

# Association between housing type and accelerated biological aging in different sexes: moderating effects of health behaviors

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## ABSTRACT

**Introduction:** Despite associated with multiple geriatric disorders, whether housing type, an indicator of socioeconomic status (SES) and environmental factors, is associated with accelerated biological aging is unknown. Furthermore, although individuals with low-SES have higher body mass index (BMI) and are more likely to smoke, whether BMI and smoking status moderate the association between SES and biological aging is unclear. We examined these questions in urbanized low-SES older community-dwelling adults.

**Methods:** First, we analyzed complete blood count data using the cox proportional hazards model and derived measures for biological age (BA) and biological age acceleration (BAA, the higher the more accelerated aging) ( $N = 376$ ). Subsequently, BAA was regressed on housing type, controlling for covariates, including four other SES indicators. Interaction terms between housing type and BMI/smoking status were separately added to examine their moderating effects. Total sample and sex-stratified analyses were performed.

**Results:** There were significant differences between men and women in housing type and BAA. Compared to residents in  $\geq 3$  room public or private housing, older adults resided in 1-2 room public housing had a higher BAA. Furthermore, BMI attenuated the association between housing type and BAA. In sex-stratified analyses, the main and interaction effects were only significant in women. In men, smoking status instead aggravated the association between housing type and BAA.

**Conclusion:** Controlling for other SES indicators, housing type is an independent socio-environmental determinant of BA and BAA in a low-SES urbanized population. There were also sex differences in the moderating effects of health behaviors on biological aging.

## INTRODUCTION

Socioeconomic status (SES) is a well-validated social determinant of health. In particular, low SES in late life represents the accumulation of lifetime stressors, resulted from the challenges and adversities experienced throughout one's life course. Low SES is thus associated with a wide range of adverse health outcomes, including increased inflammatory and metabolic biomarkers, age-related morbidities (including stroke, chronic kidney disease, coronary heart disease, and dementia [1–4]), increased hospital re-admissions [5–8], and increased healthcare utilization [8, 9]. Specifically, Singaporeans belonging to the lower SES strata had higher healthcare utilizations [9]. Due to the various barriers, they faced, they preferred alternative medicine or self-medication to manage their health issues [10], which may exacerbate their existing conditions.

Most SES studies have focused on examining the canonical SES indicators, including educational level [11–14], income [9, 15], financial adequacy [16], and occupational class [17]. However, another SES indicator, housing type, has been understudied. Apart from indicating SES, housing type is also an indicator of environmental factors. We have previously demonstrated that environmental factors are critical social determinants of health and impact aging biomarkers and social measures [18–22]. Adopting the biopsychosocial-ecological model, specifically the Transdisciplinary Neighborhood Health Framework [23], in the present study, housing type is thus being referred to as the socio-environmental indicator or determinant of health. Housing type may predominantly determine one's home environment and housing quality, including the characteristics of one's indoor built environment and the surrounding areas' environments. Another closely-relevant model, the social-determinant framework further emphasizes that amongst other determinants, improving housing and living conditions are central to improving the health of urban populations [24], which could reduce morbidity, mortality, and disparities in health [24]. Conversely, low housing quality in urban neighbourhoods has previously been linked to a variety of adverse health outcomes [25–29]. Thus, individuals living in deprived areas and public rental housing have been shown to have a higher mortality rate [9, 30–32]. Relocation to temporary housing after a disaster has also been shown to suffer from negative health effects due to health behavior [33]. In Singapore, housing policy had been employed as a social engineering tool during the nation-building period to prevent the formation of ghettos [34]. Despite seemingly homogenous, emerging evidence showed that Singaporeans staying in 1–2 room public housing

entailed higher healthcare utilization and had higher risks of hospital re-admission [9, 35].

These multiple lines of evidence underscore the importance of examining housing type as a key socio-environmental determinant, especially in health disparity research. However, there is a significant dearth of research on the association between housing type and health outcomes in vulnerable older adults [36]. The environmental characteristics of low-SES housing, such as the lack of recreational areas in these communities, may discourage involvement in physical activity, contributing to increased cases with obesity [16, 26]. In response to the psychosocial stressors, residents in low-SES housing could adopt unhealthy coping behaviors, such as smoking [16]. The lack of access to healthy foods in these neighbourhoods could also be another moderating factor of low-SES housing to adverse health outcomes [26]. Hence, the cumulative health disadvantage conferred by low housing type on older adults could potentially be ameliorated by adopting healthy behaviors [37].

Singapore is an affluent country, with a gross domestic product of approximately S\$73,000 and a multi-ethnic population of 5.6 million residents [9]. Amongst others, home ownership is a key local indicator of SES in Singapore [9, 38]. There are two general types of housing in Singapore [34, 38]; Heavily subsidized public housing is available for citizens and permanent residents to purchase from the Housing Development Board (HDB), a government agency, on a 99-year lease, with approximately 90% of Singapore residents residing in these estates. The other 10%, who are mostly residents earning higher income/belonging to the higher SES status, reside in private housing that is landed property. Apart from the public/private housing division, it is noteworthy that in Singapore, residents staying in 1–2 room public housing were considered as staying in low-SES public housing [9, 35]. Specifically, the 1–2 room apartments in Singapore are heavily subsidized by the Singaporean government's HDB to cater to the poor and needy citizens with no other housing options, i.e. households with a gross monthly income of below S\$2,000 (~USD1589) for purchase or below S\$1,500 (~1191) for rent [35]. Those residing in 1–2 room housing thus have significantly higher proportions of adverse health outcomes. Specifically, they are significantly older (based on chronological age), with a lower proportion being employed and thus significantly lower income, and have significantly worse health outcomes, including higher risks of frequent hospital admissions, readmission within 15 and 30 days, emergency department attendances, higher rates of chronic diseases, and a lower self-rated health [9, 35]. However, although low-SES housing has been demonstrated as an independent

predictor of adverse health outcomes in Singapore, those studies were limited by self-reporting nature and required linkages to hospital medical records for retrieving relevant data. The former presents the issue of subjectivity and self-recall bias, while the latter poses the issue of feasibility and data confidentiality. Furthermore, whether housing type independently acts as a risk factor while accounting for other SES indicators has not been examined. Even if positive, whether housing type could exert a biological weathering effect, in which stressors cause wear and tear of the body [16, 39, 40], and thus resulting in accelerated biological aging in older adults residing in 1–2 room public housing remains unknown. Thus, examining biological aging in this specific population may resolve these issues, while present an easy-to-measure and -monitor objective indicator to inform housing and public health policies.

The Geroscience Hypothesis proposes that biological aging is a shared and significant risk factor for developing many geriatric syndromes [41, 42]. Leukocyte telomere length (LTL) and allostatic load (AL) are two examples of canonical measures of biological aging [39, 43]. Recently, several DNA-methylation-based biological age (BA) measures have been proposed, including the Horvath's Clock [44], Hannum's Clock [45], and Levine's DNAm PhenoAge [46]. However, there have been several limitations to using some of these measures. Most prominently, many of these measures pre-screened candidate biomarkers against chronological age (CA) as their first step in deriving the respective BAs. Despite seeing the value in performing this procedure, the variability in aging intended to be captured by BA have been minimized [47, 48]. Furthermore, due to the complexity and costs involved in examining DNA methylation markers, the use of these BAs at the population level could be limited. Hence, a novel BA measure, utilizing mortality as the sole external criterion has been proposed recently [46, 48]. In this study, we employed the same approach and proposed a BA as a composite of complete blood count (CBC) and selected standard blood biochemistry parameters, a panel of easily accessible and examined clinical biomarkers. We have previously validated this BA model and the derived biological age acceleration (BAA) measure by showing their significant associations with multiple physical and mental health measures [49, 50]. Furthermore, we showed the BA was a dynamic indicator of organism health and was thus modifiable by health behaviors, including smoking status [49, 50].

Despite a small number of studies associating low-SES housing with adverse phenotypic outcomes, the underlying biological mechanisms are yet to be elucidated. We thus hypothesized that one of the mechanisms through which SES indicators and social-

environmental factors, including housing type, impact adverse health outcome could be through the biological weathering effect on BA, resulting in accelerated biological aging. However, inconsistent findings were reported on the associations between other indicators of SES and leukocyte telomere length (LTL), including studies not finding a significant association between SES and LTL [51–53]. On the other hand, several studies elucidated significant associations between SES and DNA-methylation-derived BA. For example, Simons et al. (2016) demonstrated that low-income status was robustly associated with Hannum's BA [16]. Despite the plethora of studies on other indicators, whether housing type is significantly associated with BA has been scarcely investigated. To our knowledge, only one study showed that homeownership was associated with a lower LTL-measured BA [51]. However, it is worth noting that not all older adults who resided in low-SES housing would experience accelerated biological aging. The exact aggravating factors further contributing to this susceptibility are unclear. Given that individuals with low-SES often have higher body mass index (BMI) and are more likely to smoke, it is thus unclear as to whether BMI and smoking status alleviate or aggravate the association between low-SES housing and BA and BAA. Motivated by a previous study [13], understanding the associations between housing type and BA, focusing on the moderating effects of health behaviors, may highlight intervention targets and approaches to ameliorating health disparities experienced by older adults residing in low-SES housing.

Aiming to address the gaps in knowledge, we conducted a study with a sample population comprising predominantly low-SES older community-dwelling Singaporean adults. This study has three aims:

1. The main aim of this study was to determine if there were significant associations between housing type and BA/BAA (indicating accelerated or decelerated aging);
2. We examined if BMI and smoking status, both as indicators of health behaviors, moderated the hypothesized associations between housing type and BA/BAA;
3. We explored the proposed differential associations and moderating effects in two subgroups, i.e. men and women.

## RESULTS

### Demographics and characteristics of BA

Table 1 summarizes the baseline characteristics of the 376 study participants. In the total sample, the mean CA

**Table 1. Demographic characteristics and biological age of the participants.**

<b>Demographic and biological age variables</b>	<b>Men (N = 127, 33.8%) Mean ± SD or n (%)</b>	<b>Women (N = 249, 66.2%) Mean ± SD or n (%)</b>	<b>Total (N = 376, 100%) Mean ± SD or n (%)</b>	<b>p-values</b>
<b>Housing type</b>				
1–2-room public housing	108 (85)	156 (62.7)	264 (70.2)	<b>&lt;0.001***</b>
3-room public housing and above or private housing	19 (15)	93 (37.3)	112 (29.8)	
<b>Education level</b>				
No formal education	56 (44.1)	151 (60.6)	207 (55.1)	<b>0.003**</b>
Primary education & above	71 (55.9)	98 (39.4)	169 (44.9)	
<b>Longest occupational role</b>				
Clerical level	25 (19.7)	12 (4.8)	37 (9.8)	<b>&lt;0.001***</b>
Executive level	102 (80.3)	237 (95.2)	339 (90.2)	
<b>Monthly income</b>				
< SGD 500	92 (76)	171 (74)	263 (74.7)	0.701
≥ SGD 500	29 (24)	60 (26)	89 (25.3)	
<b>Perceived income adequacy</b>				
Having difficulty	58 (46.4)	87 (35.1)	145 (38.9)	<b>0.043*</b>
Not much difficulty	67 (53.6)	161 (64.9)	228 (61.1)	
Biological age	0.451 ± 0.573	0.276 ± 0.650	0.335 ± 0.630	<b>0.008**</b>
Biological age acceleration	0.029 ± 0.524	0.0518 ± 0.583	0.044 ± 0.563	0.712
Chronological age	72.85 ± 7.958	71.86 ± 8.021	72.20 ± 8.003	0.259
<b>Ethnicity</b>				
Chinese	106 (83.5)	207 (83.1)	313 (83.2)	1
Other ethnicities	21 (16.5)	42 (16.9)	63 (16.8)	
<b>Marital Status</b>				
Married	65 (51.2)	143 (57.4)	208 (55.3)	0.273
Not married	62 (48.8)	106 (42.6)	168 (44.7)	
BMI	23.098 ± 3.835	24.900 ± 5.086	24.293 ± 4.774	<b>&lt;0.001***</b>
<b>Smoking status</b>				
Smoker	27 (21.3)	8 (3.2)	35 (9.3)	<b>&lt;0.001***</b>
Non-smoker	100 (78.7)	241 (96.8)	341 (90.7)	
<b>Alcohol consumption</b>				
Drinker	29 (22.8)	20 (8)	49 (13)	<b>&lt;0.001***</b>
Non-drinker	98 (77.2)	229 (92)	327 (87)	
Physical activity level	0.890 ± 0.857	1.104 ± 0.932	1.032 ± 0.912	<b>0.031*</b>
Social activity level	1.236 ± 0.750	1.353 ± 0.748	1.314 ± 0.750	0.152

SGD = Singapore Dollar, 1 SGD = 0.74 USD; Biological age acceleration (BAA) was calculated by subtracting the corresponding age- and sex-standardized biological age (BA) norms from the individual BA. A positive BAA value indicated accelerated biological aging, whereas a negative value indicated decelerated biological aging. Zero value represented equal rate of biological and chronological aging. \* for  $p < 0.05$ , \*\* for  $p < 0.01$ , and \*\*\* for  $p < 0.001$ .

was 72.20 (SD = 8.003, range = 54 to 95). The mean BA was 0.335 (SD = 0.63, range = -1.122 to 2.566) in log-odds units and 72.20 (SD = 1.48, range = 70.4 to 97.1) when scaled to years, whereas the mean BAA was 0.044 (SD = 0.563, range = -1.393 to 2.034) in log-odds units and 0.0 (SD = 1.37, range = -3.9 to 22.0) when scaled to years. Below we report BA and BAA in log-odds units. Most of the participants were women ( $n = 249$ , 66.2%) and Chinese ( $n = 313$ , 83.2%). Compared to women, there was a higher proportion of men staying in 1–2 room public housing ( $n = 108$ , 85% versus women,  $n = 156$ , 62.7%;  $p < 0.001$ ), longest occupation held at clerical level ( $n = 25$ , 19.7% versus women  $n = 12$ , 4.8%;  $p < 0.001$ ), having higher proportion of perceiving having difficulty in income adequacy ( $n = 58$ , 46.4% versus women,  $n = 87$ , 35.1%;  $p = 0.043$ ), higher BA (mean = 0.451, SD = 0.573 versus women mean = 0.276, SD = 0.650,  $p = 0.008$ ), higher proportion of smokers ( $n = 27$ , 21.3% versus women  $n = 8$ , 3.2%,  $p < 0.001$ ), and alcohol drinkers ( $n = 29$ , 22.8% versus women  $n = 20$ , 8%,  $p < 0.001$ ). On the other hand, there was a higher proportion of women who had no formal education ( $n = 151$ , 60.6% versus men  $n = 56$ , 44.1%,  $p = 0.003$ ). Women also had higher mean and a wider spread of BMI values (mean = 24.900, SD = 5.086 versus men mean = 23.098, SD = 3.835;  $p < 0.001$ ), and higher physical activity levels (mean = 1.104, SD = 0.932 versus men, mean = 0.890, SD = 0.857;  $p = 0.031$ ). The significant differences between men and women in both housing type and BA supported our aim 3. Hence, for all regression analyses, apart from conducting total sample analyses, we also performed sex-stratified analyses.

### Associations between housing type and BA/BAA

Table 2 presents the findings from the multivariate regression models, regressing BA and BAA separately on housing type, sequentially controlling for additional covariates.

### Total sample

The participants who resided in 1–2 room public housing had higher BA than those residing in 3 or more room public housing or private housing, even upon fully controlling for covariates (model 5:  $\beta = 0.189$ , 95% CI = 0.027 to 0.350,  $p = 0.022$ ). Similarly, there was a significant association between housing type and BAA, with the participants residing in 1–2 room public housing had accelerated biological aging (model 1:  $\beta = 0.156$ , 95% CI = 0.027 to 0.285,  $p = 0.018$ ). The relationship remained significant upon fully controlling for all the covariates (model 5:  $\beta = 0.178$ , 95% CI = 0.027 to 0.330,  $p = 0.021$ ). Notably, for all the other SES

indicators, although some were significant in the bivariate associations (Supplementary Table 1A, 1B and 1C), after controlling for each other and housing type, none were significantly associated with both BA and BAA (Supplementary Table 2A). Additional descriptive analyses can be found in the Supplementary Materials and Figure 1A and 1B.

### Sex-stratified analyses

Sex-stratified analyses showed similar results in women for both BA and BAA, upon controlling for all covariates (BA, left panel, model 5:  $\beta = 0.249$ , 95% CI = 0.054 to 0.444,  $p = 0.013$ ; BAA, right panel, model 5:  $\beta = 0.209$ , 95% CI = 0.026 to 0.392,  $p = 0.026$ ). However, in men, no significant associations were found between housing type and either BA or BAA. In men, the standardized  $\beta$  for the associations between housing type and BMI with BAA were 0.105 and 0.242, respectively (Supplementary Table 2B). While in women, for the association with BAA, the standardized  $\beta$  for the associations between housing type and BMI with BAA were 0.173 and  $< 0.001$ , respectively (Supplementary Table 2C).

### Moderation by health behaviors

#### Total sample analyses

In the total sample, there was a significant interaction effect between housing type and BMI on both BA ( $\beta = -0.041$ , 95% CI = -0.071 to -0.011,  $p = 0.007$ ) and BAA ( $\beta = -0.030$ , 95% CI = -0.058 to -0.002,  $p = 0.039$ ) (Table 3). However, no significant interaction effect was observed between housing type and smoking status on either BA ( $\beta = 0.191$ , 95% CI = -0.430 to 0.812,  $p = 0.545$ ) or BAA ( $\beta = 0.210$ , 95% CI = -0.372 to 0.792,  $p = 0.478$ ) (Table 3).

#### Sex-stratified analyses

In women, as with the total sample, the interaction effect between housing type and BMI was significant (Table 3). Women resided in 1–2 room public housing and who had higher BMI had a lower BA ( $\beta = -0.046$ , 95% CI = -0.081 to -0.012,  $p = 0.008$ ) and lower BAA ( $\beta = -0.032$ , 95% CI = 0.064 to 0.001,  $p = 0.056$ ), compared to those resided in 3 or more room public housing or private housing and with lower BMI. No significant interaction effect between housing type and smoking status was detected in women.

On the other hand, we observed the opposite trends in men; Although no significant interaction effect between housing type and BMI was found, we observed a statistically significant interaction effect between housing type and smoking status (Table 3).

**Table 2. Associations between housing type and biological age/biological age acceleration.**

Models	Biological age			Biological age acceleration			
	$\beta$ (95% CI)	<i>P</i> value	<i>R</i> <sup>2</sup>	$\beta$ (95% CI)	<i>P</i> value	<i>R</i> <sup>2</sup>	
<b>Total sample</b>							
Housing type	1	0.263 (0.120 to 0.406)	< <b>0.001</b> <sup>***</sup>	0.036	0.156 (0.027 to 0.285)	<b>0.018</b> <sup>*</sup>	0.016
	2	0.173 (0.024 to 0.323)	<b>0.023</b> <sup>*</sup>	0.091	0.166 (0.028 to 0.305)	<b>0.019</b> <sup>*</sup>	0.019
	3	0.199 (0.038 to 0.36)	<b>0.015</b> <sup>*</sup>	0.104	0.183 (0.033 to 0.334)	<b>0.017</b> <sup>*</sup>	0.025
	4	0.193 (0.032 to 0.354)	<b>0.019</b> <sup>*</sup>	0.121	0.180 (0.029 to 0.331)	<b>0.020</b> <sup>*</sup>	0.031
	5	0.189 (0.027 to 0.35)	<b>0.022</b> <sup>*</sup>	0.132	0.178 (0.027 to 0.330)	<b>0.021</b> <sup>*</sup>	0.046
<b>Men</b>							
Housing type	1	0.188 (−0.104 to 0.479)	0.204	0.014	0.202 (−0.064 to 0.467)	0.135	0.019
	2	0.148 (−0.144 to 0.440)	0.318	0.050	0.192 (−0.079 to 0.463)	0.163	0.021
	3	0.101 (−0.201 to 0.404)	0.508	0.120	0.154 (−0.130 to 0.438)	0.285	0.074
	4	0.109 (−0.188 to 0.405)	0.468	0.199	0.155 (−0.126 to 0.436)	0.277	0.136
	5	0.108 (−0.189 to 0.405)	0.471	0.212	0.154 (−0.127 to 0.436)	0.280	0.151
<b>Women</b>							
Housing type	1	0.246 (0.073 to 0.419)	<b>0.006</b> <sup>**</sup>	0.034	0.162 (0.006 to 0.319)	<b>0.042</b> <sup>*</sup>	0.018
	2	0.176 (−0.003 to 0.355)	0.054	0.086	0.163 (−0.004 to 0.329)	0.055	0.018
	3	0.256 (0.062 to 0.450)	<b>0.010</b> <sup>*</sup>	0.114	0.218 (0.036 to 0.400)	<b>0.019</b> <sup>*</sup>	0.034
	4	0.259 (0.065 to 0.452)	<b>0.009</b> <sup>**</sup>	0.139	0.221 (0.039 to 0.403)	<b>0.018</b> <sup>*</sup>	0.051
	5	0.249 (0.054 to 0.444)	<b>0.013</b> <sup>*</sup>	0.151	0.209 (0.026 to 0.392)	<b>0.026</b> <sup>*</sup>	0.072

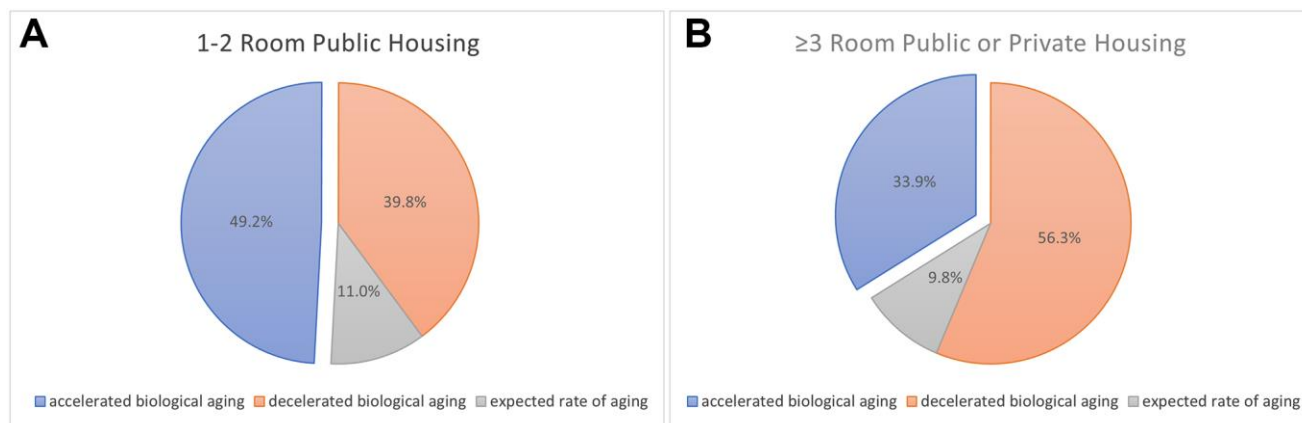
\* indicates  $p < 0.05$ , \*\* indicates  $p < 0.01$ , and \*\*\* indicates  $p < 0.001$ . Abbreviations: 95% CI: 95% confidence interval; BMI: body-mass index. Model 1: no covariates controlled for; with 3 or more room public or private housing indicating high SES-housing, which was the reference group in all regression models.

Model 2: added chronological age, sex, ethnicity.

Model 3: added marital status, education level, longest occupational role, income level, perceived income adequacy.

Model 4: added BMI, smoking status, alcohol consumption.

Model 5: added physical and social activity levels.



**Figure 1. (A)** The number and proportions of older adults resided in 1–2 room public housing who had accelerated biological aging was higher ( $N = 130$ , 49.2%), compared to those with decelerated biological aging ( $N = 105$ , 39.8%). There were 29 older adults with equal rate of biological aging with chronological aging (11%). **(B)** The number and proportions of older adults resided in 3 room or higher public housing or private housing who had accelerated biological aging was lower ( $N = 38$ , 33.9%), compared to those with decelerated biological aging ( $N = 63$ , 56.3%). There were 11 older adults with equal rate of biological aging with chronological aging (9.8%).

**Table 3. Associations between housing type and biological age/biological age acceleration, models with the additions of interaction terms for health behaviors.**

Models	Biological age			Biological age acceleration			
	$\beta$ (95% CI)	<i>P</i> -value	<i>R</i> <sup>2</sup>	$\beta$ (95% CI)	<i>P</i> -value	<i>R</i> <sup>2</sup>	
<b>Total sample</b>							
Housing Type	1	0.228 (0.067 to 0.388)	<b>0.006**</b>	0.114	0.178 (0.027 to 0.330)	<b>0.021*</b>	0.046
Housing Type	2	-0.183 (-1.402 to 1.036)	0.768	0.133	-0.231 (-1.373 to 0.912)	0.691	0.047
Smoking Status		0.104 (-0.474 to 0.682)	0.723		0.163 (-0.378 to 0.705)	0.553	
Housing Type x Smoking Status		0.191 (-0.430 to 0.812)	0.545		0.210 (-0.372 to 0.792)	0.478	
Housing Type	3	1.178 (0.438 to 1.918)	<b>0.002**</b>	0.150	0.896 (0.199 to 1.593)	<b>0.012*</b>	0.058
BMI		0.045 (0.020 to 0.071)	<b>0.001**</b>		0.030 (0.006 to 0.054)	<b>0.015*</b>	
Housing Type x BMI		-0.041 (-0.071 to -0.011)	<b>0.007**</b>		-0.030 (-0.058 to -0.002)	<b>0.039*</b>	
<b>Men</b>							
Housing Type	1	0.108 (-0.189 to 0.405)	0.471	0.212	0.154 (-0.127 to 0.436)	0.280	0.151
Housing Type	2	-1.363 (-2.761 to 0.034)	0.056	0.245	-1.259 (-2.584 to 0.066)	0.062	0.187
Smoking Status		0.611 (-0.092 to 1.314)	0.088		0.634 (-0.032 to 1.301)	0.062	
Housing Type x Smoking Status		0.795 (0.057 to 1.534)	<b>0.035*</b>		0.764 (0.063 to 1.464)	<b>0.033*</b>	
Housing Type	3	0.213 (-1.813 to 2.239)	0.835	0.212	0.267 (-1.654 to 2.188)	0.783	0.151
BMI		0.043 (-0.040 to 0.127)	0.302		0.037 (-0.041 to 0.116)	0.348	
Housing Type x BMI		-0.005 (-0.092 to 0.082)	0.918		-0.005 (-0.087 to 0.078)	0.907	
<b>Women</b>							
Housing Type	1	0.249 (0.054 to 0.444)	<b>0.013*</b>	0.151	0.209 (0.026 to 0.392)	<b>0.026*</b>	0.072
Housing Type	2	1.556 (-0.651 to 3.763)	0.166	0.157	1.397 (-0.674 to 3.468)	0.185	0.077
Smoking Status		-0.214 (-1.177 to 0.749)	0.662		-0.115 (-1.019 to 0.788)	0.802	
Housing Type x Smoking Status		-0.665 (-1.783 to 0.453)	0.243		-0.604 (-1.654 to 0.445)	0.257	
Housing Type	3	1.381 (0.521 to 2.240)	<b>0.002**</b>	0.179	0.982 (0.170 to 1.795)	<b>0.018*</b>	0.087
BMI		0.037 (0.009 to 0.065)	<b>0.009**</b>		0.020 (-0.006 to 0.046)	0.137	
Housing Type x BMI		-0.046 (-0.081 to -0.012)	<b>0.008**</b>		-0.032 (-0.064 to 0.001)	0.056	

\* indicates  $p < 0.05$ , \*\* indicates  $p < 0.01$ . Abbreviations: 95% CI: 95% confidence interval; BMI: body-mass index.

Model 1: added chronological age, sex, ethnicity, marital status, education level, longest occupational role, income level, perceived income adequacy, BMI, smoking status, alcohol consumption, physical and social activity levels (respective models 5 from Table 2).

Model 2: separately added interaction term: Housing x Smoking Status.

Model 3: separately added interaction term: Housing x BMI.

Men resided in 1–2 room public housing and who were smokers had a higher BA ( $\beta = 0.795$ , 95% CI = 0.057 to 1.534,  $p = 0.035$ ) and higher BAA ( $\beta = 0.764$ , 95% CI = 0.063 to 1.464,  $p = 0.033$ ), indicating accelerated biological aging.

#### Additional analyses

Despite not being employed as an external criterion, chronological age was significantly associated with BA ( $\beta = 3.133$ ,  $p \leq 0.001$ ). Furthermore, there were both a higher number and proportion of participants

( $p = 0.011$ ) staying in 1–2 room public housing who had accelerated biological aging ( $N = 130$ , 49.2%), compared to the reference ( $N = 29$ , 11%) and decelerated aging ( $N = 105$ , 39.8%) (Figure 1A). Whereas for participants staying in 3 room or higher public housing or private housings (Figure 1B), there were both a lower number and proportion of participants who had significantly accelerated aging ( $N = 38$ , 33.9%), compared to participants with no change/the reference ( $N = 11$ , 9.8%) and decelerated aging ( $N = 63$ , 56.3%).

## DISCUSSION

Controlling for a comprehensive panel of SES indicators, in the total sample, as compared to the high-SES housing type, we showed pilot data on the independent associations between low-SES housing and advanced BA and BAA. In sex-stratified subgroup analyses, the association was only observed in women, suggesting sex-specific vulnerability of women to the weathering effect of housing type as a socio-environmental determinant on biological aging. Furthermore, examining health behaviors as the hypothesized moderators, we showed sex-specific and differential moderating effects of BMI and smoking status on the association between housing type and biological aging. In women, higher BMI was protective for those resided in 1–2 room public housing, having moderated lower BA and BAA. In men, although the main effect of housing type was not significant, smoking status moderated the association between housing type and accelerated BAA; Men resided in 1–2 room public housing and who were smokers had both higher BA and accelerated BAA. Hence, all three hypotheses were supported by the data. Taken together, we showed pilot data on the associations between housing type, a social-environmental determinant of health, and accelerated biological aging. These findings underscore the importance of examining socio-environmental and behavioral factors in a predominantly biomedical landscape in the geroscience field.

In this study, we showed two lines of evidence supportive of the instrumental roles of housing type in biological aging. First, in the descriptive analyses, we found a higher proportion of participants resided in 1–2 room public housing who had accelerated biological aging (56.3%), compared to 39.8% of participants resided in 3 or more room public housing or private housing who had accelerated biological aging. Second, performing regression analyses, further controlling for covariates, the participants resided in 1–2 room public housing were associated with higher BA and accelerated biological aging. In contrary to this study, previous studies did not comprehensively examine the associations between SES indicators/socio-environmental determinant and biological aging, having frequently overlooked housing type as an indicator. Controlling for these SES indicators as covariates are essential, since they had been shown to confound the association between SES and BAA [13, 14]. In this study, the association between housing type and BAA remained significant upon comprehensively controlled for all the other SES indicators and covariates, including demographics, health behaviors, and social and physical activities.

The nature of the SES indicators could be the discerning factor in the association and lack thereof with biological aging. Our findings are in line with the extant literature showing that house ownership, but not the other SES indicators, was significantly associated with LTL-defined BA [51]. Housing type is more than an SES indicator, as it also captures multiple facets of the environment in which the older adults live in, thus we termed it the “socio-environmental indicator” in this study. Hence, we suggest that compared to the collective influences of SES *and* environmental factors encompassed by low housing type, the other four SES indicators had comparatively lower influences on biological aging. There are several plausible mechanistic explanations; Residing in low-SES public housing could have facilitated the accumulation of life-long stressors, exposing older adults to a health-deleterious environment, culminating in a lifetime of biological weathering effects [54] and thus premature aging [54, 55]. Amongst the health-deleterious environments in low-SES housing could be poor insulation, poor combustion appliances, cockroach, dust mites, and rodent infestations, hyper- and hypothermia, unaffordable rent, and dangerous levels of lead in soil and household paint [56]. Indeed, biological weathering is particularly prevalent in disadvantaged sample population in an urbanized population such as ours. Similarly, another study showed that female African-Americans residing in the low-SES neighbourhood experienced excess biological weathering [40]. One limitation is that these studies did not comprehensively controlled for other SES indicators. Extending previous findings, we found significant independent association between housing type and BA. SES-associated social stressors have also been shown to independently disrupt homeostasis [57]. Amongst the validated biological pathways mediating the effects of social stressors on adverse health outcomes include disrupting the hypothalamic-pituitary-adrenal (HPA) axis, autonomic nervous system, metabolic, and immune system [39], many of which were captured in our novel BA and BAA measures.

Our sex-stratified subgroup analyses revealed that only women, but not men, resided in 1–2 room public housing experienced accelerated biological aging. This finding concurs with previous observation showing that women *and* individuals in the lower social classes are more susceptible to the detrimental effects of stressors. Apart from the differential distributions of life stressors in different social classes, the psychological and social resources to cope with stressors are also unequally accessible to different sexes. For example, for women residing in high-SES housing, possibly due to the availability of and/or socially acceptable use of residential public spaces by women in these contexts



[58, 59], the effects of sex-specific stressors could be ameliorated. Conversely, for women in low-SES housing, given the unique challenges they are faced with, including marital conflicts, juggling a full-time job and the roles as a wife [60, 61], women may have less coping resources available which could be called upon in response to stressors [62]. Hence, these unique psychosocial challenges faced by women could have further compounded and reinforced the biological weathering effects exerted by low social classes, resulting in women-specific health vulnerability and disparity [62], and thus culminating in accelerated biological aging.

Lastly, exploring the moderating effects of health behaviors on the associations, in women, higher BMI counteracted the biological weathering effect of low-SES housing on biological aging. This finding is in line with the extant literature showing that in late life, in contrary to being detrimental to health, higher BMI is protective and predictive of better health [63]. Compared to their lower BMI counterparts, older adults who were obese also had lower mortality risk [57]. Conversely, epidemiological studies have shown that lower BMI could be a sign of frailty in late life [64]. According to the Asian-specific BMI standards, obesity cut-offs for women and men are 25 kg/m<sup>2</sup> and 27 kg/m<sup>2</sup>, respectively [59]. In our study, women, but not men, were borderline obese (24.9 kg/m<sup>2</sup>, compared to men, 23.10 kg/m<sup>2</sup>), further supportive of the specific moderating effect of higher BMI on lower BAA in women. On the other hand, men who resided in 1–2 room public housing who were also smokers had significantly accelerated biological aging. This finding supports the extant literature showing that low-SES individuals may be more susceptible to engage in unhealthy stress-reducing behaviors, such as smoking [13, 16], leading to accelerated biological aging [48, 50]. Due to the low percentage (3.2%) of women who smoked, compared to 21.3% of men who were smokers ( $p < 0.001$ ), future studies comprising more balanced smoker percentages between men and women are warranted to further examine the moderating effects of smoking status. Furthermore, our previous non-pharmacological trial showed that education level, an SES indicator, moderated the protective effect of the intervention on biomarker in women but not men [65], equally highlighting the importance of intersectionality among sex, social determinants of health, and biomarker.

There were several limitations in this study. The main limitation was the cross-sectional nature of the study, rendering us unable to determine the causal effects of housing type on BAA, leaving the possibility of reverse causation. However, an alternative interpretation of older adults who had accelerated biological aging

choosing to reside in low-SES housing seems rather implausible. This study also had a relatively moderate sample size, which could have limited the value of the sex-stratified exploratory analyses on health behaviors. Hence, the absence of statistical significance in some of the sex-stratified analyses does not imply the absence of a relationship [66], warranting future studies with larger sample size and more balanced variables. Furthermore, not having a nationally-representative sample, our findings warrant replication to be generalizable to the general population. Lastly, older adults staying in 1–2 room public housing have a greater risk of developing adverse health outcomes and thus have a higher mortality rate. This issue may present competing risk of death, with participants having a higher BA could have passed away before being recruited in this study. This issue could have potentially resulted in the underestimations of the detected associations and the effect sizes. If that was the case, housing type and health behaviors could have had even greater associations and moderating effects with BAA than presented.

This study extended our understanding of the associations between housing type and biological aging on several fronts. First, concurrently examining a comprehensive profile of SES indicators, we discerned the biological weathering effects of five SES indicators, showing the independent association between housing type and BAA. Second, with the associations established, we investigated the differential moderating effects of health behaviors on the associations between housing type and BAA in different sexes, contributing pilot data to untangling the complex intersections amongst multiple social and behavioral determinants of biological aging. Third, the hypotheses were tested using a novel measure of BA, which we previously derived based on CBC and selected standard blood biochemistry parameters, overcoming several limitations present in the current operationalizations of BA. Fourth, low-SES communities are more vulnerable to social stressors and have higher rates of adverse health outcomes [9, 28], all of which could be underpinned by biological aging [34, 35]. Given our study participants were recruited from predominantly low-SES communities in Singapore, our sample population is thus well-suited to test the proposed hypotheses.

To our knowledge, this is the first study showing pilot data on an independent and significant association between housing type, an indicator of socio-environmental determinant, and biological aging, which persisted after controlling for a comprehensive panel of four SES indicators. We also showed pilot exploratory data on two specific socio-behavioral determinants through which health behaviors (BMI and smoking

status) moderated accelerated biological aging in low-SES older adults. The differential moderating effects of health behaviors on these associations specific to men and women suggest sex-specific vulnerabilities of BA to social-behavioral determinants of health. The model implies that dependent on the sex, by modifying one of the risk factors/health behaviors (i.e. BMI or smoking) in older adults residing in low-SES housing, biological aging could potentially be forestalled in this group of the vulnerable population. According to the Geroscience Hypothesis, accelerated biological aging predisposes these older adults to developing a range of geriatric syndromes. Furthermore, the blood test parameters employed in this study in constructing BA are readily available for testing in commercial laboratories and routinely examined in the clinical settings. The ease of data availability, not limited by sophisticated field specimen collection procedures and laboratory examinations unlike DNA-methylation-based measures, make this BA attractive to be used at the population level. We have also previously shown that several of the BA biomarkers could be improved by non-pharmacological interventions [20, 67, 68]. Furthermore, data gathered from consumer-grade mobile and wearable device or sensor may prove as a useful tool to enroll even larger cohorts in studies of aging, as our recent work showed notable concordance between BA in blood test and wearable sensor data [50, 69, 70]. Taken together, the identifications of social and behavioral determinants of health and their associations with accelerated biological aging could highlight novel targets and approaches to preventing and closing the gaps of health disparity in low-SES communities, with the potential to inform and positively impact policies and interventions. A future direction is to validate these findings in longitudinal studies with a nationally-representative sample, especially to pinpoint the effects of specific environmental characteristics of housing types on biological aging. Despite the unique private/public divide and housing type present in Singapore, with the increasing aging population coupled with limited housing availabilities and homelessness issue worldwide, upon further validation in other countries, the findings of this study have potential implications in informing housing and public policies in other countries. Despite different cut-offs and criteria used for defining low-SES housing, studies from many other countries [25–28, 33, 36, 71] similarly found housing as a prominent social determinant of health and associated with multiple adverse health outcomes. Apart from moderating effects, whether BMI and/or smoking status also mediate the effects of low-SES housing on biological aging warrant future mediational analyses employing longitudinal cohort studies, validating intervention targets to combat health disparities in biological aging and geroscience.

## METHODS

### Study participants

The participants were recruited from the community for a behavioral randomized controlled trial (RCT) entitled Self-Care for Older PErsons (SCOPE) intervention [68, 72, 73]. This RCT was approved by the National University of Singapore Institutional Review Board (NUS-IRB Reference No: 11-111) and registered at ClinicalTrials.gov (<https://www.clinicaltrials.gov/ct2/show/NCT01672177?term=scopeandcntry=SG&rank=2>). Informed consent was obtained before screening for eligible participants. In this study, we sought to analyze the data only from the baseline to avoid intervention effects on the biomarkers.

### Independent variable: housing type

Housing type was categorized into staying in: a) 1–2 room public housing (low SES housing) and b)  $\geq 3$  room public or private housing (high SES housing, served as the reference group in all regression models).

### Dependent variable: BA and BAA

#### *Blood collection, plasma processing and biomarker measurements*

Blood samples were collected between 08:00 and 09:00 in the morning to minimize diurnal variations. We asked the participants to stop consuming foods starting from 10 pm the night before the blood draw. They were advised to only consume plain water. Research nurses obtained blood samples via performing venipuncture. Samples were kept at 4°C for a maximum of three hours before they were processed. Whole blood samples were centrifuged at 1650 g for 25 minutes at 4°C to obtain the plasma. After the completion of sample collections, they were sent to the respective laboratories for measurements. The samples were assayed for CBC and other biochemical markers on the same day to avoid the batch effect. Biomarkers were examined using commercially available assay kits and procedures as per the instructions of the respective manufacturers of the kits and laboratories.

### Covariates: other SES indicators

Education level was operationalized as two groups, no formal education and with primary school education and above. The longest occupation held was operationalized as two groups: 1) clerical level, comprising clerks, sales and production, cleaners/labourers, and housemakers, 2) executive level, comprising professional, managerial levels, and

associates. Monthly income was divided into < SGD 500 and  $\geq$  SGD 500 (1 SGD = 0.74 USD). Lastly, perceived income adequacy was operationalized as two groups: 1) having difficulty, including participants who reported having some difficulty and having much difficulty paying expenses, 2) having not much difficulty, combining participants who reported having enough and just enough money to spend.

Detailed descriptions for other covariates can be found in the Supplementary Materials.

### **Moderators: health behaviors**

BMI was defined as weight divided by squared height (unit =  $\text{kg}/\text{m}^2$ ). Smoking Status was determined by asking whether the participants were current smokers.

### **Statistical analyses**

#### ***Sample size calculation***

Based on a power calculation with 80% power at 5% significance with a 2-tailed test, a sample size of 65 could detect an effect size of 0.35 for a significant correlation. Hence, the targeted total sample size needed to be 65 or more.

### **Biological age (BA)**

The biological age (BA) model was trained using the UK Biobank data. Following [48, 74], we characterized UK Biobank participants with a binary label as disease-free if they were not diagnosed as having any of the following health conditions: cancer (C00–C99), diabetes (E10–E14), hypertension (I10–I15), Ischaemic heart diseases (I20–I25), CHF (I50), stroke (I60–I64), emphysema (J43, J44), arthritis (M00–M25), as well as self-reported data. We used the binary label for logistic regression which is an approximation to the proportional hazards model to train the model. The approximation works particularly well when the disease rate is small [75, 76] which is the case in the dataset (19% of the studied population). Analyses were performed using the *sklearn* (version 0.20.3) and *lifelines* (version 0.19.5) packages in python.

The total sample of UK Biobank (214517 female, 186480 male) was split into training (80%) and test sets. Following our previous method [50], we used CBC parameters to produce an organism state indicator. We also used selected parameters from the standard biochemistry profile to produce more robust associations with health status. The complete list of markers include: Hemoglobin (g/dL), Red blood cell count (million cells/uL), Mean cell volume (fL), Mean Cell Hgb Conc. (g/dL), Red cell distribution width (%), Platelet count

(1000 cells/uL), Lymphocyte number (1000 cells/uL), Monocyte number (1000 cells/uL), Neutrophils num (1000 cell/uL), Eosinophils number (1000 cells/uL), Basophils number (1000 cells/uL), Albumin (g/L), Creatinine (umol/L), Cholesterol (mmol/L), HDL-Cholesterol (mmol/L), LDL-cholesterol (mmol/L), Triglycerides (mmol/L). The model yielded ROC AUC for the binary label of 0.66 for both the training and test sets and concordance index for mortality follow-up of 0.64 and 0.65 for the training and test sets, respectively, which was consistent with what was reported for CBC only in our previous study [50].

Finally, we converted the predicted log-odds ratio to biological age using scaling and offset following the approach outlined previously [46]. For this study which focused on the low-SES population, we used Singapore's SCOPE dataset as the reference for scaling, since UK Biobank might represent an enrollment bias for such population [77].

### **Biological age acceleration (BAA)**

BAA, an indicator for being biologically older or younger, was calculated by subtracting the BA from the corresponding average BA for age- and sex-matched cohorts. A positive BAA value indicated accelerated aging, whereas a negative value indicated decelerated aging. Zero represented one has the expected BA based on one's CA.

### **Regression analyses**

To address aim 1, we performed linear regression analyses associating housing type (independent variable) with i) BA and ii) BAA (both as dependent variables) in separate models. In the multivariate regression analyses, all the models were conceptualized and co-variables selected *a priori*, with additional groups of covariates sequentially entered into the regression models. Model 1 did not control for any covariates, solely examining the bivariate relationships. Model 2 controlled for chronological age (CA), sex, and ethnicity. Model 3 further controlled for marital status and four other SES indicators, namely education level, the longest occupation held, income level, and perceived income adequacy. Model 4 further controlled for BMI, smoking status, and alcohol drinker. Lastly, model 5 further controlled for social and physical activities.

To address aim 2, we examined the hypothesized moderating effects of BMI and smoking status separately, by adding interaction terms between the variables with housing type in separate regression models, on top of the models examined in aim 1.

Lastly, to address aim 3, we repeated the same analyses delineated above, the only difference was that instead of the total sample, we performed sex-stratified analyses.

All the regression analyses were performed using Statistical Package for the Social Sciences (SPSS) version 24.0 (IBM SPSS Statistics for Windows, Version 24.0). A two-tailed *p*-value of < 0.05 was considered statistically significant.

## AUTHOR CONTRIBUTIONS

Conceptualization: D.B.M, A.W.C and B.K.; study design: T.K.S.N., D.B.M, and A.W.C; UK Biobank data analyses: T.V.P.; Singapore SCOPE data analyses: T.K.S.N.; data interpretation: T.K.S.N. and A.W.C; methodology: T.K.S.N., D.B.M, T.V.P, P.O.F., A.W.C and B.K.; project administration: T.K.S.N.; supervision: D.B.M, A.W.C and B.K.; writing of the first draft: T.K.S.N; revision: T.K.S.N., D.B.M, T.V.P, P.O.F., A.W.C and B.K. The corresponding author has access to all aspects of the research and manuscript preparation process. All authors have read and agreed to the final version of the manuscript.

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## CONFLICTS OF INTEREST

P.O.F. and T.V.P are current C.E.O. and employee of GERO PTE. LTD., Singapore. The authors declare no other potential conflict of interest. The funders had no role in the collection, analyses, or interpretation of data, in the writing of the manuscript, and in the decision to publish the results.

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## SUPPLEMENTARY MATERIALS

### Supplementary Materials

#### Study participants

In the main study, we recruited research participants from 14 Senior Activity Centers (SACs) which were located in low-SES areas, selected from a total of 42 in Singapore. Subsequently, from a list of individuals attached to each SAC, we randomly selected potential participants using a computerized random number generator. Participants were included if they were aged 55 years and above, affiliated with one of the SACs, had consented to future data use and blood draws. Participants were excluded if they had cognitive impairment as indicated by Abbreviated Mental Test (AMT) score  $< 5$ , had a debilitating or terminal illness, or activities of daily living (ADL) disability that rendered them physically unfit to participate at the time of screening. Participants were also excluded if they were on either chemotherapy or dialysis or received medications for major psychiatric disorders at the time.

#### Covariates

##### *Ethnicity*

Based on the distribution of our sample, we categorized ethnicity into two groups, namely Chinese and non-Chinese, which comprised the Malay and Indian.

#### Marital status

We categorized marital status into two groups, namely married and not married, which included those who were single, widowed, and divorced.

#### Physical and social activity levels

We asked three questions for each category of the activities. For physical activities, we asked how much total time the participants spent on each of the following activities: 1) performing stretching or strengthening exercises, 2) walked for exercise purposes, and 3) performing vigorous exercise. For social activities, we asked how often the participants performed any of the following in the past week: 1) attended community or neighbourhood event, 2) went out to eat, and 3) attended church, synagogue, mosque, temple or other places of worship. For physical activities, participants who performed one of the activities at least 30–60 minutes per week were given 1 point. For social activities, participants who performed one of the activities at least once a week were given 1 point. The total scores for each of the two types of activities were calculated. The total scores ranged from 0 to 3, with a higher score representing a higher level of activities.

## Supplementary Tables

**Supplementary Table 1A. Bivariate associations between each SES indicator with biological age and biological age acceleration – Total sample.**

Indicators of SES	Biological age; <i>r</i> ( <i>P</i> value)	Biological age acceleration; <i>r</i> ( <i>P</i> value)
Housing type	<b>0.191 (&lt;0.001<sup>***</sup>)</b>	<b>0.127 (0.007<sup>**</sup>)</b>
Education level	<b>0.104 (0.022<sup>*</sup>)</b>	0.013 (0.402)
Longest occupational role	-0.059 (0.126)	-0.079 (0.063)
Income level	-0.008 (0.444)	-0.002 (0.484)
Perceived income adequacy	-0.042 (0.209)	-0.014 (0.392)

**Supplementary Table 1B. Bivariate associations between each SES indicator with biological age and biological age acceleration – Men.**

Indicators of SES	Biological age; <i>r</i> ( <i>P</i> value)	Biological age acceleration; <i>r</i> ( <i>P</i> value)
Housing type	0.117 (0.095)	0.138 (0.061)
Education level	0.140 (0.059)	0.081 (0.182)
Longest occupational role	<b>-0.181 (0.021<sup>*</sup>)</b>	<b>-0.173 (0.026<sup>*</sup>)</b>
Income level	<b>0.152 (0.048<sup>*</sup>)</b>	<b>0.153 (0.047<sup>*</sup>)</b>
Perceived income adequacy	-0.124 (0.083)	-0.079 (0.190)

**Supplementary Table 1C. Bivariate associations between each SES indicator with biological age and biological age acceleration – Women.**

Indicators of SES	Biological age; <i>r</i> ( <i>P</i> value)	Biological age acceleration; <i>r</i> ( <i>P</i> value)
Housing type	<b>0.183 (0.002<sup>**</sup>)</b>	<b>0.135 (0.017<sup>*</sup>)</b>
Education level	<b>0.122 (0.027<sup>*</sup>)</b>	-0.023 (0.359)
Longest occupational role	-0.034 (0.299)	-0.005 (0.468)
Income level	-0.085 (0.099)	-0.073 (0.135)
Perceived income adequacy	-0.027 (0.334)	0.018 (0.388)

**Supplementary Table 2A. Associations between housing type and biological age/biological age acceleration – Total sample – Extension of Table 2 with all covariates and standardized  $\beta$  presented.**

Models		Biological age			Biological age acceleration		
		$\beta$ (95% CI)	Standardized $\beta$	P value	$\beta$ (95% CI)	Standardized $\beta$	P value
<b>Total Sample</b>							
1	Housing Type	0.263 (0.12 to 0.406)	0.191	< <b>0.001</b> <sup>***</sup>	0.156 (0.027 to 0.285)	0.127	<b>0.018</b> *
2	Housing Type	0.173 (0.024 to 0.323)	0.126	<b>0.023</b> *	0.166 (0.028 to 0.305)	0.135	<b>0.019</b> *
	chronological age	0.017 (0.009 to 0.025)	0.219	< <b>0.001</b> <sup>***</sup>	0 (-0.007 to 0.008)	0.001	0.98
	sex	-0.12 (-0.259 to 0.019)	-0.09	0.091	0.06 (-0.069 to 0.189)	0.05	0.361
	ethnicity	-0.03 (-0.206 to 0.145)	-0.018	0.733	-0.025 (-0.187 to 0.138)	-0.016	0.767
3	Housing Type	0.199 (0.038 to 0.36)	0.145	<b>0.015</b> *	0.183 (0.033 to 0.334)	0.149	<b>0.017</b> *
	chronological age	0.016 (0.008 to 0.025)	0.207	< <b>0.001</b> <sup>***</sup>	0 (-0.008 to 0.009)	0.005	0.936
	sex	-0.154 (-0.299 to -0.01)	-0.116	<b>0.037</b> *	0.041 (-0.093 to 0.176)	0.035	0.546
	ethnicity	-0.032 (-0.218 to 0.155)	-0.019	0.738	-0.012 (-0.186 to 0.162)	-0.008	0.893
	marital status	0.012 (-0.124 to 0.148)	0.009	0.863	0.022 (-0.105 to 0.149)	0.019	0.736
	education level	0.038 (-0.109 to 0.186)	0.03	0.609	-0.018 (-0.155 to 0.12)	-0.016	0.8
	longest occupational role	-0.157 (-0.388 to 0.074)	-0.074	0.182	-0.135 (-0.35 to 0.081)	-0.071	0.22
	income level	-0.086 (-0.24 to 0.067)	-0.06	0.269	-0.035 (-0.178 to 0.109)	-0.027	0.636
	perceived income adequacy	-0.064 (-0.204 to 0.077)	-0.049	0.372	-0.031 (-0.162 to 0.1)	-0.027	0.644
4	Housing Type	0.193 (0.032 to 0.354)	0.14	<b>0.019</b> *	0.18 (0.029 to 0.331)	0.146	<b>0.02</b> *
	chronological age	0.017 (0.008 to 0.026)	0.218	< <b>0.001</b> <sup>***</sup>	0.001 (-0.008 to 0.009)	0.01	0.867
	sex	-0.204 (-0.357 to -0.052)	-0.154	<b>0.009</b> **	0.016 (-0.127 to 0.159)	0.014	0.825
	ethnicity	0.042 (-0.152 to 0.237)	0.025	0.668	0.026 (-0.157 to 0.208)	0.017	0.782
	marital status	-0.008 (-0.144 to 0.129)	-0.006	0.909	0.011 (-0.117 to 0.139)	0.01	0.863
	education level	0.017 (-0.132 to 0.166)	0.013	0.822	-0.03 (-0.169 to 0.11)	-0.026	0.676
	longest occupational role	-0.162 (-0.392 to 0.069)	-0.076	0.169	-0.136 (-0.352 to 0.081)	-0.072	0.219
	income level	-0.112 (-0.267 to 0.043)	-0.077	0.155	-0.048 (-0.193 to 0.097)	-0.037	0.518
	perceived income adequacy	-0.057 (-0.199 to 0.084)	-0.044	0.427	-0.027 (-0.16 to 0.106)	-0.023	0.692
	BMI	0.016 (0.001 to 0.031)	0.121	<b>0.032</b> *	0.008 (-0.006 to 0.022)	0.068	0.25
	smoking status	-0.073 (-0.31 to 0.163)	-0.034	0.542	-0.03 (-0.253 to 0.192)	-0.016	0.789
	alcohol drinker	-0.081 (-0.282 to 0.121)	-0.043	0.432	-0.053 (-0.242 to 0.137)	-0.032	0.585
5	Housing Type	0.189 (0.027 to 0.35)	0.137	<b>0.022</b> *	0.178 (0.027 to 0.33)	0.145	<b>0.021</b> *
	chronological age	0.017 (0.008 to 0.026)	0.219	< <b>0.001</b> <sup>***</sup>	0.001 (-0.008 to 0.009)	0.012	0.847
	sex	-0.204 (-0.358 to -0.051)	-0.153	<b>0.009</b> **	0.014 (-0.13 to 0.157)	0.011	0.853
	ethnicity	0.027 (-0.168 to 0.222)	0.016	0.786	0.012 (-0.171 to 0.195)	0.008	0.895
	marital status	-0.014 (-0.151 to 0.123)	-0.011	0.837	0.007 (-0.122 to 0.135)	0.006	0.92
	education level	0.02 (-0.128 to 0.168)	0.016	0.792	-0.026 (-0.165 to 0.113)	-0.023	0.716
	longest occupational role	-0.18 (-0.412 to 0.051)	-0.085	0.126	-0.157 (-0.373 to 0.06)	-0.083	0.155
	income level	-0.114 (-0.269 to 0.041)	-0.079	0.148	-0.052 (-0.197 to 0.093)	-0.04	0.481
	perceived income adequacy	-0.068 (-0.21 to 0.074)	-0.053	0.347	-0.039 (-0.172 to 0.094)	-0.033	0.568
	BMI	0.017 (0.002 to 0.031)	0.127	<b>0.025</b> *	0.009 (-0.005 to 0.023)	0.075	0.201
	smoking status	-0.058 (-0.295 to 0.179)	-0.027	0.63	-0.015 (-0.237 to 0.207)	-0.008	0.894
	alcohol drinker	-0.083 (-0.284 to 0.118)	-0.044	0.416	-0.055 (-0.244 to 0.133)	-0.033	0.563
	social activity levels	-0.091 (-0.179 to -0.002)	-0.108	<b>0.046</b> *	-0.092 (-0.176 to -0.009)	-0.123	<b>0.03</b> *
	physical activity levels	0.031 (-0.043 to 0.105)	0.045	0.407	0.041 (-0.028 to 0.111)	0.067	0.243

\* indicates  $p < 0.05$ , \*\* indicates  $p < 0.01$ , and \*\*\* indicates  $p < 0.001$ . Abbreviations: 95% CI: 95% confidence interval; BMI: body-mass index.

**Supplementary Table 2B. Associations between housing type and biological age/biological age acceleration – Men subgroup analyses – Extension of Table 2 with all covariates and standardized  $\beta$  presented.**

Models		Biological Age			Biological Age Acceleration		
		$\beta$ (95% CI)	Standardized $\beta$	P value	$\beta$ (95% CI)	Standardized $\beta$	P value
<b>Total sample</b>							
1	Housing Type	0.188 (-0.104 to 0.479)	0.117	0.204	0.202 (-0.064 to 0.467)	0.138	0.135
2	Housing Type	0.148 (-0.144 to 0.44)	0.092	0.318	0.192 (-0.079 to 0.463)	0.131	0.163
	chronological age	0.014 (0 to 0.027)	0.188	<b>0.043*</b>	0.001 (-0.011 to 0.013)	0.019	0.837
	ethnicity	-0.046 (-0.326 to 0.234)	-0.03	0.746	-0.048 (-0.307 to 0.212)	-0.034	0.716
3	Housing Type	0.101 (-0.201 to 0.404)	0.063	0.508	0.154 (-0.13 to 0.438)	0.105	0.285
	chronological age	0.015 (0.001 to 0.028)	0.203	<b>0.035*</b>	0.002 (-0.01 to 0.015)	0.034	0.725
	ethnicity	-0.09 (-0.385 to 0.205)	-0.058	0.548	-0.085 (-0.361 to 0.192)	-0.06	0.544
	marital status	-0.042 (-0.264 to 0.179)	-0.037	0.705	-0.022 (-0.23 to 0.185)	-0.021	0.832
	education level	0.033 (-0.19 to 0.257)	0.029	0.768	0.001 (-0.209 to 0.211)	0.001	0.993
	longest occupational role	-0.236 (-0.515 to 0.042)	-0.165	0.095	-0.189 (-0.45 to 0.072)	-0.144	0.153
	income level	0.182 (-0.078 to 0.442)	0.136	0.168	0.175 (-0.069 to 0.418)	0.143	0.158
	perceived income adequacy	-0.102 (-0.33 to 0.125)	-0.089	0.374	-0.077 (-0.29 to 0.136)	-0.074	0.475
4	Housing Type	0.109 (-0.188 to 0.405)	0.068	0.468	0.155 (-0.126 to 0.436)	0.106	0.277
	chronological age	0.016 (0.003 to 0.029)	0.222	<b>0.02*</b>	0.004 (-0.009 to 0.016)	0.056	0.567
	ethnicity	-0.016 (-0.308 to 0.276)	-0.01	0.913	-0.031 (-0.308 to 0.247)	-0.022	0.827
	marital status	-0.053 (-0.269 to 0.162)	-0.047	0.623	-0.033 (-0.237 to 0.171)	-0.032	0.749
	education level	0.049 (-0.171 to 0.269)	0.043	0.658	0.013 (-0.196 to 0.222)	0.012	0.904
	longest occupational role	-0.271 (-0.542 to 0)	-0.189	0.05	-0.214 (-0.472 to 0.043)	-0.163	0.102
	income level	0.106 (-0.15 to 0.362)	0.079	0.413	0.116 (-0.128 to 0.359)	0.095	0.348
	perceived income adequacy	-0.042 (-0.267 to 0.184)	-0.037	0.714	-0.031 (-0.245 to 0.183)	-0.03	0.775
	BMI	0.039 (0.012 to 0.066)	0.26	<b>0.006*</b>	0.033 (0.007 to 0.059)	0.242	<b>0.013*</b>
	smoking status	-0.102 (-0.363 to 0.159)	-0.073	0.442	-0.048 (-0.296 to 0.2)	-0.038	0.701
	alcohol drinker	0.049 (-0.195 to 0.292)	0.036	0.693	0.036 (-0.195 to 0.267)	0.029	0.756
5	Housing Type	0.108 (-0.189 to 0.405)	0.068	0.471	0.154 (-0.127 to 0.436)	0.105	0.28
	chronological age	0.016 (0.002 to 0.029)	0.219	<b>0.022*</b>	0.003 (-0.009 to 0.016)	0.051	0.601
	ethnicity	-0.05 (-0.349 to 0.248)	-0.033	0.739	-0.055 (-0.338 to 0.228)	-0.039	0.702
	marital status	-0.057 (-0.276 to 0.161)	-0.05	0.605	-0.026 (-0.233 to 0.181)	-0.025	0.802
	education level	0.038 (-0.183 to 0.259)	0.033	0.734	0.005 (-0.205 to 0.215)	0.005	0.964
	longest occupational role	-0.282 (-0.554 to -0.009)	-0.196	<b>0.043*</b>	-0.222 (-0.48 to 0.037)	-0.169	0.092
	income level	0.106 (-0.152 to 0.364)	0.079	0.416	0.109 (-0.136 to 0.353)	0.089	0.381
	perceived income adequacy	-0.083 (-0.32 to 0.154)	-0.072	0.49	-0.078 (-0.303 to 0.147)	-0.075	0.492
	BMI	0.039 (0.012 to 0.067)	0.263	<b>0.005*</b>	0.033 (0.007 to 0.059)	0.242	<b>0.013*</b>
	smoking status	-0.094 (-0.355 to 0.168)	-0.067	0.479	-0.042 (-0.29 to 0.206)	-0.033	0.737
	alcohol drinker	0.04 (-0.205 to 0.285)	0.029	0.748	0.034 (-0.199 to 0.266)	0.027	0.775
	social activity levels	-0.089 (-0.233 to 0.055)	-0.117	0.221	-0.071 (-0.207 to 0.065)	-0.102	0.304
	physical activity levels	0.041 (-0.085 to 0.166)	0.061	0.523	0.069 (-0.05 to 0.188)	0.113	0.252

\* indicates  $p < 0.05$ , \*\* indicates  $p < 0.01$ , and \*\*\* indicates  $p < 0.001$ . Abbreviations: 95% CI: 95% confidence interval; BMI: body-mass index.

**Supplementary Table 2C. Associations between housing type and biological age/biological age acceleration – Women subgroup analyses – Extension of Table 2 with all covariates and standardized  $\beta$  presented.**

Models		Biological Age			Biological Age Acceleration		
		$\beta$ (95% CI)	Standardized $\beta$	P value	$\beta$ (95% CI)	Standardized $\beta$	P value
<b>Total sample</b>							
1	Housing Type	0.246 (0.073 to 0.419)	0.183	<b>0.006**</b>	0.162 (0.006 to 0.319)	0.135	<b>0.042*</b>
2	Housing Type	0.176 (−0.003 to 0.355)	0.131	0.054	0.163 (−0.004 to 0.329)	0.135	0.055
	chronological age	0.019 (0.009 to 0.03)	0.236	<b>&lt;0.001***</b>	−0.001 (−0.01 to 0.009)	−0.009	0.898
	ethnicity	−0.032 (−0.261 to 0.196)	−0.019	0.782	−0.009 (−0.222 to 0.203)	−0.006	0.932
3	Housing Type	0.256 (0.062 to 0.45)	0.191	<b>0.01**</b>	0.218 (0.036 to 0.4)	0.181	<b>0.019*</b>
	chronological age	0.02 (0.009 to 0.032)	0.252	<b>0.001***</b>	0.002 (−0.009 to 0.013)	0.024	0.759
	ethnicity	−0.017 (−0.26 to 0.227)	−0.01	0.893	0.027 (−0.201 to 0.255)	0.018	0.814
	marital status	0.091 (−0.085 to 0.267)	0.069	0.309	0.077 (−0.089 to 0.242)	0.065	0.362
	education level	0 (−0.201 to 0.201)	0	0.999	−0.058 (−0.247 to 0.13)	−0.049	0.542
	longest occupational role	0.037 (−0.365 to 0.439)	0.012	0.858	−0.011 (−0.387 to 0.366)	−0.004	0.954
	income level	−0.229 (−0.424 to −0.035)	−0.155	<b>0.021*</b>	−0.145 (−0.328 to 0.037)	−0.109	0.118
	perceived income adequacy	−0.03 (−0.21 to 0.149)	−0.022	0.74	0.007 (−0.162 to 0.175)	0.005	0.939
4	Housing Type	0.259 (0.065 to 0.452)	0.193	<b>0.009**</b>	0.221 (0.039 to 0.403)	0.183	<b>0.018*</b>
	chronological age	0.02 (0.008 to 0.032)	0.247	<b>0.001**</b>	0.001 (−0.01 to 0.012)	0.014	0.857
	ethnicity	0.048 (−0.211 to 0.308)	0.028	0.714	0.038 (−0.206 to 0.282)	0.024	0.76
	marital status	0.079 (−0.099 to 0.256)	0.06	0.383	0.079 (−0.087 to 0.246)	0.067	0.349
	education level	−0.036 (−0.239 to 0.166)	−0.027	0.723	−0.076 (−0.267 to 0.115)	−0.063	0.436
	longest occupational role	0.081 (−0.322 to 0.484)	0.027	0.692	0.02 (−0.359 to 0.4)	0.008	0.915
	income level	−0.273 (−0.47 to −0.075)	−0.184	<b>0.007**</b>	−0.169 (−0.355 to 0.017)	−0.128	0.074
	perceived income adequacy	−0.01 (−0.192 to 0.172)	−0.007	0.913	0.026 (−0.145 to 0.197)	0.021	0.763
	BMI	0.008 (−0.01 to 0.025)	0.06	0.397	0 (−0.017 to 0.016)	−0.004	0.956
	smoking status	0.23 (−0.239 to 0.699)	0.063	0.334	0.275 (−0.167 to 0.717)	0.083	0.221
	alcohol drinker	−0.361 (−0.683 to −0.039)	−0.151	<b>0.028**</b>	−0.251 (−0.555 to 0.052)	−0.117	0.104
5	Housing Type	0.249 (0.054 to 0.444)	0.185	<b>0.013*</b>	0.209 (0.026 to 0.392)	0.173	<b>0.026*</b>
	chronological age	0.02 (0.008 to 0.032)	0.248	<b>0.001**</b>	0.001 (−0.01 to 0.012)	0.016	0.841
	ethnicity	0.032 (−0.229 to 0.294)	0.019	0.807	0.019 (−0.226 to 0.264)	0.012	0.877
	marital status	0.073 (−0.105 to 0.25)	0.055	0.421	0.072 (−0.094 to 0.239)	0.061	0.393
	education level	−0.029 (−0.232 to 0.174)	−0.022	0.779	−0.067 (−0.257 to 0.123)	−0.056	0.489
	longest occupational role	0.066 (−0.338 to 0.471)	0.022	0.746	0.004 (−0.376 to 0.384)	0.001	0.984
	income level	−0.27 (−0.469 to −0.072)	−0.183	<b>0.008**</b>	−0.166 (−0.352 to 0.019)	−0.125	0.079
	perceived income adequacy	−0.008 (−0.189 to 0.173)	−0.006	0.933	0.029 (−0.141 to 0.199)	0.024	0.739
	BMI	0.008 (−0.01 to 0.026)	0.063	0.371	<0.001 (−0.017 to 0.017)	<0.001	0.995
	smoking status	0.285 (−0.187 to 0.757)	0.077	0.235	0.339 (−0.104 to 0.782)	0.103	0.133
	alcohol drinker	−0.354 (−0.676 to −0.032)	−0.148	<b>0.031*</b>	−0.243 (−0.545 to 0.059)	−0.113	0.114
	social activity levels	−0.101 (−0.214 to 0.012)	−0.116	0.081	−0.117 (−0.223 to −0.011)	−0.15	<b>0.031*</b>
	physical activity levels	0.021 (−0.071 to 0.114)	0.031	0.651	0.024 (−0.063 to 0.111)	0.038	0.59

\* indicates  $p < 0.05$ , \*\* indicates  $p < 0.01$ , and \*\*\* indicates  $p < 0.001$ . Abbreviations: 95% CI: 95% confidence interval; BMI: body-mass index.