**Supplementary Tables**

Supplementary Table 1. Variables available in ELSA that were used to implement CRIq as per Nucci et al., 2012

|  |  |
| --- | --- |
| **CRI–EDUCATION** | **Score** |
| Higher education | 15 years |
| A level | 12 years |
| Below A level | 8 years |
| No qualification | 4 years |

|  |  |
| --- | --- |
| **CRI–WORKING ACTIVITY** | **Score** |
| Low skilled manual work | 1 x (years)\* |
| Skilled manual work | 2 x (years) |
| Skilled non-manual work | 3 x (years) |
| Professional occupation | 4 x (years) |
| Highly responsible or intellectual occupation | 5 x (years) |

*Note.* For the main analysis, we used the score corresponding to each level of working activity reported.

\* For sensitivity analyses, an overall index was calculated by multiplying the score corresponding to each level of working activity by the number of years estimated from age 40 until the age 65 (considered as the retirement age) or baseline age if the participant was younger than 65 at the beginning of the study.

|  |  |  |
| --- | --- | --- |
| **CRI–CRI LEISURE TIME** | | **Score** |
| 1 | Reading newspapers and magazines |  |
| Respondent reads a daily newspaper | | 0/1 |
| 2 | Domestic chores |  |
| Access to facilities: How respondent finds getting to the supermarket | | 0/1 |
| IADL preparing a hot meal | | 0/1 |
| IADL shopping for groceries | | 0/1 |
| 3 | Driving (not biking) |  |
| Whether respondent drives a car or van themselves | | 0/1 |
| 4 | Leisure activities |  |
| Respondent has a hobby or pastime | | 0/1 |
| Frequency does mild sports or activities | | 0/1 |
| Frequency does vigorous sports or activities | | 0/1 |
| Frequency does moderate sports or activities | | 0/1 |
| 5 | Using new technologies |  |
| Respondent owns a mobile phone | | 0/1 |
| Respondent uses the internet and/or email | | 0/1 |
| Ability to use new gadgets compared to the last interview | | 0/1 |
| **Activities with monthly frequency** | |  |
| 1 | Social activities |  |
| Political party, trade union or environmental groups | | 0/1 |
| Sports clubs, gym, exercise classes | | 0/1 |
| Tenants groups, resident groups, neighbourhood watch | | 0/1 |
| Church or other religious groups | | 0/1 |
| Social club | | 0/1 |
| Any other organisations, cub or societies | | 0/1 |
| Whether the respondent has any friends | | 0/1 |
| How often the respondent meets up with their friends | | 0/1 |
| 2 | Cinema, theatre |  |
| How often the respondent goes to the cinema | | 0/1 |
| How often the respondent goes to the theatre, a concert or the opera | | 0/1 |
| 3 | Gardening, DIY, small-scale operations |  |
| IADL– Doing work around the house or garden | | 0/1 |
| 4 | Looking after grandchildren/nephews/nieces or elderly parents |  |
| Whether the respondent looked after anyone in the past week | | 0/1 |
| 5 | Voluntary work |  |
| How often does voluntary work | | 0/1 |
| Charitable associations | | 0/1 |
| 6 | Artistic activities |  |
| Education, art or music groups or evening classes | | 0/1 |
| **Activities with annual frequency** | |  |
| 1 | Exhibitions, concerts and conferences |  |
| How often respondent goes to art gallery or museum | | 0/1 |
| 2 | Journeys lasting several days |  |
| Respondent has taken a holiday in the UK in the last 12 months | | 0/1 |
| Respondent has taken a holiday aboard in the last 12 months | | 0/1 |
| 3 | Reading books |  |
|  | |  |
| **Activities with fixed frequency** | |  |
| 1 | Children |  |
| Whether the respondent has any children | | 0/1 |
| 2 | Pet care |  |
| Do you keep any household pets inside your house/flat? | | 0/1 |
| 3 | Managing one’s current account |  |
| Ability to handle financial matters compared to the last interview | | 0/1 |
| IADL – managing money | | 0/1 |

*Note.* A score of 1 signifies engagement with the activity (often/always) a score of 0 indicates a lack of engagement (never/rarely). The overall score for this CRI component was the sum of all the activities participants endorsed.

Supplementary Table 2. The thresholds used for the classification into various levels of CR by Nucci et al., 2012 on the Cognitive Reserve Index (CRIq) and the number of participants per each level in the English Longitudinal Study of Ageing

|  |  |  |  |
| --- | --- | --- | --- |
| CRIq original score thresholds as per Nucci et al., 2012 | | Re-classification of the CRIq original score thresholds as per Nucci et al., 2012 in ELSA | |
| Level and score thresholds | N (%) | Level and score thresholds | N (%) |
| Low (≤ 70) | 109 (0.9) |  |  |
| Medium-low (71-84) | 1,919 (15.6) | Low (<84) | 2 028 (16.5) |
| Medium (85-114) | 7,803 (63.6) | Medium (85-114) | 7 803 (63.5) |
| Medium-high (115-129) | 2,276 (18.5) | High (≥115) | 2 449 (20) |
| High (≥ 130) | 173 (1.4) |  |  |

CRIq: Cognitive Reserve Index questionnaire, ELSA: English Longitudinal Study of Ageing

Supplementary Table 3. Analytic sample size and attrition rates by each wave of data collection

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Wave 1  (2002-2003) | Wave 2  (2004-2005) | Wave 3  (2006-2007) | Wave 4  (2008-2009) |
| **Analytical sample**-**core members** |  |  |  |  |
| Interviewed | 9,722 | 8,650 | 7,426 | 6,542 |
| Dropped out |  | 1,072 | 1,224 | 884 |
| % Attrition |  | 11 | 16.5 | 13.5 |
| Refreshment sample |  |  | 814 | 1,744 |

Supplementary Table 4. Hazard ratios from Multivariate Cox regressions models indicating the incidence of Alzheimer’s disease by levels of CR Index *(Sensitivity Analysis 1)*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | CR Index | Hazard ratio (95% CI) | p-value | PERM |
| Model 1  (Sex + Marital status) | Low  Medium  High | 1[Reference]  0.94(0.54-1.62)  0.71(0.36-1.37) | 0.831  0.310 | …  … |
| Model 2  (Model 1 + Wealth) | Low  Medium  High | 1[Reference]  0.97(0.56-1.69)  0.80(0.40-1.58) | 0.933  0.529 | 50%  31% |
| Model 3  (Model 1 + Smoke) | Low  Medium  High | 1[Reference]  0.92(0.53-1.62)  0.69(0.35-1.36) | 0.796  0.288 | 33%  7% |
| Model 4  (Model 1 + Depressive symptoms) | Low  Medium  High | 1[Reference]  0.94(0.54-1.63)  0.70(0.36-1.38) | 0.827  0.313 | 0%  3% |
| Model 5  (Model 1 + CHD) | Low  Medium  High | 1[Reference]  0.94(0.54-1.62)  0.72(0.37-1.38) | 0.841  0.326 | 0%  3% |
| Model 6  (Model 1 + Diabetes) | Low  Medium  High | 1[Reference]  0.94(0.54-1.63)  0.71(0.37-1.38) | 0.843  0.320 | 0%  0% |
| Model 7  (Model 1 + Stroke) | Low  Medium  High | 1[Reference]  0.94(0.54-1.63)  0.71(0.37-1.38) | 0.838  0.318 | 0%  0% |
| Model 8  (Model 1 + Hypertension) | Low  Medium  High | 1[Reference]  0.94(0.54-1.62)  0.71(0.36-1.37) | 0.832  0.313 | 0%  0% |
| Model 9  (Model 1 + All covariates) | Low  Medium  High | 1[Reference]  0.96(0.55-1.68)  0.78(0.39-1.57) | 0.903  0.502 | 33%  24% |

CHD: Coronary Heart Disease, CR: Cognitive Reserve, PERM: Percentage Excess Risk Mediated

Supplementary Table 5. Hazard ratios from Multivariate Cox regressions models indicating the incidence of dementia (excluding Alzheimer’s disease) by levels of CR Index *(Sensitivity Analysis 2)*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | CR Index | Hazard ratio (95% CI) | p-value | PERM |
| Model 1  (Sex + Marital status) | Low  Medium  High | 1[Reference]  0.62(0.49-0.77)  0.55(0.44-0.70) | <0.001  <0.001 | …  … |
| Model 2  (Model 1 + Wealth) | Low  Medium  High | 1[Reference]  0.66(0.53-0.83)  0.67(0.51-0.86) | <0.001  0.002 | 11%  27% |
| Model 3  (Model 1 + Smoke) | Low  Medium  High | 1[Reference]  0.63(0.50-0.78)  0.57(0.45-0.72) | <0.001  <0.001 | 3%  4% |
| Model 4  (Model 1 + Depressive symptoms) | Low  Medium  High | 1[Reference]  0.65(0.52-0.81)  0.62(0.49-0.79) | <0.001  <0.001 | 8%  16% |
| Model 5  (Model 1 + CHD) | Low  Medium  High | 1[Reference]  0.62(0.50-0.77)  0.56(0.45-0.71) | <0.001  <0.001 | 0%  2% |
| Model 6  (Model 1 + Diabetes) | Low  Medium  High | 1[Reference]  0.62(0.50-0.77)  0.56(0.44-0.70) | <0.001  <0.001 | 0%  2% |
| Model 7  (Model 1 + Stroke) | Low  Medium  High | 1[Reference]  0.62(0.50-0.77)  0.56(0.44-0.71) | <0.001  <0.001 | 0%  2% |
| Model 8  (Model 1 + Hypertension) | Low  Medium  High | 1[Reference]  0.62(0.50-0.77)  0.56(0.44-0.70) | <0.001  <0.001 | 0%  2% |
| Model 9  (Model 1 + All covariates) | Low  Medium  High | 1[Reference]  0.70(0.56-0.88)  0.74(0.57-0.97) | 0.003  0.033 | 21%  42% |

CHD: Coronary Heart Disease, CR: Cognitive Reserve, PERM: Percentage Excess Risk Mediated.

Supplementary Table 6. Hazard ratios from Multivariate Cox regressions models indicating the incidence of dementia by levels of CR Index (tertiles) *(Sensitivity Analysis 3)*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | CR Index Tertiles | Hazard ratio (95% CI) | p-value | PERM |
| Model 1  (Sex + Marital status) | Low  Medium  High | 1[Reference]  0.60(0.49-0.73)  0.55(0.45-0.68) | <0.001  <0.001 | …  … |
| Model 2  (Model 1 + Wealth) | Low  Medium  High | 1[Reference]  0.64(0.52-0.78)  0.64(0.51-0.81) | <0.001  <0.001 | 10%  20% |
| Model 3  (Model 1 + Smoke) | Low  Medium  High | 1[Reference]  0.61(0.50-0.74)  0.56(0.46-0.70) | <0.001  <0.001 | 3%  2% |
| Model 4  (Model 1 + Depressive symptoms) | Low  Medium  High | 1[Reference]  0.63(0.52-0.77)  0.60(0.49-0.75) | <0.001  <0.001 | 8%  11% |
| Model 5  (Model 1 + CHD) | Low  Medium  High | 1[Reference]  0.60(0.50-0.74)  0.56(0.46-0.69) | <0.001  <0.001 | 0%  2% |
| Model 6  (Model 1 + Diabetes) | Low  Medium  High | 1[Reference]  0.61(0.50-0.74)  0.56(0.45-0.68) | <0.001  <0.001 | 3%  2% |
| Model 7  (Model 1 + Stroke) | Low  Medium  High | 1[Reference]  0.60(0.50-0.74)  0.56(0.45-0.68) | <0.001  <0.001 | 0%  2% |
| Model 8  (Model 1 + Hypertension) | Low  Medium  High | 1[Reference]  0.60(0.49-0.73)  0.55(0.45-0.68) | <0.001  <0.001 | 0%  0% |
| Model 9  (Model 1 + All covariates) | Low  Medium  High | 1[Reference]  0.67(0.54-0.82)  0.70(0.55-0.89) | <0.001  0.004 | 18%  33% |

CHD: Coronary Heart Disease, CR: Cognitive Reserve, PERM: Percentage of excess risk mediated

Supplementary Table 7. Hazard ratios from Multivariate Cox regressions models indicating the incidence of dementia by levels of CR Index, (Quintiles) *(Sensitivity Analysis 4)*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | CR Index | Hazard ratio (95% CI) | p-value | PERM |
| Model 1  (Sex + Marital status) | Low  Medium-low  Medium  Medium-high  High | 1[Reference]  0.84(0.66-1.06)  0.55(0.42-0.71)  0.55(0.42-0.72)  0.50(0.38-0.65) | 0.155  <0.001  <0.001  <0.001 | …  …  …  … |
| Model 2  (Model 1 + Wealth) | Low  Medium-low  Medium  Medium-high  High | 1[Reference]  0.85(0.67-1.09)  0.58(0.45-0.76)  0.61(0.46-0.81)  0.59(0.44-0.79) | 0.218  <0.001  0.001  0.001 | 6%  7%  13%  18% |
| Model 3  (Model 1 + Smoke) | Low  Medium-low  Medium  Medium-high  High | 1[Reference]  0.85(0.66-1.08)  0.55(0.42-0.72)  0.56(0.43-0.74)  0.51(0.39-0.67) | 0.189  <0.001  <0.001  <0.001 | 6%  0%  2%  2% |
| Model 4  (Model 1 + Depressive symptoms) | Low  Medium-low  Medium  Medium-high  High | 1[Reference]  0.84(0.66-1.07)  0.58(0.44-0.75)  0.58(0.45-0.77)  0.55(0.42-0.72) | 0.181  <0.001  <0.001  <0.001 | 0%  7%  7%  10% |
| Model 5  (Model 1 + CHD) | Low  Medium-low  Medium  Medium-high  High | 1[Reference]  0.84(0.66-1.07)  0.55(0.42-0.72)  0.56(0.43-0.73)  0.50(0.38-0.66) | 0.172  <0.001  <0.001  <0.001 | 0%  0%  2%  0% |
| Model 6  (Model 1 + Diabetes) | Low  Medium-low  Medium  Medium-high  High | 1[Reference]  0.84(0.66-1.07)  0.55(0.42-0.72)  0.56(0.42-0.73)  0.50(0.38-0.65) | 0.161  <0.001  <0.001  <0.001 | 0%  0%  2%  0% |
| Model 7  (Model 1 + Stroke) | Low  Medium-low  Medium  Medium-high  High | 1[Reference]  0.84(0.66-1.07)  0.55(0.42-0.72)  0.56(0.42-0.73)  0.50(0.38-0.66) | 0.164  <0.001  <0.001  <0.001 | 0%  0%  2%  0% |
| Model 8  (Model 1 + Hypertension) | Low  Medium-low  Medium  Medium-high  High | 1[Reference]  0.84(0.66-1.07)  0.55(0.42-0.71)  0.55(0.42-0.72)  0.50(0.38-0.65) | 0.161  <0.001  <0.001  <0.001 | 0%  0%  0%  0% |
| Model 9  (Model 1 + All covariates) | Low  Medium-low  Medium  Medium-high  High | 1[Reference]  0.87(0.68-1.11)  0.62(0.47-0.81)  0.65(0.49-0.87)  0.65(0.48-0.88) | 0.283  0.001  0.004  0.005 | 19%  16%  22%  30% |

CHD: Coronary Heart Disease, CR: Cognitive Reserve, 1PERM: Percentage of excess risk mediated

Supplementary Table 8. Hazard ratios from Multivariate Cox regressions models indicating the incidence of dementia by levels of CR Index, estimating the activity from age 40 onwards *(Sensitivity Analysis 5)*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | CR Index | Hazard ratio (95% CI) | p-value | PERM |
| Model 1  (Sex + Marital status) | Low  Medium  High | 1[Reference]  0.82(0.67-1.00)  0.69(0.57-0.84) | 0.060  <0.001 | …  … |
| Model 2  (Model 1 + Wealth) | Low  Medium  High | 1[Reference]  0.88(0.71-1.08)  0.81(0.66-1.00) | 0.237  0.051 | 33%  39% |
| Model 3  (Model 1 + Smoke) | Low  Medium  High | 1[Reference]  0.83(0.68-1.02)  0.71(0.58-0.86) | 0.079  0.001 | 6%  6% |
| Model 4  (Model 1 + Depressive symptoms) | Low  Medium  High | 1[Reference]  0.85(0.69-1.04)  0.74(0.61-0.90) | 0.136  0.004 | 17%  16% |
| Model 5  (Model 1 + CHD) | Low  Medium  High | 1[Reference]  0.82(0.67-1.01)  0.70(0.58-0.85) | 0.063  <0.001 | 0%  3% |
| Model 6  (Model 1 + Diabetes) | Low  Medium  High | 1[Reference]  0.82(0.67-1.00)  0.70(0.57-0.85) | 0.062  <0.001 | 0%  3% |
| Model 7  (Model 1 + Stroke) | Low  Medium  High | 1[Reference]  0.82(0.67-1.01)  0.70(0.58-0.85) | 0.066  <0.001 | 0%  3% |
| Model 8  (Model 1 + Hypertension) | Low  Medium  High | 1[Reference]  0.82(0.67-1.00)  0.70(0.57-0.85) | 0.060  <0.001 | 0%  3% |
| Model 9  (Model 1 + All covariates) | Low  Medium  High | 1[Reference]  0.91(0.74-1.12)  0.85(0.69-1.05) | 0.380  0.137 | 50%  52% |

CHD: Coronary Heart Disease, CR: Cognitive Reserve, PERM: Percentage of excess risk mediated

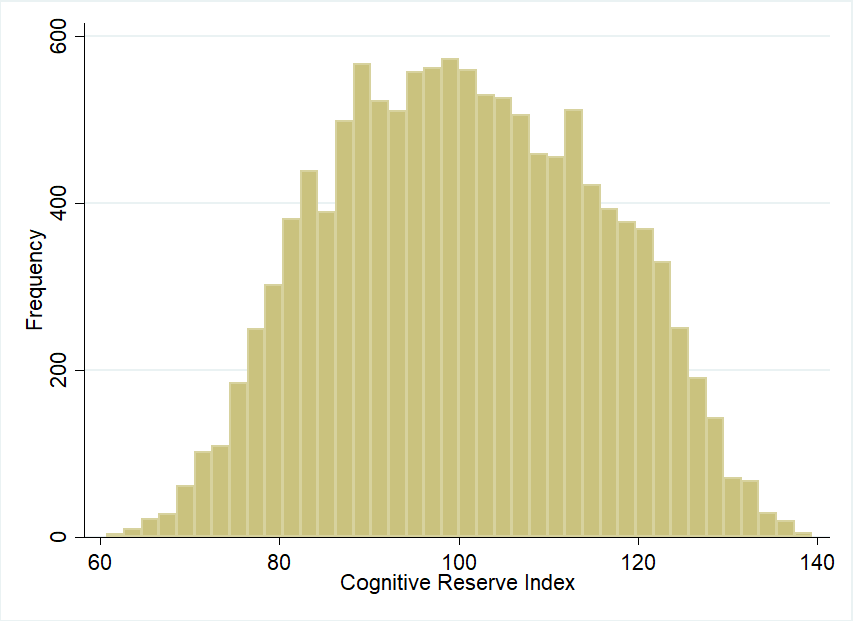
Supplementary Table 9. Hazard ratios from Multivariate Cox regressions models indicating the incidence of dementia by levels of CR Index, including APOEe4 and alcohol consumption as covariates *(Sensitivity Analysis 6, N=6,799)*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | CR Index | Hazard ratio (95% CI) | p-value | PERM |
| Model 1  (Sex + Marital status) | Low  Medium  High | 1[Reference]  0.66(0.50-0.87)  0.63(0.48-0.83) | 0.004  0.001 | …  … |
| Model 2  (Model 1 + Wealth) | Low  Medium  High | 1[Reference]  0.70(0.53-0.94)  0.77(0.57-1.06) | 0.018  0.115 | 12%  38% |
| Model 3  (Model 1 + Smoke) | Low  Medium  High | 1[Reference]  0.68(0.51-0.89)  0.66(0.50-0.87) | 0.006  0.003 | 6%  8% |
| Model 4  (Model 1 + Depressive symptoms) | Low  Medium  High | 1[Reference]  0.70(0.53-0.92)  0.68(0.51-0.91) | 0.013  0.010 | 12%  14% |
| Model 5  (Model 1 + CHD) | Low  Medium  High | 1[Reference]  0.67(0.51-0.88)  0.64(0.48-0.84) | 0.005  0.002 | 3%  3% |
| Model 6  (Model 1 + Diabetes) | Low  Medium  High | 1[Reference]  0.67(0.51-0.88)  0.63(0.48-0.83) | 0.005  0.001 | 3%  0% |
| Model 7  (Model 1 + Stroke) | Low  Medium  High | 1[Reference]  0.66(0.50-0.87)  0.63(0.48-0.83) | 0.004  0.001 | 0%  0% |
| Model 8  (Model 1 + Hypertension) | Low  Medium  High | 1[Reference]  0.66(0.50-0.87)  0.63(0.47-0.82) | 0.004  0.001 | 0%  0% |
| Model 9  (Model 1+APOEe4) | Low  Medium  High | 1[Reference]  0.66(0.50-0.87)  0.63(0.47-0.82) | 0.004  0.001 | 0%  0% |
| Model 10  (Model 1+Alcohol) | Low  Medium  High | 1[Reference]  0.63(0.44-0.91)  0.62(0.43-0.89) | 0.015  0.009 | 9%  3% |
| Model 11  (Model 1 + All covariates) | Low  Medium  High | 1[Reference]  0.74(0.50-1.10)  0.87(0.57-1.34) | 0.141  0.540 | 24%  65% |

*Note. Inclusion of APOEe4 covariate reduced the number of observations to 6,799*

CHD: Coronary Heart Disease, CR: Cognitive Reserve, PERM: Percentage Excess Risk Mediated

**Supplementary Figure**



Supplementary Figure 1. Frequency of Cognitive Reserve Index scores in the English Longitudinal Study of Ageing