

# Supplementary Material

## Study Partner Type and Adverse Event Reporting in Mild-to-Moderate Alzheimer's Disease Clinical Trials

**Supplementary Table 1.** Participants characteristics by study partner type.

	Study partner type			
	Overall (N = 934)	Spouse (N = 607)	Adult child (N = 256)	Other (N = 71)
<b>Participants</b>				
Age (y) (mean (SD))	76.07 (8.25)	74.63 (7.93)	79.68 (7.49)	75.41 (9.63)
Education (y) (mean (SD))	14.01 (3.19)	14.57 (2.89)	12.43 (3.27)	14.94 (3.48)
Education (n (%))				
<12 y	113 (12.1)	44 (7.2)	60 (23.4)	9 (12.7)
12 y	254 (27.2)	149 (24.5)	92 (35.9)	13 (18.3)
12-16 y	402 (43.0)	289 (47.6)	85 (33.2)	28 (39.4)
>16 y	165 (17.7)	125 (20.6)	19 (7.4)	21 (29.6)
Sex (n (%))				
Female	548 (58.7)	270 (44.5)	224 (87.5)	54 (76.1)
Male	386 (41.3)	337 (55.5)	32 (12.5)	17 (23.9)
Race and ethnicity (n (%))				
Non-Hispanic White	818 (87.6)	560 (92.3)	197 (77.0)	61 (85.9)
Non-Hispanic Black	53 (5.7)	17 (2.8)	30 (11.7)	6 (8.5)
Hispanic	47 (5.0)	21 (3.5)	22 (8.6)	4 (5.6)
Other	15 (1.6)	9 (1.5)	6 (2.3)	0 (0.0)
Missing	1 (0.1)	0 (0.0)	1 (0.4)	0 (0.0)
MMSE score (mean (SD))	19.90 (3.95)	20.01 (4.00)	19.53 (3.87)	20.24 (3.79)
<b>Study partner</b>				
Time spent with participant* (hours per week) (mean (SD))	115.44 (57.17)	139.20 (37.74)	67.82 (60.09)	78.10 (61.85)

\*Time spent with participant calculated from available from 6 trials (except for SIM) with overall sample of 732 participants: 480 with spousal, 194 with adult children, and 58 with other study partners.

**Supplementary Table 2.** GEE estimates of the IRR of reporting AEs by grade/severity with visit frequency.

	Grade 1 AE		Grade 2 AE		Grade 3 AE		SAE	
	Est. (95% CI)	p	Est. (95% CI)	p	Est. (95% CI)	p	Est. (95% CI)	p
Visit per year	1.12 (1.07, 1.17)	<0.001	1.08 (1.05, 1.12)	<0.001	1.03 (0.96, 1.11)	0.364	0.94 (0.88, 1.00)	0.040
Study partner								
Spouse	1		1		1		1	
Adult Child	0.96 (0.87, 1.06)	0.386	1.11 (0.88, 1.39)	0.376	1.24 (0.93, 1.64)	0.142	1.25 (0.85, 1.83)	0.262
Other	1.15 (1.08, 1.23)	<0.001	1.14 (0.90, 1.45)	0.289	1.29 (0.81, 2.07)	0.281	1.30 (1.04, 1.62)	0.023
Age (per 10 y)	0.98 (0.92, 1.04)	0.461	1.00 (0.90, 1.10)	0.951	1.20 (1.02, 1.42)	0.030	1.43 (1.16, 1.77)	0.001
Education (per year)	1.00 (0.99, 1.02)	0.724	0.99 (0.97, 1.01)	0.165	0.95 (0.91, 1.00)	0.044	0.99 (0.96, 1.03)	0.737
<12 y	1		1		1		1	
12 y	1.05 (0.93, 1.19)	0.406	1.14 (0.94, 1.38)	0.181	0.94 (0.74, 1.20)	0.617	1.06 (0.83, 1.36)	0.647
12-16 y	0.91 (0.71, 1.16)	0.440	0.93 (0.73, 1.18)	0.541	0.81 (0.66, 1.00)	0.049	1.11 (0.95, 1.30)	0.199
>16 y	1.09 (0.92, 1.29)	0.335	1.05 (0.83, 1.34)	0.677	0.80 (0.49, 1.31)	0.379	0.99 (0.65, 1.52)	0.968
Sex								
Female	1		1		1		1	
Male	1.02 (0.88, 1.19)	0.796	1.11 (0.85, 1.45)	0.458	1.07 (0.86, 1.34)	0.553	1.02 (0.73, 1.43)	0.903
Race and ethnicity								
Non-Hispanic White	1		1		1		1	
Non-Hispanic Black	0.93 (0.76, 1.14)	0.500	1.06 (0.85, 1.32)	0.625	1.01 (0.79, 1.29)	0.928	1.23 (0.80, 1.90)	0.348
Hispanic	0.89 (0.62, 1.28)	0.520	0.54 (0.43, 0.68)	<0.001	0.48 (0.22, 1.06)	0.069	0.49 (0.21, 1.17)	0.108
Other	1.29 (0.84, 1.99)	0.250	0.74 (0.44, 1.23)	0.241	1.01 (0.69, 1.48)	0.963	1.02 (0.62, 1.67)	0.947

**Supplementary Table 3.** Estimated IRR of reporting AEs by grade/severity with time spent with participants.

	Grade 1 AE		Grade 2 AE		Grade 3 AE		SAE	
	Est. (95% CI)	p	Est. (95% CI)	p	Est. (95% CI)	p	Est. (95% CI)	p
Time spent with participant (per day per week)	1.00 (0.97, 1.04)	0.844	0.96 (0.93, 1.01)	0.087	0.98 (0.90, 1.06)	0.559	0.95 (0.88, 1.02)	0.150
Age (per 10 y)	0.99 (0.91, 1.07)	0.742	0.98 (0.88, 1.10)	0.738	1.30 (1.03, 1.63)	0.025	1.48 (1.19, 1.84)	<0.001
Education (per year)	1.01 (0.99, 1.03)	0.407	0.99 (0.97, 1.02)	0.527	0.98 (0.93, 1.03)	0.370	1.01 (0.96, 1.07)	0.590
<12 y	1		1		1		1	
12 y	1.15 (0.92, 1.43)	0.215	1.19 (0.92, 1.54)	0.178	1.04 (0.61, 1.76)	0.890	1.03 (0.57, 1.84)	0.927
12-16 y	1.07 (0.87, 1.32)	0.535	1.05 (0.82, 1.36)	0.692	0.82 (0.49, 1.36)	0.437	1.05 (0.59, 1.85)	0.874
>16 y	1.17 (0.90, 1.50)	0.235	1.06 (0.78, 1.43)	0.725	1.06 (0.61, 1.86)	0.839	1.25 (0.67, 2.32)	0.482
Sex								
Female	1		1		1		1	
Male	1.07 (0.92, 1.24)	0.368	1.05 (0.88, 1.26)	0.608	1.00 (0.70, 1.44)	0.978	0.97 (0.69, 1.36)	0.852
Trial								
HU	1		1		1		1	
RES	0.64 (0.47, 0.88)	0.006	0.57 (0.34, 0.95)	0.032	0.58 (0.21, 1.57)	0.281	1.67 (0.59, 4.69)	0.330
NSAIDs	0.51 (0.38, 0.69)	<0.001	0.48 (0.32, 0.74)	0.001	0.35 (0.15, 0.80)	0.013	0.71 (0.27, 1.89)	0.494
VALPO	0.59 (0.45, 0.77)	<0.001	0.87 (0.61, 1.25)	0.454	0.64 (0.32, 1.30)	0.217	1.92 (0.79, 4.65)	0.148
DHA	0.20 (0.15, 0.26)	<0.001	0.40 (0.27, 0.57)	<0.001	0.98 (0.49, 1.95)	0.961	2.25 (0.94, 5.39)	0.068
VITB	0.36 (0.28, 0.47)	<0.001	0.49 (0.34, 0.70)	<0.001	0.56 (0.27, 1.13)	0.106	1.98 (0.81, 4.84)	0.135