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# Associations between social determinants of health and cardiovascular and cancer mortality in cancer survivors: a prospective cohort study

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## Aims

The cause-specific mortality implications of social determinants of health (SDOH) in cancer survivors were unclear. This study aimed to explore associations between SDOH and cardiovascular and cancer mortality in cancer survivors.

## Methods and results

Data from 2013 to 2017 National Health Interview Survey were used for this prospective cohort study. Social determinants of health were quantified using a 38 point, 6 domain score, with higher points indicating worse deprivation. Associations between SDOH and outcomes (primary: cardiovascular mortality; secondary: cancer and all-cause mortality) were assessed using cause-specific multivariable Cox regression, with cancer survivors and individuals without cancer modelled separately. *Post hoc* analyses were performed among cancer survivors to explore associations between each domain of SDOH and the risks of outcomes. Altogether, 37 882 individuals were analysed (4179 cancer survivors and 33 703 individuals without cancer). Among cancer survivors, worse SDOH was associated with higher cardiovascular [adjusted hazard ratio (aHR) 1.31 (1.02–1.68)], cancer [aHR 1.20 (1.01–1.42)], and all-cause mortality [aHR 1.16 (1.02–1.31)] when adjusted for demographics, comorbidities, and risk factors. Among individuals without cancer, SDOH was associated with cardiovascular mortality and all-cause when only adjusted for demographics, but not when further adjusted for comorbidities and risk factors; no associations between SDOH and cancer mortality were found. Among cancer survivors, psychological distress, economic stability, neighbourhood, physical environment and social cohesion, and food insecurity were varying associated with the outcomes.

## Conclusion

Social determinants of health were independently associated with all-cause, cardiovascular, and cancer mortality among cancer survivors but not among individuals without cancer. Different domains of SDOH may have different prognostic importance.

## Lay summary

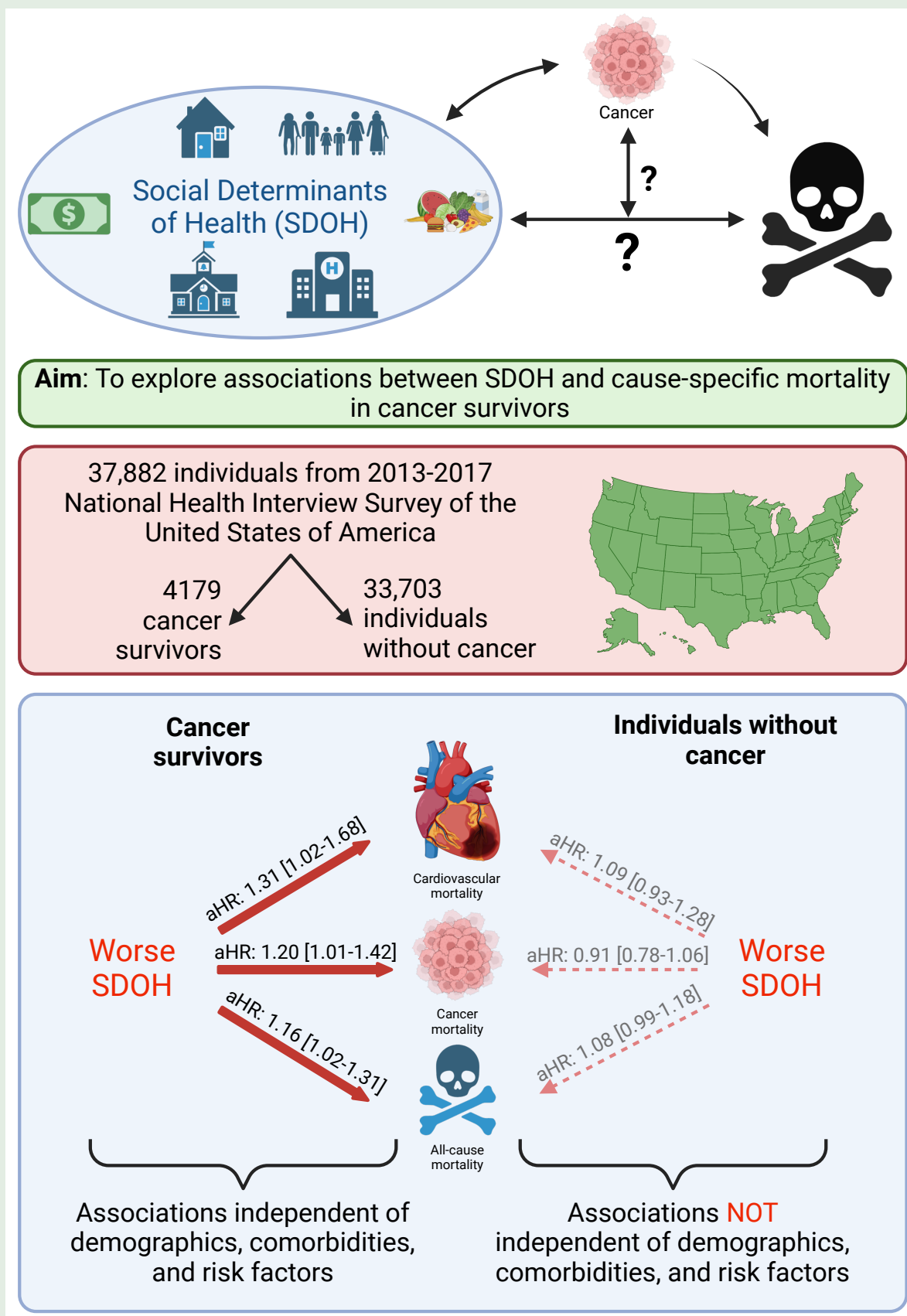
In cancer survivors, worse social deprivation contributed to higher risks of cardiovascular, cancer and overall death beyond what can be explained by demographics, coexisting illnesses, and risk factors. Specifically, psychological distress, economic stability, neighbourhood, physical environment and social cohesion, and food insecurity may be particularly influential aspects of deprivation. Meanwhile, in individuals without cancer, the contribution of social deprivation to cardiovascular and overall death may be largely explained by demographics, coexisting illnesses, and risk factors.

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## Graphical Abstract



Summary of the study aim, methods, and key results. All estimates shown were adjusted hazard ratios (aHRs; with 95% confidence intervals) for the associations between the log-transformed composite social determinants of health score and the respective risks of cardiovascular, cancer, all-cause, and other-cause mortality, adjusted for age, race, sex, comorbidities, and risk factors.

**Keywords** Disparities • Outcomes • Epidemiology • Cancer survivorship • NHIS • Death

## Introduction

Cardiovascular diseases and cancer are both common causes of death and disability worldwide—in 2021, cardiovascular diseases were accountable for 19.4 million deaths and 428 million disability-adjusted life years lost, while cancer was accountable for 9.9 million deaths and 253 million disability-adjusted life years lost.<sup>1,2</sup> Despite rising incidences of both cardiovascular diseases and cancer, cancer mortality rates have been declining due to advancing treatments and earlier detection, with an estimated 33% reduction in 2019 compared with 1991.<sup>3</sup> Such combinations in epidemiological trends have led to an increasing number of cancer survivors, who have been shown to have higher cardiovascular risks than individuals without cancer.<sup>4,5</sup> Thus, cardiovascular diseases in cancer survivors have become a growing and ever-more important clinical issue.

Among numerous factors that affect cardiovascular health, social determinants of health (SDOH) have been increasingly recognized to substantially influence cardiovascular health in both the general population and cancer survivors.<sup>6,7</sup> This was reinforced recently by a nationwide cross-sectional study of cancer survivors which found strong associations between SDOH and cardiovascular health.<sup>8</sup> However, evidence pertaining to the influence of such associations on mortality was less clear. Previous studies have shown associations between SDOH and cardiovascular/cancer mortality in the general population,<sup>9,10</sup> but these associations have rarely been studied using representative, individual-level data among cancer survivors—given their cancer history and elevated cardiovascular risk, relevant associations observed in the general population may not be directly generalizable to them. Additionally, few studies have explored SDOH comprehensively using composite metrics, with many only focusing on selected areas of SDOH. Therefore, we explored associations between SDOH and cause-specific mortality in cancer survivors using nationally representative data, specifically focusing on cardiovascular mortality as the primary outcome of interest and with SDOH quantified using a published composite score. Individuals without cancer were also studied to explore whether these associations varied with cancer survivorship.

## Methods

### Study design and source of data

Data from the National Health Interview Survey (NHIS) were used for this prospective cohort study. The NHIS, an annual health and sociodemographic survey of the US non-institutionalized population linked to the National Death Index (NDI), uses multistage probability sampling to generate nationally representative estimates. Details of NHIS and data access have been described elsewhere.<sup>8,11</sup> All data underlying this study are publicly available.<sup>11</sup> Therefore, this study is exempt from ethics review. This study and manuscript were compliant with the Strengthening the Reporting of Observational Studies in Epidemiology statement.

### Inclusion and exclusion criteria

Participants in NHIS 2013–17 with mortality follow-up data were included—only these years/iterations contained variables necessary for quantifying SDOH. Those with missing SDOH or covariate data were excluded.

### Follow-up and outcomes

All subjects were followed up from questionnaire administration to the end of 2019 or death, whichever occurred earlier, as detailed elsewhere.<sup>12</sup> The primary outcome was cardiovascular mortality. The secondary outcomes were cancer mortality and all-cause mortality. All outcomes were ascertained through the NDI using death certificate information.<sup>12</sup> There is thus no identifiable loss to follow-up.

### Data collected and ascertainment

Cancer survivorship was self-reported<sup>8</sup>; per convention, individuals with only non-melanotic skin cancer were not considered cancer survivors.<sup>8</sup> Social determinants of health was quantified using a self-reported 38 point score which has been published previously, with higher scores indicating worse deprivation.<sup>8</sup>

Covariates, including demographics (age, race, and sex) and comorbidities/risk factors (hypertension, diabetes mellitus, hypercholesterolaemia, active smoking, obesity, chronic obstructive pulmonary disease or emphysema, stroke, weekly moderate/vigorous exercise duration, weekly number of alcoholic drinks, and cardiac and liver conditions), were ascertained from self-reported data as previously detailed.<sup>8</sup>

### Statistical analysis

Survey-specific statistics with sampling weights (divided by 5 as 5 years' sample subjects were included, as per recommendations by the NHIS) were used via Stata's `svy` set of commands to produce nationally representative estimates. Due to the survey nature of the data, continuous variables were summarized as means and 95% confidence intervals (CIs), while categorical variable were summarized as proportions and 95% CIs. As individuals with missing data were excluded, there were no missing data among the analysed individuals in this study.

Due to right skewing, the composite SDOH score was analysed as standardized continuous variables after log-transformation [i.e.  $\ln(\text{SDOH} + 1)$ ; abbreviated as 'SDOH' hereafter]. As non-cardiovascular-non-cancer mortality ('other-cause mortality') constituted a competing event for cardiovascular and cancer mortality, a cause-specific approach was adopted, modelling associations between SDOH and risks of each outcome and other-cause mortality using Cox regression. Schoenfeld residual-based tests showed no violation of the proportional hazard assumption (see [Supplementary material online, Table S1 and Figures S1–S6](#)). Kaplan–Meier cumulative incidence curves (i.e. 1-KM) were used to visualize the cumulative incidence of each outcome and other-cause mortality, with grouping by quartiles of the SDOH score. Social determinants of health was quantitatively analysed as a continuous variable instead of quartiles because pairwise comparisons of individual quartiles, which are necessarily much smaller in their respective sample sizes with much fewer events than that in the overall cohort, against the lowest quartile (conventionally used as the reference group) would have led to substantially lower statistical power with additional degrees of freedom. These rendered quartile-based analysis infeasible given the already-low event rates. To account for potential non-linearity in associations, three-knot restricted cubic splines (with knots placed at the 10th, 50th, and 90th percentiles, as recommended by Harrell<sup>13</sup>) were fitted and plotted to visualize the association between SDOH and the risk of each outcome across the observed range of SDOH. Adjusted hazard ratios (aHRs) and 95% CIs were used as summary statistics, representing estimates per standard deviation increase in the SDOH score.

As the main analysis, associations in cancer survivors and individuals without cancer were modelled separately. Two multivariable models were pre-specified for each outcome based on clinical knowledge: Model 1 was adjusted for demographics, while Model 2 was adjusted for demographics, comorbidities, and risk factors. This allowed exploration of whether associations between the SDOH score and the outcomes, if any, were explained by comorbidities and risk factors, which had been shown to be associated with SDOH.<sup>8</sup>

As the main analysis found statistically significant associations between the SDOH score and cardiovascular and cancer mortality in cancer survivors with full multivariable adjustments (i.e. Model 2 as described above), a *post hoc*, exploratory analysis was performed to explore potential associations between the composite score of each domain of the SDOH score [i.e. economic stability (0–13 points), neighbourhood, physical environment, and social cohesion (NPESC; 0–5 points), psychological distress (binary), food insecurity (binary), education (0–7 points), and healthcare system (0–11 points); higher points/category indicated worse deprivation in the respective domain] and the risk of cardiovascular and cancer mortality, respectively, among cancer survivors. Similar to the above, multivariable Cox regressions (Model 2) were used. In view of the *post hoc* nature of this analysis, *P*-values were not reported, and only the aHRs and 95% CIs were reported. For non-binary-score domains, the aHRs represented estimates per point-increase in each domain's score.

*P*-values were two sided and, to avoid excessive reliance on *P*-values and potential issues with multiple hypothesis testing, were only reported for the main analysis of the primary outcome, with *P* < 0.05 considered statistically significant. All analyses were performed using Stata v16.1 (StataCorp LLC, College Station, TX, USA).

## Results

A total of 37 882 individuals were analysed (Figure 1), representing a population of 57 696 771 persons after applying sampling weights. These included 4179 cancer survivors (representing a population of 5 762 493 persons after applying sampling weights) and 33 703 individuals without cancer (representing a population of 51 934 278 persons after applying sampling weights). Their characteristics are summarized in Table 1.

Among cancer survivors, 9.9% (95% CI: 8.8–11.0%) died over a mean follow-up of 4.6 years, with cardiovascular mortality occurring in 2.2%, cancer mortality occurring in 4.6%, and other-cause mortality occurring in 3.0%. Among individuals without cancer, 2.4% died over a mean follow-up of 4.8 years, with cardiovascular mortality occurring in 0.7%, cancer mortality occurring in 0.5%, and other-cause mortality occurring in 1.1%.

### Associations between social determinants of health and mortality in cancer survivors

Among cancer survivors, worse SDOH was associated with higher cardiovascular [aHR 1.57 (1.21–2.04), *P* = 0.001], cancer [aHR 1.26 (1.06–1.50)], and all-cause [aHR 1.25 (95% CI: 1.10–1.42)] mortality when adjusted for demographics. On further adjustment for comorbidities and risk factors, point estimates were attenuated, but the corresponding 95% CIs did not include 1 [1.31 (1.02–1.68); 1.20 (1.01–1.42); and aHR 1.16 (1.02–1.31), respectively; Figure 2 and Graphical Abstract]. Restricted cubic splines showed largely linear relationships (see Supplementary material online, Figures S7–S9). No meaningful associations were found between SDOH and the competing event, i.e. other-cause mortality.

### Associations between social determinants of health and mortality in individuals without cancer

Among individuals without cancer, worse SDOH was associated with higher cardiovascular [aHR 1.28 (1.08–1.51), *P* = 0.004] and all-cause

[aHR 1.24 (1.14–1.35)] mortality only when adjusted for demographics, but not when further adjusted for comorbidities and risk factors [aHR 1.09 (0.93–1.28), *P* = 0.281 and aHR 1.08 (0.99–1.18), respectively; Figure 3]. No meaningful associations between SDOH and cancer mortality were found regardless of the multivariable model used [Model 1: aHR 1.02 (0.87–1.19); Model 2: aHR 0.91 (0.78–1.06); Figure 3]. Restricted cubic splines showed largely linear relationships for cardiovascular and cancer mortality (see Supplementary material online, Figures S10 and S11). Although the relationship for all-cause mortality displayed a slight J-shape in individuals with lower composite SDOH score, the relationship was linear in the rest of the analysed individuals (see Supplementary material online, Figure S12). Worse SDOH was associated with the competing event (other-cause mortality) in both multivariable models.

### Post hoc analysis of the components of the social determinants of health score in cancer survivors

*Post hoc*, exploratory analysis was performed for cardiovascular, cancer, and all-cause mortality in cancer survivors (Figure 4). Psychological distress was associated with higher risks of all three outcomes. Meanwhile, worse economic stability and NPESC were both associated with higher risks of cardiovascular and all-cause mortality, but not cancer mortality. Furthermore, food insecurity was associated with higher risk of cardiovascular mortality, but not cancer or all-cause mortality. Neither education nor healthcare system was associated with the risk of any of the three outcomes.

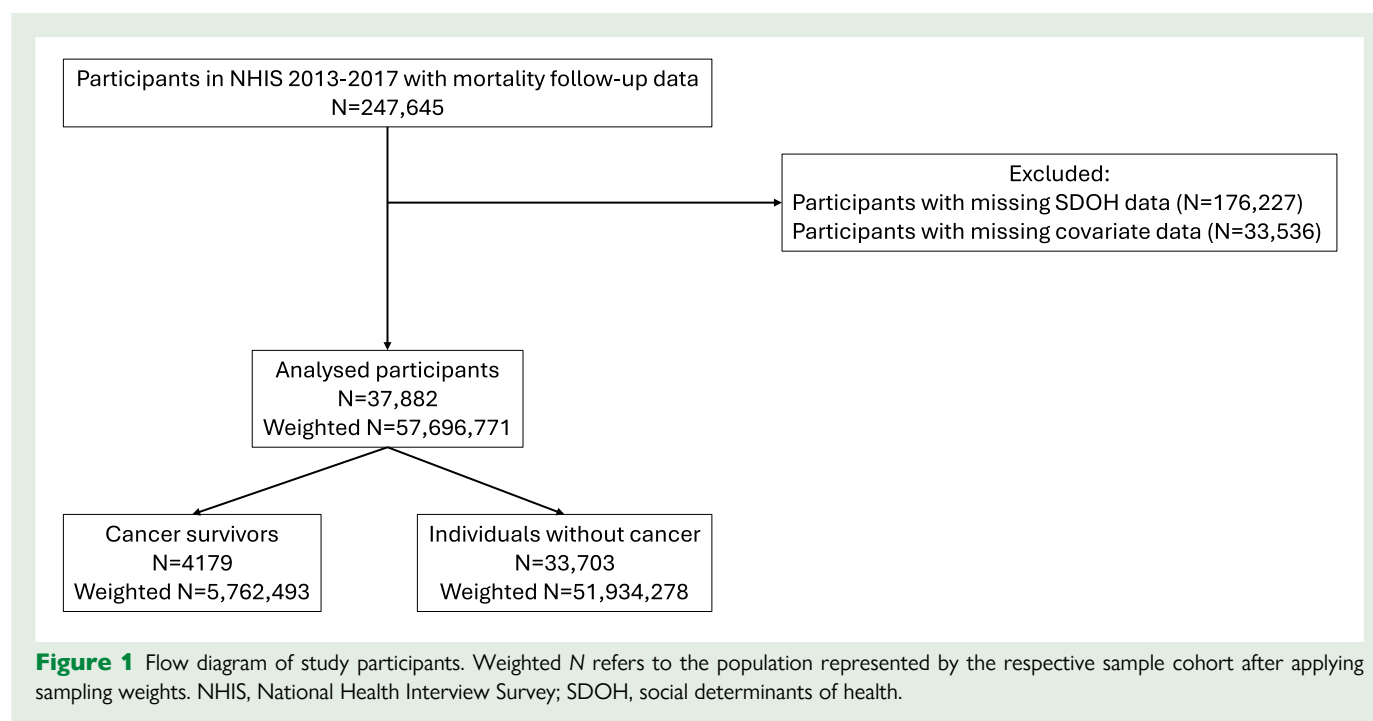
## Discussion

In this hypothesis-generating prospective cohort study using data representative of the non-institutionalized US population, associations between worse SDOH and cardiovascular, cancer, and all-cause mortality were observed among cancer survivors, which were independent of demographics, comorbidities, and risk factors. Although similar associations were observed among individuals without cancer for cardiovascular and all-cause mortality, they were not independent of and thus potentially explained by comorbidities and risk factors. Further exploratory analysis identified economic stability, NPESC, and psychological distress as domains of SDOH which were independently prognostic, albeit to different extents.

### Comparison with existing literature, implications, and actionable targets

To the best of the authors' knowledge, this was one of the first studies specifically investigating associations between SDOH and cardiovascular/cancer mortality in cancer survivors. Our findings suggested that in cancer survivors, SDOH has strong influences on cardiovascular/cancer mortality which is beyond what is explainable by comorbidities and risk factors. Contrastingly, in individuals without cancer, much of the association between SDOH and cardiovascular mortality may be 'explained away' and may therefore be driven by comorbidities and risk factors. Overall, these findings were congruent with the existing literature.<sup>9,10</sup> Particularly, the observations in individuals without cancer were not surprising, given the consistent association between worse SDOH and more comorbidities and risk factors which is likely bidirectional in nature,<sup>8,14</sup> and the strong and well-established mechanistic links between comorbidities/risk factors and cardiovascular conditions. While





these findings suggested that the relative importance of SDOH in cancer survivors may have been greater than that in individuals without cancer, they should not be seen as suggesting that SDOH are wholly unimportant for individuals without cancer, given the hypothesis-generating nature of this study, and that SDOH is known to be associated with cardiovascular morbidities—which are arguably not less important than mortality, particularly from the patients' perspective.

Our *post hoc*, exploratory analysis highlighted psychological distress as a particularly important and prognostic domain of SDOH in cancer survivors, with independent associations with all-cause, cardiovascular, and cancer mortality. Previous studies had found psychological distress and suboptimal mental health to be associated with increased cardiovascular risk both in the general population<sup>15,16</sup> and in patients with pre-existing cardiovascular conditions.<sup>17,18</sup> A previous study by our team also found associations between psychological distress and cardiovascular health in cancer survivors.<sup>19</sup> Although some of these studies suggested that such associations were largely mediated by behavioural risk factors, causal pathophysiological factors have been identified as well, such as autonomic activation, elevated cortisol levels, and endothelial dysfunction.<sup>20,21</sup> While the exact nature of such association still requires further delineation, studies have shown that rapid psychological distress screening can identify individuals at elevated cardiovascular risk, and that psychological/mental health therapies are associated with significant reductions in cardiovascular risk in both the general population and those with coronary artery disease or heart failure.<sup>22,23</sup> Although relatively little is known about the cardiovascular implications of psychological distress in cancer survivors, findings from this study—which is one of the first to report such associations in cancer survivors—highlight psychological distress as an actionable target for cardiovascular outcome improvement in cancer survivors. Further investigations confirming our observations and optimizing screening and management of psychological distress in cancer survivors are warranted.

We also observed that psychological distress was associated with higher risk of cancer mortality in cancer survivors. This was consistent

with the literature, with studies having found consistent links between psychological distress and higher risks of cancer mortality in patients with cancer.<sup>24,25</sup> Interestingly, a recent study has demonstrated that distressed patients with non-small-cell lung cancer had significantly shorter median progression-free survival compared with their non-distressed counterparts, with the association potentially driven by elevated cortisol levels in the former.<sup>26</sup> This suggested that a biological link may be at play, although the association is most likely multifactorial in nature, involving other socioeconomic factors as well. Regardless, there is evidence that mental health treatment is associated with reduced mortality in cancer survivors,<sup>27</sup> again highlighting psychological distress as a potentially actionable target for improving cancer survivors' outcomes.

In addition to psychological distress, worse economic stability and NPESC were both observed to be associated with higher risks of all-cause and cardiovascular mortality in cancer survivors. Previous studies of had shown similar associations with all-cause mortality,<sup>28,29</sup> but exploration of cardiovascular mortality has been rare. Our findings extended these associations to cardiovascular mortality and thus highlighted a window of opportunity for cardiovascular outcome improvement. Interestingly, economic stability and NPESC were associated with cardiovascular mortality, but not cancer mortality. Speculatively speaking, this may be because in cancer survivors, the risk of cancer mortality is more dependent on cancer therapy and cancer-specific healthcare, which are commonly prioritized over cardiovascular/cardo-oncology care—as the oncological issue is often more obvious—and thus is less susceptible than cardiovascular mortality to effects from social or financial vulnerability. This was partly supported by our observation that food insecurity was also associated with cardiovascular mortality but not cancer mortality—the effects of food insecurity are strongly mediated by nutritional and anthropometric factors, which are well-established cardiovascular risk factors but lack strong pathophysiological pathways affecting cancer. Overall, these findings suggested that disparity in access to cardio-oncology services

**Table 1** Summary of the characteristics of analysed individuals

	Individuals without cancer	Cancer survivors
Sample size	33 703	4179
Weighted sample size	51 934 278	5 762 493
<i>Demographic and comorbid characteristics, mean (95% CI) or proportion (%) (95% CI, %)</i>		
Age, years		
18–25	9.4 (8.8–9.9)	0.8 (0.4–1.3)
26–35	16.6 (16.1–17.2)	2.9 (2.3–3.6)
36–45	17.4 (16.9–17.9)	6.2 (5.3–7.3)
46–55	20.5 (19.9–21.1)	14.7 (13.2–16.3)
56–65	19.9 (19.3–20.5)	24.1 (22.4–25.9)
66–75	11.5 (11.1–12.0)	30.6 (28.8–32.3)
≥ 76	4.7 (4.4–5.0)	20.8 (19.3–22.3)
Male	48.8 (48.1–49.5)	49.6 (47.6–51.6)
Race		
White	85.4 (84.7–86.1)	92.2 (91.1–93.2)
Black/African American	9.2 (8.7–9.7)	5.7 (4.9–6.7)
American Indian/Alaskan native	0.8 (0.7–1.0)	0.5 (0.3–0.7)
Chinese	0.9 (0.7–1.0)	0.2 (0.1–0.7)
Filipino	1.1 (0.9–1.3)	0.4 (0.3–0.8)
Asian Indian	0.9 (0.7–1.1)	0.1 (0.0–0.2)
Other Asians	1.3 (1.1–1.5)	0.5 (0.3–0.8)
Other/multiple races	0.4 (0.4–0.5)	0.3 (0.2–0.6)
Hypertension	38.4 (37.7–39.1)	53.9 (51.8–56.0)
Diabetes mellitus	12.8 (12.3–13.2)	20.4 (18.8–22.1)
Taking insulin or diabetic pills	9.7 (9.4–10.1)	15.0 (13.7–16.5)
Hypercholesterolaemia	36.1 (35.4–36.8)	51.6 (49.6–53.7)
Active smoking	42.4 (41.6–43.2)	55.0 (52.9–57.1)
Obesity	32.9 (32.2–33.6)	31.3 (29.4–33.1)
Cardiac condition	12.5 (12.0–12.9)	25.8 (24.1–27.5)
Liver condition	2.2 (2.0–2.4)	4.4 (3.7–5.3)
Chronic obstructive pulmonary disease or emphysema	3.3 (3.0–3.5)	8.5 (7.5–9.7)
Stroke	2.3 (2.1–2.5)	5.2 (4.4–6.2)
Weekly moderate/vigorous exercise duration, minutes	262 (256–268)	238 (220–256)
Weekly number of alcoholic drink(s)	4.7 (4.4–4.9)	4.8 (4.4–5.2)
Composite social determinants of health score	6.0 (5.9–6.1)	5.3 (5.2–5.5)
Log-transformed composite social determinants of health score	1.75 (1.74–1.76)	1.62 (1.59–1.65)
Specific cancer sites/types		
Breast	N/A	20.6 (18.9–22.3) <sup>a</sup>
Prostate	N/A	17.9 (16.5–19.5) <sup>b</sup>
Lung and bronchus	N/A	3.5 (2.8–4.3)
Colorectal	N/A	6.7 (5.7–7.8)
Skin (melanomatous)	N/A	11.0 (9.9–12.2)
Bladder	N/A	3.7 (3.0–4.5)
Lymphoma	N/A	3.1 (2.5–3.9)
Uterus	N/A	3.3 (2.7–4.0) <sup>c</sup>
Pancreas	N/A	0.4 (0.3–0.8)
Leukaemia	N/A	1.9 (1.4–2.5)
Others	N/A	32.4 (30.5–34.3)
<i>Domains of the composite social determinants of health score, mean domain score (95% CI) or proportion (%) (95% CI, %)</i>		
Economic stability		
Never/previously employed	3.0 (2.7–3.2)	1.6 (1.2–2.2)
No paid sick leave	37.1 (36.4–37.9)	36.9 (34.9–38.9)
Low family income	18.1 (17.5–18.8)	16.4 (15.1–17.8)

Continued

**Table 1** Continued

	Individuals without cancer	Cancer survivors
Difficulty paying medical bills	12.9 (12.3–13.4)	11.9 (10.7–13.3)
Unable to pay medical bills	6.2 (5.8–6.5)	5.3 (4.5–6.2)
Cost-related medication non-adherence	8.7 (8.3–9.1)	8.9 (7.9–10.1)
Foregone/delayed medical care due to cost	9.2 (8.8–9.6)	7.4 (6.5–8.5)
Worried about money for retirement	47.5 (46.7–48.2)	37.9 (36.0–39.9)
Worried about medical costs of illness/accident	41.8 (41.0–42.6)	33.8 (32.0–35.7)
Worried about maintaining standard of living	37.4 (36.7–38.1)	33.5 (31.7–35.4)
Worried about medical costs of normal healthcare	25.3 (24.6–26.0)	21.8 (20.1–23.5)
Worried about paying monthly bills	24.3 (23.6–25.0)	21.8 (20.2–23.5)
Worried about paying rent/mortgage/housing costs	18.6 (18.0–19.2)	15.9 (14.5–17.5)
<i>Neighbourhood, physical environment, and social cohesion</i>		
Housing was rental/from other arrangement	27.2 (26.4–28.0)	16.7 (15.4–18.2)
People in neighbourhood did not help each other	14.4 (13.9–14.9)	11.7 (10.5–13.0)
There were not people that can be counted on in neighbourhood	14.6 (14.1–15.2)	10.9 (9.7–12.1)
People neighbourhood could not be trusted	33.6 (32.8–34.3)	31.0 (29.3–32.8)
Neighbourhood was not close-knit	12.9 (12.3–13.4)	9.5 (8.3–10.7)
Psychological distress	3.3 (3.0–3.6)	3.3 (2.7–4.1)
Food insecurity	6.5 (6.1–6.8)	5.9 (5.0–6.8)
<i>Education</i>		
Could not speak English language well/at all	1.7 (1.5–1.9)	1.3 (0.9–1.8)
Did not look up health information on internet in the past 12 months	64.7 (63.9–65.4)	59.3 (57.3–61.3)
Did not fill a prescription on the internet in the past 12 months	16.4 (15.8–17.0)	17.3 (15.8–18.9)
Did not schedule medical appointment on the internet in the past 12 months	17.2 (16.5–18.0)	15.3 (13.8–16.9)
Did not communicate with healthcare provider by email in the past 12 months	19.0 (18.3–19.8)	21.0 (19.4–22.7)
Did not use chat groups to learn about health topics in the past 12 months	4.7 (4.4–5.0)	5.4 (4.5–6.5)
Less than high school education	25.9 (25.2–26.7)	27.5 (25.8–29.2)
<i>Healthcare system</i>		
Uninsured	5.3 (5.0–5.7)	2.5 (1.9–3.1)
No usual source of care	6.2 (5.8–6.5)	2.9 (2.4–3.7)
Trouble finding a doctor/healthcare provider	3.0 (2.8–3.3)	3.7 (3.0–4.6)
Not accepted by doctor's office as new patient	2.8 (2.6–3.1)	3.5 (2.8–4.3)
Insurance not accepted by doctor's office	3.8 (3.6–4.2)	4.3 (3.6–5.2)
Delayed medical care due to not being able to get through on the phone	3.1 (2.8–3.4)	3.2 (2.6–3.9)
Delayed medical care due to not being able to get an appointment soon enough	7.9 (7.5–8.4)	8.5 (7.4–9.7)
Delayed medical care due to waiting too long at the doctor's office	4.2 (3.9–4.5)	5.4 (4.6–6.4)
Delayed medical care due to the doctor's office not being open when there was time to visit	3.7 (3.4–4.0)	3.0 (2.4–3.8)
Delayed medical care due to a lack of transportation	1.5 (1.3–1.6)	2.1 (1.6–2.7)
Dissatisfied with the quality of care/no healthcare in the past year	6.6 (6.2–6.9)	5.1 (4.3–6.1)

Continuous variables were summarized as means and 95% CIs. Categorical variables were summarized as proportions and 95% CIs.

CI, confidence interval; N/A, not applicable.

<sup>a</sup>An estimated 40.3% (95% CI: 37.5–43.0%) among female cancer survivors, and 0.5% (95% CI: 0.2–1.1%) among male cancer survivors.

<sup>b</sup>An estimated 36.1% (95% CI: 33.4–38.9%) among male cancer survivors.

<sup>c</sup>An estimated 6.5% (95% CI: 5.4–7.9%) among female cancer survivors.

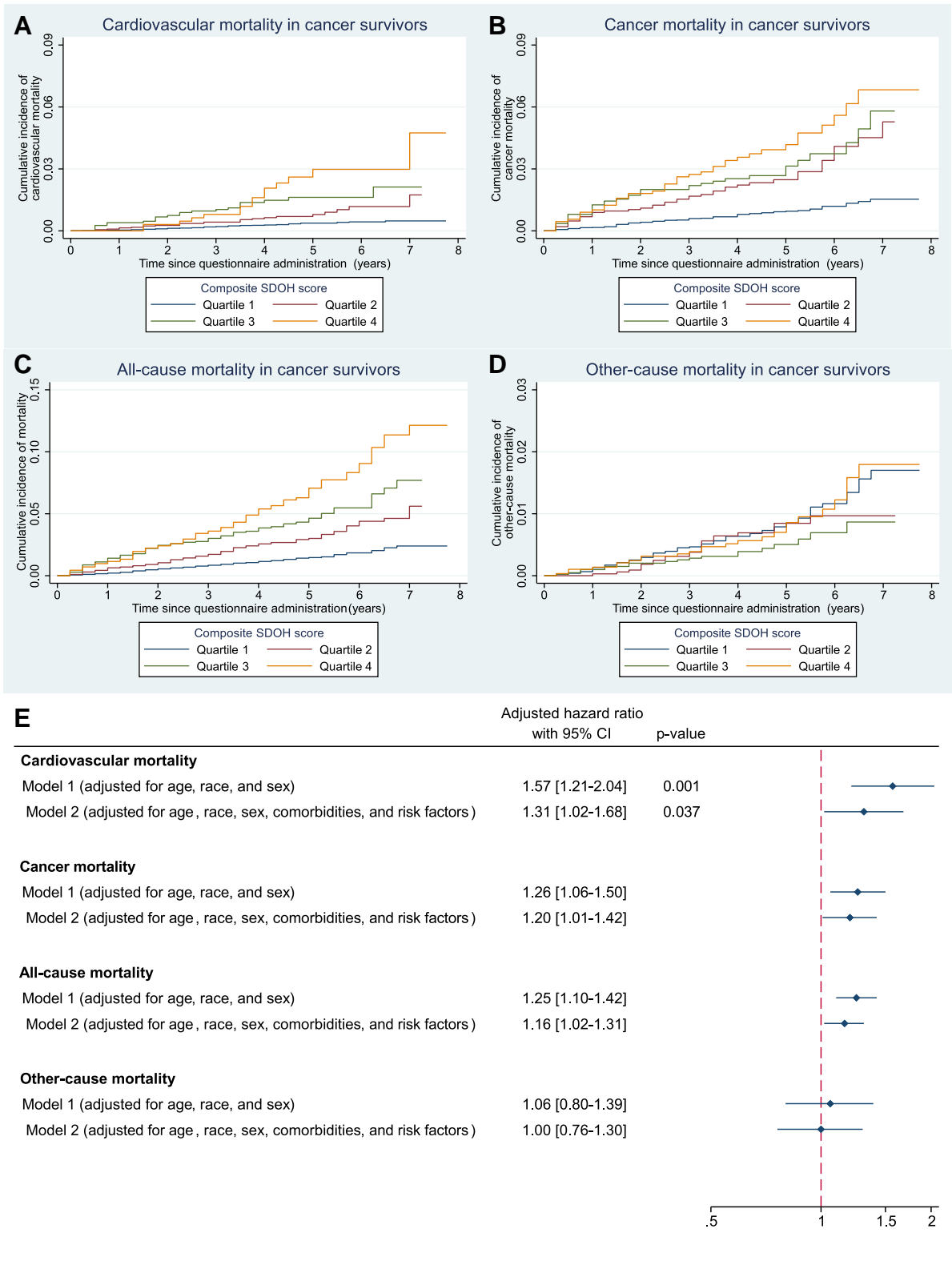
may be an important actionable target for cardiovascular outcome improvement in cancer survivors.<sup>30</sup>

## Gaps in evidence

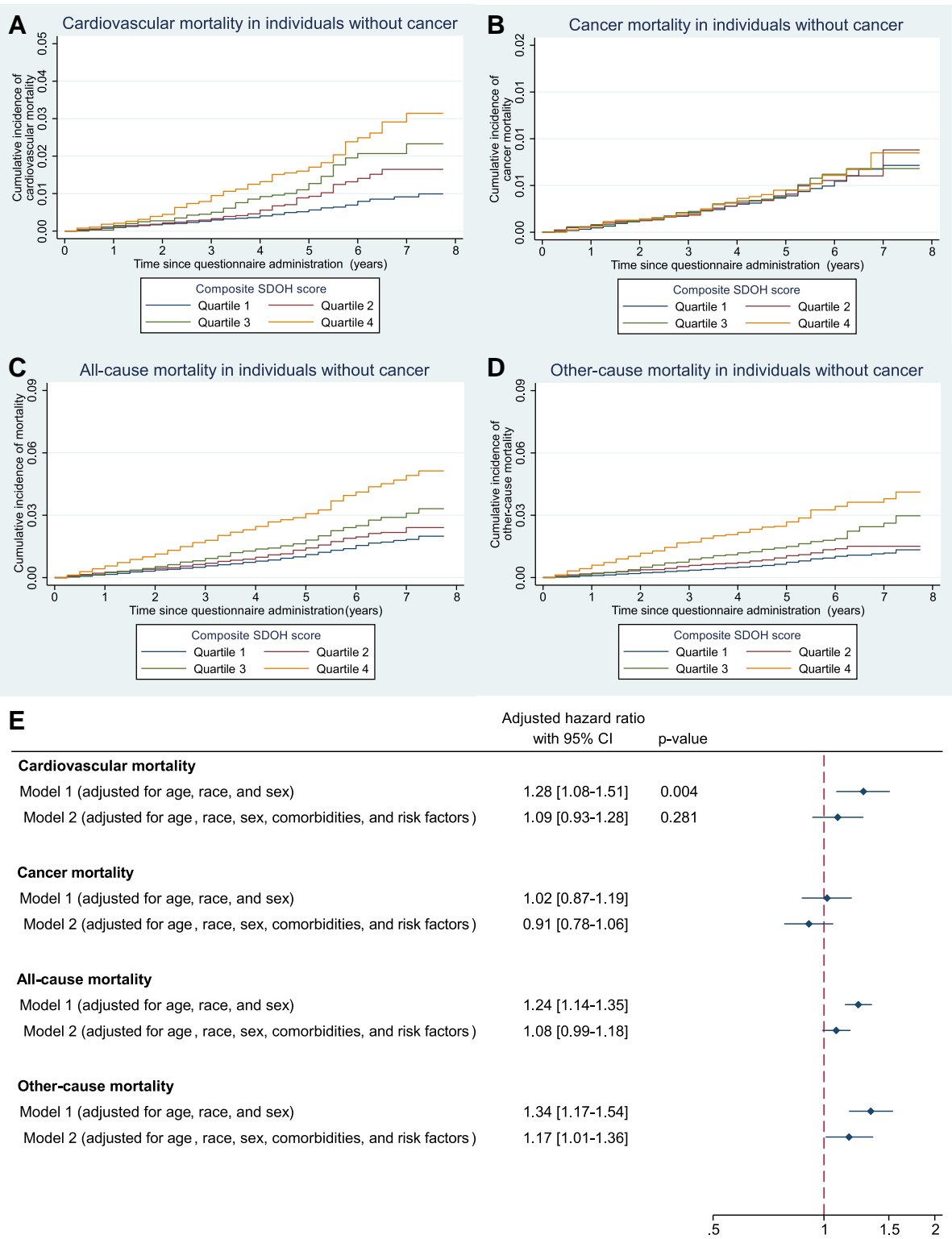
While our findings—which were hypothesis-generating in nature—highlighted several key areas of focus, further studies remain required to confirm these findings, as well as exploring the underlying drivers for better mechanistic understanding and identification of more specific/lower level actionable targets.

Meanwhile, whether the observed SDOH–mortality associations differ by race/ethnicity warrants further research.<sup>6,31</sup> This was not possible in the current study due to the low rates of cardiovascular and cancer mortality preventing subgroup analyses with meaningful statistical power. Nevertheless, others had shown that socioeconomic deprivation may have significantly different effects on cardiovascular and cancer outcomes depending on race/ethnicity.<sup>32</sup> These effects and SDOH–race/ethnicity interactions may also vary geographically due to differences in racial/ethnic distributions and other sociocultural factors.

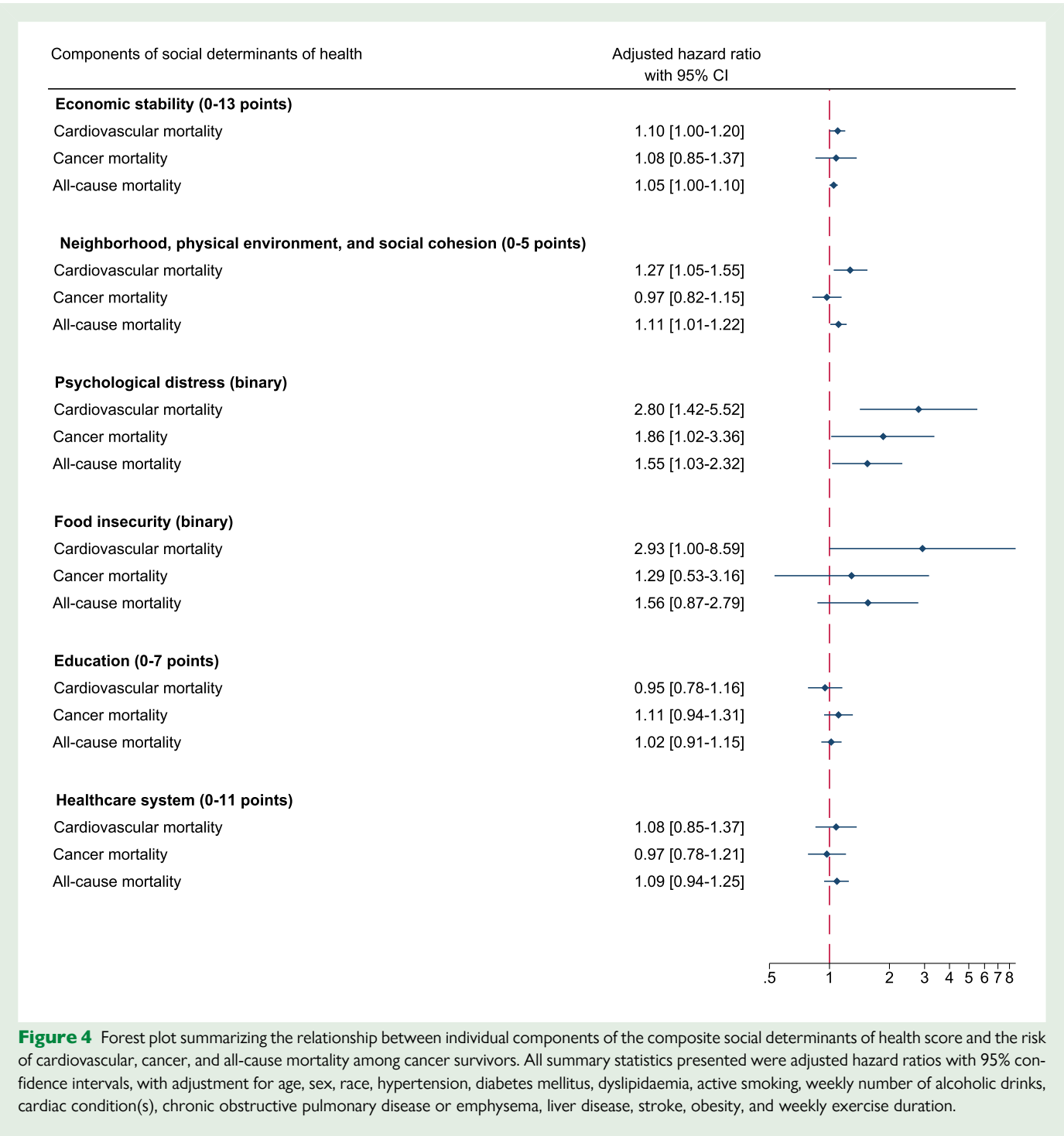




**Figure 2** Kaplan–Meier cumulative incidence curves of cardiovascular (A), cancer (B), all-cause (C), and other-cause (D) mortality in cancer survivors. Associations between the log-transformed composite social determinants of health score and each outcome were visualized in forest plots (E). All summary statistics presented were adjusted hazard ratios with 95% confidence intervals. Comorbidities and risk factors in Model 2 included hypertension, diabetes mellitus, dyslipidaemia, active smoking, weekly number of alcoholic drinks, cardiac condition(s), chronic obstructive pulmonary disease or emphysema, liver disease, stroke, obesity, and weekly exercise duration.



**Figure 3** Kaplan–Meier cumulative incidence curves of cardiovascular (A), cancer (B), all-cause (C), and other-cause (D) mortality in individuals without cancer. Associations between the log-transformed composite social determinants of health score and each outcome were visualized in forest plots (E). All summary statistics presented were adjusted hazard ratios with 95% confidence intervals. Comorbidities and risk factors in Model 2 included hypertension, diabetes mellitus, dyslipidaemia, active smoking, weekly number of alcoholic drinks, cardiac condition(s), chronic obstructive pulmonary disease or emphysema, liver disease, stroke, obesity, and weekly exercise duration.



**Figure 4** Forest plot summarizing the relationship between individual components of the composite social determinants of health score and the risk of cardiovascular, cancer, and all-cause mortality among cancer survivors. All summary statistics presented were adjusted hazard ratios with 95% confidence intervals, with adjustment for age, sex, race, hypertension, diabetes mellitus, dyslipidaemia, active smoking, weekly number of alcoholic drinks, cardiac condition(s), chronic obstructive pulmonary disease or emphysema, liver disease, stroke, obesity, and weekly exercise duration.

Furthermore, the aforementioned potential importance of access to cardio-oncology services may not only be related to socio-economic barriers in access, but also physicians' awareness of cardio-oncology considerations in cancer survivors. Studies have demonstrated that, despite drastic increases in the volume of cardio-oncology research and evidently increasing cardiovascular burden among cancer survivors,<sup>33–35</sup> healthcare professionals' knowledge of cardio-oncology and adherence with guideline-recommended practices have remained poor.<sup>36,37</sup> Raising awareness of cardio-oncology among healthcare professionals and aligning

practice with guidelines may be important steps in improving cardiovascular outcomes in cancer survivors.

In addition, further studies of the interactions between different domains of SDOH are warranted. Various domains of SDOH are often interrelated. For instance, financial difficulties have been associated with psychological distress.<sup>38</sup> This contributes to the difficulty of quantifying SDOH in general. While the current study made use of a well-published composite SDOH score, the simple, additive nature of the score may not be optimal in capturing the health implications of SDOH. Further studies refining tools for

quantifying SDOH with consideration of these complex interactions are warranted.

## Limitations

Notwithstanding this study's nationally representative nature, it was limited by NHIS' self-reported nature which predisposes to information and recall bias, and the lack of individual data adjudication potentially predisposing to mortality data miscoding. Among cancer survivors, there was also no information on the status of cancer (active, remitted, recurred, second primary, and etcetera) or the cancer therapy which have been or were being used, both of which have a significant impact on cardiovascular risks.<sup>6</sup> Despite having accounted for a large number of potential confounders, the existence of residual confounding and unobserved confounders cannot be ruled out, which is a limitation inherent to observational studies in general. Also, a large proportion of individuals were excluded due to missing data, potentially introducing selection bias which may have influenced the findings. Additionally, low event rates precluded subgroup/exploratory analyses, and the observational nature precluded causal inferences. Furthermore, although the composite SDOH score used in this study has been used in other research studies, it was designed for the American population, and so our findings may not be directly generalizable to populations in other countries/regions. Lastly, despite the prognostic nature of this study, we could not use the Fine and Gray subdistribution model to account for competing risks. This was solely due to software limitations, as neither Stata nor R had readily available packages for Fine–Gray competing risk regression that could account for complex survey designs. We have therefore handled the competing risk scenario with a cause-specific approach, with all competing events modelled and described separately. This approach has been used by other teams in numerous prior studies, including researchers at the authoritative National Center for Health Statistics of the United States.<sup>39–41</sup> Overall, given these limitations, our findings are hypothesis-generating in nature, and further confirmatory/mechanistic studies are necessary.

## Conclusions

Social determinants of health were independently associated with all-cause, cardiovascular and cancer mortality among cancer survivors but not among individuals without cancer. Different domains of SDOH may have different prognostic importance, with psychological distress, economic stability, NPESC, and food insecurity possibly being particularly prognostic domains of SDOH. Further studies are required to confirm these hypothesis-generating findings and explore underlying mechanisms.

## Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

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## Author contribution

J.S.K.C.: conceptualization, methodology, data curation, formal analysis, visualization, writing—original draft, and writing—review and editing;

D.I.S.: conceptualization and writing—review and editing; Y.L.A.C., Q.L., and O.H.-I.C.: writing—review and editing; E.C.D., K.N., T.L., and A.L.: supervision and writing—review and editing; G.T.: resources, funding acquisition, and writing—review and editing.

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## Ethical approval

This study was exempt from ethics review due to the use of deidentified and publicly available data.

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## Data availability

All data underlying this study are publicly available.

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