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	Low	1[Reference]		
(Sex + Marital status)	Medium	0.94(0.54-1.62)	0.831	…
	High	0.71(0.36-1.37)	0.310	…
Model 2	Low	1[Reference]		
(Model 1 + Wealth)	Medium	0.97(0.56-1.69)	0.933	50%
	High	0.80(0.40-1.58)	0.529	31%
Model 3	Low	1[Reference]		
(Model 1 + Smoke)	Medium	0.92(0.53-1.62)	0.796	33%
	High	0.69(0.35-1.36)	0.288	7%
Model 4	Low	1[Reference]		
(Model 1 + Depressive	Medium	0.94(0.54-1.63)	0.827	0%
symptoms)	High	0.70(0.36-1.38)	0.313	3%
Model 5	Low	1[Reference]		
(Model 1 + CHD)	Medium	0.94(0.54-1.62)	0.841	0%
	High	0.72(0.37-1.38)	0.326	3%
Model 6	Low	1[Reference]		
(Model 1 + Diabetes)	Medium	0.94(0.54-1.63)	0.843	0%
	High	0.71(0.37-1.38)	0.320	0%
Model 7	Low	1[Reference]		
(Model 1 + Stroke)	Medium	0.94(0.54-1.63)	0.838	0%
	High	0.71(0.37-1.38)	0.318	0%
Model 8	Low	1[Reference]		
(Model 1 + Hypertension)	Medium	0.94(0.54-1.62)	0.832	0%
	High	0.71(0.36-1.37)	0.313	0%
Model 9	Low	1[Reference]		
(Model 1 + All covariates)	Medium	0.96(0.55-1.68)	0.903	33%
	High	0.78(0.39-1.57)	0.502	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	1[Reference]		
	Medium	0.62(0.49-0.77)	<0.001	…
	High	0.55(0.44-0.70)	<0.001	…
Model 2 (Model 1 + Wealth)	Low	1[Reference]		
	Medium	0.66(0.53-0.83)	<0.001	11%
	High	0.67(0.51-0.86)	0.002	27%
Model 3 (Model 1 + Smoke)	Low	1[Reference]		
	Medium	0.63(0.50-0.78)	<0.001	3%
	High	0.57(0.45-0.72)	<0.001	4%
Model 4 (Model 1 + Depressive symptoms)	Low	1[Reference]		
	Medium	0.65(0.52-0.81)	<0.001	8%
	High	0.62(0.49-0.79)	<0.001	16%
Model 5 (Model 1 + CHD)	Low	1[Reference]		
	Medium	0.62(0.50-0.77)	<0.001	0%
	High	0.56(0.45-0.71)	<0.001	2%
Model 6 (Model 1 + Diabetes)	Low	1[Reference]		
	Medium	0.62(0.50-0.77)	<0.001	0%
	High	0.56(0.44-0.70)	<0.001	2%
Model 7 (Model 1 + Stroke)	Low	1[Reference]		
	Medium	0.62(0.50-0.77)	<0.001	0%
	High	0.56(0.44-0.71)	<0.001	2%
Model 8 (Model 1 + Hypertension)	Low	1[Reference]		
	Medium	0.62(0.50-0.77)	<0.001	0%
	High	0.56(0.44-0.70)	<0.001	2%
Model 9 (Model 1 + All covariates)	Low	1[Reference]		
	Medium	0.70(0.56-0.88)	0.003	21%
	High	0.74(0.57-0.97)	0.033	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	1[Reference]		
	Medium	0.60(0.49-0.73)	<0.001	…
	High	0.55(0.45-0.68)	<0.001	…
Model 2 (Model 1 + Wealth)	Low	1[Reference]		
	Medium	0.64(0.52-0.78)	<0.001	10%
	High	0.64(0.51-0.81)	<0.001	20%
Model 3 (Model 1 + Smoke)	Low	1[Reference]		
	Medium	0.61(0.50-0.74)	<0.001	3%
	High	0.56(0.46-0.70)	<0.001	2%
Model 4 (Model 1 + Depressive symptoms)	Low	1[Reference]		
	Medium	0.63(0.52-0.77)	<0.001	8%
	High	0.60(0.49-0.75)	<0.001	11%
Model 5 (Model 1 + CHD)	Low	1[Reference]		
	Medium	0.60(0.50-0.74)	<0.001	0%
	High	0.56(0.46-0.69)	<0.001	2%
Model 6 (Model 1 + Diabetes)	Low	1[Reference]		
	Medium	0.61(0.50-0.74)	<0.001	3%
	High	0.56(0.45-0.68)	<0.001	2%
Model 7 (Model 1 + Stroke)	Low	1[Reference]		
	Medium	0.60(0.50-0.74)	<0.001	0%
	High	0.56(0.45-0.68)	<0.001	2%
Model 8 (Model 1 + Hypertension)	Low	1[Reference]		
	Medium	0.60(0.49-0.73)	<0.001	0%
	High	0.55(0.45-0.68)	<0.001	0%
Model 9 (Model 1 + All covariates)	Low	1[Reference]		
	Medium	0.67(0.54-0.82)	<0.001	18%
	High	0.70(0.55-0.89)	0.004	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	Low	1[Reference]		
(Sex + Marital status)	Medium-low	0.84(0.66-1.06)	0.155	…
	Medium	0.55(0.42-0.71)	<0.001	…
	Medium-high	0.55(0.42-0.72)	<0.001	…
	High	0.50(0.38-0.65)	<0.001	…
Model 2	Low	1[Reference]		
(Model 1 + Wealth)	Medium-low	0.85(0.67-1.09)	0.218	6%
	Medium	0.58(0.45-0.76)	<0.001	7%
	Medium-high	0.61(0.46-0.81)	0.001	13%
	High	0.59(0.44-0.79)	0.001	18%
Model 3	Low	1[Reference]		
(Model 1 + Smoke)	Medium-low	0.85(0.66-1.08)	0.189	6%
	Medium	0.55(0.42-0.72)	<0.001	0%
	Medium-high	0.56(0.43-0.74)	<0.001	2%
	High	0.51(0.39-0.67)	<0.001	2%
Model 4	Low	1[Reference]		
(Model 1 + Depressive	Medium-low	0.84(0.66-1.07)	0.181	0%
symptoms)	Medium	0.58(0.44-0.75)	<0.001	7%
	Medium-high	0.58(0.45-0.77)	<0.001	7%
	High	0.55(0.42-0.72)	<0.001	10%
Model 5	Low	1[Reference]		
(Model 1 + CHD)	Medium-low	0.84(0.66-1.07)	0.172	0%
	Medium	0.55(0.42-0.72)	<0.001	0%
	Medium-high	0.56(0.43-0.73)	<0.001	2%
	High	0.50(0.38-0.66)	<0.001	0%
Model 6	Low	1[Reference]		
(Model 1 + Diabetes)	Medium-low	0.84(0.66-1.07)	0.161	0%
	Medium	0.55(0.42-0.72)	<0.001	0%
	Medium-high	0.56(0.42-0.73)	<0.001	2%
	High	0.50(0.38-0.65)	<0.001	0%
Model 7	Low	1[Reference]		
(Model 1 + Stroke)	Medium-low	0.84(0.66-1.07)	0.164	0%
	Medium	0.55(0.42-0.72)	<0.001	0%
	Medium-high	0.56(0.42-0.73)	<0.001	2%
	High	0.50(0.38-0.66)	<0.001	0%
Model 8	Low	1[Reference]		
(Model 1 + Hypertension)	Medium-low	0.84(0.66-1.07)	0.161	0%
	Medium	0.55(0.42-0.71)	<0.001	0%
	Medium-high	0.55(0.42-0.72)	<0.001	0%
	High	0.50(0.38-0.65)	<0.001	0%
Model 9	Low	1[Reference]		
(Model 1 + All covariates)	Medium-low	0.87(0.68-1.11)	0.283	19%
	Medium	0.62(0.47-0.81)	0.001	16%
	Medium-high	0.65(0.49-0.87)	0.004	22%
	High	0.65(0.48-0.88)	0.005	30%

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

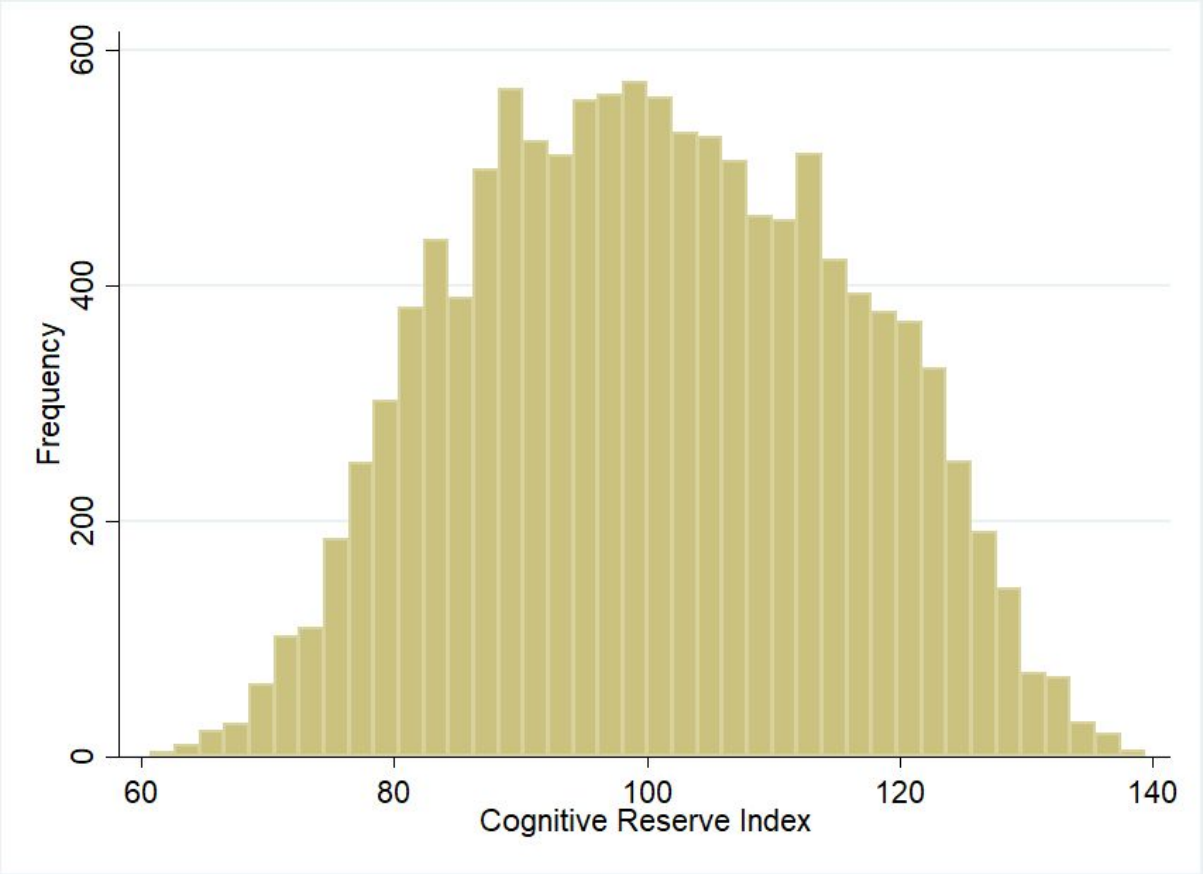
CHD: Coronary Heart Disease, CR: Cognitive Reserve, PERM: Percentage of excess risk mediated

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