Journal Pre-proof

Body Composition, Vascular Health, Cardiorespiratory Fitness, Lung
Function, Muscle Architecture, and Physical Activity in People with
Young Onset Dementia: A Case-Control Study

Lawrence D. Hayes PhD , Ethan C.J. Berry BSc (Hons) ,
Nilihan E.M. Sanal-Hayes PhD , Nicholas F. Sculthorpe PhD ,
Duncan S. Buchan PhD , Marie Mclaughlin PhD ,
Sowmya Munishankar MBChB, MRCPsych, MSc ,
Debbie Tolson PhD

Please cite this article as: Lawrence D. Hayes PhD , Ethan C.J. Berry BSc (Hons) ,
Nilihan E.M. Sanal-Hayes PhD , Nicholas F. Sculthorpe PhD , Duncan S. Buchan PhD ,
Marie Mclaughlin PhD , Sowmya Munishankar MBChB, MRCPsych, MSc , Debbie Tolson PhD ,
Body Composition, Vascular Health, Cardiorespiratory Fitness, Lung Function, Muscle Architecture,
and Physical Activity in People with Young Onset Dementia: A Case-Control Study, *The American
Journal of Medicine* (2024), doi: https://doi.org/10.1016/j.amjmed.2024.08.027

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition
of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of
record. This version will undergo additional copyediting, typesetting and review before it is published
in its final form, but we are providing this version to give early visibility of the article. Please note that,
during the production process, errors may be discovered which could affect the content, and all legal
disclaimers that apply to the journal pertain.

Clinical Research Study

Body Composition, Vascular Health, Cardiorespiratory Fitness, Lung Function, Muscle Architecture, and Physical Activity in People with Young Onset Dementia: A Case-Control Study

Running head: Health and Fitness in Young Onset Dementia

Lawrence D. Hayes, PhD[1,2], Ethan C.J. Berry, BSc (Hons)[1,*], Nilihan E.M. Sanal-Hayes, PhD[1,3], Nicholas F. Sculthorpe, PhD[1], Duncan S. Buchan, PhD[1], Marie Mclaughlin, PhD[1,4], Sowmya Munishankar MBChB, MRCPsych, MSc[5], Debbie Tolson, PhD[6]

[1]Sport and Physical Activity Research Institute, School of Health and Life Sciences, University of the West of Scotland, Glasgow, UK

[2]Lancaster Medical School, Lancaster University, Lancaster, UK

[3]School of Health and Society, University of Salford, Salford, UK

[4]Physical Activity for Health Research Centre, Institute for Sport, P.E. and Health Sciences, University of Edinburgh, Moray House School of Education and Sport, Holyrood Road, Edinburgh, EH8 8AQ, UK

[5]Clydesdale CMHT and Young Onset Dementia Service, Clinical Director for Old Age Psychiatry, Foundation Programme Director W10, Enhanced Appraiser, NHS Lanarkshire

[6]Alzheimer Scotland Centre for Policy and Practice, University of the West of Scotland

[*]Corresponding author.
Ethan.Berry@UWS.ac.uk

This article is formatted in British English

Abstract

BACKGROUND: Body composition, blood pressure, estimated maximal oxygen uptake (VO_{2max}), lung function, physical activity, muscle architecture, and endothelial function had not previously been examined in people with young onset dementia. Therefore, the study measured these variables in a young onset dementia group, compared them to age-matched controls.

METHODS: Estimated VO_{2max} (via the Astrand-Rhyming test), body composition, blood pressure, lung function (via spirometry), muscle architecture (via ultrasonography) and endothelial function (via flow mediated dilation) were assessed. Physical activity was measured using ActiGraph accelerometers for 7 days.

RESULTS: We recruited 33 participants (16 young onset dementia, 17 controls). The young onset dementia group had shorter fascicle lengths of the vastus lateralis, were sedentary for longer over a seven-day period, and completed less moderate-vigorous physical activity than controls ($p=0.028$, $d=0.81$; large effect, $p=0.029$, $d=0.54$; moderate effect, and $p=0.014$, $d=0.97$; large effect, respectively for pairwise comparisons). Pairwise comparisons suggest no differences at the $p<0.05$ level between young onset dementia and controls for estimated VO_{2max} (despite a moderate effect size [$d=0.66$]), height, body mass, BMI, blood pressure, light physical activity, lung function, muscle thickness, pennation angle, or endothelial function.

CONCLUSION: This study highlights differences between people with young onset dementia and controls, underscoring the need for multicomponent exercise interventions. Future interventions should target muscle architecture, increase moderate-vigorous physical activity, and reduce sedentariness, with the goal of improving quality of life and promoting functional independence.

Key words

Young-onset dementia; neurodegenerative disease; body composition; blood pressure; physical fitness; lung function; physical activity; muscle architecture; endothelial function

<u>Clinical Significance</u>

- Key differences exist muscle architecture, physical activity levels, and sedentariness in people with young onset dementia compared to age-matched controls.

- Physicians should be aware of these impairments in patients with young onset dementia.

- Physicians should encourage tailored, multicomponent exercise interventions to address these specific deficits.

- Implementing such targeted strategies could improve quality of life, maintain functional independence, and reduce the overall burden on caregivers and healthcare systems.

Introduction

Dementia is a neurodegenerative condition which leads to partial or complete loss of cognitive function[1]. There are several risk factors associated with dementia such as age, level of education, diet, alcohol use, sleep, smoking, and a range of other factors including chronic comorbidities[2]. In 2015, 50 million people were diagnosed with dementia worldwide[3], which represents ~10% of everyone over 65 years of age[7]. By 2050, this prevalence will mean an incidence of 152 million[4]. This will result in a global cost of dementia of between $1.6 and 2.4 trillion by 2050[5].

Young onset dementia is the onset of dementia before the age of 65 years of age[8] and represents 5% of all dementia cases in the UK, and 3.9 million cases worldwide[9]. A systematic review highlighted an average of 4.4 years between symptom onset and young onset dementia diagnosis, severely impacting upon the support for people with young onset dementia[8]. Possibly in part due to the poor rates of early diagnosis, average life expectancy from young onset dementia diagnosis is 7.9 years, emphasising the aggressiveness of the condition[10.] In young onset dementia, the early age at which symptoms are experienced initiate a cascade of physical and mental decline at a faster rate than late onset dementia[11]. Exercise has been proposed as a non-pharmacological intervention for people with dementia to improve fitness, disease progression, and quality of life[12]. There are several mechanisms by which exercise has been proposed to slow dementia progression[13], including increased serum brain derived neurotrophic factor[14], increased carotid blood flow[15], and reduced cerebral beta amyloid accumulation[16]. However, much mechanistic research excludes those with dementia, and utilises rodent or *in vitro* models[17 18], meaning there is uncertainly whether these mechanisms extend to humans with young onset dementia or late onset dementia. Moreover, whether mechanisms that exist in rodents or *in vitro* correspond to clinically meaningful of even detectable changes at the human level in people with late onset dementia in uncertain, and this lack of data is even more pronounced in young onset dementia.

Dost et al.[21] reported that 53% of 166 people with Alzheimer's disease presented with sarcopenia, highlighting the multi-systems effect of ageing. Cadore et al.[22] attempted to combat this multimorbidity with a lower extremity resistance training, observing improved muscular strength

post-intervention, the absence of a control group means these results should be interpreted with caution. With regards to the 'combined training' approach, Bossers et al.[23] found that balance and leg endurance improved in a combined training group more than an aerobic only training group, highlighting benefits of a multi-component exercise approach.

Although exercise is known to exert beneficial effects on several parameters in late onset dementia, there is scant literature concerning young onset dementia is. Concerningly, a recent scoping review revealed not a single study investigated effects of physical exercise on cognition, physical performance, well-being, or quality of life in young onset dementia[25]. Further, there are no cross-sectional studies comparing young onset dementia and healthy controls. Whilst exercise intervention studies in young onset dementia are lacking, implementing such interventions without a pragmatic dependent variable would be impractical. Before targeted support strategies can be developed, we conducted this case-control study to identify physiological differences in young onset dementia compared to age-matched healthy controls. We aimed to compare body composition, blood pressure, physical fitness, lung function, physical activity, muscle architecture, and endothelial function between individuals with young onset dementia and age-matched healthy controls. We hypothesised people with young onset dementia would show poorer values across all variables.

Methods

The study protocol was informed by research involvement activities which included volunteers with young onset dementia viewing demonstration films of the tests to be included. With support of healthcare professionals, the volunteers provided feedback on the acceptability of each test. These involvement activities are discussed fully elsewhere.

Participants

Sample size was based on estimated aerobic capacity using the Astrand-Rhyming cycle ergometer test[26]. To detect a mean difference of 1-metabolic equivalent (MET; 3.5 mL·kg·min^{-1}), with a standard deviation of 3.6 mL·kg·min^{-1}, a desired power of 0.80, and α of 0.05, we required n=17 per group. We recruited 33 participants (16 young onset dementia, 17 controls), as one young onset dementia participant withdrew due to injury unrelated to the study. Groups were age- and sex-matched. Young

onset dementia participants were recruited via NHS partners in Scotland. The South Lanarkshire young onset dementia team shared details of the study with those diagnosed with young onset dementia during consultations and contact details were passed on. Controls were recruited through social media advertisement, attending a single visit to the Cardiovascular Imaging Laboratory at the University of the West of Scotland between January 2023 and May 2024. The study adhered to Helsinki Declaration principles, with informed consent obtained and ethical approval was given by the NHS London Riverside Ethics Committee. Descriptive statistics for participants are in table 1.

Protocol

Body Composition and Blood Pressure

Stature was measured with a wall-mounted stadiometer (SECA, CE0123, Germany) and recorded in centimetres. Body mass was measured using electronic scales (SECA 876, CE0123, Germany) and recorded in kilograms. Body composition was assessed following ISAK guidelines, and BMI was calculated (BMI = kg/m²). Resting blood pressure was measured with an automated sphygmomanometer (Omron, the Netherlands). Participants were seated with the BP cuff on the left arm, which was inflated to 200 mmHg, and deflated to 0 mmHg. This was repeated three times with a one-minute rest between repetitions. The mean of the three repetitions was recorded.

Physical Fitness

Aerobic capacity was assessed using the submaximal Astrand-Rhyming test[26] on a cycle ergometer (ProTrainer, Wattbike, England) over six minutes. This test was chosen instead of a maximal test with consideration for participants comfort and clinical condition. Each participant wore a heart rate chest strap (PC.15.11, SIGMA, Germany). Resting HR was recorded, and the target heart rate was 125-175 b·min^{-1}, as justified previously[26]. Participants performed a three-minute warm-up without resistance, and then resistance was increased until the target heart rate was achieved. Heart rate and power output (W) were recorded every minute. If heart rate was stable within 5 b·min^{-1} during minutes five and six, the test concluded. If not, adjustments were made, and further minutes were added until the target heart rate was achieved. After the test, participants completed a one-minute cool-down and

dismounted the ergometer. The average heart rate from the final two minutes was used with the Astrand-Rhyming nomogram to predict maximal oxygen uptake (VO_{2max}) in mL·kg^{-1}·min^{-1}, with age correction applied.

Lung Function

A plastic peak flow meter (Mini Wright, PEA001, Clement Clarke, New York, USA), was used to assess lung function. The participant sat on a chair/plinth in the laboratory, relaxed, and performed a maximal inhalation before a subsequent maximal exhalation as quickly and forcefully as possible. The participant performed three trials allowing a one-minute rest between trials. The maximum of the three measurements was taken as the final value of peak flow.

Physical Activity

To determine physical activity, each participant wore an wGT3X-BT ActiGraph accelerometer (ActiGraph LLC, Pensacola, FL, USA) on their non-dominant wrist and were instructed to wear the device for 24h across seven days. Further details of the methodological decisions taken when assessing physical activity can be found in supplementary file 1.

To determine physical activity, each participant wore an wGT3X-BT ActiGraph accelerometer (ActiGraph LLC, Pensacola, FL, USA) on their non-dominant wrist. All accelerometer devices were initialized in ActiLife v6.13.4 (ActiGraph, Pensacola, FL, USA) to collect data at 100 Hz, and commence data collection. The "idle sleep mode" in ActiLife v6.13.4 was not enabled. Each participant was instructed to wear the device 24 hours per day for seven days, only removing the device during water-based activities. Once devices were returned, data were downloaded as raw .gt3x files which were processed using the GGIR package version 3.0-5 in R statistical software (R Foundation for Statistical Computing, Vienna, Austria, http://cran.r-project.org/[27]). In GGIR, files were processed to detect abnormally high values, detect nonwear[27], and calibrated using local gravity[28]. Files were excluded from analyses if post calibration error was >0.01 g, or if participants had less than one valid wear day (defined as ≥16 hr per day) or wear data was not present for each 15-min period of the 24-hr cycle[29]. The default non-wear setting was applied during processing within

GGIR[30]. Alongside wear time (days), the time spent inactive (<30 mg[31]), in light physical activity (between 30 and 100 mg) and moderate-vigorous physical activity (>100 mg[32]) was determined. Inactive time is provided exclusive of sleep time after applying the automated Heuristic Algorithm looking at Change of Z-Angle (HDCZA) algorithm within GGIR as previously described[3334]. For participants to be included in analysis, they had to provide a minimum of four days (three weekdays and one weekend day)[35].

Muscle Architecture

Muscle architecture of the vastus lateralis muscle was assessed using ultrasound with a 7-10 MHz, 4.7 cm linear array transducer (Vivid I, GE Healthcare, Horton, Norway). Participants lay supine on a plinth. Scans were taken at the distal third of the vastus lateralis, 35% of the distance between the greater trochanter (100%) and the distal femoral condyle (0%). Femur length was measured with a measuring tape (SECA 201, Germany), and the 35% mark was noted on the leg with a marker pen. The transducer was placed on this mark to capture images. Muscle architecture was analysed using ImageJ software (version 1.42q, National Institute of Health, USA), measuring fascicle length (distance between fascicle insertions at the deep and superficial aponeurosis), muscle thickness (distance between the deep and superficial aponeurosis), and pennation angle (angle between the fascicle and tendon axis). Ultrasound sarcopenia index was calculated by dividing fascicle length and muscle thickness[37 44].

Endothelial Function

Vascular endothelial function was assessed using an ultrasound scan of the brachial artery, focusing on vascular reactivity via flow-mediated dilation, as previously described[38]. Semi-automated edge detection software (Brachial Analyzer, Medical Imaging Applications LLC, Coralville, IA) measured arterial diameter, flow, and shear stress. The software tracked vessel walls and blood velocity, calculating shear stress and arterial diameter over three-second periods. Absolute (mm), relative (%), and shear-normalised flow-mediated dilation (%) were also determined.

Statistical Analysis

All data were assessed for normal distribution and homogeneity of variance and to assess differences, independent samples t-tests were performed. Data were analysed using R Studio (2023.12.0+369). Data are presented without subjective terminology and α levels are reported as exact p values, without dichotomous interpretation of 'significant' or 'non-significant' as advised by the American Statistical Association[36]. Effect size for paired comparisons was conducted using Cohen's d whereby the difference in means between two samples was divided by the pooled standard deviation (SD). Thresholds of 0.2, 0.5, and 0.8 for small, moderate, and large effects were used for Cohen's d[39]. Figures were generated in R Studio (2023.12.0+369) and displayed as grouped dot plots with mean lines as recommended by Drummond and Vowler[40,41].

Results

For physical activity data, all participants met the wear time criteria with a mean of 11 valid hours for both groups and a mean of 6 valid days for both groups. Estimated VO_{2max} (figure 1), lung function (figure 2), physical activity (figure 3), muscular architecture (figure 4), and vascular function (figure 5) are displayed below. Pairwise comparisons suggest no differences between young onset dementia and controls for estimated VO_{2max} (p=0.119, d=0.66; moderate effect). No differences were apparent in the lung function data (p=0.496, d=0.24; small effect). Differences were evident in sedentary time (p=0.029, d=0.54; moderate effect) and moderate-vigorous physical activity (p=0.014, d=0.97; large effect) between the groups. There were no differences observed for light physical activity (p=0.374, d=0.34; small effect). Muscle architecture displayed differences in fascicle length (p=0.028, d=0.81; large effect) and no differences on the remaining parameters (p=0.702, d=0.14; trivial effect). Vascular baseline diameter (p=0.162, d=0.53; moderate effect) and flow-mediated dilation % (p=0.118, d=0.60; moderate effect) was not different between groups. Further to this no differences in handgrip strength were observed between the groups (p=0.284, d=0.39; small effect).

INSERT TABLE 1 NEAR NERE
INSERT FIGURES 1-5 NEAR HERE

Discussion

This study addressed the knowledge gap in young onset dementia by examining body composition, blood pressure, estimated VO_{2max}, lung function, physical activity, muscle architecture, and endothelial function. The main findings revealed differences in fascicle length, sedentary time, and moderate-vigorous physical activity between groups. However, no differences were observed in estimated VO_{2max}, vascular function, pennation angle, muscle thickness, ultrasound sarcopenia index, lung function, functional capacity, and light physical activity. Thus, our hypothesis that all parameters would be deficient in people with young onset dementia compared to controls is only partially supported.

Estimated VO_{2max} was 5.3 mL·kg·min^{-1} greater in controls (although not reaching p<0.05) with a difference of this magnitude suggesting a greater risk of diabetes and cardiovascular disease[52]. A meta-analysis by Kodama et al.[53] showed that a 1-MET (3.5 mL·kg^{-1}·min^{-1}) increase in maximal oxygen uptake was associated with a 13% reduction in all-cause mortality. Despite not reaching the p<0.05 level in the present study, this area warrants further consideration and aerobic capacity should be considered in support for people with young onset dementia. There is a known association with maximal oxygen uptake and quality of life[55] and longevity[56], although these data are not in people with young onset dementia, so this could be an area of further investigation. Lower aerobic capacity may exist as young onset dementia participants were more sedentary than controls and completed less moderate-vigorous physical activity than controls, which also heightens their risk of obesity and diabetes[49].

Vascular function was similar across both groups, in line with previous studies which measured flow-mediated dilation in those with dementia[57]. However, some previous research has shown a specific link between endothelial dysfunction and Alzheimer's disease due to the reduced availability of nitric oxide which can exacerbate amyloid levels[58]. While our findings do not fall in line with this previous work, it is possible this is due to our smaller sample or due to the fact the young onset dementia group

were younger, and so vascular function is likely higher in terms of baseline diameter and reactivity regardless of diagnosis[59].

Fascicle length of the vastus lateralis was shorter in the young onset dementia group compared to controls, with a mean difference of 7.6 mm. A difference in fascicle length of this magnitude may suggest greater predisposition to frailty in young onset dementia [42]. Moreover, it is possible the shorter fascicle length increases metabolic cost of locomotion[43], which could result in a downward cycle of metabolically costly locomotion resulting in increased perception of effort, resulting in less physical activity, exacerbated by physical inactivity. Considering sarcopenia, while fascicle length is important, frailty and/or sarcopenia is more determined by muscle thickness[44], and whether fascicle length is plastic remains a matter of debate[45-48].

Implications

Our novel findings reported herein can guide future research to support exercise or physical activity interventions. We have highhighlighted areas of impairment, suggesting physical activity promotion for people with young onset dementia should be explored as less sedentary time may improve muscle architecture and aerobic fitness. A multi-disciplinary, multi-component approach is recommended[9], as these have improved physiological and psychological parameters in late onset dementia[64].

Strengths and Limitations

A key strength of the current study was the target population, focussing on those with young onset dementia addressed an under-represented population, paving the way for further research in the area. By using a case-control design, we isolated effects of young onset dementia on outcome variables. This study is not without limitations, including a modest sample size. To address this, we communicated magnitude-based inferences and precise α values instead of binary 'significance' classifications. This was necessary due to scant normative values in young onset dementia. Secondly, young onset dementia is progressive and therefore data from this study may not be extrapolated to all

people with young onset dementia. Future research could stratify participants by young onset dementia stage.

Conclusion

The identified deficits in muscle architecture and physical activity may contribute to disease burden, emphasising the need to recognise and address these issues to improve quality of life. We identified differences between the young onset dementia group and controls in muscle architecture and physical activity. These disparities underscore the need for tailored support interventions incorporating exercise/physical activity.

Authorship contributions according to the CRediT taxonomy

Conceptualisation, L.D.H., N.E.M.S-H., N.F.S., S.M., D.T.; methodology, L.D.H., E.C.J.B., N.E.M.S-H., N.F.S., D.S.B., M.M., D.T.; software, L.D.H., E.C.J.B., N.F.S., D.S.B., M.M.; validation, L.D.H., E.C.J.B., N.E.M.S-H., N.F.S., D.S.B., M.M., S.M., B.C., D.T.; formal analysis, L.D.H., E.C.J.B., N.E.M.S-H., D.S.B., ; investigation, L.D.H., E.C.J.B., N.E.M.S-H., N.F.S., D.S.B., M.M.; resources, L.D.H., N.E.M.S-H., N.F.S., D.S.B., S.M., D.T.; data curation, E.C.J.B.; writing—original draft preparation, L.D.H., E.C.J.B.; writing—review and editing, L.D.H., E.C.J.B., N.E.M.S-H., N.F.S., D.S.B., M.M., S.M., B.C., D.T. ; visualisation, E.C.J.B.; supervision, L.D.H.; project administration, L.D.H., E.C.J.B., S.M., B.C., D.T.; funding acquisition, L.D.H., N.E.M.S-H., N.F.S., D.S.B., S.M., D.T. All authors have read and agreed to the published version of the manuscript.

Supplementary File 1:

Participants were asked to wear an wGT3X-BT ActiGraph accelerometer (ActiGraph LLC, Pensacola, FL, USA) on their self-reported non-dominant wrist. Prior to distribution, all accelerometer devices were initialized in ActiLife v6.13.4 (ActiGraph, Pensacola, FL, USA) to collect data at 100 Hz, and commence data collection shortly after distribution. The "idle sleep mode" in ActiLife v6.13.4 was not enabled. Participants were instructed to wear the device 24 hours per day for a seven-day period, only removing the device during water-based activities (swimming, bathing, and showering).

Once devices were returned, data were downloaded as raw .gt3x files which were subsequently processed using the GGIR package version 3.0-5 in R statistical software (R Foundation for Statistical Computing, Vienna, Austria, http://cran.r-project.org/; Migueles, Rowlands, et al., 2019). In GGIR, files were processed to detect abnormally high values, detect nonwear (Migueles, Rowlands, et al., 2019), and calibrated using local gravity as a reference (van Hees et al., 2014). Files were excluded from subsequent analyses if post calibration error was >0.01 g, or if participants had less than one valid wear day (defined as ≥16 hr per day) or wear data was not present for each 15-min period of the 24-hr cycle (Buchan, 2022). The default nonwear setting was applied during processing within GGIR (van Hees et al., 2013).

Alongside wear time (days), the time spent inactive (<30 mg; Bakrania et al., 2016), in light physical activity (LPA) (between 30 and 100 mg) and moderate-vigorous physical activity (MVPA) (>100 mg; Hilderbrand et al., (2014)) was provided. Inactive time is provided exclusive of sleep time after applying he automated Heuristic Algorithm looking at Change of Z-Angle (HDCZA) algorithm within GGIR as previously described (van Hees et al., 2018; Buchan et al, 2024). For participants to be included in subsequent analysis, they had to provide a minimum of four days (three weekdays and one weekend day) as recommended (Migueles et al., 2017).

Acknowledgements

Declaration of competing interest

The submitted work was not carried out in the presence of any personal, professional, or financial relationships that could potentially be construed as a conflict of interest.

References

1. Aarsland, D. (2020) 'Epidemiology and Pathophysiology of Dementia-Related Psychosis', The Journal of Clinical Psychiatry, 81(5). Available at: https://doi.org/10.4088/JCP.AD19038BR1C.

2. Anstey, K.J., Ee, N., Eramudugolla, R., Jagger, C. and Peters, R. (2019) 'A Systematic Review of Meta-Analyses that Evaluate Risk Factors for Dementia to Evaluate the Quantity, Quality, and Global Representativeness of Evidence', Journal of Alzheimer's Disease. Edited by K. Anstey and R. Peters, 70(s1), pp. S165–S186. Available at: https://doi.org/10.3233/jad-190181.

3. Handley, M., Bunn, F. and Goodman, C. (2017) 'Dementia-friendly interventions to improve the care of people living with dementia admitted to hospitals: a realist review', BMJ Open, 7(7), p. e015257. Available at: https://doi.org/10.1136/bmjopen-2016-015257.

4. GBD 2019 Dementia Forecasting Collaborators (2022) 'Estimation of the Global Prevalence of Dementia in 2019 and Forecasted Prevalence in 2050: an Analysis for the Global Burden of Disease Study 2019', The Lancet Public Health, 7(2). Available at: https://doi.org/10.1016/s2468-2667(21)00249-8.

5. Pedroza, P., Chakrabarti, S., Chapin, A., Liu, A., Matyasz, T. and Dieleman, J.L. (2019) 'COSTS OF ALZHEIMER'S DISEASE AND DEMENTIA IN 188 COUNTRIES', Alzheimer's & Dementia, 15(7), p. P1635. Available at: https://doi.org/10.1016/j.jalz.2019.06.4877.

6. Rizzi, L., Rosset, I. and Roriz-Cruz, M. (2014) 'Global Epidemiology of Dementia: Alzheimer's and Vascular Types', BioMed Research International, 2014, pp. 1–8. Available at: https://doi.org/10.1155/2014/908915. priority_highIssue numberclose

7. Mosconi, L. (2013) 'Glucose metabolism in normal aging and Alzheimer's disease: methodological and physiological considerations for PET studies', Clinical and Translational Imaging, 1(4), pp. 217–233. Available at: https://doi.org/10.1007/s40336-013-0026-y.

8. Hendriks, S., Peetoom, K., Bakker, C., van der Flier, W.M., Papma, J.M., Koopmans, R., Verhey, F.R.J., de Vugt, M., Köhler, S., Withall, A., Parlevliet, J.L., Uysal-Bozkir, Ö., Gibson, R.C., Neita, S.M., Nielsen, T.R., Salem, L.C., Nyberg, J., Lopes, M.A., Dominguez, J.C. and De Guzman, M.F. (2021) 'Global Prevalence of Young-Onset Dementia', JAMA Neurology, 78(9). Available at: https://doi.org/10.1001/jamaneurol.2021.2161.

9. Rodgers, C., Rogerson, D., Stevenson, J. and Porock, D. (2018) 'Physical activity for people with young-onset dementia and carers: protocol for a scoping review', Systematic Reviews, 7(1). Available at: https://doi.org/10.1186/s13643-018-0698-5.

10. Brodaty, H., Seeher, K. and Gibson, L. (2012) '24:7, 1034-1045 C International Psychogeriatric Association', International Psychogeriatrics [Preprint]. Available at: https://doi.org/10.1017/S1041610211002924. priority_highVolume numberclosepriority_highIssue numberclose

11. Tolhurst, E., Bhattacharyya, S. and Kingston, P. (2012) 'Young onset dementia: The impact of emergent age-based factors upon personhood', Dementia, 13(2), pp. 193–206.

12. Alty, J., Farrow, M. and Lawler, K. (2020) 'Exercise and dementia prevention', *Practical Neurology*, 20(3), pp. 234–240. Available at: https://doi.org/10.1136/practneurol-2019-002335.

13. Gholamnezhad, Z., Boskabady, M.H. and Jahangiri, Z. (2020) 'Exercise and Dementia', *Physical Exercise for Human Health*, 1228, pp. 303–315. doi:10.1007/978-981-15-1792-1_20.

14. Damirchi, A., Hosseini, F. and Babaei, P. (2017) 'Mental Training Enhances Cognitive Function and BDNF More Than Either Physical or Combined Training in Elderly Women With MCI: A Small-Scale Study', *American Journal of Alzheimer's Disease & Other Dementiasr*, 33(1), pp. 20–29. doi:10.1177/1533317517727068.

15. Tan, Z.-X., Dong, F., Wu, L.-Y., Feng, Y.-S. and Zhang, F. (2021) 'The Beneficial Role of Exercise on Treating Alzheimer's Disease by Inhibiting β-Amyloid Peptide', *Molecular Neurobiology*, 58(11), pp. 5890–5906. doi:10.1007/s12035-021-02514-7.

16. Thomas, R., Zimmerman, S.D., Yuede, K.M., Cirrito, J.R., Tai, L.M., Timson, B.F. and Yuede, C.M. (2020) 'Exercise Training Results in Lower Amyloid Plaque Load and Greater Cognitive Function in an Intensity Dependent Manner in the Tg2576 Mouse Model of Alzheimer's Disease', *Brain Sciences*, 10(2), p. 88. doi:10.3390/brainsci10020088.

17. Ayari, S., Abellard, A., Carayol, M., Guedj, É. and Gavarry, O. (2023) 'A systematic review of exercise modalities that reduce pro-inflammatory cytokines in humans and animals' models with mild cognitive impairment or dementia', *Experimental Gerontology*, 175, p. 112141. Available at: https://doi.org/10.1016/j.exger.2023.112141.

18. Poon, C.H., Wang, Y., Fung, M.-L., Zhang, C. and Lim, L.W. (2020) 'Rodent Models of Amyloid-Beta Feature of Alzheimer's Disease: Development and Potential Treatment Implications', *Aging and disease*, 11(5), p. 1235. Available at: https://doi.org/10.14336/ad.2019.1026.

19. Sobol, N.A., Hoffmann, K., Frederiksen, K.S., Vogel, A., Vestergaard, K., Braendgaard, H., Gottrup, H., Lolk, A., Wermuth, L., Jakobsen, S., Laugesen, L., Gergelyffy, R., Høgh, P., Bjerregaard, E., Siersma, V., Andersen, B.B., Johannsen, P., Waldemar, G., Hasselbalch, S.G. and Beyer, N. (2016) 'Effect of aerobic exercise on physical performance in patients with Alzheimer's disease', *Alzheimer's & Dementia*, 12(12), pp. 1207–1215. doi:10.1016/j.jalz.2016.05.004.

20. Salisbury, D., Mathiason, M.A. and Yu, F. (2021) 'Exercise Dose and Aerobic Fitness Response in Alzheimer's Dementia in the FIT-AD Trial', *International Journal of Sports Medicine*, 43(10). doi:10.1055/a-1639-2307.

21. Dost, F.S., Ates Bulut, E., Dokuzlar, O., Kaya, D., Mutlay, F., Yesil Gurel, B.H. and Isik, A.T. (2022) 'Sarcopenia is as common in older patients with dementia with Lewy bodies as it is in those with Alzheimer's disease', *Geriatrics & Gerontology International*, 22(5), pp. 418–424. doi:10.1111/ggi.14383.

22. Cadore, E.L., Moneo, A.B.B., Mensat, M.M., Muñoz, A.R., Casas-Herrero, A., Rodriguez-Mañas, L. and Izquierdo, M. (2013) 'Positive effects of resistance training in frail elderly patients with dementia after long-term physical restraint', *AGE*, 36(2), pp. 801–811. doi:10.1007/s11357-013-9599-7.

23. Bossers, W.J.R., van der Woude, L.H.V., Boersma, F., Hortobágyi, T., Scherder, E.J.A. and van Heuvelen, M.J.G. (2015) 'A 9-Week Aerobic and Strength Training Program Improves Cognitive and Motor Function in Patients with Dementia: A Randomized, Controlled Trial', *The American Journal of Geriatric Psychiatry*, 23(11), pp. 1106–1116. doi:10.1016/j.jagp.2014.12.191.

24. Groot, C., Hooghiemstra, A.M., Raijmakers, P.G.H.M., van Berckel, B.N.M., Scheltens, P., Scherder, E.J.A., van der Flier, W.M. and Ossenkoppele, R. (2016) 'The effect of physical activity on cognitive function in patients with dementia: A meta-analysis of randomized control trials', *Ageing Research Reviews*, 25, pp. 13–23. doi:10.1016/j.arr.2015.11.005.

25. Roman de Mettelinge, T., Calders, P. and Cambier, D. (2021) 'The Effects of Aerobic Exercise in Patients with Early-Onset Dementia: A Scoping Review', Dementia and Geriatric Cognitive Disorders, 50(1), pp. 1–8. Available at: .

26. Åstrand, P.-O. . and Ryhming, I. (1954) 'A Nomogram for Calculation of Aerobic Capacity (Physical Fitness) From Pulse Rate During Submaximal Work', *Journal of Applied Physiology*, 7(2), pp. 218–221. Available at: https://doi.org/10.1152/jappl.1954.7.2.218.

27. Migueles, J.H., Cadenas-Sanchez, C., Rowlands, A.V., Henriksson, P., Shiroma, E.J., Acosta, F.M., Rodriguez-Ayllon, M., Esteban-Cornejo, I., Plaza-Florido, A., Gil-Cosano, J.J., Ekelund, U., van Hees, V.T. and Ortega, F.B. (2019) 'Comparability of accelerometer signal aggregation metrics across placements and dominant wrist cut points for the assessment of physical activity in adults', Scientific Reports, 9(1). Available at: https://doi.org/10.1038/s41598-019-54267-y.

28. van Hees, V.T., Fang, Z., Langford, J., Assah, F., Mohammad, A., da Silva, I.C.M., Trenell, M.I., White, T., Wareham, N.J. and Brage, S. (2014) 'Autocalibration of accelerometer data for free-living physical activity assessment using local gravity and temperature: an evaluation on four continents', Journal of Applied Physiology, 117(7), pp. 738–744. Available at: https://doi.org/10.1152/japplphysiol.00421.2014.

29. Buchan, D.S. (2021) 'Equivalence of activity outcomes derived from three research grade accelerometers worn simultaneously on each wrist', Journal of Sports Sciences, pp. 1–11. Available at: https://doi.org/10.1080/02640414.2021.2019429. priority_highVolume numberclosepriority_highIssue numberclose

30. van Hees, V.T., Gorzelniak, L., Dean León, E.C., Eder, M., Pias, M., Taherian, S., Ekelund, U., Renström, F., Franks, P.W., Horsch, A. and Brage, S. (2013) 'Separating Movement and Gravity Components in an Acceleration Signal and Implications for the Assessment of Human Daily Physical Activity', PLoS ONE. Edited by M. Müller, 8(4), p. e61691. Available at: https://doi.org/10.1371/journal.pone.0061691.

31. Bakrania, K., Edwardson, C.L., Bodicoat, D.H., Esliger, D.W., Gill, J.M.R., Kazi, A., Velayudhan, L., Sinclair, A.J., Sattar, N., Biddle, S.J.H., Khunti, K., Davies, M. and Yates, T. (2015) 'Associations of mutually exclusive categories of physical activity and sedentary time with markers of cardiometabolic health in English adults: a cross-sectional analysis of the Health Survey for England', BMC Public Health, 16(1). Available at: https://doi.org/10.1186/s12889-016-2694-9.

32. HILDEBRAND, M., VAN HEES, V.T., HANSEN, B.H. and EKELUND, U. (2014) 'Age Group Comparability of Raw Accelerometer Output from Wrist- and Hip-Worn Monitors', Medicine & Science in Sports & Exercise, 46(9), pp. 1816–1824. Available at: https://doi.org/10.1249/mss.0000000000000289.

33. van Hees, V.T., Sabia, S., Jones, S.E., Wood, A.R., Anderson, K.N., Kivimäki, M., Frayling, T.M., Pack, A.I., Bucan, M., Trenell, M.I., Mazzotti, D.R., Gehrman, P.R., Singh-Manoux, B.A. and Weedon, M.N. (2018) 'Estimating sleep parameters using an accelerometer without sleep diary', Scientific Reports, 8(1). Available at: https://doi.org/10.1038/s41598-018-31266-z.

34. Buchan, D.S. (2024) 'Comparison of Sleep and Physical Activity Metrics From Wrist-Worn ActiGraph wGT3X-BT and GT9X Accelerometers During Free-Living in Adults', Journal for the Measurement of Physical Behaviour, 7(1). Available at: https://doi.org/10.1123/jmpb.2023-0026.

35. Migueles, J.H., Cadenas-Sanchez, C., Ekelund, U., Delisle Nyström, C., Mora-Gonzalez, J., Löf, M., Labayen, I., Ruiz, J.R. and Ortega, F.B. (2017) 'Accelerometer Data Collection and Processing Criteria to Assess Physical Activity and Other Outcomes: A Systematic Review and Practical Considerations', Sports Medicine, 47(9), pp. 1821–1845. Available at: https://doi.org/10.1007/s40279-017-0716-0.

36. Hurlbert, S.H., Levine, R.A. and Utts, J. (2019) 'Coup de Grâce for a Tough Old Bull: "Statistically Significant" Expires', The American Statistician, 73(sup1), pp. 352–357. Available at: https://doi.org/10.1080/00031305.2018.1543616.

37. Di Lenarda, L., Buoite Stella, A., Ratti, C., Ruggiero, L., Bernard, M., Cavarzerani, L.P., Canton, G. and Murena, L. (2024) 'Assessing Muscle Mass in the Orthopedic Clinical Setting: Application of the Ultrasound Sarcopenia Index in Elderly Subjects with a Recent Femoral Fracture', Nutrients, 16(5), p. 711. Available at: https://doi.org/10.3390/nu16050711.

38. McLaughlin, M., Nilihan E. M. Sanal-Hayes, Hayes, L.D., Berry, E.W. and Sculthorpe, N. (2023) 'People With Long COVID and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) Exhibit Similarly Impaired Vascular Function', The American Journal of Medicine [Preprint]. Available at: https://doi.org/10.1016/j.amjmed.2023.09.013.

39. Lakens, D. (2013) 'Calculating and reporting effect sizes to facilitate cumulative science: A practical primer for t-tests and ANOVAs', Frontiers in Psychology, 4(863). Available at: https://doi.org/10.3389/fpsyg.2013.00863.

40. Drummond, G.B. and Vowler, S.L. (2012) 'Do as you would be done by: write as you would wish to read', The Journal of Physiology, 590(24), pp. 6251–6254. Available at: https://doi.org/10.1113/jphysiol.2012.248278.

41. Drummond, G. and Vowler, S. (2011) 'Show the data, don't conceal them', British Journal of Pharmacology, 163(2), pp. 208–210. Available at: https://doi.org/10.1111/j.1476-5381.2011.012.

42. Mpampoulis, T., Methenitis, S., Papadopoulos, C., Papadimas, G., Spiliopoulou, P., Stasinaki, A.-N., Bogdanis, G.C., Karampatsos, G. and Terzis, G. (2021) 'Weak Association between

Vastus Lateralis Muscle Fiber Composition and Fascicle Length in Young Untrained Females', *Sports*, 9(5), p. 56. Available at: https://doi.org/10.3390/sports9050056.

43. Beck, O.N., Trejo, L.H., Schroeder, J.N., Franz, J.R. and Sawicki, G.S. (2022) 'Shorter muscle fascicle operating lengths increase the metabolic cost of cyclic force production', *Journal of Applied Physiology*, 133(3), pp. 524–533. Available at: https://doi.org/10.1152/japplphysiol.00720.2021.

44. Narici, M., McPhee, J., Conte, M., Franchi, M.V., Mitchell, K., Tagliaferri, S., Monti, E., Marcolin, G., Atherton, P.J., Smith, K., Phillips, B., Lund, J., Franceschi, C., Maggio, M. and Butler-Browne, G.S. (2021) 'Age-related alterations in muscle architecture are a signature of sarcopenia: the ultrasound sarcopenia index', *Journal of Cachexia, Sarcopenia and Muscle* [Preprint]. doi:https://doi.org/10.1002/jcsm.12720.

45. Baroni, B.M., Geremia, J.M., Rodrigues, R., De Azevedo Franke, R., Karamanidis, K. and Vaz, M.A. (2013) 'Muscle architecture adaptations to knee extensor eccentric training: Rectus femoris vs. vastus lateralis', *Muscle & Nerve*, 48(4), pp. 498–506. Available at: https://doi.org/10.1002/mus.23785.

46. BLAZEVICH, A.J. and GIORGI, A. (2001) 'Effect of testosterone administration and weight training on muscle architecture', *Medicine & Science in Sports & Exercise*, 33(10), pp. 1688–1693. Available at: https://doi.org/10.1097/00005768-200110000-00012.

47. Erskine, R.M., Jones, D.A., Williams, A.G., Stewart, C.E. and Degens, H. (2010) 'Inter-individual variability in the adaptation of human muscle specific tension to progressive resistance training', *European journal of applied physiology*, 110(6), pp. 1117–25. Available at: https://doi.org/10.1007/s00421-010-1601-9.

48. Potier, T.G., Alexander, C.M. and Seynnes, O.R. (2009) 'Effects of eccentric strength training on biceps femoris muscle architecture and knee joint range of movement', *European Journal of Applied Physiology*, 105(6), pp. 939–944. Available at: https://doi.org/10.1007/s00421-008-0980-7.

49. Park, J.H., Moon, J.H., Kim, H.J., Kong, M.H. and Oh, Y.H. (2020) 'Sedentary lifestyle: Overview of Updated Evidence of Potential Health Risks', *Korean Journal of Family Medicine*, 41(6), pp. 365–373. Available at: https://doi.org/10.4082/kjfm.20.0165.

50. Long, A., Di Lorito, C., Logan, P., Booth, V., Howe, L., Hood-Moore, V. and van der Wardt, V. (2020) 'The Impact of a Dementia-Friendly Exercise Class on People Living with

Dementia: A Mixed-Methods Study', *International Journal of Environmental Research and Public Health*, 17(12), p. 4562. Available at: https://doi.org/10.3390/ijerph17124562.

51. Chudasama, Y.V., Khunti, K.K., Zaccardi, F., Rowlands, A.V., Yates, T., Gillies, C.L., Davies, M.J. and Dhalwani, N.N. (2019) 'Physical activity, multimorbidity, and life expectancy: a UK Biobank longitudinal study', *BMC Medicine*, 17(1). Available at: https://doi.org/10.1186/s12916-019-1339-0.

52. Bye, A., Røsjø, H., Aspenes, S.T., Condorelli, G., Omland, T. and Wisløff, U. (2013) 'Circulating MicroRNAs and Aerobic Fitness – The HUNT-Study', *PLoS ONE*. Edited by M. Fehlings, 8(2), p. e57496. Available at: https://doi.org/10.1371/journal.pone.0057496.

53. Kodama, S. (2009) 'Cardiorespiratory Fitness as a Quantitative Predictor of All-Cause Mortality and Cardiovascular Events in Healthy Men and Women', JAMA, 301(19), p. 2024. Available at: https://doi.org/10.1001/jama.2009.681.

54. Brain, J., Greene, L., Tang, E.Y.H., Louise, J., Salter, A., Beach, S., Turnbull, D., Siervo, M., Stephan, B.C.M. and Tully, P.J. (2023) 'Cardiovascular disease, associated risk factors, and risk of dementia: An umbrella review of meta-analyses', *Frontiers in Epidemiology*, 3. Available at: https://doi.org/10.3389/fepid.2023.1095236.

55. Casla, S., López-Tarruella, S., Jerez, Y., Marquez-Rodas, I., Galvão, D.A., Newton, R.U., Cubedo, R., Calvo, I., Sampedro, J., Barakat, R. and Martín, M. (2015) 'Supervised physical exercise improves VO2max, quality of life, and health in early stage breast cancer patients: a randomized controlled trial', *Breast Cancer Research and Treatment*, 153(2), pp. 371–382. Available at: https://doi.org/10.1007/s10549-015-3541-x.

56. Strasser, B. and Burtscher, M. (2018) 'Survival of the fittest: VO2max, a key predictor of longevity?', *Frontiers in Bioscience*, 23(8), pp. 1505–1516. Available at: https://doi.org/10.2741/4657.

57. Garg, P.K., Tan, A.X., Odden, M.C., Gardin, J.M., Lopez, O.L., Newman, A.B., Rawlings, A.M. and Mukamal, K.J. (2020) 'Brachial Flow-mediated Dilation and Risk of Dementia', *Alzheimer Disease & Associated Disorders*, 34(3), pp. 272–274. Available at: https://doi.org/10.1097/wad.000000000000394.

58. Tachibana, H., Washida, K., Kowa, H., Kanda, F. and Toda, T. (2016) 'Vascular Function in Alzheimer's Disease and Vascular Dementia', *American Journal of Alzheimer's Disease & Other Dementiasr*, 31(5), pp. 437–442. Available at: https://doi.org/10.1177/1533317516653820.

59. Tsao, C.W., Seshadri, S., Beiser, A.S., Westwood, A.J., DeCarli, C., Au, R., Himali, J.J., Hamburg, N.M., Vita, J.A., Levy, D., Larson, M.G., Benjamin, E.J., Wolf, P.A., Vasan, R.S. and Mitchell, G.F. (2013) 'Relations of arterial stiffness and endothelial function to brain aging in the community', *Neurology*, 81(11), pp. 984–991. Available at: https://doi.org/10.1212/wnl.0b013e3182a43e1c.

60. Waite, S.J., Maitland, S., Thomas, A. and Yarnall, A.J. (2021) 'Sarcopenia and frailty in individuals with dementia: A systematic review', *Archives of Gerontology and Geriatrics*, 92, p. 104268. Available at: https://doi.org/10.1016/j.archger.2020.104268.

61. Xiao, T., Wijnant, S.R.A., Licher, S., Terzikhan, N., Lahousse, L., Ikram, M.K., Brusselle, G.G. and Ikram, M.A. (2021) 'Lung Function Impairment and the Risk of Incident Dementia: The Rotterdam Study', *Journal of Alzheimer's Disease*, 82(2), pp. 621–630. Available at: https://doi.org/10.3233/jad-210162.

62. Alencar, M.A., Dias, J.M.D., Figueiredo, L.C. and Dias, R.C. (2012) 'Handgrip strength in elderly with dementia: study of reliability', *Brazilian Journal of Physical Therapy*, 16, pp. 510–514. doi:10.1590/S1413-35552012005000059.

63. Vermeulen, J., Neyens, J.C., Spreeuwenberg, M.D., van Rossum, E., Boessen, A.B., Sipers, W. and de Witte, L.P. (2015) 'The Relationship Between Balance Measured With a Modified Bathroom Scale and Falls and Disability in Older Adults: A 6-Month Follow-Up Study', *Journal of Medical Internet Research*, 17(5), p. e131. Available at: https://doi.org/10.2196/jmir.3802.

64. Toots, A., Wiklund, R., Littbrand, H., Nordin, E., Nordström, P., Lundin-Olsson, L., Gustafson, Y. and Rosendahl, E. (2019) 'The Effects of Exercise on Falls in Older People With Dementia Living in Nursing Homes: A Randomized Controlled Trial', *Journal of the American Medical Directors Association*, 20(7), pp. 835-842.e1. Available at: https://doi.org/10.1016/j.jamda.2018.10.009.

65. Chen, Y., Hou, L., Li, Y., Lou, Y., Li, W., Struble, L.M. and Yang, H. (2023) 'Barriers and motivators to promotion of physical activity participation for older adults with mild cognitive impairment or dementia: An umbrella
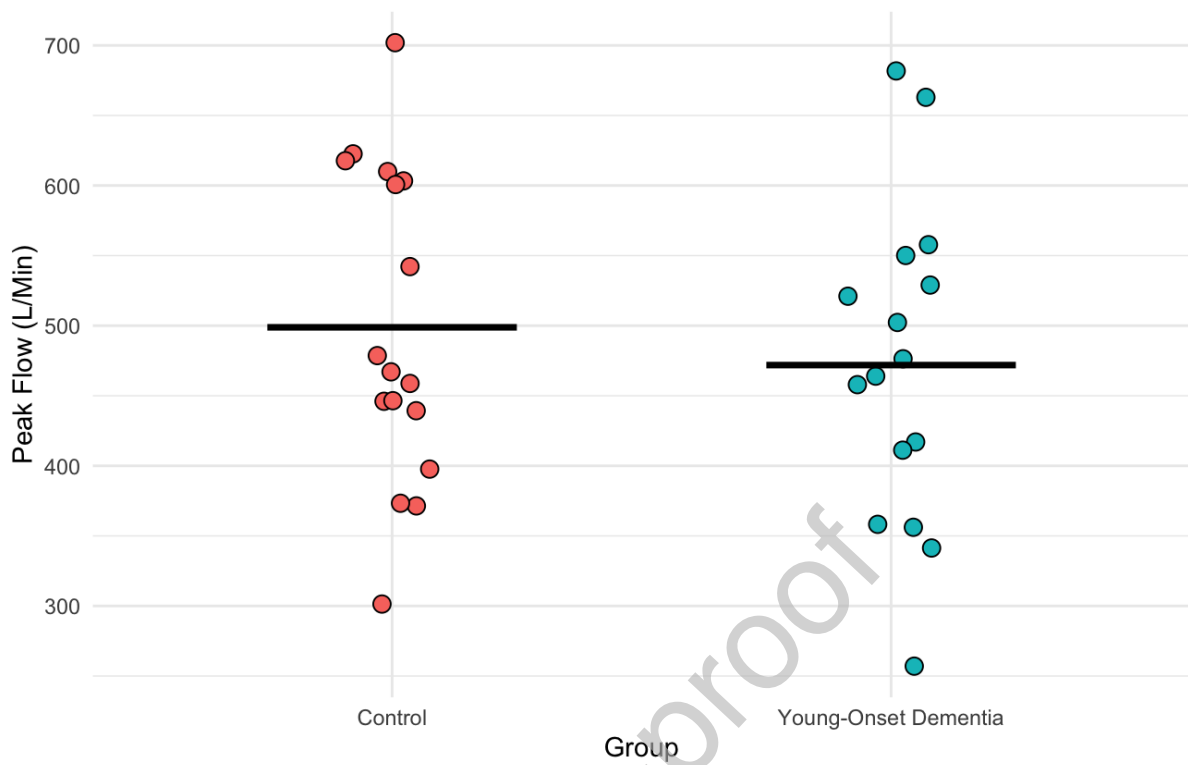
review', *International Journal of Nursing Studies*, p. 104493. Available at: https://doi.org/10.1016/j.ijnurstu.2023.104493.

66. Baptista, M.A.T., Santos, R.L., Kimura, N., Lacerda, I.B., Johannenssen, A., Barca, M.L., Engedal, K. and Dourado, M.C.N. (2016) 'Quality of life in young onset dementia: an updated systematic review', *Trends in Psychiatry and Psychotherapy*, 38(1), pp. 6–13. doi:10.1590/2237-6089-2015-0049

Figure 1. Estimated VO$_{2max}$ data from people with young onset dementia (Young onset dementia; n = 16) and controls (n = 17) from a submaximal Astrand-Rhyming test. Data are presented as individual dot plots with accompanying mean line.
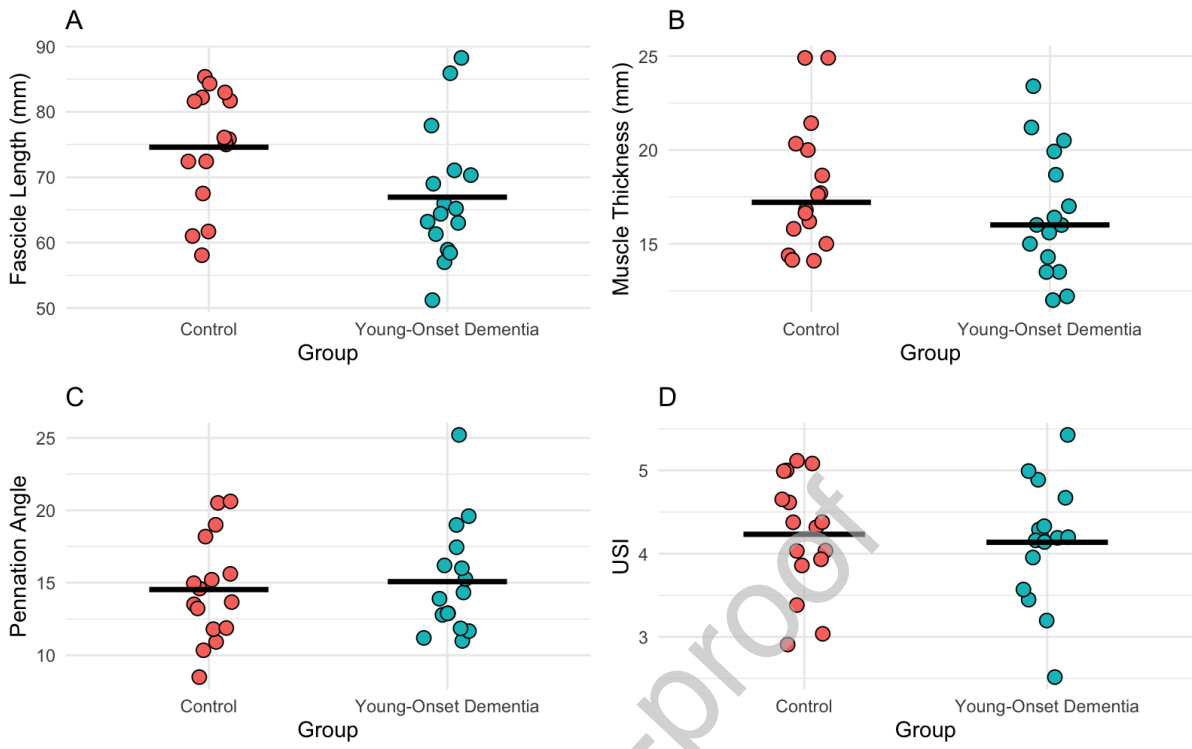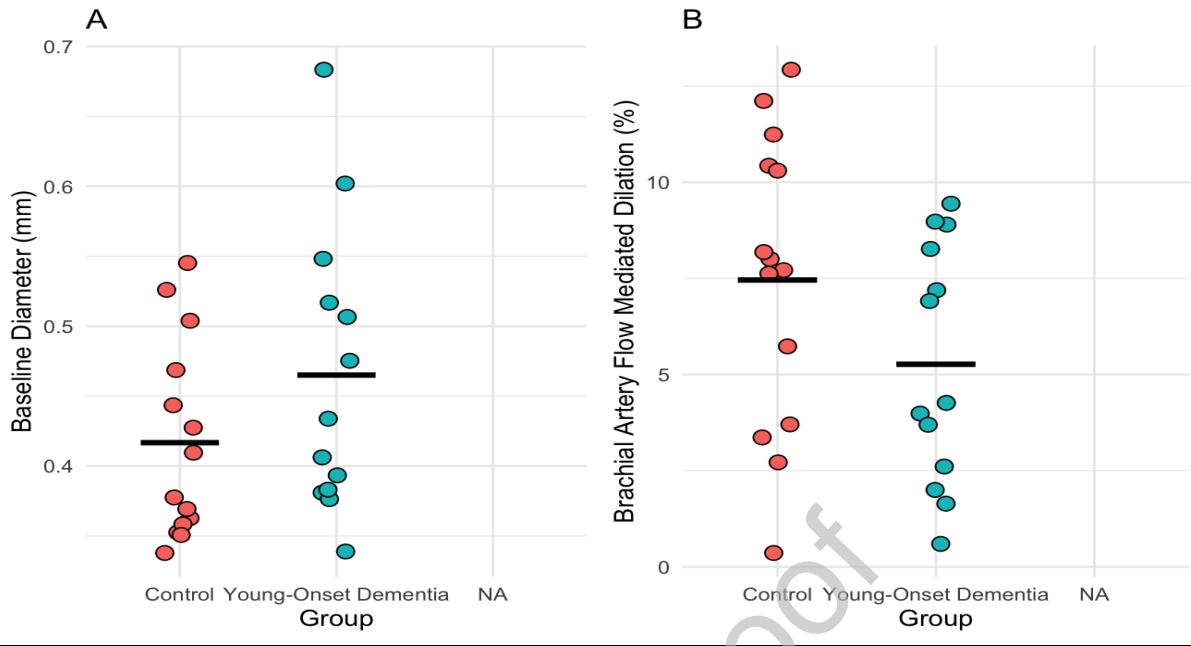
Figure 2. Peak flow data from people with young onset dementia (Young onset dementia; n = 16) and controls (n = 17). Data are presented as individual dot plots with accompanying mean line.
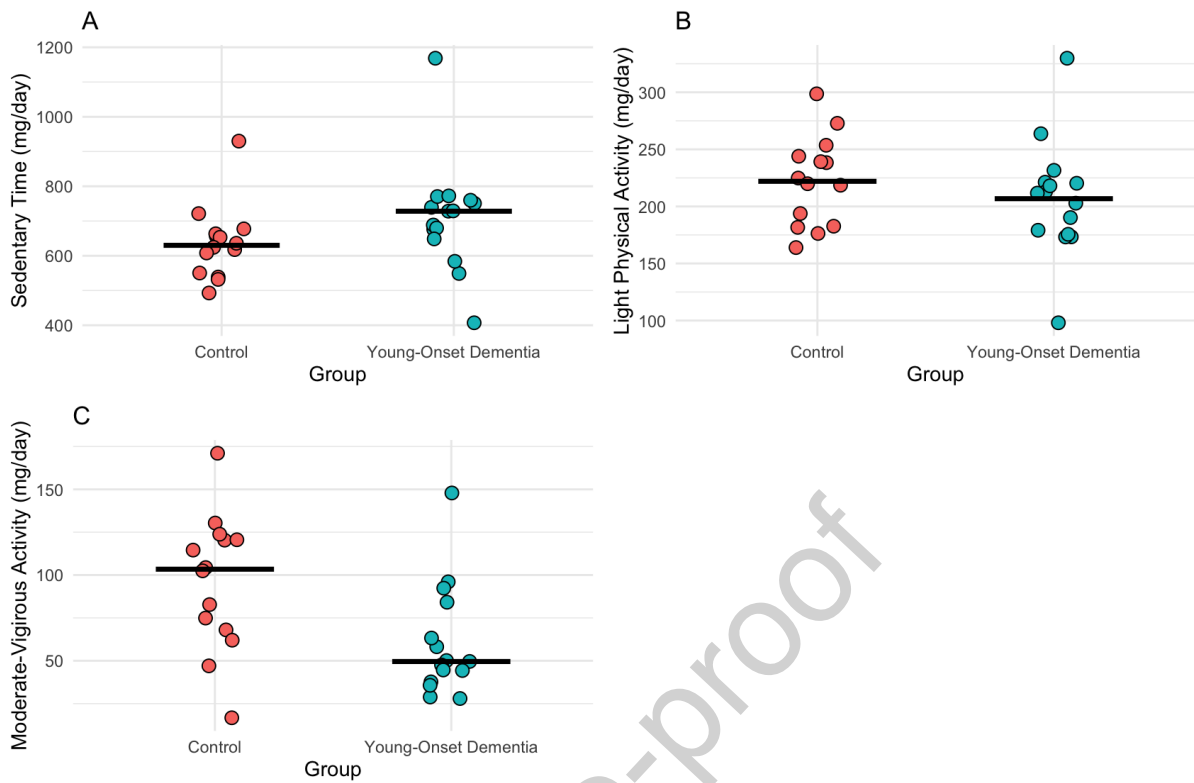
Figure 3. Physical activity parameters from people with young onset dementia (Young onset dementia; n = 16) and controls (n = 17). Data are presented as individual dot plots with accompanying mean line (LPA and MVPA) and median line (sedentary time).
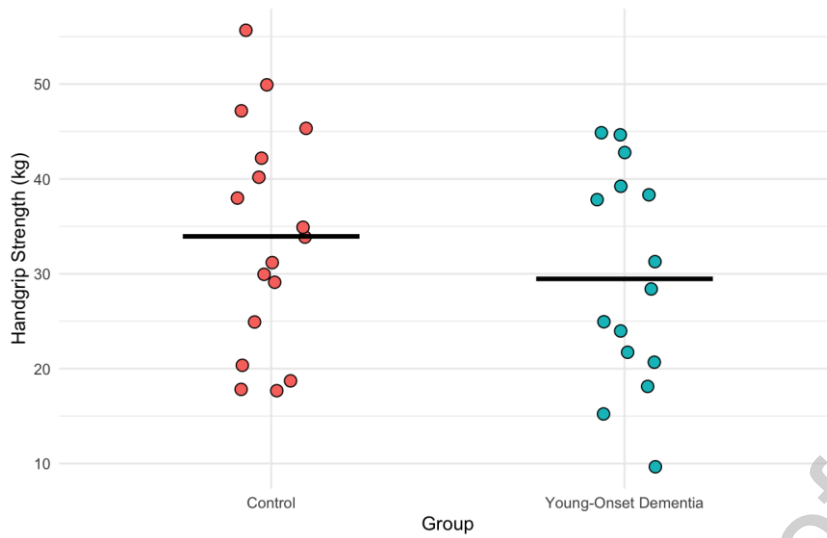
Figure 4. Muscle architecture parameters from people with young onset dementia (Young onset dementia; n = 16) and controls (n = 17). Data are presented as individual dot plots with accompanying mean line (fascicle length, pennation angle and USI) and median line (muscle thickness).

Figure 5. Endothelial function parameters from people with young onset dementia (Young onset dementia; n = 16) and controls (n = 17). Data are presented as individual dot plots with accompanying mean line.

Figure 6. Handgrip strength data from people with young onset dementia (Young onset dementia; n = 16) and controls (n = 17). Data are presented as individual dot plots with accompanying mean line.

Table 1: Descriptive data of participants at enrolment.

Variable	Group	Mean ± SD	T-test p value and Cohen's *d*
Age (years)	Young onset dementia (n = 16)	60 ± 7	p=0.577 *d*= 0.20
	Control (n= 17)	58 ± 10	
Stature (cm)	Young onset dementia (n = 16)	167 ± 7	p=0.487 *d*=0.25
	Control (n= 17)	169 ± 7	
Body Mass (kg)	Young onset dementia (n = 16)	79.2 ± 16.5	p=0.501 *d*=0.24
	Control (n= 17)	83.6 ± 20.9	
Body Mass Index (kg/m^2)	Young onset dementia (n = 16)	28.1 ± 4.9	p=0.631 *d*=0.17
	Control (n= 17)	29 ± 6	
Systolic blood pressure (mmHg)	Young onset dementia (n = 16)	150 ± 19	p=0.365 *d*=0.32
	Control (n= 17)	143 ± 24	
Diastolic blood pressure (mmHg)	Young onset dementia (n = 16)	83 ± 9	p=0.465 *d*=0.26
	Control (n= 17)	81 ± 10	
Resting Heart Rate (bpm)	Young onset dementia (n = 16)	76 ± 11	p=0.751 *d*=0.17

	Control (n= 17)	75 ± 15	