Community-based complex interventions to sustain independence in older people, stratified by frailty: a systematic review and network meta-analysis

Thomas Frederick Crocker,[1] Natalie Lam,[1] Joie Ensor,[2] Magda Jordão,[1] Ram Bajpai,[2] Matthew Bond,[2] Anne Forster,[1] Richard D Riley,[2] Deirdre Andre,[3] Caroline Brundle,[1] Alison Ellwood,[1] John Green,[1] Matthew Hale,[1] Jessica Morgan,[4] Eleftheria Patetsini,[1] Matthew Prescott,[1] Ridha Ramiz,[1] Oliver Todd,[1] Rebecca Walford,[4] John Gladman[5] and Andrew Clegg[1*]

[1]Academic Unit for Ageing and Stroke Research (University of Leeds), Bradford Institute for Health Research, Bradford Teaching Hospitals NHS Foundation Trust, Bradford, UK
[2]Centre for Prognosis Research, Keele School of Medicine, Keele University, Keele, Staffordshire, UK
[3]Research Support Team, Leeds University Library, University of Leeds, Leeds, West Yorkshire, UK
[4]Geriatric Medicine, Bradford Teaching Hospitals NHS Foundation Trust, Bradford, UK
[5]Centre for Rehabilitation & Ageing Research, Academic Unit of Injury, Inflammation and Recovery Sciences, University of Nottingham and Health Care of Older People, Nottingham University Hospitals NHS Trust, Nottingham, UK

[*]Corresponding author a.p.clegg@leeds.ac.uk

Scientific summary

Community-based complex interventions to sustain independence in older people, stratified by frailty: a systematic review and network meta-analysis

Scientific summary

Background

The number and proportion of older people are growing in the UK and worldwide. Maintaining independence is a goal of community health and care services for older people. The concept of frailty can be used to distinguish between people who remain in robust health in later life and those who are at greater risk of losing independence and needing care. Previous research has suggested that community-based complex interventions are generally effective for supporting independence for older people, but only broad service models have been explored. There is insufficient guidance about which services to implement and the appropriateness of different services for different levels of frailty. We aimed to provide a rigorous, contemporary synthesis of trial evidence to identify how interventions might best be configured to improve outcomes for older people, and inform the commissioning and delivery of evidence-based services.

Objectives (list of research questions)

1. Do community-based complex interventions to sustain independence in older people increase living at home, independence and health-related quality of life?
2. Do community-based complex interventions to sustain independence in older people reduce home-care usage, depression, loneliness, falls, hospitalisation, care-home placement, costs and mortality?
3. How should interventions be grouped for network meta-analysis (NMA)?
4. What is the optimal configuration of community-based complex interventions to sustain independence in older people?
5. Do intervention effects differ by a population's frailty level (robust; pre-frailty; frailty)?

Methods

Systematic review with NMA of trials evaluating community-based complex interventions to sustain independence in older people (mean age 65 years and over), compared with usual care or another complex intervention meeting our criteria, with follow-up for at least 24 weeks. We followed Cochrane methods, Grading of Recommendations Assessment, Development and Evaluation (GRADE) and Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) NMA guidance.

Information sources
We searched the following databases and trial registers from inception between 9 and 11 August 2021: Cochrane Central Register of Controlled Trials (CENTRAL) Wiley (1992–); MEDLINE Ovid (1946–); Embase and Embase Classic Ovid (1947–); CINAHL EBSCOhost (1972–); APA PsycINFO Ovid (1806–); US National Institutes of Health Ongoing Trials Register, ClinicalTrials.gov (www.clinicaltrials.gov); World Health Organization, International Clinical Trials Registry Platform (https://trialsearch.who.int). We scanned the reference lists of included studies.

Study selection

Eligibility criteria

- Randomised controlled trials (RCTs) or cluster-RCTs.

- Participants were older people living at home (mean age 65 years or older). Participants living in residential/nursing homes were excluded.
- With an intervention that:
  ◦ was both initiated and mainly provided in the community
  ◦ included two or more interacting components (intervention practices, structural elements and contextual factors)
  ◦ was targeted at the individual person, with provision of appropriate specialist care
  ◦ focused on sustaining (maintaining or improving) the person's independence.
- Usual care, 'placebo' or attention control or a different complex intervention which met our criteria were eligible comparators.
- Outcome data were measured at a minimum 24 weeks (approximately 6 months) time point.

Study selection process
Two researchers independently evaluated eligibility of records (title and abstract) and reports (full text). Disagreements were resolved by consensus.

Data collection process
Two researchers independently collected data.

Main outcomes

- Living at home.
- Activities of daily living (ADL): personal ADL (PADL)/instrumental ADL (IADL).
- Hospitalisation.
- Care-home placement.
- Homecare services (non-healthcare professional) usage.
- Costs.
- Cost-effectiveness.

Additional outcomes

- Health status/health-related quality of life.
- Depression.
- Loneliness.
- Falls.
- Mortality.

Data were extracted (including treatment effect estimates) and categorised into three time frames:

- short term (around 6 months): 24 weeks to 9 months
- medium term (around 12 months): > 9 months to 18 months
- long term (around 24 months): > 18 months

with the medium term as our main time frame.

Intervention grouping
We grouped all eligible interventions (including comparators) in preparation for NMA in a three-stage process of coding and summarising based on the Template for Intervention Description and Replication framework, categorisation and grouping.

Assessment of frailty

Two reviewers with extensive clinical academic frailty expertise (AC and JG) independently categorised study level frailty (robust, pre-frailty, frailty) based on validated measures where available or participant characteristics and study inclusion criteria using the phenotype model as a framework.

Risk-of-bias assessment

Two reviewers independently assessed risk of bias (RoB) in each result of interest from each included study, using the Revised Cochrane risk-of-bias tool for randomised trials (RoB 2).

Data synthesis

Meta-analysis was conducted for living at home, PADL, IADL and care-home placement for each of the three time frames separately, and for hospitalisation, health status and depression in the medium term only. Other outcomes were narratively synthesised.

Meta-analysis

We meta-analysed the extracted effect estimates using modules within Stata. Random-effects meta-analyses were conducted.

Initially, for each outcome and time frame, we performed a separate meta-analysis for each type of intervention versus control, to provide summary effectiveness results based only on direct evidence.

An NMA was then conducted (for each outcome and time frame separately) using a multivariate random-effects meta-analysis framework via the network module in Stata using restricted maximum likelihood estimation. We produced summary (pooled) effect estimates for each pair of treatments in the network, with 95% confidence intervals (CIs). Based on the results, the ranking of intervention groups was calculated using resampling methods.

The consistency assumption (that direct and indirect evidence are consistent with each other) was examined for each treatment comparison where possible and across the whole network.

The effect of study-level frailty on each intervention group effect was examined where data allowed. Sensitivity analyses were conducted excluding results at the highest RoB, and funnel plots examined for small-study effects.

Confidence in cumulative evidence

We used the GRADE framework, adapted for NMA, to rate the certainty of the results of our NMA.

Summary of economic evidence

We followed the brief economic commentary framework to summarise, compare and contrast the principal findings from the included studies.

Results

We screened 40,112 records and assessed 973 reports for eligibility. We included 129 studies consisting of 496 reports.

The studies assigned 74,946 participants (three studies missing data) to 266 eligible intervention arms. They were predominantly conducted in developed countries and most participants were described as white. Nonetheless, the overall population included a broad range of demographic characteristics. Study populations included all frailty levels.

We identified 19 separate components of included interventions which were evaluated in 63 combinations including the absence of all of these components, which we termed available care (ac), and homecare (a common control group in populations where all participants were receiving homecare). Homecare involved frequent visits at home by professionals who typically supported domestic and self-care tasks. Five components were primarily about a process of ascertainment or assessment and planning with subsequent action: **multifactorial-action** from care planning (a process of individualised multidomain assessment and management) with or without routine **review** (scheduled, regular follow-ups), **medication-review**, **monitoring** and routine **risk-screening**. The 14 other components and their short labels (bold) were **ADL** training, providing **aids** and adaptations, **alternative medicine**, **care voucher** provision, **cognitive training**, health **education**, physical **exercise**, formal **homecare**, engagement in **meaningful-activities**, **nutrition**al support, psychological (mood) therapy (**psychology**), **social skills** training, technology for communication and engagement (**telecoms**), **welfare** rights advice. Multifactorial-action was further delineated based on the presence or absence of an embedded medication-review and specific self-management strategies.

We judged most results to be at high RoB, primarily due to missing outcome data. This led to serious concerns with RoB for many of the GRADE ratings of evidence.

Findings

Most networks were small and sparse, with few included studies contributing to most networks. We found little evidence of inconsistency but there was usually low power to detect this. All outcomes except mortality needed to be analysed in two separate NMAs as the networks were disconnected: one with ac as the reference comparator ('available-care network') and one with homecare as the reference comparator ('homecare network'). Estimates are reported here only in comparison with the reference comparator. Comparisons with ac can be thought of as the effect of adding the intervention for a population who are not all receiving any particular care; comparisons with homecare are similarly an alternative intervention for a population already in receipt of homecare without associated reablement or multifactorial-action from care planning. Most estimates were low certainty or very low certainty due to RoB, imprecision or their combination, and we do not describe very low-certainty evidence below.

Living at home

For living at home in the medium term there were 21 studies (n = 16,937) with 14 intervention groups in the available-care network. There was moderate-certainty evidence that multifactorial-action and review with medication-review probably results in a slight increase in the chance of living at home [odds ratio (OR) 1.22, 95% CI 0.93 to 1.59; moderate certainty]. There was low-certainty evidence that multifactorial-action with medication-review [OR 2.55 (large), 95% CI 0.61 to 10.60]; cognitive training, medication-review, nutrition and exercise [OR 1.93 (large), 95% CI 0.79 to 4.77]; and ADL, nutrition and exercise [OR 1.79 (large), 95% CI 0.67 to 4.76] may result in an increase in the chance of living at home, and that risk-screening; education, multifactorial-action and review with medication-review; and education, multifactorial-action and review with medication-review and self-management may each result in some reduction in chance of living at home. Other comparisons with ac were of very low certainty.

In the short- and long-term time frames, results were at best low certainty. For multifactorial-action and review with medication-review; and ADL, nutrition and exercise, estimates were similarly of small increases in the long term but of little to no difference in the short term. There were similar results in other time frames for education, multifactorial-action and review with medication-review and self-management; and risk-screening, but contrasting evidence of reduction followed by an increase in living at home for education, multifactorial-action and review with medication-review.

The homecare network for living at home was smaller (five studies, n = 1978 in the medium term). In the short- and medium-term time frames, there was low-certainty evidence that homecare, ADL,

multifactorial-action and review with self-management may result in a moderate or large reduction in the chance of living at home compared with homecare alone.

Instrumental activities of daily living

For the medium-term instrumental activities of daily living (IADL) available-care network there were 16 studies (*n* = 5309) with 14 intervention groups. Multifactorial-action and review with medication-review was associated with very slightly increased independence in IADL versus ac [standardised mean difference (SMD) 0.11, 95% CI 0.00 to 0.21; moderate-certainty evidence]. Two intervention groups may result in some reduction in IADL: ADL, aids and exercise; and ADL, aids, education, exercise, multifactorial-action and review with medication-review and self-management.

There were contrasting findings for multifactorial-action and review with medication-review in the long term, with moderate-certainty evidence of a very slight reduction in IADL (SMD −0.08, 95% CI −0.21 to 0.05).

For the homecare network, there was one low certainty finding in the short-term time frame of little to no difference for homecare, ADL, multifactorial-action and review with self-management with all other estimates being very low certainty.

Personal activities of daily living

For personal activities of daily living (PADL), 20 trials (*n* = 8583 participants) with 16 intervention groups contributed to the medium-term available-care network. One comparison was judged low certainty. Exercise, multifactorial-action and review with medication-review and self-management may result in a very slight increase in PADL (SMD 0.16, 95% CI −0.51 to 0.82).

The homecare network included four trials (*n* = 632 participants) in the medium term. As for ac, only one comparison with homecare was low certainty: homecare, multifactorial-action and review with medication-review may result in an increase in PADL [SMD 0.60 (moderate), 95% CI 0.32 to 0.88].

Other outcomes

For the service outcome of hospitalisation, there were low-certainty estimates of some reductions for education, exercise, multifactorial-action and review with medication-review and self-management; and education, multifactorial-action and review with medication-review; and of an increase for exercise, multifactorial-action and review with medication-review and self-management. For care-home placement, all estimates were rated very low certainty in the medium term. There was some evidence of both increases and decreases in use of homecare services with little pattern (not meta-analysed).

For our additional outcomes, there was little evidence of any effect on self-reported health status, only low certainty beneficial findings regarding depression, very little evidence regarding loneliness and more complex interventions were associated with less falling than more falling (12 studies vs. 4 studies). For mortality, there was a large network of 65 studies (*n* = 38,351) and 41 intervention groups. There was low-certainty evidence of reductions for two, and increases for five, intervention groups.

The summary of economic evidence included 39 studies. Based on the conclusions of 22 studies that performed a full economic evaluation, five intervention groups appeared promising compared with a standard intervention or ac from an economic perspective: ADL (medium-term time horizon); homecare, multifactorial-action and review with medication-review and self-management (short-term time horizon); meaningful-activities and education (short- and medium-term time horizon); multifactorial-action and review with medication-review (short- but not medium- or long-term time horizon); and exercise and multifactorial-action with medication-review (long-term time horizon).

Summary across outcomes

We found evidence that multifactorial-action and review with medication-review probably improves some important outcomes slightly (living at home, IADL), but there was also contradictory evidence for IADL in the long term. For some other intervention groups there was low-certainty evidence that they may improve or worsen particular outcomes but for most intervention groups evidence was either absent or very uncertain.

Conclusions

Available evidence suggests the community-based complex interventions most likely to sustain independence in older people involve multifactorial-action from multidomain assessment and individualised care planning, routine review and the incorporation of medication-review. There was also some positive evidence for the combination of exercise and nutritional support and multiple other intervention combinations. Decision-makers should be aware that there is plausible evidence that some community-based complex interventions may worsen outcomes such as living at home and ADL independence and that all of these findings are tentative.

We recommend the uncertainty in these findings be addressed by:

1. realist synthesis to explore the mechanisms and broader contextual factors relating to individual benefit or harm
2. future robust, large-scale trials which compare alternative interventions with multifactorial-action and review with medication-review
3. future Individual Participant Data meta-analysis (IPDMA) focusing on interventions with multifactorial action to explore factors relating to individual benefit or harm
4. greater reporting of the organisational aspects of intervention implementation in complex intervention research.

Study registration

This study is registered as PROSPERO CRD42019162195.

Funding

Health Technology Assessment

> **Criteria for inclusion in the *Health Technology Assessment* journal**
> Manuscripts are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.
>
> Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

This article