The multicausality of declines in wellbeing and cognition in older adults with multimorbidity

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We commend Wei-Ju Lee and colleagues for the TIGER study, published in *The Lancet Healthy Longevity*, which is a scientifically sound evaluation of a complex integrated care intervention to improve healthy ageing in older inhabitants of Taiwan with multiple chronic conditions.[1] The study embraces the value-based health care paradigm, which makes it relevant for the global aim of sustainable and cost-effective health care. 398 community-dwelling older adults (mean age 73·2 years [SD 6·3]; 60% female) with three or more chronic diseases participated in the study and were randomly assigned to the 12-month multidomain intervention (n=199) or to usual care (n=199). The intervention consisted of 16 sessions lasting 2 h each, with a combination of aerobic and non-aerobic exercise, cognitive training, and nutrition-related lifestyle education. Most participants had cardiovascular health problems. However, only 5% were current smokers and 9% used alcohol, which limited the room for improvement in lifestyle factors.

After only 12 months, the multidomain intervention group showed improvements in physical domain score and some mental subdomains of quality of life according to the 36-item Short Form Health Survey, with a clinically relevant improvement in physical role limitation score. Small but statistically significant improvements were also observed in some of the secondary outcomes, including some of the metrics of the International Consortium of Health Outcomes score (ICHOM; effect size 0·14) and the Montreal Cognitive Assessment battery (odds ratio 0·5, 95% CI 0·4–0·7). These small improvements hold promise of becoming clinically relevant if the intervention were to be implemented for a longer time.

This trial has some major strengths. First, the study was conducted at six sites across New Taipei City. Because only 26% declined to participate, the study seems to have been successful in including a representative sample of older community-dwelling inhabitants, despite their multimorbidity and the complexity of the intervention. Second, the researchers had the courage to use a value-based outcome (ICHOM). Although the ICHOM was specifically designed for evaluating interventions in older adults, it is hardly used in trials. Most older people with multimorbidity prioritise wellbeing over disease severity or biomarker outcomes. Therefore, this outcome choice is a best practice example. However, because wellbeing is not always closely related to the intervention target, it can be a more risky outcome for researchers to use (due to smaller anticipated effect sizes), which probably is the main reason for underuse of ICHOM. Moreover, underuse of ICHOM keeps it trapped in a vicious cycle of scarce validated data on responsiveness and minimal important change, which can only be reversed by increasing its use in trials. The promising TIGER results for some ICHOM outcomes advocate for prioritising and funding ICHOM (or similar wellbeing-related outcomes) as the primary outcome in future trials done in older people. Third, the light to moderate intensity of the intervention ensures feasibility of widespread roll-out given the limited costs, burden, and labour. Finally, incorporating the comprehensive geriatric assessment and management plan allowed genuine personalisation.

The study also has some weaknesses, which are understandable given the target population and the complex intervention. The blinding of participants is questionable because it fully depends on their own non-disclosure of their group assignment to other participants and researchers involved in data acquisition. This could have led to overestimation of the effects. The randomisation done at individual research sites carries the risk of contamination within each site, which could have led to underestimation of net effects. Unfortunately, the researchers do not present a process analysis, which obscures the role of the geriatric assessment in the intervention. Also, little information is provided on the usual care component. The slight improvements in the control group might reflect high quality usual care. The short intervals between assessments could have introduced repeat measurement bias, and multiple comparisons on the subscales of outcomes increase the risk of type I errors. The fact that all statistically significant outcomes are found in the same direction, however, increases confidence in the positive findings.

In summary, the positive findings of the TIGER study are clearly relevant in the search for effective interventions to improve quality of life and physical and mental functioning in older people with multimorbidity. So far, most randomised trials that evaluated the efficacy of multidomain preventive interventions targeting either multimorbidity[2,3] or cognitive functioning[4,5] have not shown positive effects. An exception is the FINGER trial in older people with elevated cardiovascular and cerebrovascular risk, which showed similar effect sizes (ie, 0·2) but with a longer intervention period.[6] The TIGER and FINGER studies clearly show the direction in which health care services could cost-effectively improve healthy ageing. A key element is targeting older adults with multiple health problems who receive inadequate care. This point might seem obvious but is probably the reason why some trials (eg, preDIVA) did not find positive effects in similar age groups with similar interventions. Next, multidomain interventions should activate physical and mental functions, improve self-management, and address vascular risk factors in a personalised manner. Such an intervention route is physiologically in line with the complexity of health in older people and the multiple interacting mechanisms of ageing that are responsible for most multimorbidity. An important challenge is to integrate these multicomponent interventions into routine clinical care. The FINGER study shows that this is possible, because this multicomponent intervention is now being implemented in community-based care in several parts of the world, but it requires adaptation to local health systems. To bridge the gap between the TIGER study and widespread roll-out, implementation studies are needed, similar to the FINGER study upscaling, to adapt the intervention to other health systems and patient populations. Feasibility, adherence, and benefits could differ from country to country, as we showed in the implementation of a multicomponent occupational therapy intervention for people with dementia across Europe.[7]

The fact that these multicomponent interventions are effective, including on those cognitive outcomes that have been shown to be more difficult to modify (delayed memory and executive functioning), is important supporting evidence for the multicausality of cognitive decline in older adults. This theory is strongly supported by a reduction of dementia incidence over the past 30 years evidenced in eight large studies across seven high-income countries (USA, UK, Germany, Spain, Sweden, France, and the Netherlands), and in the meta-analysis of Livingston and colleagues.[8] These researchers explained that the decrease is likely caused by improvement of multilevel, multiple lifestyle conditions (cardiovascular risks, education, nutrition, exercise, and working conditions) over decades, suggesting that various pathophysiological mechanisms are involved in causing dementia. Lee and colleagues built on these epidemiological studies and corroborated the overarching multicausality paradigm with use of the positive results from their complex multidomain study. This line of reasoning should be continued, because with the rise of comorbidity, quality of life is decreasing and costs of health care are rapidly increasing.[9,10]

We declare no competing interests.

*Marcel G M Olde Rikkert, G M E E (Geeske) Peeters
marcel.olderikkert@radboudumc.nl

Department of Geriatric Medicine, Radboudumc Alzheimer Centre, Radboud University Medical Center, Nijmegen 6500 HB, Netherlands

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