocode the 7,423 participant addresses. We geocoded the participant addresses using Nomatim to query Open Street Map (OSM) (OpenStreetMap contributors, 2017), as the accuracy for addresses in Edinburgh is between 1-3 m and the coverage is excellent (Grosso et al., 2015). The output contained the latitude, longitude and the comma separated OSM-derived address string (e.g. 82, Home Street, Edinburgh, United Kingdom). This address string was then compared with what was supplied by the participant, which was recorded in the same format. 15% of the participant addresses were not able to be geocoded or had lost information (i.e. the difference in the number of comma separated 'information bits' was negative). As we hypothesised that this may be due to misspellings or imperfect matches, the Google Maps geocoding API was used as it employs a fuzzy string matching algorithm. We then manually compared the Google maps geocoding API quality output (i.e. 'rooftop', 'range_interpolated', 'geometric_center' and 'approximate') to the address supplied by the participant. 6% of the google-derived geocodes did not contain the same level of information

supplied by the participant and were manually geocoded using historic building repositories such as Canmore.org.uk (i.e. using the 8-digit National Grid Reference, 1m resolution)."

We have also updated the discussion to highlight the assumptions of the geocoding method and a discussion of the precision of the earlier period exposure estimates on Pg 17 ln 413-421:

"In addition, by geocoding using contemporary sources, we have assumed that the street layout was the same as it is today for the majority of the addresses, with only minor changes to the street content. However we acknowledge that these small changes could have affected the precision of the park exposure estimate for the earlier time periods. Given that we were geocoding a relatively small number of addresses, we were able to employ a system to detect information lost compared with what was supplied, so that if the results were unsatisfactory they would be geocoded manually. This ensured that addresses that had changed significantly (e.g. demolished) would be geocoded to the same accuracy as those that were able to be geocoded with contemporary sources (<3m)."

3. "With regards to my comment on the adjustment of analyses for BMI, although the authors have conducted a sensitivity analysis showing that removing BMI from analyses does not change the findings notably (which is great), still I believe it is more appropriate if the results of the analyses are only presented without adjustment for BMI. We adjust our analyses for confounders which by definitions are factors that are associated with both exposure and outcome of interest but do not fall in the causal pathway of these two. If they fall, then they are mediators (and not confounders) and the analyses should be adjusted for them because it results in underestimation of the association (due to the fact that the mediator could explain a part of the association between the exposure and outcome)."

As suggested, we have removed BMI from the analyses.

Green Space and cognitive ageing: a retrospective life course analysis in the Lothian Birth Cohort 1936

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Manuscript Title: Green Space and cognitive ageing: a retrospective life course analysis in the Lothian Birth Cohort 1936 Social Science & Medicine

Highlights

- Lifecourse approaches are necessary to investigate green space and cognitive ageing
- Better cognitive ageing depended on more park provision in childhood and adulthood
- Childhood park provision was modified by adulthood park provision
- Association was strongest in females, without an APOE e4 alelle and in a lower SES

1   *Abstract*

2   International evidence suggests that green space has beneficial effects on general and mental health

3   but little is known about how lifetime exposure to green space influences cognitive ageing.

4   Employing a novel, longitudinal, life course approach, we examined the association between lifetime

5   availability of public parks and cognitive ageing. Lifetime residential information was gathered from

6   the participants of the Lothian Birth Cohort 1936 using a "life-grid" questionnaire at age 78 years.

7   Parks information from 1949, 1969 and 2009 was used to determine a percentage of parks within a

8   1,500 m buffer zone surrounding residence for childhood, adulthood, and later adulthood periods.

9   Linear regressions were undertaken to test for association with age-standardised, residualised

10   change in cognitive function (Moray House Test score) from age 11 to 70 years, and from age 70 to

11   76 (n=281). The most appropriate model was selected using the results of a partial F-test, and then

12   stratified by demographic, genetic and socioeconomic factors. The local provision of park space in

13   childhood and adulthood were both important in explaining the change in cognitive function in later

14   life. The association between childhood and adulthood park availability and change in the Moray

15   House Test Score from age 70 to 76 was strongest for women, those without an *APOE* e4 allele (a

16   genetic risk factor), and those in the lowest socioeconomic groups.

17   Greater neighbourhood provision of public parks from childhood through to adulthood may help to

18   slow down the rate of cognitive decline in later life, recognising that such environmental associations

19   are always sensitive to individual characteristics.

20

21   *Keywords:* UK; Green space; public parks; cognitive function; cognitive ageing; life course;

22   longitudinal

23

24

1

Introduction

With the global increase in life expectancy, there is an urgent need to identify factors that affect changes in cognitive abilities as people age. Explanatory models of cognitive ageing posit a variety ~~of~~ ~~demographic~~of demographic, genetic, behavioural and environmental factors contributing to cognitive function (Anstey, 2014). The focus of the current research is on how environmental conditions – or more specifically local green spaces - throughout life affect people's cognitive ageing relative to one another. There have been significant advances made in understanding the range of demographic, genetic, and behavioural factors affecting cognitive ageing. For instance, women tend to have greater resilience to age-related decline (McCarrey et al., 2016). The major genetic predictor responsible for increased susceptibility to non-normative cognitive ageing is the presence of the APOE (apolipoprotein) e4 allele (Davies et al., 2014; Deary et al., 2012b; Schiepers et al., 2012). Behavioural factors, including diet, physical activity, smoking and alcohol consumption, closely related to an individual's socioeconomic status, are often associated with cognitive function in older age, although, apart from smoking, results differ between studies and some associations are prone to confounding by prior cognitive function (Deary et al., 2009; Plassman et al., 2010). Little work has considered specific built, social or environmental features of local areas, with previous research relying on aggregate measures of social deprivation (Lang et al., 2009). Yet cognitive function could be affected by a range of environmental or neighbourhood conditions including: local social capital; residential segregation; perceived safety and incivilities; availability of community resources such as food shops and other services; walkability; and the availability of public open space or local greenness (Y. T. Wu et al., 2015a).

It is well established that public open space and greenness is often beneficial for the physical and mental health of local residents (van den Berg et al., 2015). It is also feasible that public open space and greenness may help to optimise cognitive function. Several studies with differing population, design and outcome measures are suggestive of a direct positive benefit of natural environments to

50   directed attention (Ohly et al., 2016). Increased support and motivation for social interaction and

51   physical activity, reductions in stress and exposure to higher air quality offer indirect benefits to

52   cognitive capability, evidenced by a large body of research on changes in physiological markers and

53   emotional states (Hartig et al., 2014). Other indirect benefits such as exposure to beneficial

54   microbiota could indirectly affect cognitive processes through facilitating a reduction in blood

55   pressure and boost to immune function (M. Kuo, 2015). Some of these mechanisms have been

56   shown to directly link with change in cognitive ~~functio~~function;~~n,~~ for example, in participants over 70

57   years old, low levels of leisure-time physical activity were associated with a decline in cognitive

58   function five years later (Willey et al., 2016). The only previous longitudinal study of area-level

59   greenness and cognitive change focused on children. The authors found that greenness surrounding

60   a child's home, school and commute was correlated positively with improvements in memory and a

61   reduction in inattentiveness (Dadvand et al., 2015a). However, the study only considered these

62   associations over a 12-month period during early life, and therefore the influence of green space on

63   cognitive function over an individual's lifetime remains unknown.

64   In the present study, we examined whether availability of green space (using a measure of nearby

65   public parks) was associated with age-related changes in cognitive function between age 11 and 70

66   years, and between age 70 and 76 years. Three life course models (critical periods, accumulation,

67   and effect modification) were used to address three key hypotheses. First, early childhood has been

68   shown to be a critical period for brain growth due to heightened brain plasticity (Lyu & Burr, 2016).

69   Therefore, we hypothesised that greater public park availability during childhood has positive

70   associations with cognitive change in later life (critical period model). Second, we hypothesised that

71   a greater accumulation of park availability over life is required to promote successful cognitive

72   ageing in later life (accumulation model). This was based on the assumption that cross-sectional

73   effects of access to parks on cognitive function are consistent, albeit weaker, over time (Dadvand et

74   al. 2015a) and that for significant cognitive ageing to be observed a threshold must be surpassed

75   (Anstey 2014). Finally, by combining the critical periods and accumulation models, we hypothesised

76   that availability during adulthood is important for determining the extent of cognitive reserve, with

77   the capacity to modify the effect of exposure on the sensitive childhood period (effect modification

78   model). As mentioned previously, demographic, genetic and behavioural factors will set an individual

79   on a unique cognitive health trajectory. Therefore, with the aim to determine which groups would

80   benefit most from greater park availability, we stratified the life course model by sex, the presence

81   of an *APOE* e4 allele, and occupational social class (as a marker of individual socioeconomic status).

82   ***Methods***

83   *Study design and setting*

84   A retrospective life course study was designed using data from the Lothian Birth Cohort 1936

85   (LBC1936) (Deary et al., 2012a; Deary et al., 2007). The participants, who were all born in 1936, were

86   recruited from Edinburgh and the Lothians in Scotland. Most had taken part in a nationwide

87   assessment of their general intelligence in 1947 (Scottish Mental Survey 1947; N=70,805) (SCRE

88   1949). The cohort participants were re-contacted in 2004 and, from 2,318 responses, 1,091 were

89   eligible for wave 1 data collection (Deary, Gow et al. 2012). Cohort participants were subsequently

90   contacted and tested at mean ages of approximately 70 years (Jul 2004- May 2007), 73 (Oct 2007-

91   May 2010) and 76 (Jul 2011-Nov 2013). At mean age 78, a stand-alone questionnaire booklet was

92   posted out with returns received between July 2014 and April 2015.

93   *Operationalising change in cognitive function*

94   We operationalised the outcome of cognitive ageing using the participant's Moray House Test No.

95   12 (MHT) scores from mean ages of 11, 70 and 76 years (SCRE, 1949). The MHT is a validated

96   measure of cognitive function, which correlates highly with the current "gold standard" cognitive

97   tests (Deary et al., 2004). The MHT is a general intelligence test that is composed of 71 items,

98   measuring the participant's ability on a variety of mental tasks including verbal reasoning,

99   arithmetic, and following directions. Each score was adjusted for age in days at the time of

100   examination by taking the standardised residuals from a linear regression with age as the

101   independent variable. The score was then standardised to have a mean of 100 and standard

102   deviation of 15. Change was calculated by generating the standardised residual from a linear

103   regression model with previous MHT score (e.g. change from 11 to 70 calculated by taking age 70

104   score as the dependent and age 11 as the independent variable). This statistical technique to

105   calculate change in score is superior to an arithmetic difference as the outcome is independent of

106   baseline level (Prochaska et al., 2008), and has been used in relation to changes in cognitive function

107   previously (Gow et al., 2005). The procedure above provided two outcomes: residualised change in

108   MHT score from age 11 to 70 and residualised change in MHT score from age 70 to 76.

109   *Operationalising LBC1936 covariates*

110   During the structured interview as part of the cognitive testing appointment at age 70, respondents

111   provided the information required for all the covariates except for father's social class, which was

112   obtained via a questionnaire, and BMI, which was obtained during the physical examination.

113   Covariates were selected *a priori* based on previous literature (Deary et al., 2009)*,* including sex,

114   Occupational Social Class (OSC) (Office of Population Censuses and Surveys, 1980) of participant's

115   father, people per room in childhood household, childhood smoking status, OSC of participant,

116   smoking status and alcohol consumption (Deary et al., 2007). OSC of the participant's father was

117   used as a measure of socioeconomic status from childhood and dichotomised into Professional-

118   managerial (I and II) and Skilled, partly skilled, unskilled (III, IV and V). Additionally, we used

119   childhood overcrowding as a secondary measure of socioeconomic status, defined as the number of

120   people per household room. Participants were asked at what age they started smoking and were

121   categorised as a childhood smoker if they responded that they had started before age 16, as per

122   convention (Hopkinson et al., 2014). Smoking status at age 70 was dichotomised as smoker or non-

123   smoker. Similarly, alcohol consumption was dichotomised as drinks alcohol or doesn't drink alcohol.

124   BMI at age 70 was calculated as weight divided by height squared. Socioeconomic status during

125   adulthood was defined by OSC of the participant's main job from their career and dichotomised in

126   the same way as their father's OSC. For females, husband's OSC was used if higher than their own.

127   We selected a number of variables as effect modifiers *a priori* including sex, adulthood OSC and

128   *APOE* e4 allele. Sex and adulthood OSC at age 70 were operationalised as above. Blood samples

129   were taken during examination and participants were genotyped for *APOE* allele status using

130   TaqMan technology at the Wellcome Trust Clinical Research Facility Genetics Core (Deary et al.,

131   2012a). Participants were dichotomised into having at least one *APOE* e4 allele or having none. In

132   addition to the variables above, we selected several variables to act as auxiliary variables in the

133   imputation of missing data. Due to the association with cognitive ageing, these included the Hospital

134   Anxiety and Depression Scale score (Zigmond & Snaith, 1983), history of stroke (Yes or No) and

135   family history of heart disease, stroke, or problems with blood vessels (Yes or No).

136   *Operationalising public parks information*

137   We identified four open space surveys that recorded public parks in Edinburgh during the 20th and

138   21st century (Pearce et al., 2016). Public parks were deemed a suitable indicator of urban green

139   space because they promote social interaction and a range of uses, including physical activity, to a

140   greater extent than ambient greenery (such as road side verges or river corridors) (E. Richardson et

141   al., 2010). Public parks data were scanned from paper maps from the Edinburgh Civic Survey 1949

142   (Abercrombie et al., 1949) and the Open space survey 1969 (Town Planning Department Edinburgh,

143   1969), georeferenced and converted to geographic information system vector data using ArcMap

144   10.1 GIS software (ESRI, Redlands, CA). Contemporary public parks data were derived from the Open

145   Space Audit 2009 (The City of Edinburgh Council, 2009). Although descriptions of the parks changed

146   slightly between surveys (e.g. "public parks" and "public recreation grounds"), consistency was

147   confirmed by the continued presence in certain spaces over time. Hereafter we refer to these spaces

148   simply as 'parks'.

149   *Operationalising lifetime residential address history*

150 The surviving participants of the LBC1936 were re-contacted in 2014 (mean age 78) (n=704/1,091),

151 and asked to fill out a residential (i.e. Life grid) questionnaire (Blane, 1996), with a response rate of

152 87% (n=612/704). From these responses, a total of 593 participants had useable life grid data; these

153 participants are referred to as the "Life grid sample". The participants were given the option to recall

154 the dates of personal events in their life, and to fill them in next to a column containing global events

155 such as the Falklands War. These events acted as memory prompts for participants to provide

156 information on their residential address and occupation (of self or father) for each decade from

157 birth. We have utilised contemporary sources to geocode the 7,423 participant addresses. We

158 geocoded the participant addresses using Nomatim to query Open Street Map (OSM)

159 (OpenStreetMap contributors, 2017), as the accuracy for addresses in Edinburgh is between 1-3 m

160 and the coverage is excellent (Grosso et al., 2015). The output contained the latitude, longitude and

161 the comma separated OSM-derived address string (e.g. 82, Home Street, Edinburgh, United

162 Kingdom). This address string was then compared with what was supplied by the participant, which

163 was recorded in the same format. 15% of the participant addresses were not able to be geocoded or

164 had lost information (i.e. the difference in the number of comma separated 'information bits' was

165 negative). As we hypothesised that this may be due to misspellings or imperfect matches, the

166 Google Maps geocoding API was used as it employs a fuzzy string matching algorithm. We then

167 manually compared the Google maps geocoding API quality output (i.e. 'rooftop',

168 'range_interpolated', 'geometric_center' and 'approximate') to the address supplied by the

169 participant. 6% of the google-derived geocodes did not contain the same level of information

170 supplied by the participant and were manually geocoded using historic building repositories such as

171 Canmore.org.uk (i.e. using the 8-digit National Grid Reference, 1m resolution). Participants were

172 eligible for the "Analysis sample" (n=281) if they recorded Edinburgh addresses during the decades

173 when parks were surveyed (i.e. childhood: 1949; adulthood: 1969; later adulthood: 2009). This

174 approach was markedly less restrictive than an analysis sample where participants had to have all of

175 their previous addresses within Edinburgh (n=174) and only resulted in a modest drop in the mean

176   percentage of the participant's total number of addresses that were within Edinburgh (i.e. from

177   100% to 94%).

178   *Determining park availability using lifetime residential address history*

179   Park availability for the LBC1936 participants was calculated by taking the percentage of park area

180   that intersected with a 1,500 m buffer zone surrounding the participant's address at each time

181   period (childhood, adulthood, and later adulthood). A 1,500 m buffer zone was selected as it

182   corresponds to approximately a 15-25 minute walk to the edge of the buffer zone, based upon data

183   on mean walk speeds of between 1-1.5 m/s for ages 20-80 (Ferrucci et al., 2016). Also, a 1,500 m

184   circular buffer was used as approximately 90% of the 500 people surveyed in the 1969 Open space

185   survey reported travelling up to 1.6 km (as the crow flies) to reach public parks within the city (Town

186   Planning Department Edinburgh 1969). A sensitivity analysis was undertaken by repeating the

187   analysis using buffer zones of 500 m and 1,000 m. The availability of parks metric was analysed as a

188   continuous variable, for each 10% increase in park area within the 1,500 buffer zone.

189   *Main Analyses*

190   All statistical analysis was performed in R version 3.3.1. To investigate the relationship between

191   availability of parks measured at three time periods (childhood, adulthood and later adulthood) and

192   cognitive ageing, we adapted an established method to detect the most appropriate life course

193   model (Mishra et al. 2009). The general premise was to build a series of linear regression models

194   that represent the life course models under investigation ("accumulation", "critical periods", and

195   "effect modification"). The model fit was then compared, via the partial F test, with a "saturated"

196   model. The "saturated" model was specified by including all the individual park terms, three two-

197   way multiplicative interactions and a three-way multiplicative interaction (Fig. 1; see Model 1). The

198   saturated model represents the full complexity of combinations of park availability through life. We

199   determined whether parks have an effect on cognitive ageing or not by comparing the fit statistics of

200   the saturated model with a "no effects" model which contained only the intercept (Fig. 1; see Model

201   5). This "no effects" model crudely predicted an individual's cognitive change as the mean of the

202   cognitive change experienced by all the participants. Thus, if park availability was important for

203   cognitive ageing then the inclusion of all park terms would explain more of the variance in cognitive

204   change than just using the mean. This was established by comparison of the two models using a

205   partial F-test. If the "no effects" model fitted the data just as well as the saturated model, then a p-

206   value above 0.05 was obtained and we could assume that parks did not have an association with

207   cognitive ageing. If the p-value was lower than 0.05, it signified that the "no effects" model was not

208   superior and we could assume that parks had an effect on cognitive ageing. We could also,

209   subsequently, repeat this procedure to compare life course analyses and determine the most

210   appropriate models.

211   The Accumulation models were categorised into strict and relaxed. The strict model was defined as

212   the park terms summed (i.e. sum of parks from childhood, adulthood and later adulthood), which

213   assumed that parks had an equal association with cognitive ageing, irrespective of the time they

214   were measured (Fig. 1; see Model 2a). The relaxed model contained each of the park terms as

215   individual predictors; i.e. parks from childhood, adulthood and later adulthood were mutually

216   adjusted for one another, which allowed any differences in the strength of association by time of

217   park measurement, to be observed (Fig. 1; see Model 2b).

218   The Critical Periods models were tested by running separate models for each park term from a single

219   point in time. This assumed that the other park terms did not influence cognitive ageing or modify

220   the association of the parks under investigation (e.g. Fig. 1; see Model 3a).

221   The Effect Modification models were defined at two points in time, early and later, and were

222   specified by including a multiplicative interaction term between parks from the two successive time

223   periods (i.e. an interaction between childhood parks and adulthood parks) (Fig. 1; see Model 4a).

224   These models emphasised the temporal sequence of exposure during early or later life as being

225   important for the eventual association with cognitive ageing. As before, we compared the partial F-

9

226 statistics of each life course model with the "saturated" model. A p-value of over 0.05 signified that

227 the life course model fitted the data as well as the "saturated model". The life course model with the

228 highest p-value was deemed the most appropriate as this meant that it not only fit the data as well

229 as the "saturated model", but was more parsimonious. All models were adjusted for sex in a

230 complete-case analysis. A positive regression coefficient represented higher residualised change in

231 cognitive function between the time points (i.e. relatively better cognitive change) whereas a

232 negative regression coefficient represented decreasing residualised change in cognitive function

233 between the time points (i.e. relatively worse cognitive change). The multiplicative interaction

234 regression coefficient was interpreted as the coefficient of one park term being conditional on

235 another.

236 *Adjusted and stratified analyses*

237 After identifying the most appropriate life course model we continued to the multiple regression

238 analysis, adjusting for childhood and adulthood covariates. Some data were missing for covariates

239 and the two outcomes. These were assumed missing at random and imputed by chained equations

240 using the 'mice' package (van Buuren & Groothuis-Oudshoorn, 2011). We imputed 20 datasets using

241 the following sociodemographic and behaviour variables that were proposed to be related to the

242 missing structure: sex, OSC, smoking, alcohol consumption and BMI; and variables proposed to be

243 associated with cognitive ageing: Hospital Anxiety and Depression Scale total score, history of stroke,

244 and family history of heart disease, stroke or problems with blood vessels. The estimates from the

245 imputed datasets were pooled using Rubin's rules. We then ran a linear regression for three nested

246 models with adjustment for: (i) sex; (ii) father's OSC, number of people per rooms in childhood

247 household, childhood smoking status, (iii) adulthood OSC, alcohol consumption and adulthood

248 smoking status. Finally, using the fully adjusted model we stratified by sex, the presence of the *APOE*

249 *e4* allele and adulthood OSC.

250 **Results**

251   We found few discernible differences between the Full sample and the Analysis sample for most of

252   the selected characteristics, as shown by chi-square and two sample t-tests (Table 1). The Analysis

253   sample had significantly higher levels of individuals recorded as Skilled, partly skilled, unskilled OSC

254   during the adulthood period. The frequency of missing data was low at below 6% for all the

255   variables. We found similar rates of missing data in the outcomes, with 6.7% for MHT change from

256   11 to 70, and 4.6% for change in MHT score from 70 and 76. On average, MHT scores increased from

257   11 to 70 and decreased from 70 to 76. There were differences in age standardised MHT scores by

258   the selected characteristics (Table 2). Men had lower scores at age 11, but were similar to women at

259   age 70 and 76. Those in the sSkilled, partly skilled, unskilled OSC and carriers of the *APOE* e4 allele

260   also performed worse at each age. We compared the availability of parks at the three measurement

261   periods using Pearson correlation coefficients and found the highest correlation between adulthood

262   and later adulthood parks (0.63) compared to the lowest between childhood and later adulthood

263   parks (0.19) (See Supplementary material; see Fig. S1). Median percentage of parks surrounding

264   participant residence increased with measurement period: from childhood at 7.0%, to adulthood at

265   7.7%, and later adulthood at 8.4%. This mirrored the increase in parks in Edinburgh during these

266   periods (See supplementary material; see Fig. S2).

267   *Associations between availability of parks and cognitive change*

268   There was no significant association between the availability of parks and cognitive change from age

269   11 to 70, as shown by the comparison between the "no effects" model and the saturated model

270   yielding a p-value of over 0.05 (p=0.780) (Table 3). However, there was an association between park

271   availability and cognitive change from age 70 to 76, with the same comparison yielding a p-value

272   below 0.05 (p=0.027) (Table 3). The life course model with the best fit was the "early effect

273   modification" model (i.e. the interaction between childhood and adulthood parks), given that this

274   model recorded the highest p-value (p=0.071) and the lowest AIC (758.1). The coefficient for the

275   interaction term was positive and statistically significant (β=0.31; 95% CI 0.02-0.59) (Figure 2). Figure

276   2A shows the marginal effects of childhood park availability on cognitive change from age 70 to 76,

277   conditional on the percentage of parks in adulthood. This shows that childhood park availability had

278   an increasingly positive/advantageous association with cognitive change from 70 to 76 years as the

279   person's adulthood park availability increases. This was found predominantly at the highest levels

280   (i.e. top tertile) of adulthood park availability (Figure 2B).

281   *Moderating role of demographic, genetic and socio-economic factors*

282   As the most parsimonious model, we undertook further analysis using the early effect modification

283   model with adjustment for childhood (i.e. father's OSC, childhood smoking status, people per room

284   in childhood home) and adulthood covariates (i.e. adulthood OSC, adulthood smoking status and

285   adulthood alcohol consumption status). In the adjusted models, the coefficient was attenuated, to

286   the extent that in the fully adjusted model (i.e. model 3) the association was no longer significant

287   (β=0.26; 95% CI -0.06 – 0.57) (Table 4). In analyses stratified by these variables we found that the

288   "early effect modification model" was moderated by sex, the presence of the *APOE* e4 allele and

289   adulthood OSC. We found the association to be strongest in women (β=0.64; 95% CI 0.24 – 1.05),

290   those without an *APOE* e4 allele (β=0.29; 95% CI -0.05 – 0.63) and in a Skilled, partly skilled, unskilled

291   OSC during adulthood (β=0.66; 95% CI 0.15 – 1.18) (Table 5).

292   *Sensitivity Analyses*

293   We found similar results when we used a stricter definition for the Analysis sample (See

294   Supplementary material; see Table S1). We also tested how sensitive the results were to the buffer

295   zone size. In the sensitivity analysis, we found that the results for the 1,000 m buffer zone were

296   similar to those using the 1,500 m buffer zone, but no association between parks availability and

297   cognitive change was found using the 500 m buffer zone (see Supplementary material; see Table S2).

298   A case-complete analysis was undertaken to test our assumptions of data being missing at random

299   and we found that the coefficients varied marginally. As we found that the interaction was most

300   significant at the highest levels of adulthood park availability, we present the adjusted and stratified

12

301   results using tertiles of adulthood park availability (Table S3 and Table S4). Finally, in the current

302   analysis, we acknowledge that the meaning and purpose of public parks may differ depending on

303   level of urbanity (see Supplementary material; see Figure S3). As a proxy for degree of urbanity we

304   have extracted the population density from the Edinburgh Civic survey 1947 (for 1941) and

305   1951/1961 censuses and appended this information to the participant addresses. In the fully

306   adjusted model (model 3), the early effect modification model coefficient for participants residing in

307   areas with greater population density (27.4-76 people per hectare) was 0.43 (95% CI; 0.00-0.86)

308   compared with -0.03 (95% CI; -0.52-0.47) for those residing in a lower population density area (3.06-

309   27.4 people per hectare).

310   ***Discussion***

311   This research is the first to consider the role of green space in influencing cognitive ageing, and

312   identifies an important new line of enquiry for understanding the factors promoting successful

313   cognitive ageing. We examined the association between combinations of park availability over an

314   individual's lifetime and cognitive ageing. Our key finding was that greater availability of parks in

315   both childhood and adulthood were associated with successful cognitive ageing in later life.

316   Although the effect size is modest, the result makes a valuable contribution to understanding how

317   aspects of physical environment may be protective against poorer cognitive ageing. These findings

318   are amongst the first to suggest that environmental conditions in childhood might have significant

319   implications for health outcomes much later in life. The work is also novel because it is the first to

320   examine the role of green space over a participant's lifetime in influencing any health outcome;

321   examining a wider set of health outcomes and environmental characteristics are important next

322   steps for researchers in this field.

323   We observed greater park availability in childhood to have a positive association with the stability of

324   cognitive functioning in older adulthood, conditional on early adulthood environment. Previous work

325   on children pre-post home relocation have shown cognitive function to be highest amongst children

326   who moved to greener neighbourhoods (Wells, 2000). Other studies have found the school

327   environment to be important for childhood cognitive development, with significant positive effects

328   on academic performance with higher surrounding greenness of schools (Dadvand et al., 2015b; C.

329   D. Wu et al., 2014). In addition, objective measures of a child's residential neighbourhood and self-

330   reported greenness of their activity spaces have been associated with fewer symptoms of social,

331   emotional and behavioural difficulties (F. E. Kuo & Taylor, 2004; E. A. Richardson et al., 2017).

332   Parks may represent a feature of the urban environment that are more stimulating cognitively than

333   other kinds of green spaces, including those found in rural environments (Cassarino et al., 2016).

334   Whilst it has been shown that a lower percentage of surrounding green space and private gardens is

335   associated with a higher likelihood of cognitive impairment and dementia (Y. T. Wu et al., 2015b),

336   this is not uniformly the case (Clarke et al., 2012). Conflicting results in these previous studies may

337   be due to the age of participants. As the majority of the participants in the Clarke et al. study were

338   under 70 years old, null findings may be because there were smaller variations in cognitive ageing

339   trajectories.

340   Whilest we hypothesised that adulthood park availability modifies the influence of childhood park

341   exposure, due to childhood being a sensitive period for brain development, the reverse may also be

342   true. It is feasible that modification of park availability during adulthood by childhood exposure

343   relates to the theory of the "childhood factor", whereby the frequency of visits and positive

344   experiences with natural spaces in childhood predicts use in adulthood (Thompson et al., 2008).

345   Those who participated in nature-based recreation when they were children may be better able to

346   mitigate any constraints they face to participation in adulthood (Asah et al., 2012). Other

347   researchers stress the importance of unstructured play for infants and structured support from the

348   family, school and social clubs thereafter strengthening the link with nature-based recreation in

349   adulthood (Lovelock et al., 2016; Wang et al., 2013). Both interpretations emphasise the importance

350   of childhood exposure and the associated opportunity for brain development and acculturation

351 ~~which~~acculturation, which, if not realised, could result in much lower accumulated benefits from

352 green space throughout life.

353 We found that associations were strongest in those without the *APOE* e4 allele, women and those

354 with skilled, partly skilled and unskilled occupations; these results may be explained by differences in

355 outcome subtype and interaction with parks. The presence of the *APOE* e4 allele has been shown as

356 the single biggest predictor of older age cognitive change using the LBC1936 (Ritchie et al., 2016).

357 Ritchie et al., found that women in the LBC1936 were more likely to retain cognitive functions, in

358 particular under the specific domain of acquired knowledge, as they aged (Ritchie et al., 2016).

359 Previous studies have found that biomarkers of inflammation consistently associate with cognitive

360 ageing (Marioni et al., 2010; Rafnsson et al., 2007), but in some cases, associations have also only

361 been found in women and those without the APOE e4 allele (Metti et al., 2014). These results could

362 be due to differences in the pathology of cognitive ageing. The presence of APOE e4 alleles is mainly

363 associated with Alzheimer's dementia (Corder et al., 1993) and women experience cardiovascular

364 health problems 7-10 years later than men (Maas & Appelman, 2010). Taken together, our result

365 may suggest that park availability, through the potential mechanism of inflammatory biomarker

366 variability, could have a greater impact on vascular dementia, thus explaining heightened

367 significance in these groups. Our finding of a stronger association for lower socioeconomic

368 individuals is consistent with previous evidence showing that the greenest areas have the lowest

369 inequality in mortality (R. Mitchell & Popham, 2008) and mental wellbeing (R. J. Mitchell et al.,

370 2015). This may be because those in a lower socioeconomic status have less resource to take

371 advantage of spaces outside of their immediate environment, and therefore spend more time closer

372 to home.

373 A major strength of the study is the availability of childhood measures of cognitive function and

374 repeated measures in older age from the LBC1936 study, thus reducing the issue of reverse causality

375 associated with cognitive testing being undertaken within older age only. We have used change in

376 cognitive function rather than level at one point in time, thus avoiding cohort-specific differences in

377 ageing and measurement error (Liu et al., 2010). Our outcome is complemented by our

378 environmental exposure being the most consistently used measure of historical natural space

379 currently available (Pearce et al., 2016). We have also considered parks throughout life, decreasing

380 differential assessment error which can occur from using an address from a single point in time (e.g.

381 birth or last known address) (Brokamp et al., 2016). However, given the lengthy time frame of

382 exposure we were unable to classify subtypes of green space (e.g. golf courses, allotments) or the

383 quality of green space, which has been shown to be important in contemporary analyses (Wheeler

384 et al., 2015). The life course method we applied has been validated (Mishra et al., 2009). We used

385 continuous variables in the life course models, hence slight modifications to the specifications

386 presented elsewhere., Nnamely, we did not constrain the effect modification models to have fixed

387 effects to be 0, which would have resulted in a decrease in the model degrees of freedom and

388 therefore errors in the nested model comparison. We conducted a sensitivity analysis dichotomising

389 the variables, based on being within the highest quartile for public park availability, with the fixed

390 effects constrained to 0, and the results were congruous to the continuous analysis. Findings from

391 the sensitivity analysis suggest that level of urbanity, defined by residential population density in

392 childhood, has an impact on the effect size and significance of the associations. The non-significant

393 relationship in suburban areas may be in part due to the differences in use of public parks, whereby

394 suburban residents have lower reliance on public parks, as private gardens and other types of green

395 space (e.g. river/canal corridors and forests) may be used more often (Mitchell and Popham 2007).

396 We did not perform sensitivity analyses with different buffer methods as we would expect the same

397 results regardless of whether a circular or network buffer was used (Bodicoat et al. 2014).

398 A weakness of thise study is the retrospective data collection of residential address history, which

399 can be prone to recall bias. We were also limited by the numbers available for the analysis sample

400 due to the criteria for eligibility being based on continued lifetime residence in a small geographic

401 area. It was necessary to dichotomise OSC as to provide greater statistical power for stratified

402   models (i.e. to keep cell sizes to an appropriate size). This dichotomisation was also appropriate

403   when this variable was used as a covariate, as previous research found that significant differences in

404   health outcomes were only found between "professional or managerial occupations" compared to

405   the rest (Gale et al., 2016). We dichotomised other covariates (e.g. smoking status) as they were not

406   recorded in the same way for~~in~~ childhood and adulthood and therefore dichotomisation was used to

407   aid interpretation of change over time. The analysis sample was broadly similar in terms of selected

408   characteristics compared with the full cohort at age 70, but selection bias may have caused a higher

409   number of participants from lower socioeconomic groups being included. The issue of selection bias

410   was partly addressed by running the sensitivity analysis using a sample with different assumptions.

411   For addresses within the Edinburgh area, the precision of the addresses supplied varied and

412   therefore, for a small number of addresses that did not have a house number, the error between

413   actual participant residence and geocoded address was larger as we took the centre of their street.

414   In addition, by geocoding using contemporary sources, we have assumed that the street layout was

415   the same as it is today for the majority of the addresses, with only minor changes to the street

416   content. However we acknowledge that these small changes could have affected the precision of the

417   park exposure estimate for the earlier time periods. Given that we were geocoding a relatively small

418   number of addresses, we were able to employ a system to detect information lost compared with

419   what was supplied, so that if the results were unsatisfactory they would be geocoded manually. This

420   ensured that addresses that had changed significantly (e.g. demolished) would be geocoded to the

421   same accuracy as those that were able to be geocoded with contemporary sources (<3m). Given the

422   complexity of the existing analysis, with multiple exposures from different time points, we were

423   unable to include the examination of non-linearity.~~,~~ ~~H~~however, we would encourage this in future

424   analyses, especially using the forthcoming cognitive data waves in the LBC1936.

425   Availability of parks represents a 'cumulative opportunity' indicator of urban green space, which was

426   shown recently to represent the sum of intentional and incidental interactions to a greater extent

427   than proximity based measures (Ekkel and de Vries 2017).~~,~~ ~~H~~however, we were still unable to

428   distinguish how the space was being used and therefore the specific mechanisms by which green

429   spaces were beneficial to health. It has been argued that the sum of a range of mechanisms could

430   have a large effect on health through the pathway of enhanced immune function (M. Kuo, 2015).

431   Even though the effect of individual mechanisms may only contribute slightly to this effect, the

432   ability to define the function of specific green spaces, and use these individual, function-based

433   accessibility metrics to examine the association with mechanisms via responses or biomarkers from

434   cohort participants is still warranted to determine their relative importance. The challenge for future

435   research will be to collect accurate information on historical function and use of public parks and

436   green space by individuals over time.

437   This is the first study to consider the association between area-level green space on ~~long term~~long-

438   term cognitive ageing but, unlike recent studies over shorter time frames (Dadvand et al., 2015a),

439   we did not estimate the effect of school, work or commuting green space. Due to the longitudinal

440   nature and complexity of the analysis, we concentrated on one feature of the residential

441   environment (green space) that may affect cognitive ageing; however, in cross-sectional analyses,

442   multiple features have been examined (Clarke et al., 2012). In addition, we have tested multiple

443   temporal combinations of one feature of the urban environment, as advised previously (Mishra et

444   al., 2009), but this may have led to significant results by chance using conventional p-value

445   thresholds of 0.05; therefore, we recommend the replication of these results in further studies.

446   Future studies in other settings can learn from the approach used in this study in collecting and

447   harmonising historical green space data (Pearce et al., 2016). Comparable green space surveys are

448   available in other large urban areas of the UK and could be linked to cohorts with longitudinal health

449   outcomes in later life. Further automation, using techniques such as Optical Character Recognition

450   on paper maps (e.g. those produced periodically in the UK by the Ordnance Survey), offers

451   significant analytical promise for extracting historical environmental information for larger areas, up

452   to the national level. Temporal environmental data collected at this spatial scale can then be

453   integrated with nationwide cohorts (e.g. the various British birth cohort studies). This approach is

454   contingent on the availability of participants' residential addresses over time, which are increasingly

455   being made available for studies of health and place over the life course.

456   **Conclusions**

457   This study has demonstrated that environmental circumstances in early life, in particular the

458   availability of local parks, may have life-long impacts on cognitive ageing, particularly for women,

459   people without an *APOE* e4 allele, and those in lower socioeconomic groups during adulthood. The

460   findings are not only novel but also have relevance for policymakers. The results emphasise the need

461   to ensure a good level of access to parks throughout the life course, but particularly during

462   childhood. Encouraging parents to help their children's use of parks become regular and frequent

463   may also be warranted, as this can inspire lifelong green space usage as well as providing continued

464   positive effects for the parent (Refshauge et al., 2012). Future research could usefully investigate the

465   geographic nature of availability of parks (e.g. accounting for movement from home to work and

466   school) and which features (e.g. safety, number of amenities) are important for both children and

467   adults, to encourage lifelong use for health-promoting behaviours, as well as considering how

468   exposure to a wider set of environmental features across the life course affect health and wellbeing

469   in later life.

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Tables

Table 1: Descriptive statistics of LBC 1936 participants by sample

Characteristic at age 70 [a]	LBC Full Sample at age 70 (n=1,091)	LBC Life grid sample at age 78 [c] n=(593)	LBC Analysis Sample at age 78 (n=281)
Sex			
Women	543 (50)	279 (47)	135 (48)
Age (days)	25,397 ± 303	25,385 ± 306	25,308 ± 252
Family history of Heart Disease			
Yes	672 (62)	377 (63)	167 (59)
NA [b]	7(0)	5 (1)	2 (1)
APOE e4 allele			
Yes	304 (28)	167 (28)	76 (27)
NA	64 (6)	34 (6)	12 (4)
Father's OSC			
Professional-managerial (I/II)	260 (24)	153 (26)	57 (20)
Skilled, partly skilled, unskilled (III/IV/V)	700 (64)	403 (68)	208 (74)
NA	131 (12)	37 (6)	16 (6)
Childhood smoker (≤16 y)			
Yes	226 (21)	103 (17)	54 (19)
NA	-	-	-
Childhood number of people per room	1.38 ± 0.79	1.32 ± 0.75	1.41 ± 0.78
NA	4 (0)	3 (1)	-
Adulthood OSC			
Professional-managerial (I, II)	592 (54)	354 (60)	133 (47)*
Skilled, partly skilled, unskilled (III, IV,V)	478 (44)	231 (39)	146 (52)*
NA	22 (2)	8 (1)	2 (1)
Adulthood Smoker (>16 y)			
Yes	125 (11)	39 (7)	23 (8)
NA	1 (0)	1 (0.2)	-
Alcohol consumption			
Yes	947 (87)	533 (90)	248 (88)
NA	1 (0)	1 (0.2)	-
Adulthood History of Stroke			
Yes	54 (5)	22 (4)	11 (4)
NA	1 (0)	1 (0.2)	-
Adulthood HADS Score	7.68 ± 4.52	7.37 ± 4.41	7.52 ± 4.33
NA	6 (0)	5 (1)	2 (1)
Adulthood BMI	27.78 ± 4.36	27.22 ± 4.15	27.76 ± 4.37
NA	2 (0)	1 (0.2)	-

[a] Number and percentages for categorical data; mean and standard deviation for continuous variables

[b] "NA" is missing

[c] Descriptions of samples as follows: Full sample- participants at age 70; Life grid sample- participants with complete address history at age 78; Analysis sample- Participants had at

least one Edinburgh address during the decade of park measurement (childhood: 1949; adulthood: 1969; later adulthood: 2009).

Chi- square test for independence for categorical data and Welch two sample t-test for continuous data with significance presented as follows: * P<0.05 ** p<0.01

Table 2: Descriptive statistics by Moray House Test Score at ages 11, 70 and 76 for LBC Analysis sample

Characteristic at age 70 [a]	Age standardised MHT Score at age 11	Age standardised MHT Score at age 70	Age standardised MHT Score at age 76
Sex			
Men	99.7 ± 15.0	100.8 ± 14.8	99.2 ± 12.5
Women	102.1 ± 13.7	100.2 ± 13.0	100.0 ± 12.5
APOE E4 allele			
No	101.4 ± 14.7	101.1 ± 13.7	100.7 ± 15.6
Yes	98.9 ± 14.0	98.6 ± 15.0	95.8 ± 13.5
Father's OSC			
Professional-managerial (I, II)	104.2 ± 13.5	103.7 ± 10.4	102.6 ± 12.6
Skilled, partly skilled, unskilled (III, IV,V)	99.6 ± 14.5	99.4 ± 14.9	98.7 ± 14.5
Childhood smoker (≤16 y)			
No	101.6 ± 13.6	101.2 ± 13.2	100.5 ± 13.2
Yes	97.6 ± 17.0	97.3 ± 16.5	95.6 ± 16.9
Childhood number of people per room			
<2	101.6 ± 14.7	101.5 ± 12.9	100.5 ± 13.5
>2	98.3 ± 12.5	96.5 ± 16.9	96.1 ± 15.7
Adulthood OSC			
Professional-managerial (I, II)	-	103.7 ± 15.1	102. 4 ± 23.7
Skilled, partly skilled, unskilled (III, IV,V)	-	97.0 ± 15.1	96.3 ± 15.1
Adulthood Smoker (≥16 y)			
No	-	100.8 ± 13.8	99.9 ± 14.0
Yes	-	98.1 ± 15.0	96.2 ± 14.2
Adulthood Alcohol consumption			
No	-	101.2 ± 11.9	101.3 ± 13.6
Yes	-	100.5 ± 14.2	99.4 ± 14.1
Adulthood Adiposity			
Normal (BMI <30 kg/m^2)	-	100.8 ± 14.0	100.1 ± 13.8
Obese (BMI ≥30 kg/m^2)	-	99.5 ± 13.7	97.8 ± 14.7
Parks availability [b]			
Childhood			
Low (0.34-7.01%)	99.2 ± 15.5	98.1 ± 16.3	98.0 ± 15.6
High (7.01-31.3%)	100.3 ± 13.4	100.8 ± 12.0	98.7 ± 13.2
Adulthood			
Low (0.73-7.74%)	-	98.6 ± 14.2	98.1 ± 13.8
High (7.74-30.7%)	-	100.3 ± 14.4	98.6 ± 15.0
Later Adulthood			
Low (0-7.07%)	-	99.1 ± 14.7	97.9 ± 14.7
High (7.07-40.9%)	-	99.8 ± 14.0	98.8 ± 14.2

[a] Mean and standard deviation presented

[b] Residential parks availability dichotomised by median

Table 3: Association between park life course model and cognitive change from age 11-70 and 70-76

	MHT Score change 11-70					MHT Score change 70-76				
Park life course model [a]	AIC	P [b]	β	95%CI LL	95%CI UL	AIC	P	β	95%CI LL	95%CI UL
a) Accumulation										
- Strict	728.466	0.711	-0.018	-0.100	0.063	761.454	0.016	-0.010	-0.094	0.075
- Relaxed	731.475	0.628				762.036	0.018			
Childhood			0.024	-0.181	0.230			-0.149	-0.340	0.041
Adulthood			0.060	-0.204	0.323			0.006	-0.293	0.305
Later adulthood			-0.096	-0.265	0.072			0.112	-0.121	0.346
b) Critical Time Period										
- Childhood	728.624	0.692	0.020	-0.172	0.212	759.368	0.034	-0.130	-0.305	0.045
- Adulthood	728.666	0.687	0.002	-0.220	0.224	761.488	0.016	0.014	-0.210	0.238
- Later adulthood	727.689	0.799	-0.074	-0.223	0.074	760.605	0.022	0.089	-0.097	0.275
c) Effect modification										
- Early	732.511	0.453	-0.019	-0.313	0.274	758.135	0.071	0.308*	0.024	0.591
- Later	731.291	0.621	-0.007	-0.210	0.195	763.304	0.010	0.114	-0.124	0.352
No effect	726.619	0.780	-0.037	-0.155	0.080	759.458	0.027	0.017	-0.102	0.137

[a] Per 10% of parks within 1,500 m residential buffer zone

[b] P-value for partial F test in comparison with the saturated model

[c] MHT score change is residualised on previous MHT score and standardised for age

*p<0.05 **p<0.01

Table 4: Association between childhood and adulthood park availability, as modelled by an interaction term, and cognitive change from age 70-76 [a]

| Covariate model [c] | Model term [b] | |
| | Childhood*Adulthood | |
	β	CI (95%CI)
Model 1	0.31*	0.02 - 0.59
Model 2	0.26	-0.05 - 0.58
Model 3	0.26	-0.06 - 0.57

[a] MHT score change is residualised on previous MHT score and age

[b] Per 10% of parks within 1,500 m residential buffer zone

[c] Model 1 adjusted for sex; Model 2 additionally adjusted for father's Occupational Social Class (OSC), childhood smoking status and people per room in childhood home; Model 3 additionally adjusted for adulthood OSC, adulthood smoking status and adulthood alcohol consumption status

*p<0.05 **p<0.01

Table 5: Stratified analysis on the association between childhood and adulthood public park availability, as modelled by an interaction term, and cognitive change from age 70-76

	Model term [b]	
	Childhood*Adulthood Parks	
	β	CI (95%CI)
Effect modifier [a]		
Sex		
Male	0.06	-0.42 – 0.54
Female	0.64**	0.24 – 1.05
APOE e4 allele		
Yes	-0.02	-0.78 – 0.74
No	0.29	-0.05 – 0.63
Adulthood OSC		
Professional-managerial (I, II)	0.02	-0.38 – 0.44
Skilled, partly skilled, unskilled (III, IV,V)	0.66*	0.15 – 1.18

[a] Additionally adjusted for childhood OSC, people per room in childhood home, childhood smoking status, adulthood smoking status andadulthood alcohol consumption status

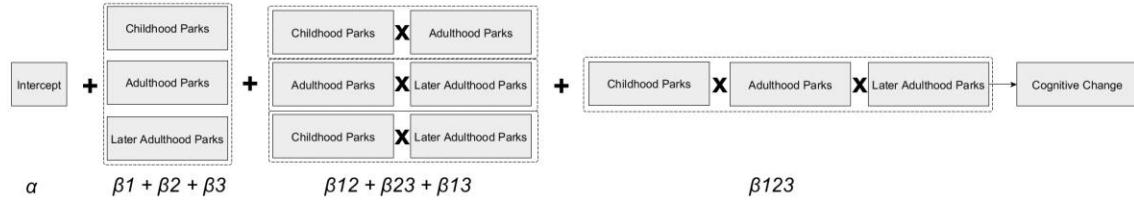[b] Per 10% of parks within 1,500 m residential buffer zone

*p<0.05 **p<0.01

Figure

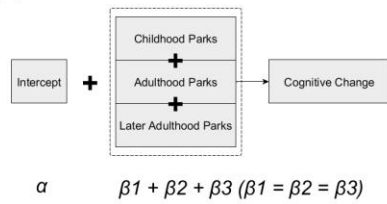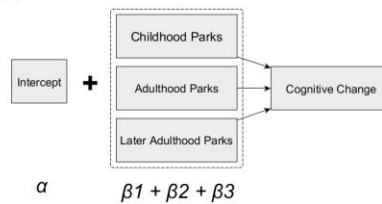Figure 1: Conceptual model with specifications for life course analysis

<u>**Figure 1**</u>

α = intercept

β = coefficient

Figure 2: Marginal effects of park availability, conditional on parks availability from adulthood on cognitive change from age 70-76, presented continuously (A) and in tertiles (B)

1   *Abstract*

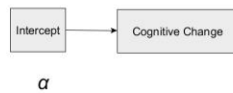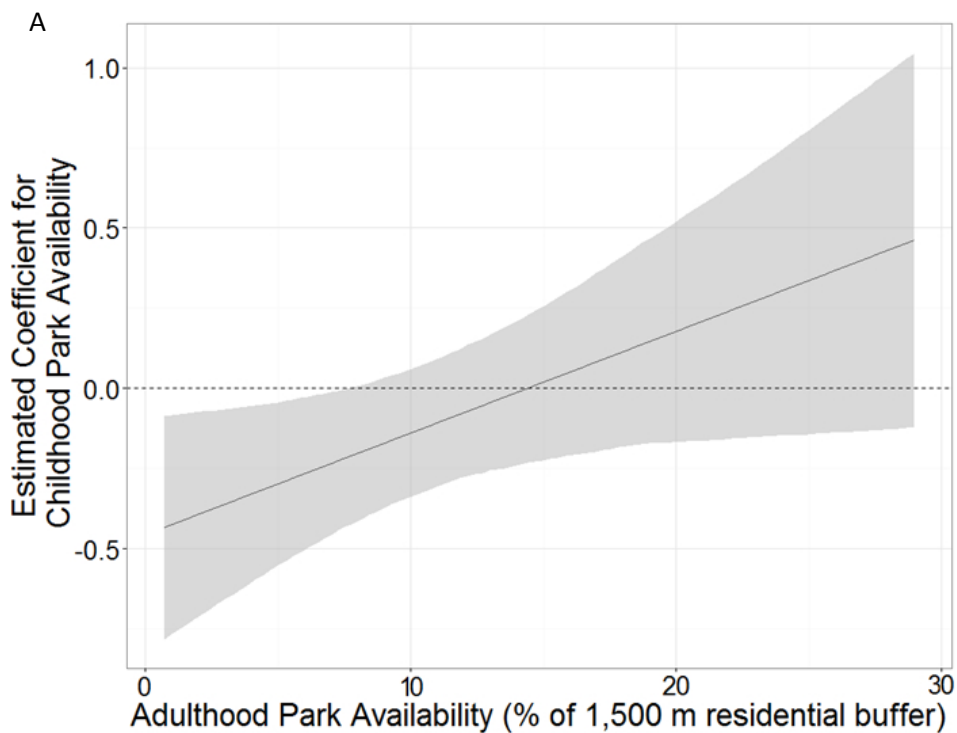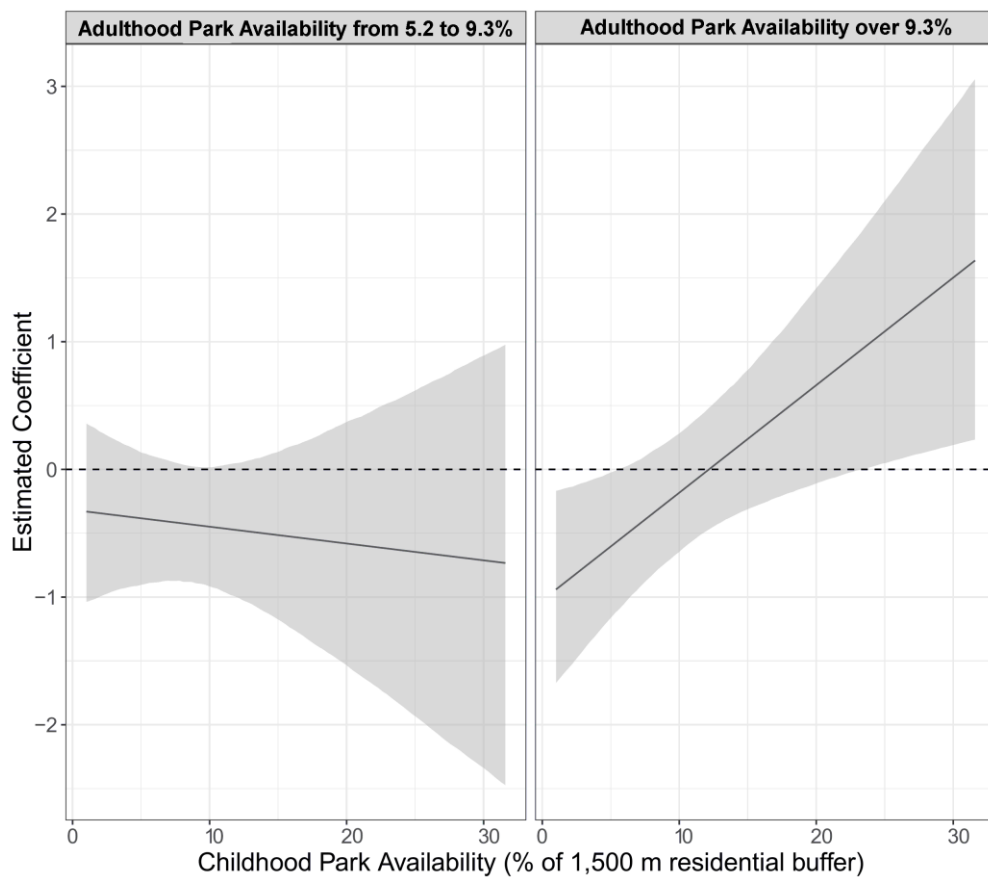2   International evidence suggests that green space has beneficial effects on general and mental health

3   but little is known about how lifetime exposure to green space influences cognitive ageing.

4   Employing a novel longitudinal life course approach, we examined the association between lifetime

5   availability of public parks and cognitive ageing. Lifetime residential information was gathered from

6   the participants of the Lothian Birth Cohort 1936 using a "life-grid" questionnaire at age 78 years.

7   Parks information from 1949, 1969 and 2009 was used to determine a percentage of parks within a

8   1,500 m buffer zone surrounding residence for childhood, adulthood, and later adulthood periods.

9   Linear regressions were undertaken to test for association with age-standardised, residualised

10   change in cognitive function (Moray House Test score) from age 11 to 70 years, and from age 70 to

11   76 (n=281). The most appropriate model was selected using the results of a partial F-test, and then

12   stratified by demographic, genetic and socioeconomic factors. The local provision of park space in

13   childhood and adulthood were both important in explaining the change in cognitive function in later

14   life. The association between childhood and adulthood park availability and change in the Moray

15   House Test Score from age 70 to 76 was strongest for women, those without an *APOE* e4 allele (a

16   genetic risk factor), and those in the lowest socioeconomic groups.

17   Greater neighbourhood provision of public parks from childhood through to adulthood may help to

18   slow down the rate of cognitive decline in later life, recognising that such environmental associations

19   are always sensitive to individual characteristics.

20

21   *Keywords:* UK; Green space; public parks; cognitive function; cognitive ageing; life course;

22   longitudinal

23

24

25 *Introduction*

26 With the global increase in life expectancy, there is an urgent need to identify factors that affect

27 changes in cognitive abilities as people age. Explanatory models of cognitive ageing posit a variety of

28 demographic, genetic, behavioural and environmental factors contributing to cognitive function

29 (Anstey, 2014). The focus of the current research is on how environmental conditions – or more

30 specifically local green spaces - throughout life affect people's cognitive ageing relative to one

31 another. There have been significant advances made in understanding the range of demographic,

32 genetic, and behavioural factors affecting cognitive ageing. For instance, women tend to have

33 greater resilience to age-related decline (McCarrey et al., 2016). The major genetic predictor

34 responsible for increased susceptibility to non-normative cognitive ageing is the presence of the

35 APOE (apolipoprotein) e4 allele (Davies et al., 2014; Deary et al., 2012b; Schiepers et al., 2012).

36 Behavioural factors, including diet, physical activity, smoking and alcohol consumption, closely

37 related to an individual's socioeconomic status, are often associated with cognitive function in older

38 age, although, apart from smoking, results differ between studies and some associations are prone

39 to confounding by prior cognitive function (Deary et al., 2009; Plassman et al., 2010). Little work has

40 considered specific built, social or environmental features of local areas, with previous research

41 relying on aggregate measures of social deprivation (Lang et al., 2009). Yet cognitive function could

42 be affected by a range of environmental or neighbourhood conditions including: local social capital;

43 residential segregation; perceived safety and incivilities; availability of community resources such as

44 food shops and other services; walkability; and the availability of public open space or local

45 greenness (Y. T. Wu et al., 2015a).

46 It is well established that public open space and greenness is often beneficial for the physical and

47 mental health of local residents (van den Berg et al., 2015). It is also feasible that public open space

48 and greenness may help to optimise cognitive function. Several studies with differing population,

49 design and outcome measures are suggestive of a direct positive benefit of natural environments to

50   directed attention (Ohly et al., 2016). Increased support and motivation for social interaction and

51   physical activity, reductions in stress and exposure to higher air quality offer indirect benefits to

52   cognitive capability, evidenced by a large body of research on changes in physiological markers and

53   emotional states (Hartig et al., 2014). Other indirect benefits such as exposure to beneficial

54   microbiota could indirectly affect cognitive processes through facilitating a reduction in blood

55   pressure and boost to immune function (M. Kuo, 2015). Some of these mechanisms have been

56   shown to directly link with change in cognitive function; for example, in participants over 70 years

57   old, low levels of leisure-time physical activity were associated with a decline in cognitive function

58   five years later (Willey et al., 2016). The only previous longitudinal study of area-level greenness and

59   cognitive change focused on children. The authors found that greenness surrounding a child's home,

60   school and commute was correlated positively with improvements in memory and a reduction in

61   inattentiveness (Dadvand et al., 2015a). However, the study only considered these associations over

62   a 12-month period during early life, and therefore the influence of green space on cognitive function

63   over an individual's lifetime remains unknown.

64   In the present study, we examined whether availability of green space (using a measure of nearby

65   public parks) was associated with age-related changes in cognitive function between age 11 and 70

66   years, and between age 70 and 76 years. Three life course models (critical periods, accumulation,

67   and effect modification) were used to address three key hypotheses. First, early childhood has been

68   shown to be a critical period for brain growth due to heightened brain plasticity (Lyu & Burr, 2016).

69   Therefore, we hypothesised that greater public park availability during childhood has positive

70   associations with cognitive change in later life (critical period model). Second, we hypothesised that

71   a greater accumulation of park availability over life is required to promote successful cognitive

72   ageing in later life (accumulation model). This was based on the assumption that cross-sectional

73   effects of access to parks on cognitive function are consistent, albeit weaker, over time (Dadvand et

74   al. 2015a) and that for significant cognitive ageing to be observed a threshold must be surpassed

75   (Anstey 2014). Finally, by combining the critical periods and accumulation models, we hypothesised

76   that availability during adulthood is important for determining the extent of cognitive reserve, with

77   the capacity to modify the effect of exposure on the sensitive childhood period (effect modification

78   model). As mentioned previously, demographic, genetic and behavioural factors will set an individual

79   on a unique cognitive health trajectory. Therefore, with the aim to determine which groups would

80   benefit most from greater park availability, we stratified the life course model by sex, the presence

81   of an *APOE* e4 allele, and occupational social class (as a marker of individual socioeconomic status).

82   ***Methods***

83   *Study design and setting*

84   A retrospective life course study was designed using data from the Lothian Birth Cohort 1936

85   (LBC1936) (Deary et al., 2012a; Deary et al., 2007). The participants, who were all born in 1936, were

86   recruited from Edinburgh and the Lothians in Scotland. Most had taken part in a nationwide

87   assessment of their general intelligence in 1947 (Scottish Mental Survey 1947; N=70,805) (SCRE

88   1949). The cohort participants were re-contacted in 2004 and, from 2,318 responses, 1,091 were

89   eligible for wave 1 data collection (Deary, Gow et al. 2012). Cohort participants were subsequently

90   contacted and tested at mean ages of approximately 70 years (Jul 2004- May 2007), 73 (Oct 2007-

91   May 2010) and 76 (Jul 2011-Nov 2013). At mean age 78, a stand-alone questionnaire booklet was

92   posted out with returns received between July 2014 and April 2015.

93   *Operationalising change in cognitive function*

94   We operationalised the outcome of cognitive ageing using the participant's Moray House Test No.

95   12 (MHT) scores from mean ages of 11, 70 and 76 years (SCRE, 1949). The MHT is a validated

96   measure of cognitive function, which correlates highly with the current "gold standard" cognitive

97   tests (Deary et al., 2004). The MHT is a general intelligence test that is composed of 71 items,

98   measuring the participant's ability on a variety of mental tasks including verbal reasoning,

99   arithmetic, and following directions. Each score was adjusted for age in days at the time of

4

100   examination by taking the standardised residuals from a linear regression with age as the

101   independent variable. The score was then standardised to have a mean of 100 and standard

102   deviation of 15. Change was calculated by generating the standardised residual from a linear

103   regression model with previous MHT score (e.g. change from 11 to 70 calculated by taking age 70

104   score as the dependent and age 11 as the independent variable). This statistical technique to

105   calculate change in score is superior to an arithmetic difference as the outcome is independent of

106   baseline level (Prochaska et al., 2008), and has been used in relation to changes in cognitive function

107   previously (Gow et al., 2005). The procedure above provided two outcomes: residualised change in

108   MHT score from age 11 to 70 and residualised change in MHT score from age 70 to 76.

109   *Operationalising LBC1936 covariates*

110   During the structured interview as part of the cognitive testing appointment at age 70, respondents

111   provided the information required for all the covariates except for father's social class, which was

112   obtained via a questionnaire, and BMI, which was obtained during the physical examination.

113   Covariates were selected *a priori* based on previous literature (Deary et al., 2009)*,* including sex,

114   Occupational Social Class (OSC) (Office of Population Censuses and Surveys, 1980) of participant's

115   father, people per room in childhood household, childhood smoking status, OSC of participant,

116   smoking status and alcohol consumption (Deary et al., 2007). OSC of the participant's father was

117   used as a measure of socioeconomic status from childhood and dichotomised into Professional-

118   managerial (I and II) and Skilled, partly skilled, unskilled (III, IV and V). Additionally, we used

119   childhood overcrowding as a secondary measure of socioeconomic status, defined as the number of

120   people per household room. Participants were asked at what age they started smoking and were

121   categorised as a childhood smoker if they responded that they had started before age 16, as per

122   convention (Hopkinson et al., 2014). Smoking status at age 70 was dichotomised as smoker or non-

123   smoker. Similarly, alcohol consumption was dichotomised as drinks alcohol or doesn't drink alcohol.

124   BMI at age 70 was calculated as weight divided by height squared. Socioeconomic status during

125 adulthood was defined by OSC of the participant's main job from their career and dichotomised in

126 the same way as their father's OSC. For females, husband's OSC was used if higher than their own.

127 We selected a number of variables as effect modifiers *a priori* including sex, adulthood OSC and

128 *APOE* e4 allele. Sex and adulthood OSC at age 70 were operationalised as above. Blood samples

129 were taken during examination and participants were genotyped for *APOE* allele status using

130 TaqMan technology at the Wellcome Trust Clinical Research Facility Genetics Core (Deary et al.,

131 2012a). Participants were dichotomised into having at least one *APOE* e4 allele or having none. In

132 addition to the variables above, we selected several variables to act as auxiliary variables in the

133 imputation of missing data. Due to the association with cognitive ageing, these included the Hospital

134 Anxiety and Depression Scale score (Zigmond & Snaith, 1983), history of stroke (Yes or No) and

135 family history of heart disease, stroke, or problems with blood vessels (Yes or No).

136 *Operationalising public parks information*

137 We identified four open space surveys that recorded public parks in Edinburgh during the 20th and

138 21st century (Pearce et al., 2016). Public parks were deemed a suitable indicator of urban green

139 space because they promote social interaction and a range of uses, including physical activity, to a

140 greater extent than ambient greenery (such as road side verges or river corridors) (E. Richardson et

141 al., 2010). Public parks data were scanned from paper maps from the Edinburgh Civic Survey 1949

142 (Abercrombie et al., 1949) and the Open space survey 1969 (Town Planning Department Edinburgh,

143 1969), georeferenced and converted to geographic information system vector data using ArcMap

144 10.1 GIS software (ESRI, Redlands, CA). Contemporary public parks data were derived from the Open

145 Space Audit 2009 (The City of Edinburgh Council, 2009). Although descriptions of the parks changed

146 slightly between surveys (e.g. "public parks" and "public recreation grounds"), consistency was

147 confirmed by the continued presence in certain spaces over time. Hereafter we refer to these spaces

148 simply as 'parks'.

149 *Operationalising lifetime residential address history*

150   The surviving participants of the LBC1936 were re-contacted in 2014 (mean age 78) (n=704/1,091),

151   and asked to fill out a residential (i.e. Life grid) questionnaire (Blane, 1996), with a response rate of

152   87% (n=612/704). From these responses, a total of 593 participants had useable life grid data; these

153   participants are referred to as the "Life grid sample". The participants were given the option to recall

154   the dates of personal events in their life, and to fill them in next to a column containing global events

155   such as the Falklands War. These events acted as memory prompts for participants to provide

156   information on their residential address and occupation (of self or father) for each decade from

157   birth. We have utilised contemporary sources to geocode the 7,423 participant addresses. We

158   geocoded the participant addresses using Nomatim to query Open Street Map (OSM)

159   (OpenStreetMap contributors, 2017), as the accuracy for addresses in Edinburgh is between 1-3 m

160   and the coverage is excellent (Grosso et al., 2015). The output contained the latitude, longitude and

161   the comma separated OSM-derived address string (e.g. 82, Home Street, Edinburgh, United

162   Kingdom). This address string was then compared with what was supplied by the participant, which

163   was recorded in the same format. 15% of the participant addresses were not able to be geocoded or

164   had lost information (i.e. the difference in the number of comma separated 'information bits' was

165   negative). As we hypothesised that this may be due to misspellings or imperfect matches, the

166   Google Maps geocoding API was used as it employs a fuzzy string matching algorithm. We then

167   manually compared the Google maps geocoding API quality output (i.e. 'rooftop',

168   'range_interpolated', 'geometric_center' and 'approximate') to the address supplied by the

169   participant. 6% of the google-derived geocodes did not contain the same level of information

170   supplied by the participant and were manually geocoded using historic building repositories such as

171   Canmore.org.uk (i.e. using the 8-digit National Grid Reference, 1m resolution). Participants were

172   eligible for the "Analysis sample" (n=281) if they recorded Edinburgh addresses during the decades

173   when parks were surveyed (i.e. childhood: 1949; adulthood: 1969; later adulthood: 2009). This

174   approach was markedly less restrictive than an analysis sample where participants had to have all of

175   their previous addresses within Edinburgh (n=174) and only resulted in a modest drop in the mean

176   percentage of the participant's total number of addresses that were within Edinburgh (i.e. from

177   100% to 94%).

178   *Determining park availability using lifetime residential address history*

179   Park availability for the LBC1936 participants was calculated by taking the percentage of park area

180   that intersected with a 1,500 m buffer zone surrounding the participant's address at each time

181   period (childhood, adulthood, and later adulthood). A 1,500 m buffer zone was selected as it

182   corresponds to approximately a 15-25 minute walk to the edge of the buffer zone, based upon data

183   on mean walk speeds of between 1-1.5 m/s for ages 20-80 (Ferrucci et al., 2016). Also, a 1,500 m

184   circular buffer was used as approximately 90% of the 500 people surveyed in the 1969 Open space

185   survey reported travelling up to 1.6 km (as the crow flies) to reach public parks within the city (Town

186   Planning Department Edinburgh 1969). A sensitivity analysis was undertaken by repeating the

187   analysis using buffer zones of 500 m and 1,000 m. The availability of parks metric was analysed as a

188   continuous variable, for each 10% increase in park area within the 1,500 buffer zone.

189   *Main Analyses*

190   All statistical analysis was performed in R version 3.3.1. To investigate the relationship between

191   availability of parks measured at three time periods (childhood, adulthood and later adulthood) and

192   cognitive ageing, we adapted an established method to detect the most appropriate life course

193   model (Mishra et al. 2009). The general premise was to build a series of linear regression models

194   that represent the life course models under investigation ("accumulation", "critical periods", and

195   "effect modification"). The model fit was then compared, via the partial F test, with a "saturated"

196   model. The "saturated" model was specified by including all the individual park terms, three two-

197   way multiplicative interactions and a three-way multiplicative interaction (Fig. 1; see Model 1). The

198   saturated model represents the full complexity of combinations of park availability through life. We

199   determined whether parks have an effect on cognitive ageing or not by comparing the fit statistics of

200   the saturated model with a "no effects" model which contained only the intercept (Fig. 1; see Model

201 5). This "no effects" model crudely predicted an individual's cognitive change as the mean of the

202 cognitive change experienced by all the participants. Thus, if park availability was important for

203 cognitive ageing then the inclusion of all park terms would explain more of the variance in cognitive

204 change than just using the mean. This was established by comparison of the two models using a

205 partial F-test. If the "no effects" model fitted the data just as well as the saturated model, then a p-

206 value above 0.05 was obtained and we could assume that parks did not have an association with

207 cognitive ageing. If the p-value was lower than 0.05, it signified that the "no effects" model was not

208 superior and we could assume that parks had an effect on cognitive ageing. We could also,

209 subsequently, repeat this procedure to compare life course analyses and determine the most

210 appropriate models.

211 The Accumulation models were categorised into strict and relaxed. The strict model was defined as

212 the park terms summed (i.e. sum of parks from childhood, adulthood and later adulthood), which

213 assumed that parks had an equal association with cognitive ageing, irrespective of the time they

214 were measured (Fig. 1; see Model 2a). The relaxed model contained each of the park terms as

215 individual predictors; i.e. parks from childhood, adulthood and later adulthood were mutually

216 adjusted for one another, which allowed any differences in the strength of association by time of

217 park measurement to be observed (Fig. 1; see Model 2b).

218 The Critical Periods models were tested by running separate models for each park term from a single

219 point in time. This assumed that the other park terms did not influence cognitive ageing or modify

220 the association of the parks under investigation (e.g. Fig. 1; see Model 3a).

221 The Effect Modification models were defined at two points in time, early and later, and were

222 specified by including a multiplicative interaction term between parks from the two successive time

223 periods (i.e. an interaction between childhood parks and adulthood parks) (Fig. 1; see Model 4a).

224 These models emphasised the temporal sequence of exposure during early or later life as being

225 important for the eventual association with cognitive ageing. As before, we compared the partial F-

226 statistics of each life course model with the "saturated" model. A p-value of over 0.05 signified that

227 the life course model fitted the data as well as the "saturated model". The life course model with the

228 highest p-value was deemed the most appropriate as this meant that it not only fit the data as well

229 as the "saturated model", but was more parsimonious. All models were adjusted for sex in a

230 complete-case analysis. A positive regression coefficient represented higher residualised change in

231 cognitive function between the time points (i.e. relatively better cognitive change) whereas a

232 negative regression coefficient represented decreasing residualised change in cognitive function

233 between the time points (i.e. relatively worse cognitive change). The multiplicative interaction

234 regression coefficient was interpreted as the coefficient of one park term being conditional on

235 another.

236 *Adjusted and stratified analyses*

237 After identifying the most appropriate life course model we continued to the multiple regression

238 analysis, adjusting for childhood and adulthood covariates. Some data were missing for covariates

239 and the two outcomes. These were assumed missing at random and imputed by chained equations

240 using the 'mice' package (van Buuren & Groothuis-Oudshoorn, 2011). We imputed 20 datasets using

241 the following sociodemographic and behaviour variables that were proposed to be related to the

242 missing structure: sex, OSC, smoking, alcohol consumption and BMI; and variables proposed to be

243 associated with cognitive ageing: Hospital Anxiety and Depression Scale total score, history of stroke,

244 and family history of heart disease, stroke or problems with blood vessels. The estimates from the

245 imputed datasets were pooled using Rubin's rules. We then ran a linear regression for three nested

246 models with adjustment for: (i) sex; (ii) father's OSC, number of people per rooms in childhood

247 household, childhood smoking status, (iii) adulthood OSC, alcohol consumption and adulthood

248 smoking status. Finally, using the fully adjusted model we stratified by sex, the presence of the *APOE*

249 *e4* allele and adulthood OSC.

250 **Results**

251   We found few discernible differences between the Full sample and the Analysis sample for most of

252   the selected characteristics, as shown by chi-square and two sample t-tests (Table 1). The Analysis

253   sample had significantly higher levels of individuals recorded as Skilled, partly skilled, unskilled OSC

254   during the adulthood period. The frequency of missing data was low at below 6% for all the

255   variables. We found similar rates of missing data in the outcomes, with 6.7% for MHT change from

256   11 to 70, and 4.6% for change in MHT score from 70 and 76. On average, MHT scores increased from

257   11 to 70 and decreased from 70 to 76. There were differences in age standardised MHT scores by

258   the selected characteristics (Table 2). Men had lower scores at age 11, but were similar to women at

259   age 70 and 76. Those in the skilled, partly skilled, unskilled OSC and carriers of the *APOE* e4 allele

260   also performed worse at each age. We compared the availability of parks at the three measurement

261   periods using Pearson correlation coefficients and found the highest correlation between adulthood

262   and later adulthood parks (0.63) compared to the lowest between childhood and later adulthood

263   parks (0.19) (See Supplementary material; see Fig. S1). Median percentage of parks surrounding

264   participant residence increased with measurement period: from childhood at 7.0%, to adulthood at

265   7.7%, and later adulthood at 8.4%. This mirrored the increase in parks in Edinburgh during these

266   periods (See supplementary material; see Fig. S2).

267   *Associations between availability of parks and cognitive change*

268   There was no significant association between the availability of parks and cognitive change from age

269   11 to 70, as shown by the comparison between the "no effects" model and the saturated model

270   yielding a p-value of over 0.05 (p=0.780) (Table 3). However, there was an association between park

271   availability and cognitive change from age 70 to 76, with the same comparison yielding a p-value

272   below 0.05 (p=0.027) (Table 3). The life course model with the best fit was the "early effect

273   modification" model (i.e. the interaction between childhood and adulthood parks), given that this

274   model recorded the highest p-value (p=0.071) and the lowest AIC (758.1). The coefficient for the

275   interaction term was positive and statistically significant (β=0.31; 95% CI 0.02-0.59) (Figure 2). Figure

276   2A shows the marginal effects of childhood park availability on cognitive change from age 70 to 76,

277   conditional on the percentage of parks in adulthood. This shows that childhood park availability had

278   an increasingly positive/advantageous association with cognitive change from 70 to 76 years as the

279   person's adulthood park availability increases. This was found predominantly at the highest levels

280   (i.e. top tertile) of adulthood park availability (Figure 2B).

281   *Moderating role of demographic, genetic and socio-economic factors*

282   As the most parsimonious model, we undertook further analysis using the early effect modification

283   model with adjustment for childhood (i.e. father's OSC, childhood smoking status, people per room

284   in childhood home) and adulthood covariates (i.e. adulthood OSC, adulthood smoking status and

285   adulthood alcohol consumption status). In the adjusted models, the coefficient was attenuated, to

286   the extent that in the fully adjusted model (i.e. model 3) the association was no longer significant

287   (β=0.26; 95% CI -0.06 – 0.57) (Table 4). In analyses stratified by these variables we found that the

288   "early effect modification model" was moderated by sex, the presence of the *APOE* e4 allele and

289   adulthood OSC. We found the association to be strongest in women (β=0.64; 95% CI 0.24 – 1.05),

290   those without an *APOE* e4 allele (β=0.29; 95% CI -0.05 – 0.63) and in a Skilled, partly skilled, unskilled

291   OSC during adulthood (β=0.66; 95% CI 0.15 – 1.18) (Table 5).

292   *Sensitivity Analyses*

293   We found similar results when we used a stricter definition for the Analysis sample (See

294   Supplementary material; see Table S1). We also tested how sensitive the results were to the buffer

295   zone size. In the sensitivity analysis, we found that the results for the 1,000 m buffer zone were

296   similar to those using the 1,500 m buffer zone, but no association between parks availability and

297   cognitive change was found using the 500 m buffer zone (see Supplementary material; see Table S2).

298   A case-complete analysis was undertaken to test our assumptions of data being missing at random

299   and we found that the coefficients varied marginally. As we found that the interaction was most

300   significant at the highest levels of adulthood park availability, we present the adjusted and stratified

301   results using tertiles of adulthood park availability (Table S3 and Table S4). Finally, in the current

302   analysis, we acknowledge that the meaning and purpose of public parks may differ depending on

303   level of urbanity (see Supplementary material; see Figure S3). As a proxy for degree of urbanity we

304   have extracted the population density from the Edinburgh Civic survey 1947 (for 1941) and

305   1951/1961 censuses and appended this information to the participant addresses. In the fully

306   adjusted model (model 3), the early effect modification model coefficient for participants residing in

307   areas with greater population density (27.4-76 people per hectare) was 0.43 (95% CI; 0.00-0.86)

308   compared with -0.03 (95% CI; -0.52-0.47) for those residing in a lower population density area (3.06-

309   27.4 people per hectare).

310   ***Discussion***

311   This research is the first to consider the role of green space in influencing cognitive ageing, and

312   identifies an important new line of enquiry for understanding the factors promoting successful

313   cognitive ageing. We examined the association between combinations of park availability over an

314   individual's lifetime and cognitive ageing. Our key finding was that greater availability of parks in

315   both childhood and adulthood were associated with successful cognitive ageing in later life.

316   Although the effect size is modest, the result makes a valuable contribution to understanding how

317   aspects of physical environment may be protective against poorer cognitive ageing. These findings

318   are amongst the first to suggest that environmental conditions in childhood might have significant

319   implications for health outcomes much later in life. The work is also novel because it is the first to

320   examine the role of green space over a participant's lifetime in influencing any health outcome;

321   examining a wider set of health outcomes and environmental characteristics are important next

322   steps for researchers in this field.

323   We observed greater park availability in childhood to have a positive association with the stability of

324   cognitive functioning in older adulthood, conditional on early adulthood environment. Previous work

325   on children pre-post home relocation have shown cognitive function to be highest amongst children

who moved to greener neighbourhoods (Wells, 2000). Other studies have found the school

environment to be important for childhood cognitive development, with significant positive effects

on academic performance with higher surrounding greenness of schools (Dadvand et al., 2015b; C.

D. Wu et al., 2014). In addition, objective measures of a child's residential neighbourhood and self-

reported greenness of their activity spaces have been associated with fewer symptoms of social,

emotional and behavioural difficulties (F. E. Kuo & Taylor, 2004; E. A. Richardson et al., 2017).

Parks may represent a feature of the urban environment that are more stimulating cognitively than

other kinds of green spaces, including those found in rural environments (Cassarino et al., 2016).

Whilst it has been shown that a lower percentage of surrounding green space and private gardens is

associated with a higher likelihood of cognitive impairment and dementia (Y. T. Wu et al., 2015b),

this is not uniformly the case (Clarke et al., 2012). Conflicting results in these previous studies may

be due to the age of participants. As the majority of the participants in the Clarke et al. study were

under 70 years old, null findings may be because there were smaller variations in cognitive ageing

trajectories.

While we hypothesised that adulthood park availability modifies the influence of childhood park

exposure due to childhood being a sensitive period for brain development, the reverse may also be

true. It is feasible that modification of park availability during adulthood by childhood exposure

relates to the theory of the "childhood factor", whereby the frequency of visits and positive

experiences with natural spaces in childhood predicts use in adulthood (Thompson et al., 2008).

Those who participated in nature-based recreation when they were children may be better able to

mitigate any constraints they face to participation in adulthood (Asah et al., 2012). Other

researchers stress the importance of unstructured play for infants and structured support from the

family, school and social clubs thereafter strengthening the link with nature-based recreation in

adulthood (Lovelock et al., 2016; Wang et al., 2013). Both interpretations emphasise the importance

of childhood exposure and the associated opportunity for brain development and acculturation,

351   which, if not realised, could result in much lower accumulated benefits from green space throughout

352   life.

353   We found that associations were strongest in those without the *APOE* e4 allele, women and those

354   with skilled, partly skilled and unskilled occupations; these results may be explained by differences in

355   outcome subtype and interaction with parks. The presence of the *APOE* e4 allele has been shown as

356   the single biggest predictor of older age cognitive change using the LBC1936 (Ritchie et al., 2016).

357   Ritchie et al., found that women in the LBC1936 were more likely to retain cognitive functions, in

358   particular under the specific domain of acquired knowledge, as they aged (Ritchie et al., 2016).

359   Previous studies have found that biomarkers of inflammation consistently associate with cognitive

360   ageing (Marioni et al., 2010; Rafnsson et al., 2007), but in some cases, associations have also only

361   been found in women and those without the APOE e4 allele (Metti et al., 2014). These results could

362   be due to differences in the pathology of cognitive ageing. The presence of APOE e4 alleles is mainly

363   associated with Alzheimer's dementia (Corder et al., 1993) and women experience cardiovascular

364   health problems 7-10 years later than men (Maas & Appelman, 2010). Taken together, our result

365   may suggest that park availability, through the potential mechanism of inflammatory biomarker

366   variability, could have a greater impact on vascular dementia, thus explaining heightened

367   significance in these groups. Our finding of a stronger association for lower socioeconomic

368   individuals is consistent with previous evidence showing that the greenest areas have the lowest

369   inequality in mortality (R. Mitchell & Popham, 2008) and mental wellbeing (R. J. Mitchell et al.,

370   2015). This may be because those in a lower socioeconomic status have less resource to take

371   advantage of spaces outside of their immediate environment, and therefore spend more time closer

372   to home.

373   A major strength of the study is the availability of childhood measures of cognitive function and

374   repeated measures in older age from the LBC1936 study, thus reducing the issue of reverse causality

375   associated with cognitive testing being undertaken within older age only. We have used change in

376 cognitive function rather than level at one point in time, thus avoiding cohort-specific differences in

377 ageing and measurement error (Liu et al., 2010). Our outcome is complemented by our

378 environmental exposure being the most consistently used measure of historical natural space

379 currently available (Pearce et al., 2016). We have also considered parks throughout life, decreasing

380 differential assessment error which can occur from using an address from a single point in time (e.g.

381 birth or last known address) (Brokamp et al., 2016). However, given the lengthy time frame of

382 exposure we were unable to classify subtypes of green space (e.g. golf courses, allotments) or the

383 quality of green space, which has been shown to be important in contemporary analyses (Wheeler

384 et al., 2015). The life course method we applied has been validated (Mishra et al., 2009). We used

385 continuous variables in the life course models, hence slight modifications to the specifications

386 presented elsewhere. Namely, we did not constrain the effect modification models to have fixed

387 effects to be 0, which would have resulted in a decrease in the model degrees of freedom and

388 therefore errors in the nested model comparison. We conducted a sensitivity analysis dichotomising

389 the variables, based on being within the highest quartile for public park availability with the fixed

390 effects constrained to 0, and the results were congruous to the continuous analysis. Findings from

391 the sensitivity analysis suggest that level of urbanity, defined by residential population density in

392 childhood, has an impact on the effect size and significance of the associations. The non-significant

393 relationship in suburban areas may be in part due to the differences in use of public parks, whereby

394 suburban residents have lower reliance on public parks, as private gardens and other types of green

395 space (e.g. river/canal corridors and forests) may be used more often (Mitchell and Popham 2007).

396 We did not perform sensitivity analyses with different buffer methods as we would expect the same

397 results regardless of whether a circular or network buffer was used (Bodicoat et al. 2014).

398 A weakness of this study is the retrospective data collection of residential address history, which can

399 be prone to recall bias. We were also limited by the numbers available for the analysis sample due to

400 the criteria for eligibility being based on continued lifetime residence in a small geographic area. It

401 was necessary to dichotomise OSC as to provide greater statistical power for stratified models (i.e. to

402   keep cell sizes to an appropriate size). This dichotomisation was also appropriate when this variable

403   was used as a covariate, as previous research found that significant differences in health outcomes

404   were only found between "professional or managerial occupations" compared to the rest (Gale et

405   al., 2016). We dichotomised other covariates (e.g. smoking status) as they were not recorded in the

406   same way for childhood and adulthood and therefore dichotomisation was used to aid

407   interpretation of change over time. The analysis sample was broadly similar in terms of selected

408   characteristics compared with the full cohort at age 70, but selection bias may have caused a higher

409   number of participants from lower socioeconomic groups being included. The issue of selection bias

410   was partly addressed by running the sensitivity analysis using a sample with different assumptions.

411   For addresses within the Edinburgh area, the precision of the addresses supplied varied and

412   therefore, for a small number of addresses that did not have a house number, the error between

413   actual participant residence and geocoded address was larger as we took the centre of their street.

414   In addition, by geocoding using contemporary sources, we have assumed that the street layout was

415   the same as it is today for the majority of the addresses, with only minor changes to the street

416   content. However we acknowledge that these small changes could have affected the precision of the

417   park exposure estimate for the earlier time periods. Given that we were geocoding a relatively small

418   number of addresses, we were able to employ a system to detect information lost compared with

419   what was supplied, so that if the results were unsatisfactory they would be geocoded manually. This

420   ensured that addresses that had changed significantly (e.g. demolished) would be geocoded to the

421   same accuracy as those that were able to be geocoded with contemporary sources (<3m). Given the

422   complexity of the existing analysis, with multiple exposures from different time points, we were

423   unable to include the examination of non-linearity. However, we would encourage this in future

424   analyses, especially using the forthcoming cognitive data waves in the LBC1936.

425   Availability of parks represents a 'cumulative opportunity' indicator of urban green space, which was

426   shown recently to represent the sum of intentional and incidental interactions to a greater extent

427   than proximity based measures (Ekkel and de Vries 2017). However, we were still unable to

428   distinguish how the space was being used and therefore the specific mechanisms by which green

429   spaces were beneficial to health. It has been argued that the sum of a range of mechanisms could

430   have a large effect on health through the pathway of enhanced immune function (M. Kuo, 2015).

431   Even though the effect of individual mechanisms may only contribute slightly to this effect, the

432   ability to define the function of specific green spaces, and use these individual function-based

433   accessibility metrics to examine the association with mechanisms via responses or biomarkers from

434   cohort participants is still warranted to determine their relative importance. The challenge for future

435   research will be to collect accurate information on historical function and use of public parks and

436   green space by individuals over time.

437   This is the first study to consider the association between area-level green space on long-term

438   cognitive ageing but, unlike recent studies over shorter time frames (Dadvand et al., 2015a), we did

439   not estimate the effect of school, work or commuting green space. Due to the longitudinal nature

440   and complexity of the analysis, we concentrated on one feature of the residential environment

441   (green space) that may affect cognitive ageing; however, in cross-sectional analyses, multiple

442   features have been examined (Clarke et al., 2012). In addition, we have tested multiple temporal

443   combinations of one feature of the urban environment, as advised previously (Mishra et al., 2009),

444   but this may have led to significant results by chance using conventional p-value thresholds of 0.05;

445   therefore, we recommend the replication of these results in further studies. Future studies in other

446   settings can learn from the approach used in this study in collecting and harmonising historical green

447   space data (Pearce et al., 2016). Comparable green space surveys are available in other large urban

448   areas of the UK and could be linked to cohorts with longitudinal health outcomes in later life.

449   Further automation, using techniques such as Optical Character Recognition on paper maps (e.g.

450   those produced periodically in the UK by the Ordnance Survey), offers significant analytical promise

451   for extracting historical environmental information for larger areas up to the national level.

452   Temporal environmental data collected at this spatial scale can then be integrated with nationwide

453   cohorts (e.g. the various British birth cohort studies). This approach is contingent on the availability

454   of participants' residential addresses over time, which are increasingly being made available for

455   studies of health and place over the life course.

Conclusions

457   This study has demonstrated that environmental circumstances in early life, in particular the

458   availability of local parks, may have life-long impacts on cognitive ageing, particularly for women,

459   people without an *APOE* e4 allele, and those in lower socioeconomic groups during adulthood. The

460   findings are not only novel but also have relevance for policymakers. The results emphasise the need

461   to ensure a good level of access to parks throughout the life course, but particularly during

462   childhood. Encouraging parents to help their children's use of parks become regular and frequent

463   may also be warranted, as this can inspire lifelong green space usage as well as providing continued

464   positive effects for the parent (Refshauge et al., 2012). Future research could usefully investigate the

465   geographic nature of availability of parks (e.g. accounting for movement from home to work and

466   school) and which features (e.g. safety, number of amenities) are important for both children and

467   adults to encourage lifelong use for health-promoting behaviours, as well as considering how

468   exposure to a wider set of environmental features across the life course affect health and wellbeing

469   in later life.

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Tables

Table 1: Descriptive statistics of LBC 1936 participants by sample

Characteristic at age 70 [a]	LBC Full Sample at age 70 (n=1,091)	LBC Life grid sample at age 78 [c] n=(593)	LBC Analysis Sample at age 78 (n=281)
Sex			
Women	543 (50)	279 (47)	135 (48)
Age (days)	25,397 ± 303	25,385 ± 306	25,308 ± 252
Family history of Heart Disease			
Yes	672 (62)	377 (63)	167 (59)
NA [b]	7(0)	5 (1)	2 (1)
APOE e4 allele			
Yes	304 (28)	167 (28)	76 (27)
NA	64 (6)	34 (6)	12 (4)
Father's OSC			
Professional-managerial (I/II)	260 (24)	153 (26)	57 (20)
Skilled, partly skilled, unskilled (III/IV/V)	700 (64)	403 (68)	208 (74)
NA	131 (12)	37 (6)	16 (6)
Childhood smoker (≤16 y)			
Yes	226 (21)	103 (17)	54 (19)
NA	-	-	-
Childhood number of people per room	1.38 ± 0.79	1.32 ± 0.75	1.41 ± 0.78
NA	4 (0)	3 (1)	-
Adulthood OSC			
Professional-managerial (I, II)	592 (54)	354 (60)	133 (47)*
Skilled, partly skilled, unskilled (III, IV,V)	478 (44)	231 (39)	146 (52)*
NA	22 (2)	8 (1)	2 (1)
Adulthood Smoker (>16 y)			
Yes	125 (11)	39 (7)	23 (8)
NA	1 (0)	1 (0.2)	-
Alcohol consumption			
Yes	947 (87)	533 (90)	248 (88)
NA	1 (0)	1 (0.2)	-
Adulthood History of Stroke			
Yes	54 (5)	22 (4)	11 (4)
NA	1 (0)	1 (0.2)	-
Adulthood HADS Score	7.68 ± 4.52	7.37 ± 4.41	7.52 ± 4.33
NA	6 (0)	5 (1)	2 (1)
Adulthood BMI	27.78 ± 4.36	27.22 ± 4.15	27.76 ± 4.37
NA	2 (0)	1 (0.2)	-

[a] Number and percentages for categorical data; mean and standard deviation for continuous variables

[b] "NA" is missing

[c] Descriptions of samples as follows: Full sample- participants at age 70; Life grid sample- participants with complete address history at age 78; Analysis sample- Participants had at

least one Edinburgh address during the decade of park measurement (childhood: 1949; adulthood: 1969; later adulthood: 2009).

Chi- square test for independence for categorical data and Welch two sample t-test for continuous data with significance presented as follows: * P<0.05 ** p<0.01

Table 2: Descriptive statistics by Moray House Test Score at ages 11, 70 and 76 for LBC Analysis sample

Characteristic at age 70 [a]	Age standardised MHT Score at age 11	Age standardised MHT Score at age 70	Age standardised MHT Score at age 76
Sex			
Men	99.7 ± 15.0	100.8 ± 14.8	99.2 ± 12.5
Women	102.1 ± 13.7	100.2 ± 13.0	100.0 ± 12.5
APOE E4 allele			
No	101.4 ± 14.7	101.1 ± 13.7	100.7 ± 15.6
Yes	98.9 ± 14.0	98.6 ± 15.0	95.8 ± 13.5
Father's OSC			
Professional-managerial (I, II)	104.2 ± 13.5	103.7 ± 10.4	102.6 ± 12.6
Skilled, partly skilled, unskilled (III, IV,V)	99.6 ± 14.5	99.4 ± 14.9	98.7 ± 14.5
Childhood smoker (≤16 y)			
No	101.6 ± 13.6	101.2 ± 13.2	100.5 ± 13.2
Yes	97.6 ± 17.0	97.3 ± 16.5	95.6 ± 16.9
Childhood number of people per room			
<2	101.6 ± 14.7	101.5 ± 12.9	100.5 ± 13.5
>2	98.3 ± 12.5	96.5 ± 16.9	96.1 ± 15.7
Adulthood OSC			
Professional-managerial (I, II)	-	103.7 ± 15.1	102. 4 ± 23.7
Skilled, partly skilled, unskilled (III, IV,V)	-	97.0 ± 15.1	96.3 ± 15.1
Adulthood Smoker (≥16 y)			
No	-	100.8 ± 13.8	99.9 ± 14.0
Yes	-	98.1 ± 15.0	96.2 ± 14.2
Adulthood Alcohol consumption			
No	-	101.2 ± 11.9	101.3 ± 13.6
Yes	-	100.5 ± 14.2	99.4 ± 14.1
Adulthood Adiposity			
Normal (BMI <30 kg/m^2)	-	100.8 ± 14.0	100.1 ± 13.8
Obese (BMI ≥30 kg/m^2)	-	99.5 ± 13.7	97.8 ± 14.7
Parks availability [b]			
Childhood			
Low (0.34-7.01%)	99.2 ± 15.5	98.1 ± 16.3	98.0 ± 15.6
High (7.01-31.3%)	100.3 ± 13.4	100.8 ± 12.0	98.7 ± 13.2
Adulthood			
Low (0.73-7.74%)	-	98.6 ± 14.2	98.1 ± 13.8
High (7.74-30.7%)	-	100.3 ± 14.4	98.6 ± 15.0
Later Adulthood			
Low (0-7.07%)	-	99.1 ± 14.7	97.9 ± 14.7
High (7.07-40.9%)	-	99.8 ± 14.0	98.8 ± 14.2

[a] Mean and standard deviation presented

[b] Residential parks availability dichotomised by median

Table 3: Association between park life course model and cognitive change from age 11-70 and 70-76

	Outcome [c]									
	MHT Score change 11-70					MHT Score change 70-76				
Park life course model [a]	AIC	P [b]	β	95%CI LL	95%CI UL	AIC	P	β	95%CI LL	95%CI UL
a) Accumulation										
- Strict	728.466	0.711	-0.018	-0.100	0.063	761.454	0.016	-0.010	-0.094	0.075
- Relaxed	731.475	0.628				762.036	0.018			
Childhood			0.024	-0.181	0.230			-0.149	-0.340	0.041
Adulthood			0.060	-0.204	0.323			0.006	-0.293	0.305
Later adulthood			-0.096	-0.265	0.072			0.112	-0.121	0.346
b) Critical Time Period										
- Childhood	728.624	0.692	0.020	-0.172	0.212	759.368	0.034	-0.130	-0.305	0.045
- Adulthood	728.666	0.687	0.002	-0.220	0.224	761.488	0.016	0.014	-0.210	0.238
- Later adulthood	727.689	0.799	-0.074	-0.223	0.074	760.605	0.022	0.089	-0.097	0.275
c) Effect modification										
- Early	732.511	0.453	-0.019	-0.313	0.274	758.135	0.071	0.308*	0.024	0.591
- Later	731.291	0.621	-0.007	-0.210	0.195	763.304	0.010	0.114	-0.124	0.352
No effect	726.619	0.780	-0.037	-0.155	0.080	759.458	0.027	0.017	-0.102	0.137

[a] Per 10% of parks within 1,500 m residential buffer zone

[b] P-value for partial F test in comparison with the saturated model

[c] MHT score change is residualised on previous MHT score and standardised for age

*p<0.05 **p<0.01

Table 4: Association between childhood and adulthood park availability, as modelled by an interaction term, and cognitive change from age 70-76 [a]

Covariate model [c]	Model term [b] Childhood*Adulthood	
	β	CI (95%CI)
Model 1	0.31*	0.02 - 0.59
Model 2	0.26	-0.05 - 0.58
Model 3	0.26	-0.06 - 0.57

[a] MHT score change is residualised on previous MHT score and age

[b] Per 10% of parks within 1,500 m residential buffer zone

[c] Model 1 adjusted for sex; Model 2 additionally adjusted for father's Occupational Social Class (OSC), childhood smoking status and people per room in childhood home; Model 3 additionally adjusted for adulthood OSC, adulthood smoking status and adulthood alcohol consumption status

*p<0.05 **p<0.01

Table 5: Stratified analysis on the association between childhood and adulthood public park availability, as modelled by an interaction term, and cognitive change from age 70-76

| | Model term [b] | |
| | Childhood*Adulthood Parks | |
	β	CI (95%CI)
Effect modifier [a]		
Sex		
Male	0.06	-0.42 – 0.54
Female	0.64**	0.24 – 1.05
APOE e4 allele		
Yes	-0.02	-0.78 – 0.74
No	0.29	-0.05 – 0.63
Adulthood OSC		
Professional-managerial (I, II)	0.02	-0.38 – 0.44
Skilled, partly skilled, unskilled (III, IV,V)	0.66*	0.15 – 1.18

[a] Additionally adjusted for childhood OSC, people per room in childhood home, childhood smoking status, adulthood smoking status andadulthood alcohol consumption status

[b] Per 10% of parks within 1,500 m residential buffer zone

*p<0.05 **p<0.01

Figure

Figure 1: Conceptual model with specifications for life course analysis

<u>**Figure 1**</u>
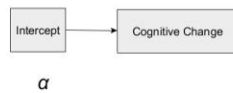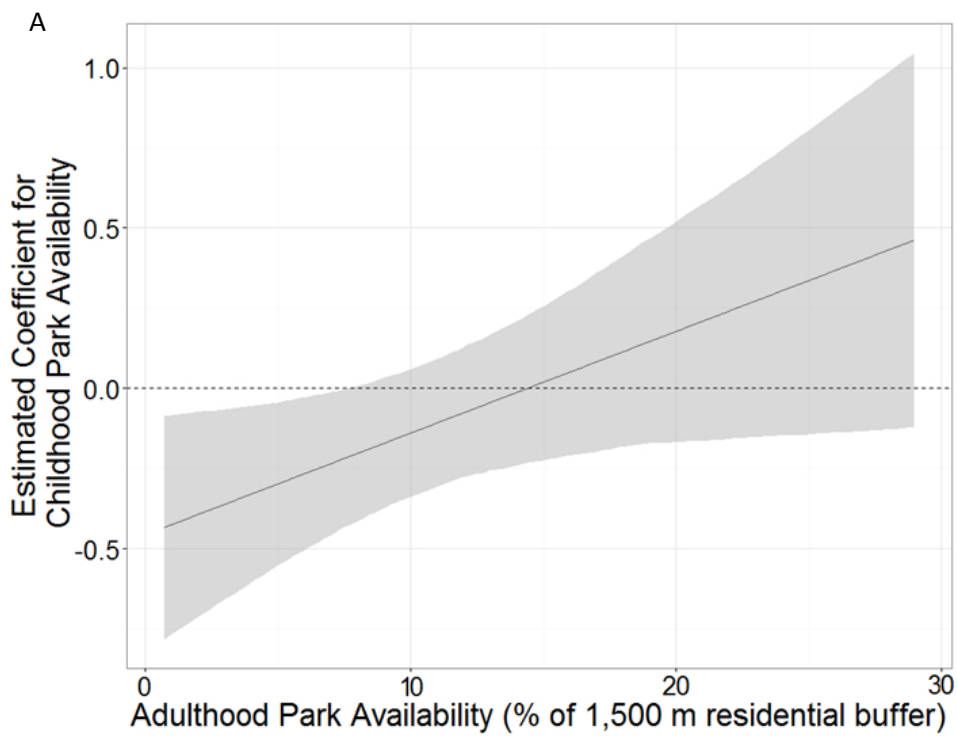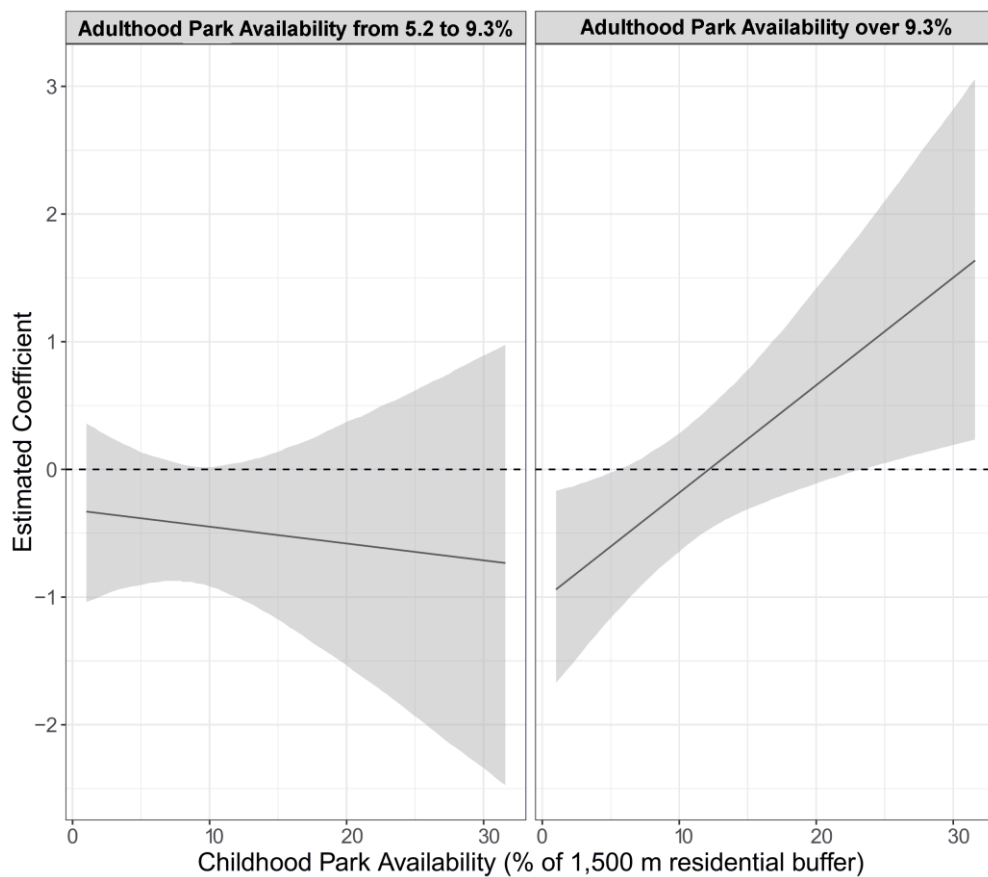

α = intercept

β = coefficient

Figure 2: Marginal effects of park availability, conditional on parks availability from adulthood on cognitive change from age 70-76, presented continuously (A) and in tertiles (B)

Ethical Statement

Ethical approval was attained from The Lothian Research Ethics Committee (LREC/2003/2/29) for wave 1 and the Multi-Centre Research Ethics Committee for Scotland (MREC/01/0/56) and The Scotland Research Ethics Committee (07/MRE00/58) for wave 2, 3 and 4. The MMP project gained ethical approval from the Edinburgh College of Art and University of Edinburgh School of Geosciences.