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The association of health literacy and cognitive ability with self-reported diabetes in the

English Longitudinal Study of Ageing

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ABSTRACT

Background Lower health literacy and cognitive ability – variables which are moderately correlated – have associations with greater diabetes risk. This study investigated whether health literacy and cognitive ability were associated with diabetes risk when examined individually and simultaneously.

Method Participants were 8,669 English Longitudinal Study of Ageing participants (mean age=66.7, SD=9.7) who completed health literacy and cognitive ability tests at wave 2 (2004-2005), and who answered a self-reported question on whether a doctor had ever diagnosed them with diabetes. Logistic regression was used to examine cross-sectional associations of health literacy and cognitive ability with diabetes status. Cox regression was used to test the associations of health literacy and cognitive ability with risk of diabetes over a median of 9.5 years follow-up.

Results Adequate (compared to limited) health literacy (OR=0.72, 95% CI=0.61 to 0.84) and higher cognitive ability (OR per 1 SD=0.73, 95% CI=0.67 to 0.80) were associated with lower odds of diabetes. Adequate health literacy (HR=0.64; 95% CI=0.53 to 0.77) and higher cognitive ability (HR=0.77, 95% CI=0.69 to 0.85) were associated with lower risk of diabetes during follow-up. When both health literacy and cognitive ability were added to the same model, these associations were slightly attenuated. Additionally adjusting for health behaviours and BMI fully attenuated cross-sectional associations between health literacy and cognitive ability with diabetes status, and partly attenuated associations between health literacy and cognitive ability with risk of diabetes during follow-up.

Conclusions Adequate health literacy and better cognitive ability were independently associated with reduced risk of diabetes.

Keywords Health literacy, cognition, diabetes risk, prospective studies

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Strengths and limitations of this study

- This study used data from the English Longitudinal Study of Ageing, a large prospective • cohort study designed to be representative of community-dwelling adults aged over 50 years living in England.
- Participants were followed-up for a median of 9.5 years to determine whether they were • abet... diagnosed with diabetes.
- Diabetes status was self-reported. •

INTRODUCTION

Diabetes is a common chronic condition in older adulthood and is associated with substantial morbidity and mortality.[1] Type 2 diabetes, the most common type of diabetes, is at least partly preventable.[1] Understanding the characteristics of those most at risk of developing diabetes is important for appropriately targeting diabetes education and interventions. Risk factors for developing diabetes include older age, deprivation, and obesity.[1]

Lower cognitive ability may be a risk factor for diabetes. Whereas one study[2] found that childhood cognitive ability did not predict diabetes in midlife, others have found that lower cognitive ability in early life was associated with higher risk of diabetes in adulthood.[3, 4] In a sample of Scottish older adults who had their cognitive ability tested in childhood,[3] a 1 SD advantage in cognitive ability was associated with 26% lower odds of reporting diabetes in older age. Individuals with higher cognitive ability might have the cognitive skills required to self-manage their health, take better care of themselves throughout life, and thus reduce the risk of developing diabetes.[3, 5]

Health literacy – the "capacity to obtain, process and understand basic health information and services needed to make basic health decisions"[6] – might also play a role in diabetes risk. In cross-sectional studies, rates of diabetes are higher in those with low health literacy.[7, 8] In one study, participants with inadequate health literacy were 48% more likely to report having diabetes when compared to participants with adequate health literacy after adjusting for sociodemographic and health variables.[8] Individuals with lower health literacy might lack the health-related skills required to obtain, understand and follow health advice, such as eating well and exercising, which might reduce the risk of diabetes.[6]

In patients with diabetes, higher health literacy has consistently been associated with greater diabetes knowledge.[9-11] A very small association between higher health literacy and lower

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HbA_{1C} levels in patients with diabetes has been reported in a meta-analysis of 26 studies (r=-0.048, p=0.027).[10] Whereas studies have investigated the association between health literacy and disease management in people with diabetes, little is known about whether health literacy is associated with risk of developing diabetes.

Health literacy and cognitive ability test scores are positively correlated.[12, 13] Rank-order correlations between general cognitive ability and three health literacy tests ranged from 0.37 to 0.50.[13] Researchers have sought to determine the role of cognitive ability in the association between health literacy and a range of health outcomes. Most (but not all)[14] studies have found that cognitive ability partly or entirely attenuates the association between health literacy and health.[15-18] Any association between health literacy and diabetes may be attenuated when also measuring cognitive ability.

The aim of the current study was to better understand the associations of health literacy and cognitive ability with risk of diabetes. Using data from the English Longitudinal Study of Ageing (ELSA), a cohort study designed to be representative of adults aged 50 years and over living in England,[19] the present study investigated whether health literacy and cognitive ability were independently associated with self-reported diabetes status. First, the cross-sectional associations between health literacy, cognitive ability, and self-reported diabetes were investigated. Second, participants without diabetes at baseline were followed-up for up to 10 years to determine whether health literacy and cognitive ability were independently associated with risk of diabetes in mid-to-later life.

METHODS

Participants

This study used data from core members of the ELSA study, a prospective cohort study of community-dwelling adults residing in England. The wave 1 (2002-2003) sample consisted of

11,391 participants who had previously participated in the Health Survey for England and who were living in a private household.[19] ELSA participants have been followed up every two years.

A face-to-face interview was used to measure topics including health, lifestyle and economic circumstances. Participants answered a self-completion questionnaire including questions about diet and alcohol consumption. A nurse visit was carried out every second wave to assess physical measurements including height and weight, and blood and saliva samples were taken to measure biomarkers of disease. Detailed descriptions of the sample design and data collected in ELSA are reported elsewhere.[19] The present study used data from waves 2 to 7, and baseline, here, was considered to be Wave 2 (2004-2005; n=8,726), which was when the health literacy assessment was introduced.

Ethical approval was obtained from the NHS Multicentre Research Ethics Committee, London (reference: MREC/01/2/91). Written informed consent was obtained from all ELSA participants. This study confirmed to the principles embodied in the Declaration of Helsinki.

Patient and Public Involvement

Participants were not involved in the development of any part of this study.

Measures

Diabetes

Two measures of diabetes were used as outcome variables.

Baseline diabetes status: Individuals who answered "yes" to "Has a doctor ever told you that you have diabetes?" at wave 2 were categorised as having diabetes. This question did not differentiate which type of diabetes the participant was diagnosed with.

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Incident diabetes: For incident diabetes, the analysis was restricted to participants who did not self-report diabetes at wave 2 and who had at least one wave of follow-up between waves 3 and 7. Participants who did not self-report diabetes at wave 2 and who subsequently answered "yes" to "Has a doctor ever told you that you have diabetes?" any time between waves 3 and 7 were categorised as having incident diabetes. As all participants were aged over 50 years at diagnosis, these cases are probably cases of type 2 diabetes.

Date of diabetes diagnosis: Individuals who self-reported diabetes were asked which month and year they were diagnosed. Date of diabetes diagnosis was used to calculate the time between wave 2 assessment and diabetes diagnosis.

Health literacy

A brief 4-item health literacy test was administered during the interview at wave 2. This test assessed health-related reading comprehension skills which are thought to be required to successfully understand written health materials commonly encountered in healthcare. Participants were presented with a piece of paper containing a label for a packet of over-the-counter medication. Participants were asked four questions about the information on this label (e.g., "what is the maximum number of days you may take this medicine?"). The score was the number of correctly answered questions. As has been done in other studies,[20, 21] performance was categorised as adequate (4/4 correct) or limited (<4 correct).

Cognitive ability

Four tests administered during the wave 2 interview were used to measure general cognitive ability. Immediate and delayed word recall tests were used to assess verbal declarative memory. For immediate and delayed recall, participants were read a list of 10 words and were asked to immediately recall as many of the words as possible. The score was the number of words recalled immediately. After a short delay, in which the words were not repeated,

participants were asked to remember the 10 words again. The score was the number of words recalled after a delay. Executive function was assessed with verbal fluency. Participants were instructed to name as many animals as possible. The score was the number of animals named within 60 seconds. Letter cancellation was used to assess processing speed. Participants were presented with a piece of paper containing letters of the alphabet arranged in rows and columns. The task was to scan the piece of paper and score out all Ps and Ws. The score was the combined number of Ps and Ws scored out in 60 seconds.

Scores of 0 on animal fluency (n=48) and letter cancellation (n=3) were removed as this suggests participants did not complete the task or did not understand the task. Scores of \geq 50 on animal fluency (n=4), and \geq 60 on the letter cancellation (n=3) were removed as these scores were questionably high given the time limits. Scores on the four cognitive ability tests were entered into a principal component analysis (PCA). Only the first component had an eigenvalue >1. The scree plot also indicated one component. Scores from the first principal component were saved and used as a measure of cognitive ability (mean=0.00, SD=1.00). The first component accounted for 57% of the variance in the scores on the four cognitive tests. The loadings were: Immediate word recall=0.83, delayed word recall=0.85, animal fluency=0.72, and letter cancellation=0.58.

Covariates

 Age (in years), sex, BMI, health behaviours, number of cardiovascular comorbidities, and measures of socioeconomic status were used as covariates. Unless otherwise stated, all were self-reported at the wave 2 interview. Participants aged over 90 years had their age set to 90 as there were so few of them. Participants were asked whether they smoked cigarettes nowadays and were categorised as current smokers or non-smokers. Participants were asked how often they took part in moderate and vigorous physical activity (more than once a week, once a

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week, one to three times a month, and hardly ever/never). Physical activity levels were categorised as vigorous activity at least once per week, moderate activity at least once per week, and physically inactive. Participants were asked about their frequency of alcohol consumption in the past 12 months in the self-completion questionnaire. This was categorised as never, rarely, at least once a month, at least once a week, and daily/almost daily. Height and weight, measured during the wave 2 nurse interview, were used to calculate BMI (kg/m²). Cardiovascular comorbidities were assessed by counting the number of self-reported cardiovascular conditions from hypertension, angina, heart attack, heart murmur, abnormal heart rhythm, stroke, and high cholesterol. Age that participants left full-time education was categorised as: age 14 or under, 15-16 years, 17-18 years, and age 19 or older. Social class was categorised using the National Statistics Socioeconomic Classification 3 categories;[22] managerial and professional, intermediate, and routine and manual.

Analysis

Independent t-tests were used to compare those with and without diabetes at wave 2 and those who did and did not develop diabetes at follow-up on normally-distributed continuous variables. Mann-Whitney U tests were used for non-normal continuous variables, and Chi-squared tests were used for categorical variables. Spearman rank-order correlations were calculated between all predictor variables and co-variables.

Binary logistic regression was used to test the cross-sectional association of health literacy and cognitive ability with wave 2 diabetes status. Cox regression was used to investigate whether health literacy and cognitive ability test scores at wave 2 predicted risk of developing diabetes between waves 2 and 7. In the Cox regression analysis, time-to-event was taken as the difference, in days, between date of wave 2 and date of diabetes diagnosis for those who self-reported diabetes. For other participants, time-to-event was the difference between date of

wave 2 interview and the date of last interview. Month and year, but not day, were recorded for date of interview and date of diabetes diagnosis. To create a date variable (yyyy.mm.dd), the day was set to the middle of the month.

For the logistic regressions and Cox regressions, 7 models were run. Age and sex were entered into all models. Health literacy and cognitive ability were entered individually in models 1 and 2, respectively. Both health literacy and cognitive ability were added in Model 3 to determine whether the size of the health literacy-diabetes and cognitive ability-diabetes associations changed when simultaneously entering both these variables. Health literacy and cognitive ability were also entered together in models 4-7. To assess whether BMI and health behaviours accounted for these associations, BMI, smoking status, alcohol consumption, and physical activity were added in Model 4. Diabetes is a risk factor for cardiovascular disease.[23] Associations between poorer cognitive ability and cardiovascular disease are also well established. [24, 25] It is possible that any association between health literacy and cognitive ability with diabetes may be because of these associations with cardiovascular disease. To determine whether any association between health literacy and cognitive ability with diabetes was attenuated when adjusting for cardiovascular disease, number of cardiovascular comorbidities was added in Model 5. Age of leaving full-time education and occupational social class were added in Model 6 to determine whether the association between health literacy, cognitive ability and diabetes was attenuated when accounting for these commonlyused indicators of socioeconomic status. A fully-adjusted model (Model 7) adjusted for health literacy, cognitive ability, and all covariates.

This study was interested in the associations of health literacy and cognitive ability with selfreported diabetes and the independence of these associations with respect to other health and socioeconomic-related variables. In the main text we report the ORs (95% CIs) and the HRs

(95% CIs) for health literacy and cognitive ability only. The estimates for all covariates entered into the models are reported in the Supplementary materials.

RESULTS

Of the 8,726 ELSA participants who completed wave 2, 3 participants were removed who answered "don't know" to whether a doctor had diagnosed them with diabetes. A further 54 participants were removed because they selected that they had "diabetes or high blood sugar" from a Showcard listing cardiovascular conditions, but, when asked whether a doctor had ever told them they had diabetes, they answered "no". The analytic sample consisted of 8,669 participants. Participant characteristics are reported in Table 1.

Baseline diabetes status

At baseline, 708 (8.2%) participants self-reported a diagnosis of diabetes. Compared to those without diabetes, those with diabetes were more likely to have limited health literacy (42.2% versus 32.3%; p<0.001) and have lower cognitive ability (diabetes mean=-0.36, SD=0.97; no diabetes mean=0.03, SD=1.00; Cohen's d=0.40; p<0.001). Compared to participants without diabetes, participants with diabetes were older, more likely to be male, leave full-time education at a younger age, be from a less professional social class, have a higher BMI, consume less alcohol, be inactive, and self-report more cardiovascular comorbidities. Rank-order correlations between predictor variables and co-variables are reported in Table 2. Adequate health literacy was moderately correlated with higher cognitive ability (rho=0.31, p<0.001).

ORs and 95% CIs for the associations between health literacy and cognitive ability with selfreported diabetes at wave 2 are reported in Table 3 (and Supplementary Table S1). A Box-Tidwell test found the assumption of linearity of the logit was violated. Therefore an agesquared term was included in all models, and a squared term for number of cardiovascular

comorbidities was included in Model 5. Participants with adequate health literacy were 29% less likely to self-report diabetes (Model 1 OR=0.71; 95% CI=0.61 to 0.84). A 1 SD higher cognitive ability was associated with 27% lower odds of self-reported diabetes (Model 2 OR=0.73; 95% CI=0.67 to 0.80). The association between health literacy and diabetes was attenuated by 38% (OR=0.82; 95% CI=0.69 to 0.98) and the association between cognitive ability and diabetes was attenuated by 19% (OR=0.78; 95% CI= 0.70 to 0.86) when entering both health literacy and cognitive ability in Model 3. Both remained significantly associated with diabetes.

BMI and health behaviours were added in Model 4. The associations between health literacy and cognitive ability with diabetes were attenuated and no longer significant. The cognitive ability-diabetes association was not attenuated after adjusting for cardiovascular comorbidities (Model 5) or when adjusting for education and social class (Model 6). Cognitive ability remained significantly associated with diabetes in these models. The association between health literacy and diabetes was slightly attenuated and no longer significant when adjusting for cardiovascular comorbidities (Model 5) and education and social class (Model 6). In the fully adjusted model (Model 7), the size of the associations between health literacy and cognitive ability with diabetes were reduced further and were non-significant.

In the fully-adjusted model (Model 7; Supplementary Table S1) older age, male sex, having a higher BMI, and reporting more cardiovascular comorbidities were associated with higher odds of having diabetes. The association between number of cardiovascular comorbidities and diabetes became less strong as the number of comorbidities increased. Those who reported drinking alcohol at least once per month, rarely, or who never drank alcohol in the last 12 months were more likely to self-report diabetes when compared to those who reported drinking daily/almost daily. Compared to those who reported being physically inactive, those who took

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part in moderate or vigorous physical activity at least once per week were less likely to selfreport diabetes.

Risk of incident diabetes

Of the 7,961 participants who did not self-report diabetes at wave 2, 6,961 participants had at least one wave of follow-up between waves 3 and 7. They form the analytic sample for the association between health literacy, cognitive ability and risk of incident diabetes. A total of 506 (7.3%) participants reported a new diagnosis of diabetes between wave 3 and wave 7, whereas 6,455 (92.7%) participants did not. Median time to follow-up was 9.5 years. Mean time to censor was 4.7 years (SD=3.1) for those with diabetes and 7.8 years (SD=2.9) for those not diagnosed with diabetes. Participant characteristics are reported in Table 1. Compared to participants who did not have incident diabetes, those who did were more likely to have limited health literacy (38.8% versus 30.3%, p<0.001) and had lower cognitive ability (diabetes mean=-0.04, SD=0.89; no diabetes mean=0.10, SD=0.98, Cohen's d=0.15, p<0.001) at wave 2. Compared to those who did not develop diabetes, participants who did were older, more likely to be male, have left full-time education at a younger age, be from a less professional social class, smoke, consume less alcohol, be inactive, and to report more cardiovascular comorbidities at wave 2.

The HRs and 95% CIs for the association between health literacy, cognitive ability and risk of diabetes are reported in Table 4 (and Supplementary Table S2). Adequate health literacy at wave 2 was associated with a 36% lower risk of diabetes (Model 1 HR=0.64; 95% CI=0.53 to 0.77). A 1 SD higher cognitive ability at wave 2 was associated with a 23% lower risk of diabetes (Model 2 HR=0.77; 95% CI=0.69 to 0.85). The association between health literacy and risk of diabetes was attenuated by 22% after adjustment for cognitive ability (Model 3 HR=0.72; 95% CI=0.59 to 0.87), and the association between cognitive ability and risk of

diabetes was attenuated by 9% after adjusting for health literacy (HR=0.79; 95% CI=0.71 to 0.88). Both health literacy and cognitive ability remained significant predictors of diabetes risk. BMI and health behaviours were added in Model 4. The associations of health literacy and cognitive ability with diabetes risk were further attenuated but remained statistically significant. When adjusting for number of cardiovascular comorbidities, the association between health literacy and cognitive ability with risk of diabetes remained almost unchanged (Model 5) and both remained significantly associated with diabetes risk. Education and social class was added in Model 6. The size of the association between health literacy and cognitive ability reduced but remained statistically significant. In the fully adjusted model (Model 7) the associations between health literacy and cognitive ability and risk of diabetes were further reduced and no longer significant.

In the fully-adjusted model (Model 7; Supplementary Table S2) male participants, those with a higher BMI, current smokers, and those who reported consuming alcohol rarely (compared to daily/almost daily) at wave 2 had increased risk of diabetes. Participants who reported leaving education at age 19 years or older had a lower risk of diabetes compared to those who left at age 14 years or younger.

Sensitivity analysis

There were some missing data. For the cross-sectional analyses, 70% of participants had complete data. For the longitudinal analyses, 75% of participants had complete data. All models were re-run using only participants with complete data on all variables entered into the models. These results are reported in Supplementary Tables S3 and S4. The pattern of associations were generally similar; however, the sizes of the associations tended to be slightly weaker compared to the full sample. For the cross-sectional analysis, health literacy was no longer significantly associated with diabetes status in Model 3 when adjusting for health

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literacy and cognitive ability (Supplementary Table S3). For the longitudinal analysis, when adjusting for BMI and health behaviours (Model 4; Supplementary Table S4), health literacy was no longer associated with risk of diabetes.

DISCUSSION

Using a sample of middle-aged and older adults living in England, the present study found that adequate health literacy and better cognitive ability were associated with lower odds of reporting diabetes. These associations were attenuated when health literacy and cognitive ability were entered in the same model, though both independently contributed to diabetes. Adequate health literacy and better cognitive ability, measured at wave 2, were associated with reduced risk of developing diabetes during a median of 9.5 years follow-up. Health literacy and cognitive ability predicted risk of diabetes when examined individually and when examined simultaneously. Health literacy and cognitive ability were no longer associated with cross-sectional diabetes status or with risk of diabetes when adjusting for health behaviours and BMI. Cross-sectional associations between cognitive ability and diabetes status at wave 2, and associations the between health literacy and cognitive ability with risk of developing diabetes during follow-up persisted after adjusting for cardiovascular comorbidities and indicators of socioeconomic status.

Previous cross-sectional studies have found that individuals with lower health literacy are more likely to report having diabetes[7, 8] and longitudinal studies have found that that lower cognitive ability earlier in life is associated with an increased risk of diabetes.[3, 4] The present study is the first longitudinal study to examine whether health literacy is associated with risk of developing diabetes, and the first to examine whether cognitive ability and health literacy have independent associations with diabetes. The results reported here suggest that cognitive

capabilities and health-related skills, though related, contribute independently to risk of diabetes.

Some have suggested that health literacy variance is mostly overlapping with cognitive ability.[17, 26] If this were true, one would expect the association between health literacy and diabetes to be fully attenuated when adjusting for cognitive ability. This is not what was found here. The association between health literacy and diabetes was only moderately attenuated (by 38% for baseline diabetes status and by 22% for diabetes risk) when adjusting for cognitive ability; moreover, both remained significant predictors of diabetes. The results suggest that only some of the association of health literacy and diabetes was accounted for by cognitive ability. However, the cognitive ability measure used here included four brief cognitive ability tests that assessed memory, executive function and processing speed, and did not include other important domains of cognitive function, such as reasoning, that are known to load highly on general cognitive ability that was not picked up by the relatively brief measures of cognitive ability used here.[28]

This study was also interested in examining whether health literacy and cognitive ability were associated with diabetes risk independent of other health-related and socioeconomic risk factors for diabetes. The largest attenuation was seen when entering health behaviours and BMI into the models. BMI and health behaviours fully attenuated the relationship between health literacy, cognitive ability and reporting diabetes at baseline, and partly attenuated the relationship between health literacy, cognitive ability has been associated with health promoting behaviours such as follow-up. Better cognitive ability has been associated with health promoting behaviours such as following a healthy diet and taking part in regular exercise.[2, 29-31] Whereas some studies have found associations between better health literacy and taking part in health promoting behaviours behaviours.[32] others have not.[33] Individuals with higher health literacy and cognitive

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ability might be better equipped with the health-related skills and knowledge, and the general cognitive capabilities (e.g., to plan, reason and learn) needed to take better care of themselves[5, 34] and to follow health advise such as eating well and exercising, which, in turn, could reduce the risk of developing diabetes.[1]

Education also partly attenuated the association between health literacy and cognitive ability with risk of diabetes. The association between better health literacy and cognitive ability with higher levels of education are well established.[6, 35] Education may lead to better cognitive ability and health literacy, which in turn may lead to better health-related skills and lower rates of diabetes.[17] Higher early life cognitive ability has been found to predict later educational attainment.[35] An alternative, but not mutually exclusive, explanation could be that higher cognitive ability may equip an individual with the skills needed to obtain higher educational qualifications. Higher educational attainment, in turn, may lead to better health (and lower risk of diabetes) by, for example, increasing health-related knowledge and decision-making skills.[17]

This study has a number of strengths and limitations. A key strength is that it examined the association of health literacy, cognitive ability and risk of diabetes longitudinally. Another strength is the relatively large sample size. One limitation is that only a subsample of participants had complete data. Those with missing data may be those with the lowest health literacy and cognitive ability scores. ELSA may also suffer from selective attrition such that those with increased risk of diabetes may be less likely to return for follow-up. The results reported here may not generalise to those with the lowest health literacy and/or cognitive ability, and those with the highest risk of diabetes. Diabetes status was self-reported; however, there is a relatively high rate of agreement between self-reported diabetes and fasting blood glucose in ELSA.[36] In a sub-sample of ELSA participants with data on both self-reported diabetes, which is

much lower than has been found in other cohort studies.[36] The health literacy test used in the current study was a brief, four-item test which had limited variance (67% of participants scored the highest score). Although brief, this test was sensitive enough to predict diabetes risk in the current study, and it has previously been found to predict mortality.[16]

This study found that adequate health literacy and higher cognitive ability were independently associated with lower odds of self-reported diabetes and with reduced risk of developing diabetes during a median of 9.5 years follow-up. Individuals with poor health literacy and/or cognitive ability might lack the health-related skills and knowledge and the cognitive abilities required to look after their health throughout life, which in turn, may increase the risk of diabetes. Future studies should investigate whether interventions designed to improve the knowledge and skills required to better self-manage health reduce the risk of developing diabetes in individuals with low health literacy and cognitive ability. literary

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Conflict of Interest No potential conflicts of interest were reported.

Author Contributions Chloe Fawns-Ritchie contributed to the conception and design of the project, analysed the data, interpreted the data, drafted the initial manuscript, and critically revised the manuscript. Jackie Price contributed to the conception and design of the project, interpreted the data, and critically revised the manuscript. Ian J. Deary contributed to the conception and design of the project, interpreted the data, and critically revised the manuscript.

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Data accessibility Anonymised data from the English Longitudinal Study of Ageing is available from the UK Data Service (<u>https://https://www.ukdataservice.ac.uk/</u>).

REFERENCES

- Hussain A, Claussen B, Ramachandran A, *et al.* Prevention of type 2 diabetes: a review.
 Diabetes Res Clin Pract 2007;76:317-26.
- 2 Batty GD, Deary IJ, Macintyre S. Childhood IQ in relation to risk factors for premature mortality in middle-aged persons: the Aberdeen Children of the 1950s study. *J Epidemiol Community Health* 2007;61:241-7.
- 3 Mõttus R, Luciano M, Starr JM, *et al.* Diabetes and life-long cognitive ability. *J Psychosom Res* 2013;75:275-8.
- 4 Twig G, Gluzman I, Tirosh A, *et al.* Cognitive function and the risk for diabetes among young men. *Diabetes care* 2014;37:2982-8.
- 5 Gottfredson LS. Intelligence: is it the epidemiologists' elusive "fundamental cause" of social class inequalities in health? *J Pers Soc Psychol* 2004;86:174-99.
- 6 Nielsen-Bohlman L, Panzer AM, Kindig DA. *Health Literacy: A Prescription to End Confusion*. Washinton, DC: The National Academies Press 2004.
- 7 Adams RJ, Appleton SL, Hill CL, *et al.* Risks associated with low functional health literacy in an Australian population. *Med J Aust* 2009;191:530-4.
- 8 Wolf MS, Gazmararian JA, Baker DW. Health literacy and functional health status among older adults. *Arch Intern Med* 2005;165:1946-52.
- 9 Caruso R, Magon A, Baroni I, *et al.* Health literacy in type 2 diabetes patients: a systematic review of systematic reviews. *Acta Diabetol* 2018;55:1-12.
- 10 Marciano L, Camerini AL, Schulz PJ. The Role of Health Literacy in Diabetes Knowledge, Self-Care, and Glycemic Control: a Meta-analysis. *J Gen Intern Med* 2019;34:1007-17.
- 11 Al Sayah F, Majumdar SR, Williams B, *et al.* Health literacy and health outcomes in diabetes: a systematic review. *J Gen Intern Med* 2013;28:444-52.

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2	
3 4	12 Bennett JS, Boyle PA, James BD, et al. Correlates of health and financial literacy in older
5 6	adults without dementia. BMC Geriatrics 2012;12:30.
7 8 9	13 Murray C, Johnson W, Wolf MS, et al. The Association between Cognitive Ability across
9 10 11	the Lifespan and Health Literacy in Old Age: The Lothian Birth Cohort 1936. Intelligence
12 13	2011;39:178-87.
14 15	14 Lamar M, Wilson RS, Yu L, et al. Associations of literacy with diabetes indicators in older
16 17 18	adults. J Epidemiol Community Health 2019;73:250-5.
19 20	15 Baker DW, Wolf MS, Feinglass J, et al. Health literacy, cognitive abilities, and mortality
21 22	among elderly persons. J Gen Intern Med 2008;23:723-6.
23 24 25	16 Bostock S, Steptoe A. Association between low functional health literacy and mortality in
26 27	older adults: longitudinal cohort study. BMJ 2012;344:e1602.
28 29	17 Mõttus R, Johnson W, Murray C, et al. Towards understanding the links between health
30 31 32	literacy and physical health. Health Psychol 2014;33:164-73.
33 34	18 Fawns-Ritchie C, Starr JM, Deary IJ. Role of cognitive ability in the association between
35 36	functional health literacy and mortality in the Lothian Birth Cohort 1936: a prospective
37 38 20	cohort study. BMJ Open 2018;8:e022502.
39 40 41	19 Steptoe A, Breeze E, Banks J, et al. Cohort profile: the English Longitudinal Study of
42 43	Ageing. Int J Epidemiol 2013;42:1640-8.
44 45	20 Kobayashi LC, Wardle J, von Wagner C. Limited health literacy is a barrier to colorectal
46 47 48	cancer screening in England: evidence from the English Longitudinal Study of Ageing. Prev
49 50	<i>Med</i> 2014;61:100-5.
51 52	21 Gale CR, Deary IJ, Wardle J, et al. Cognitive ability and personality as predictors of
53 54	participation in a national colorectal cancer screening programme: the English Longitudinal
55 56 57	Study of Ageing. J Epidemiol Community Health 2015;69:530-5.
58 59	

- 22 Rose D, Pevalin DJ, O'Reilly K. *The National Statistics Socio-economic Classification: origins, development and use*: Palgrave Macmillan Basingstoke 2005.
- 23 Sarwar N, Gao P, Seshasai SR, *et al.* Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet* 2010;375:2215-22.
- 24 Rostamian S, Mahinrad S, Stijnen T, *et al.* Cognitive impairment and risk of stroke: a systematic review and meta-analysis of prospective cohort studies. *Stroke* 2014;45:1342-8.
- 25 Hart CL, Taylor MD, Smith GD, *et al.* Childhood IQ and cardiovascular disease in adulthood: prospective observational study linking the Scottish Mental Survey 1932 and the Midspan studies. *Social Science & Medicine* 2004;59:2131-8.
- 26 Reeve CL, Basalik D. Is health literacy an example of construct proliferation? A conceptual and empirical evaluation of its redundancy with general cognitive ability. *Intelligence* 2014;44:93-102.
- 27 Salthouse TA. Localizing age-related individual differences in a hierarchical structure. *Intelligence* 2004;32:541-61.
- 28 Fawns-Ritchie C, Starr JM, Deary IJ. Health literacy, cognitive ability and smoking: a crosssectional analysis of the English Longitudinal Study of Ageing. *BMJ Open* 2018;8:e023929.
- 29 Batty GD, Deary IJ, Schoon I, *et al.* Childhood mental ability in relation to food intake and physical activity in adulthood: the 1970 British Cohort Study. *Pediatrics* 2007;119:e38-45.
- 30 Wraw C, Der G, Gale CR, *et al.* Intelligence in youth and health behaviours in middle age. *Intelligence* 2018;69:71-86.
- 31 Batty GD, Deary IJ, Schoon I, *et al.* Mental ability across childhood in relation to risk factors for premature mortality in adult life: the 1970 British Cohort Study. *J Epidemiol Community Health* 2007;61:997-1003.

25 of 41	BMJ Open
	32 von Wagner C, Knight K, Steptoe A, et al. Functional health literacy and health-promoting
	behaviour in a national sample of British adults. J Epidemiol Community Health
	2007;61:1086-90.
	33 Wolf MS, Gazmararian JA, Baker DW. Health literacy and health risk behaviors among
	older adults. Am J Prev Med 2007;32:19-24.
	34 Deary IJ, Weiss A, Batty GD. Intelligence and Personality as Predictors of Illness and
	Death: How Researchers in Differential Psychology and Chronic Disease Epidemiology Are
	Collaborating to Understand and Address Health Inequalities. Psychol Sci Public Interest
	2010;11:53-79.
	35 Deary IJ, Strand S, Smith P, et al. Intelligence and educational achievement. Intelligence
	2007;35:13-21.
	36 Pierce MB, Zaninotto P, Steel N, et al. Undiagnosed diabetes-data from the English
	longitudinal study of ageing. Diabetic Med 2009;26:679-85.

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	Ba	seline diabetes sta	atus reported at	wave 2	In	Incident diabetes reperted at follow-up*				
		No diabetes	Diabetes		_	No diabetes	Diabetes			
	n	(n = 7961)	(n = 708)	р	n	(n = 6455)	ີສູກ = 506)	р		
Age, mean (SD)	8669	66.46 (9.70)	69.38 (9.16)	< 0.001	6961	66.02 (9.53)	85.51 (8.59)	< 0.001		
Sex, n (%)	8669			< 0.001	6961		22.	< 0.00		
Male		3522 (44.2%)	379 (53.5%)			2791 (43.2%)	§ 62 (51.8%)			
Female		4439 (55.8%)	329 (46.5%)			3664 (56.8%)	हैं44 (48.2%)			
Age left full-time education,							ade			
n (%)	8468			< 0.001	6809		d fro	< 0.00		
≤ 14 years		1641 (21.1%)	210 (30.6%)			1222 (19.3%)	∎07 (21.8%)			
15-16 years		4085 (52.5%)	349 (50.8%)			3283 (52.0%)	3 02 (61.6%)			
17-18 years		1009 (13.0%)	55 (8.0%)			870 (13.8%)	4 5 (9.2%)			
≥ 19 years		1046 (13.4%)	73 (10.6%)			944 (14.9%)	ਭ ੱ6 (7.3%)			
Social class, n (%)	8508			< 0.001	6846		en.t	< 0.00		
Managerial and) M.			
professional		2444 (31.2%)	194 (28.4%)			2067 (32.6%)	§33 (26.7%)			
Intermediate		1979 (25.3%)	131 (19.2%)			1662 (26.2%)	do4 (20.9%)			
Routine and manual		3403 (43.5%)	357 (52.3%)			2619 (41.3%)	2 61 (52.4%)			
Health literacy, n (%)	8293			< 0.001	6736		rii 1	< 0.00		
Adequate		5172 (67.7%)	376 (57.8%)			4351 (69.7%)	300 (61.2%)			
Limited		2471 (32.3%)	274 (42.2%)			1895 (30.3%)	段90 (38.8%)			
Cognitive ability, mean (SD)	8335	0.03 (1.00)	-0.36 (0.97)	< 0.001	6746	0.10 (0.98)	₹0.04 (0.89)	< 0.00		
BMI, mean (SD)	7179	27.71 (4.79)	30.45 (5.37)	< 0.001	5997	27.46 (4.64)	ଞ୍ଚି1.21 (5.28)	< 0.00		
Current smoker, n (%)	8622			0.377	6929		st. F	< 0.00		
Yes		1216 (15.4%)	99 (14.1%)			934 (14.5%)	ğ 05 (20.8%)			
No		6704 (84.6%)	603 (85.9%)			5490 (85.5%)	g00 (79.2%)			
Alcohol, n (%)	7577			< 0.001	6239		d D	< 0.00		
Never		723 (10.3%)	112 (19.3%)			565 (9.7%)	§ 9 (11.2%)			
Rarely		1076 (15.4%)	124 (21.3%)			863 (14.9%)	90 (20.6%)			

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Page 27 of 41				BMJ Open			86/bmjope	
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26	At least once a month At least once a week Daily/almost daily Physical activity, n (%) Vigorous activity Moderate activity Inactive Number of cardiovascular comorbidities, mean (SD) BMI, body mass index. *Incident diabetes reported a wave 2 and with at least one	827 (11.8%) 2662 (38.1%) 1708 (24.4%) 2236 (28.1%) 3888 (48.9%) 1833 (23.0%) 0.67 (0.91) up comparisons a follow-up.	85 (14.6%) 171 (29.4%) 89 (15.3%) 108 (15.2%) 305 (43.1%) 295 (41.7%) 1.28 (1.13)	< 0.001	6958 6961 f participar	669 (11.5%) 2255 (38.9%) 1451 (25.0%) 1938 (30.0%) 3194 (49.5%) 1320 (20.5%) 0.64 (0.88) hts who did not	66/bmjopen-2021-0 56/bmjopen-2021-0 56/bmjopen-2021-0 57 (31.0%) 57 (31.0%) 58 (1.04) 59 (1.04)	<0.001 <0.001 iagnosis of c
							http://bmjopen.bmj.com/ on April 17, 2024 by guest. Protected b	

 *Incident diabetes reported at follow-up comparisons are based on a subsample of participants who did not set f-report a diagnosis of diabetes at

http://bmjopen.bmj.com/ on April 17, 2024 by guest. Protected by copyright

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				Social	Health	Cognitive			on on	Physical	CV
	Age	Sex	Education	class	literacy	ability	BMI	Smoking	Alcophol	activity	comorbid
Age									lune		
Sex	-0.03**								2022		
Education	-0.41***	0.02							•		
Social class	0.08***	-0.09***	-0.41***						Dov		
Health literacy	-0.16***	0.01	0.23***	-0.18***					vnlo		
Cognitive ability	-0.47***	-0.09***	0.39***	-0.27***	0.31***				Downloaded		
BMI	-0.07***	0.02	-0.06***	0.08***	-0.04**	-0.01					
Smoking	-0.13***	0.01	-0.05***	0.12***	-0.04***	-0.02	-0.09***		from		
Alcohol	-0.11***	0.21***	0.22***	-0.20***	0.09***	0.16***	-0.11***	-0.04***	http:/		
Physical activity	-0.26***	0.10***	0.23***	-0.15***	0.14***	0.26***	-0.11***	-0.09***	0.18***		
CV comorbid	0.18***	0.00	-0.11***	0.05***	-0.06***	-0.11***	0.14***	-0.03*	-0.0 ***	-0.14***	

Sex is coded 0 for female, 1 for male; Education is age of leaving full-time education and is coded 1 for age 4 years or less, 2 for age 15-16 years, 3 for age 17-18 years, and 4 for 19 years or older; Social class is coded 1 for managerial and professional, 2 for intermediate, and 3 for routine and manual; Health literacy is coded 0 for limited and 1 for adequate; Smoking is coded 0 for current from smoker and 1 for current smoker; Alcohol is the frequency of alcohol consumed in the last 12 months and is coded 0 for never, 1 for rately, 2 for at least once a month, 3 for at least once a week, 4 for daily/almost daily; Physical activity is coded 0 for inactive, 1 for moderate activity at least once per week, 2 for vigorous activity at least once per week; CV comorbid is the number of cardiovascular comorbidities self-reported from hypertension, angina, heart attack, heart failure, heart murmur, abnormal heart rhythm, stroke, and high cholesterol. guest. Protected by copyright

Table 3 Od	lds ratios (95% CI) from logistic regression models of the association between health lite	eracy and cognitive ability with self-reported
diabetes at v	wave 2	

	Model 1:	Model 2:	Model 3: Health	Model 4: +BMI	Model 5: +CV	Model 6:	Model 7: Fully
	Health literacy	Cognitive	literacy and	and health	comorbidities	+Education and	adjusted
		ability	cognitive ability	behaviours	ne	social class	
Adequate health literacy	0.71***	-	0.82*	0.97	0.85	0.84	0.98
	(0.61, 0.84)		(0.69, 0.98)	(0.78, 1.21)	(0.72, 1.02)	(0.70, 1.01)	(0.78, 1.23)
Cognitive ability	-	0.73***	0.78***	0.90	0.78*** Š	0.78***	0.87
		(0.67, 0.80)	(0.70, 0.86)	(0.80, 1.02)	(0.71, 0.87)	. (0.71, 0.87)	(0.76, 1.00)

*p < .05, **p < .01, ***p < .001 $\overleftarrow{\mathbf{g}}$ BMI, body mass index; CV, cardiovascular. $\overrightarrow{\mathbf{g}}$ All models adjusted for age, age-squared, and sex. Models 1 n=8,293, Model 2 n=8,335, Model 3 n=8,185. Model 4 (n=6,302) adjusted for body mass index, frequency of alcohol consumption in the past 12 months, and physical activity. Model 5 (n=8,185) adjusted for number of cardiovascular comorbidities reported, and a squared term for number of cardiovascular comorbidities reported. Model 6 (n=7,861) adjusted for 1 7 (n=6,086) adjusted for all covariates. age left full-time education, and occupational social class. Model 7 (n=6,086) adjusted for all covariates.

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BMJ Open Table 4 Hazard ratios (95% CI) from Cox regression models of the association between health literacy and cognitive ability with risk of incident diabetes

Model 1:	Model 2:	Model 3:	Model 4: +BMI	Model 5: +CV	⁵ Model 6:	Model 7: Fully
Health literacy	Cognitive ability	Health literacy and cognitive ability	and health behaviours	comorbidities	Section and Sectio	adjusted
0.64***	-	0.72***	0.79*	0.73**	0.79*	0.85
(0.53, 0.77)		(0.59, 0.87)	(0.64, 0.99)	(0.60, 0.88)	§(0.65, 0.97)	(0.68, 1.06)
-	0.77***	0.79***	0.85*	0.80***	<u>0.84**</u>	0.88
	(0.69, 0.85)	(0.71, 0.88)	(0.74, 0.96)	(0.71, 0.89)	8 (0.75, 0.95)	0.77, 1.01)
	Health literacy 0.64***	Health literacy Cognitive ability 0.64*** (0.53, 0.77) - 0.77***	Health literacy Cognitive ability Health literacy and cognitive ability 0.64*** - 0.72*** (0.53, 0.77) (0.59, 0.87) - 0.77***	Health literacy abilityCognitive abilityHealth literacy and cognitive abilityand health behaviours ability 0.64^{***} - 0.72^{***} 0.79^{*} $(0.53, 0.77)$ (0.59, 0.87)(0.64, 0.99)- 0.77^{***} 0.79^{***} 0.85^{*}	Health literacy ability Cognitive ability Health literacy and cognitive ability and health behaviours comorbidities 0.64*** - 0.72*** 0.79* 0.73** (0.53, 0.77) (0.59, 0.87) (0.64, 0.99) (0.60, 0.88) - 0.77*** 0.79*** 0.85* 0.80***	Health literacy abilityCognitive abilityHealth literacy and cognitive abilityand health behaviourscomorbidities $\overset{\omega}{}_{1}$ +Education and social class0.64*** (0.53, 0.77) -0.72***0.79*0.73**0.79*0.59, 0.87) -(0.64, 0.99)(0.60, 0.88) 0.85* $\underbrace{0.60, 0.88}_{0.80***}$ $\underbrace{0.80***}_{0.80***}$

BMI, body mass index, CV, cardiovascular.

All models adjusted for age and sex. Models 1 (n=6,736) had 490 diabetes events, Model 2 (n=6,746) had 494 diabetes events, Model 3 (n=6,654) had 484 diabetes events. Model 4 (n=5,357; 377 diabetes events) adjusted for body mass index, frequency of alcohol consumption in the past 12 months, and physical activity. Model 5 (n=6,654; 484 diabetes events) adjusted for number of cardiovascular comorbidities reported. Model 6 (n=6,409; 492 diabetes events) adjusted for age left full-time education, and occupational social class. Model 7 (n=5,186, 360 diabetes events) adjusted for all covariates. com/ on April 17, 2024 by guest. Protected by copyright

1 2 3	Supplementary material for:
4 5 6 7	The association of health literacy and cognitive ability with self-reported diabetes in the English Longitudinal Study of Ageing
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	Model 1: Health literacy n=8,293	Model 2: Cognitive ability n=8,335	Model 3: Health literacy and cognitive ability n=8,185	Model 4: +BMI and health behaviours n=6,302	Model 5: +CV comorbidities n=8,185	S S S Model 6: S Social class S Social class S S S S S S S S S S S S S	Model 7: Fully- adjusted n=6,086
Health literacy						N N NReference	
Limited	Reference	-	Reference	Reference	Reference	Reference	Reference
Adequate	0.71***		0.82*	0.97	0.85	80.84	0.98
•	(0.61, 0.84)		(0.69, 0.98)	(0.78, 1.21)	(0.72, 1.02)	Š(0.70, 1.01)	(0.78, 1.23)
Cognitive ability	-	0.73***	0.78***	0.90	0.78***	a.78***	0.87
0 1		(0.67, 0.80)	(0.70, 0.86)	(0.80, 1.02)	(0.71, 0.87)	ີ້ສີ(0.71, 0.87)	(0.76, 1.00)
Age	1.04***	1.03***	1.03***	1.04***	1.02***	a (0.71, 0.87) 1.03***	1.03***
e	(1.03, 1.05)	(1.02, 1.04)	(1.02, 1.04)	(1.03, 1.06)	(1.01, 1.03)	≤(1.02, 1.04)	(1.02, 1.05)
Age ²	0.998***	0.998***	0.998***	0.998**	0.998***	⊇ 0.998***	0.999
e	(0.997, 0.999)	(0.997, 0.998)	(0.997, 0.999)	(0.997, 0.999)	(0.997, 0.999)	5(0.997, 0.999)	(0.998, 1.000)
Sex							· · · · ·
Female	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Male	1.50***	1.41***	1.43	2.16***	1.45***	6 1.44***	2.09***
	(1.28, 1.77)	(1.20, 1.66)	(1.22, 1.69)	(1.75, 2.68)	(1.23, 1.71)	2 (1.22, 1.71)	(1.67, 2.62)
BMI				1.10***			1.09***
				(1.08, 1.12)		8	(1.07, 1.11)
Current smoking						Ę	· · · /
Non-smoker				Reference		on	Reference
Smoker				0.91		Ap	0.93
				(0.66, 1.23)		rii	(0.66, 1.27)
Alcohol consumption						17,	
Daily/almost daily				Reference		20	Reference
At least once per				1.21)24	1.24
week				(0.90, 1.65)		by	(0.91, 1.70)
At least once per				1.78**		gu	1.77**
month				(1.24, 2.56)		est	(1.21, 2.57)
Rarely				1.95***		רי ס	1.95***
-				(1.38, 2.76)		rot	(1.36, 2.79)
Never				2.40***		ect	2.12***
				(1.67, 3.44)		ed	(1.45, 3.11)
Physical activity						by	
Inactive				Reference		mj.com/ on April 17, 2024 by guest. Protected by copyright.	Reference
						руг	
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BMJ Open Supplementary Table S1 Odds ratios (95% CI) from logistic regression models of the association between health literacy and cognitive ability with self-

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Page 33 of 41		BMJ Open 0.65*** (0.51, 0.83) (0.51, 0.83) (0.50*** (0.37, 0.68) 2.08*** (1.84, 2.36) (0.88*** (0.84, 0.93) 0.68** (0.84, 0.94) 0.68** (0.84, 0.94) 0.68** (0.84, 0.94) 0.68** (0.84, 0.94)				
1				ben-202		
2 3 4	Moderate activity	0.65*** (0.51, 0.83)		1-0584	0.68** (0.53, 0.87)	
5	Vigorous activity	(0.31, 0.83) 0.50*** (0.37, 0.68)		96 on 3	(0.53, 0.87) 0.56^{***} (0.41, 0.76)	
7	Number of CV		2.08***	3 J	1.98***	
8	comorbidities		(1.84, 2.36)	Ine	(1.70, 2.32)	
9	Number of CV		0.88***	÷ 20	0.88***	
10	comorbidities ²		(0.84, 0.93)	022	(0.82, 0.93)	
11	Age left full-time					
12	education			00W		
13	≤14 years			- O Reference	Reference	
14	15-16 years			81.06	1.16	
15	2			<u>a</u> (0.84, 1.34)	(0.87, 1.56)	
16	17-18 years			a 0.81	0.98	
17	2			5 (0.56, 1.14) 5 1.06	(0.63, 1.50)	
	≥19 years			1.06	1.32	
18				3 (0.74, 1.50)	(0.85, 2.05)	
19	Social class			<u>n</u>		
20	Managerial and			Reference	Reference	
21	professional			9 90.79		
22	Intermediate			5 0.79	0.79	
23				$\overline{o}(0.61, 1.02)$	(0.58, 1.07)	
24	Routine and			§ 1.08	1.01	
25	manual			q (0.87, 1.35)	(0.77, 1.32)	
26	* <i>p</i> <.05, ** <i>p</i> <.01, *** <i>p</i> <.001	dex; CV, cardiovascular; number of CV cormorbidities ² , numb				
27	Age^2 , age squared: BMI, body mass inc	dex; CV, cardiovascular; number of CV cormorbidities ² , numb	er of cardiovas	cuter comorbidities	s squared.	
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	Model 1: Health literacy n=6,736 Events=490	Model 2: Cognitive ability n=6,746 Events=491	Model 3: Health literacy and cognitive ability n=6,654 Events=484	Model 4: +BMI health behaviours n=5,357 Events=377	Model 5: +CV comorbidities n=6654 Events=484	GModel 6: ⇔Education and Gocial class M=6409 Wents=462	Model 7: Fully- adjusted n=5,186 Events=360
Health literacy						Ņ	
Limited	Reference	-	Reference	Reference	Reference	Reference	Reference
Adequate	0.64***		0.72***	0.79*	0.73**	Š .79*	0.85
	(0.53, 0.77)		(0.59, 0.87)	(0.64, 0.99)	(0.60, 0.88)	3 0.65, 0.97)	(0.68, 1.06)
Cognitive ability	-	0.77***	0.79***	0.85*	0.80***	ð .84**	0.88
2		(0.69, 0.85)	(0.71, 0.88)	(0.74, 0.96)	(0.71, 0.89)	$\frac{2}{4}$ 0.75, 0.95)	(0.77, 1.01)
Age	1.01	1.00	1.00	1.01	0.99	9.00	1.01
-	(1.00, 1.02)	(0.99, 1.01)	(0.98, 1.01)	(1.00, 1.02)	(0.98, 1.00)	1 0.98, 1.01)	(0.99, 1.02)
Sex					/	ਰਿ	/
Female	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Male	1.43***	1.39***	1.38***	1.84***	1.38***	1 .39***	1.82***
	(1.20, 1.71)	(1.16, 1.66)	(1.15, 1.65)	(1.49, 2.29)	(1.16, 1.66)	6 1.15, 1.68)	(1.45, 2.28)
BMI				1.12***			1.12***
				(1.10, 1.14)		<u></u>	(1.10, 1.13)
Current smoking						.8	
Non-smoker				Reference		۳,	Reference
Smoker				1.77***		on	1.69***
				(1.35, 2.31)		Ap	(1.28, 2.22)
Alcohol consumption				()		oril	()
Daily/almost daily				Reference		17	Reference
At least once per week				1.11		22	1.01
				(0.83, 1.49)		024	(0.75, 1.37)
At least once per				1.53*		.bmj.com/ on April 17, 2024 by guest. Protected by copyright.	1.40
month				(1.07, 2.19)		, Gr	(0.97, 2.01)
Rarely				1.78***		les	1.53*
				(1.27, 2.50)		÷ T	(1.08, 2.17)
Never				1.42		ro	1.15
1.0.01				(0.95, 2.11)		lec	(0.76, 1.73)
Physical activity				(0.90, 2.11)		ted	(0.70, 1.75)
Inactive				Reference		ça.	Reference
Moderate activity				0.78		ò	0.79
moderate activity				0.70		уру	0.19
						rig	
						ht.	

BMJ Open Supplementary Table S2 Hazard ratios (95% CI) from Cox regression models of the association between health literacy and cognitive ability with risk of

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1 2 3 4 Vigorous activity 5 6 Number of CV 7 comorbidities 8 Age left full-time	BMJ Open (0.61, 1.01) 0.72* (0.54, 0.98) 1.34*** (1.22, 1.46)	2021-058496 on 3 June 20221-058496 on 3 June 20221-058496 on 3 June 2022 ference 0.93 0.71, 1.22) 0.71, 1.22) 0.72, 1.07) 0.71, 1.22) 0.72, 1.07) 0.72, 1.17	(0.61, 1.03) 0.76 (0.56, 1.04) 1.17** (1.05, 1.30) Reference 1.00 (0.74, 1.36) 0.73 (0.47, 1.15) 0.58* (0.35, 0.96) Reference 0.91 (0.66, 1.24) 1.17	
27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42	eer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	com/ on April 17, 2024 by guest. Protected by copyright.	(0.89, 1.53)	5

		Model 4: +BMI Model 5: +CV	9 Model 6:	Model 7: Fully-			
	literacy	Cognitive ability	literacy and cognitive	and health	comorbidities	ω +Education and	adjusted
	•	0	ability	behaviours		social class	0
Health literacy			•			ē	
Limited	Reference	-	Reference	Reference	Reference	No. 20 Reference	Reference
Adequate	0.79*		0.88	0.96	0.92	N 0.90	0.98
-	(0.64, 0.97)		(0.71, 1.10)	(0.77, 1.20)	(0.74, 1.15)	0.72, 1.12)	(0.78, 1.23)
Cognitive ability	-	0.78***	0.79***	0.88	0.80***	Download (0.72, 1.12) 0.82** (0.72, 0.93) 1.04*** (1.02, 1.05) 0.999*	0.88
		(0.69, 0.88)	(0.70, 0.90)	(0.77, 1.00)	(0.70, 0.91)	<u>o</u> (0.72, 0.93)	(0.77, 1.00)
Age	1.04***	1.03***	1.03***	1.04***	1.02**	g 1.04***	1.03***
	(1.03, 1.06)	(1.02, 1.05)	(1.02, 1.05)	(1.02, 1.05)	(1.01, to 1.04)	$\frac{d}{d}$ (1.02, 1.05)	(1.02, 1.05)
Age ²	0.999*	0.999**	0.999**	0.998**	0.999	g 0.999*	0.999
	(0.997, 1.000)	(0.997, 1.000)	(0.997, 1.000)	(0.997, 1.000)	(0.998, 1.000)	= (0.997, 1.000)	(0.998, 1.000)
Sex						б ./	
Female	Reference	Reference	Reference	Reference	Reference	http://bmjopen.bmj.com/ on April 17, 2024 by guest. Protected by copyright.	Reference
Male	1.66***	1.58***	1.58***	2.17***	1.63***] 1.56	2.09***
	(1.36, 2.03)	(1.29, 1.93)	(1.29, 1.94)	(1.74, 2.70)	(1.33, 2.00)	6 (1.27, 1.92)	(1.67, 2.62)
BMI				1.10***		D.b	1.09***
				(1.08, 1.12)		<u>,</u>	(1.07, 1.11)
Current smoking						ğ	
Non-smoker				Reference			Reference
Smoker				0.89		ŭ N	0.93
				(0.64, 1.22)		₽ ₽	(0.66, 1.27)
Alcohol consumption							
Daily/almost daily				Reference		7	Reference
At least once per week				1.21		202	1.24
				(0.90, 1.66)		4	(0.91, 1.70)
At least once per				1.76**			1.77**
month				(1.21, 2.54)		gue	(1.21, 2.57)
Rarely				2.01***		st.	1.95***
N				(1.42, 2.87)		P	(1.36, 2.79)
Never				2.24***		ote	2.12***
				(1.55, 3.26)		cte	(1.45, 3.11)
Physical activity				D C		d D	D C
Inactive				Reference		х́ о	Reference
Moderate activity				0.65***		Ö	0.68**
						yrig	
						ht	

BMJ Open Supplementary Table S3 Odds ratios (95% CI) for the association between health literacy and cognitive ability with diabetes status at wave 2 in a sub-sample of 6,086 participants with data on all variables of interest.

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of 41		BMJ Open		6/bmjopen-2021-058496	
		(0.51, 0.82)		n-2021-05	(0.53, 0.87)
Vigorous act	vity	0.51***		8496	0.56***
Number of CV		(0.37, 0.69)	2.22***	on 3	(0.41, 0.76) 1.98***
comorbidities			(1.91, 2.59)	ω	(1.70, 2.32)
Number of CV			(1.91, 2.39) 0.87^{***}	June	0.88***
comorbidities ²			(0.81, 0.92)	le v	(0.82, 0.93)
Education			(0.81, 0.92)	2022	(0.82, 0.93)
				N Defense	Defense
≤ 14 years				\bigcirc 1.07	Reference 1.17
15-16 years				Reference 1.07 (0.81, 1.42) 0.78 (0.51, 1.18)	
17 10				\overline{O} (0.81, 1.42)	(0.87, 1.56)
17-18 years				$\frac{\overline{0}}{\Phi}$ (0.51, 1.10)	0.98
>10				ਰ (0.51, 1.18) ਤੋਂ 0.94	(0.64, 1.50)
≥ 19 years					1.32
0 1 1				B (0.62, 1.43)	(0.85, 2.05)
Social class	1			đ.	D (
Managerial a	.d			Reference	Reference
professional				0.79 (0.59, 1.07) 1.09	0.70
Intermediate				ස් 0.79 (0.50 1.07)	0.79
	1			(0.59, 1.07)	(0.58, 1.07)
Routine and 1	ianual			<u><u> </u></u>	1.01
				<u><u><u></u></u> (0.84, 1.42)</u>	(0.77, 1.32)
* <i>p</i> <.05, ** <i>p</i> <.0 Age ² , age squar	l, *** <i>p</i> <.001 ed; BMI, body mass index; CV, cardiovascul	lar; number of CV cormorbidities ² , numb		m/ of a April 17, 2024 by guest. Protected by copyright.	squared.
				yht.	,
				•	

	Model 1: Health literacy	Model 2: Cognitive ability	Model 3: Health literacy and cognitive ability	Model 4: +BMI and health behaviours	Model 5: +CV comorbidities	9 Model 6: ω+Education and Social class	Model 7: Fully- adjusted
Health literacy						le N	
Limited	Reference	-	Reference	Reference	Reference	Reference	Reference
Adequate	0.64***		0.73**	0.80	0.74**	N0.79*	0.85
-	(0.52, 0.80)		(0.58, 0.91)	(0.64, 1.01)	(0.59, 0.93)	[0.63, 0.98]	(0.68, 1.06)
Cognitive ability	<u> </u>	0.72***	0.76***	0.84**	0.76***	≦0.83**	0.88
		(0.63, 0.82)	(0.66, 0.86)	(0.73, 0.96)	(0.67, 0.87)	$\overline{\underline{0}}(0.72, 0.95)$	(0.77, 1.01)
Age	1.01	1.00	1.00	1.01	0.99	0 1.00	1.01
2	(0.997, 1.02)	(0.98, 1.01)	(0.98, 1.01)	(0.997, 1.03)	(0.98, 1.01)	a(0.92, 0.99) a(0.92, 0.99) a(0.98, 1.01)	(0.99, 1.02)
Sex						rom	
Female	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Male	1.47***	1.38**	1.40**	1.82***	1.40**	1.42**	1.82***
	(1.20, 1.81)	(1.12, 1.70)	(1.13, 1.72)	(1.46, 2.27)			(1.45, 2.28)
BMI	- / - /			1.12***	() -)	nic i i i i i i i i i i i i i i i i i i	1.12***
				(1.10, 1.14)		ope	(1.10, 1.13)
Current smoking						n.b	(-) -)
Non-smoker				Reference		<u>ă</u>	Reference
Smoker				1.79***			1.69***
2				(1.36, 2.34)		Ĩ.	(1.28, 2.22)
Alcohol consumption				(1100, 2101)		on	(1120, 2122)
Daily/almost daily				Reference		Ą	Reference
At least once per week				1.10		oril	1.01
The loast once per week				(0.80, 1.46)		17	(0.75, 1.36)
At least once per				1.49*		, 20	1.40
month				(1.03, 2.14)		024	(0.97, 2.01)
Rarely				1.70**		- b	1.53*
ruitiy				(1.20, 2.40)		1 gl	(1.08, 2.17)
Never				1.30		Jes	1.15
110101				(0.86, 1.96)		řť.	(0.76, 1.73)
Physical activity				(0.00, 1.90)		oro	(0.70, 1.75)
Inactive				Reference		tec	Reference
Moderate activity				0.76*		tec	0.79
				(0.59, 0.99)		b b	(0.61, 1.03)
Vigorous activity				(0.39, 0.99) 0.71*			0.76
vigorous activity				0./1		(dc	0.70
						(1.15, 1.76) (1.15, 1.76) (1.15, 1.76) on April 17, 2024 by guest. Protected by copyright.	
						ht.	

BMJ Open diabetes. Models are run on a sub-sample of 5,186 (360 with incident diabetes) participants with data on all variables opinterest.

Page 39 of 41		BMJ Open	86/bmjc	
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	* <i>p</i> <.05, ** <i>p</i> <.01, *** <i>p</i> <.001 BMI, body mass index; CV, cardiovascular.	(0.52, 0.96) 1.30*** (1.17, 1.45)	65bmjopen-2021-058496 on Gradient Control Co	(0.56, 1.04) 1.17^{**} (1.05, 1.30) Reference 1.00 (0.74, 1.36) 0.73 (0.47, 1.15) 0.58^* (0.35, 0.96) Reference 0.91 (0.66, 1.24) 1.16 (0.89, 1.53)
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 STROBE Statement-checklist of items that should be included in reports of observational studies

4 5	Item No	Recommendation	
⁵ Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
3		(b) Provide in the abstract an informative and balanced summary of what was	Page 2
0		done and what was found	-
1 Introduction			
3 Background/rationale	2	Explain the scientific background and rationale for the investigation being	Pages
4		reported	5-6
⁵ Objectives	3	State specific objectives, including any prespecified hypotheses	Page 6
6 7 Methods			
8 Study design	4	Present key elements of study design early in the paper	Pages
9			6-8
0 1 ^{Setting}	5	Describe the setting, locations, and relevant dates, including periods of	Pages
2	C	recruitment, exposure, follow-up, and data collection	6-7
² ³ Participants	6	(<i>a</i>) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of	Pages
4	Ũ	selection of participants. Describe methods of follow-up	6-7
5		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods	0 /
6 7		of case ascertainment and control selection. Give the rationale for the choice	
8		of cases and controls	
9		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and	
0		methods of selection of participants	
1		(b) Cohort study—For matched studies, give matching criteria and number of	NA
2 3		exposed and unexposed	INA
4		<i>Case-control study</i> —For matched studies, give matching criteria and the	
5		number of controls per case	
6 7 Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	Dagag
8	/		Pages 7-10
0	0*	effect modifiers. Give diagnostic criteria, if applicable	
⁹ Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of	Pages
1 2		assessment (measurement). Describe comparability of assessment methods if	7-10
3 Bias	0	there is more than one group	D
4 Bias	9	Describe any efforts to address potential sources of bias	Pages
5	10		15-16 P
6 Study size 7	10	Explain how the study size was arrived at	Pages
ō	11		7,12
^o Quantitative variables 9	11	Explain how quantitative variables were handled in the analyses. If applicable,	Pages
0	10	describe which groupings were chosen and why	10-11
1 Statistical methods 2	12	(<i>a</i>) Describe all statistical methods, including those used to control for	Pages
3		confounding	10-11
4		(b) Describe any methods used to examine subgroups and interactions	NA
5		(c) Explain how missing data were addressed	Pages
6 7			15-16
8		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	Pages
59		Case-control study—If applicable, explain how matching of cases and	15-16
50		controls was addressed	
		Cross-sectional study—If applicable, describe analytical methods taking	

		(\underline{e}) Describe any sensitivity analyses	Pag 15-
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study-eg numbers	Pages
		potentially eligible, examined for eligibility, confirmed eligible, included in the	12, 14
		study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	Pages
			12, 14
		(c) Consider use of a flow diagram	NA
Descriptive	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	Pages
data		and information on exposures and potential confounders	12, 14,
		(h) In direct much as a first state with an indirect data for such as side a first such	Table 1
		(b) Indicate number of participants with missing data for each variable of interest(c) <i>Cohort study</i>—Summarise follow-up time (eg, average and total amount)	Table 1 Pages 7-
		(c) <i>Conort study</i> —Summarise follow-up time (eg, average and total amount)	Pages /-
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over	Tables 3
	10	time	and 4
		Case-control study—Report numbers in each exposure category, or summary	
		measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary	Table 3
		measures	and 4
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates	Tables
		and their precision (eg, 95% confidence interval). Make clear which confounders	1-4
		were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for	NA
		a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and	Pages 7-
		sensitivity analyses	10
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or	Pages
		imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	Pages
		limitations, multiplicity of analyses, results from similar studies, and other	16-19
Generalisability	21	relevant evidence Discuss the generalisability (external validity) of the study results	Dagas
Generalisability	21	Discuss the generalisability (external validity) of the study results	Pages 18-19
Other informati			10-17
Other informati Funding	on 22	Give the source of funding and the role of the funders for the present study and,	Page 20
1 ununig	<u> </u>	if applicable, for the original study on which the present article is based	1 age 20
		in apprease, for the original study on which the present atticle is based	

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The association of functional health literacy and cognitive ability with self-reported diabetes in the English Longitudinal Study of Ageing: A prospective cohort study

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The association of functional health literacy and cognitive ability with self-reported diabetes in the English Longitudinal Study of Ageing: A prospective cohort study Chloe Fawns-Ritchie^{1,2}, Jackie Price³, and Ian J Deary^{1,2}

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ABSTRACT

Objectives: We investigated whether functional health literacy and cognitive ability were associated with self-reported diabetes.

Design: Prospective cohort study.

Setting: Data was from waves 2 (2004-05) to 7 (2014-15) of the English Longitudinal Study of Ageing (ELSA), a cohort study designed to be representative of adults aged 50 years and older living in England.

Participants: 8,669 ELSA participants (mean age=66.7, SD=9.7) who completed a brief functional health literacy test assessing health-related reading comprehension, and 4 cognitive tests assessing declarative memory, processing speed and executive function at wave 2.

Primary outcome measure: Self-reported doctor diagnosis of diabetes.

Results: Logistic regression was used to examine cross-sectional (wave 2) associations of functional health literacy and cognitive ability with diabetes status. Adequate (compared to limited) functional health literacy (OR=0.72, 95% CI=0.61 to 0.84) and higher cognitive ability (OR per 1 SD=0.73, 95% CI=0.67 to 0.80) were associated with lower odds of self-reporting diabetes at wave 2. Cox regression was used to test the associations of functional health literacy and cognitive ability measured at wave 2 with self-reporting diabetes over a median of 9.5 years follow-up (n=6,961). Adequate functional health literacy (HR=0.64; 95% CI=0.53 to 0.77) and higher cognitive ability (HR=0.77, 95% CI=0.69 to 0.85) at wave 2 were associated with lower risk of self-reporting diabetes during follow-up. When both functional health literacy and cognitive ability were added to the same model, these associations were slightly attenuated. Additionally adjusting for health behaviours and body mass index fully attenuated cross-sectional associations between functional health literacy and cognitive ability with

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diabetes status, and partly attenuated associations between functional health literacy and cognitive ability with self-reporting diabetes during follow-up.

Conclusions: Adequate functional health literacy and better cognitive ability were independently associated with lower likelihood of reporting diabetes.

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Keywords Health literacy, cognition, diabetes, prospective studies

Strengths and limitations of this study

- This study used data from the English Longitudinal Study of Ageing, a large prospective cohort study designed to be representative of community-dwelling adults aged over 50 years living in England.
- Participants were followed-up for a median of 9.5 years to determine whether they were diagnosed with diabetes.

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- Diabetes status was self-reported.
- Health literacy and cognitive ability assessments were brief.

INTRODUCTION

 Diabetes is a common chronic condition in older adulthood and is associated with substantial morbidity and mortality.[1] Type 2 diabetes, the most common type of diabetes, is at least partly preventable.[1] Understanding the characteristics of those most at risk of developing diabetes is important for appropriately targeting diabetes education and interventions. Risk factors for developing diabetes include older age, deprivation, and obesity.[1]

Lower cognitive ability may be a risk factor for diabetes. Cognitive ability can be conceptualised as a composite term for a range of different but overlapping mental capabilities, including the ability to learn, plan, problem solve and process information.[2] Cognitive ability is closely related to but distinct from educational attainment and correlations between cognitive ability and education range from 0.40 to 0.80.[3] This general mental capability has been found to be associated with many different aspects of health.[2] Studies examining the association between cognitive ability and diabetes have found mixed results. One study[4] found that childhood cognitive ability did not predict diabetes in midlife when individually adjusting for a range of demographic variables including education. Others have found that lower cognitive ability in early life was associated with higher risk of diabetes in adulthood.[5, 6] Whereas the first study[5] did not adjust for educational attainment or measures of socioeconomic status, the latter[6] found that individuals with lower cognitive ability in early adulthood had higher rates of diabetes in midlife, even after adjusting for education and indicators of socioeconomic status. Individuals with higher cognitive ability might have the cognitive skills required to selfmanage their health, take better care of themselves throughout life, and thus reduce the risk of developing diabetes.[2, 5]

Health literacy is the "capacity to obtain, process and understand basic health information and services needed to make basic health decisions"[7], and it might also play a role in diabetes.

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Health literacy is a multifaceted construct thought to encompass all of the skills required to make decisions about one's health, including the ability to access, appraise and apply health information.[8, 9] One component of health literacy is functional health literacy – the reading, writing and numeracy skills needed to understand basic health information.[10] These skills are thought to be required, for example, to understand and correctly follow the instructions on a packet of prescription medication. In cross-sectional studies, rates of diabetes are higher in those with low functional health literacy, even after adjusting for age, sex, income and education.[11, 12] In one study, participants with inadequate functional health literacy were 48% more likely to report having diabetes when compared to participants with adequate health literacy, adjusting for sociodemographic and health variables.[12] Associations between health literacy and diabetes may differ by sex. Women with low health literacy were found to be more than twice as likely to have diabetes compared to those with high literacy after adjusting for age, race, income, education, body mass index (BMI), and smoking and alcohol status, however, health literacy was not associated with diabetes status in men.[13] Individuals with lower functional health literacy – at least in women – might lack the health-related reading and writing skills required to obtain, understand and follow health advice, such as eating well and exercising, which might reduce the risk of diabetes.[7]

In patients with diabetes, higher functional health literacy has consistently been associated with greater diabetes knowledge.[14-16] A very small association between higher functional health literacy and lower glycated haemoglobin (HbA_{1C}) levels in patients with diabetes has been reported in a meta-analysis of 26 studies (r=-0.048, p=0.027).[15] Whereas studies have investigated the association between functional health literacy and disease management in people with diabetes, little is known about whether functional health literacy is associated with risk of developing diabetes.

Functional health literacy and cognitive ability test scores are positively correlated.[17-19] Rank-order correlations between general cognitive ability and three functional health literacy tests ranged from 0.37 to 0.50.[18] Researchers have sought to determine the role of cognitive ability in the association between functional health literacy and a range of health outcomes. Most (but not all)[20] studies have found that cognitive ability partly or entirely attenuates the association between functional health literacy and health.[21-24]. One study[19] sought to determine whether health literacy and cognitive ability had independent associations with performance on various health-related tasks, including comprehending written and videopresented health information and using health-related props, such as a pill bottle. Using three different measures of functional health literacy, the association between functional health literacy and performance on the health-related tasks were attenuated by between 70.6% and 77.7% when including cognitive ability in the same model compared to models not including cognitive ability.[19] Any association between functional health literacy and diabetes may be attenuated when also measuring cognitive ability.

The aim of the current study was to better understand the associations of functional health literacy and cognitive ability with diabetes. Using data from the English Longitudinal Study of Ageing (ELSA),[25] the present study investigated whether functional health literacy and cognitive ability were independently associated with diabetes. First, the cross-sectional associations between functional health literacy, cognitive ability, and self-reported diabetes were investigated. Second, participants without diabetes at baseline were followed-up for up to 10 years to determine whether functional health literacy and cognitive ability were independently associated with newly reporting diabetes during follow-up.

METHODS

Participants

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This study used data from core members of the ELSA study, a prospective cohort study of community-dwelling adults residing in England. ELSA was designed to be representative of adults aged 50 years and older living in England.[25] The wave 1 (2002-03) sample consisted of 11,391 participants who had previously participated in the Health Survey for England between 1998 and 2001, who were born before 1 March 1952, and who were living in a private household in England.[25] ELSA participants have been followed up every two years and the sample has been refreshed at waves 3, 4, 6 and 7 to ensure the sample is representative of adults aged over 50 years. The present study used data from waves 2 (2004-05) to 7 (2014-15), and baseline, here, was considered to be wave 2 (n=8,726), which was when the functional health literacy assessment was introduced.

At each wave, a face-to-face interview was used to measure topics including health, lifestyle and economic circumstances. Face-to-face interviews were carried out in the participant's own home using computer-assisted interviewing. Participants answered a self-completion questionnaire including questions about diet and alcohol consumption. A nurse interview was carried out at waves 2, 4 and 6 to assess physical measurements including height and weight, and blood and saliva samples were taken to measure biomarkers of disease. Detailed descriptions of the sample design and data collected in ELSA are reported elsewhere.[25] Ethical approval was obtained from the NHS Multicentre Research Ethics Committee, London (reference: MREC/01/2/91). Written informed consent was obtained from all ELSA participants. This study conformed to the principles embodied in the Declaration of Helsinki.

Patient and Public Involvement

Participants were not involved in the development of any part of this study.

Measures

Diabetes

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Baseline diabetes status: Individuals who answered "yes" to "Has a doctor ever told you that you have diabetes?" at wave 2 were categorised as having diabetes. This question did not differentiate which type of diabetes the participant was diagnosed with.

Diabetes during follow-up: This analysis was restricted to participants who did not self-report diabetes at wave 2 and who had at least one wave of follow-up between waves 3 and 7. Participants who did not self-report diabetes at wave 2 and who subsequently answered "yes" to "Has a doctor ever told you that you have diabetes?" any time between waves 3 and 7 were categorised as having newly diagnosed diabetes during follow-up. As all participants were aged over 50 years at diagnosis, these cases are probably cases of type 2 diabetes.

Date of diabetes diagnosis: Individuals who self-reported diabetes were asked which month and year they were diagnosed. Date of diabetes diagnosis was used to calculate the time between wave 2 assessment and diabetes diagnosis.

Functional health literacy

A 4-item functional health literacy test taken from the Adult Literacy and Life Skills Survey,[26] and the International Adult Literacy Survey[27] was administered during the wave 2 interview. This test assessed health-related reading comprehension skills which are thought to be required to successfully understand written materials commonly encountered in healthcare. Participants were presented with a piece of paper containing a label for a packet of over-the-counter medication. Participants were asked four questions about the information on this label (e.g., "what is the maximum number of days you may take this medicine?"). The score was the number of correctly answered questions. As has been done in other studies,[28, 29] performance was categorised as adequate (4/4 correct) or limited (<4 correct).

Cognitive ability

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Scores on different cognitive tests tend to be positively correlated.[30] Data reduction techniques such as principal component analysis (PCA) are often used to capture the covariance among a range of difference cognitive tests. This shared variance can then be used as a measure of general cognitive ability.[31] Four tests administered during the wave 2 interview that are designed to assess cognitive domains that decline with increasing age[32] were entered into a PCA to create a measure general cognitive ability.

Word list learning tests, in which participants are required to remember a list of words immediately and then after a delay are commonly used to assess verbal declarative memory and learning.[33] Here, the immediate and delayed word recall tests were used. Participants were read a list of 10 words and were asked to immediately recall as many of the words as possible. The score was the number of words recalled immediately. After a short delay, in which the words were not repeated, participants were asked to remember the 10 words again. The score was the number of words recalled after a delay. Verbal fluency tests, in which participants are asked to produce as many words as possible in a set time following a set of rules, are often used to measure executive function.[33] Category fluency was used to assess executive function in ELSA. Participants were instructed to name as many animals as possible. The score was the number of animals named in 60 seconds. Tests of processing speed involve completing a simple task as quickly as possible and common tests include using a code to write as many symbols as possible, or finding symbols amongst distractors and scoring them out as quickly as possible.[33, 34] Letter cancellation was used to assess processing speed. Participants were presented with a piece of paper containing letters of the alphabet arranged in rows and columns. The task was to scan the piece of paper and score out all Ps and Ws. The score was the combined number of Ps and Ws scored out in 60 seconds.

Scores of 0 on animal fluency (n=48) and letter cancellation (n=3) were removed as scores of 0 on these tests suggest participants either did not complete the task or did not understand the

task. Scores of \geq 50 on animal fluency (n=4), and \geq 60 on the letter cancellation (n=3) were removed as these scores were extremely high given the 60 second time limit for these tests and these values are greater than 4 SDs from the mean.

We did not include tests of self-reported memory, prospective memory or orientation in time in the measure of general cognitive ability. Self-reported memory was not included because this is a subjective test. Prospective memory was not included because the test consists of only one trial. Orientation in time is a four item test in which participants are asked to recall the date. It has limited variance and is most frequently used as a brief screening tool for cognitive impairment.

Only the first principal component had an eigenvalue >1. The scree plot also indicated one component. Scores from the first principal component were saved and used as a measure of cognitive ability (mean=0.00, SD=1.00). The first component accounted for 57% of the variance in the scores on the four cognitive tests. The loadings were: Immediate word recall=0.83, delayed word recall=0.85, animal fluency=0.72, and letter cancellation=0.58.

Covariates

 Age (in years), sex, BMI, health behaviours, number of cardiovascular comorbidities, and indicators of socioeconomic status were used as covariates. Unless otherwise stated, all were self-reported at the wave 2 interview. Prior to releasing data, ELSA set the age of all participants aged over 90 years to 90 years to reduce the risk of disclosure. Participants were asked whether they smoked cigarettes nowadays and were categorised as current smokers or non-smokers. Participants were asked how often they took part in moderate and vigorous physical activity (more than once a week, once a week, one to three times a month, and hardly ever/never). Physical activity levels were categorised as vigorous activity at least once per week, moderate activity at least once per week, and physically inactive. Participants were

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asked about their frequency of alcohol consumption in the past 12 months in the selfcompletion questionnaire. This was categorised as never, rarely, at least once a month, at least once a week, and daily/almost daily. Height and weight, measured during the wave 2 nurse interview, were used to calculate BMI (kg/m²). Cardiovascular comorbidities were assessed by counting the number of self-reported cardiovascular conditions from hypertension, angina, heart attack, heart murmur, abnormal heart rhythm, stroke, and high cholesterol. Age that participants left full-time education was categorised as: age 14 or under, 15-16 years, 17-18 years, and age 19 or older. Social class was categorised using the National Statistics Socioeconomic Classification 3 categories;[35] managerial and professional, intermediate, and routine and manual.

Analysis

All analyses was performed in R. Independent t-tests were used to compare those with and without diabetes at wave 2 and those who did and did not self-report diabetes at follow-up on normally-distributed continuous variables. Mann-Whitney U tests were used for non-normal continuous variables, and Chi-squared tests were used for categorical variables. Spearman rank-order correlations were calculated between all predictor variables and co-variables.

Binary logistic regression was used to test the cross-sectional association of functional health literacy and cognitive ability with diabetes reported at wave 2. Cox regression was used to investigate whether functional health literacy and cognitive ability test scores at wave 2 were associated with newly reported diabetes between waves 2 and 7. In the Cox regression analysis, time-to-event was taken as the difference, in days, between date of wave 2 interview and date of diabetes diagnosis for those who self-reported diabetes. For other participants, time-to-event was the difference between date of wave 2 interview and the date of last interview. Month and

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year, but not day, were recorded for date of interview and date of diabetes diagnosis. To create a date variable (yyyy.mm.dd), the day was set to the middle of the month.

For the logistic regressions and Cox regressions, 7 models were run. Age and sex were entered into all models. Functional health literacy and cognitive ability were entered individually in models 1 and 2, respectively. Both functional health literacy and cognitive ability were added in Model 3 to determine whether the size of the functional health literacy-diabetes and cognitive ability-diabetes associations changed when simultaneously entering both these variables. Functional health literacy and cognitive ability were also entered together in models 4-7. To assess whether BMI and health behaviours accounted for these associations, BMI, smoking status, alcohol consumption, and physical activity were added in Model 4. Diabetes is a risk factor for cardiovascular disease.[36] Associations between poorer cognitive ability and cardiovascular disease are also well established.[37, 38] It is possible that any association between functional health literacy and cognitive ability with diabetes may be because of these associations with cardiovascular disease. To determine whether any association between functional health literacy and cognitive ability with diabetes was attenuated when adjusting for cardiovascular disease, number of cardiovascular comorbidities was added in Model 5. Age of leaving full-time education and occupational social class were added in Model 6. A fullyadjusted model (Model 7) adjusted for functional health literacy, cognitive ability, and all covariates.

This study was interested in the associations of functional health literacy and cognitive ability with self-reported diabetes and the independence of these associations with respect to other health and socioeconomic-related variables. In the main text we report the odd ratios (ORs) and hazard ratios (HRs) for functional health literacy and cognitive ability only. The estimates for all variables entered into the models are reported in the Supplementary materials.

RESULTS

Of the 8,726 ELSA participants who completed wave 2, 3 participants were removed who answered "don't know" to whether a doctor had diagnosed them with diabetes. A further 54 participants were removed because they selected that they had "diabetes or high blood sugar" from a Showcard listing cardiovascular conditions, but when asked whether a doctor had ever told them they had diabetes, they answered "no". The analytic sample consisted of 8,669 participants. Participant characteristics are reported in Table 1.

Baseline diabetes status

At baseline, 708 (8.2%) participants self-reported a diagnosis of diabetes. Compared to those without diabetes, those with diabetes were more likely to have limited functional health literacy (42.2% versus 32.3%) and have lower cognitive ability (diabetes mean=-0.36, SD=0.97; no diabetes mean=0.03, SD=1.00; Cohen's d=0.40). Participants with diabetes were older (diabetes mean=69.36, SD=9.16; no diabetes mean=66.46, SD=9.70) and more likely to be male (53.5% versus 44.2%) than those without. Those with diabetes were also more likely to leave full-time education at a younger age, be from a less professional social class, have a higher BMI, consume less alcohol, be inactive, and self-report more cardiovascular comorbidities (Table 1). Rank-order correlations between predictor variables and co-variables are reported in Table 2. Adequate functional health literacy was moderately correlated with higher cognitive ability (rho=0.31, p<0.001).

ORs and 95% confidence intervals (CIs) for the associations between functional health literacy and cognitive ability with self-reported diabetes at wave 2 are reported in Table 3 (and Supplementary Table S1). Box-Tidwell tests were performed whereby an interaction term between each continuous predictor variable and the log of that variable were added to the model to check the assumption that there is a linear relationship between each continuous

predictor and the logit of the outcome. The interaction between age and log(age) and the interaction between number of cardiovascular comorbidities and log(number of cardiovascular comorbidities) was significant. Therefore the assumptions of the linearity of the logit was violated. To overcome this, an age-squared term was included in all models, and a squared term for number of cardiovascular comorbidities was included in Models 5 and 7.

Participants with adequate functional health literacy were 29% less likely to self-report diabetes (Model 1 OR=0.71; 95% CI=0.61 to 0.84). A 1 SD higher cognitive ability was associated with 27% lower odds of self-reported diabetes (Model 2 OR=0.73; 95% CI=0.67 to 0.80). The association between functional health literacy and diabetes was attenuated by 38% (OR=0.82; 95% CI=0.69 to 0.98) and the association between cognitive ability and diabetes was attenuated by 19% (OR=0.78; 95% CI=0.70 to 0.86) when entering both functional health literacy and cognitive ability in Model 3. Both remained significantly associated with diabetes.

BMI and health behaviours were added in Model 4. The associations between functional health literacy and cognitive ability with diabetes were attenuated and no longer significant. The cognitive ability-diabetes association was not attenuated after adjusting for cardiovascular comorbidities (Model 5) or when adjusting for education and social class (Model 6). Cognitive ability remained significantly associated with diabetes in these models. The association between functional health literacy and diabetes was slightly attenuated and no longer significant when adjusting for cardiovascular comorbidities (Model 5) and education and social class (Model 6). In the fully adjusted model (Model 7), the size of the associations between functional health literacy and cognitive ability with diabetes were reduced further and were non-significant.

In the fully-adjusted model (Model 7; Supplementary Table S1) older age, male sex, having a higher BMI, and reporting more cardiovascular comorbidities were associated with higher odds

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of having diabetes. The association between number of cardiovascular comorbidities and diabetes became less strong as the number of comorbidities increased. Those who reported drinking alcohol at least once per month, rarely, or who never drank alcohol in the last 12 months were more likely to self-report diabetes when compared to those who reported drinking daily/almost daily. Compared to those who reported being physically inactive, those who took part in moderate or vigorous physical activity at least once per week were less likely to self-report diabetes.

Diabetes during follow-up

Of the 7,961 participants who did not self-report diabetes at wave 2, 6,961 participants had at least one wave of follow-up between waves 3 and 7. They form the analytic sample for the association between functional health literacy, cognitive ability and self-reported diabetes during follow-up. A total of 506 (7.3%) participants reported a new diagnosis of diabetes between wave 3 and wave 7, whereas 6,455 (92.7%) participants did not. Median time to follow-up was 9.5 years. Mean time to censor was 4.7 years (SD=3.1) for those with diabetes and 7.8 years (SD=2.9) for those without. Participant characteristics are reported in Table 1. Compared to participants who did not self-report diabetes during follow-up, those who did were more likely to have limited functional health literacy (38.8% versus 30.3%) and had lower cognitive ability (diabetes mean=-0.04, SD=0.89; no diabetes mean=0.10, SD=0.98, Cohen's d=0.15) at wave 2. Participants who reported diabetes were younger (diabetes mean=65.51, SD=8.59; no diabetes mean=66.0; SD=9.53) and more likely to be male (51.8%versus 43.2%) than those without. Compared to those without diabetes, participants who reported diabetes during follow-up were more likely to have left full-time education at a younger age, be from a less professional social class, smoke, consume less alcohol, be inactive, and to report more cardiovascular comorbidities at wave 2 (Table 1).

The HRs and 95% CIs for the association between functional health literacy, cognitive ability and self-reporting diabetes during follow-up are reported in Table 4 (and Supplementary Table S2). Adequate functional health literacy at wave 2 was associated with a 36% lower risk of reporting diabetes (Model 1 HR=0.64; 95% CI=0.53 to 0.77). A 1 SD higher cognitive ability at wave 2 was associated with a 23% lower risk of reporting diabetes (Model 2 HR=0.77; 95% CI=0.69 to 0.85). The association between functional health literacy and diabetes was attenuated by 22% after adjustment for cognitive ability (Model 3 HR=0.72; 95% CI=0.59 to 0.87), and the association between cognitive ability and diabetes was attenuated by 9% after adjusting for functional health literacy (HR=0.79; 95% CI=0.71 to 0.88). Both functional health literacy and cognitive ability remained significant predictors of reporting diabetes during follow-up.

BMI and health behaviours were added in Model 4. The associations of functional health literacy and cognitive ability with reporting diabetes were further attenuated but remained statistically significant. When adjusting for number of cardiovascular comorbidities, the association between functional health literacy and cognitive ability with diabetes remained almost unchanged (Model 5) and both remained significantly associated with diabetes. Education and social class was added in Model 6. The size of the association between functional health literacy ability with diabetes were slightly reduced but remained statistically significant. In the fully-adjusted model (Model 7) the associations between functional health literacy and cognitive ability and reporting diabetes were further reduced and no longer significant.

In the fully-adjusted model (Model 7; Supplementary Table S2) male participants, those with a higher BMI, current smokers, and those who reported consuming alcohol rarely (compared to daily/almost daily) at wave 2 were more likely to report diabetes during follow-up. Participants

who reported leaving education at age 19 years or older were less likely to report diabetes during follow-up compared to those who left at age 14 years or younger.

Sensitivity analysis

Missing data

There was missing data. For the cross-sectional analyses, 70% of participants had complete data. For the longitudinal analyses, 75% of participants had complete data. All models were rerun using only participants with complete data on all variables. These results are reported in Supplementary Tables S3 and S4. The pattern of associations were generally similar; however, the sizes of the associations tended to be slightly weaker compared to the full sample. For the cross-sectional analysis, functional health literacy was no longer significantly associated with diabetes status in Model 3 when adjusting for functional health literacy and cognitive ability (Supplementary Table S3). For the longitudinal analysis, when adjusting for BMI and health behaviours (Model 4; Supplementary Table S4), functional health literacy was no longer associated with reporting diabetes during follow-up.

Undiagnosed diabetes

It is possible that some participants not reporting diabetes may have undiagnosed diabetes. To identify participants who may have undiagnosed diabetes HbA_{1c} levels collected by blood draw during the nurse interview (waves 2, 4, and 6) were used.[25] Participants who did not report diabetes but who had HbA_{1c} levels of \geq 47.5 mmol/mol (6.5%) were categorised as having suspected undiagnosed diabetes. The models were re-run after removing these individuals to determine whether the results differ from those reported in the main models.

A total of 5,783 participants who formed the analytical sample for the cross-sectional analysis had HbA_{1c} levels available from the wave 2 nurse interview (399 self-reporting diabetes; 5,384 not self-reporting diabetes). Of the 5,384 participants who did not self-report diabetes at wave

2 and who had HbA_{1c} levels available at wave 2, 112 (2.1%) participants had HbA_{1c} levels of \geq 47.5 mmol/mol (6.5%). Models were re-run on this sub-sample after removal of these 112 participants with suspected undiagnosed diabetes (n=5,671). The results are reported in Supplementary Table S5. The associations between cognitive ability and diabetes status at wave 2 are very similar to those reported in the main model. Using this sub-sample, the size of the associations between functional health literacy and diabetes were reduced and were no longer significant in Model 1 (functional health literacy only; Supplementary Table S5) and Model 3 (functional health literacy and cognitive ability; Supplementary Table S5).

The Cox regressions were also re-run after removal of participants with suspected undiagnosed diabetes. The follow-up period was restricted to waves 3 to 6 (mean follow-up=7.5 years), as HbA_{1c} levels were not available at wave 7. A total of 4,425 participants who formed the analytical sample for the Cox models had HbA_{1c} levels collected at wave 4 and/or wave 6 (279 self-reporting diabetes between waves 3 and 6; 4,146 not self-reporting diabetes during followup). 147 participants who reported not having diabetes at waves 3 and 4 had HbA_{1c} levels of \geq 47.5 mmol/mol (6.5%) at wave 4 and were removed. A further 72 participants reported not having diabetes between waves 3 and 6 but had HbA_{1c} levels of \geq 47.5 mmol/mol (6.5%) at wave 6 and were removed. The Cox regression models were re-run on this sample (n=4,206; 212 reporting diabetes during follow-up; 3,994 not reporting diabetes during follow-up). The results are reported in Supplementary Table S6. The size of the associations between limited functional health literacy and self-reporting diabetes during follow-up became even stronger. In the fully-adjusted model (Model 7, Supplementary Table S6), the association between limited functional health literacy and diabetes remained significant. For cognitive ability, the strength of the associations were generally similar to the main models. However, after adjusting for BMI and health behaviours (Model 4, Supplementary Table S6) the size of the association between cognitive ability and diabetes was slightly attenuated and no longer significant.

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DISCUSSION

Using a sample of middle-aged and older adults living in England, the present study found that adequate functional health literacy and better cognitive ability were associated with lower odds of self-reporting diabetes. These associations were attenuated when functional health literacy and cognitive ability were entered in the same model, though both independently contributed to diabetes. These associations were further attenuated and non-significant when adjusting for BMI and health behaviours. Adjusting for cardiovascular comorbidities and indicators of socioeconomic status did not attenuate the association between cognitive ability and diabetes, however, for functional health literacy there was a small attenuation and these associations were no longer significant. When adjusting for all covariates simultaneously, neither functional health literacy nor cognitive ability was associated with diabetes at wave 2.

Adequate health literacy and better cognitive ability, measured at wave 2, were associated with reduced risk of self-reporting diabetes during a median of 9.5 years follow-up. Both functional health literacy and cognitive ability were independently associated with self-reported diabetes when both were entered in the same model. These associations remained when separately adjusting for BMI and health behaviours, cardiovascular comorbidities, and education and social class. However, neither health literacy nor cognitive ability were associated with reporting diabetes during follow-up when all covariates were entered together.

Previous cross-sectional studies have found that individuals with lower functional health literacy are more likely to report having diabetes[11, 12] and longitudinal studies have found that that lower cognitive ability earlier in life is associated with an increased risk of diabetes.[5, 6] The present study is the first longitudinal study to examine whether functional health literacy is associated with self-reporting a new diagnosis of diabetes, and the first to examine whether cognitive ability and functional health literacy have independent associations with

diabetes. The results reported here suggest that cognitive capabilities and health-related reading comprehension skills, though related, contribute independently to diabetes.

There are obvious similarities between tests of cognitive ability and functional health literacy. The Rapid Estimate of Adult Literacy in Medicine (REALM)[39] is a popular health literacy test which involves the ability to read and pronounce health-related words of varying complexity. More ecologically valid assessments of functional health literacy such as the Test of Functional Health Literacy in Adults (TOFHLA)[10] and the health literacy test used in the current study involve participants using mock health-related props, such as prescription labels or a medical appointment slips, and answering questions about the information presented. Successful completion of these tests will require the ability to process information, plan and problem solve (i.e., cognitive ability).[2]

Some have suggested that functional health literacy variance is mostly overlapping with cognitive ability.[23, 40] If this were true, one would expect the association between functional health literacy and diabetes to be fully attenuated when adjusting for cognitive ability. This is not what was found here. Only some of the association of functional health literacy and diabetes was accounted for by cognitive ability. The level of independence between health literacy and cognitive ability may vary depending on the assessments used to measure health literacy and cognitive ability.[22] The cognitive ability measure used here included four brief cognitive ability tests that assessed memory, executive function and processing speed, and did not include other important domains of cognitive function, such as reasoning, that are known to load highly on general cognitive ability.[41] The health literacy assessment was also very brief. Some of the unique contribution of functional health literacy might be residual cognitive capability that was not picked up by the relatively brief measures of cognitive ability used here.[42] However, unique associations of health literacy and cognitive ability with health have been reported when using a variety of different functional health literacy tests, including the

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REALM[23], the TOFHLA[21, 23] and the ELSA health literacy test[22]. Though attenuated, functional health literacy has also been found to have had unique associations with health after adjusting for cognitive ability created using a comprehensive test battery consisting of well-validated cognitive tests[23]. Therefore, low health literacy and poorer cognitive ability may contribute unique disadvantages in terms of navigating healthcare and looking after one's own health.[22]

This study was also interested in examining whether functional health literacy and cognitive ability were associated with reporting diabetes independent of other health-related and socioeconomic risk factors for diabetes. The largest attenuation was seen when entering health behaviours and BMI into the models. BMI and health behaviours fully attenuated the relationship between functional health literacy, cognitive ability and reporting diabetes at baseline, and partly attenuated the relationship between functional health literacy, cognitive ability has been associated with health promoting behaviours such as follow-up. Better cognitive ability has been associated with health promoting behaviours such as following a healthy diet and taking part in regular exercise.[4, 43-45] Whereas some studies have found associations between tot.[47] Individuals with higher functional health literacy and cognitive ability might be better equipped with the health-related skills and knowledge, and the general cognitive capabilities needed to take better care of themselves[2, 48] and to follow health advise such as eating well and exercising, which, in turn, could reduce the risk of developing diabetes.[1]

Education also partly attenuated the association between functional health literacy and cognitive ability with reporting diabetes during follow-up. The association between better functional health literacy and cognitive ability with higher levels of education are well established.[7, 49] Education may lead to better cognitive ability and functional health literacy, which in turn may lead to better health-related skills and lower rates of diabetes.[23] Higher

cognitive ability in early life has been found to predict later educational attainment.[49] An alternative but not mutually exclusive explanation could be that higher cognitive ability may equip an individual with the skills needed to obtain higher educational qualifications. Higher educational attainment, in turn, may lead to better health (and lower risk of diabetes) by, for example, increasing health-related knowledge and decision-making skills.[23] In the current study, social class was not found to have associations with diabetes and did not appear to play an attenuating role in the association between health literacy and cognitive ability with diabetes.

This study has a number of strengths and limitations. A key strength is that it examined the association of functional health literacy, cognitive ability and reporting diabetes longitudinally. Another strength is the relatively large sample size. One limitation is that only a sub-sample of participants had complete data. Those with missing data may be those with the lowest functional health literacy and cognitive ability scores. ELSA may also suffer from selective attrition such that those with increased risk of developing diabetes may be less likely to return for follow-up. The results reported here may not generalise to those with the lowest functional health literacy and/or cognitive ability. The rates of diabetes reported here do not fully match those reported in national statistics. Compared to the 2004/05 National Diabetes Audit for England and Wales, rates of diabetes in the current study were lower for those aged 55 to 69 years (this study: 8.4% in men and 5.6% in womer; National Diabetes Audit: approximately 10% in men, and 7% in women; National Diabetes Audit: approximately 13.6% in men and 9.9% in women; National Diabetes Audit: approximately 13.6% in men and 10% in women). [50] Therefore the current sample is not fully representative of people with diabetes living in England.

Another limitation is that diabetes status was self-reported. As has been shown in other ELSA studies, there is a relatively high rate of agreement between self-reported diabetes and fasting

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blood glucose in ELSA; however, 1.7% of participants had undiagnosed diabetes.[51] Sensitivity analysis was performed in the current study to try to identify and remove individuals with undiagnosed diabetes. Although the results were generally similar after removal of those with suspected undiagnosed diabetes, we found that health literacy was no longer associated with cross-sectional diabetes status in the sub-sample of participants with HbA_{1c} levels. It is not clear whether these differences are due to removal of participants with suspected undiagnosed diabetes, or if it was due to bias caused by using a smaller sub-sample of participants who also attended the nurse interview and provided a blood sample.

The functional health literacy test used here was a brief, four-item test which had limited variance (67% of participants scored the highest score) and the psychometric properties of this measure are unknown. Although brief, this test was sensitive enough to have associations with self-reported diabetes during follow-up, and it has previously been found to have associations with mortality.[22] This brief measure only assessed functional health literacy and did not measure other components of health literacy.[8] More detailed, self-report measures of health literacy are available that assess a range of other health literacy skills, including the (self-reported) ability to access, appraise and apply health information.[52] An important next step would be to test the associations between health literacy and cognitive ability with diabetes using more detailed tests of health literacy that cover a range of other health literacy skills in addition to health-related reading comprehension.

This study found that adequate functional health literacy and higher cognitive ability were independently associated with lower odds of self-reporting diabetes at wave 2 and with reduced rates of self-reporting a new diagnosis of diabetes during a median of 9.5 years follow-up. Individuals with poor functional health literacy and/or cognitive ability might lack the healthrelated reading and writing skills and the general cognitive capabilities required to look after

their health throughout life, which in turn, may increase the risk of being diagnosed with diabetes.

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Conflict of Interest No potential conflicts of interest were reported.

Author Contributions Chloe Fawns-Ritchie contributed to the conception and design of the project, analysed the data, interpreted the data, drafted the initial manuscript, and critically revised the manuscript. Jackie Price contributed to the conception and design of the project, interpreted the data, and critically revised the manuscript. Ian J. Deary contributed to the conception and design of the project, interpreted the data, and critically revised the manuscript.

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Data accessibility Anonymised data from the English Longitudinal Study of Ageing is available from the UK Data Service (<u>https://https://www.ukdataservice.ac.uk/</u>).

REFERENCES

1 Hussain A, Claussen B, Ramachandran A, *et al.* Prevention of type 2 diabetes: a review. *Diabetes Res Clin Pract* 2007;76:317-26.

2 Gottfredson LS. Intelligence: is it the epidemiologists' elusive "fundamental cause" of social class inequalities in health? *J Pers Soc Psychol* 2004;86:174-99.

3 Malanchini M, Rimfeld K, Allegrini AG, *et al.* Cognitive ability and education: How behavioural genetic research has advanced our knowledge and understanding of their association. *Neuroscience & Biobehavioral Reviews* 2020;111:229-45.

4 Batty GD, Deary IJ, Macintyre S. Childhood IQ in relation to risk factors for premature mortality in middle-aged persons: the Aberdeen Children of the 1950s study. *J Epidemiol Community Health* 2007;61:241-7.

5 Mõttus R, Luciano M, Starr JM, *et al.* Diabetes and life-long cognitive ability. *J Psychosom Res* 2013;75:275-8.

6 Twig G, Gluzman I, Tirosh A, *et al.* Cognitive function and the risk for diabetes among young men. *Diabetes care* 2014;37:2982-8.

7 Nielsen-Bohlman L, Panzer AM, Kindig DA. *Health Literacy: A Prescription to End Confusion*. Washinton, DC: The National Academies Press 2004.

8 Sørensen K, Van Den Broucke S, Fullam J, *et al.* Health literacy and public health: A systematic review and integration of definitions and models. *BMC Public Health* 2012;12:80-.

9 Nutbeam D. The evolving concept of health literacy. *Social Science & Medicine*2008;67:2072-8.

10 Parker RM, Baker DW, Williams MV, *et al.* The test of functional health literacy in adults: A new instrument for measuring patients' literacy skills. *Journal of General Internal Medicine* 1995;10:537-41.

BMJ Open

11 Adams RJ, Appleton SL, Hill CL, *et al.* Risks associated with low functional health literacy in an Australian population. *Med J Aust* 2009;191:530-4.

12 Wolf MS, Gazmararian JA, Baker DW. Health literacy and functional health status among older adults. *Arch Intern Med* 2005;165:1946-52.

13 Quartuccio M, Simonsick EM, Langan S, *et al.* The relationship of health literacy to diabetes status differs by sex in older adults. *Journal of Diabetes and its Complications* 2018;32:368-72.

14 Caruso R, Magon A, Baroni I, *et al.* Health literacy in type 2 diabetes patients: a systematic review of systematic reviews. *Acta Diabetol* 2018;55:1-12.

15 Marciano L, Camerini AL, Schulz PJ. The Role of Health Literacy in Diabetes Knowledge, Self-Care, and Glycemic Control: a Meta-analysis. *J Gen Intern Med* 2019;34:1007-17.

16 Al Sayah F, Majumdar SR, Williams B, *et al.* Health literacy and health outcomes in diabetes: a systematic review. *J Gen Intern Med* 2013;28:444-52.

17 Bennett JS, Boyle PA, James BD, *et al.* Correlates of health and financial literacy in older adults without dementia. *BMC Geriatrics* 2012;12:30.

18 Murray C, Johnson W, Wolf MS, *et al.* The Association between Cognitive Ability across the Lifespan and Health Literacy in Old Age: The Lothian Birth Cohort 1936. *Intelligence* 2011;39:178-87.

19 Wolf MS, Curtis LM, Wilson EA, *et al.* Literacy, cognitive function, and health: results of the LitCog study. *General Internal Medicine* 2012;27:1300-7.

20 Lamar M, Wilson RS, Yu L, *et al.* Associations of literacy with diabetes indicators in older adults. *J Epidemiol Community Health* 2019;73:250-5.

21 Baker DW, Wolf MS, Feinglass J, *et al.* Health literacy, cognitive abilities, and mortality among elderly persons. *J Gen Intern Med* 2008;23:723-6.

> 22 Bostock S, Steptoe A. Association between low functional health literacy and mortality in older adults: longitudinal cohort study. *BMJ* 2012;344:e1602.

23 Mõttus R, Johnson W, Murray C, *et al.* Towards understanding the links between health literacy and physical health. *Health Psychol* 2014;33:164-73.

Fawns-Ritchie C, Starr JM, Deary IJ. Role of cognitive ability in the association between functional health literacy and mortality in the Lothian Birth Cohort 1936: a prospective cohort study. *BMJ Open* 2018;8:e022502.

25 Steptoe A, Breeze E, Banks J, *et al.* Cohort profile: the English Longitudinal Study of Ageing. *Int J Epidemiol* 2013;42:1640-8.

26 Desjardins R, Murray S, Clermont Y, *et al.* Learning a living: First results of the adult literacy and life skills survey. *Statistics Canada catalogue* 2005.

27 Kirsch IS. The International Adult Literacy Survey (IALS): Understanding What is Measured. 2001;2001:i-61.

28 Kobayashi LC, Wardle J, von Wagner C. Limited health literacy is a barrier to colorectal cancer screening in England: evidence from the English Longitudinal Study of Ageing. *Prev Med* 2014;61:100-5.

Gale CR, Deary IJ, Wardle J, *et al.* Cognitive ability and personality as predictors of participation in a national colorectal cancer screening programme: the English Longitudinal Study of Ageing. *J Epidemiol Community Health* 2015;69:530-5.

30 Spearman C. "General Intelligence", objectively determined and measured. *The American Journal of Psychology* 1904;15:201-92.

31 Salthouse T. *Major issues in cognitive aging*: Oxford University Press 2010.

32 Salthouse TA. Selective review of cognitive aging. *Journal of the International Neuropsychological Society* 2010;16:754-60.

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33 Lara J, Cooper R, Nissan J, *et al.* A proposed panel of biomarkers of healthy ageing.*BMC Medicine* 2015;13:222.

34 Lezak MD, Howieson DB, Bigler ED, *et al. Neuropsychological Assessment*. Oxford:Oxford University Press 2012.

35 Rose D, Pevalin DJ, O'Reilly K. *The National Statistics Socio-economic Classification: origins, development and use*: Palgrave Macmillan Basingstoke 2005.

36 Sarwar N, Gao P, Seshasai SR, *et al.* Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet* 2010;375:2215-22.

37 Rostamian S, Mahinrad S, Stijnen T, *et al.* Cognitive impairment and risk of stroke: a systematic review and meta-analysis of prospective cohort studies. *Stroke* 2014;45:1342-8.

38 Hart CL, Taylor MD, Smith GD, *et al.* Childhood IQ and cardiovascular disease in adulthood: prospective observational study linking the Scottish Mental Survey 1932 and the Midspan studies. *Social Science & Medicine* 2004;59:2131-8.

39 Davis TC, Long SW, Jackson RH, *et al.* Rapid estimate of adult literacy in medicine: a shortened screening instrument. *Family Medicine* 1993;25:391-5.

40 Reeve CL, Basalik D. Is health literacy an example of construct proliferation? A conceptual and empirical evaluation of its redundancy with general cognitive ability. *Intelligence* 2014;44:93-102.

41 Salthouse TA. Localizing age-related individual differences in a hierarchical structure. *Intelligence* 2004;32:541-61.

42 Fawns-Ritchie C, Starr JM, Deary IJ. Health literacy, cognitive ability and smoking: a cross-sectional analysis of the English Longitudinal Study of Ageing. *BMJ Open* 2018;8:e023929.

43 Batty GD, Deary IJ, Schoon I, *et al.* Childhood mental ability in relation to food intake and physical activity in adulthood: the 1970 British Cohort Study. *Pediatrics* 2007;119:e38-45.

44 Wraw C, Der G, Gale CR, *et al.* Intelligence in youth and health behaviours in middle age. *Intelligence* 2018;69:71-86.

45 Batty GD, Deary IJ, Schoon I, *et al.* Mental ability across childhood in relation to risk factors for premature mortality in adult life: the 1970 British Cohort Study. *J Epidemiol Community Health* 2007;61:997-1003.

46 von Wagner C, Knight K, Steptoe A, *et al.* Functional health literacy and healthpromoting behaviour in a national sample of British adults. *J Epidemiol Community Health* 2007;61:1086-90.

47 Wolf MS, Gazmararian JA, Baker DW. Health literacy and health risk behaviors among older adults. *Am J Prev Med* 2007;32:19-24.

48 Deary IJ, Weiss A, Batty GD. Intelligence and Personality as Predictors of Illness and Death: How Researchers in Differential Psychology and Chronic Disease Epidemiology Are Collaborating to Understand and Address Health Inequalities. *Psychol Sci Public Interest* 2010;11:53-79.

49 Deary IJ, Strand S, Smith P, *et al.* Intelligence and educational achievement. *Intelligence* 2007;35:13-21.

50 The Information Centre. National Diabetes Audit: Key findings about the quality of care for people with diabetes in England, incorporating registrations from Wales. Report for the audit period 2004/05. 2006.

51 Pierce MB, Zaninotto P, Steel N, *et al.* Undiagnosed diabetes-data from the English longitudinal study of ageing. *Diabetic Med* 2009;26:679-85.

52	Sørensen K, Pelikan JM, Rothlin F, et al. Health literacy in Europe: comparative results
of the	European health literacy survey (HLS-EU). European Journal of Public Health
2015;2	25:1053-8.

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Table 1 Participant character	ristics by	diabetes status					584	
		Diabetes rep	orted at wave 2			Diabetes reported	<u> </u>	up*
		No diabetes	Diabetes			No diabetes	Diabetes	- F
	n	(n = 7961)	(n = 708)	р	n	(n = 6455)	$f_{m} = 506$)	р
Age, mean (SD)	8669	66.46 (9.70)	69.38 (9.16)	<0.001	6961	66.02 (9.53)	85.51 (8.59)	<0.00
Sex, n (%)	8669			< 0.001	6961		22.	< 0.00
Male		3522 (44.2%)	379 (53.5%)			2791 (43.2%)	2 62 (51.8%)	
Female		4439 (55.8%)	329 (46.5%)			3664 (56.8%)	add (48.2%)	
Age left full-time education,			. ,			``	ade	
n (%)	8468			< 0.001	6809		ă fr	< 0.00
≤14 years		1641 (21.1%)	210 (30.6%)			1222 (19.3%)	9 1 07 (21.8%)	
15-16 years		4085 (52.5%)	349 (50.8%)			3283 (52.0%)	3 02 (61.6%)	
17-18 years		1009 (13.0%)	55 (8.0%)			870 (13.8%)	45 (9.2%)	
≥19 years		1046 (13.4%)	73 (10.6%)			944 (14.9%)	9 6 (7.3%)	
Social class, n (%)	8508			< 0.001	6846		en.	< 0.00
Managerial and							omj.	
professional		2444 (31.2%)	194 (28.4%)			2067 (32.6%)	§ 33 (26.7%)	
Intermediate		1979 (25.3%)	131 (19.2%)			1662 (26.2%)	₫04 (20.9%)	
Routine and manual		3403 (43.5%)	357 (52.3%)			2619 (41.3%)	261 (52.4%)	
Health literacy, n (%)	8293			< 0.001	6736		oril 1	< 0.00
Adequate		5172 (67.7%)	376 (57.8%)			4351 (69.7%)	300 (61.2%)	
Limited		2471 (32.3%)	274 (42.2%)			1895 (30.3%)	190 (38.8%)	
Cognitive ability, mean (SD)	8335	0.03 (1.00)	-0.36 (0.97)	< 0.001	6746	0.10 (0.98)	, 3 0.04 (0.89)	< 0.00
BMI, mean (SD)	7179	27.71 (4.79)	30.45 (5.37)	< 0.001	5997	27.46 (4.64)	g1.21 (5.28)	< 0.00
Current smoker, n (%)	8622			0.377	6929		st.	< 0.00
Yes		1216 (15.4%)	99 (14.1%)			934 (14.5%)	д 05 (20.8%)	
No		6704 (84.6%)	603 (85.9%)			5490 (85.5%)	2 00 (79.2%)	
Alcohol, n (%)	7577			< 0.001	6239		ā.	< 0.00
Never		723 (10.3%)	112 (19.3%)			565 (9.7%)	ଞ୍ ଖ୍ 9 (11.2%)	
Rarely		1076 (15.4%)	124 (21.3%)			863 (14.9%)	90 (20.6%)	

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Page 35 of 53					BMJ Open			86/bmjope	
1 2 3 4 5 6 7	At least once a month At least once a week Daily/almost daily Physical activity, n (%)	8665	827 (11.8%) 2662 (38.1%) 1708 (24.4%)	85 (14.6%) 171 (29.4%) 89 (15.3%)	< 0.001	6958	669 (11.5%) 2255 (38.9%) 1451 (25.0%)	¹ -2021 500 (16.1%) 549 (34.2%) 58 (17.9%) 500 (16.1%) 510 (16	<0.001
8 9 10 11 12	Vigorous activity Moderate activity Inactive Number of cardiovascular		2236 (28.1%) 3888 (48.9%) 1833 (23.0%)	108 (15.2%) 305 (43.1%) 295 (41.7%)			1938 (30.0%) 3194 (49.5%) 1320 (20.5%)	Ф16 (22.9%) 233 (46.0%) 457 (31.0%)	
13 14	comorbidities, mean (SD)	8669	0.67 (0.91)	1.28 (1.13)	< 0.001	6961	0.64 (0.88)	9 .89 (1.04)	< 0.001

BMI, body mass index.

 *Diabetes reported at follow-up comparisons are based on a sub-sample of participants who did not self-repoint diabetes at wave 2 and with at mparisons are based on a sub-sample of participants who did not self-report d

least one wave of follow-up.

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				Social	Health	Cognitive			- 6 On	Physical	CV
	Age	Sex	Education	class	literacy	ability	BMI	Smoking	Alcophol	activity	comorbid
Age									lune		
Sex	-0.03**								\$ 2022		
Education	-0.41***	0.02							22.		
Social class	0.08***	-0.09***	-0.41***						Dov		
Health literacy	-0.16***	0.01	0.23***	-0.18***					vnlo		
Cognitive ability	-0.47***	-0.09***	0.39***	-0.27***	0.31***				ade		
BMI	-0.07***	0.02	-0.06***	0.08***	-0.04**	-0.01			Downloaded from		
Smoking	-0.13***	0.01	-0.05***	0.12***	-0.04***	-0.02	-0.09***				
Alcohol	-0.11***	0.21***	0.22***	-0.20***	0.09***	0.16***	-0.11***	-0.04***	http:		
Physical activity	-0.26***	0.10***	0.23***	-0.15***	0.14***	0.26***	-0.11***	-0.09***	0.18***		
CV comorbid	0.18***	0.00	-0.11***	0.05***	-0.06***	-0.11***	0.14***	-0.03*	-0.0 ***	-0.14***	

p*<.05, *p*<.01, ****p*<.001

 BMI, body mass index; CV comorbid, number of cardiovascular comorbidities.

Sex is coded 0 for female, 1 for male; Education is age of leaving full-time education and is coded 1 for age 14 years or less, 2 for age 15-16 years, 3 for age 17-18 years, and 4 for 19 years or older; Social class is coded 1 for managerial and professional, 2 for intermediate, and 3 for routine and manual; Health literacy is coded 0 for limited and 1 for adequate; Smoking is coded 0 for current smoker; Alcohol is the frequency of alcohol consumed in the last 12 months and is coded 0 for never, 1 for rately, 2 for at least once a month, 3 for at least once a week, 4 for daily/almost daily; Physical activity is coded 0 for inactive, 1 for moderate activity at least once per week; 2 for vigorous activity at least once per week; CV comorbid is the number of cardiovascular comorbidities self-reported from hypertension, angina, heart attack, heart failure, heart murmur, abnormal heart rhythm, stroke, and high cholesterol.

Table 3 Odds ratios (95% CIs) from logistic regression models of the association between functional health	Atteracy and cognitive ability with
self-reported diabetes at wave 2	1 96

	Model 1:	Model 2:	Model 3: Health	Model 4: +BMI	Model 5: +CV	Model 6:	Model 7: Fully
	Health literacy	Cognitive	literacy and	and health	comorbidities 🗧	+Education and	adjusted
		ability	cognitive ability	behaviours	ne	social class	
Adequate health literacy	0.71***	-	0.82*	0.97	0.85	0.84	0.98
	(0.61, 0.84)		(0.69, 0.98)	(0.78, 1.21)	(0.72, 1.02)	(0.70, 1.01)	(0.78, 1.23)
Cognitive ability	-	0.73***	0.78***	0.90	0.78***	0.78***	0.87
		(0.67, 0.80)	(0.70, 0.86)	(0.80, 1.02)	(0.71, 0.87)	(0.71, 0.87)	(0.76, 1.00)

*p < .05, **p < .01, ***p < .001BMI, body mass index; CV, cardiovascular.All models adjusted for age, age-squared, and sex. Model 1 n=8,293, Model 2 n=8,335, Model 3 n=8,185.Mgdel 4 (n=6,302) adjusted for body mass index, frequency of alcohol consumption in the past 12 months, and physical activity. Model 5 (n=8,185) adjusted for number of cardiovascular comorbidities reported, and a squared term for number of cardiovascular comorbidities reported. Model 6 (n=7,861) adjusted for nber of cardiovascular comorbidities reported. 1 7 (n=6,086) adjusted for all covariates. age left full-time education, and occupational social class. Model 7 (n=6,086) adjusted for all covariates.

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BMJ Open Table 4 Hazard ratios (95% CIs) from Cox regression models of the association between functional health literacy and cognitive ability with self-reporting diabetes during follow-up

	Model 1:	Model 2:	Model 3:	Model 4: +BMI	Model 5: +CV	⁵ Model 6:	Model 7: Fully
	Health literacy	Cognitive ability	Health literacy and cognitive ability	and health behaviours	comorbidities	Section and Section and Section and Section and Section and Section 2000	adjusted
Adequate health literacy	0.64***	-	0.72***	0.79*	0.73**	0.79*	0.85
	(0.53, 0.77)		(0.59, 0.87)	(0.64, 0.99)	(0.60, 0.88)	§(0.65, 0.97)	(0.68, 1.06)
Cognitive ability	-	0.77***	0.79***	0.85*	0.80***	a 0.84**	0.88
		(0.69, 0.85)	(0.71, 0.88)	(0.74, 0.96)	(0.71, 0.89)	$\overline{B}(0.75, 0.95)$	0.77, 1.01)

All models adjusted for age and sex. Models 1 (n=6,736) had 490 diabetes events, Model 2 (n=6,746) had 494 diabetes events, Model 3 (n=6,654) had 484 diabetes events. Model 4 (n=5,357; 377 diabetes events) adjusted for body mass index, frequency of alcohol consumption in the past 12 months, and physical activity. Model 5 (n=6,654; 484 diabetes events) adjusted for number of cardiovascular comorbidities reported. Model 6 (n=6,409; 492 diabetes events) adjusted for age left full-time education, and occupational social class. Model 7 (n=5,186, 360 diabetes events) adjusted for all covariates. com/ on April 17, 2024 by guest. Protected by copyright

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6	The association of functional health literacy and cognitive ability with self-reported diabetes in the English Longitudinal Study of Ageing: A prospective cohort study
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Reference		n=8,185	behaviours n=6,302	comorbidities n=8,185	↔Education and Social class n=7,861	adjusted n=6,086
Reference					N N N N Reference	
		Reference	Reference	Reference	NReference	Reference
0.71***		0.82*	0.97	0.85	2 0.84	0.98
(0.61, 0.84)		(0.69, 0.98)	(0.78, 1.21)	(0.72, 1.02)	<u>≦(</u> 0.70, 1.01)	(0.78, 1.23)
-		0.78***	0.90	0.78***		0.87
	(0.67, 0.80)	(0.70, 0.86)	(0.80, 1.02)	(0.71, 0.87)	ଗ୍ ଟି(0.71, 0.87)	(0.76, 1.00)
1.04***	1.03***	1.03***	1.04***	1.02***		1.03***
(1.03, 1.05)	(1.02, 1.04)	(1.02, 1.04)	(1.03, 1.06)	(1.01, 1.03)		(1.02, 1.05)
0.998***	0.998***	0.998***	0.998**	0.998***	⊒ 0.998***	0.999
(0.997, 0.999)	(0.997, 0.998)	(0.997, 0.999)	(0.997, 0.999)	(0.997, 0.999)	(0.997, 0.999)	(0.998, 1.000)
					br	
Reference	Reference	Reference	Reference	Reference		Reference
1.50***	1.41***	1.43	2.16***	1.45***	<u>6</u> 1.44***	2.09***
(1.28, 1.77)	(1.20, 1.66)	(1.22, 1.69)	(1.75, 2.68)	(1.23, 1.71)	d (1.22, 1.71)	(1.67, 2.62)
			1.10***		<u>, </u>	1.09***
			(1.08, 1.12)		8	(1.07, 1.11)
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			Reference		on	Reference
			0.91		Ap	0.93
			(0.66, 1.23)		<u></u>	(0.66, 1.27)
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	1.04*** (1.03, 1.05) 0.998*** (0.997, 0.999) Reference 1.50***	- 0.73*** (0.67, 0.80) 1.04*** (1.03, 1.05) (1.02, 1.04) 0.998*** 0.998*** (0.997, 0.999) (0.997, 0.998) Reference Reference 1.50*** 1.41***	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$

BMJ Open Supplementary Table S1 Odds ratios (95% CI) from logistic regression models of the association between functional deealth literacy and cognitive ability

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1 2				en-2021	
- 3 4	Moderate activity	0.65^{***} (0.51, 0.83)		-0584	0.68** (0.53, 0.87)
5 6	Vigorous activity	(0.37, 0.63) 0.50*** (0.37, 0.68)		96 on	(0.41, 0.76)
7	Number of CV	()	2.08***	3 J	1.98***
	comorbidities		(1.84, 2.36)	Ine	(1.70, 2.32)
	Number of CV		0.88***	20	0.88***
	comorbidities ²		(0.84, 0.93)	22	(0.82, 0.93)
	Age left full-time			ঢ়	
12 .	education			0 W	
13	≤14 years			Reference	Reference
14	15-16 years			81.06	1.16
15				<u>a</u> (0.84, 1.34)	(0.87, 1.56)
16	17-18 years			<u>j</u> 0.81	0.98
17				₹0.81 ₹(0.56, 1.14) ₹1.06	(0.63, 1.50)
18	≥19 years			= 1.06	1.32
10				(0.74, 1.50)	(0.85, 2.05)
20	Social class			<u>ă</u> .	
20	Managerial and			Reference	Reference
22	professional			5 0.79	
22	Intermediate			3 0.79	0.79
				o(0.61, 1.02)	(0.58, 1.07)
24	Routine and			ě 1.08	1.01
25	manual			<u>q</u> (0.87, 1.35)	(0.77, 1.32)
26 */	<i>p</i> <.05, ** <i>p</i> <.01, *** <i>p</i> <.001	CV, cardiovascular; number of CV cormorbidities ² ;		Ap	
27 A	.ge ² , age squared; BMI, body mass index	CV, cardiovascular; number of CV cormorbidities ² ,	, number of cardiovas	cufar comorbiditie	s squared.
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	Model 1:	Model 2:	Model 3: Health	Model 4: +BMI	Model 5: +CV	<u>5</u> Model 6:	Model 7: Fully-
	Health literacy	Cognitive ability	literacy and cognitive	health	comorbidities	Generation and	adjusted
	n=6,736	n=6,746	ability	behaviours	n=6654	Social class	n=5,186
	Events=490	Events=491	n=6,654	n=5,357	Events=484	¶=6409	Events=360
	2.000		Events=484	Events=377	2.000	&vents=462	2.000 000
Health literacy						<u>N</u>	
Limited	Reference	-	Reference	Reference	Reference	Reference	Reference
Adequate	0.64***		0.72***	0.79*	0.73**	Š .79*	0.85
1	(0.53, 0.77)		(0.59, 0.87)	(0.64, 0.99)	(0.60, 0.88)	a 0.65, 0.97)	(0.68, 1.06)
Cognitive ability	-	0.77***	0.79***	0.85*	0.80***	ð .84**	0.88
e ognici ve donity		(0.69, 0.85)	(0.71, 0.88)	(0.74, 0.96)	(0.71, 0.89)	$\frac{1}{4}$ 0.75, 0.95)	(0.77, 1.01)
Age	1.01	1.00	1.00	1.01	0.99	91.00	1.01
Age	(1.00, 1.02)	(0.99, 1.01)	(0.98, 1.01)	(1.00, 1.02)	(0.98, 1.00)	$\pm 0.98, 1.01$	(0.99, 1.02)
Sex	(1.00, 1.02)	(0.99, 1.01)	(0.90, 1.01)	(1.00, 1.02)	(0.90, 1.00)		(0.99, 1.02)
Female	Reference	Reference	Reference	Reference	Reference	Reference	Reference
	1.43***	1.39***	1.38***	1.84***	1.38***	39***	1.82***
Male							
	(1.20, 1.71)	(1.16, 1.66)	(1.15, 1.65)	(1.49, 2.29)	(1.16, 1.66)	§ 1.15, 1.68)	(1.45, 2.28)
BMI				1.12***		.bn	1.12***
				(1.10, 1.14)		j.	(1.10, 1.13)
Current smoking						ğ	
Non-smoker				Reference		2	Reference
Smoker				1.77***		n .	1.69***
				(1.35, 2.31)		Api	(1.28, 2.22)
Alcohol consumption							
Daily/almost daily				Reference		17,	Reference
At least once per week				1.11		20	1.01
1				(0.83, 1.49)		24	(0.75, 1.37)
At least once per				1.53*		by	1.40
month				(1.07, 2.19)		ŋŋ	(0.97, 2.01)
Rarely				1.78***		es	1.53*
-,				(1.27, 2.50)		. . TI	(1.08, 2.17)
Never				1.42		ro	1.15
1.0.01				(0.95, 2.11)		lec	(0.76, 1.73)
Physical activity				(0.93, 2.11)		.bmj.com/ on April 17, 2024 by guest. Protected by copyright.	(0.70, 1.75)
Inactive				Reference		l by	Reference
Moderate activity				0.78		10	0.79
wouchate activity				0.70		(dc	0.19
						/ric	
						Int.	

BMJ Open Supplementary Table S2 Hazard ratios (95% CI) from Cox regression models of the association between functional health literacy and cognitive ability with _

Page 43 of 53		BMJ Ope	n		6/bmjop		
1 2 3			(0.61, 1.01)		6/bmjopen-2021-058496 on 3 June 2022	(0.61, 1.03)	
4 5	Vigorous activity		(0.01, 1.01) 0.72* (0.54, 0.98)		8496	(0.01, 1.05) 0.76 (0.56, 1.04)	
6	Number of CV		(0.0.1, 0.5.0)	1.34***	on	1.17**	
7	comorbidities			(1.22, 1.46)	3 J	(1.05, 1.30)	
8	Age left full-time				Jne		
9	education				20		
10	≤14 years					Reference	
11	15-16 years				. Ө.93	1.00	
12 13	17-18 years				≩ 0.71, 1.22) ₹ .61*	(0.74, 1.36) 0.73	
14 15	≥19 years				80.41, 0.91) 8.44***	(0.47, 1.15) 0.58*	
16					र्देव.28, 0.68)	(0.35, 0.96)	
17	Social class					5.0	
18	Managerial and				Reference	Reference	
19	professional				1 9.81	0.01	
20 21	Intermediate Routine and manual				40.62, 1.07)	0.91 (0.66, 1.24) 1.17	
22	Routine and manual				$\frac{1}{3}(0.93, 1.49)$	(0.89, 1.53)	
24	* <i>p</i> <.05, ** <i>p</i> <.01, *** <i>p</i> <.001 BMI, body mass index; CV, cardiovascular		Ch			(0.09, 1.09)	
26	Bivii, body mass mdex, C v, cardiovascular				.com/ on April 17, 2024 by gues		
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44		i el pecificación entre interior entre interior perioritori		galacinics.Antini			
45							
46							

Limited Adequate Reference 0.79* - Reference 0.88 Reference 0.96 Reference 0.92 Reference 0.90 Reference 0.82** Reference 0.82** Reference 0.82** Reference 0.82** Reference 0.82** Reference 0.82** Reference 0.999 Reference 0		Model 1: Health literacy	Model 2: Cognitive ability	Model 3: Health literacy and cognitive ability	Model 4: +BMI and health behaviours	Model 5: +CV 9	$\begin{array}{c} 45\\ 65\\ 9\\ 9\\ 10\\ 10\\ 10\\ 10\\ 10\\ 10\\ 10\\ 10\\ 10\\ 10$	Model 7: Fully adjusted
Cognitive ability $(0.64, 0.97)$ $(0.71, 1.10)$ $(0.77, 1.20)$ $(0.74, 1.15)$ 0.62^{**} 0.82^{**} 0.88 Cognitive ability 0.78^{***} 0.79^{***} 0.88 0.80^{***} 0.80^{***} 0.82^{**} $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.02^{*}$ $0.77, 1.00$ $0.97, 1.00$ 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**}	Health literacy						0	
Cognitive ability $(0.64, 0.97)$ $(0.71, 1.10)$ $(0.77, 1.20)$ $(0.74, 1.15)$ 0.62^{**} 0.82^{**} 0.88 Cognitive ability 0.78^{***} 0.79^{***} 0.88 0.80^{***} 0.80^{***} 0.82^{**} $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.02^{*}$ $0.77, 1.00$ $0.97, 1.00$ 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**}	Limited	Reference	-	Reference	Reference	Reference	Reference	Reference
Cognitive ability $(0.64, 0.97)$ $(0.71, 1.10)$ $(0.77, 1.20)$ $(0.74, 1.15)$ 0.62^{**} 0.82^{**} 0.88 Cognitive ability 0.78^{***} 0.79^{***} 0.88 0.80^{***} 0.80^{***} 0.82^{**} $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.00$ $0.77, 1.02^{*}$ $0.77, 1.00$ $0.97, 1.00$ 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**} 0.999^{**}	Adequate	0.79*				0.92	N 0.90	0.98
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1							
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Cognitive ability	_	0.78***			0.80***	≦ 0.82**	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	eogina ve donity					(0.70, 0.91)	$\frac{5}{2}$ (0.72 0.93)	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	A ge	1 0/***				1 02**	$\frac{0}{2}$ (0.72, 0.95)	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Age					$(1.01 \text{ to } 1.04)^{-1}$	$\frac{1}{2}$ (1.02 1.05)	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$\Lambda a a^2$					(1.01, 101.04)	$\frac{1}{2}$ (1.02, 1.03)	
Sex Reference Refe	Age					(0.009 1.000)	= (0.007, 1.000)	
Sex Male Reference 1.66*** Reference 1.58*** Reference 1.58*** Reference 1.58*** Reference 1.33, 2.00 Reference 1.56 Reference 2.09*** BMI (1.29, 1.93) (1.29, 1.93) (1.29, 1.94) (1.74, 2.70) (1.33, 2.00) (1.27, 1.92) (1.67, 2.62) Non-smoker Non-smoker Reference 0.89 (0.64, 1.22) (0.66, 1.27) Alcohol consumption Reference 0.89 (0.64, 1.22) (0.66, 1.27) Alcohol consumption Reference 1.21 (0.91, 1.70) 1.24 At least once per month (1.21, 2.54) (1.42, 2.87) (1.42, 2.87) 2.01*** Never 2.24*** (1.55, 3.26) (1.45, 3.11) 1.95*** Physical activity Inactive Moderate activity Reference 0.65*** 0.65*** Reference 0.65*** Reference 0.65*** Reference 0.65***	G	(0.997, 1.000)	(0.997, 1.000)	(0.997, 1.000)	(0.997, 1.000)	(0.998, 1.000)	(0.997, 1.000)	(0.998, 1.000)
remaie Reference R		D	D	D	D	D	D.C.	D
Male 1.65*** 1.58*** 1.58*** 1.65***						Kelerence	Keterence	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Male					1.03***	0 1.30 (1.07 1.02)	
BMI 1.10*** 1.00*** 1.00*** Current smoking (1.08, 1.12) (1.07, 1.11) Non-smoker Reference 0.89 0.93 Smoker 0.64, 1.22) (0.64, 1.22) (0.66, 1.27) Alcohol consumption Reference 1.21 (0.90, 1.66) (0.91, 1.70) Daily/almost daily Reference 1.21 (1.21, 2.54) (1.21, 2.57) At least once per month (1.21, 2.54) (1.21, 2.57) (1.21, 2.57) Rarely 2.01*** (1.36, 2.79) (1.36, 2.79) Never 2.24*** (1.45, 3.11) (1.45, 3.11) Physical activity Reference 0.65*** 0.68**		(1.36, 2.03)	(1.29, 1.93)	(1.29, 1.94)		(1.33, 2.00)	g (1.27, 1.92)	
Current smoking Non-smoker (1.08, 1.12) (1.07, 1.11) Non-smoker 0.89 0.93 Smoker (0.64, 1.22) (0.66, 1.27) Alcohol consumption Reference 1.21 Daily/almost daily Reference 1.24 At least once per week (0.90, 1.66) (0.91, 1.70) At least once per 1.76** (1.21, 2.54) month (1.22, 87) (1.36, 2.79) Never 2.24*** (1.35, 3.26) Physical activity Reference 0.65*** Inactive Reference 0.65***	BMI						ġ	
Current smoking Non-smoker Reference OP Reference Smoker 0.89 (0.64, 1.22) (0.66, 1.27) Alcohol consumption Reference 1.21 (1.24, 1.24) Daily/almost daily Reference 1.21 (0.90, 1.70) At least once per week 1.21 (1.21, 2.54) (0.91, 1.70) At least once per 1.76** 1.95*** 1.95*** month (1.22, 2.87) (1.36, 2.79) (1.36, 2.79) Never 2.24*** (1.155, 3.26) (1.45, 3.11) Physical activity Reference 0.65*** 0.68**					(1.08, 1.12)		<u>Di</u> .	(1.07, 1.11)
Non-smoker Reference Op Reference Smoker 0.89 0.93 0.93 Alcohol consumption 0.64, 1.22) 0.66, 1.27) Daily/almost daily Reference 1.21 At least once per week 1.21 0.93 Month 1.24 0.90, 1.66) 0.91, 1.70) At least once per 1.76** 1.77** month (1.21, 2.54) (1.21, 2.57) Rarely 2.01*** 1.36, 2.79) Never 2.24*** 2.12*** Physical activity Inactive Reference Moderate activity Reference 0.65***							ğ	
Smoker 0.89 09 0.93 Alcohol consumption (0.64, 1.22) (0.66, 1.27) Daily/almost daily Reference 1.21 At least once per week 1.21 (0.90, 1.66) At least once per 1.76** 1.77** month (1.21, 2.54) (1.21, 2.57) Rarely 2.01*** 1.36, 2.79) Never 2.24*** (1.42, 2.87) Physical activity (1.55, 3.26) (1.45, 3.11) Inactive Reference 0.65***								
Alcohol consumption (0.64, 1.22) (0.66, 1.27) Daily/almost daily Reference 1.7 At least once per 1.21 1.24 (0.90, 1.66) (0.91, 1.70) At least once per 1.76** (1.21, 2.54) month (1.21, 2.54) (1.24, 2.87) Never 2.24*** (1.36, 2.79) Physical activity (1.55, 3.26) (1.45, 3.11) Physical activity Reference 0.65*** Moderate activity 0.65*** 0.68**	Smoker				0.89			0.93
Alcohol consumption Paily/almost daily Reference Provide the second secon					(0.64, 1.22)		Ap	(0.66, 1.27)
Daily/almost daily Reference 7.7 Reference At least once per week 1.21 1.24 (0.90, 1.66) (0.91, 1.70) At least once per 1.76** U 1.77** month (1.21, 2.54) (1.21, 2.57) (1.21, 2.57) Rarely 2.01*** 1.95*** (1.36, 2.79) Never 2.24*** 2.12*** (1.45, 3.11) Physical activity Inactive Reference V Moderate activity 0.65*** 0.65*** 0.68**	Alcohol consumption						<u></u>	
At least once per week 1.21 D0 4 (0.91, 1.70) At least once per 1.76** 1.77** month (1.21, 2.54) 90 Rarely 2.01*** 1.95*** Never 2.24*** (1.36, 2.79) Physical activity (1.55, 3.26) (1.45, 3.11) Physical activity Reference 0.65*** 0.68**	Daily/almost daily				Reference		17.	Reference
At least once per (0.90, 1.66) (0.91, 1.70) At least once per 1.76** (1.21, 2.54) month (1.21, 2.54) (1.21, 2.57) Rarely 2.01*** 1.95*** Never 2.24*** (1.36, 2.79) Physical activity (1.55, 3.26) (1.45, 3.11) Physical activity Reference 0.65*** 0.68**	5 5						20	1.24
At least once per 1.76** 1.77** month (1.21, 2.54) (1.21, 2.57) Rarely 2.01*** 1.95*** Never 2.24*** (1.36, 2.79) Physical activity (1.55, 3.26) (1.45, 3.11) Physical activity Reference 0.65*** Moderate activity 0.65*** 0.68**	The reason of the Pert we can						024	
month (1.21, 2.54) (1.21, 2.57) Rarely 2.01*** 1.95*** Never 2.24*** (1.36, 2.79) Physical activity (1.55, 3.26) (1.45, 3.11) Physical activity Reference 0.65*** Moderate activity 0.65*** 0.68**	At least once per						p p	1.77**
Rarely 2.01*** 1.95*** Never 2.24*** (1.42, 2.87) Physical activity (1.55, 3.26) (1.45, 3.11) Inactive Reference 0.65*** Moderate activity 0.65*** 0.68**						ű		
Never (1.42, 2.87) (1.36, 2.79) Never (1.55, 3.26) (1.45, 3.11) Physical activity Reference Reference Moderate activity 0.65*** 0.68**							Jes	
Never(1.42, 2.37)PD(1.50, 2.79)Never2.24***2.12***(1.55, 3.26)(1.45, 3.11)Physical activityReferenceReferenceInactiveReference0.65***Moderate activity0.65***0.68**	itarely						<u>.</u>	
Interver2.24Off2.12 m(1.55, 3.26)(1.45, 3.11)Physical activityReferenceVReferenceInactiveReference0.65***0.68**	Never							
Physical activity Inactive Reference V Reference Moderate activity 0.65*** Open 0.68**							tec	
Inactive Reference Reference 0.65*** 6 0.68**	Dhymical activity				(1.33, 5.20)		tec	(1.43, 5.11)
Inactive Reference Reference Moderate activity 0.65*** 0.68**					D	2	σ	D
Moderate activity 0.65*** Ö 0.68**						· · · · · · · · · · · · · · · · · · ·	<	
	Moderate activity				0.65***		0	0.68**
							vric	
						Ű	aht	

BMJ Open Supplementary Table S3 Odds ratios (95% CI) for the association between functional health literacy and cognitive ability with cross-sectional diabetes status at wave 2 in a sub-sample of 6,086 participants with data on all variables of interest

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	Vigorous activity	(0.51, 0.82) 0.51*** (0.37, 0.69)	6/bmjopen-2021-058496 o	(0.53, 0.87) 0.56*** (0.41, 0.76)
	Number of CV comorbidities Number of CV comorbidities ² Education	$\begin{array}{c} 2.22^{***} \\ (1.91, \ 2.59) \\ 0.87^{***} \\ (0.81, \ 0.92) \end{array}$	on 3 June 2022	1.98*** (1.70, 2.32) 0.88*** (0.82, 0.93)
	≤14 years 15-16 years 17-18 years	(0.81, 0.92)	Reference 1.07 (0.81, 1.42) 0.78	Reference 1.17 (0.87, 1.56) 0.98
	≥19 years		e (0.51, 1.18) fo 0.94 (0.62, 1.43)	(0.64, 1.50) 1.32 (0.85, 2.05)
	Social class Managerial and professional		Reference	Reference
	Intermediate Routine and manual		0.79 0.59, 1.07) 1.09	0.79 (0.58, 1.07) 1.01
	* <i>p</i> <.05, ** <i>p</i> <.01, *** <i>p</i> <.001 Age ² , age squared; BMI, body mass index; CV, car	rdiovascular; number of CV cormorbidities ² , number of cardiovasc		(0.77, 1.32) squared.
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	Model 1:	Model 2:	Model 3: Health	Model 4: +BMI	Model 5: +CV	9 Model 6:	Model 7: Fully-
	Health literacy	Cognitive ability	literacy and cognitive	and health	comorbidities	ω +Education and	adjusted
		-	ability	behaviours		social class	-
Health literacy			•			le .	
Limited	Reference	-	Reference	Reference	Reference	Reference	Reference
Adequate	0.64***		0.73**	0.80	0.74**	N _{0.79} *	0.85
1	(0.52, 0.80)		(0.58, 0.91)	(0.64, 1.01)	(0.59, 0.93)	[0.63, 0.98]	(0.68, 1.06)
Cognitive ability		0.72***	0.76***	0.84**	0.76***	₹0.83**	0.88
c :		(0.63, 0.82)	(0.66, 0.86)	(0.73, 0.96)	(0.67, 0.87)	$\overline{\overline{0}}(0.72, 0.95)$	(0.77, 1.01)
Age	1.01	1.00	1.00	1.01	0.99	d 1.00 f(0.98, 1.01)	1.01
0	(0.997, 1.02)	(0.98, 1.01)	(0.98, 1.01)	(0.997, 1.03)	(0.98, 1.01)	œ_(0.98, 1.01)	(0.99, 1.02)
Sex	/			/	× · · /	on` ´	
Female	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Male	1.47***	1.38**	1.40**	1.82***	1.40**	1.42**	1.82***
	(1.20, 1.81)	(1.12, 1.70)	(1.13, 1.72)	(1.46, 2.27)	(1.14, 1.73)	g (1.15, 1.76)	(1.45, 2.28)
BMI				1.12***		njo (1.12***
				(1.10, 1.14)		pe	(1.10, 1.13)
Current smoking						n.b	
Non-smoker				Reference		<u>, , , , , , , , , , , , , , , , , , , </u>	Reference
Smoker				1.79***		<u>S</u>	1.69***
				(1.36, 2.34)		ار	(1.28, 2.22)
Alcohol consumption						on	
Daily/almost daily				Reference		Ap	Reference
At least once per week				1.10		<u>n</u> i	1.01
-				(0.80, 1.46)		17,	(0.75, 1.36)
At least once per				1.49*		20	1.40
month				(1.03, 2.14)		24	(0.97, 2.01)
Rarely				1.70**		by	1.53*
				(1.20, 2.40)		(1.15, 1.76) (bmjopen.bmj.com/ on April 17, 2024 by guest. Protected by copyright.	(1.08, 2.17)
Never				1.30		est	1.15
				(0.86, 1.96)		ש	(0.76, 1.73)
Physical activity				,		rote	
Inactive				Reference		ect	Reference
Moderate activity				0.76*		be	0.79
-				(0.59, 0.99)		by	(0.61, 1.03)
Vigorous activity				0.71*		co	0.76
						зуг	
						igh	
						.+	

BMJ Open self-reporting diabetes during follow-up. Models are run on a sub-sample of 5,186 (360 with diabetes) participants with data on all variables of interest. _____

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	5021-C
Supplementary Table S5 Odds ratios (95% CI) from logistic regression models of the association between functional	ealth literacy and cognitive ability
with self-reported diabetes at wave 2. Models are run on a sub-sample of participants with HbA1c levels recorded wave	\$2, removing participants with
suspected undiagnosed diabetes (n=5,671; 399 with diabetes)	3

	Model 1: Health literacy n= 5533	Model 2: Cognitive ability n=5534	Model 3: Health literacy and cognitive ability n=5470	Model 4: +BMI and health behaviours n=4845	Model 5: +CV comorbidities n=5470	Hodel 6: HEducation and Noocial class M==5271	Model 7: Fully adjusted n=4674
Health literacy	D (D.C.	D. C	D. C	P QReference	D (
Limited	Reference		Reference	Reference	Reference	Reference	Reference
Adequate	0.91		1.04	1.17	1.07	⊒.04	1.14
	(0.73, 1.14)		(0.82, 1.32)	(0.90, 1.53)	(0.84, 1.36)	≥1.04 ≥(0.82, 1.33) ≥(0.80**	(0.87, 1.51)
Cognitive ability	-	0.78***	0.78***	0.88	0.78***	<u>@</u> 0.80**	0.85
		(0.69, 0.88)	(0.69, 0.89)	(0.76, 1.03)	(0.69, 0.89)	ਤੁ(0.69, 0.92)	(0.73, 1.01)
Age	1.04***	1.03***	1.03***	1.04***	1.02*	∃1.03***	1.03**
	(1.03, 1.05)	(1.02, 1.05)	(1.01, 1.04)	(1.02, 1.05)	(1.00, 1.03)	∃ (1.01, 1.04)	(1.01, 1.05)
Age ²	0.998***	0.997***	0.998***	0.998**	0.998**	0.998**	0.999
	(0.996, 0.999)	(0.996, 0.999)	(0.996, 0.999)	(0.996, 0.999)	(0.997, 0.999)	<u>ਤ</u> (0.996, 0.999)	(0.997, 1.000)
Sex						o	
Female	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Male	1.45***	1.39**	1.38**	2.16***	1.40**	<u>5</u> 1.38**	2.09***
	(1.17, 1.79)	(1.13, 1.72)	(1.11, 1.71)	(1.67, 2.79)	(1.13, 1.74)	1.10, 1.72) on April 17, 2024 by guest. Protected by copyright.	(1.60, 2.74)
BMI				1.11***		m∕ o	1.10***
				(1.09, 1.14)		n A	(1.07, 1.12)
Current smoking						pri.	
Non-smoker				Reference		1	Reference
Smoker				0.83		, ⁿ N	0.86
A1 1 1 /				(0.56, 1.20)		024	(0.57, 1.26)
Alcohol consumption Daily/almost daily				Reference		t by	Reference
At least once per				1.33		gu	1.42
week				(0.94, 1.92)		est	(0.98, 2.08)
At least once per				1.87**		D	1.95**
month				(1.22, 2.87)		rot	(1.25, 3.07)
Rarely				2.08***		ect	2.22***
imory				(1.38, 3.16)		ed	(1.44, 3.44)
Never				2.23***		by	1.85*
1,0,01				(1.43, 3.49)		co	(1.14, 3.00)
				(1.10, 0.17)		oyri	(, 5.00)
						ight	

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					jope	
					6/bmjopen-2021-058496 on 3 June 2022.	
	Physical activity				058	
	Inactive		eference		49	Reference
	Moderate activity	0.0	65**		0 0	0.68*
			.49, 0.87)		n S	(0.50, 0.92)
	Vigorous activity		40***		Ju	0.43***
		(0.	.27, 0.57)		ne	(0.29, 0.63)
	Number of CV			2.30***	202	2.08***
	comorbidities			(1.96, 2.70)		(1.73, 2.50)
	Number of CV			0.88***	Do	0.90**
	comorbidities ²			(0.82, 0.94)	Ň	(0.82, 0.97)
	Age left full-time				Download	
	education				a Reference	Defener
	≤ 14 years				akeference	Reference 1.31
	15-16 years				(0.74, 1.37)	(0.92, 1.87)
	17-18 years				=0.63	0.92, 1.87)
					(0.39, 1.00)	(0.55, 1.58)
	≥19 years				30.84	1.23
	_17 jours				$\frac{1}{2}(0.53, 1.32)$	(0.72, 2.08)
	Social class	ndex: CV_cardiovascular: number of CV cormo				(0.72, 2.00)
	Managerial and				Reference	Reference
	professional					
	Intermediate					0.62*
					g(0.46, 0.89) ∞0.94	(0.42, 0.89)
	Routine and				0.94ھ	0.89
	manual				<u>5</u> (0.71, 1.24)	(0.65, 1.22)
	*p<.05, **p<.01, ***p<.001				17,	
	Age ² , age squared; BMI, body mass in	ndex; CV, cardiovascular; number of CV cormon	rbidities ² , numb	er of cardiovase		squared.
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	Model 1:	Model 2:	Model 3: Health	Model 4: +BMI	Model 5: +CV	Model 6:	Model 7: Fully-
	Health literacy	Cognitive ability	literacy and cognitive	health	comorbidities	Education and	adjusted
	n=3675	n=3674	ability	behaviours	n=3641	Social class	n=3095
	Events=203	Events=205	n=3641	n=3184	Events=201	ສ=3530	Events=159
		$\mathbf{\wedge}$	Events=201	Events=165		Events=195	
Health literacy						ον	
Limited	Reference	-	Reference	Reference	Reference	Reference	Reference
Adequate	0.50***		0.58***	0.63**	0.59***	a .61***	0.65*
L	(0.38, 0.67)		(0.43, 0.77)	(0.45, 0.88)	(0.44, 0.79)	$\overline{\mathbf{g}}_{0.45, 0.82}$	(0.46, 0.90)
Cognitive ability	-	0.71***	0.78**	0.91	0.78**	₹9.83*	0.93
<i>6j</i>		(0.60, 0.84)	(0.65, 0.94)	(0.74, 1.11)	(0.66, 0.94)	₹0.68, 0.997)	(0.76, 1.16)
Age	1.02*	1.01	1.01	1.02*	1.00	1 .01	1.01
	(1.00, 1.03)	(0.99, 1.03)	(0.99, 1.03)	(1.00, 1.04)	(0.98, 1.02)	9.99, 1.03)	(0.99, 1.04)
Sex	(1.00, 1.05)	(0.55, 1.05)	(0.55), 1.05)	(1.00, 1.01)	(0.90, 1.02)	b, 1.03)	(0.55, 1.01)
Female	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Male	1.57**	1.50**	1.51**	2.22 ***	1.53**	9.50**	2.11***
1,1uio	(1.19, 2.06)	(1.14, 1.98)	(1.14, 2.00)	(1.59, 3.10)	(1.15, 2.02)	(1.12, 2.00)	(1.49, 2.97)
BMI	(111), 2100)	(111, 1190)	(1.1.1, 2.00)	1.12***	(1.10, 2.02)		1.11***
				(1.10, 1.15)		8	(1.08, 1.14)
Current smoking				(1.10, 1.15)		ع ا	(1.00, 1.14)
Non-smoker				Reference		on	Reference
Smoker				2.12***		Ap	2.04***
Smoker				(1.43, 3.15)		<u> </u>	(1.36, 3.06)
Alcohol consumption				(1.43, 5.15)		17,	(1.30, 3.00)
Daily/almost daily				Reference		20	Reference
				1.09		024	1.00
At least once per week						by	
A 4 1				(0.70, 1.71)		g	(0.64, 1.57)
At least once per				1.48		les	1.34
month Demotor				(0.86, 2.55) 2.10***		.+ ™	(0.77, 2.34) 1.78*
Rarely						rot	
N				(1.27, 3.48)		nj.com/ on April 17, 2024 by guest. Protected by copyright.	(1.06, 2.98)
Never				1.54		ted	1.27
				(0.85, 2.80)		ç	(0.69, 2.35)
Physical activity				D C		20	D (
Inactive				Reference		б	Reference

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age 51 of 53		BMJ Ope	en		6/bmjopen-2021-058496 on 3 June 2022.		
					en-2021		
	Moderate activity		0.64*		1-058	0.65*	
			(0.43, 0.94)		3496	(0.44, 0.96)	
	Vigorous activity		0.61* (0.39, 0.95)		on	0.65 (0.41, 1.02)	
	Number of CV		()	1.43***	з Ju	1.22*	
	comorbidities			(1.25, 1.64)	Ine	(1.04, 1.44)	
	Age left full-time				20		
C	education				22.		
1	≤ 14 years				Beference	Reference	
2	15-16 years				§ .01	0.91	
3 1	17 10				₹ 0.66, 1.54)	(0.57, 1.44)	
	17-18 years				80.71	0.78	
	> 10				Φ0.39, 1.29) ₹	(0.41, 1.48)	
	≥19 years				4 0.39, 1.29) 5 .52 4 0.27, 1.02)	0.59	
	Social class				10.27, 1.02)	(0.28, 1.23)	
	Managerial and				5 Pafaranaa	Reference	
	professional				Reference	Reference	
	Intermediate				.83	0.84	
	memouate				₹0.54, 1.27)	(0.52, 1.35)	
	Routine and manual				1.22	1.20	
	-				6 0.85, 1.74)	(0.80, 1.79)	
	*p<.05, **p<.01, ***p<.001	r.					
	BMI, body mass index; CV, cardiovascula	r.			on		
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STROBE Statement—checklist of items that should be included in reports of observational studies

4 5	Item No	Recommendation	
6 Title and abstract 7	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
8 9		(b) Provide in the abstract an informative and balanced summary of what was	Page 2
10		done and what was found	_
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1			
12 13 Background/rationale	2	Explain the scientific background and rationale for the investigation being	Pages
14		reported	5-7
¹⁵ Objectives	3	State specific objectives, including any prespecified hypotheses	Page 7
16 17 Methods			
18 Study design	4	Present key elements of study design early in the paper	Pages
19			6-8
20 21 ^{Setting}	5	Describe the setting, locations, and relevant dates, including periods of	Pages
22		recruitment, exposure, follow-up, and data collection	7-8
23 Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of	Pages
24		selection of participants. Describe methods of follow-up	7
25 26		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods	
20 27		of case ascertainment and control selection. Give the rationale for the choice	
28		of cases and controls	
29		Cross-sectional study—Give the eligibility criteria, and the sources and	
30 31		methods of selection of participants	
32		(b) Cohort study—For matched studies, give matching criteria and number of	NA
33		exposed and unexposed	
34		Case-control study—For matched studies, give matching criteria and the	
35 36		number of controls per case	
37 Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	Pages
38		effect modifiers. Give diagnostic criteria, if applicable	8-12
³⁹ Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of	Pages
41		assessment (measurement). Describe comparability of assessment methods if	8-12
42		there is more than one group	
4 ³ Bias	9	Describe any efforts to address potential sources of bias	Pages
14 15			18-19
46 Study size	10	Explain how the study size was arrived at	Pages
17			8, 14,
18 19			16
50 Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,	Pages
51		describe which groupings were chosen and why	12-13
52 Statistical methods	12	(a) Describe all statistical methods, including those used to control for	Pages
53 54		confounding	12-13
55		(b) Describe any methods used to examine subgroups and interactions	NA
56		(c) Explain how missing data were addressed	Pages
57			18
58 59		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	Pages
60		Case-control study-If applicable, explain how matching of cases and	13
		controls was addressed	

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		(\underline{e}) Describe any sensitivity analyses	F 1
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study-eg numbers	Pages
		potentially eligible, examined for eligibility, confirmed eligible, included in the	14, 10
		study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	Pages
			14, 10
		(c) Consider use of a flow diagram	NA
Descriptive	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	Pages
data Outcome data		and information on exposures and potential confounders	14, 10
			Table
		(b) Indicate number of participants with missing data for each variable of interest	Table
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Pages
			16
	15*	Cohort study—Report numbers of outcome events or summary measures over	Table
			and 4
		<i>Case-control study</i> —Report numbers in each exposure category, or summary	
		measures of exposure	TT 11
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary	Table
	1.6	measures	and 4
Main results	16	(<i>a</i>) Give unadjusted estimates and, if applicable, confounder-adjusted estimates	Table
		and their precision (eg, 95% confidence interval). Make clear which confounders	1-4
		were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	N 14
		(c) If relevant, consider translating estimates of relative risk into absolute risk for	NA
	17	a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and	Pages
		sensitivity analyses	18-19
Discussion	10		D
Key results	18	Summarise key results with reference to study objectives	Page
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or	Pages
Intormatation	20	imprecision. Discuss both direction and magnitude of any potential bias	22-24
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	Pages
		limitations, multiplicity of analyses, results from similar studies, and other	24-25
Conoralizatilit	21	relevant evidence	Dar
Generalisability	21	Discuss the generalisability (external validity) of the study results	Pages 24-25
			24-23
Other informati		Cive the source of funding and the relative funders for the supervised at 1 = 1	Dati
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and , f.e he ,/www.pidem. /// published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.