Effectiveness of holistic assessment-based interventions in improving outcomes in adults with multiple long-term conditions and/or frailty

Review title

Effectiveness of holistic assessment-based interventions in improving outcomes in adults with multiple long-term conditions and/or frailty: an umbrella review protocol

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Declarations

None

Author contributions

41
42 SA, NL, AA, ML, LF, NM, SM and BG conceptualized the umbrella review. BG, SM, NL, ML and AA
43 secured funding. SA and BG developed the search strategy. SA and BG developed the first draft of
44 the manuscript; all co-authors contributed to the review and editing of the final manuscript.
45
46 **Conflict of interest**
47 Authors declare no conflict of interest
48

Abstract

Objective: This umbrella review aims to synthesize evidence on the effectiveness of holistic assessment-based interventions (HABIs) in improving health outcomes in adults (aged ≥ 18) with multiple long-term conditions (MLTCs) and/or frailty in community and hospital settings.

Introduction: Health systems need evidence-based, effective interventions to improve health outcomes for adults with MLTCs. Holistic assessment-based interventions are effective in older people admitted to the hospital (usually called Comprehensive Geriatric Assessment in that context) but the evidence that similar interventions are effective in the community is inconclusive.

Inclusion criteria: We will include systematic reviews published since 2010 in English which examine the effectiveness of community and/or hospital HABIs in improving health outcomes among community-dwelling and hospitalized adults aged ≥ 18 with MLTCs and/or frailty.

Methods: We will perform systematic searches in MEDLINE, EMBASE, PsycINFO, CINAHL Plus, Scopus, ASSIA, Cochrane Library, and TRIP Medical Database and manually search reference lists of included reviews for additional eligible reviews. Two reviewers will independently screen titles and abstracts for eligibility, and then screen potentially eligible full-texts against selection criteria. We will assess the methodological quality of included reviews using the JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses tool and extract data using an adapted and piloted JBI data extraction tool. The summary of findings will be presented in tabular form, with narrative descriptions and visual indications accompanying the tabulated results. The citation matrix will be generated and the corrected covered area calculated to analyze the overlap in primary studies included in reviews.

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Introduction

As the global population is ageing, the burden of multiple long-term conditions (MLTCs) is also on the rise.[1-5] An estimated 42% (95% CI 38.9%-46.0%) of the global adult population has MLTCs, with no significant difference in prevalence rates observed between low- or middle-income (36.8%) and high-income countries (44.3%). [2] In the US, around 32.9% of adults report receiving treatment for ≥2 long-term conditions in a single year, with 20.7% having ≥3 and 12.3% ≥4 long-term conditions. [3] The prevalence rates in the UK are around 23-27%, with higher rates observed among the elderly and the less affluent. [4-6] Over 60% of UK older adults (aged >65) are affected by MLTCs, [5,7] with predictions suggesting a doubling of rates of older people with ≥4 long-term conditions by 2035. [8]

MLTCs are associated with functional declines and contribute to frailty. [9, 10] Frailty is an age-related progressive decline in physiological reserves and functions across multiple organ systems, leading to a vulnerable state of health due to poor homeostatic resources. [11] An estimated 72% of people with frailty have MLTCs, and 16% of people with MLTCs are also frail. [9] Frailty is associated with decreased resistance to stressors, resulting in rapid changes in health status following a minor event. Frailty-related health deterioration may lead to the development of comorbidities and MLTCs. [9, 10]

People with MLTCs and/or frailty are at increased risk of adverse events including unscheduled hospital admissions, adverse drug events, and premature death. [1] This is, in part, because people with MLTCs and/or frailty require access to comprehensive care, but often experience single disease-oriented, fragmented, and poorly-coordinated care. [12] They often receive complex treatments resulting in polypharmacy, which puts them at risk for adverse drug events. [13] They often attend multiple appointments, self-manage their conditions, and adhere to lifestyle changes, resulting in a treatment burden. Given the presence of MLTCs is socially patterned, the effects are worse in adults from disadvantaged communities among whom earlier onset, more complex needs, [14] and higher treatment burden [15] are observed. The experiences and care needs of people with MLTCs are heterogeneous, which adds to the challenges of providing effective care.

MLTCs are one of the major challenges facing health services.[1, 13] Health systems urgently need evidence-based, effective interventions to improve health outcomes (e.g., quality of life, physical, mental and cognitive functions, outpatient and inpatient services utilization rates, treatment burden) for people with MLTCs and/or frailty who need additional support services. [12, 13, 16] Holistic assessment-based interventions (HABIs), which consider individuals' health, functional and social conditions, followed by the formulation of personalized care and follow-up plans, [17] are viewed as a promising model of care provision for this population. [4] Hospital HABIs are commonly used in geriatric practice with frail older adults, [4, 18] referred to as comprehensive geriatric assessment (CGA). [19] CGA is a form of integrated care delivered by a multidisciplinary team based on the holistic assessment of older people's unique needs in function, cognition, depression, nutrition, and medication use. [19] The Cochrane review on the effectiveness of CGA in the hospital setting found that initiating CGA on hospital admission increases the likelihood of older adults being alive and living in their homes

compared to those receiving standard care. [20] The UK NICE guidance on the management of MLTCs (2016) [4] suggests that community low-intensity HABI is effective in improving health outcomes in older adults (aged >65) with MLTCs and frailty. A recent systematic review by Sum et al. [18] found evidence of the effectiveness of CGA in improving functional status, frailty, fall and mental health outcomes as well as self-rated health and quality of life of community-dwelling older adults (aged ≥75). The effectiveness of community HABIs in improving patient-centred health outcomes and reducing the risk for adverse events in adults (aged ≥ 18) with MLTCs is unclear.

A systematic review by Smith et al.[16] found that community interventions led by multidisciplinary teams and targeted at better care coordination, self-management support, and medicine review have the potential to improve experiences of care and health behaviours in older people with MLTCs. However, there is no conclusive evidence that these interventions are effective in improving quality of life and mental health or reducing healthcare utilization rates. For example, a phase 3 randomized control trial – the 3D Study – incorporating patient-centred strategies that reflect an international consensus on optimal management of MLTCs found positive effects on patients' experience of, and satisfaction with care. At 15 months of follow-up, however, no effects were observed in relation to the primary outcome of quality of life, or on mental health, polypharmacy, and mortality. [21] A phase 2 RCT – the CARE Plus Study – targeted at adults with MLTCs from deprived communities, on the other hand, found some evidence of the benefits of a whole system primary-care complex intervention in improving patients' wellbeing and quality of life. This intervention included longer GP consultations to allow for structured holistic assessment, relational continuity, practitioner training and support, and patient self-management support. [22] The Cochrane review evaluating community interventions for people with MLTCs established no clear evidence of benefit in clinical outcomes [23] but included studies had to be targeting people with MLTCs. This means that potentially relevant interventions from other disciplines using different terminology (including literature on CGA) were not included.

Recent reviews signal that there remain uncertainties about effective models of care and interventions for adults (aged ≥ 18) with MLTCs, [16, 23] calling for further research into complex interventions prioritizing patient-identified needs and outcomes. The NICE guidelines specifically called for research evaluating the effectiveness of "holistic assessment and intervention", reflecting that this is often a core component of complex interventions in this field but with variations in implementation modalities and other elements included. [13] Further, interventions targeting people with MLTC with very similar components (e.g., multidisciplinary review with a whole person focus) can be included or excluded by reviews based on how they are named. This umbrella review, therefore, aims to provide a comprehensive evaluation of evidence-based literature on holistic assessment-based complex interventions targeted at adults with MLTCs and/or frailty. A preliminary search of JBI Evidence Synthesis, the Cochrane Database, JBI Library, and PROSPERO was conducted; no current or in-progress umbrella reviews on the topic were identified.

Review questions

(i) What is the effectiveness of community HABIs in improving outcomes in adults (aged ≥ 18) with MLTCs and/or frailty?
(ii) What is the effectiveness of hospital HABIs in improving outcomes in adults (aged ≥ 18) with MLTCs and/or frailty?

Inclusion criteria

Participants

We will include systematic reviews that are focusing on community-dwelling and hospitalized adults aged ≥ 18 with MLTCs and/or frailty. Multiple long-term conditions (or multimorbidity) will be operationalized based on the NICE guideline definition [13] as the presence of two or more long-term health conditions in an individual, including (a) physical and mental health conditions; (b) ongoing conditions such as learning disability; (c) symptom complexes such as frailty or chronic pain; (d) sensory impairments such as sight or hearing loss; (e) alcohol and substance misuse. We will adopt the WHO's definition of long-term conditions described as persistent "health problems that require ongoing management over a period of years or decades".[24] Frailty is not an easily described syndrome for which there is universal consensus on its operational definition.[11] Further, tools and assessments of frailty vary in their complexity. Therefore, systematic reviews considering both the phenotype of frailty (weight loss, exhaustion, weakness, low physical activity, slowness) and/or accumulation of deficits (loss in ≥ 1 domain of human functioning such as physical, psychological, social domains) approaches or using multidimensional specific frailty validated scale, measurement or index will be considered for inclusion. We will exclude reviews that focus on children or young people aged <18; adults aged ≥ 18 receiving end-of-life care; adults aged ≥ 18 who have a single long-term condition, or those where the focus is on people with a single long-term condition with an interest in comorbidity.

Interventions

We will include studies that evaluate HABIs in the community (home, primary care, outpatient clinic, care or nursing home), hospital (acute care, general medicine and geriatric care) or both settings. A holistic assessment is broadly defined as a multidimensional process based on the assessment of individuals' medical, psychological, social conditions and functional capabilities, and the development of an integrated treatment and follow-up plan. It is a complex intervention itself that responds to all factors relevant to the health or illness of a person. [17] The terminology used to describe HABIs may differ across disciplines; we will, therefore, consider reviews describing interventions based on the assessment of needs in two or more domains of health and using alternative terminology to describe holistic interventions. Table 1 presents detailed descriptions of the selection criteria.

<<Include Table 1 here>>

Comparators

We will consider reviews reporting on any type of comparator intervention including context-specific standard or usual care.

Outcomes

We will consider systematic reviews reporting on health outcomes important to people with MLTCs [25] and/or frailty. [26] Guided by a consensus-based core set of outcomes for MLTCs (COSmm) [25] and frailty (FOCUS), [26] the primary outcomes of interest will be quality of life, physical and cognitive function, mortality, unscheduled hospital admission (times/year), unscheduled care attendance (provider visits/year), and care home admission (yes/no) measured by validated instruments or any clinically meaningful metrics. Secondary outcomes are adverse drug events, length of stay (bed days/year), 'geriatric syndromes' (e.g., falls, delirium). We will include reviews reporting on key outcomes of interest assessed using validated measures. These may include for (a) quality of life - EuroQol 5-Dimension (EQ-5D); Health Survey (SF-12 (Short Form), SF-36); Global quality of life (WHOQOL-BREF); Assessment of Quality of Life (AQoL 8); (b) cognitive function - Mini-Mental State Exam (MMSE); General Practitioner Assessment of Cognition (GPCOG); Memory Impairment Screen (MIS); Mini-Cog™; (c) physical function - Sheehan Disability scale; Sherbrooke Postal Q; Frenchay Activities Index (FAI); Instrumental for Activities of Daily Living questionnaire (ADL/ IADL); Barthel's Index (BI); PROMIS Physical Function. This list is not exhaustive and other validated measures of outcomes will also be considered.

Types of studies

We define a systematic review as an evidence synthesis that has a clearly stated set of objectives with pre-defined eligibility criteria for the studies; an explicit, reproducible methodology; a systematic search that attempts to identify all the studies that would meet the eligibility criteria; an assessment of the validity of the findings of the included studies and a systematic synthesis of the characteristics and findings of the included studies. We will include systematic reviews of various types (e.g., integrative systematic reviews, mixed-methods systematic reviews, combined scoping and systematic intervention reviews) with and without meta-analyses reporting on experimental and quasi-experimental study designs, such as randomized controlled trials, non-randomized controlled trials, controlled before-after studies, interrupted time series study designs. These are study designs acceptable to the Cochrane Effective Practice and Organisation of Care group criteria for the evaluation of the effectiveness of organisational interventions. We will exclude systematic reviews that will report only on observational study designs (e.g., case series, individual case reports, descriptive cross-sectional studies, case-control, cohort studies) and pharmacological studies. We will additionally exclude narrative reviews without a systematic formal search, screening, quality

appraisal, extraction and synthesis of evidence as well as systematic reviews reporting on qualitative and theoretical studies or published opinions only (see Table 1 for details).

Methods

This protocol was developed adhering to the guidelines of Methodology for JBI Umbrella Reviews, [27] Reporting of Overviews of Reviews of Healthcare Intervention (PRIOR), [28] and Preferred Reporting Items for Systematic Review and Meta-Analysis protocols (PRISMA-P). [29] The protocol was registered with PROSPERO (CRD42022363217).

Search strategy

Systematic searches will be performed in MEDLINE (Ovid), EMBASE (Ovid), PsycINFO (Ovid), CINAHL Plus (EBSCOhost), Scopus, ASSIA (ProQuest), Cochrane Library (Wiley) and TRIP Medical Database for peer-reviewed literature published since 2010. The date limit is applied to capture the most recent and relevant intervention reviews, given that MLCTs and integrated holistic care are relatively new concepts in health care. The search strategy will apply subject terms and keywords relating to the target population and intervention. The search terms will be combined with the Scottish Intercollegiate Guidelines Network (SIGN) database-specific filters for systematic reviews, with no language restrictions applied. An information specialist will be consulted to finalize the search strategy tailored to each database. A search strategy used in MEDLINE is appended (see Appendix I). We will additionally manually search the reference lists of included reviews for eligible reviews.

Study selection

Retrieved records will then be imported to EndNote v20.3 (Clarivate Analytics, PA, USA) for de-duplication. The de-duplicated RIS file will be transferred into a Covidence platform (Veritas Health Innovation, Melbourne, Australia) for screening. Two reviewers will independently screen the inclusion eligibility of retrieved records, initially based on the titles and abstracts and followed by full-texts. At the full-text screening stage, only reviews in English will be included due to resources and time constraints. Reasons for the exclusion of full-text studies will be recorded. Disagreement between the two reviewers will be resolved by discussion and consensus. If no consensus is reached, a third reviewer will be invited to help with decision-making. Search and screening results will be presented in a PRISMA flow diagram. [29]

Data collection

We will extract data using an adapted and piloted JBI data extraction tool [27] (see Appendix III). Data on (a) systematic review characteristics (title, first author, country, year of publication, objective); (b) included populations (age, gender, number of conditions, definitions, and measures used); (c) search strategy; (d) complex interventions (names/types of interventions, country in which interventions were tested, intervention components, holistic-assessment domains (if reported), who led assessments (if

reported), type of controls, total sample sizes, the number of meta-analyses); (e) setting (community vs hospital); (f) analysis, health outcomes (types/measures used) and results will be extracted. For reviews with no meta-analyses, a summary of the authors' primary interpretation of findings will be extracted. For meta-analyses, data on pooled effect sizes e.g., rate ratio, risk ratio, odds ratio (for dichotomous data) and mean difference or standardized mean difference (for continuous data) and corresponding 95% CIs and p-values will be extracted. From integrative systematic reviews, mixed-methods systematic reviews, combined scoping and systematic intervention reviews reporting on experimental and quasi-experimental study designs, data on pooled effect sizes, 95% CIs, p-values, and/or a statement summarising the authors' primary interpretation of results will be extracted.

Analysis of the degree of overlap in studies

Systematic reviews exploring similar topics may have considerable overlap in included primary studies. We will create a citation matrix and calculate the corrected covered area (CCA) index to analyse the overlap in primary studies included in reviews. [30] We will consult the guidance developed by Hennessy and Johnson (2020) [31] to further examine the reasons for overlap based on CCA value (see Appendix IV for details). The reviews with complete/near complete overlap will be examined for reasons of high overlap and considered for exclusion; higher quality and/or most recent reviews (if ratings are similar) will be retained.

Assessment of methodological quality

The quality appraisal will be done by two reviewers using the JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses (CACSRRS) tool. [27] The tool comprises 11 items (Is) evaluating the clarity of review question (I1); appropriateness of inclusion criteria (I2) and search strategy (I3); adequateness of sources and resources used for searching the studies (I4); appropriateness of appraisal criteria (I5); duplicate conduct of quality appraisal (I6); applications used to minimize errors in data extraction (I7); appropriateness of methods used to combine the studies (I8); assessment of publication bias (I9); soundness of arrived recommendations for policy and practice (I10); appropriateness of proposed new research directives (I11). The items are scored based on the checklist as 'Y=met', 'N=not met', '?=unclear' and 'NA=not applicable'.

The JBI CACSRRS tool is not intended to generate an overall score, and the rating of overall quality may be based on certain criteria being met. [27] We differentiated items 1-3, and 5-10 as critical domains (see Appendix II). Rating the confidence of review results will be based on weaknesses in critical domains, ranging from high (no or one non-critical weakness), moderate (more than one non-critical weakness), low (one critical flaw with or without non-critical weaknesses), and critically low (more than one critical flaw with or without non-critical weaknesses). The results of the critical appraisal will be reported in a table with an accompanying narrative. All studies will undergo data extraction and synthesis; however, depending on the overall results of the critical appraisal, sensitivity analyses might be performed to test the robustness of our conclusions.

Data summary

The extracted data will be synthesized manually. The summary of findings will be presented in tabular form, with narrative descriptions and visual indications accompanying the tabulated results. Where possible, analysis will be stratified by setting. We will classify interventions using an existing taxonomy of health interventions (e.g., EPOC) and use a "stop-light" visual indicator to summarise the effectiveness of interventions. [27] We will collate the pooled estimates reported in each meta-analysis, providing narrative synthesis to these findings.

In summarising findings across the reviews, we will use the principles from Grading of Recommendations, Assessment, Development, and Evaluation [32] for an overall assessment of the quality of evidence across the reviews with meta-analyses for outcomes of interest. [27] Quality of evidence for a given outcome will be graded as high, moderate or low based on the overall quality of systematic reviews and risk of bias in primary studies and consistency of results in relation to an outcome (see Appendix V for details).

312 **Table 1: Review selection criteria**

Domain	Inclusion criteria	Exclusion criteria
Publication type	Peer-reviewed systematic review publications in English	Conference proceedings, abstracts, meta-analyses published in the letter-to-editor format, scoping reviews, narrative reviews or overviews, systematic review protocols, grey literature
Publication timeline	Published between January 2010-September 2022	Published before 2010
Population	Community-dwelling or hospitalized adults (aged ≥18) with MLTCs and/or frailty	Children and/or young people (aged <18) with multimorbidity People who only have two or more mental health problems and no physical health condition People who receive end-of-life or palliative care People with a single long-term health condition People with a single long-term condition with an interest in comorbidity (e.g., cancer comorbidities)
Intervention	Holistic assessment-based intervention (HABI) which has ≥2 assessment domains Assessed domains may include physical health, psychological or mental health, functional status, cognitive status Terminology for HABI can be explicit or not Alternative terminology may include holistic evaluation or consultation or management; comprehensive needs assessment or evaluation or consultation; comprehensive geriatric assessment or evaluation or consultation	Holistic assessment-based intervention which has <2 assessment domains Complex interventions not including holistic assessment as a component
Comparator	Any, context-specific standard or usual care	Complementary and/or alternative care (care that falls outside of mainstream healthcare)
Outcomes: Primary	Quality of life, physical and/or cognitive function, mortality, unscheduled hospital admission, unscheduled care attendance, care home admission	Adverse events not associated with healthcare (e.g., air/rail/road traffic injuries, occupational injuries).
Secondary	Adverse drug events, length of stay (bed days/year), 'geriatric syndrome' (e.g., falls, delirium)	
Context	Community setting (community home, primary care, outpatient clinic, care or nursing home) Hospital setting (acute hospital or emergency care, general medicine or geriatric care)	Hospice, end-of-life care setting
Study designs	Systematic reviews (with or without meta-analyses) reporting on randomized controlled trials, non-randomized controlled	Systematic reviews including only observational study designs not acceptable to Cochrane EPOC (case series, individual

	trials, controlled before-after studies, interrupted time series Mixed-methods, combined or integrative systematic reviews (with or without meta-analyses) including randomized controlled trials, non-randomized controlled trials, controlled before-after studies, interrupted time series	case reports, descriptive cross-sectional studies, case-control, and cohort studies) and pharmacological studies Systematic reviews reporting qualitative meta-synthesis only Systematic reviews reporting theoretical studies or published opinions only

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Appendix I. Search strategy for MEDLINE (Ovid interface)

The search conducted on 26 September 2022 returned 1909 results.

1. Multimorbidity/
2. Chronic Disease/
3. Comorbidity/
4. (multimorbid* or multi-morbid* or chronic disease$ or comorbid* or co-morbid* or polymorbid* or poly-morbid* or multidisease* or multi-disease* or disease cluster* or multiple long-term condition* or multiple chronic disease$).tw.
5. ((coocur* or co-ocur* or coexist* or co-exist* or multipl* or concord* or discord*) adj3 (disease$ or ill* or care or condition$ or disorder* or health* or symptom* or syndrom*)).tw.
6. or/1-5
7. Frailty/
8. Frail Elderly/
9. Frailty Syndrome/
10. (frail* or frail* syndrome or geriatric* syndrom* or vulnerabil* or function*).tw.
11. or/7-10
12. 6 or 11
13. Adult/
14. Young adult/
15. Middle aged/
16. Aged/
17. (adult* or young adult* or middle aged or old* or elder* or geriatric* or gerontol* or ageing or aged).tw.
18. or/13-17
19. Needs assessment/
20. Geriatric assessment/
21. Risk Assessment/
22. Patient-centered Care/
23. Health Services/
24. health services for the aged/
25. Delivery of Health Care, Integrated/
26. ((holistic or whole or comprehens* or complet*) adj3 (assess* or evaluat* or consult* or manag*)).tw.
27. ((integrat* or co-ordinat* or multidisciplin* or patient-centr* or person-centr*) adj2 (care or service$)).tw.
28. ((geriatric or aged or elderly or old age) adj3 (assess* or evaluat* or consult*)).tw.
29. (team$ adj2 (care or treat* or assess* or consult*)).tw.
30. (multidiscipline* adj3 assess*).tw.
31. or/19-30
32. Meta-Analysis as Topic/
33. meta analy$.tw.
34. metaanaly$.tw.
35. Meta-Analysis/
36. (systematic adj (review$1 or overview$1)).tw.
37. exp Review Literature as Topic/
38. or/32-37
39. cochrane.ab.
40. embase.ab.
41. (psychlit or psyclit).ab.
42. (psychinfo or psycinfo).ab.

43. (cinahl or cinhal).ab.
44. science citation index.ab.
45. bids.ab.
46. cancerlit.ab.
47. or/39-46
48. reference list$.ab.
49. bibliograph$.ab.
50. hand-search$.ab.
51. relevant journals.ab.
52. manual search$.ab.
53. or/48-52
54. selection criteria.ab.
55. data extraction.ab
56. 54 or 55
57. Review/
58. 56 and 57
59. Comment/
60. Letter/
61. Editorial/
62. animal/
63. human/
64. 62 not (62 and 63)
65. or/59-61,64
66. 38 or 47 or 53 or 58
67. 66 not 65
68. 12 and 18 and 31 and 67
69. limit 68 to yr="2010 -Current"

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Appendix II: Quality appraisal instrument

JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses

Reviewer:		Date:			
Author:		Year:			
		Record Number:			
		Yes	No	Unclear	NA
I1	Is the review question clearly and explicitly stated?				
I2	Where the inclusion criteria appropriate for the review question?				
I3	Was the search strategy appropriate?				
I4	Were the sources and resources used to search for studies adequate?				
I5	Were the criteria for appraising studies appropriate?				
I6	Was critical appraisal conducted by two or more reviewers independently?				
I7	Were there methods to minimize errors in data extraction?				
I8	Were the methods used to combine studies appropriate?				
I9	Was the likelihood of publication bias assessed?				
I10	Were the recommendations for policy/and or practice supported by the reported data?				
I11	Were the specific directives for new research appropriate?				

Overall confidence in the review results based on weaknesses in critical domains*

High (no or one non-critical weakness)	
Moderate (more than one non-critical weakness)	
Low (one critical flaw with or without non-critical weaknesses)	
Critically low (more than one critical flaw with or without non-critical weaknesses)	

**Critical domains: Items 1-3, 5-10*

Appendix III: Data extraction instrument

Systematic review details	
Title First author/year Country	
Objective	
Included population	
Age (mean, SD)	
Gender	
Number of conditions	
Definitions/measures used	
Total number of participants	
Search details	
Sources searched	
Range (years) of included studies	
Number of studies included	
Type of studies included	
Country of origin of included studies	
Complex interventions	
Names	
Types included in a meta-analysis	
Intervention components	
Holistic assessment domains (if reported)	
Multidisciplinary teams/who led the assessments (if reported)	
Type of controls	
Total sample sizes	
Number of meta-analyses	
Setting/context	
Quality appraisal	
Analysis	
Methods of analysis	
Outcomes assessed (measures used)	
Results	
Significance/direction	
Heterogeneity	
Comments	

Appendix IV: Analysis of the degree of overlap in primary studies

Step 1: Create citation matrix (CM)

The citation matrix (CM) will allow for assessing the amount of overlap at the review as opposed to the outcome level. The CM will list all primary studies (*r*=rows) included for each review (*c*=columns). The duplicate rows will be removed to ensure that a primary study appearing across reviews is noted in a line. The first occurrence of a primary study will be defined as an index publication (see Table A).

Table A. Citation matrix

	Review 1	Review 2	Review 3
Primary study 1	x		x
Primary study 2	x	x	
Primary study 3	x		x
Primary study 4	x	x	x

Step 2: Calculate Corrected Covered Area (CCA) across the matrix

The overlap in studies across the matrix will be calculated based on the corrected covered area (CCA) method [30] by dividing the frequency of repeated occurrences of the index publication in other reviews by the product of index publications and reviews, reduced by the number of index publications (see below).

$$CCA\ (Corrected\ Covered\ Area) = \frac{N - r}{rc - r}$$

where *N* is the number of included publications (irrespective of overlaps) in evidence synthesis (this is the sum of the ticked boxes in the citation matrix); *r* is the number of rows (number of index publications) and *c* is the number of columns (number of reviews).

The degree of overlap across the matrix can vary from 0–5 slight overlap; 6–10 moderate overlap; 11–15 high overlap to >15 very high overlap. Depending on CCA value, a decision tree developed by Hennessy and Johnson (2020) [31] will be used to guide our further steps.

Step 3: Examine the CM for reviews with complete/near complete overlap

The reviews with complete/near complete overlap will be examined for reasons of high overlap and considered for exclusion; higher quality and/or most recent reviews (if ratings are similar) will be retained.

Appendix V: Quality of evidence across systematic reviews for the outcome*

Quality of evidence	Criteria
High-quality evidence	One or more updated, high-quality systematic reviews that are based on at least 2 high-quality primary studies with consistent results
Moderate-quality evidence	One or more updated systematic reviews of high or moderate quality: -based on at least 1 high-quality primary study -based on at least 2 primary studies of moderate quality with consistent results
Low-quality evidence	One or more systematic reviews of variable quality: -based on primary studies of moderate quality -based on inconsistent results in the reviews -based on inconsistent results in primary studies

** Based on principles from Grading of Recommendations Assessment, Development, and Evaluation*

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