

Supplementary Table 1: MR results with AD as outcome using four different GWAS for AD

Data Sets		IVW estimate				MR Egger estimate				Weighted median MR estimate				Heterogeneity statistics					
Exposure & Dataset	Outcome & Dataset	Number of Instruments	Instrument Strength	IVW estimate				MR Egger estimate				Weighted median MR estimate				Degrees of freedom			
				estimate	95% CI LB	95% CI UB	p-value	estimate	95% CI LB	95% CI UB	p-value	estimate	95% CI LB	95% CI UB	p-value	Cochran's Q	p-value	I ²	
Education Okby et al., 2016	Bellenguez et al., 2022	70	45.793	0.657	0.049	1.265	0.034	0.306	-2.765	3.378	0.845	0.464	-0.221	1.149	0.184	138.398	69	>.00001	50.1%
	Kunkle et al., 2019	72	45.650	-1.135	-2.121	-0.149	0.024	-2.483	-7.556	2.590	0.337	-1.299	-2.441	-0.158	0.026	121.596	71	0.000	41.6%
	Lambert et al., 2013	71	45.818	-1.488	-2.441	-0.536	0.002	-3.618	-8.842	1.605	0.175	-1.187	-2.455	0.080	0.066	89.283	70	0.060	21.6%
	Schwarzentruber et al., 2021	72	45.686	0.694	0.111	1.277	0.020	-0.769	-3.725	2.187	0.610	0.494	-0.250	1.239	0.193	98.699	71	0.017	28.1%
Alcohol consumption et al., 2019	Bellenguez et al., 2022	72	60.889	0.170	-0.167	0.507	0.323	0.011	-0.542	0.563	0.969	0.063	-0.275	0.401	0.715	183.606	71	>.00001	61.3%
	Kunkle et al., 2019	73	61.287	-0.071	-0.180	0.038	0.201	0.944	-3.823	5.711	0.698	-0.078	-0.204	0.048	0.226	127.835	72	0.000	43.7%
	Lambert et al., 2013	70	61.204	-0.024	-0.594	0.545	0.933	0.001	-0.941	0.943	0.999	-0.352	-1.042	0.339	0.318	119.991	69	0.000	42.5%
	Schwarzentruber et al., 2021	73	61.264	0.233	-0.117	0.582	0.192	-0.022	-0.624	0.580	0.943	-0.138	-0.573	0.297	0.533	137.708	72	>.00001	47.7%
BMI Pulit et al., 2018	Bellenguez et al., 2022	542	55.264	-0.139	-0.200	-0.079	0.000	-0.165	-0.321	-0.009	0.038	-0.171	-0.264	-0.078	0.000	870.906	541	>.00001	37.9%
	Kunkle et al., 2019	544	55.368	-0.184	-0.433	0.066	0.149	-0.749	-1.394	-0.105	0.023	-0.110	-0.268	0.048	0.173	4736.082	543	>.00001	88.5%
	Lambert et al., 2013	538	55.433	-0.054	-0.281	0.172	0.639	-0.538	-1.131	0.055	0.076	0.029	-0.158	0.216	0.760	3106.162	537	>.00001	82.7%
	Schwarzentruber et al., 2021	544	55.359	-0.287	-0.515	-0.059	0.014	-0.572	-1.161	0.017	0.057	-0.126	-0.220	-0.031	0.009	9183.831	543	>.00001	94.1%
Systolic Blood Pressure UKBB	Bellenguez et al., 2022	219	45.411	-0.106	-0.204	-0.008	0.035	-0.100	-0.408	0.209	0.527	-0.166	-0.273	-0.058	0.002	472.711	218	>.00001	53.9%
	Kunkle et al., 2019	218	45.262	-0.128	-0.269	0.012	0.074	-0.180	-0.628	0.267	0.430	-0.073	-0.258	0.113	0.443	306.713	217	0.000	29.2%
	Lambert et al., 2013	217	45.240	-0.157	-0.305	-0.008	0.038	-0.270	-0.747	0.206	0.266	-0.160	-0.368	0.047	0.130	275.843	216	0.004	21.7%
	Schwarzentruber et al., 2021	218	45.268	-0.217	-0.320	-0.113	0.000	-0.270	-0.599	0.059	0.108	-0.273	-0.396	-0.149	0.000	386.483	217	>.00001	43.9%
Age related hearing loss Kalra et al., 2020	Bellenguez et al., 2022	30	43.403	0.061	-0.165	0.287	0.598	0.723	-0.152	1.598	0.105	0.052	-0.235	0.339	0.721	37.267	29	0.140	22.2%
	Kunkle et al., 2019	30	43.392	0.026	-0.333	0.385	0.889	-0.223	-1.809	1.364	0.783	-0.144	-0.651	0.364	0.579	20.179	29	0.887	0.0%
	Lambert et al., 2013	28	43.462	0.038	-0.370	0.445	0.856	-0.440	-2.568	1.689	0.686	0.090	-0.470	0.651	0.752	26.100	27	0.513	0.0%
	Schwarzentruber et al., 2021	30	43.369	-0.115	-0.387	0.157	0.407	-0.403	-1.537	0.731	0.486	-0.178	-0.523	0.167	0.312	39.495	29	0.093	26.6%
Depression Howard et al., 2019	Bellenguez et al., 2022	76	42.782	0.016	-0.086	0.119	0.752	-0.361	-0.924	0.202	0.209	0.029	-0.090	0.148	0.637	125.995	75	0.000	40.5%
	Kunkle et al., 2019	79	42.426	-0.167	-0.332	-0.001	0.049	-0.854	-1.786	0.078	0.072	-0.201	-0.408	0.006	0.057	113.362	78	0.006	31.2%
	Lambert et al., 2013	78	42.430	-0.116	-0.285	0.053	0.180	-0.776	-1.719	0.167	0.107	-0.109	-0.338	0.120	0.351	93.851	77	0.093	18.0%
	Schwarzentruber et al., 2021	79	42.426	-0.068	-0.190	0.054	0.274	-0.414	-1.093	0.265	0.232	-0.046	-0.185	0.093	0.517	141.493	78	>.00001	44.9%
Type 2 Diabetes, Scott et al., 2017	Bellenguez et al., 2022	39	62.187	0.006	-0.036	0.049	0.776	-0.009	-0.123	0.104	0.871	-0.013	-0.061	0.035	0.596	95.862	38	>.00001	60.4%
	Kunkle et al., 2019	40	61.953	-0.201	-0.679	0.278	0.411	-0.332	-1.614	0.951	0.612	-0.006	-0.085	0.073	0.887	4047.441	39	>.00001	99.0%
	Lambert et al., 2013	40	62.226	-0.101	-0.523	0.320	0.638	-0.247	-1.371	0.877	0.667	-0.007	-0.091	0.076	0.862	2524.884	39	>.00001	98.5%
	Schwarzentruber et al., 2021	40	62.013	-0.200	-0.654	0.255	0.389	-0.271	-1.499	0.957	0.665	0.005	-0.044	0.053	0.851	8393.471	39	>.00001	99.5%
Loneliness Day et al., 2019	Bellenguez et al., 2022	15	36.105	0.206	-0.270	0.682	0.396	-0.814	-3.230	1.603	0.509	0.081	-0.395	0.557	0.738	29.810	14	0.008	53.0%
	Kunkle et al., 2019	15	36.097	0.045	-1.114	1.204	0.939	0.479	-5.663	6.620	0.879	-0.390	-1.232	0.453	0.365	54.771	14	>.00001	74.4%
	Lambert et al., 2013	14	36.131	0.195	-0.885	1.274	0.723	0.786	-5.414	6.987	0.804	-0.396	-1.345	0.553	0.413	34.207	13	0.001	62.0%
	Schwarzentruber et al., 2021	15	36.083	-0.146	-0.827	0.534	0.674	-1.611	-5.074	1.852	0.362	-0.328	-0.853	0.196	0.220	44.367	14	0.000	68.4%
Physical Activity Klimentidis et al., 2018	Bellenguez et al., 2022	7	37.958	-0.724	-2.279	0.832	0.362	5.031	-8.337	18.399	0.461	-0.197	-1.395	1.001	0.748	28.695	6	0.000	79.1%
	Kunkle et al., 2019	7	37.952	-0.012	-1.512	1.489	0.988	-5.161	-18.158	7.836	0.436	-0.188	-1.909	1.532	0.830	8.553	6	0.200	29.8%
	Lambert et al., 2013	7	38.362	-0.747	-2.516	1.021	0.407	-5.295	-21.854	11.265	0.531	-0.942	-2.880	0.995	0.340	9.466	6	0.149	36.6%
	Schwarzentruber et al., 2021	7	37.952	-0.293	-1.441	0.854	0.617	-3.783	-13.894	6.328	0.463	-0.272	-1.419	0.876	0.643	11.361	6	0.078	47.2%
Smoking Wootton et al., 2019	Bellenguez et al., 2022	126	42.693	-0.229	-0.372	-0.086	0.002	-0.719	-1.286	-0.152	0.013	-0.169	-0.339	0.000	0.050	221.479	125	>.00001	43.6%
	Kunkle et al., 2019	126	42.617	-0.037	-0.259	0.185	0.746	-0.794	-1.691	0.102	0.082	-0.042	-0.336	0.252	0.781	169.390	125	0.005	26.2%
	Lambert et al., 2013	125	42.533	0.039	-0.218	0.295	0.767	-0.555	-1.640	0.530	0.316	0.022	-0.310	0.355	0.896	181.590	124	0.001	31.7%
	Schwarzentruber et al., 2021	126	42.625	-0.316	-0.477	-0.154	0.000	-0.713	-1.361	-0.066	0.031	-0.342	-0.538	-0.146	0.001	208.446	125	>.00001	40.0%

Supplementary Table2: MR results with DLB as outcome

Data Sets				IVW estimate				MR Egger estimate				Weighted median MR estimate				Heterogeneity statistics			
Exposure & Dataset	Outcome & Dataset	Number of Instruments	Instrument Streight	IVW estimate	95% CI LB	95% CI UB	p-value	MR Egger	95% CI LB	95% CI UB	p-value	Weighted median MR estimate	95% CI LB	95% CI UB	p-value	Cochran's Q	Degrees of freedom	p-value	I ²
Education Okbay et al., 2016	DLB Chia et al., 2021	67	45.517	0.688	-1.411	2.787	0.521	-1.338	-11.753	9.077	0.801	2.185	-0.741	5.111	0.143	73.913	66	0.236	10.7%
Alcohol Consumption Evangelou et al., 2019	DLB Chia et al., 2021	69	58.002	-0.515	-1.737	0.706	0.408	0.222	-3.588	4.033	0.909	-1.217	-3.102	0.667	0.205	71.462	68	0.364	48.0%
Body Mass Index Pulit et al., 2018	DLB Chia et al., 2021	538	55.504	-0.286	-0.565	-0.006	0.045	-0.563	-1.289	0.163	0.129	-0.024	-0.406	0.359	0.904	881.655	537	>.00001	39.1%
Systolic Blood Pressure UK BioBank	DLB Chia et al., 2021	213	45.574	0.110	-0.196	0.416	0.481	-0.380	-1.367	0.607	0.451	0.002	-0.461	0.464	0.994	204.133	212	0.639	0.0%
Age-related hearing impairment Kalra et al., 2020	DLB Chia et al., 2021	29	43.436	-0.282	-1.193	0.630	0.545	-2.504	-6.182	1.174	0.182	-0.606	-1.875	0.664	0.350	25.491	28	0.601	0.0%
Depression Howard et al., 2019	DLB Chia et al., 2021	71	42.191	-0.008	-0.452	0.437	0.972	0.965	-1.579	3.510	0.457	-0.314	-0.899	0.270	0.292	94.768	70	0.026	26.1%
Type 2 Diabetes, Scott et al., 2017	DLB Chia et al., 2021	38	62.483	0.024	-0.149	0.197	0.784	0.027	-0.420	0.473	0.907	0.048	-0.168	0.265	0.661	27.353	37	0.877	0.0%
Loneliness Day et al., 2019	DLB Chia et al., 2021	14	34.957	-1.524	-3.434	0.387	0.118	-1.575	-11.135	7.985	0.747	-1.811	-3.988	0.367	0.103	20.702	13	0.079	37.2%
Physical Activity Klimentidis et al., 2018	DLB Chia et al., 2021	7	38.048	-2.679	-7.705	2.347	0.296	-17.324	-61.638	26.990	0.444	-3.330	-8.120	1.459	0.173	14.169	6	0.028	57.7%
Smoking Wootton et al., 2019	DLB Chia et al., 2021	119	42.782	-0.181	-0.717	0.354	0.507	-0.159	-2.248	1.930	0.881	-0.417	-1.165	0.331	0.275	134.921	118	0.137	12.5%

Supplementary Table 3: MR results with FTD as outcome

Data Sets				IVW estimate				MR Egger estimate				Weighted median MR estimate				Heterogeneity statistics			
Exposure & Dataset	Outcome & Dataset	Number of Instruments	Instrument Strength	IVW estimate	95% CI LB	95% CI UB	p-value	MR Egger	95% CI LB	95% CI UB	p-value	Weighted median MR estimate	95% CI LB	95% CI UB	p-value	Cochran's Q	Degrees of freedom	p-value	I ²
Education Okbay et al., 2016	FTD Ferreri et al., 2014	71	45.976	1.044	-1.427	3.514	0.408	-7.489	-21.785	6.807	0.305	0.326	-2.989	3.641	0.847	84.386	70	0.116	17.0%
Alcohol Consumption Evangelou et al., 2019	FTD Ferreri et al., 2014	65	61.944	0.431	-0.664	1.526	0.440	0.557	-1.164	2.278	0.526	0.124	-1.543	1.791	0.884	62.995	64	0.512	0.0%
Body Mass Index Pult et al., 2018	FTD Ferreri et al., 2014	525	55.268	-0.287	-0.540	-0.034	0.026	-0.318	-0.976	0.340	0.344	-0.191	-0.649	0.268	0.415	543.364	524	0.270	3.6%
Systolic Blood Pressure UK Biobank	FTD Ferreri et al., 2014	212	45.081	-0.047	-0.406	0.312	0.798	0.165	-1.005	1.335	0.782	0.106	-0.431	0.642	0.700	222.056	211	0.287	5.0%
Age-related hearing impairment Kalra et al., 2020	FTD Ferreri et al., 2014	26	43.494	-0.111	-1.201	0.979	0.842	-1.268	-8.039	5.503	0.714	-0.342	-1.899	1.216	0.667	26.110	25	0.402	4.3%
Depression Howard et al., 2019	FTD Ferreri et al., 2014	78	41.904	0.004	-0.411	0.420	0.983	-0.561	-2.827	1.705	0.627	0.083	-0.506	0.672	0.782	79.237	77	0.408	2.8%
Type 2 Diabetes Scott et al., 2017	FTD Ferreri et al., 2014	38	62.478	0.024	-0.149	0.197	0.784	0.027	-0.420	0.473	0.907	0.048	-0.168	0.265	0.661	59.181	37	0.012	37.5%
Loneliness Day et al., 2019	FTD Ferreri et al., 2014	14	36.429	1.334	-0.390	3.059	0.129	0.760	-8.418	9.938	0.871	0.816	-1.588	3.219	0.506	12.524	13	0.483	0.0%
Physical Activity Klimentidis et al., 2018	FTD Ferreri et al., 2014	7	38.177	1.520	-2.158	5.198	0.418	10.857	-20.400	42.114	0.496	0.885	-4.058	5.829	0.726	6.080	6	0.414	1.3%
Smoking Wootton et al., 2019	FTD Ferreri et al., 2014	123	42.593	-0.344	-0.973	0.284	0.283	0.458	-2.180	3.097	0.733	-0.116	-0.970	0.738	0.790	153.749	122	0.027	20.6%

Supplementary Table 4: Additional sample statistics

Dataset	Meta-analyses?	Heterogeneity statistics		Maximum number of participants	Maximum exposure sample overlaps with outcome sample population						
		p-value	I ²		Alzheimer's Disease				Dementia with Lewy Bodies	Frontotemporal Dementia	Coronary Artery Disease
					Bellenguez et al., 2022	Kunkle et al., 2019	Lambert et al., 2013	Schwartzentruber et al., 2022	DLB: Chia et al., 2021	FTD: Ferreri et al., 2014	Nelson et al., 2017
Education Okbay et al., 2016	Yes	>.05	ranged from 0.0 to 38.3	293723	2.6%	0.0%	0.0%	0.0%	0.0%	0.0%	N/A
Alcohol consumption et al., 2019	Yes	>.05	ranged from 0.0 to 77.8	480842	80.6%	0.0%	0.0%	89.6%	0.0%	0.0%	N/A
BMI Pulit et al., 2018	No	-	-	694649	55.8%	0.0%	0.0%	62.0%	0.0%	0.0%	100.0%
Systolic Blood Pressure UKBB	No	-	-	475142	81.6%	0.0%	0.0%	90.7%	0.0%	0.0%	100.0%
Age related hearing loss Kalra et al., 2020	No	-	-	330759	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	N/A
Depression Howard et al., 2019	No	-	-	322580	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	N/A
Type 2 Diabetes, Scott et al., 2017	Yes	-	-	159208	3.7%	0.0%	0.0%	0.0%	0.0%	0.0%	N/A
Loneliness Day et al., 2019	No	-	-	452302	85.7%	0.0%	0.0%	95.3%	0.0%	0.0%	N/A
Physical Activity Klimentidis et al., 2018	No	-	-	377234	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	N/A
Smoking Wootton et al., 2019	No	-	-	462690	83.8%	0.0%	0.0%	93.2%	0.0%	0.0%	100.0%

