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Title

Assessing frailty in clinical trials for dementia or cognitive impairment

Priority 1 (Research Category)

Geriatrics

Presenters

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Abstract

Context: Frailty is a state in which physiological reserve is depleted across multiple systems, leading to an increased risk of decompensation in response to stressor events. Frailty is a risk factor for dementia and complicates its management. However, frailty is rarely reported in clinical trials for dementia and mild cognitive impairment (MCI) which limits assessment of trial applicability. Objective: This analysis will assess the feasibility of using a frailty index (FI) and individual participant data (IPD) to measure frailty in clinical trials for MCI and dementia. It will assess the prevalence of frailty and its association with serious adverse events (SAEs) and trial attrition. Study design: Secondary analysis of IPD from randomised controlled trials. Dataset: IPD from trials for dementia (n=1) or MCI (n=2). Population: Trial participants were analysed at baseline (dementia trial n=408, MCI trials n=987 and n=1064). Instrument: Two FIs were created, one based exclusively on physical deficits, the other based on physical and cognitive deficits. Outcomes: Frailty prevalence (FI>0.24) was assessed along with the distribution of the FI in each trial. The relationship between FI and SAEs and trial attrition were assessed using Poisson and logistic regression, respectively. Estimates were pooled in random effects meta-analysis. Analyses were adjusted for age and sex. Results: The mean physical FI was 0.13 and 0.14 in the MCI trials and 0.25 in the dementia trial. Frailty prevalence (FI>0.24) was 5.1%, 5.4% in MCI trials and 55.6% in dementia. After including cognitive deficits, prevalence was similar in MCI (4.6% and 4.9%) but higher in dementia (80.7%). 99th percentile (0.29 in MCI, 0.44 in dementia) of FI was lower than in most general population studies. Frailty was associated with SAEs (physical FI IRR = 1.63 [1.43, 1.87]; physical/cognitive FI IRR = 1.67 [1.45, 1.93]). Frailty was not associated with trial attrition (physical FI OR = 1.18 [0.92, 1.53]; physical/cognitive FI OR = 1.17 [0.92, 1.49]). Conclusion: Measuring frailty from baseline IPD in dementia and MCI trials is feasible. Those living with more severe frailty may be under-represented. Frailty is associated with clinically significant outcomes. Including only physical deficits may underestimate frailty in dementia. Frailty can and should be measured in future and existing trials for dementia and MCI, and efforts should be made to facilitate inclusion of people living with frailty.