

Mediterranean diet adherence and cognitive function in older, UK adults

Shannon, Oliver M; Stephan, Blossom C M; Granic, Antoneta; Lentjes, Marleen; Hayat, Shabina; Mulligan, Angela; Brayne, Carol; Khaw, Kay-tee; Bundy, Rafe; Aldred, Sarah; Hornberger, Michael; Paddick, Stella-maria; Muniz-tererra, Graciela; Minihane, Anne-marie; Mathers, John C; Siervo, Mario

DOI:
[10.1093/ajcn/nqz114](https://doi.org/10.1093/ajcn/nqz114)

License:
None: All rights reserved

Document Version
Peer reviewed version

Citation for published version (Harvard):
Shannon, OM, Stephan, BCM, Granic, A, Lentjes, M, Hayat, S, Mulligan, A, Brayne, C, Khaw, K, Bundy, R, Aldred, S, Hornberger, M, Paddick, S, Muniz-tererra, G, Minihane, A, Mathers, JC & Siervo, M 2019, 'Mediterranean diet adherence and cognitive function in older, UK adults: The European Prospective Investigation into Cancer and Nutrition-Norfolk (EPIC-Norfolk) Study', *American Journal of Clinical Nutrition*, vol. 110, no. 4, pp. 938-948. <https://doi.org/10.1093/ajcn/nqz114>

[Link to publication on Research at Birmingham portal](#)

Publisher Rights Statement:
Checked for eligibility: 16/08/2019

This is a pre-copyedited, author-produced PDF of an article accepted for publication in *American Journal of Clinical Nutrition* following peer review. The version of record Oliver M Shannon, Blossom C M Stephan, Antoneta Granic, Marleen Lentjes, Shabina Hayat, Angela Mulligan, Carol Brayne, Kay-Tee Khaw, Rafe Bundy, Sarah Aldred, Michael Hornberger, Stella-Maria Paddick, Graciela Muniz-Tererra, Anne-Marie Minihane, John C Mathers, Mario Siervo, Mediterranean diet adherence and cognitive function in older UK adults: the European Prospective Investigation into Cancer and Nutrition–Norfolk (EPIC-Norfolk) Study, *The American Journal of Clinical Nutrition*, is available online at: <https://doi.org/10.1093/ajcn/nqz114>

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

ONLINE SUPPORTING MATERIAL

Shannon et al. Mediterranean diet adherence and cognitive function in older, UK adults: The EPIC-Norfolk study

Contents

| | |
|---|----|
| Supplementary Table 1: Components and scoring of the MEDAS and MEDAS Continuous Mediterranean diet adherence scales..... | 2 |
| Supplementary Table 2: Components and scoring of the Pyramid Mediterranean diet adherence scale | 4 |
| Supplementary Table 3: Additional participant characteristics at baseline (HC1) of the EPIC-Norfolk study according to Mediterranean diet adherence score | 6 |
| Supplementary Table 4: Mediterranean diet adherence at HC1 and the risk of poor cognitive performance at HC3 of the EPIC-Norfolk study..... | 7 |
| Supplementary Table 5: Mediterranean diet adherence at HC1 and risk of poor cognitive performance at HC3 in maximally adjusted models, with participants stratified by CVD risk..... | 9 |
| Supplementary Table 6: Mediterranean diet adherence at HC2 and cognitive function at HC3 of the EPIC-Norfolk study | 10 |
| Supplementary Table 7: Mediterranean diet adherence at HC2 and the risk of poor cognitive performance at HC3 of the EPIC-Norfolk study..... | 11 |
| Supplementary Table 8: Sensitivity analysis exploring the influence of each component of the MedDiet in the MEDAS and MEDAS Continuous scale at HC1 on cognitive function at HC3 of the EPIC-Norfolk study in maximally adjusted models | 13 |
| Supplementary Table 9: Sensitivity analysis exploring the influence of each component of the MedDiet in the Pyramid score at HC1 on cognitive function at HC3 of the EPIC-Norfolk study in maximally adjusted models..... | 14 |
| Supplementary Table 10: Sensitivity analysis excluding potential under- or over-reporters for energy intake in maximally adjusted models exploring associations between Mediterranean diet adherence at HC1 and cognitive function at HC3 of the EPIC-Norfolk study. | 15 |
| Supplementary Table 11: Interaction between Mediterranean diet adherence at HC1 and CVD risk status and risk of poor cognitive performance at HC3 in maximally adjusted models..... | 16 |
| Supplementary Table 12: A comparison of participant characteristics at HC3 of the EPIC-Norfolk study between individuals with complete and incomplete cognitive test data..... | 17 |
| Supplementary Figure 1: Participant flow chart. Participants for the current study were individuals who provided both dietary data at HC1 and cognitive function data at HC3 of the EPIC-Norfolk study. | 18 |

Supplementary Material

Supplementary Table 1: Components and scoring of the MEDAS and MEDAS Continuous Mediterranean diet adherence scales

| Food component | Contributing foods from the EPIC-Norfolk food frequency questionnaire | MEDAS ¹ | | MEDAS Continuous ² | |
|---|--|--|------------------------------------|--------------------------------|------------------------------------|
| | | Servings required for 0 points | Servings required for 1 point | Servings required for 0 points | Servings required for 1 point |
| Olive oil ⁵ | Main fat used for frying? Main fat used for baking? | Non-consumption | Consumption | Non-consumption | Consumption |
| Olive oil ³ | Based on standardised recipe quantities for fat/olive oil associated with FFQ items AND answer to main fat question where relevant | <4 tbsp/d | ≥4 tbsp/d | 0 tbsp/d | ≥4 tbsp/d |
| Vegetables ^{3,7} | Vegetable soup, ketchup, pickles, carrots, spinach, broccoli/ sprint greens/ kale, sprouts, cabbage, marrow/ courgettes, cauliflower, parsnip/ turnip/ swede, leeks, onions, garlic, mushrooms, peppers, green salad/ lettuce/ cucumber/ celery, beansprouts, green beans/ broad beans/ runner beans, watercress, tomatoes, sweetcorn, beetroot, coleslaw, avocado | <2/d (and/or not including 1/d raw or salad) | ≥2/d (including ≥1/d raw or salad) | 0/d | ≥2/d (including ≥1/d raw or salad) |
| Fruit ³ | Apples, pears, oranges/satsumas/mandarins, grapefruits, bananas, grapes, melon, peaches/plums/apricots, strawberries/raspberries/kiwi, tinned fruit, fruit from pies/ tarts, fruit juice | <3/d | ≥3/d | 0/d | ≥3/d |
| Red meat ⁴ | Beef, pork, lamb, beefburgers, red meat soups (e.g. oxtail), bacon, ham, corned beef, sausages, savoury pie, liver, lasagne | >1/d | <1/d | ≥2/d | <1/d |
| Butter, margarine or cream ⁴ | Single cream, double cream, butter, low fat spread | >1/d | <1/d | ≥2/d | <1/d |
| Sweetened or carbonated drinks ⁴ | Fizzy soft drinks, fruit squash/ cordial | >1/d | <1/d | ≥2/d | <1/d |
| Wine ³ | Wine | <7/wk | ≥7/wk | 0/wk | ≥7/wk |
| Legumes ³ | Peas, baked beans, dried lentils/ beans/ peas | <3/wk | ≥3/wk | 0/wk | ≥3/wk |
| Seafood ³ | Fried fish, fish fingers/fish cakes, white fish, oily fish, shellfish, fish roe/taramasalata | <3/wk | ≥3/wk | 0/wk | ≥3/wk |
| Sweets or pastries ⁴ | Chocolate biscuits, plain biscuits, readymade cakes, readymade buns/ pastries, readymade fruit pies, readymade sponge, milk puddings, ice cream, chocolates, chocolate bars, sweets/ toffees/ mints | >2/wk | <2/wk | ≥4/wk | <2/wk |
| Nuts ³ | Nuts, peanut butter | <3/wk | ≥3/wk | 0/wk | ≥3/wk |
| White meat ⁶ | Chicken and other poultry, white meat soups (e.g. chicken) | Less white meat than red meat | More white meat than red meat | Less white meat than red meat | More white meat than red meat |
| Sofrito ³ | Lasagne | <2/wk | ≥2/wk | 0/wk | ≥2/wk |

¹Scoring for the MEDAS scale was calculated according to the methods detailed by Martínez-González et al. (2012). A score of 1 point was awarded if participants achieved a dietary target. Otherwise, participants were awarded 0 points. ²Scoring for the MEDAS Continuous scale used the same dietary components as the standard MEDAS scale. However, rather than awarding points on a binary basis, points were awarded continuously based on linear equation principles ($y = ax+b$, where y is the number of points scored between 0 and 1, a is the slope and b is the intercept). ³A high intake of olive oil, vegetables, fruit, wine, legumes, seafood, nuts, and sofrito was recommended. For

Supplementary Material

the MEDAS Continuous scale, points were allocated between 0 for no consumption and 1 for meeting the recommended intake. ³A low intake of red meat, butter, margarine or cream, sweetened or carbonated drinks, and sweets or pastries was recommended. For the MEDAS Continuous scale, points were allocated continuously between 0 points for double the recommended intake and 1 point for below the recommended intake. ⁵For olive oil (item 1), individuals who reported consumption received a score of 1 point, whilst non-consumers received 0 points. ⁶For white meat, participants were awarded a point if the total amount of white meat consumed exceeded red meat consumption. ⁷A maximum score of 0.5 points was awarded for participants who did not also consume 1 serving per day of raw vegetables or salad as part of the MEDAS Continuous scale. Conversely, 0 points were awarded for participants who did not consume 1 serving per day of raw vegetables or salad as part of the MEDAS scale, irrespective of their total vegetable intake.

Supplementary Material

Supplementary Table 2: Components and scoring of the Pyramid Mediterranean diet adherence scale

| Food component | Contributing foods from the EPIC-Norfolk food frequency questionnaire | Recommended intake | Servings required for 0 points | Servings required for 1 point |
|-----------------------------|---|------------------------------------|--------------------------------|--------------------------------------|
| Vegetables ¹ | Vegetable soup, ketchup, pickles, carrots, spinach, broccoli/ sprint greens/ kale, sprouts, cabbage, marrow/ courgettes, cauliflower, parsnip/ turnip/ swede, leeks, onions, garlic, mushrooms, peppers, green salad/ lettuce/ cucumber/ celery, watercress, tomatoes, sweetcorn, beetroot, coleslaw, avocado | ≥6/d | 0/d | ≥6/d |
| Legumes ¹ | Peas, green beans/ broad beans/ runner beans, beansprouts, baked beans, dried lentils/ beans/ peas, tofu | ≥2/wk | 0/wk | ≥2/wk |
| Fruits ² | Apples, pears, oranges/satsumas/mandarins, grapefruits, bananas, grapes, melon, peaches/plums/apricots, strawberries/raspberries/kiwi, tinned fruit, dried fruit | 3-6/d | 0/d | 3-6/d |
| Nuts ² | Nuts, peanut butter | 1-2/d | 0/d | 1-2/d |
| Cereals ² | White bread and bread rolls, brown bread and bread rolls, wholemeal bread and bread rolls, crackers, crispbread, porridge/ readybrek, breakfast cereals, white rice, brown rice, white pasta, wholemeal pasta, lasagne/ moussaka, pizza | 3-6/d | 0/d | 3-6/d |
| Dairy ² | Single or sour cream, double or clotted cream, low fat yoghurt/fromage frais, full fat yogurt or Greek yoghurt, dairy desserts, cheese, cottage cheese, milk | 2/d | 0/d | 1.5-2.5/d |
| Fish ¹ | Fried fish, fish fingers/fish cakes, white fish, oily fish, shellfish, fish roe/taramasalata | ≥2/wk | 0/wk | ≥2/wk |
| Red meat ³ | Beef, pork, lamb, beefburgers, red meat soups (e.g. oxtail) | <2/wk | ≥4/wk | <2/wk |
| Processed meat ³ | Bacon, ham, corned beef, sausages, savoury pie, liver | ≤1/wk | ≥2/wk | ≤1/wk |
| White meat ² | Chicken and other poultry, white meat soups (e.g. chicken) | 2/wk | 0/wk | 1.5-2.5/wk |
| Egg ² | Eggs, quiche | 2-4/wk | 0/wk | 2-4/wk |
| Potato ³ | Boiled/mashed/instant/jacket potatoes, chips, roast potatoes, potato salad | ≤3/wk | ≥6/wk | ≤3/wk |
| Sweets ³ | Chocolate biscuits, plain biscuits, cakes, buns/ pastries, fruit pies, sponge, milk puddings, ice cream, chocolates, chocolate bars, sweets/ toffees/ mints, sugar, jam, low calorie/ diet fizzy soft drinks, fizzy soft drinks, fruit squash/ cordial | ≤2/wk | ≥4/wk | ≤2/wk |
| Alcohol ⁴ | Wine, beer/lager/cider, port/sherry/vermouth/liqueurs, spirits | 2/d for men 1/d for women | Men = ≥4/d Women = ≥2/d | Men = 1.5-2.5/d Women = 0.5-1.5/d |
| Olive oil ⁵ | Principal fat used for cooking | Principal source of dietary lipids | Non-consumption | Consumption |

Scoring for the Pyramid scale was calculated according to the methods of Tong et al. (2016). ¹A high intake of vegetables, legumes, and fish was recommended. Points were allocated continuously between 0 for no consumption and 1 for meeting the recommended intake. ²A Moderate intake of fruits, nuts, cereals, dairy, white meat, and eggs was recommended. Points were allocated continuously between 0 for no consumption and 1 for achieving an intake within the recommended level. Overconsumption, defined as consuming an amount double the mid-point of the recommended intake, was penalised and received a maximum of 0.5 points, with points allocated proportionally between

Supplementary Material

the recommended level and the penalty point. ³A low intake of red meat, processed meat, potato, and sweets was recommended. Points were allocated continuously between 0 points for double the recommended intake and 1 point for below the recommended intake. ⁴Sex-specific recommendations were provided for alcohol consumption. Consumption within the recommended intake received 1 point, whilst overconsumption received 0 points, and non-consumption received a score of 0.5 points. Points were allocated proportionally between 0.5 points and 1 point for intake between non-consumption and the recommended level for alcohol intake. ⁵For olive oil, individuals who reported consumption received a score of 1 point, whilst non-consumers received 0 points.

Supplementary Material

Supplementary Table 3: Additional participant characteristics at baseline (HC1) of the EPIC-Norfolk study according to Mediterranean diet adherence score

| Characteristic | Mediterranean diet score | | | | | | | | | | | | |
|--|--------------------------|--------------------------|-----------------------------|----------------------------|------------------|--------------------------------|-----------------------------------|----------------------------------|------------------|--------------------------------|-----------------------------------|--------------------------------|------------------|
| | Overall | MEDAS ¹ | | | <i>P</i> | MEDAS Continuous | | | <i>P</i> | Pyramid | | | <i>P</i> |
| | | Low = 0 - 2 n=2400 | Medium = 3 - 4 n=4198 | High = 5 - 10 n=1411 | | Low = 1.31 - 4.97 n=2670 | Medium = 4.98 - 6.04 n=2670 | High = 6.05 - 10.87 n=2669 | | Low = 3.47 - 7.53 n=2687 | Medium = 7.54 - 8.66 n=2673 | High = 8.67-12.93 n=2649 | |
| Waist circumference, cm (n=7999) | 85.7 (77.0, 94.7) | 87.8 (78.0, 96.0) | 85.6 (76.7, 94.8) | 82.4 (75.0, 92.0) | <0.001 | 87.5 (78.0, 95.5) | 86.0 (77.0, 95.3) | 83.6 (75.3, 93.0) | <0.001 | 88.0 (78.2, 96.3) | 85.6 (77.0, 94.8) | 83.0 (75.0, 92.8) | <0.001 |
| Marital status, % married (n=7974) | 85 | 88 | 86 | 82 | <0.001 | 86 | 86 | 85 | 0.606 | 88 | 86 | 83 | <0.001 |
| Occupational status, % currently employed (n=7983) | 63 | 64 | 63 | 64 | 0.376 | 61 | 63 | 65 | 0.010 | 65 | 62 | 63 | 0.026 |
| Medication use | | | | | | | | | | | | | |
| Anti-hypertensive, % | 12 | 11 | 12 | 13 | 0.565 | 12 | 11 | 12 | 0.370 | 12 | 12 | 11 | 0.734 |
| Lipid-lowering, % | 1 | 1 | 1 | 2 | 0.008 | 1 | 1 | 2 | 0.002 | 1 | 1 | 1 | 0.103 |
| Steroids, % | 2 | 3 | 2 | 2 | 0.358 | 2 | 2 | 2 | 0.622 | 2 | 2 | 2 | 0.692 |
| Diabetes, % | 1 | 1 | 1 | 1 | 0.497 | 1 | 1 | 1 | 0.407 | 1 | 1 | 1 | 0.718 |
| Self-reported medical condition | | | | | | | | | | | | | |
| Diabetes, % (n=8008) | 1 | 1 | 1 | 1 | 0.826 | 1 | 1 | 1 | 0.368 | 1 | 1 | 1 | 0.220 |
| MI, % (n=8009) | 2 | 1 | 1 | 2 | 0.171 | 2 | 1 | 2 | 0.046 | 2 | 1 | 2 | 0.768 |
| Migraine, % (n=7927) | 13 | 13 | 13 | 14 | 0.505 | 13 | 14 | 13 | 0.847 | 13 | 13 | 14 | 0.300 |
| Stroke, % (n=8011) | 1 | 1 | 1 | 1 | 0.222 | 1 | 1 | 1 | 0.568 | 1 | 0 | 1 | 0.166 |
| Arrhythmia, % (n=8012) | 5 | 4 | 5 | 6 | 0.197 | 4 | 4 | 6 | 0.003 | 4 | 5 | 5 | 0.005 |
| Depression, % (n=8004) | 15 | 14 | 15 | 15 | 0.542 | 14 | 14 | 15 | 0.768 | 14 | 15 | 15 | 0.453 |
| Other psychiatric illness, % (n=8010) | 3 | 3 | 3 | 3 | 0.478 | 2 | 3 | 3 | 0.108 | 3 | 3 | 3 | 0.877 |

Participant characteristics were compared between low, medium and high Mediterranean diet adherence groups for each score using the Kruskal-Wallis test for ordered and non-normally distributed continuous variables and the chi squared test for nominal variables. Data are presented as median (IQR) for non-normally distributed continuous data and % for nominal/ categorical data. Where measurements were not obtained in the full set of 8009 participants, the exact number of participants for the variable is stated in brackets under the variable name. ¹For the MEDAS score, it was not possible to divide participants into approximately equal sized groups, given a large number of participants achieved the same score. Therefore, participants were split into three groups where all individuals with the same score were categorised together.

Supplementary Material

Supplementary Table 4: Mediterranean diet adherence at HC1 and the risk of poor cognitive performance at HC3 of the EPIC-Norfolk study

| Outcome | Cognitive domain | Model | Comparison | MEDAS OR (95% CI) | <i>P</i> | MEDAS Continuous OR (95% CI) | <i>P</i> | Pyramid OR (95% CI) | <i>P</i> |
|------------------------|---|-------|------------|----------------------|--------------|---------------------------------|------------------|------------------------|------------------|
| SF-EMSE | Global cognition | 1 | M vs. L | 0.936 (0.866, 1.011) | 0.393 | 0.879 (0.811, 0.954) | 0.116 | 0.848 (0.781, 0.921) | 0.044 |
| | | | H vs. L | 0.800 (0.718, 0.890) | 0.038 | 0.731 (0.671, 0.797) | <0.001 | 0.694 (0.653, 0.736) | <0.001 |
| | | 2 | M vs. L | 0.932 (0.800, 1.086) | 0.366 | 0.884 (0.752, 1.038) | 0.132 | 0.857 (0.729, 1.008) | 0.062 |
| | | | H vs. L | 0.790 (0.638, 0.976) | 0.029 | 0.726 (0.613, 0.861) | <0.001 | 0.698 (0.589, 0.828) | <0.001 |
| | | 3 | M vs. L | 0.982 (0.842, 1.146) | 0.820 | 0.941 (0.800, 1.108) | 0.466 | 0.946 (0.803, 1.115) | 0.510 |
| | | | H vs. L | 0.910 (0.734, 1.129) | 0.392 | 0.829 (0.697, 0.986) | 0.034 | 0.841 (0.706, 1.002) | 0.053 |
| | | 4 | M vs. L | 0.982 (0.841, 1.146) | 0.817 | 0.940 (0.799, 1.107) | 0.458 | 0.946 (0.803, 1.115) | 0.510 |
| | | | H vs. L | 0.908 (0.732, 1.128) | 0.384 | 0.828 (0.696, 0.985) | 0.033 | 0.841 (0.706, 1.002) | 0.053 |
| HVLТ | Retrospective memory (verbal episodic memory) | 1 | M vs. L | 0.909 (0.832, 0.993) | 0.278 | 0.904 (0.823, 0.992) | 0.279 | 0.789 (0.719, 0.867) | 0.011 |
| | | | H vs. L | 0.718 (0.704, 0.732) | 0.009 | 0.724 (0.656, 0.799) | 0.001 | 0.668 (0.553, 0.806) | <0.001 |
| | | 2 | M vs. L | 0.903 (0.751, 1.085) | 0.247 | 0.902 (0.750, 1.083) | 0.269 | 0.793 (0.659, 0.953) | 0.014 |
| | | | H vs. L | 0.707 (0.551, 0.908) | 0.007 | 0.715 (0.587, 0.870) | 0.001 | 0.668 (0.548, 0.812) | <0.001 |
| | | 3 | M vs. L | 0.941 (0.795, 1.113) | 0.496 | 0.949 (0.788, 1.143) | 0.583 | 0.868 (0.720, 1.046) | 0.138 |
| | | | H vs. L | 0.800 (0.621, 1.030) | 0.084 | 0.800 (0.655, 0.976) | 0.028 | 0.786 (0.643, 0.961) | 0.019 |
| | | 4 | M vs. L | 0.941 (0.790, 1.121) | 0.497 | 0.948 (0.787, 1.142) | 0.577 | 0.866 (0.719, 1.044) | 0.132 |
| | | | H vs. L | 0.796 (0.618, 1.026) | 0.078 | 0.797 (0.653, 0.973) | 0.026 | 0.784 (0.641, 0.959) | 0.018 |
| CANTAB-PAL | Retrospective memory (non- verbal episodic memory) | 1 | M vs. L | 1.018 (0.929, 1.115) | 0.845 | 0.918 (0.834, 1.010) | 0.371 | 0.865 (0.786, 0.952) | 0.131 |
| | | | H vs. L | 1.081 (0.859, 1.360) | 0.514 | 0.936 (0.850, 1.031) | 0.494 | 0.846 (0.768, 0.933) | 0.086 |
| | | 2 | M vs. L | 1.014 (0.848, 1.213) | 0.880 | 0.926 (0.766, 1.118) | 0.422 | 0.874 (0.723, 1.057) | 0.165 |
| | | | H vs. L | 1.088 (0.860, 1.377) | 0.481 | 0.942 (0.773, 1.142) | 0.543 | 0.861 (0.710, 1.044) | 0.127 |
| | | 3 | M vs. L | 1.054 (0.880, 1.262) | 0.566 | 0.975 (0.806, 1.180) | 0.796 | 0.940 (0.777, 1.138) | 0.528 |
| | | | H vs. L | 1.207 (0.951, 1.532) | 0.121 | 1.036 (0.852, 1.259) | 0.722 | 0.983 (0.807, 1.196) | 0.862 |
| | | 4 | M vs. L | 1.054 (0.880, 1.263) | 0.567 | 0.975 (0.806, 1.180) | 0.796 | 0.940 (0.776, 1.138) | 0.526 |
| | | | H vs. L | 1.207 (0.951, 1.532) | 0.122 | 1.036 (0.852, 1.259) | 0.725 | 0.983 (0.807, 1.196) | 0.861 |
| Letter Cancellation | Attention | 1 | M vs. L | 1.022 (0.942, 1.109) | 0.789 | 0.908 (0.833, 0.990) | 0.265 | 0.909 (0.834, 0.991) | 0.270 |
| | | | H vs. L | 0.912 (0.815, 1.020) | 0.411 | 0.831 (0.760, 909) | 0.038 | 0.832 (0.695, 0.995) | 0.041 |
| | | 2 | M vs. L | 1.020 (0.878, 1.185) | 0.812 | 0.910 (0.768, 1.079) | 0.277 | 0.991 (0.771, 1.075) | 0.283 |
| | | | H vs. L | 0.898 (0.720, 1.121) | 0.344 | 0.824 (0.691, 0.984) | 0.033 | 0.834 (0.698, 0.995) | 0.045 |
| | | 3 | M vs. L | 1.050 (0.894, 1.233) | 0.555 | 0.943 (0.795, 1.118) | 0.499 | 0.961 (0.809, 1.141) | 0.648 |
| | | | H vs. L | 0.972 (0.777, 1.216) | 0.803 | 0.887 (0.741, 1.061) | 0.189 | 0.924 (0.771, 1.107) | 0.392 |
| | | 4 | M vs. L | 1.050 (0.894, 1.233) | 0.556 | 0.943 (0.795, 1.118) | 0.500 | 0.961 (0.809, 1.141) | 0.650 |
| | | | H vs. L | 0.972 (0.777, 1.217) | 0.805 | 0.887 (0.742, 1.061) | 0.190 | 0.924 (0.771, 1.108) | 0.393 |

Supplementary Material

| | | | | | | | | | |
|-------------------------|--------------------------|---|---------|----------------------|-------|----------------------|--------------|----------------------|------------------|
| VST-Simple | Simple processing speed | 1 | M vs. L | 0.942 (0.857, 1.036) | 0.531 | 0.960 (0.869, 1.061) | 0.685 | 0.836 (0.756, 0.923) | 0.072 |
| | | | H vs. L | 0.960 (0.752, 1.224) | 0.742 | 0.863 (0.779, 0.956) | 0.151 | 0.756 (0.682, 0.839) | 0.007 |
| | | 2 | M vs. L | 0.934 (0.769, 1.135) | 0.476 | 0.958 (0.787, 1.166) | 0.667 | 0.836 (0.687, 1.017) | 0.074 |
| | | | H vs. L | 0.950 (0.743, 1.215) | 0.682 | 0.851 (0.695, 1.042) | 0.120 | 0.753 (0.614, 0.923) | 0.006 |
| | | 3 | M vs. L | 0.970 (0.807, 1.165) | 0.750 | 0.999 (0.819, 1.217) | 0.989 | 0.893 (0.732, 1.088) | 0.260 |
| | | | H vs. L | 1.042 (0.814, 1.333) | 0.748 | 0.926 (0.755, 1.135) | 0.461 | 0.845 (0.687, 1.040) | 0.113 |
| | | 4 | M vs. L | 0.970 (0.808, 1.165) | 0.750 | 0.998 (0.820, 1.217) | 0.988 | 0.892 (0.732, 1.087) | 0.259 |
| | | | H vs. L | 1.041 (0.814, 1.332) | 0.751 | 0.925 (0.754, 1.136) | 0.458 | 0.845 (0.687, 1.040) | 0.112 |
| VST-Complex | Complex processing speed | 1 | M vs. L | 0.927 (0.844, 1.019) | 0.423 | 0.789 (0.714, 0.872) | 0.017 | 0.789 (0.723, 0.880) | 0.021 |
| | | | H vs. L | 1.046 (0.926, 1.182) | 0.711 | 0.821 (0.743, 0.907) | 0.048 | 0.706 (0.637, 0.782) | 0.001 |
| | | 2 | M vs. L | 0.920 (0.767, 1.104) | 0.380 | 0.786 (0.646, 0.955) | 0.016 | 0.792 (0.654, 0.961) | 0.018 |
| | | | H vs. L | 1.033 (0.812, 1.314) | 0.793 | 0.814 (0.668, 0.992) | 0.041 | 0.696 (0.569, 0.852) | <0.001 |
| | | 3 | M vs. L | 0.939 (0.784, 1.125) | 0.505 | 0.803 (0.660, 0.978) | 0.029 | 0.821 (0.677, 0.996) | 0.047 |
| | | | H vs. L | 1.090 (0.855, 1.389) | 0.488 | 0.853 (0.699, 1.041) | 0.117 | 0.741 (0.603, 0.910) | 0.004 |
| | | 4 | M vs. L | 0.939 (0.782, 1.128) | 0.506 | 0.803 (0.660, 0.977) | 0.029 | 0.820 (0.675, 0.995) | 0.045 |
| | | | H vs. L | 1.087 (0.853, 1.386) | 0.501 | 0.850 (0.697, 1.038) | 0.111 | 0.739 (0.601, 0.907) | 0.004 |
| Prospective memory task | Prospective memory | 1 | M vs. L | 0.901 (0.842, 0.964) | 0.121 | 0.963 (0.896, 1.036) | 0.606 | 0.919 (0.855, 0.987) | 0.235 |
| | | | H vs. L | 0.898 (0.820, 0.984) | 0.238 | 0.933 (0.867, 1.004) | 0.344 | 0.773 (0.717, 0.833) | 0.001 |
| | | 2 | M vs. L | 0.896 (0.786, 1.022) | 0.106 | 0.962 (0.835, 1.109) | 0.595 | 0.923 (0.802, 1.062) | 0.265 |
| | | | H vs. L | 0.888 (0.742, 1.061) | 0.193 | 0.928 (0.802, 1.073) | 0.315 | 0.773 (0.668, 0.894) | 0.001 |
| | | 3 | M vs. L | 0.920 (0.805, 1.051) | 0.220 | 0.993 (0.861, 1.145) | 0.924 | 0.966 (0.839, 1.113) | 0.633 |
| | | | H vs. L | 0.953 (0.796, 1.141) | 0.602 | 0.993 (0.875, 1.151) | 0.927 | 0.842 (0.726, 0.977) | 0.025 |
| | | 4 | M vs. L | 0.920 (0.805, 1.051) | 0.220 | 0.993 (0.861, 1.145) | 0.920 | 0.965 (0.837, 1.112) | 0.619 |
| | | | H vs. L | 0.951 (0.793, 1.140) | 0.586 | 0.992 (0.856, 1.149) | 0.912 | 0.841 (0.724, 0.977) | 0.023 |

SF-EMSE, Short Form Extended Mini Mental State Exam (n = 7917); HVLT, Hopkins Verbal Learning Test (n = 7589); CANTAB-PAL, Paired Associates Learning Test from the Cambridge Automated Neuropsychological Test Battery (n = 6970); Letter cancellation (n = 7847); VST-Simple, Visual Sensitivity Test, simple version (n = 6685); VST-Complex, Visual Sensitivity Test, complex version (n = 6685); Prospective memory task (n = 7841). Associations were explored via logistic regression. Model 1 was adjusted for age, sex, BMI, waist circumference, marital status, and employment status. Model 2 was additionally adjusted for self-reported medical conditions (heart attack, stroke, arrhythmia, diabetes, depression, and other psychological illness), self-reported medication (BP lowering, lipid lowering, steroids, diabetes medication), HDL and LDL cholesterol, total triglycerides, smoking status, physical activity status, systolic BP and diastolic BP. Model 3 was additionally adjusted for education. Model 4 was additionally adjusted for *APOE E4* genotype. Contrasts are medium versus low adherence (M vs. L) and high versus low adherence (H vs. L).

Supplementary Material

Supplementary Table 5: Mediterranean diet adherence at HC1 and risk of poor cognitive performance at HC3 in maximally adjusted models, with participants stratified by CVD risk

| Outcome | Cognitive domain | CVD risk profile | Comparison | MEDAS OR (95% CI) | <i>P</i> | MEDAS Continuous OR (95% CI) | <i>P</i> | Pyramid OR (95% CI) | <i>P</i> |
|------------------------|---|------------------|------------|----------------------|----------|---------------------------------|--------------|------------------------|--------------|
| SF-EMSE | Global cognition | Low | M vs. L | 1.070 (0.812, 1.408) | 0.631 | 0.941 (0.710, 1.248) | 0.675 | 0.957 (0.718, 1.275) | 0.764 |
| | | | H vs. L | 0.997 (0.689, 1.442) | 0.986 | 0.753 (0.557, 1.017) | 0.065 | 0.890 (0.661, 1.198) | 0.441 |
| | | High | M vs. L | 0.944 (0.781, 1.142) | 0.553 | 0.906 (0.740, 1.109) | 0.340 | 0.952 (0.778, 1.165) | 0.634 |
| | | | H vs. L | 0.891 (0.679, 1.168) | 0.403 | 0.888 (0.717, 1.101) | 0.279 | 0.806 (0.647, 1.005) | 0.055 |
| HVLТ | Retrospective memory (verbal episodic memory) | Low | M vs. L | 1.031 (0.729, 1.458) | 0.862 | 1.010 (0.701, 1.455) | 0.958 | 0.779 (0.540, 1.123) | 0.181 |
| | | | H vs. L | 0.789 (0.490, 1.300) | 0.365 | 0.871 (0.595, 1.277) | 0.480 | 0.721 (0.493, 1.054) | 0.091 |
| | | High | M vs. L | 0.910 (0.741, 1.118) | 0.370 | 0.896 (0.720, 1.115) | 0.324 | 0.898 (0.721, 1.119) | 0.339 |
| | | | H vs. L | 0.779 (0.567, 1.055) | 0.106 | 0.756 (0.596, 0.958) | 0.021 | 0.793 (0.624, 1.009) | 0.059 |
| CANTAB-PAL | Retrospective memory (non- verbal episodic memory) | Low | M vs. L | 1.080 (0.776, 2.502) | 0.650 | 1.038 (0.741, 1.454) | 0.828 | 0.822 (0.579, 1.168) | 0.275 |
| | | | H vs. L | 0.965 (0.622, 1.497) | 0.874 | 0.816 (0.569, 1.170) | 0.269 | 0.869 (0.613, 1.232) | 0.430 |
| | | High | M vs. L | 1.031 (0.830, 1.281) | 0.781 | 0.913 (0.724, 1.152) | 0.443 | 0.971 (0.771, 1.222) | 0.801 |
| | | | H vs. L | 1.332 (0.998, 1.777) | 0.052 | 1.145 (0.906, 1.447) | 0.258 | 1.036 (0.815, 1.318) | 0.770 |
| Letter cancellation | Attention | Low | M vs. L | 1.119 (0.845, 1.481) | 0.448 | 0.867 (0.641, 1.174) | 0.357 | 0.977 (0.727, 1.367) | 0.984 |
| | | | H vs. L | 0.985 (0.672, 1.443) | 0.937 | 0.863 (0.638, 1.167) | 0.341 | 0.989 (0.726, 1.347) | 0.944 |
| | | High | M vs. L | 1.027 (0.842, 1.252) | 0.793 | 0.971 (0.787, 1.197) | 0.781 | 0.951 (0.771, 1.173) | 0.640 |
| | | | H vs. L | 0.979 (0.739, 1.297) | 0.884 | 0.901 (0.720, 1.128) | 0.364 | 0.893 (0.712, 1.120) | 0.328 |
| VST-Simple | Simple processing speed | Low | M vs. L | 0.927 (0.690, 1.244) | 0.613 | 0.912 (0.673, 1.237) | 0.558 | 0.886 (0.654, 1.201) | 0.443 |
| | | | H vs. L | 1.170 (0.810, 1.692) | 0.403 | 0.820 (0.599, 1.124) | 0.219 | 0.839 (0.612, 1.151) | 0.281 |
| | | High | M vs. L | 0.988 (0.770, 1.267) | 0.923 | 1.020 (0.784, 1.327) | 0.883 | 0.879 (0.676, 1.143) | 0.336 |
| | | | H vs. L | 0.956 (0.677, 1.350) | 0.797 | 1.027 (0.781, 1.352) | 0.847 | 0.841 (0.638, 1.109) | 0.223 |
| VST-Complex | Complex processing speed | Low | M vs. L | 0.888 (0.658, 1.198) | 0.437 | 0.912 (0.664, 1.252) | 0.568 | 1.040 (0.885, 1.223) | 0.807 |
| | | | H vs. L | 0.962 (0.653, 1.419) | 0.846 | 0.848 (0.614, 1.172) | 0.319 | 0.867 (0.620, 1.213) | 0.405 |
| | | High | M vs. L | 0.977 (0.769, 1.242) | 0.851 | 0.728 (0.565, 0.939) | 0.015 | 0.707 (0.551, 0.908) | 0.007 |
| | | | H vs. L | 1.185 (0.861, 1.629) | 0.298 | 0.852 (0.658, 1.103) | 0.225 | 0.667 (0.551, 0.871) | 0.003 |
| Prospective memory | Prospective memory | Low | M vs. L | 0.882 (0.704, 1.104) | 0.273 | 0.902 (0.706, 1.151) | 0.406 | 0.849 (0.667, 1.081) | 0.185 |
| | | | H vs. L | 0.975 (0.730, 1.302) | 0.862 | 1.042 (0.820, 1.323) | 0.738 | 0.859 (0.674, 1.095) | 0.220 |
| | | High | M vs. L | 0.950 (0.803, 1.123) | 0.546 | 1.050 (0.879, 1.256) | 0.589 | 1.039 (0.870, 1.241) | 0.673 |
| | | | H vs. L | 0.944 (0.746, 1.194) | 0.629 | 0.971 (0.804, 1.173) | 0.760 | 0.826 (0.681, 1.002) | 0.052 |

SF-EMSE, Short Form Extended Mini Mental State Exam (low risk n = 3942, high risk n = 3914); HVLТ, Hopkins Verbal Learning Test (low risk n = 3847, high risk n = 3685); CANTAB-PAL, Paired Associates Learning Test from the Cambridge Automated Neuropsychological Test Battery (low risk n = 3549, high risk n = 3366); Letter cancellation (low risk n = 3931, high risk n = 3855); VST-Simple, Visual Sensitivity Test, simple version (low risk n = 3424, high risk n = 3207); VST-Complex, Visual Sensitivity Test, complex version (low risk n = 3424, high risk n = 3207); Prospective memory task (low risk n = 3925, high risk n = 3855). Associations were explored via logistic regression. Contrasts are medium versus low adherence (M vs. L) and high versus low adherence (H vs. L). Participants are stratified in to low and high CVD risk by the QRISK2 score median.

Supplementary Material

Supplementary Table 6: Mediterranean diet adherence at HC2 and cognitive function at HC3 of the EPIC-Norfolk study

| Outcome | Cognitive domain | Model | MEDAS | | MEDAS Continuous | | Pyramid | |
|---------------------|---|-------|----------------|--------------|------------------|------------------|----------------|------------------|
| | | | β + SE | <i>P</i> | β + SE | <i>P</i> | β + SE | <i>P</i> |
| SF-EMSE | Global cognition | 1 | -0.007 ± 0.002 | 0.001 | -0.011 ± 0.002 | <0.001 | -0.018 ± 0.002 | <0.001 |
| | | 2 | -0.007 ± 0.002 | 0.001 | -0.011 ± 0.002 | <0.001 | -0.018 ± 0.002 | <0.001 |
| | | 3 | -0.002 ± 0.002 | 0.273 | -0.004 ± 0.003 | 0.056 | -0.011 ± 0.002 | <0.001 |
| | | 4 | -0.002 ± 0.002 | 0.266 | -0.004 ± 0.003 | 0.053 | -0.011 ± 0.002 | <0.001 |
| HVLТ | Retrospective memory (verbal episodic memory) | 1 | -0.006 ± 0.002 | 0.007 | -0.007 ± 0.002 | 0.002 | -0.010 ± 0.002 | <0.001 |
| | | 2 | -0.006 ± 0.002 | 0.008 | -0.007 ± 0.002 | 0.004 | -0.010 ± 0.002 | <0.001 |
| | | 3 | -0.001 ± 0.002 | 0.501 | 0.000 ± 0.002 | 0.869 | 0.002 ± 0.002 | 0.309 |
| | | 4 | -0.002 ± 0.002 | 0.467 | 0.000 ± 0.002 | 0.831 | 0.002 ± 0.002 | 0.291 |
| CANTAB-PAL | Retrospective memory (non-verbal episodic memory) | 1 | -0.019 ± 0.040 | 0.632 | 0.026 ± 0.043 | 0.553 | 0.115 ± 0.042 | 0.007 |
| | | 2 | -0.023 ± 0.040 | 0.562 | 0.019 ± 0.044 | 0.672 | 0.122 ± 0.043 | 0.004 |
| | | 3 | -0.075 ± 0.040 | 0.061 | -0.059 ± 0.044 | 0.175 | 0.031 ± 0.043 | 0.468 |
| | | 4 | -0.074 ± 0.040 | 0.063 | -0.059 ± 0.044 | 0.181 | 0.032 ± 0.043 | 0.463 |
| Letter Cancellation | Attention | 1 | -0.066 ± 0.054 | 0.218 | -0.055 ± 0.058 | 0.257 | 0.067 ± 0.058 | 0.248 |
| | | 2 | -0.067 ± 0.054 | 0.217 | -0.057 ± 0.059 | 0.701 | 0.070 ± 0.058 | 0.227 |
| | | 3 | -0.113 ± 0.054 | 0.037 | -0.125 ± 0.060 | 0.036 | -0.006 ± 0.059 | 0.918 |
| | | 4 | -0.113 ± 0.054 | 0.037 | -0.125 ± 0.060 | 0.037 | -0.006 ± 0.059 | 0.921 |
| VST-Simple | Simple processing speed | 1 | -0.002 ± 0.001 | 0.005 | -0.003 ± 0.001 | 0.001 | -0.004 ± 0.001 | <0.001 |
| | | 2 | -0.002 ± 0.001 | 0.005 | -0.003 ± 0.001 | 0.001 | -0.004 ± 0.001 | <0.001 |
| | | 3 | -0.002 ± 0.001 | 0.037 | -0.002 ± 0.001 | 0.016 | -0.003 ± 0.001 | 0.004 |
| | | 4 | -0.002 ± 0.001 | 0.034 | -0.002 ± 0.001 | 0.015 | -0.003 ± 0.001 | 0.003 |
| VST-Complex | Complex processing speed | 1 | -0.001 ± 0.001 | 0.244 | -0.002 ± 0.001 | 0.028 | -0.002 ± 0.001 | 0.007 |
| | | 2 | -0.001 ± 0.001 | 0.272 | -0.002 ± 0.001 | 0.035 | -0.002 ± 0.001 | 0.009 |
| | | 3 | -0.001 ± 0.001 | 0.389 | -0.002 ± 0.001 | 0.074 | -0.002 ± 0.001 | 0.026 |
| | | 4 | -0.001 ± 0.001 | 0.377 | -0.002 ± 0.001 | 0.070 | -0.002 ± 0.001 | 0.025 |

SF-EMSE, Short Form Extended Mini Mental State Exam (n = 5851); HVLТ, Hopkins Verbal Learning Test (n = 5605); CANTAB-PAL, Paired Associates Learning Test from the Cambridge Automated Neuropsychological Test Battery (n = 5120); Letter cancellation task (n = 5769); VST-Simple, Visual Sensitivity Test, simple version (n = 4887); VST-Complex, Visual Sensitivity Test, complex version (n = 4887). Associations were explored via linear regression. Model 1 was adjusted for age, sex, BMI, waist circumference, marital status, and employment status. Model 2 was additionally adjusted for self-reported medical conditions (heart attack, stroke, arrhythmia, diabetes, depression, and other psychological illness), self-reported medication (BP lowering, lipid lowering, steroids, diabetes medication), HDL and LDL cholesterol, total triglycerides, smoking status, physical activity status, systolic and diastolic BP. Model 3 was additionally adjusted for education. Model 4 was additionally adjusted for *APOE E4* genotype. Scores for the SF-EMSE and HVLТ were negatively skewed, and therefore log and reverse score transformed variables were derived. Lower transformed scores on these tests reflect better cognitive performance (i.e. greater original scores). VST-Simple and VST-Complex scores were log transformed (log10), whilst untransformed variables were used for the CANTAB-PAL and Letter Cancellation Task.

Supplementary Material

Supplementary Table 7: Mediterranean diet adherence at HC2 and the risk of poor cognitive performance at HC3 of the EPIC-Norfolk study

| Outcome | Cognitive domain | Model | Comparison | MEDAS OR (95% CI) | <i>P</i> | MEDAS Continuous OR (95% CI) | <i>P</i> | Pyramid OR (95% CI) | <i>P</i> |
|------------------------|---|-------|------------|----------------------|--------------|---------------------------------|--------------|------------------------|--------------|
| SF-EMSE | Global cognition | 1 | M vs. L | 0.912 (0.829, 1.003) | 0.333 | 0.999 (0.908, 1.099) | 0.990 | 1.002 (0.838, 1.197) | 0.985 |
| | | | H vs. L | 0.812 (0.637, 1.034) | 0.082 | 0.824 (0.777, 0.874) | 0.054 | 0.752 (0.616, 0.917) | 0.005 |
| | | 2 | M vs. L | 0.909 (0.753, 1.097) | 0.321 | 0.990 (0.820, 1.196) | 0.919 | 0.998 (0.827, 1.204) | 0.983 |
| | | | H vs. L | 0.802 (0.632, 1.016) | 0.068 | 0.814 (0.667, 0.994) | 0.044 | 0.749 (0.612, 0.916) | 0.005 |
| | | 3 | M vs. L | 0.965 (0.798, 1.168) | 0.716 | 1.040 (0.860, 1.259) | 0.684 | 1.103 (0.912, 1.335) | 0.312 |
| | | | H vs. L | 0.914 (0.718, 1.162) | 0.463 | 0.943 (0.770, 1.156) | 0.574 | 0.883 (0.718, 1.085) | 0.236 |
| | | 4 | M vs. L | 0.962 (0.795, 1.164) | 0.693 | 1.038 (0.857, 1.256) | 0.704 | 1.105 (0.913, 1.337) | 0.306 |
| | | | H vs. L | 0.911 (0.716, 1.159) | 0.446 | 0.938 (0.765, 1.150) | 0.541 | 0.882 (0.718, 1.084) | 0.234 |
| HVLT | Retrospective memory (verbal episodic memory) | 1 | M vs. L | 0.895 (0.728, 1.100) | 0.296 | 0.905 (0.812, 1.008) | 0.353 | 1.011 (0.823, 1.243) | 0.917 |
| | | | H vs. L | 0.785 (0.602, 1.024) | 0.075 | 0.802 (0.644, 0.998) | 0.050 | 0.820 (0.656, 1.025) | 0.083 |
| | | 2 | M vs. L | 0.891 (0.722, 1.099) | 0.280 | 0.900 (0.727, 1.114) | 0.331 | 1.013 (0.819, 1.253) | 0.904 |
| | | | H vs. L | 0.797 (0.609, 1.042) | 0.097 | 0.816 (0.653, 1.021) | 0.075 | 0.829 (0.661, 1.039) | 0.104 |
| | | 3 | M vs. L | 0.937 (0.758, 1.158) | 0.546 | 0.942 (0.760, 1.168) | 0.587 | 1.115 (0.899, 1.383) | 0.332 |
| | | | H vs. L | 0.884 (0.674, 1.160) | 0.373 | 0.921 (0.734, 1.157) | 0.481 | 0.961 (0.763, 1.212) | 0.739 |
| | | 4 | M vs. L | 0.929 (0.751, 1.148) | 0.495 | 0.936 (0.755, 1.162) | 0.550 | 1.122 (0.904, 1.392) | 0.297 |
| | | | H vs. L | 0.869 (0.662, 1.141) | 0.312 | 0.906 (0.721, 1.138) | 0.396 | 0.958 (0.760, 1.209) | 0.720 |
| CANTAB-PAL | Retrospective memory (non- verbal episodic memory) | 1 | M vs. L | 0.952 (0.852, 1.065) | 0.661 | 1.151 (1.030, 1.287) | 0.205 | 0.935 (0.752, 1.161) | 0.543 |
| | | | H vs. L | 1.158 (0.961, 1.396) | 0.269 | 1.051 (0.937, 1.178) | 0.666 | 0.912 (0.734, 1.132) | 0.416 |
| | | 2 | M vs. L | 0.959 (0.769, 1.195) | 0.707 | 1.153 (0.928, 1.438) | 0.197 | 0.940 (0.755, 1.171) | 0.583 |
| | | | H vs. L | 1.183 (0.910, 1.538) | 0.210 | 1.076 (0.857, 1.351) | 0.528 | 0.935 (0.747, 1.172) | 0.561 |
| | | 3 | M vs. L | 1.000 (0.801, 1.248) | 1.000 | 1.194 (0.958, 1.488) | 0.114 | 1.007 (0.807, 1.256) | 0.951 |
| | | | H vs. L | 1.274 (0.977, 1.660) | 0.073 | 1.173 (0.931, 1.477) | 0.176 | 1.040 (0.827, 1.309) | 0.735 |
| | | 4 | M vs. L | 1.000 (0.802, 1.248) | 0.999 | 1.194 (0.958, 1.489) | 0.114 | 1.007 (0.807, 1.256) | 0.951 |
| | | | H vs. L | 1.274 (0.977, 1.660) | 0.073 | 1.173 (0.931, 1.477) | 0.176 | 1.040 (0.827, 1.309) | 0.735 |
| Letter Cancellation | Attention | 1 | M vs. L | 1.141 (1.027, 1.267) | 0.210 | 1.007 (0.908, 1.116) | 0.946 | 0.964 (0.800, 1.162) | 0.718 |
| | | | H vs. L | 1.211 (0.951, 1.542) | 0.128 | 1.058 (0.848, 1.321) | 0.586 | 0.870 (0.712, 1.062) | 0.184 |
| | | 2 | M vs. L | 1.139 (0.926, 1.400) | 0.218 | 1.004 (0.820, 1.230) | 0.969 | 0.960 (0.786, 1.171) | 0.686 |
| | | | H vs. L | 1.202 (0.938, 1.540) | 0.145 | 1.054 (0.858, 1.293) | 0.617 | 0.858 (0.697, 1.057) | 0.150 |
| | | 3 | M vs. L | 1.177 (0.956, 1.448) | 0.124 | 1.029 (0.839, 1.261) | 0.786 | 1.008 (0.824, 1.232) | 0.940 |
| | | | H vs. L | 1.286 (1.002, 1.651) | 0.049 | 1.134 (0.921, 1.396) | 0.235 | 0.929 (0.752, 1.147) | 0.494 |
| | | 4 | M vs. L | 1.178 (0.958, 1.450) | 0.121 | 1.030 (0.840, 1.263) | 0.777 | 1.007 (0.824, 1.231) | 0.946 |
| | | | H vs. L | 1.288 (1.003, 1.654) | 0.047 | 1.137 (0.923, 1.400) | 0.226 | 0.929 (0.752, 1.148) | 0.496 |

Supplementary Material

| | | | | | | | | | |
|-------------------------|--------------------------|---|---------|----------------------|--------------|----------------------|--------------|----------------------|--------------|
| VST-Simple | Simple processing speed | 1 | M vs. L | 0.913 (0.887, 0.940) | 0.423 | 0.950 (0.849, 1.064) | 0.653 | 0.811 (0.722, 0.910) | 0.070 |
| | | | H vs. L | 0.635 (0.474, 0.849) | 0.002 | 0.687 (0.543, 0.870) | 0.002 | 0.749 (0.595, 0.943) | 0.016 |
| | | 2 | M vs. L | 0.913 (0.731, 1.142) | 0.426 | 0.954 (0.763, 1.192) | 0.679 | 0.807 (0.642, 1.014) | 0.065 |
| | | | H vs. L | 0.634 (0.472, 0.852) | 0.002 | 0.683 (0.536, 0.871) | 0.002 | 0.744 (0.588, 0.942) | 0.014 |
| | | 3 | M vs. L | 0.946 (0.756, 1.184) | 0.628 | 0.978 (0.782, 1.223) | 0.845 | 0.869 (0.690, 1.095) | 0.234 |
| | | | H vs. L | 0.685 (0.509, 0.922) | 0.013 | 0.748 (0.585, 0.956) | 0.020 | 0.841 (0.661, 1.069) | 0.158 |
| | | 4 | M vs. L | 0.945 (0.755, 1.182) | 0.618 | 0.978 (0.781, 1.223) | 0.843 | 0.870 (0.691, 1.095) | 0.236 |
| | | | H vs. L | 0.684 (0.508, 0.920) | 0.012 | 0.746 (0.583, 0.954) | 0.019 | 0.840 (0.661, 1.069) | 0.157 |
| VST-Complex | Complex processing speed | 1 | M vs. L | 0.960 (0.856, 1.077) | 0.726 | 0.750 (0.668, 0.842) | 0.013 | 0.841 (0.751, 0.942) | 0.126 |
| | | | H vs. L | 0.957 (0.739, 1.239) | 0.754 | 0.822 (0.732, 0.922) | 0.088 | 0.695 (0.617, 0.784) | 0.002 |
| | | 2 | M vs. L | 0.970 (0.773, 1.217) | 0.790 | 0.761 (0.605, 0.957) | 0.020 | 0.844 (0.675, 1.055) | 0.136 |
| | | | H vs. L | 0.981 (0.743, 1.296) | 0.893 | 0.836 (0.665, 1.052) | 0.126 | 0.701 (0.553, 0.888) | 0.003 |
| | | 3 | M vs. L | 0.987 (0.786, 1.240) | 0.914 | 0.772 (0.613, 0.971) | 0.027 | 0.873 (0.698, 1.094) | 0.238 |
| | | | H vs. L | 1.023 (0.774, 1.354) | 0.871 | 0.877 (0.695, 1.105) | 0.265 | 0.739 (0.581, 0.940) | 0.014 |
| | | 4 | M vs. L | 0.986 (0.785, 1.239) | 0.906 | 0.772 (0.613, 0.971) | 0.027 | 0.874 (0.698, 1.094) | 0.239 |
| | | | H vs. L | 1.021 (0.772, 1.351) | 0.882 | 0.874 (0.694, 1.103) | 0.257 | 0.739 (0.581, 0.940) | 0.014 |
| Prospective memory task | Prospective memory | 1 | M vs. L | 0.973 (0.845, 1.120) | 0.741 | 1.048 (0.966, 1.138) | 0.565 | 0.966 (0.816, 1.145) | 0.678 |
| | | | H vs. L | 0.817 (0.668, 0.999) | 0.049 | 0.891 (0.757, 1.048) | 0.173 | 0.870 (0.737, 1.025) | 0.100 |
| | | 2 | M vs. L | 0.966 (0.822, 1.135) | 0.672 | 1.043 (0.887, 1.226) | 0.612 | 0.963 (0.818, 1.133) | 0.650 |
| | | | H vs. L | 0.815 (0.665, 0.998) | 0.048 | 0.896 (0.757, 1.060) | 0.201 | 0.870 (0.735, 1.029) | 0.103 |
| | | 3 | M vs. L | 0.994 (0.845, 1.168) | 0.937 | 1.066 (0.906, 1.254) | 0.444 | 1.010 (0.857, 1.190) | 0.909 |
| | | | H vs. L | 0.865 (0.705, 1.061) | 0.164 | 0.958 (0.807, 1.136) | 0.622 | 0.940 (0.792, 1.115) | 0.476 |
| | | 4 | M vs. L | 0.989 (0.841, 1.164) | 0.898 | 1.062 (0.902, 1.250) | 0.469 | 1.010 (0.857, 1.190) | 0.905 |
| | | | H vs. L | 0.861 (0.701, 1.056) | 0.151 | 0.951 (0.802, 1.129) | 0.568 | 0.937 (0.790, 1.112) | 0.458 |

SF-EMSE, Short Form Extended Mini Mental State Exam (n = 5851); HVLT, Hopkins Verbal Learning Test (n = 5605); CANTAB-PAL, Paired Associates Learning Test from the Cambridge Automated Neuropsychological Test Battery (n = 5120); Letter cancellation task (n = 5769); VST-Simple, Visual Sensitivity Test, simple version (n = 4887); VST-Complex, Visual Sensitivity Test, complex version (n = 4887); Prospective memory task (n = 5801). Associations were explored via logistic regression. Model 1 was adjusted for age, sex, BMI, waist circumference, marital status, and employment status. Model 2 was additionally adjusted for self-reported medical conditions (heart attack, stroke, arrhythmia, diabetes, depression, and other psychological illness), self-reported medication (BP lowering, lipid lowering, steroids, diabetes medication), HDL and LDL cholesterol, total triglycerides, smoking status, physical activity status, systolic BP and diastolic BP. Model 3 was additionally adjusted for education. Model 4 was additionally adjusted for *APOE E4* genotype. Contrasts are medium versus low adherence (M vs. L) and high versus low adherence (H vs. L).

Supplementary Material

Supplementary Table 8: Sensitivity analysis exploring the influence of each component of the MedDiet in the MEDAS and MEDAS Continuous scale at HC1 on cognitive function at HC3 of the EPIC-Norfolk study in maximally adjusted models

| Component | MEDAS | B + SE | MEDAS Continuous | P |
|-------------------------------|----------------|--------------|------------------|-------------------|
| | SF-EMSE | | SF-EMSE | |
| | B + SE | | B + SE | |
| Full score | -0.004 ± 0.002 | 0.018 | -0.005 ± 0.002 | 0.008 |
| Minus olive oil | -0.004 ± 0.002 | 0.040 | -0.005 ± 0.002 | 0.018 |
| Minus vegetables | -0.005 ± 0.002 | 0.015 | -0.006 ± 0.002 | 0.006 |
| Minus fruit | -0.004 ± 0.002 | 0.076 | -0.005 ± 0.002 | 0.029 |
| Minus red meat | -0.004 ± 0.002 | 0.032 | -0.005 ± 0.002 | 0.010 |
| Minus high fat dairy | -0.007 ± 0.002 | 0.001 | -0.008 ± 0.002 | < 0.001 |
| Minus sugar sweetened drinks | -0.005 ± 0.002 | 0.014 | -0.006 ± 0.002 | 0.004 |
| Minus wine | -0.004 ± 0.002 | 0.063 | -0.003 ± 0.002 | 0.206 |
| Minus legumes | -0.005 ± 0.002 | 0.010 | -0.006 ± 0.002 | 0.002 |
| Minus seafood | -0.004 ± 0.002 | 0.039 | -0.006 ± 0.002 | 0.008 |
| Minus sweets | -0.005 ± 0.002 | 0.008 | -0.007 ± 0.002 | 0.001 |
| Minus nuts | -0.004 ± 0.002 | 0.036 | -0.005 ± 0.002 | 0.029 |
| Minus preferential white meat | -0.004 ± 0.002 | 0.041 | -0.005 ± 0.002 | 0.020 |
| Minus sofrito | -0.004 ± 0.002 | 0.019 | -0.005 ± 0.002 | 0.013 |

SF-EMSE, Short Form Extended Mini Mental State Exam (n = 7917). Associations were explored via linear regression. Scores for the SF-EMSE were negatively skewed, and therefore log and reverse score transformed variables were derived. Lower transformed scores reflect better cognitive performance (i.e. greater original scores).

Supplementary Material

Supplementary Table 9: Sensitivity analysis exploring the influence of each component of the MedDiet in the Pyramid score at HC1 on cognitive function at HC3 of the EPIC-Norfolk study in maximally adjusted models

| Component | SF-EMSE | | HVLTL | | VST-Simple | |
|----------------------|----------------|--------|----------------|--------|----------------|--------------|
| | B + SE | P | B + SE | P | B + SE | P |
| Full score | -0.012 ± 0.002 | <0.001 | -0.009 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.013 |
| Minus vegetables | -0.014 ± 0.002 | <0.001 | -0.009 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.016 |
| Minus legumes | -0.012 ± 0.002 | <0.001 | -0.009 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.013 |
| Minus fruits | -0.013 ± 0.002 | <0.001 | -0.009 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.013 |
| Minus nuts | -0.013 ± 0.002 | <0.001 | -0.009 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.018 |
| Minus cereals | -0.011 ± 0.002 | <0.001 | -0.008 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.027 |
| Minus dairy | -0.012 ± 0.002 | <0.001 | -0.009 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.024 |
| Minus fish | -0.014 ± 0.002 | <0.001 | -0.009 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.024 |
| Minus red meat | -0.013 ± 0.002 | <0.001 | -0.011 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.005 |
| Minus processed meat | -0.013 ± 0.002 | <0.001 | -0.010 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.007 |
| Minus white meat | -0.011 ± 0.002 | <0.001 | -0.008 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.028 |
| Minus eggs | -0.012 ± 0.002 | <0.001 | -0.009 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.020 |
| Minus potato | -0.013 ± 0.002 | <0.001 | -0.009 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.012 |
| Minus sweets | -0.013 ± 0.002 | <0.001 | -0.009 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.011 |
| Minus alcohol | -0.012 ± 0.002 | <0.001 | -0.009 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.022 |
| Minus olive oil | -0.012 ± 0.002 | <0.001 | -0.009 ± 0.002 | <0.001 | -0.002 ± 0.001 | 0.013 |

SF-EMSE, Short Form Extended Mini Mental State Exam (n = 7917); HVLTL, Hopkins Verbal Learning Test (n = 7589); VST, Visual Sensitivity Test (n = 6685). Associations were explored via linear regression. Scores for the SF-EMSE and HVLTL were negatively skewed, and therefore log and reverse score transformed variables were derived. Lower transformed scores on these tests reflect better cognitive performance (i.e. greater original scores). VST-Simple scores were log transformed (log10).

Supplementary Material

Supplementary Table 10: Sensitivity analysis excluding potential under- or over-reporters for energy intake in maximally adjusted models exploring associations between Mediterranean diet adherence at HC1 and cognitive function at HC3 of the EPIC-Norfolk study.

| Outcome | Cognitive domain | MEDAS | | MEDAS Continuous | | Pyramid | |
|---------------------|---|----------------|----------|------------------|--------------|----------------|------------------|
| | | β + SE | <i>P</i> | β + SE | <i>P</i> | β + SE | <i>P</i> |
| SF-EMSE | Global cognition | -0.004 ± 0.002 | 0.057 | -0.005 ± 0.002 | 0.060 | -0.013 ± 0.002 | <0.001 |
| HVLT | Retrospective memory (verbal episodic memory) | -0.003 ± 0.002 | 0.139 | -0.006 ± 0.002 | 0.021 | -0.010 ± 0.002 | <0.001 |
| CANTAB-PAL | Retrospective memory (non-verbal episodic memory) | -0.006 ± 0.045 | 0.889 | -0.014 ± 0.049 | 0.781 | 0.043 ± 0.047 | 0.360 |
| Letter Cancellation | Attention | 0.020 ± 0.061 | 0.747 | 0.071 ± 0.066 | 0.279 | 0.056 ± 0.063 | 0.376 |
| VST-Simple | Simple processing speed | -0.002 ± 0.001 | 0.090 | -0.002 ± 0.001 | 0.071 | -0.003 ± 0.001 | 0.005 |
| VST-Complex | Complex processing speed | -0.001 ± 0.001 | 0.112 | -0.002 ± 0.001 | 0.062 | -0.002 ± 0.001 | 0.019 |

SF-EMSE, Short Form Extended Mini Mental State Exam (n = 5349); HVLT, Hopkins Verbal Learning Test (n = 5131); CANTAB-PAL, Paired Associates Learning Test from the Cambridge Automated Neuropsychological Test Battery (n = 4711); VST, Visual Sensitivity Test (n = 4502). Associations were explored via linear regression. Scores for the SF-EMSE and HVLT were negatively skewed, and therefore log and reverse score transformed variables were derived. Lower transformed scores on these tests reflect better cognitive performance (i.e. greater original scores). VST-Simple and VST-Complex scores were log transformed (log10), whilst untransformed variables were used for the CANTAB-PAL and Letter Cancellation Task.

Supplementary Material

Supplementary Table 11: Interaction between Mediterranean diet adherence at HC1 and CVD risk status and risk of poor cognitive performance at HC3 in maximally adjusted models

| Outcome | Cognitive domain | Contrast | MEDAS OR (95% CI) | <i>P for interaction</i> | MEDAS Continuous OR (95% CI) | <i>P for interaction</i> | Pyramid OR (95% CI) | <i>P for interaction</i> |
|---------------------|---|--------------------|----------------------|------------------------------|---------------------------------|------------------------------|------------------------|------------------------------|
| SF-EMSE | Global cognition | M vs. L * CVD risk | 0.976 (0.765, 1.246) | 0.847 | 0.994 (0.748, 1.320) | 0.965 | 0.893 (.871, 1.189) | 0.438 |
| | | H vs. L * CVD risk | 0.941 (0.639, 1.385) | 0.757 | 0.792 (0.585, 1.073) | 0.132 | 0.963 (0.715, 1.296) | 0.803 |
| HVLТ | Retrospective memory (verbal episodic memory) | M vs. L * CVD risk | 1.034 (0.773, 1.384) | 0.823 | 1.010 (0.718, 1.420) | 0.956 | 0.889 (0.628, 1.260) | 0.510 |
| | | H vs. L * CVD risk | 0.944 (0.580, 1.538) | 0.818 | 1.021 (0.710, 1.469) | 0.911 | 0.921 (0.639, 1.327) | 0.658 |
| CANTAB-PAL | Retrospective memory (non-verbal episodic memory) | M vs. L * CVD risk | 0.993 (0.747, 1.319) | 0.961 | 1.088 (0.781, 1.515) | 0.619 | 0.485 (0.351, 0.670) | <0.001 |
| | | H vs. L * CVD risk | 0.648 (0.419, 1.001) | 0.050 | 0.652 (0.462, 0.921) | 0.015 | 0.516 (0.375, 0.709) | <0.001 |
| Letter cancellation | Attention | M vs. L * CVD risk | 0.686 (0.543, 0.867) | 0.002 | 0.953 (0.704, 1.289) | 0.753 | 1.046 (0.774, 1.413) | 0.770 |
| | | H vs. L * CVD risk | 0.682 (0.463, 1.006) | 0.054 | 1.075 (0.792, 1.459) | 0.643 | 1.129 (0.833, 1.530) | 0.436 |
| VST-Simple | Simple processing speed | M vs. L * CVD risk | 0.992 (0.743, 1.324) | 0.956 | 1.012 (0.726, 1.469) | 0.946 | 1.047 (0.751, 1.461) | 0.785 |
| | | H vs. L * CVD risk | 1.262 (0.826, 1.928) | 0.283 | 0.911 (0.648, 1.280) | 0.590 | 0.992 (0.704, 1.398) | 0.964 |
| VST-Complex | Complex processing speed | M vs. L * CVD risk | 1.003 (0.751, 1.340) | 0.983 | 1.227 (0.873, 1.722) | 0.239 | 1.317 (0.946, 1.833) | 0.102 |
| | | H vs. L * CVD risk | 0.861 (0.564, 1.314) | 0.488 | 0.955 (0.680, 1.340) | 0.789 | 1.105 (0.779, 1.566) | 0.576 |
| Prospective memory | Prospective memory | M vs. L * CVD risk | 0.862 (0.700, 1.063) | 0.165 | 0.793 (0.620, 1.014) | 0.064 | 0.772 (0.605, 0.986) | 0.038 |
| | | H vs. L * CVD risk | 0.940 (0.686, 1.289) | 0.701 | 0.974 (0.764, 1.243) | 0.833 | 0.979 (0.764, 1.256) | 0.870 |

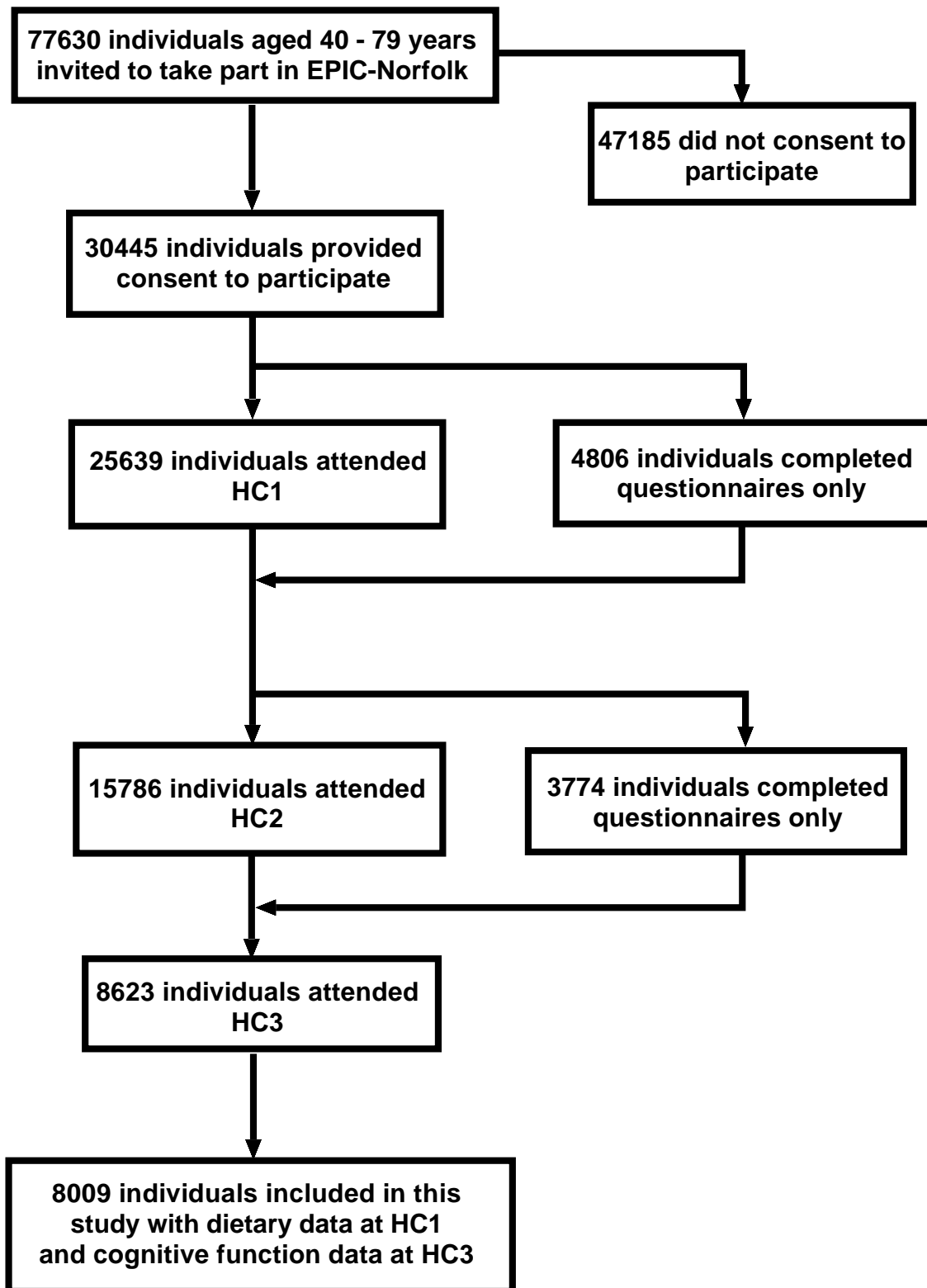
SF-EMSE, Short Form Extended Mini Mental State Exam (n = 7856); HVLТ, Hopkins Verbal Learning Test (n = 7532);, CANTAB-PAL, Paired Associates Learning Test from the Cambridge Automated Neuropsychological Test Battery (n = 6915); Letter cancellation (n = 7786); VST-Simple, Visual Sensitivity Test, simple version (n = 6631); VST-Complex, Visual Sensitivity Test, complex version (n = 6631); Prospective memory task (n = 7780). Analyses explored, via logistic regression, whether the associations between MedDiet adherence and risk of poor cognitive performance varied by CVD risk status (0 (low risk), 1(high risk)) by including a diet * CVD risk group interaction term in maximally adjusted models. Odds ratios indicate whether those with high CVD status compared to those with low CVD status had increased or decreased risk of poor cognitive performance if belonging to medium versus low (M vs. L) and high versus low (H vs. L) MedDiet group. Significant *P* for interactions are presented in bold.

Supplementary Material

Supplementary Table 12: A comparison of participant characteristics at HC3 of the EPIC-Norfolk study between individuals with complete and incomplete cognitive test data

| Characteristic | All cognitive tests completed (n = 5861) | Partial completion of cognitive tests (n=2148) | <i>P</i> |
|----------------------------|---|---|------------------|
| Age, Years | 67 (62, 74) | 70 (64, 78) | <0.001 |
| Sex, % males | 44 | 45 | 0.568 |
| BMI, kg/m ² | 26 (24, 29) | 26 (24, 29) | 0.693 |
| Smoking status, % | | | 0.558 |
| Current | 4 | 4 | |
| Former | 46 | 47 | |
| Never | 50 | 49 | |
| Physical activity level, % | | | <0.001 |
| Inactive | 36 | 41 | |
| Moderately inactive | 29 | 29 | |
| Moderately active | 19 | 16 | |
| Active | 16 | 15 | |
| Education status, % | | | 0.001 |
| No education | 25 | 30 | |
| O-levels | 13 | 10 | |
| A-levels | 45 | 43 | |
| Degree | 18 | 17 | |
| Systolic BP, mmHg | 136 (125, 146) | 138 (127, 148) | 0.001 |
| Diastolic BP, mmHg | 78 (72, 84) | 77 (72, 84) | 0.003 |
| HDL cholesterol, mM | 1.5 (1.2,1.8) | 1.5 (1.2,1.8) | 0.580 |
| LDL cholesterol, mM | 3.2 (2.5, 3.8) | 3.1 (2.5, 3.9) | 0.685 |
| Total triglycerides, mM | 1.5 (1.0, 2.1) | 1.4 (1.0, 2.0) | 0.381 |
| QRISK2 score | 17.1 (9.9, 28.2) | 21.2 (12.1, 34.8) | <0.001 |

Participant characteristics were compared between individuals with complete and incomplete cognitive test data at HC3 of the EPIC-Norfolk study using the Kruskal-Wallis test or Mann Whitney U test for ordered and non-normally distributed continuous variables and the Chi squared test for nominal variables. Data are presented as median (IQR) for non-normally distributed continuous data and % for nominal/categorical data. Results show that participants who completed all cognitive tests were typically younger, more physically active, better educated, had lower systolic BP and a lower QRISK2 score (all $P < 0.05$).



Supplementary Figure 1: Participant flow chart. Participants for the current study were individuals who provided both dietary data at HC1 and cognitive function data at HC3 of the EPIC-Norfolk study.

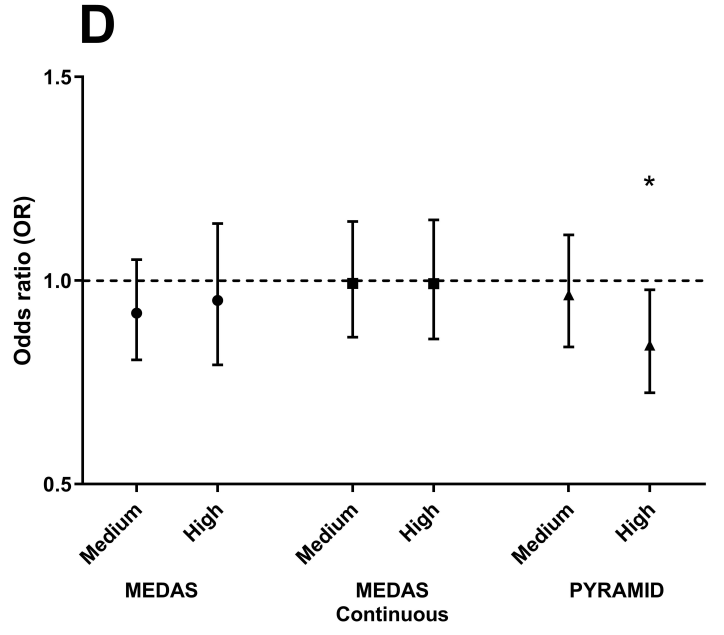
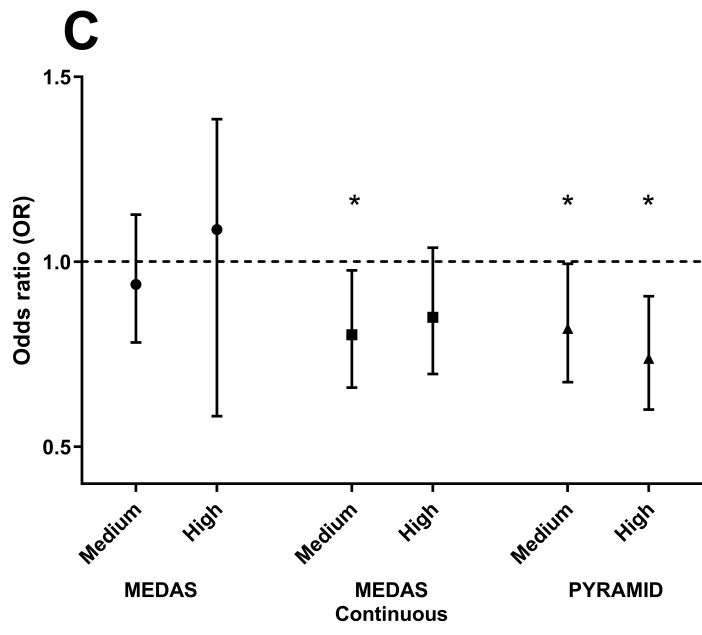
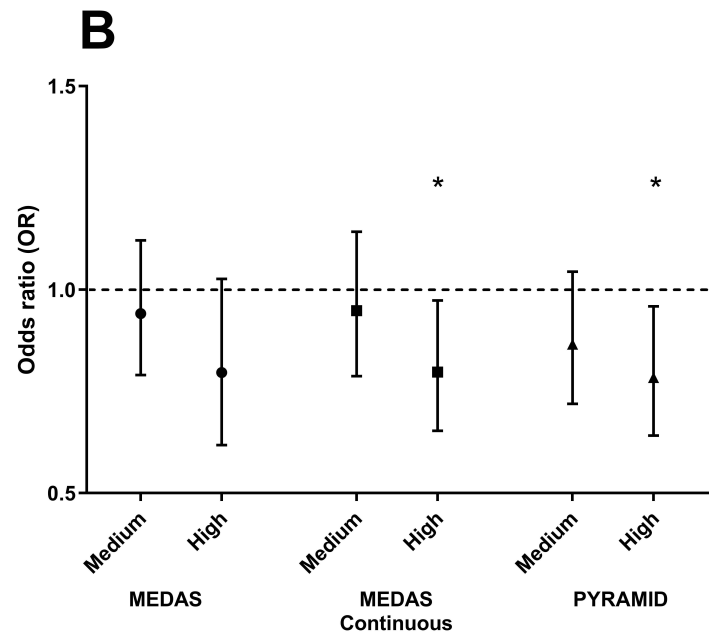
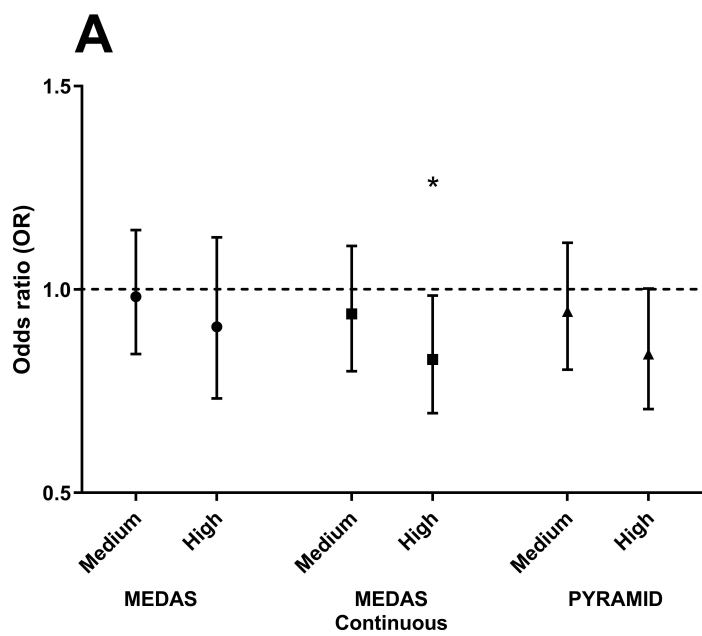


Figure 1

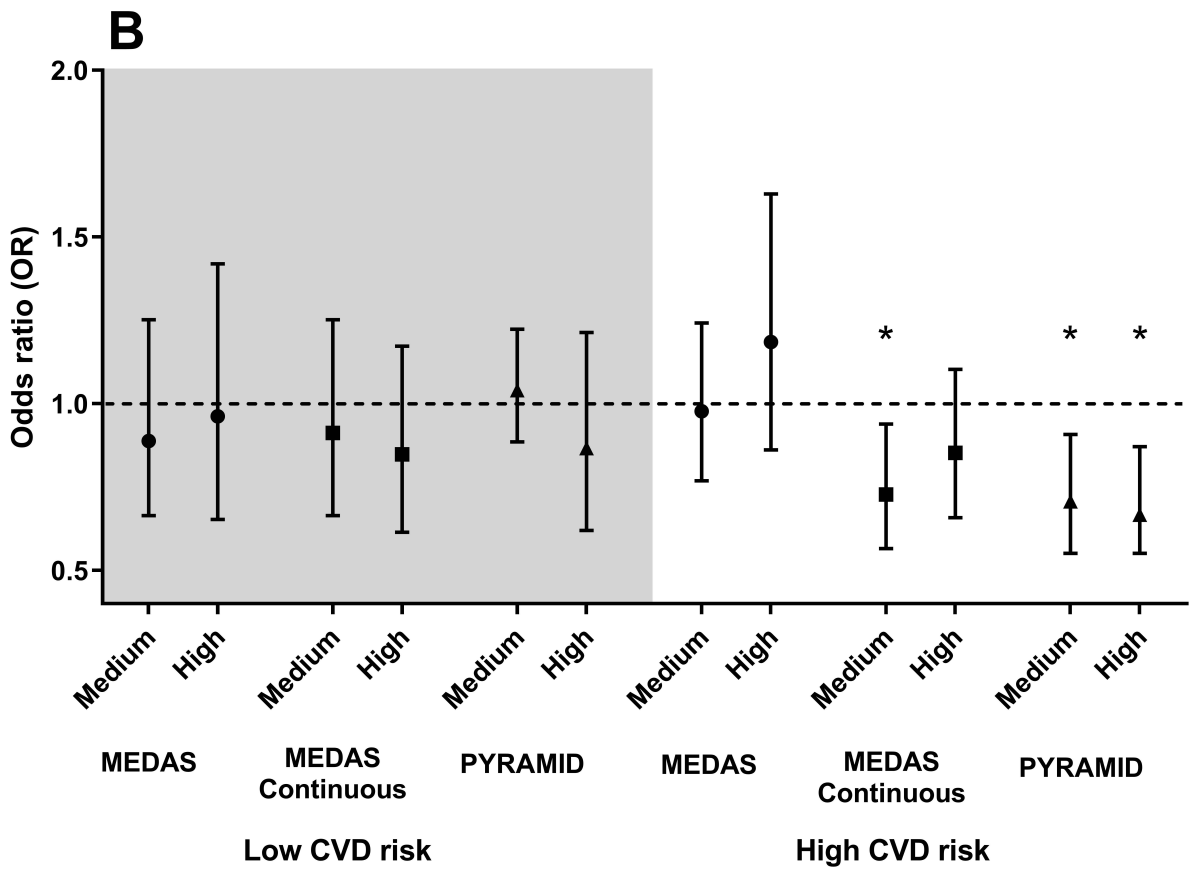
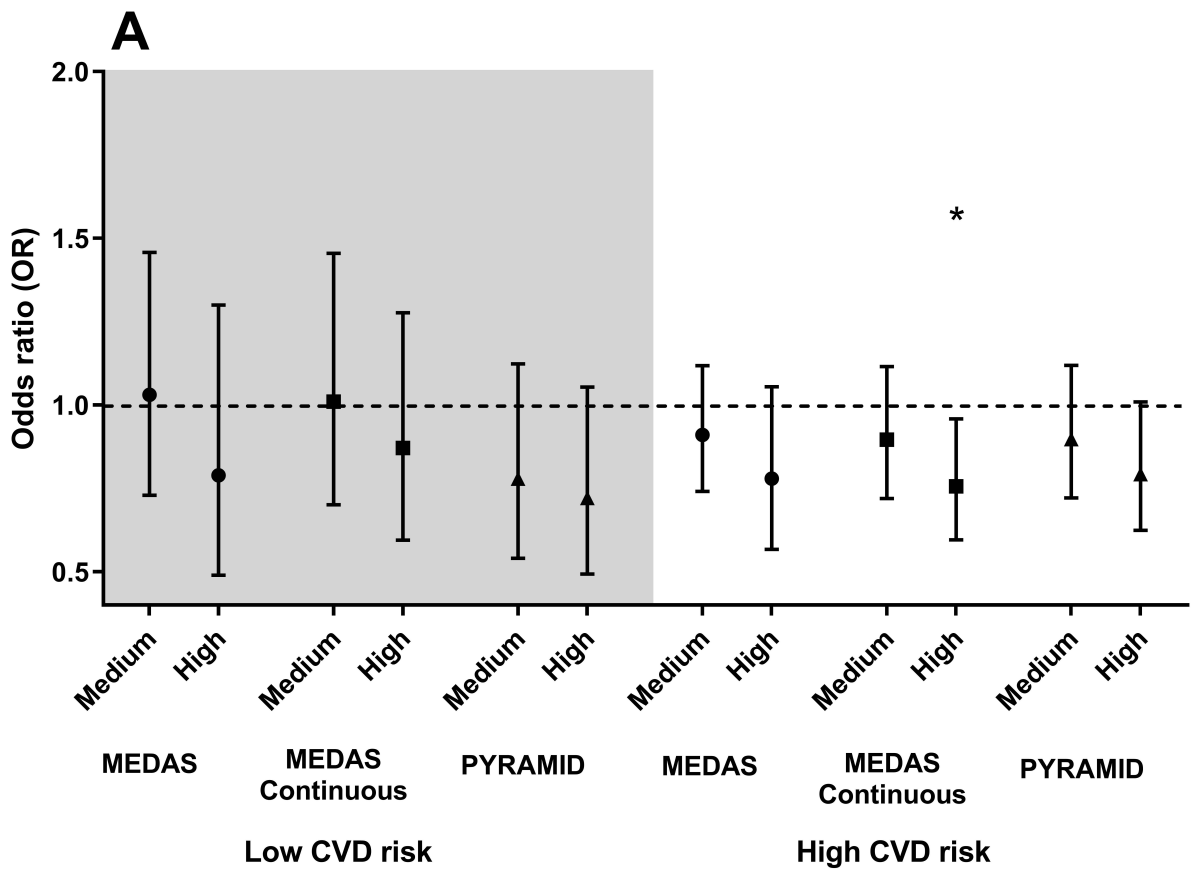


Figure 2