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Abbreviated score to assess adherence to the 2018 WCRF/AICR Cancer Prevention Recommendations and risk of cancer in the UK Biobank

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Conflict of Interest

The authors declare no potential conflicts of interest.

Abstract

Background

The WCRF/AICR Cancer Prevention Recommendations are lifestyle-based guidelines which aim to reduce cancer risk. This study investigated, in the UK Biobank, associations between an abbreviated score to assess adherence to these Recommendations and the risk of all cancers combined and of 14 cancers for which there is strong evidence for links with diet, adiposity, and physical activity.

Methods

We used data from 288,802 UK Biobank participants (mean age 56.2 years), cancer-free at baseline. An abbreviated version of the 2018 WCRF/AICR Score was calculated to assess adherence to five Recommendations on i) body weight, ii) physical activity, iii) fruits, vegetables and dietary fibre, iv) red and processed meat, and v) alcohol. Multivariable Cox proportional hazards models were used to analyse associations between the abbreviated score (range 0-5 points) and cancer incidence, adjusting for confounders.

Results

During a median follow-up of 8.2 years (IQR 7.4-8.9), 23,448 participants were diagnosed with cancer. The abbreviated score was inversely associated with risk of cancer overall (HR:0.93; 95% CI:0.92-0.95 per 1-point increment), and breast (HR:0.90; 95% CI:0.87–0.94), colorectal (HR:0.86; 95% CI: 0.83–0.90), lung (HR:0.89; 95% CI:0.84-0.94), kidney (HR:0.83; 95% CI:0.76-0.90), pancreatic (HR:0.86; 95% CI: 0.79-0.94), uterine (HR:0.79; 95% CI: 0.73-0.86), oesophageal (HR:0.82; 95% CI: 0.75-0.90), stomach (HR:0.89; 95% CI: 0.79-0.99), and liver (HR:0.80; 95% CI:0.72–0.90) cancers.

Conclusions

Greater adherence to the Cancer Prevention Recommendations, assessed using an abbreviated score, was associated with reduced risk of all cancers combined and of nine site-specific cancers.

Impact

Our findings support compliance to these Recommendations for cancer prevention.

Keywords: Cancer Prevention Recommendations, lifestyle, cancer risk, UK Biobank

Abbreviations and Acronyms: A levels: Advanced levels, AS levels: Advance Subsidiary levels, AICR: American Institute for Cancer Research; BMI: body mass index; CSE: Certificate of Secondary Education; CVD: cardiovascular disease GCSE: General Certificate of Secondary Education; HNC: Higher National Certificate; HND: Higher National Diploma; IPAQ: International Physical Activity Questionnaire, MET: metabolic-equivalent, MVPA: moderate to vigorous physical activity, NDNS: National Diet and Nutrition Survey, NVQ: National Vocational Qualifications, O levels: General Certificate of Education Ordinary Level; PA: physical activity; UPF: ultra-processed food; WCRF: World Cancer Research Fund.

Introduction

The risk of developing several common cancers is modulated by lifestyle factors including diet, physical activity, and body weight and composition and, in the UK, approximately 40% of all cancers are attributable to such factors(1). The World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) Cancer Prevention Recommendations aim to promote a healthier lifestyle and reduce the risk of cancer(2). Following the publication of the latest update to the recommendations in 2018, a scoring system, known as the '2018 WCRF/AICR Score', was created to standardise the assessment of adherence to these recommendations and to facilitate comparability of findings across studies(3,4). The score includes seven of the recommendations, with an optional eighth regarding breastfeeding(3). Several studies have reported inverse associations between greater adherence to the 2018 Cancer Prevention Recommendations and the risk of cancer overall as well as of cancer at a few individual sites, mainly breast(5-11), colorectal(12-14) and lung(9,15).

We have previously described operationalisation of the 2018 WCRF/AICR Score in the UK Biobank (which recruited >500,000 people) to derive a total score ranging from 0 to 7 points, including the use of dietary data collected using a touchscreen questionnaire completed by all participants at baseline, as well as using a 24-hour dietary assessment tool (Oxford WebQ) which is available for a subset of participants only(16). However, the use of the 24-hour dietary assessment data reduced the cohort available for analysis to <100,000 participants. The creators of the 2018 WCRF/AICR score encourage researchers to fully apply the standardised scoring system, but appreciate that this may not always be possible due to limited data collection. Our recent systematic review revealed that the majority of studies to date have used adapted versions of the score - in particular, the waist circumference sub-component and the recommendation to "limit the intake of 'fast foods' and other processed foods high in fat, starches or sugar" (assessed as ultra-processed foods (UPFs)) tended to be excluded(17). Data collection methods yielding more granular dietary

data, such as 24-hour dietary recalls, are associated with greater participant and researcher burdens and higher costs compared with other methods such as food frequency questionnaires (FFQs); therefore this type of granular data is often not collected in large-scale epidemiological studies(18).

The dietary data collected in UK Biobank using the touchscreen questionnaire allow for assessment of adherence to five out of the seven recommendations in the 2018 WCRF/AICR Score concerning i) body weight, ii) physical activity, iii) fruits, vegetables and fibre intake, iv) red and processed meats intake, and v) alcohol consumption. The aim of the current study is to investigate associations between an 'abbreviated score' comprising these five recommendations to assess adherence to the 2018 WCRF/AICR Cancer Prevention Recommendations among participants in the UK Biobank and the risk of all invasive cancers as well as of 14 specific cancers (prostate, breast, colorectal, lung, uterine, kidney, bladder, ovarian, pancreatic, head and neck, oesophageal, stomach, liver, and gallbladder) for which there is strong evidence for a relationship with diet, nutrition and/or physical activity(19).

Materials and Methods

Study participants

The UK Biobank prospective cohort study recruited >500,000 participants aged 37 to 73 years between 2006 and 2010. Eligibility criteria and methods are reported elsewhere(20). At the baseline assessment centre visit, participants completed the touchscreen questionnaire which collected data on participant characteristics including sociodemographic factors, habitual diet, physical activity, and health, and anthropometric measurements were made by trained staff. The UK Biobank study was conducted according to the Declaration of Helsinki and ethical approval was granted by the North West Multi-Centre Research Ethics Committee (reference: 06/MRE08/65). All participants provided informed consent.

Abbreviated score to assess adherence to the WCRF/AICR Cancer Prevention Recommendations

We created an abbreviated score to assess adherence to the 2018 WCRF/AICR Cancer Prevention Recommendations as described in detail in the **Supplementary Methods** with a summary of the scoring system in **Table 1**. The abbreviated score included five of the Recommendations (namely, body weight; physical activity; fruits, vegetables and dietary fibre; red and processed meat; alcohol), and included the sub-components of the recommendations to 'be a healthy weight' and 'eat a diet rich in wholegrains, vegetables, fruits and beans', and had a possible range of 0-5 points.

Briefly, adherence to the 'Be a healthy weight' recommendation was assessed using data on BMI, calculated from data on weight and height, and on waist circumference. Physical activity data were self-reported using a validated short form of the International Physical Activity Questionnaire (IPAQ)(21). Time spent in moderate and vigorous physical activity (MVPA) was used to allocate scores for this recommendation.

Touchscreen questionnaire data on daily consumption of fresh fruit, dried fruit, cooked vegetables and raw vegetables were used to calculate total fruit and vegetable intake, which was converted to intake in grams per day by multiplying the frequency by the corresponding mean portion size in grams(22,23). We calculated a partial fibre score based on the intake of fresh fruit, dried fruit, raw vegetables, cooked vegetables, bread and breakfast cereals as described by Bradbury and colleagues(23) to assess adherence to the dietary fibre sub-component. As the partial fibre score(23) does not fully estimate total fibre intake, we applied a tertile-based approach to allocate points to this sub-component(3,4).

We used data on the intake of beef, lamb/mutton, and pork to estimate red meat intake, and responses to the question "How often do you eat processed meats (such as bacon, ham, sausages, meat pies, kebabs, burgers, chicken nuggets)?" to estimate processed meat

intake. Intakes in grams per week were calculated by multiplying the frequency by standard portion sizes(22) and by 52.5g for red and processed meats, respectively.

To assess adherence to the recommendation on alcohol consumption, we used data for the intake of red wine, white wine or champagne, beer or cider, spirits or liqueurs, fortified wine, and other alcoholic drinks. The number of units per week were calculated by multiplying the frequency of intake per week by the number of units corresponding to each drink. We applied the guidelines for alcohol consumption in the UK(24), as Shams-White et al. advise using national guidelines to assess adherence to this recommendation, where applicable(4).

Participants were allocated 1 point for fully meeting, 0.5 points for partially meeting or 0 points for not meeting each score component (recommendation). Scores for individual components were summed to yield a total score for each individual ranging from 0 to 5 points.

Covariates

Data on sociodemographic and lifestyle factors, including sex, ethnicity, and smoking status, were self-reported and collected using a touchscreen questionnaire during the baseline assessment centre visit. Age was calculated from date of birth. Townsend Deprivation Index, an area-based measure of deprivation, was derived from each participant's postcode at the time of study recruitment, and was based on data from the preceding national census(25). Smoking status was categorised as 'never', 'previous' or 'current' smoker.

Assessment of outcomes

We used electronically-linked, population-based cancer registry data (National Cancer Data Repository, Scottish Cancer Registry and Welsh Cancer Surveillance & Intelligence Unit) to identify prevalent and incident cancer cases. Data were available until July 2019 for England and Wales and October 2015 for Scotland. Cancers were classified using the International Classification of Diseases, 10th revision (ICD-10) and we included: i) overall incident cancer (i.e. all cancers combined, C00-C97, excluding non-melanoma skin cancer (C44)) and ii) 14

individual lifestyle-related cancers (26): head & neck (C00-C14), oesophageal (C15), stomach (C16), colorectal (C18-C20), liver (C22), gallbladder (C23-24), pancreatic (C25), lung (C33-34), breast (C50), uterine (C54-C55), ovarian (C56), prostate (C61), kidney (C64-C65) and bladder (C67). We also considered sub-sites within the colorectum individually: colon (C18.0), proximal colon (C18.0-18.4), distal colon (C18.5, C18.7) and rectum (C19-C20).

Statistical analyses

We excluded UK Biobank participants for whom we were not able to derive the abbreviated score (i.e., who had missing data for one or more components of the score); with a prevalent cancer at baseline; and with missing covariate data (see below and **Supplementary Figure 1**).

Cox-proportional hazard models were used to investigate associations between the abbreviated score and the risk of all cancers combined, as well as the 14 cancer sites individually. UK Biobank participants were followed over time from recruitment to cancer diagnosis or date of death, or end of follow-up (July 2019 for England and Wales and October 2015 for Scotland), whichever occurred first. We conducted a landmark analysis to minimise the effect of reverse causation by excluding participants diagnosed with cancer in the first two years of follow-up. The abbreviated score was analysed as a continuous variable by estimating the hazard ratio (HR) and 95% confidence interval (CI) associated with a 1-point increment in score. We also ran the model according to approximate score tertiles of the study population, with the lowest score tertile as the reference group.

In model 1, we included age, sex (if applicable), Townsend Deprivation Index and ethnicity as covariates. We also re-ran model 1 stratified according to smoking status. Model 2 included the covariates from model 1 plus smoking status. Further, we tested for interactions with the score (continuous) by sex and by smoking. Additional analyses were performed for incident breast cancer by stratifying according to menopausal status, which was estimated

by calculating age at diagnosis or follow-up, as appropriate, and categorising women aged ≤50 years as pre-menopausal and those aged >50 years as post-menopausal.

For comparative purposes, we compared the abbreviated score with the 'total' score computed in our previous analysis (which used the 24-hour dietary assessment data and included seven components), calculating Spearman's correlation and mean differences for the subgroup of participants for whom both scores could be computed.

Finally, we compared HRs for associations between the abbreviated (5-point) score and the total 2018 WCRF/AICR score (7 points) for those participants for whom both scores were available (n=76,550, free from cancer at baseline and without missing covariate data).

Statistical analyses were performed using StataMP v16 (Stata Corp, College Station, TX, USA).

Data Availability Statement

The data generated in this study will be available from UK Biobank for all bona fide researchers who are granted access to UK Biobank data.

Results

Participant characteristics

A total abbreviated score was calculated for 314,616 UK Biobank participants, of whom 288,702 participants did not have a cancer diagnosis at baseline and had complete data for the covariates included in model 1 (**Supplementary Figure 1**). Comparisons between the characteristics of the included vs. excluded participants are presented in **Supplementary Table 1**. **Table 2** describes the characteristics of all included participants according to approximate score tertiles. The mean age was 56.2 years (range 38-72 years), and the majority of participants were recruited in England and were White. Most participants were

educated to the O level/GCSE or equivalent level or above. Over half of the participants had never smoked and approximately a third were former smokers. Those with higher adherence scores were more likely to be female and to be never smokers and less likely to be White.

Total abbreviated scores

The mean abbreviated score across all participants was 2.64 (0.91) points (**Supplementary Figure 2**)**.** Participants adhered most frequently to the recommendations on body weight, physical activity and the sub-recommendation on fruit and vegetable intake; fewer participants fully adhered to the recommendations on red and processed meat intake and on alcohol consumption (**Figure 1**). The original 'total' score and the abbreviated score were positively correlated (Spearman's rho=0.80, p<0.001, n=127,667). The mean difference between the total score and the abbreviated score was 1.2 (SD 0.6) points, with 3.6% of points lying outside the lower and upper agreement limits, and there was no evidence to suggest proportional bias (**Supplementary Figure 3**).

Associations between abbreviated score and cancer risk

During a median follow-up of 8.2 years (IQR 7.4-8.9), 23,448 participants were diagnosed with cancer. When the abbreviated score was assessed as a continuous variable, there were statistically significant associations with the risk of all cancers combined (HR per 1-unit increment in score: 0.93 (95% CI 0.92-0.95)), as well as breast (HR:0.90 (95% CI: 0.87-0.94)), colorectal (HR:0.86 (95% CI: 0.83-0.90)), lung (HR:0.89 (95% CI: 0.84-0.94)), kidney (HR:0.83 (95% CI: 0.76-0.90)), pancreatic (HR:0.86 (95% CI: 0.79-0.94)), uterine (HR:0.79 (95% CI: 0.73-0.86)), oesophageal (HR:0.82 (95% CI: 0.75-0.90)), stomach (HR:0.89 (95% CI 0.79-0.99)) and liver (HR:0.80 (95% CI 0.72-0.90)) cancers (**Table 3**). When analyses were stratified by smoking status (**Supplementary Table 3**), statistically significant associations between the abbreviated score and lung cancer were present among former and current smokers only, associations with kidney cancer were present among never smokers only, among those with pancreatic, uterine, and liver cancer associations were

present among non-smokers (i.e., never and former smokers) only, and associations with oesophageal and stomach cancer among former smokers only.

Participants in the highest approximate score tertile (scoring 3.25-5 points) had reduced risk of all cancers combined (HR:0.88 (95% CI 0.85-0.90) and of breast (HR:0.83 (95% CI 0.77-0.90)), colorectal (HR:0.75 (95% CI 0.69-0.83)), lung (HR:0.81 (95% CI 0.72-0.91)), kidney (HR:0.69 (95% CI 0.58-0.83)), pancreatic (HR:0.74 (95% CI 0.62-0.89]), uterine (HR:0.62 (95% CI 0.52-0.75)), oesophageal (HR:0.64 (95% CI 0.51-0.81)), stomach (HR:0.75 (95% CI 0.58-0.98)), and liver (HR:0.74 (95% CI 0.57-0.98)) cancers compared with participants in the lowest tertile (scoring ≤2.25 points) (**Table 4**). Further, participants in the middle tertile, with scores between 2.5 to 3 points, had lower risk of all cancers combined, and of colorectal, lung, kidney, pancreatic, uterine, and oesophageal cancers compared with those in the lowest tertile (**Table 4**).

When we tested for interactions between the continuous score and sex (when applicable), we found evidence for an interaction for colorectal cancer ($p<0.001$), oesophageal cancer ($p=0.036$), head and neck cancer ($p=0.013$), and liver cancer ($p<0.001$). For colorectal and oesophageal cancers, the risk of cancer per unit increase in adherence was greater in men than in women. For head and neck and liver cancers, risk of cancer increased with increasing adherence in women and decreased with increasing adherence in men. When assessing interactions with score tertiles, these were statistically significant for colorectal and liver cancers only. There was no evidence to suggest interactions between the score and smoking status for any of the cancers investigated.

When incident breast cancer analyses were stratified according to estimated menopausal status, there was a statistically significant reduced risk for post-menopausal women (aged >50 years at diagnosis) (**Table 3** and **Table 4**). When the analyses for colorectal cancer were stratified according to sub-site, risk was significantly lower for all sub-sites (**Table 3** and **Table 4**).

We observed no significant associations between the abbreviated score and the risk of prostate, ovarian, bladder, head and neck or gallbladder cancers.

When we compared the HRs for associations between i) the abbreviated (5-point) score and ii) the total 2018 WCRF/AICR score (7 points) as continuous variables for participants for whom both scores were available, we found similar associations in terms of HRs and p-values for both scores (**Supplementary Table 4**). The exceptions to this were: the associations with bladder, oesophageal, and liver cancer that were significant for the abbreviated score but not for the total score. In contrast, in these participants, there were significant associations with kidney cancer when using the total score (HR:0.80 (95% CI 0.69-0.93), p=0.004), but not the abbreviated score (HR:0.86 (95% CI 0.73-1.02), p=0.077).

Discussion

This study describes the creation of a five-point abbreviated score, based on the 2018 WCRF/AICR Score(3), to assess adherence to the 2018 WCRF/AICR Cancer Prevention Recommendations and its association with the risk of lifestyle-related cancers in almost 300,000 UK Biobank participants. Participants with a higher abbreviated score, representing greater adherence to five of the Recommendations, had a 12% lower risk of all cancers combined compared with those in the lowest tertile, and each 1-point increment in score reduced risk by 7%. In our previous analysis using the total 7-point score, we also observed a 7% reduction in risk per 1-point increment in score and, compared with those in the lowest score tertile (≤3.5 points), participants in the highest score tertile (4.5–7 points) had a 16% lower risk of developing all cancers combined(27). Only one other study has investigated associations between adherence score and the risk of all cancers combined. The Cohort of Swedish Men and the Swedish Mammography Cohort included 12,693 incident cancers over 15 years of follow-up and reported a 3% reduction in cancer risk per 1-point increment in score(28). In that study, participants with highest scores (4.1–7 points) had a 12% lower risk compared with those scoring 0-2 points(28), patterns similar to those seen here. While any findings relating to all cancers combined need to be interpreted with caution as they include

cancers with different aetiologies (and a slightly different “mix” of cancers in each setting), these findings underscore the importance of encouraging compliance to the Recommendations to yield widespread benefits in reducing overall cancer risk. We also assessed associations between the abbreviated score and the risks of 14 lifestyle-related cancers individually. The significant associations found here for lung, pancreatic, uterine, and stomach cancers were not seen in our previous analysis using the total score(27), likely due, at least in part, to the considerably larger numbers of cancers in the current analysis.

We observed a 10% lower risk of breast cancer per 1-point increment in abbreviated score, in line with findings from our previous analyses of the total score(27). However, when stratified according to menopausal status, this association was only statistically significant for breast cancers diagnosed in women aged >50 years. This finding should be interpreted with care because the number of pre-menopausal cancers was relatively low (*n* 359) and the point estimate for the HR was 0.91. To date, breast cancer is the most studied cancer in relation to adherence to the 2018 Cancer Prevention Recommendations, and there have been seven studies(17), of which five(7-11) reported a reduction in breast cancer risk with greater adherence scores. One study which used UK Biobank data found no associations between a 6-point version of the score and breast cancer *in situ* risk (we included invasive cancers only), although there was an 8% reduction in risk per 1-point increment in score in the fully-adjusted model among women who did not report dietary changes in the past five years(8). Direct comparisons of findings between studies should be interpreted cautiously because of differences in the way in which adherence to the Recommendations has been assessed and, therefore, between scores(17).

We also observed a 14% reduction in colorectal cancer risk per 1-point increment in the abbreviated score, and participants in the highest score tertile had a 25% lower risk compared with those scoring ≤2.25 points (lowest tertile). This is a stronger association than in our previous analyses where we found a 10% reduction in risk per 1-point increment in total score(27). When running the present analyses according to colorectal cancer subsites,

we detected significant associations between the abbreviated score and risk of proximal colon cancers and of rectal cancers, which we did not observe previously(27). To our knowledge, five studies(9,12-14,29) have assessed associations between adherence to the 2018 Cancer Prevention Recommendations and colorectal cancer risk, and all reported lower risk with higher adherence scores.

One of the stronger associations observed in this study was for lung cancer, where we found 11% lower risk per 1-point increase in the abbreviated score, and participants scoring ≥3.25 points had a 19% lower risk compared with those scoring ≤2.25 points. These associations were limited to those who were current or former smokers. In a study which used an adapted version of the 2018 WCRF/AICR Score specific to lung cancer (Ad-LC WCRF/AICR Score), which included an additional eighth component regarding smoking(15), lung cancer risk was 47% lower in participants with higher adherence (>5 points) compared with participants scoring ≤3 points, and each 1-point increase in Ad-LC WCRF/AICR Score reduced risk by 34%(15). In the NIH-AARP Diet and Health study, significant reductions in lung cancer risk with higher scores were observed only among male former smokers (16% decrease per 1-point increment in score) and female current smokers (11% decrease per 1-point increment in score)(9). These findings, and ours, suggest aetiological differences in lung cancer subtypes. Specifically, they raise the possibility that lifestyle factors may be more aetiologically important in small cell carcinomas (which occur more commonly in smokers) than in adenocarcinomas (which occur more often in never smokers(30)); further research on this issue is warranted.

In the present study, we observed no significant associations between the abbreviated score and risk of prostate cancer, in line with our earlier analyses using the total 2018 WCRF/AICR score(27). These findings are in agreement with findings from the NIH-AARP Diet and Health study(9). One other case-control study has investigated associations between 2018 WCRF/AICR Score and prostate cancer risk, including 398 cases and 302 controls, and

reported a 19% risk reduction per 1-point increase in score, but no differences when comparing score tertiles(31).

Each 1-point increment in the abbreviated score resulted in a 14% reduction in the risk of pancreatic cancer, and risk was 26% lower in participants in the highest, compared with the lowest, score tertiles. In one other study that fully-operationalised the 2018 WCRF/AICR Score in 95,962 participants in the US, a 12% reduction in pancreatic cancer risk per 1-point increment in score and a 33% lower risk in participants in the highest compared with the lowest tertile was reported(32). These findings add to the WCRF/AICR assessment of the role of lifestyle in pancreatic cancer (i.e., strong evidence for increased risk with greater body fatness, limited evidence for additional lifestyle and dietary components such as red and processed meat, sugar-sweetened beverages, and alcoholic drinks)(2) and suggest more attention should be paid to lifestyle in the prevention of this cancer .

A recent case-control study including 454 cases and 908 age-matched controls reported an inverse association between adherence score and the risk of uterine cancer, with a 28% reduction in risk per 1-point increment in score(33). In our study, which included 684 cases, a 1-point increase in the abbreviated score was associated with a 21% reduction in risk. Consequently, it seems likely that adherence to the Cancer Prevention Recommendations lowers risk of uterine cancer.

As anticipated, the mean abbreviated score was significantly lower than the original total score, but the two scores were positively and significantly correlated and there was no evidence of proportional bias. By using this abbreviated score, we increased the sample size to from 93,630 to 288,702 participants (without a prevalent cancer at baseline), and the number of incident cancers by over three-fold from 7,296 to 23,448, thus increasing the statistical power to detect associations. This is particularly important for the less common cancers, which are also those less investigated in relation to adherence score (and lifestyle factors more generally) and disease risk.

Strengths and limitations

The main strength of our study is that, as noted above, using the touchscreen questionnaire for whom data are available for all UK Biobank participants at baseline, we could derive an abbreviated adherence score for a much larger number of participants than was possible for the 'total' 7-point score(27). Such an abbreviated score may be useful to researchers who have data on more "core" aspects of lifestyle, but insufficient data to assess adherence to the recommendations to limit consumption of sugar-sweetened drinks and of fast foods and other processed foods high in fat, starches or sugar. The biological consequences of adherence to these two components may be captured to some extent through adherence to the components relating to body weight since sugar-sweetened drinks and UPFs promote excess energy intake and thus weight gain, overweight and obesity, and greater body fatness increases the risk of several cancers(2). Further, in their exploratory analyses of 2018 WCRF/AICR Score weightings using data from the NIH-AARP Diet and Health Study, Korn and colleagues found that both the 'fast foods' and sugar-sweetened drinks components received zero weight across all weighting approaches and that the penalised weighted scoring approach, which excluded these two components, had a similar predictive performance for estimating cancer risk and mortality outcomes as the original version of the score(9).

We assessed adherence to the sub-component for dietary fibre intake using a partial fibre score, which captures intakes of fibre from fruit, vegetables, bread and cereals, food groups that are estimated to contribute 54-60% of total fibre intake(23). Bradbury and colleagues have shown reliable ranking of participants according to partial fibre score when compared with Englyst fibre intakes derived from the 24-hour dietary assessments(23). Further, associations between partial fibre score and cancer incidence have been reported(34). As advised by the score creators(3,4), we used subjective cut-points based on tertiles within our dataset to allocate points for this score sub-component so that intake score is relative to

other participants in our study, and thus accounting for differences in measurements of fibre and the variation of fibre sources included across studies.

Another strength of our study is that we were able to compare associations with cancer incidence between the abbreviated (5-point) score created in the present study and the original 'total' 2018 WCRF/AICR Score. We found that, broadly, associations were similar when using both scores, with the exception of bladder, oesophageal, and liver cancer that were significant for the abbreviated score only, and kidney cancer that was significant when applying the total score only. These findings highlight that the additional two score components (regarding the intake of sugar-sweetened drinks and of 'fast foods' and other processed foods high in fat, starches or sugars) may be of more importance for certain cancer sites. Further research to explore which specific Recommendation(s) are driving the observed associations with cancer risk, and to investigate the weightings allocated to the individual components within the scoring system is warranted and is in progress.

Although our analyses included 14 individual cancer sites, we did not have information on sub-types of cancers, such as HER2 positive or triple negative breast cancers and, therefore, we were not able to investigate lifestyle-related risk factors may affect cancer subtypes differently(35). We carefully considered potential confounders to be included in our analyses by adding these individually to model 1 and, finally, included age, sex, ethnicity, Townsend deprivation index, and smoking status. However, our analyses may be subject to residual or unmeasured confounding. For example, tobacco exposure was controlled by including self-reported smoking status at baseline; this measure does not include information on smoking intensity or the timing of when former smokers quit.

Conclusion

In conclusion, we found significant inverse associations between an abbreviated, 5-point version of the 2018 WCRF/AICR Score and the risk of all cancers combined and of nine individual lifestyle-related cancers including breast and colorectal among participants in UK

Biobank. Building on our previous study where we were the first to report that greater adherence is associated with lower risk of kidney, oesophageal, and liver cancers(27), we now show that greater adherence is also associated with lower risk of lung, pancreatic, uterine, and stomach cancers.

These findings provide further evidence to support interventions designed to improve compliance with the 2018 Cancer Prevention Recommendations. Our findings are particularly valuable for researchers who have access to limited data that do not allow assessment of adherence to all seven (or eight) score components. Where possible, we encourage researchers to operationalise the 2018 WCRF/AICR Score as fully as possible to allow for comparability of findings across studies, but the findings from this study suggest that abbreviated versions of the score may be useful to detect associations between adherence to the Recommendations and the risk of cancer.

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TABLES

Table 1: Abbreviated score to assess adherence to the 2018 WCRF/AICR Cancer Prevention Recommendations

2018 WCRF/AICR Recommendation	Operationalization of Recommendations	Points
1. Be a healthy weight	**BMI (kg/m^2)**	
	18.5–24.9	0.5
	25–29.9	0.25
	<18.5 or ≥30	0
	Waist circumference (cm (in))	
	Men: <94 (<37) Women: <80 (<31.5)	0.5
	Men: 94–<102 (37–<40) Women: 80–<88 (31.5–<35)	0.25
	Men: ≥102 (≥40) Women: ≥88 (≥35)	0
2. Be physically active	**Total moderate-vigorous physical activity (MET min/wk)**	
	≥600	1
	300–<600	0.5
	<300	0
3. Eat a diet rich in wholegrains, vegetables, fruit and beans	**Fruits and vegetables (g/day)**	
	≥400	0.5
	200–<400	0.25
	<200	0
	Partial fibre score	
	Highest tertile	0.5
	Middle tertile	0.25
	Lowest tertile	0
4. Limit consumption of red and processed meat	**Total red meat and processed meat (g/wk)**	
	Red meat ≤500 and processed meat <21	1
	Red meat ≤500 and processed meat 21–<100	0.5
	Red meat >500 or processed meat ≥100	0
5. Limit alcohol consumption	**Total ethanol (UK guidelines) (units/week)**	
	0	1
	≤14	0.5
	>14	0

Table 2: UK Biobank participant characteristics at baseline according to approximate score tertiles of the study population[1]

	Overall (0-5)	Low (0 - 2.25)	Middle (2.5 - 3)	High (3.25 - 5)
Total score (points)	2.64 (0.91)	1.70 (0.51)	2.75 (0.20)	3.66 (0.40)
Number of participants (%)	288,702 (100)	108,907 (37.7)	90,126 (31.2)	89,669 (31.1)
Sex, n (%)				
Females	148,517 (51.4)	44,516 (40.9)	46,454 (51.5)	57,547 (64.2)
Males	140,185 (48.6)	64,391 (59.1)	43,672 (48.5)	32,122 (35.8)
Age at baseline (years)	56.2 (8.1)	56.1 (8.0)	56.4 (8.1)	56.3 (8.3)
Country of recruitment, n (%)				
England	256,148 (88.7)	96,294 (88.4)	80,062 (88.8)	79,792 (89.0)
Scotland	20,559 (7.1)	7,759 (7.1)	6,389 (7.1)	6,411 (7.2)
Wales	11,995 (4.2)	4,854 (4.5)	3,675 (4.1)	3,466 (3.9)
Education, n (%)				
College or University degree	101,344 (35.1)	34,620 (31.8)	31,895 (35.4)	34,829 (52.0)
A levels/AS levels or equivalent	33,775 (11.7)	13,150 (12.1)	10,347 (11.5)	10,278 (11.5)
O levels/GCSEs or equivalent	61,874 (21.4)	24,766 (22.7)	19,065 (21.2)	18,043 (20.1)
CSEs or equivalent	15,087 (5.2)	6,108 (5.6)	4,836 (5.4)	4,143 (4.6)
NVQ or HND or HNC or equivalent	19,059 (6.6)	7,936 (7.3)	6,004 (6.7)	5,119 (5.7)
Other professional qualifications	14,723 (5.1)	5,258 (4.8)	4,670 (5.2)	4,795 (5.4)
None of the above	41,063 (14.2)	16,467 (15.1)	12,769 (14.2)	11,827 (13.2)
Do not know/prefer not to answer	1,776 (0.6)	601 (0.6)	540 (0.6)	635 (0.7)
Townsend deprivation index	-1.55 (2.95)	-1.47 (2.99)	-1.62 (2.91)	-1.57 (2.94)
Ethnicity, n (%)				
White	275,943 (95.6)	105,681 (97.0)	86,351 (95.8)	83,911 (93.6)
Mixed	3,519 (1.2)	993 (0.9)	1,041 (1.2)	1,485 (1.7)
South Asian	4,834 (1.7)	993 (0.9)	1,315 (1.5)	2,526 (2.8)
Black	3,795 (1.3)	1,146 (1.1)	1,253 (1.4)	1,396 (1.6)
Chinese	611 (0.2)	94 (0.1)	166 (0.2)	351 (0.4)
Smoking status at baseline, n (%)				
Never	164,876 (57.1)	55,411 (50.9)	51,756 (57.4)	57,709 (64.4)
Former smoker	98,836 (34.2)	41,261 (37.9)	30,956 (34.4)	26,619 (29.7)
Current smoker	24,313 (8.4)	11,957 (11.0)	7,198 (8.0)	5,158 (5.8)
Unknown	677 (0.2)	278 (0.3)	216 (0.2)	183 (0.2)

[1]Participants with a total abbreviated score, without prevalent cancer at baseline, and full data for covariates in model 1.

Data are presented as means and standard deviation in brackets (SD) for total score, age, and Townsend Deprivation Index. Data for sex, education, ethnicity, and smoking are presented as number of participants (n) and percentage in brackets (%).

Table 3: Associations between 1-point increment in abbreviated 5-point adherence score and risk of all cancers combined and of cancer at individual anatomical sites

			Model 1		Model 2	
Cancer site	**Total**	**Incident cancers**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
All cancers combined	284,553	23,448	**0.92 (0.91; 0.93)**	**<0.001**	**0.93 (0.92; 0.95)**	**<0.001**
Prostate	139,240	5,677	**1.03 (1.00; 1.06)**	**0.046**	1.02 (0.99; 1.05)	0.192
Breast	147,655	4,014	**0.90 (0.87; 0.93)**	**<0.001**	**0.90 (0.87; 0.94)**	**<0.001**
Pre-Menopausal	2,705	359	0.93 (0.82; 1.04)	0.183	0.91 (0.81; 1.02)	0.123
Post-Menopausal	144,950	3,655	**0.89 (0.86; 0.93)**	**<0.001**	**0.90 (0.86; 0.93)**	**<0.001**
Colorectal	288,191	2,689	**0.86 (0.82; 0.90)**	**<0.001**	**0.86 (0.83; 0.90)**	**<0.001**
Colon	288,361	1,812	**0.84 (0.80; 0.89)**	**<0.001**	**0.85 (0.80; 0.89)**	**<0.001**
Distal	288,537	756	**0.84 (0.77; 0.91)**	**<0.001**	**0.84 (0.77; 0.91)**	**<0.001**
Proximal	288,554	965	**0.85 (0.79; 0.91)**	**<0.001**	**0.86 (0.80; 0.92)**	**<0.001**
Rectum	288,518	1,052	**0.86 (0.80; 0.92)**	**<0.001**	**0.87 (0.81; 0.93)**	**<0.001**
Lung	288,493	1,805	**0.79 (0.75; 0.83)**	**<0.001**	**0.89 (0.84; 0.94)**	**<0.001**
Kidney	288,593	764	**0.81 (0.75; 0.88)**	**<0.001**	**0.83 (0.76; 0.90)**	**<0.001**
Pancreas	288,629	745	**0.85 (0.79; 0.92)**	**<0.001**	**0.86 (0.79; 0.94)**	**<0.001**
Uterus	148,395	684	**0.81 (0.74; 0.88)**	**<0.001**	**0.79 (0.73; 0.86)**	**<0.001**
Oesophagus	288,627	555	**0.78 (0.71; 0.86)**	**<0.001**	**0.82 (0.75; 0.90)**	**<0.001**
Ovary	148,434	482	1.00 (0.90; 1.11)	0.983	1.00 (0.90; 1.11)	0.940
Bladder	288,603	549	**0.88 (0.80; 0.97)**	**0.001**	0.93 (0.84; 1.02)	0.118
Head and Neck	288,626	445	0.96 (0.87; 1.07)	0.464	1.01 (0.91; 1.12)	0.888
Stomach	288,645	389	**0.86 (0.77; 0.97)**	**0.011**	**0.89 (0.79; 0.99)**	**0.038**
Liver	288,653	356	**0.79 (0.70; 0.89)**	**<0.001**	**0.80 (0.72; 0.90)**	**<0.001**
Gallbladder	288,687	153	0.94 (0.78; 1.12)	0.483	0.94 (0.78; 1.12)	0.483

Data are presented as hazard ratio (HR) with 95% confidence intervals in parentheses (95% CIs) per 1-point increment in score. 2-year landmark analysis was conducted. Model 1 was adjusted for age, sex, Townsend deprivation index and ethnicity. Model 2 was additionally adjusted for smoking status at baseline (never, former, or current smoker).

Table 4: Associations between abbreviated 5-point adherence score, categorised according to approximate score tertiles of the study population, and risk of all cancers combined and of cancers at individual anatomical sites

			Low score (0 - 2.25)	Mid Score (2.5 – 3)				Higher score (3.25 – 5)			
				Model 1		Model 2		Model 1		Model 2	
Cancer site	**Total**	**Incident cancers**	**HR (95% CI)**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
All cancers combined	284,553	23,448	1.00 (ref)	**0.90 (0.88; 0.93)**	**<0.001**	**0.92 (0.89; 0.95)**	**<0.001**	**0.85 (0.83; 0.88)**	**<0.001**	**0.88 (0.85; 0.90)**	**<0.001**
Prostate	139,240	5,677	1.00 (ref)	1.06 (0.99; 1.13)	0.055	1.05 (0.99; 1.12)	0.099	1.06 (0.99; 1.14)	0.069	1.04 (0.97; 1.11)	0.233
Breast	147,655	4,014	1.00 (ref)	0.93 (0.86; 1.00)	0.060	0.93 (0.86; 1.00)	0.067	**0.83 (0.77; 0.90)**	**<0.001**	**0.83 (0.77; 0.90)**	**<0.001**
Pre-menopausal	2,705	359	1.00 (ref)	0.89 (0.68; 1.16)	0.386	0.87 (0.67; 1.13)	0.289	0.86 (0.67; 1.11)	0.248	0.84 (0.65; 1.07)	0.164
Post-menopausal	143,043	3,655	1.00 (ref)	**0.92 (0.85; 0.99)**	**0.049**	0.93 (0.85; 1.00)	0.059	**0.82 (0.75; 0.88)**	**<0.001**	**0.82 (0.76; 0.89)**	**<0.001**
Colorectal	288,191	2,689	1.00 (ref)	**0.80 (0.73; 0.87)**	**<0.001**	**0.80 (0.73; 0.88)**	**<0.001**	**0.74 (0.67; 0.82)**	**<0.001**	**0.75 (0.69; 0.83)**	**<0.001**
Colon	288,361	1,812	1.00 (ref)	**0.80 (0.71; 0.89(**	**<0.001**	**0.80 (0.72; 0.89)**	**<0.001**	**0.74 (0.66; 0.84)**	**<0.001**	**0.75 (0.67; 0.85)**	**<0.001**
Distal	288,537	756	1.00 (ref)	**0.76 (0.64; 0.91)**	**0.002**	**0.76 (0.64; 0.91)**	**0.002**	**0.74 (0.61; 0.88)**	**0.001**	**0.74 (0.62; 0.89)**	**0.001**
Proximal	288,554	965	1.00 (ref)	**0.84 (0.72; 0.97)**	**0.020**	**0.84 (0.73; 0.98)**	**0.028**	**0.76 (0.65; 0.89)**	**0.001**	**0.77 (0.66; 0.90)**	**0.001**
Rectum	288,518	1,052	1.00 (ref)	**0.79 (0.69; 0.92)**	**0.001**	**0.80 (0.70; 0.93)**	**0.003**	**0.69 (0.59; 0.80)**	**<0.001**	**0.70 (0.60; 0.82)**	**<0.001**
Lung	288,493	1,805	1.00 (ref)	**0.72 (0.64; 0.80)**	**<0.001**	**0.81 (0.72; 0.90)**	**<0.001**	**0.63 (0.56; 0.71)**	**<0.001**	**0.81 (0.72; 0.91)**	**<0.001**
Kidney	288,593	764	1.00 (ref)	**0.68 (0.57; 0.81)**	**<0.001**	**0.69 (0.58; 0.82)**	**<0.001**	**0.67 (0.56; 0.80)**	**<0.001**	**0.69 (0.58; 0.83)**	**<0.001**
Pancreas	288,629	745	1.00 (ref)	**0.83 (0.70; 0.99)**	**0.037**	**0.84 (0.71; 0.99)**	**0.046**	**0.72 (0.60; 0.87)**	**0.001**	**0.74 (0.62; 0.89)**	**0.002**
Uterus	148,395	684	1.00 (ref)	0.85 (0.71; 1.01)	0.070	**0.83 (0.69; 0.99)**	**0.045**	**0.64 (0.53; 0.77)**	**<0.001**	**0.62 (0.52; 0.75)**	**<0.001**
Oesophagus	299,627	555	1.00 (ref)	**0.78 (0.64; 0.94)**	**0.011**	**0.82 (0.67; 0.99)**	**0.040**	**0.58 (0.46; 0.72)**	**<0.001**	**0.64 (0.51; 0.81)**	**<0.001**
Ovary	148,434	482	1.00 (ref)	0.95 (0.76; 1.19)	0.653	0.95 (0.76; 1.19)	0.664	0.96 (0.77; 1.19)	0.706	0.96 (0.77; 1.20)	0.740
Bladder	288,603	549	1.00 (ref)	0.82 (0.67; 1.00)	0.050	0.87 (0.71; 1.06)	0.175	0.83 (0.67; 1.03)	0.095	0.93 (0.75; 1.16)	0.540
Head and Neck	288,626	445	1.00 (ref)	0.96 (0.77; 1.19)	0.696	1.01 (0.81; 1.26)	0.954	0.89 (0.71; 1.13)	0.354	0.99 (0.78; 1.25)	0.916
Stomach	288,645	389	1.00 (ref)	0.87 (0.69; 1.10)	0.246	0.90 (0.71; 1.13)	0.352	**0.71 (0.55; 0.92)**	**0.011**	**0.75 (0.58; 0.98)**	**0.034**
Liver	288,653	356	1.00 (ref)	0.87 (0.68; 1.11)	0.273	0.89 (0.70; 1.14)	0.359	**0.71 (0.54; 0.93)**	**0.014**	**0.74 (0.57; 0.98)**	**0.033**
Gallbladder	288,687	153	1.00 (ref)	1.09 (0.75; 1.58)	0.667	1.09 (0.74; 1.58)	0.668	0.84 (0.56; 1.27)	0.410	0.84 (0.56; 1.27)	0.410

Data are presented as hazard ratio (HR) with 95% confidence intervals in parentheses (95% CIs). 2-year landmark analysis was conducted. Lowest score tertile was the reference group. Model 1 was adjusted for age, sex, Townsend deprivation index and ethnicity. Model 2 was additionally adjusted for smoking status at baseline (never, former, or current smoker).

FIGURE LEGENDS

Figure 1: Adherence to individual components and sub-components of the abbreviated score (n=288,702). The recommendation '1. Healthy weight' is divided into two sub-components: a. BMI and b. waist circumference. The recommendation '3. Wholegrains, vegetables, fruit, and beans' is divided into two sub-components: a. fruit and vegetables intake and b. dietary fibre intake. BMI: body mass index, PA: physical activity, F&V: fruit and vegetables

STATEMENTS & DECLARATIONS

Conflict of Interest

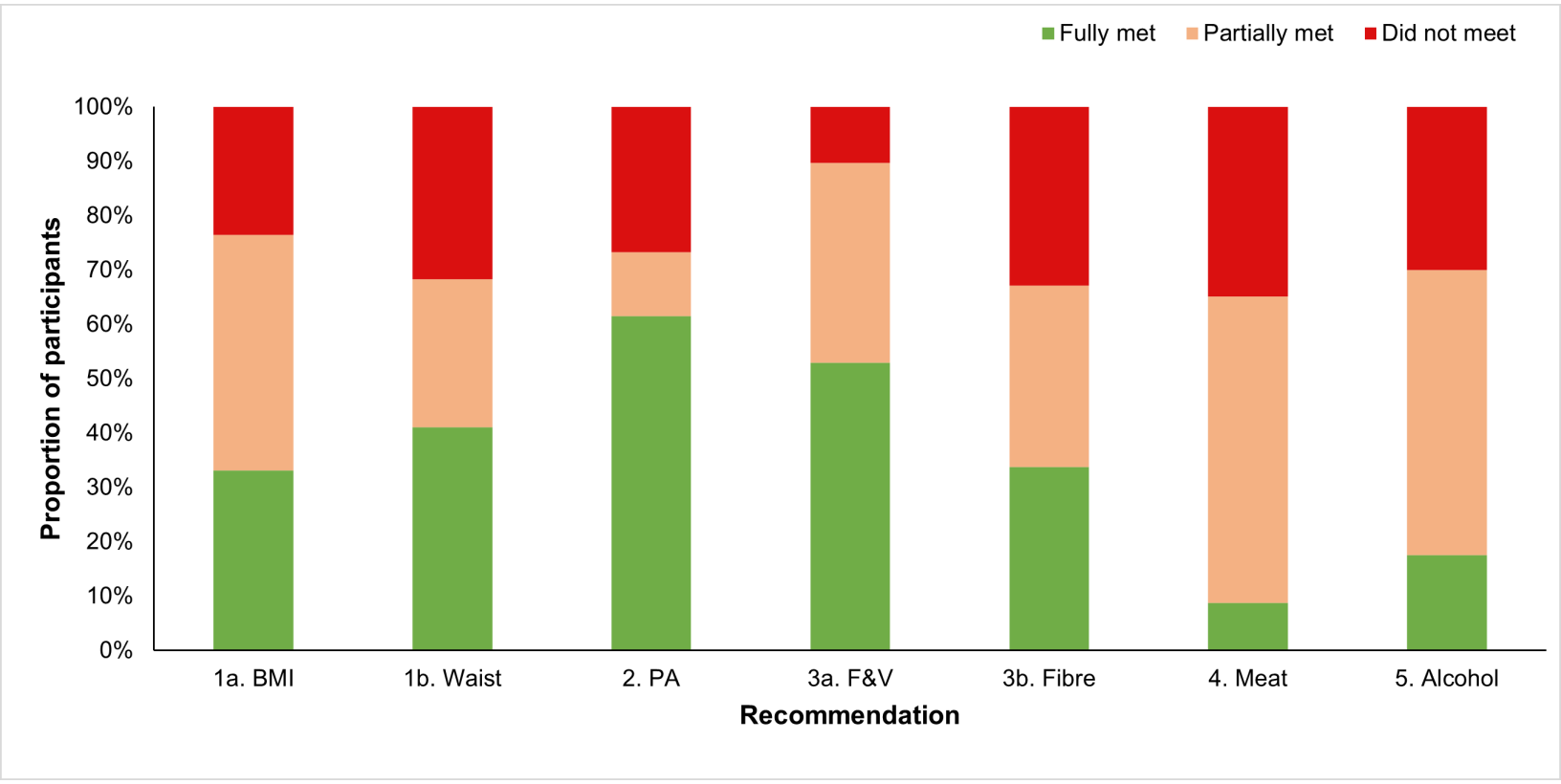
The authors declare no potential conflicts of interest.

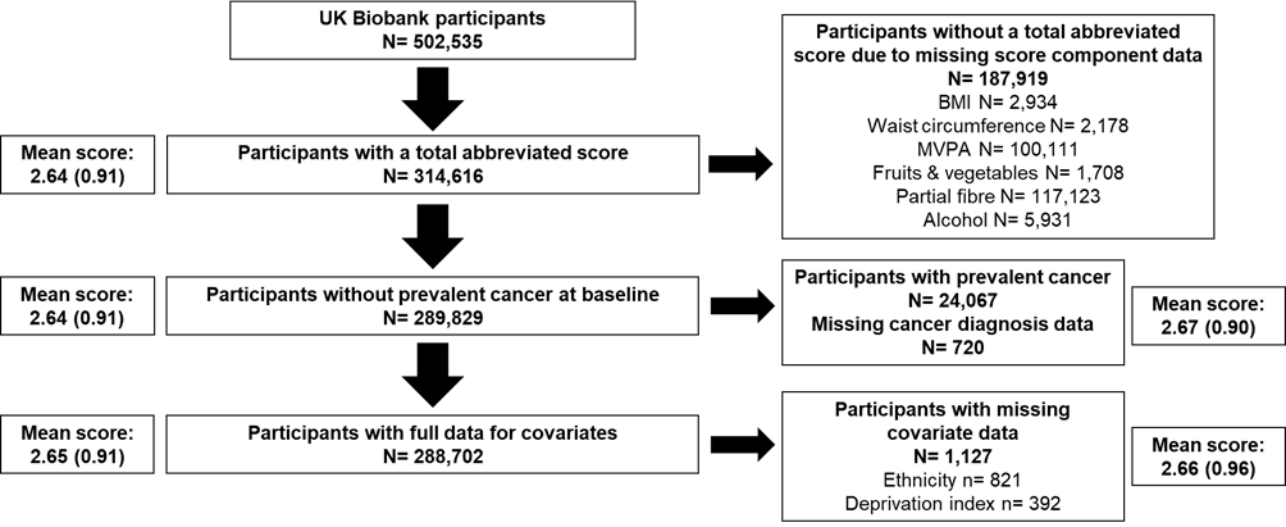
Ethical approval

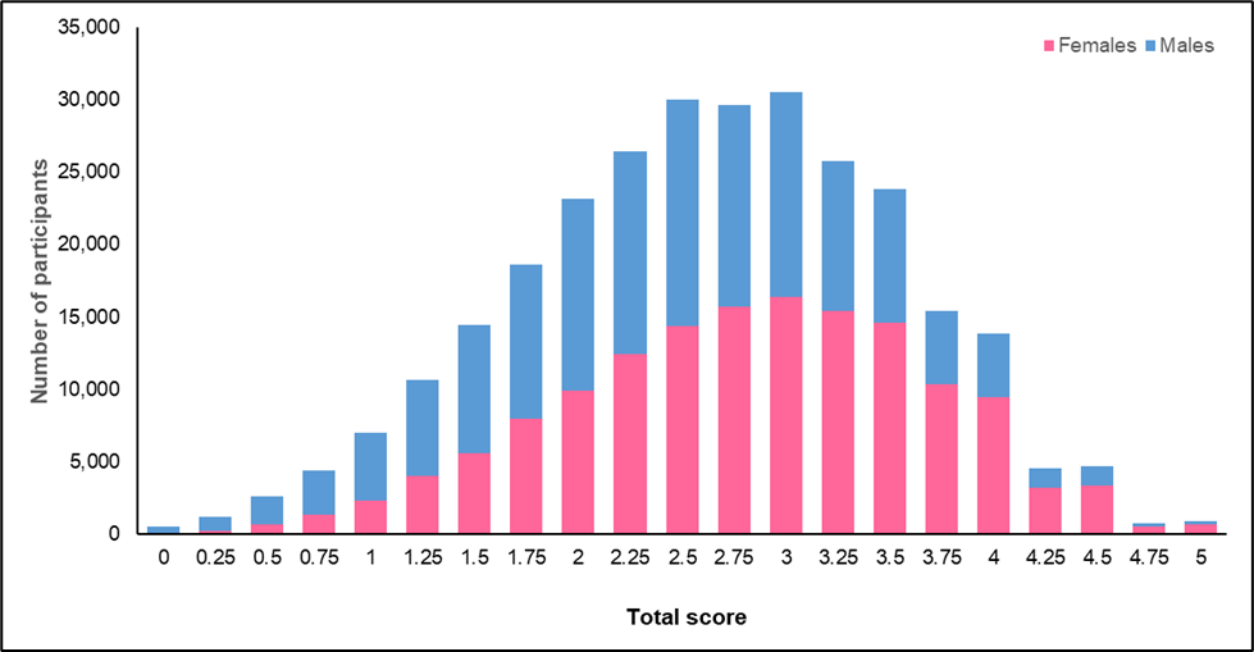
The UK Biobank study was conducted in accordance with the Declaration of Helsinki and was approved by the North West Multi-centre Research Ethics Committee (REC reference: 12/NW/03820).

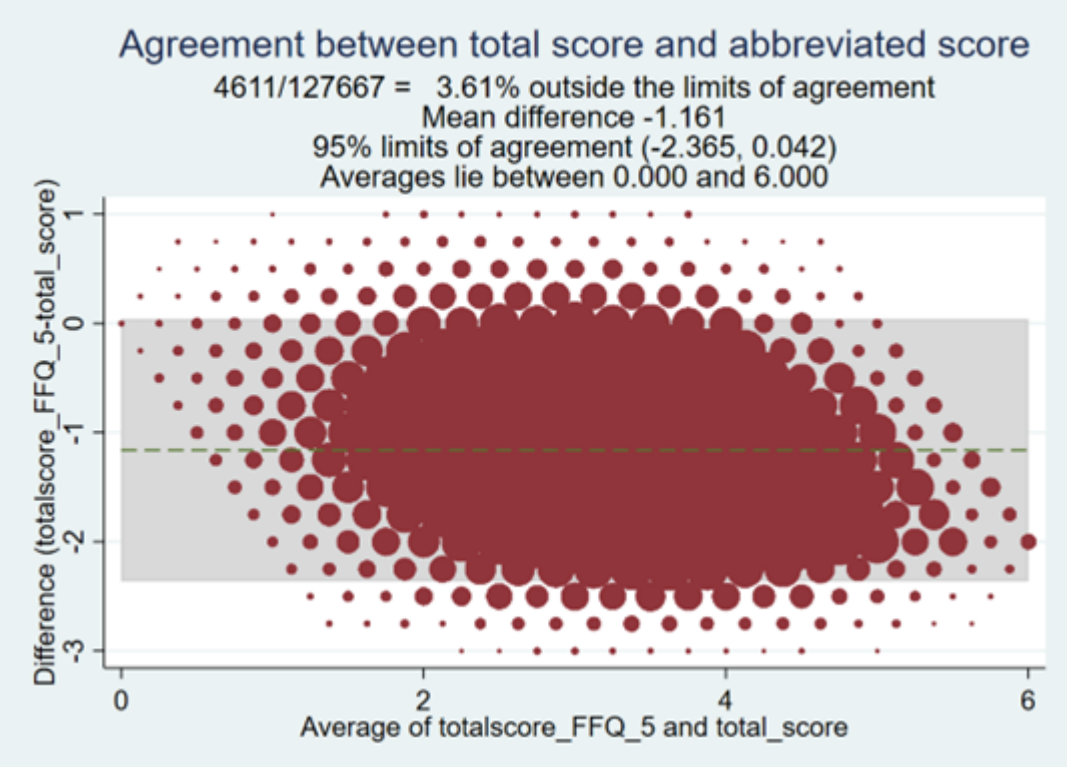
Consent to participate

Informed consent was obtained from all individual participants included in the UK Biobank study.


Fully met
Partially met
Did not meet
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Proportion of participants
1a. BMI
1b. Waist
2. PA
3a. F&V
3b. Fibre
4. Meat
5. Alcohol
Recommendation


UK Biobank participants
N= 502,535
Participants without a total abbreviated score due to missing score component data
N= 187,919
BMI N= 2,934
Waist circumference N= 2,178
MVPA N= 100,111
Fruits & vegetables N= 1,708
Partial fibre N= 117,123
Alcohol N= 5,931
Mean score: 2.64 (0.91)
Participants with a total abbreviated score
N= 314,616
Participants with prevalent cancer
N= 24,067
Missing cancer diagnosis data
N= 720
Mean score: 2.67 (0.90)
Mean score: 2.64 (0.91)
Participants without prevalent cancer at baseline
N= 289,829
Participants with missing covariate data
N= 1,127
Ethnicity n= 821
Deprivation index n= 392
Mean score: 2.66 (0.96)
Mean score: 2.65 (0.91)
Participants with full data for covariates
N= 288,702


Females
Males
Number of participants
35,000
30,000
25,000
20,000
15,000
10,000
5,000
0
0
0.25
0.5
0.75
1
1.25
1.5
1.75
2
2.25
2.5
2.75
3
3.25
3.5
3.75
4
4.25
4.5
4.75
5
Total score


Agreement between total score and abbreviated score
4611/127667 = 3.61% outside the limits of agreement
Mean difference -1.161
95% limits of agreement (-2.365, 0.042)
Averages lie between 0.000 and 6.000
Difference (totalscore_FFQ_5-total_score)
1
0
-1
-2
-3
0
2
4
6
Average of totalscore_FFQ_5 and total_score