1	Benefits of Physical Activity Not Affected by Air Pollution: A Prospective Cohort Study
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22	
23	Word count: 4134

#### 24 Abstract

25 Background: Physical activity (PA) is beneficial to human health, whereas long-term exposure to air pollution is harmful. However, their combined effects remain unclear. We 26 27 aimed to estimate the combined (interactive) mortality effects of PA and long-term exposure 28 to fine particulate matter (PM<sub>2.5</sub>) among older adults in Hong Kong. Methods: Participants aged 65 years or older from the Elderly Health Service Cohort (n=66 29 30 820) reported their habitual PA at baseline (1998 to 2001) and were followed up till 31 December 2011. We used a satellite-based spatiotemporal model to estimate PM<sub>2.5</sub> 31 32 concentration at the residential address for each participant. We used Cox proportional 33 hazards regression to assess the interaction between habitual PA and long-term exposure to 34 PM<sub>2.5</sub> on cardiovascular and respiratory mortality. We tested for additive interaction by 35 estimating relative excess risk due to interaction and multiplicative interaction employing p-36 value for the interaction term. 37 **Results:** The death risks were inversely associated with higher volume of PA and were 38 positively associated with long-term exposure to PM2.5. The benefits of PA were more 39 pronounced for participation in traditional Chinese exercise (e.g., Tai Chi) and aerobic 40 exercise (e.g., cycling). We found little evidence of interaction between PA (volume and 41 type) and long-term exposure to PM<sub>2.5</sub> on either additive or multiplicative scales. 42 **Conclusions**: In this cohort of older Chinese adults, PA may decrease the risk of mortality, 43 be it in areas of relatively good or bad air quality. The beneficial mortality effects of habitual 44 PA outweighed the detrimental effects of long-term exposure to air pollution in Hong Kong. 45

46 Keywords: Air pollution; Physical activity; Cohort study; Older

# 47 Key Messages

- 48 Moderate to high volume of physical activity is associated with a lower risk of
  49 cardiovascular and respiratory mortality.
- Traditional Chinese exercise and aerobic exercise are two recommended types of
   physical exercise for older adults.
- The long-term benefits of physical activity (volume and type) did not moderate by
  physical exercise environment of good or bad air quality.
- Physical activity might still be recommended to older adults residing in relatively
  more polluted areas.

### 56 Introduction

Physical inactivity is a significant lifestyle-related risk factor and potentially modifiable.<sup>1</sup>
There is convincing evidence that physical activity reduces risks of non-accidental and
cardiovascular mortality over a wide range of age.<sup>2-5</sup> The global and country-specific physical
activity guidelines recommend people to improve their health through regular physical
activity.<sup>6-8</sup>

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Air pollution is recognized as the world's largest single environmental risk factor,<sup>9</sup> associated
with an elevated risk of cardiopulmonary diseases.<sup>10, 11</sup> An estimated 4.2 million deaths
globally are attributable to ambient air pollution each year.<sup>12</sup> Due to an increased ventilation
rate, the uptake of air pollution during physical activity increases considerably, potentially
intensifying the detrimental health effects of air pollution.

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It is of significant public health interest to examine the risk-benefit relationship between health benefits of physical activity and the intensified harmful effects of air pollution during physical activity. Emerging evidence showed that the benefits of physical activity were lost after acute exposure to higher level of air pollution (temporal changes in air pollution).<sup>13-15</sup> However, evidence on the modification effects of long-term exposure to air pollution (levels of air pollution at where people usually perform physical activity) on the health benefits of physical activity is scarce.

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To our best knowledge, we totally identified six related studies, including the Danish Diet,
Cancer, and Health Cohort,<sup>16-18</sup> the Swiss Cohort Study on Air Pollution and Lung and Heart
Diseases,<sup>19</sup> a cohort in Taiwan,<sup>20</sup> and a cohort in southern California.<sup>21</sup> These studies were all
conducted in countries with relatively good air quality, which may limit the power to assess

81 the modification effects of air pollution on the health benefits of physical activity. No study82 has been conducted in areas with relatively high air pollution levels.

84	Hong Kong is one of the world's most populous territories located in the Pearl River Delta
85	areas, one of the most polluted areas in China. The annual mean concentration of air pollution
86	in Hong Kong greatly exceeds the World Health Organization (WHO) air quality
87	guidelines. <sup>22</sup> We sought to evaluate the combined mortality effects of habitual physical
88	activity and long-term exposure to air pollution defined by annual concentration of fine
89	particulate matter (PM <sub>2.5</sub> ) among ~70 000 older adults in Hong Kong. Findings of this study
90	should provide evidence on physical exercises recommendation and air pollution control.
91	
92	Methods
93	Study population
94	The Chinese Elderly Health Service Cohort is a prospective cohort, into which all Hong
95	Kong residents aged 65 years and older were eligible to enrol. From 1998 to 2001, 66 820
96	elders, about 9% of Hong Kong older population, enrolled into the 18 Elderly Health Centres
97	of the Department of Health, one in each of the 18 districts, and were followed up till
98	December 2011. Face-to-face interview for each participant was carried out by registered
99	nurses and doctors using a standardized and structured questionnaire. <sup>23, 24</sup> The collected
100	information included demographic characteristics (e.g., age and sex), socioeconomic status
101	(e.g., education attainment and personal monthly expenditure), lifestyle (e.g., smoking status
102	and alcohol consumption), body mass index (BMI), and pre-existing chronic conditions (e.g.,
103	hypertension and cerebrovascular accident). Details of cohort profile and data collection have
104	been published elsewhere. <sup>23, 24</sup> Ethics approval was obtained from the Ethics Committee of

the Faculty of Medicine, The University of Hong Kong and of the Department of Health ofHong Kong.

107

## **108 Definition of physical activity**

109 Physical activity was collected by structured interview using questions regarding types of physical activity, the frequency of physical activity per week, and duration per session. 110 111 Participants were asked to report their most frequently performed type of physical activity, 112 which included walking slowly (level ground), stretching exercise, traditional Chinese 113 exercise (Tai Chi, Pak Tuen Kam, and Luk Tung Kuen), aerobic exercise (jogging, cycling, 114 swimming, walking uphill, and playing ball games), other types not mentioned above (<3%), 115 and no physical exercise. The frequency of physical exercise was specified as 0 to 7 or  $\geq 8$ 116 times per week, and duration for each session was classified as none (no physical exercise), 117 <30 minutes, and  $\geq30$  minutes. We used a standard metabolic equivalent of task (MET) value 118 to assign the intensity of each physical exercise type according to the Ainsworth 119 compendium: < 1.0 (never), 2.0 (walking slowly), 2.5 (stretching exercises), 4.0 (traditional Chinese exercise), and 6.0 (aerobic exercise).<sup>25</sup> We then quantified physical activity volume 120 of each participant by calculating hours of MET per week (MET-h/wk) based on the reported 121 type, frequency, and duration of physical activity. We finally categorized MET-h/wk as <1.0, 122 1.0-20.9, and  $\geq$ 21.0.<sup>26</sup> These methods to define physical activity have been used in earlier 123 studies using this cohort to reveal the beneficial effects of physical activity.<sup>26, 27</sup> 124

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#### 126 **Prospective follow-up**

127 Participants were followed from the date of recruitment to date of death or 31 December

128 2011, whichever came first. We used a common unique identifier to link the cohort with the

129 death registration in Department of Health, which covered all deaths in Hong Kong.<sup>28</sup> We

130 coded deaths according to International Classification of Diseases, 10<sup>th</sup> revision (ICD-10):

131 cardiovascular cause (I00-I99) and respiratory disease (J00-J47, J80-J99).

132

## **133** Air pollution assessment

We selected PM<sub>2.5</sub> as a proxy for air pollution exposure since PM<sub>2.5</sub> is the most commonly 134 used proxy indicator of air pollution.<sup>29</sup> We used a satellite-based spatiotemporal model to 135 estimate the annual concentration of PM2.5 at the residential address of each participant 136 between 1998 and 2011, as previously described.<sup>30, 31</sup> Briefly, Aerosol Optical Depth (AOD), 137 138 an indicator of PM<sub>2.5</sub> concentrations in the troposphere, was retrieved from the remote sensing data of the two National Aeronautics and Space Administration (NASA) Earth 139 Observing System satellites.<sup>32</sup> It was initially retrieved at a  $10 \times 10$  km resolution and then 140 141 refined into 1×1 km resolution by modifying the Moderate Resolution Imaging Spectroradiometer (MODIS) algorithm.<sup>33</sup> The annual Surface Extinction Coefficients (SEC) 142 from AOD were regressed on the yearly PM<sub>2.5</sub> concentration measured from the ground-level 143 144 air monitoring stations using grid cells with both SEC and  $PM_{2.5}$  measurements. We then used this calibration to estimate yearly PM<sub>2.5</sub> concentrations at the geocoded residential 145 addresses for all participants. The estimated PM<sub>2.5</sub> has been validated and was used to assess 146 the associations of long-term exposure to  $PM_{2.5}$  with morbidity<sup>34, 35</sup> and mortality<sup>30</sup> in this 147 148 cohort.

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We used the baseline concentration of PM<sub>2.5</sub> at the residential address of each participant as a
proxy for long-term air pollution exposure (Figure 1)<sup>30, 34-37</sup> given the temporal trend of
PM<sub>2.5</sub> concentrations change in parallel spatially in Hong Kong (Supplementary Figure S1).
In sensitivity analyses we also used the average concentrations of PM<sub>2.5</sub> over the follow-up to
define long-term air pollution exposure.

155

## 156 Covariates

Potential confounders were selected according to the literature.<sup>30, 34, 35</sup> We controlled for 157 158 individual-level confounders, including age (strata variable, continuous), sex, BMI (kg/m<sup>2</sup>, a 159 natural spline with 3 degrees of freedom), smoking status, education attainment, personal monthly expenditure, medication taken, and pre-existing chronic conditions (hypertension, 160 161 cerebrovascular accident, heart disease, and chronic obstructive pulmonary disease). Tertiary 162 Planning Unit (TPU) is the smallest administrative area unit used in the Hong Kong 163 population census report (Supplementary Figure S2), we also controlled for three TPU-164 level covariates including % of population aged  $\geq 65$  years, % with tertiary education, and % with income  $\geq$  \$1923 USD per month. We additionally adjusted for smoking rate among 165 residents over 15 years old at the district-level. 166 167 **Statistical analyses** 168 169 Cox proportional hazards regression with follow-up time as the underlying time scale was 170 used to estimate the associations of physical activity (volume and type) and long-term exposure to PM<sub>2.5</sub> with cardiovascular and respiratory mortality. To allow for possible non-171 proportionality of hazard, age in year was treated as a stratification variable. We estimated 172

hazard ratio (HR) adjusted for individual-, TPU-, and district-level confounders as mentionedabove.

175

To investigate whether the beneficial effects of physical activity outweigh the detrimental
effects of air pollution, we examined the combined effects of physical activity and air
pollution and tested their interaction on both additive and multiplicative scales.

180 To assess the additive interaction, we first classified participants into those resided in low (lower 50<sup>th</sup> percentile of exposure range:  $<35.3\mu g/m^3$ ) and high PM<sub>2.5</sub> areas (upper 50<sup>th</sup> 181 percentile of exposure range:  $\geq 35.3 \mu g/m^3$ ). Together with physical activity volume (<1.0, 182 183 1.0-20.9, and  $\geq$ 21.0 MET-h/wk), we then created a new variable with six categories representing six combinations of physical activity volume and PM<sub>2.5</sub> exposure. We also 184 created a new variable with ten categories representing ten combinations of exercise types 185 186 (no exercise, walking slowly, stretching exercise, traditional Chinese exercise, and aerobic exercise) and PM<sub>2.5</sub> exposure. 187

188

To test the additive interaction, we calculated the relative excess risk due to interaction 189 (RERI) and corresponding 95% confidence interval.<sup>38</sup> When calculating RERI, it has been 190 recommended to recode preventive factors to risk factors.<sup>39</sup> In the present study, we recoded 191 192 physical activity as physical inactivity, and set the highest volume or intensity of physical activity (≥21.0 MET-h/wk or aerobic exercise) and low air pollution as the joint reference 193 194 group. A RERI of 0 indicates no additive interaction (i.e., the combined excess risk 195 calculated as HR-1 is exactly the sum of their individual excess risks), a RERI of more than 0 196 indicates positive interaction (i.e., the combined excess risk is more than the sum of their 197 individual excess risks), and a RERI of less than 0 means negative interaction, or that the 198 combined excess risk is less than the sum of their individual excess risks. A positive RERI 199 value in the present study would indicate that air pollution diminishes the health benefits of physical exercise. 200

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We further evaluated the multiplicative interaction and tested the multiplicative interaction by
adding a product term between PM<sub>2.5</sub> (low and high) and volume (<1.0, 1.0-20.9, and ≥21.0</li>
MET-h/wk) or types (no exercise, walking slowly, stretching exercise, traditional Chinese

exercise, and aerobic exercise) of physical activity. We used likelihood tests to evaluate the product term by comparing the model with and without the interaction term. p<0.05 of the product term indicates a multiplicative interaction.

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In the secondary analyses, we conducted stratified analysis to examine whether the additive and multiplicative interaction between physical activity and long-term exposure to  $PM_{2.5}$ varied by sex.

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213 We performed a series of sensitivity analyses to confirm the robustness of our findings. First, 214 to check the suitability of baseline PM<sub>2.5</sub>, we used the average concentrations of PM<sub>2.5</sub> over 215 the follow-up to define long-term exposure to air pollution. Second, to exclude the possibility 216 of reverse causality, we excluded participants who died within the first year after enrolment. 217 Participants who had severe diseases at baseline were prone to be physically inactive. Third, 218 to reduce air pollution exposure misclassification due to participants' movement, we did 219 analyses by excluding participants who moved during the follow-up period. Fourth, to be 220 aware of the influence of changing physical activity habits, we stratified participants by 221 baseline pre-existing chronic conditions. Participants with pre-existing diseases are more 222 likely to change their physical activity habits due to their deteriorating health. Fifth, we 223 varied cut-offs defined by percentiles of PM<sub>2.5</sub> to dichotomize air pollution and refitted the 224 regression models to test the multiplicative interactions. All analyses were two-sided and p-225 value < 0.05 was considered as statistically significant. We conducted all analyses in R 226 software (version 3.4.3) with "survival" package (version 2.44-1.1) for survival analysis. 227

228 **Results** 

229	A total of 66 820 older adults were enrolled in the initial study cohort. After excluding 5352
230	(8.0%) participants due to problems in geocoding or satellite data, 1259 (1.9%) with missing
231	covariates, and 1566 (2.3%) reported types of physical activity that were listed as others in
232	the questionnaire, a total of 58 643 (87.8%) participants were included in the final analyses
233	(Figure 1). During the follow-up, there were 4600 deaths from cardiovascular disease and
234	3106 from respiratory disease (Table 1).
235	
236	[Figure 1 here]
237	
238	The mean age of the 58 643 participants at baseline was 71.9 years old, and approximately
239	65.7% of the participants were females. Only 4.4% of the participants were current smokers,
240	about one half received primary education or above (54.4%) or took medications regularly
241	(52.9%), and more than one third (35.9%) had hypertension ( <b>Table 1</b> ).
242	
243	Most participants (80.9%) performed low to moderate volume of physical activity (1.0-20.9
244	MET-h/wk). For types of physical exercise, about one third of participants (38.1%) chose
245	stretching exercise, followed by walking slowly (18.4%), traditional Chinese exercise
246	(17.8%), and aerobic exercise (10.0%). We found males were more likely to participate in
247	activities of walking slowly or aerobic exercise, whereas females were more likely to
248	participate in stretching exercise or traditional Chinese exercise (Table 1).
249	
250	[Table 1 here]
251	
252	After adjusted for individual-, TPU-, and district-level confounders, the HR per 10 $\mu\text{g}/\text{m}^3$
253	increase in $PM_{2.5}$ concentration was 1.19 (95% CI: 1.05, 1.35) for cardiovascular and 1.02

(95% CI: 0.87, 1.19) for respiratory mortality. We found elders resided in high PM<sub>2.5</sub> areas
were positively associated with a higher risk of cardiovascular mortality compared with
participants resided in low PM<sub>2.5</sub> areas in the fully adjusted models (**Table 2**). The elevated
risk of mortality associated with PM<sub>2.5</sub> was also observed across gender (**Supplementary Figure S3**).

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# [Table 2 here]

261

262 Participation in higher volume of physical activity was associated with a lower risk of 263 mortality (Table 2). For example, compared with low volume of physical activity (<1.0 264 MET-h/wk), the HR of cardiovascular mortality was 0.91 (95% CI: 0.88, 0.95) and 0.75 265 (95% CI: 0.68, 0.83) for low to moderate (1.0-20.9 MET-h/wk) and high (≥21 MET-h/wk) 266 volume of physical activity, respectively. We found the beneficial effects of physical activity 267 were more pronounced for aerobic exercise such as jogging and cycling and traditional 268 Chinese exercises such as Tai Chi. We also found suggestive benefits of walking and 269 stretching exercises, although the association did not reach statistical significance. The 270 decreased mortality risk associated with physical activity was more pronounced among 271 females than males (Supplementary Figure S3).

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**Table 3** shows the combined effects of physical activity volume and long-term exposure to PM<sub>2.5</sub> using the high volume of physical activity ( $\geq$ 21.0 MET-h/wk)-low PM<sub>2.5</sub> (<35.3 µg/m<sup>3</sup>) participants as the reference. The HR of cardiovascular disease for performing low volume of physical activity (<1.0 MET-h/wk) was 1.46 (95% CI: 1.11, 1.92) in low PM<sub>2.5</sub> areas (<35.3µg/m<sup>3</sup>) and 1.53 (95% CI: 1.17, 2.00) in high PM<sub>2.5</sub> areas ( $\geq$ 35.3 µg/m<sup>3</sup>), and the corresponding HR for respiratory disease was 1.31 (95% CI: 0.95, 1.82) and 1.50 (95% CI:

279	1.09, 2.06), respectively. We found little evidence of interaction on either additive or
280	multiplicative scales in overall analysis (Table 3) and gender-specific subgroup analysis
281	(Supplementary Table S1).
282	
283	[Table 3 here]
284	
285	Table 4 represents the combined mortality effects of physical activity types and long-term
286	exposure to $PM_{2.5}$ using aerobic exercise and low air pollution as the joint reference group.
287	Lower intensity exercise was associated with a higher risk of mortality irrespective of high or
288	low $PM_{2.5}$ concentrations. For example, compared with the joint reference group, the
289	cardiovascular mortality risk for no exercise was 1.53 (95% CI: 1.27, 1.84) in low $PM_{2.5}$
290	areas and 1.61 (95% CI: 1.34, 1.92) in high PM <sub>2.5</sub> areas. We found little evidence of
291	interaction between physical activity types (no exercise, stretching exercise, traditional
292	Chinese exercise, and aerobic exercise) and long-term $PM_{2.5}$ exposure (low and high) on
293	either additive or multiplicative scales, but we found a significant positive RERI [0.301 (95%
294	CI: 0.024, 0.578)] for walking slowly for cardiovascular mortality (Table 4). We also found
295	little evidence of interaction in the subgroup analysis for males or females (Supplementary
296	Table S2).
297	
298	[Table 4 here]
299	
300	Sensitivity analyses excluding participants who died within the first year of follow-up or who
301	moved during the follow-up did not materially change our findings (Supplementary Table
302	$\mathbf{S3}$ ). When stratified by pre-existing diseases, participants with and without pre-existing
303	conditions showed similar findings of little evidence of interaction (Supplementary Table

S4). Using the average annual PM<sub>2.5</sub> concentration over the follow-up to define long-term
exposure to air pollution (Supplementary Tables S5 & S6) or varying cut-off selected by
percentile of PM<sub>2.5</sub> to define low and high air pollution areas did not change our findings of
little evidence of interaction between physical activity (volume and type) and long-term
exposure to PM<sub>2.5</sub> (Supplementary Figure S4).

309

## 310 Discussion

In this large prospective elderly cohort, habitual physical activity was associated with a lower 311 312 risk of cardiovascular and respiratory mortality. The beneficial effects of habitual physical 313 activity were more pronounced for higher volume of physical activity or higher intensity 314 exercise like traditional Chinese exercise or aerobic exercise. Long-term exposure to PM<sub>2.5</sub> 315 was associated with a higher risk of mortality. We found little evidence of interaction 316 between habitual physical activity (volume and type) and long-term exposure to PM<sub>2.5</sub> in 317 either additive or multiplicative models, which suggest that the benefits of habitual physical 318 activity outweigh the amplified detrimental effects of air pollution among older adults in 319 Hong Kong.

320

Our findings of decreased mortality risks associated with physical activity are consistently with numerous cohort studies.<sup>5, 40</sup> A recent systematic review and meta-analysis summarised 323 33 cohort studies with a total of 883 372 participants and reported that physical exercise was associated with a 35% (95% CI: 30%, 40%) lower risk of cardiovascular mortality and 33% (95% CI: 28%, 37%) lower risk of all-cause mortality.<sup>5</sup> A recent multi-country cohort study with ~130 000 participants from seventeen low-, middle-, and high-income countries found the protective effects of physical activity were consistently observed among countries with

different economic levels.<sup>41</sup> We found health benefits of physical activity were more
pronounced among females than males, which were also consistent with previous studies.<sup>5,41</sup>

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We found long-term exposure to  $PM_{2.5}$  was associated with a higher risk of cardiovascular mortality, which corroborates the evidence of a positive association between long-term exposure to  $PM_{2.5}$  and mortality.<sup>42, 43</sup> We found that each 10 µg/m<sup>3</sup> increase in  $PM_{2.5}$  was associated with an HR of 1.19 (95% CI: 1.05, 1.35) for cardiovascular mortality, which was similar with most previous studies.<sup>44, 45</sup>

336

A few studies have investigated the interaction between acute or intermediary exposure to air 337 pollution and physical activity, but findings are mixed.<sup>13-15, 46-50</sup> Some studies reported that 338 the health benefits from physical exercises were lost in high air pollution days.<sup>13-15</sup> For 339 340 example, lung function of asthma patients decreased after walking on a polluted street in London for only two hours.<sup>14</sup> A randomized crossover study among 135 participants in UK 341 342 also found that acute exposure to traffic related air pollutants diminished the beneficial 343 cardiopulmonary effects of walking for participants with or without chronic cardiopulmonary diseases.<sup>13</sup> On the contrary, a few other studies found no evidence on cancellation of physical 344 activity benefits by acute or intermediary air pollution exposure.<sup>48-50</sup> For example, a panel 345 346 study of 122 healthy adults in three European cities (Antwerp, Barcelona, and London) 347 reported no evidence of modification effects of short-term or intermediary exposure to black carbon on the benefits of physical activity on blood pressure<sup>49</sup> and subclinical cardiovascular 348 disease (heart rate variability and retinal vessel diameters).<sup>48</sup> Although acute effects of air 349 350 pollution studies provide a useful context, our findings of the cumulative interaction between physical activity and long-term exposure to air pollution are not directly comparable with the 351

352 short-term or intermediary exposure studies that assess the acute interplay between physical353 activity and air pollution.

354

355 Our findings of the combined relationships between habitual physical activity and long-term 356 exposure to air pollution are novel. To our knowledge, we only identified six related epidemiologic studies,<sup>16-21</sup> and these studies were all conducted in relatively good air quality 357 areas. Consistent with the mortality study,<sup>17</sup> we also found little evidence of interaction 358 359 between habitual physical activity and long-term exposure to air pollution. Our findings were 360 also consistent with a health impact modelling study, which tested the risk-benefit balance 361 between physical activity and background PM<sub>2.5</sub> concentration, and they found that the health 362 benefits of physical activity generally outweighed the harmful effects of air pollution except in the most extreme air pollution scenario.<sup>51</sup> We found some evidence that the cardiovascular 363 364 benefits of walking were reduced in more polluted areas, which was consistent with the randomized crossover study.<sup>13</sup> Although the exact reason to explain the general protective 365 366 effects of physical activity on mortality regardless of different PM2.5 concentrations have not 367 been elucidated, one potential hypothesis is that the additional inhaled air pollutants due to physical activity only account for a small fraction of the total inhaled air pollutants.<sup>52</sup> It is 368 also possible that the long-term health benefits of habitual physical activity may reverse the 369 370 acute adverse mortality effects associated with exposure to higher level of air pollution during physical activity.<sup>17</sup> 371

372

Our findings should be interpreted with caution. First, we did not collect information on
whether participants performed physical activity indoors or outdoors. However, a territorywide survey among the elderly in Hong Kong found that up to 85% of their physical activity
were performed outdoors.<sup>53</sup> Second, we assessed habits of physical activity at baseline.

377 Changing physical activity habits during the follow-up might influence our results. However, 378 we conducted a series of sensitivity analyses by excluding participants who died within the 379 first year of follow-up or stratifying by pre-existing chronic conditions. Results of these 380 sensitivity analyses suggests that changing habits of physical activity during the follow-up 381 would not influence our findings significantly. Third, we used SEC from AOD within 1 km of ground level to predict concentrations of PM<sub>2.5</sub>. Due to the high population density in 382 383 Hong Kong, PM<sub>2.5</sub> maps of higher resolution will be needed in future studies to better differentiate the PM<sub>2.5</sub> exposure among participants. Fourth, we used PM<sub>2.5</sub> concentration at 384 385 residential address as a proxy of long-term air pollution exposure encountered during 386 physical activity. This should work well for this cohort of older participants, as it is reasonable to assume that most of them perform physical activity near their residences.<sup>54</sup> Last 387 388 but not least, our study is based on a cohort of Chinese older adults (mean age of ~72 years at 389 baseline). Results of this study may not be generalizable to younger populations or 390 populations in other countries.

391

392 On the other hand, our study is one of the few studies to evaluate the combined mortality 393 effects of habitual physical activity (volume and type) and long-term exposure to air pollution. Our findings add to the scarce evidence of the risk-benefit relationship between 394 395 long-term health benefits of habitual physical activity and air pollution. Furthermore, our 396 analyses were conducted in Hong Kong (annual mean concentration of PM2.5 among study participants was  $\sim 35 \mu g/m^3$ ), a top 20% most polluted city globally, where levels of air 397 pollution greatly exceed the WHO air quality guidelines  $(10\mu g/m^3)$ . Thus, findings of this 398 399 study should provide a more comprehensive picture of the combined effects of habitual 400 physical activity and long-term air pollution exposure.

401

403	In this cohort of Chinese older adults, we found little evidence of the modification effects of
404	long-term exposure to air pollution on the benefits of physical activity on mortality. The
405	beneficial effects of habitual physical activity outweigh the mortality risk associated with air
406	pollution. Findings of this study may support current guidelines on promoting physical
407	activity for diseases prevention even for people residing in relatively more polluted areas.
408	Additional studies in higher air pollution areas or among younger population are still needed
409	to confirm or refute these findings.
410	
411	Declaration of interests
412	None.
413	
414	Funding: None.
415	
416	Acknowledgments
417	The authors would like to thank the Elderly Health Service of the Department of Health for
418	providing the cohort data and the Environmental Protection Department for providing the air
419	pollution data.

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562	Figure legends
563	
564	Figure 1. Spatial distribution of air pollution exposure and participants of Elderly Health
565	Service Cohort in Hong Kong.
566	
567	The left panel shows varying levels of surface extinction coefficients (SEC) indicating the
568	concentrations of fine particulate matter (PM <sub>2.5</sub> ) at baseline. The right panel shows the spatial
569	distribution of participants of Elderly Health Service Cohort (n=58 643)