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Supplementary Data

Physical Activity in Middle-Age and Dementia in Later Life: Findings from a Prospective Cohort of Men in Caerphilly, South Wales and a Meta-Analysis

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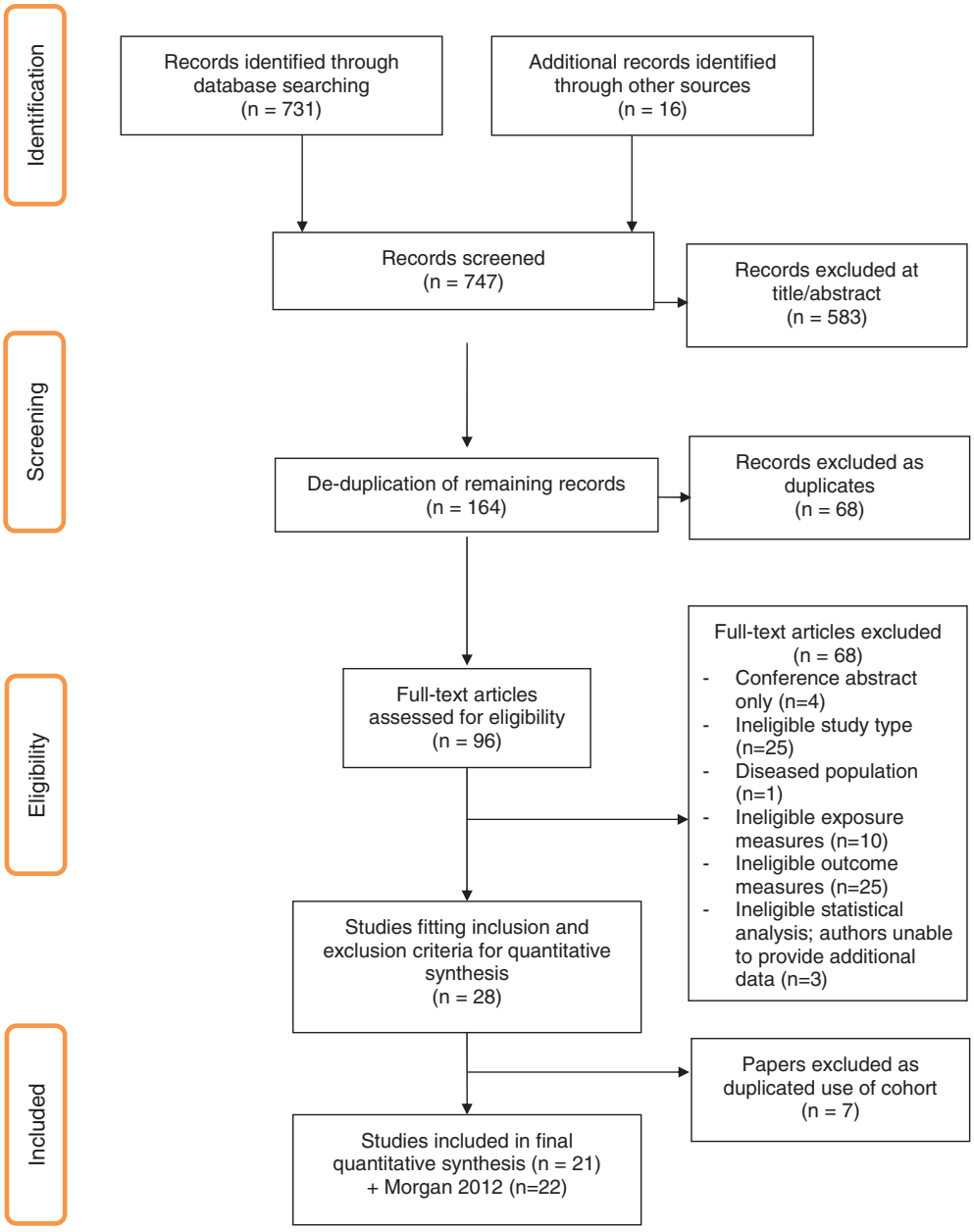

Supplementary Figure 1. PRISMA flow diagram.

Supplementary Table 1
Inclusion and exclusion criteria for systematic review

Inclusion criteria
– Prospective cohort design
– Measured association between physical activity (composite measure of total activity or measure of a specific activity) and cognitive impairment or dementia, as a primary or secondary outcome
– Studies reporting a validated, clinically-relevant outcome measure of cognitive impairment or a pre-specified decline in cognitive function from baseline
– Studies reporting an outcome measure of dementia, or if not dementia Alzheimer's disease, or if not Alzheimer's disease vascular dementia
Exclusion criteria
– Cohorts from specific diseased populations
– Studies not reporting a relative effect estimate and/or measure of precision (confidence interval)
– Studies not describing clear methods of assessing outcomes using standardized and validated operational criteria for diagnosing cognitive impairment or dementia/Alzheimer's disease/vascular dementia
– Studies not documenting clear, operationalized methods of obtaining prospective data on physical activity
– Studies not providing a relative measure of effect between highest/lowest categories of physical activity
– Studies using an identical control group as an already-included study

Supplementary Table 2
Distribution of potential confounders by level of each physical exposure

	Work-related physical activity				Leisure-time physical activity				
	Low	Middle	High	*p*	Low	Middle	High	Total	*p**
Mean age, y	56	56	56	**0.35**^	57	56	56	–	**0.04**^
Social Class									
Non-manual (%)	262 (64)	107 (26)	40 (10)	**<0.001***	118 (29)	147 (36)	144 (35)	409 (100)	**0.93***
Manual (%)	123 (21)	279 (47)	194 (33)		173 (29)	215 (36)	208 (35)	596 (100)	
Marital status									
Married (%)	349 (38)	353 (39)	211 (23)	**0.91***	261 (29)	330 (36)	322 (35)	913 (100)	**0.44***
Not married (%)	36 (39)	33 (36)	23 (25)		30 (33)	32 (35)	30 (33)	92 (100)	
BMI									
Underweight or normal	122 (40)	115 (37)	70 (23)	**0.60***	77 (25)	106 (35)	124 (40)	307 (100)	**0.02***
Overweight or obese (%)	263 (38)	271 (39)	164 (24)		214 (31)	256 (37)	228 (33)	698 (100)	
Alcohol consumption									
Non-drinker (%)	22 (42)	18 (34)	13 (25)	**0.85***	22 (42)	21 (40)	10 (19)	53 (100)	**<0.01***
Light alcohol intake (%)	130 (41)	124 (39)	64 (20)		100 (31)	109 (34)	109 (34)	318 (100)	
Moderate alcohol intake (%)	116 (38)	126 (41)	65 (21)	**0.85***	84 (27)	107 (35)	116 (37)	307 (100)	**0.272***
High alcohol intake (%)	117 (36)	118 (36)	92 (28)		85 (26)	125 (38)	117 (36)	327 (100)	
Smoking status									
Never smoked (%)	96 (41)	79 (34)	60 (26)		76 (32)	93 (40)	66 (28)	235 (100)	
Ex-smoker or pipe/cigar (%)	207 (40)	205 (40)	104 (20)	**0.11***	142 (28)	181 (35)	193 (37)	516 (100)	**0.11***
Regular smoker (%)	82 (32)	102 (40)	70 (28)		73 (29)	88 (35)	93 (37)	254 (100)	
Mean NART index score	111	106	103	**<0.001**^	107	108	107	–	**0.28**^
Vascular Disease$									
No (%)	319 (39)	316 (38)	189 (23)	**0.51***	234 (28)	299 (36)	291 (35)	824 (100)	**0.47***
Yes (%)	66 (36)	70 (39)	45 (25)		57 (31)	63 (35)	61 (34)	181 (100)	
Common Mental Disorder+									
No (%)	308 (38)	297 (37)	188 (24)	**0.93***	221 (28)	277 (35)	295 (37)	793 (100)	**0.01***
Yes (%)	77 (36)	89 (42)	46 (22)		70 (33)	85 (40)	57 (27)	212 (100)	
Mean STAI score	34	35	35	**0.02**~	36	34	34	–	**0.02**~

BMI, body mass index, kg/m^3; NART, National Adult Reading Test; CIND, Cognitive impairment not dementia; STAI, Spielberger's State-Trait Anxiety Index; *Chi-square test for trend, ^oneway ANOVA, ~oneway ANOVA on log-transformed data; $Self reported presence of at least one of: heart attack, angina, ischemic heart disease, stroke, claudication; +Defined as a score of ≥5 on the General Health Questionnaire.

Supplementary Table 3
Details of studies included in meta-analysis

Name	Country	Gender	Age	Exposure measurement	Outcome measurement	Follow-up (y)	Sample size
Akbaraly, 2009 [51]	France	M&F	>65 y at baseline (mean 74 y–78 y)	Self-report questionnaires on frequency of activities: "doing odd jobs, gardening, and going for a walk"	Neuropsychological tests, neurologist examination, independent clinical consensus decision. DSM-IV criteria (dementia), NINCDS-ADRDA (AD), NINDS-AIREN (VaD)	4	5698
Chang, 2010 [52]	Iceland	M&F	Mean 51 y at baseline	Asked if ever regularly played sports/exercise and if so how many hours per week spent exercising	MMSE, further cognitive tests, neurological test and proxy medical history - diagnosis made by consensus according to DSM-IV	26	4945
Etgen, 2010 [53]	Germany	M&F	>55 y at baseline, (mean 66 y–71 y)	Self-report on number of days/wk spent performing various activities	6CIT (Short Blessed Test) by primary care physician	2	3485
Fabrigoule, 1995 [54]	France	M&F	Mean 74.8 y at baseline	Binary question on baseline survey: sports or gymnastics participation - yes/no	Psychometric tests, standardized questionnaire. Diagnoses made using DSM-III-R criteria (dementia), NINCDS-ADRDA (AD) by neurologist	3	2040
Gureje, 2011 [55]	Nigeria	M&F	>65 y at baseline	International Physical Activity Questionnaire	Screening using 10-Word Delayed Recall Test, assessment by Clinician Home-based Interview to assess Function, final diagnosis made by psychiatrist	3	1225
Larson, 2006 [56]	US	M&F	>65 y at baseline	Structured questionnaire on number of days/wk during the past year that they did activities (walking, hiking, bicycling, aerobics, swimming, etc, or other exercise) for at least 15 mins	Screening using Cognitive Ability Screening Instrument; diagnoses made by consensus between physicians and neuropsychologist	6.2	1740
Lytle, 2004 [57]	US	M&F	Mean age 76.8 y	Self-report whether participant exercised, type of activity, frequency, duration	Cognitive decline: MMSE decline of $\geq$3 points versus <3 points, controlling for baseline MMSE	3	1146
Middleton, 2008 [46]	Canada	M&F	>65 y	Self-reported lifestyle factors including frequency and intensity of exercise	Screening using mMMSE, clinical examination, consensus diagnoses using DSM	5	4683
Podewils, 2005 [58]	US	M&F	>65 y at baseline, mean 74.8 y	Modified Minnesota Leisure Time Activity Questionnaire, over the previous 2 weeks	Screening using 3MS/TICS/history, medical record review, neuropsychiatric examination. Diagnoses made by Adjudication Committee including neurology and psychiatry clinicians, using NINCDS-ADRDA (AD)	5.4	3375
Ravaglia, 2008 [59]	Italy	M&F	>65 y at baseline, mean age 73 y	Interviews at baseline using Paffenbarger Physical Activity Questionnaire	Screening (history, MMSE, clinical and neurological examination) and neuropsychological assessment (mental deterioration battery). Diagnoses made using DSM (dementia), NINCDS-ADRDA (AD), and NINDS-AIREN (VaD)	3.9	749
Rovio, 2005 [42]	Finland	M&F	Mean 50 y (39 y–64 y)	Self-report health behavior: "how often do you participate in leisure-time physical activity that lasts at least 20–30 mins and causes breathlessness and sweating"	Screening (MMSE) and further neurological and cardiovascular examinations, detailed neuropsychological examination. Diagnoses made using DSM and NINCDS-ADRDA criteria	21	1449

Supplementary Table 3
(Continued)

Name	Country	Gender	Age	Exposure measurement	Outcome measurement	Follow-up (y)	Sample size
Scarmeas, 2009 [60]	US	M&F	Mean 77.2 y	Godin leisure-time questionnaire: frequency and duration of vigorous/moderate/light activities over 2 w	Neuropsychological battery, CDR. Diagnoses made by consensus agreement based on criteria from DSM and NINCDS-ADRDA (AD)	5.4	1880
Schuit, 2001 [61]	Netherlands	M	Mean 74.6 y at baseline	Self-report questionnaire about frequency and duration of walking and bicycling, hobbies, gardening, odd jobs and sport	Diagnosis made if decrease of ≥3 points in the Dutch version of the MMSE	3	347
Sumic, 2007 [62]	US	M, F	Mean age 88.5 y	Self-report questionnaire on how many city blocks walked daily, and frequency of light physical exercise and strenuous exercise	Face-to-face interview using MMSE and CDR. Diagnosis made if repeated abnormal scores on the MMSE (<24) or CDR (= 0.5) on two consecutive assessments	4.7	66
Taaffe, 2008 [13]	US	M	71 y–92 y at baseline	Self-report 24-hour physical activity using frequency and duration of basal/sedentary/slight/moderate/heavy physical activity	Screening (age and cognitive performance using CASI), repeat CASI and Informant Questionnaire on Cognitive Decline in Elderly, standardized interview, neuropsychological battery, proxy interview, neurological examination, neuroimaging	6.1	2263
Verghese, 2006 [12]	US	M&F	>75 y at baseline	Self-reported participation in ten physical activities (tennis, golf, swimming, bicycling, dancing)	Blessed test score change ≥ 4points, worsening neuropsychological test scores. Dementia diagnosis made using DSM and amnestic MCI diagnosed if not meeting criteria for dementia, and objective memory impairment	5.6	437
Verghese, 2003 [63]	US	M&F	>75 y at baseline	Self-reported participation in eleven physical activities (e.g. tennis, golf, swimming, bicycling, dancing)	Blessed test score change ≥4points, worsening neuropsychological test scores. Dementia diagnosis made using DSM and NINCDS-ADRDA (AD)	5.1	469
Wang, 2002 [64]	Sweden	M&F	Mean 81.1 y	Interview by trained nurses about engagement in any particular activities, type and frequency of e.g. “doing sport”, “walking”, “doing outdoor activities”	Clinical examination following a standardized protocol including: personal and family history, clinical examination by physicians, psychological tests by trained personnel. Diagnoses made by consensus agreement using criteria in DSM-III	6.4	776
Wilson, 2002 [65]	US	M&F	>65 y at baseline	Self-report on frequency and duration of activities included: walking for exercise, jogging or running, gardening or yard work, dancing, general exercise, bowling, bicycle riding, swimming	Structured clinical evaluation including medical history, neurological examination, detailed cognitive function testing, imaging. Diagnoses made by neurologist according to NINCDS-ADRDA criteria	4.1	842
Yaffe, 2001 [45]	US	F	>65 y at baseline	Self-reported “city blocks” and stairs walked each day; modified Paffenbarger Scale	Cognitive decline defined as decrease of ≥3 points on MMSE from baseline at follow-up	7.5	5925
Yoshitake, 1995 [66]	Japan	M&F	M: 73 y (64 y–92 y). F: 74 y (65 y–98 y)	Self-report baseline data on physical activity	MMSE and Hasegawa’s dementia scale. Neuropsychological interview and examination. Diagnoses made using DSM (dementia), NINCDS-ADRDA (AD), NINDS-AIREN (VaD)	7	828

AD, Alzheimer’s disease; CASI, Cognitive Abilities Screening Instrument; CDR, Clinical Dementia Rating, MCI, mild cognitive impairment; MMSE, Mini-Mental Status Examination, VaD, vascular dementia.