Supplemental Material Table of Contents

Supplemental Text 1	ASPREE Study design and population
Supplemental Text 2	Incident Dementia Outcome and Dementia Assessment
Supplemental Table 1	Sample sizes for those who had cognitive assessments at each Annual Visit (AV)
Supplemental Table 2	Summary of cognitive tests at baseline and Annual Visits (AV)
Supplemental Table 3	Association between renal function and cognitive function at baseline: parameter estimates for the interaction terms between eGFR and UACR
Supplemental Table 4	Association between baseline renal function and change in cognitive function: parameter estimates for the interaction terms between eGFR and UACR and time
Supplemental Table 5	Association between baseline renal functions and CIND and dementia: parameter estimates for the interaction terms between eGFR and UACR
Supplemental Figure 1	Consolidated Standards of Reporting Trials (CONSORT) flow diagram of participants in the Aspirin in Reducing Events in the Elderly (ASPREE) trial ¹

$\begin{tabular}{ll} \textbf{Supplemental Table 1.} Sample sizes for those who had cognitive assessments at each Annual Visit (AV) \end{tabular}$

Test	Baseline	AV1	AV2	AV3	AV4	AV5	AV6
3MS	19114	17869	27	14729	1728	6984	1654
COWAT	19083	17807	17	14614	1718	6924	1640
HVLT4	19007	17663	20	14364	1692	6738	1603
SDMT	19030	17701	17	14456	1704	6787	1616

Supplemental Table 2. Summary of cognitive tests at baseline and Annual Visits (AV)

Characteristic	3MS	COWAT	HVLT4	SDMT
Baseline				
N	19,114	19,083	19,007	19,030
Mean (SD)	93.4 (4.6)	12.1 (4.6)	7.7 (2.8)	36.7 (10.1)
Median (IQR)	94 (91, 97)	12 (9, 15)	8 (6, 10)	37 (30, 44)
Range	75, 100	0, 36	0, 12	1, 99
Annual visit 1				
N	17,869	17,807	17,663	17,701
Mean (SD)	94.2 (4.7)	13.2 (4.8)	8.2 (3.0)	36.9 (10.1)
Median (IQR)	95 (92, 98)	13 (10, 16)	9 (6, 11)	37 (30, 44)
Range	56, 100	0, 46	0, 12	0, 84
Annual visit 2				
N	27	17	20	17
Mean (SD)	84.2 (9.0)	10.7 (4.9)	5.0 (3.5)	27.6 (11.9)
Median (IQR)	81 (78, 92)	10 (6, 14)	5 (2, 8)	23 (19, 35)
Range	67, 100	5, 20	0, 11	12, 50
Annual visit 3				
N	14,729	14,614	14,364	14,456
Mean (SD)	93.9 (5.4)	13.3 (5.0)	8.2 (3.2)	35.9 (10.1)
Median (IQR)	95 (92, 98)	13 (10, 16)	9 (6, 11)	36 (29, 43)
Range	30, 100	0, 45	0, 12	0, 80
Annual visit 4				
N	1,728	1,718	1,692	1,704
Mean (SD)	93.9 (5.8)	13.4 (4.9)	8.2 (3.2)	35.7 (10.4)
Median (IQR)	95 (92, 98)	13 (10, 16)	9 (6, 11)	36 (29, 43)
Range	33, 100	1, 35	0, 12	1, 68
Annual visit 5				
N	6,984	6,924	6,738	6,787
Mean (SD)	93.5 (6.4)	13.6 (5.1)	8.2 (3.3)	35.0 (10.2)
Median (IQR)	95 (91, 98)	13 (10, 17)	9 (6, 11)	35 (28, 42)
Range	1, 100	0, 51	0, 12	1, 68
Annual visit 6				
N	1,654	1,640	1,603	1,616
Mean (SD)	94.0 (6.7)	14.0 (5.0)	8.5 (3.3)	35.8 (10.5)
Median (IQR)	96 (92, 98)	14 (10, 17)	9 (6, 11)	36 (29, 43)
Range	30, 100	1, 39	0, 12	1, 71

Supplemental Table 3. Association between renal function and cognitive function at baseline: parameter estimates for the interaction terms between eGFR and UACR

Characteristic	N	Beta	95% CI ¹	p-value
3MS	17,753			
eGFR < 45: UACR ≥3		0.32	-0.50, 1.1	0.4
eGFR < 60: UACR ≥3		-0.33	-0.79, 0.13	0.2
COWAT	17,725			
eGFR < 45: UACR ≥3		0.12	-0.72, 1.0	0.8
eGFR < 60: UACR ≥3		-0.01	-0.48, 0.45	>0.9
SDMT	17,679			
eGFR < 45: UACR ≥3		0.64	-1.1, 2.4	0.5
eGFR < 60: UACR ≥3		-0.53	-1.5, 0.45	0.3
HVLT4	17,663			
eGFR < 45: UACR ≥3		0.02	-0.50, 0.53	>0.9
eGFR < 60: UACR ≥3		0.07	-0.21, 0.36	0.6

¹CI = Confidence Interval

All models were adjusted for Age, Gender, Education (<12 and ≥12 years), Diabetes, Treatment group, Hypertension, and Race (White/Australia, White/US, Black, Hispanic, and Other)

Supplemental Table 4. Association between baseline renal function and change in cognitive function: parameter estimates for the interaction terms between eGFR and UACR and time

Characteristic	Beta	95% CI ¹	p-value
3MS			
eGFR < 45: UACR ≥3: time (+5 years)	0.36	-0.97, 1.68	0.6
eGFR < 60: UACR ≥3: time (+5 years)	-0.18	-0.92, 0.56	0.6
COWAT			
eGFR < 45: UACR ≥3: time (+5 years)	1.02	0.01, 2.03	0.049
eGFR < 60: UACR ≥3: time (+5 years)	0.01	-0.56, 0.58	>0.9
SDMT			
eGFR < 45: UACR ≥3: time (+5 years)	0.57	-1.20, 2.33	0.5
eGFR < 60: UACR ≥3: time (+5 years)	-0.28	-1.27, 0.70	0.6
HVLT4			
eGFR < 45: UACR ≥3: time (+5 years)	0.28	-0.35, 0.91	0.4
eGFR < 60: UACR ≥3: time (+5 years)	-0.21	-0.56, 0.15	0.3

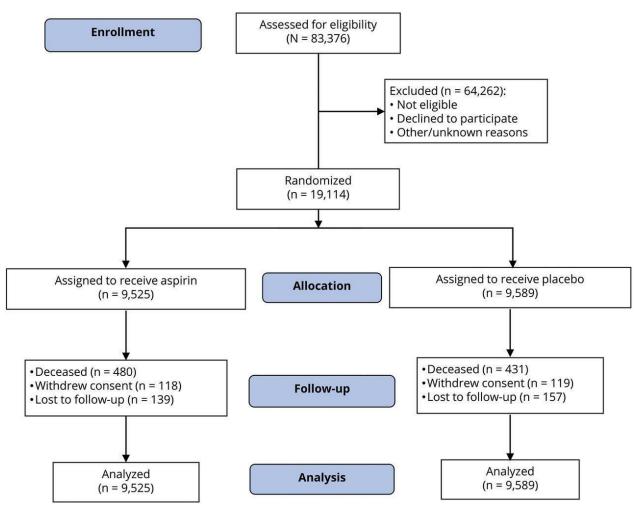
¹CI = Confidence Interval. All models were adjusted for Age, Gender, Education (<12 and ≥12 years), Diabetes, Treatment group, Hypertension, and Race (White/Australia, White/US, Black, Hispanic, and Other)

Supplemental Table 5. Association between baseline renal functions and CIND and dementia: parameter estimates for the interaction terms between eGFR and UACR

Characteristic	HR ¹	95% CI ¹	p-value
CIND			
eGFR < 45: UACR ≥3	1.07	0.69, 1.68	0.8
eGFR < 60: UACR ≥3	1.04	0.81, 1.33	8.0
Dementia			
eGFR < 45: UACR ≥3	0.49	0.14, 1.74	0.3
eGFR < 60: UACR ≥3	1.00	0.60, 1.64	>0.9

¹HR = Hazard Ratio, CI = Confidence Interval. All models were adjusted for Age, Gender, Education (<12 and ≥12 years), Diabetes, Treatment group, Hypertension, and Race (White/Australia, White/US, Black, Hispanic, and Other)

Supplemental Figure 1. Consolidated standards of reporting trials (CONSORT) flow diagram of participants in the Aspirin in Reducing Events in the Elderly (ASPREE) trial¹



All randomized participants were included in the final analysis. For participants who withdrew from the trial or died, all information up to the point of withdrawal/death was included in the analysis.

¹Ryan J, Storey E, Murray AM, et al. Randomized placebo-controlled trial of the effects of aspirin on dementia and cognitive decline. *Neurology*. 2020;95(3):e320-e331. doi:10.1212/WNL.00000000000009277