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METHOD ARTICLE

A theory-informed mixed-methods approach for early implementation assessment in clinical trials of complex interventions

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Abstract

Background

Clinical trials of complex interventions often face challenges when translating interventions developed under research conditions into routine practice. Implementation science offers approaches to examine this research-to-practice gap, but strategies for assessing early implementation within clinical trials remain limited. This is particularly relevant to rehabilitation interventions, which are individualized, context-dependent, and delivered through interactions among patients, healthcare professionals, and organizations.

Methods

A hybrid type 1 design was used to evaluate a palliative rehabilitation intervention. A theory-informed methodological approach was developed to guide early implementation assessment within the clinical trial. The EPIS process model structured assessment across trial phases, while Proctor's taxonomy guided selection of implementation outcomes. Outcome measures were mapped and reviewed, prioritizing validated measures where available. Quantitative questionnaires and qualitative topic guides were developed for patients, healthcare professionals, and institutional representatives. The approach was designed to remain adaptable to trial phase and objectives.

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Results

The resulting mixed-methods strategy combined quantitative assessment of selected implementation outcomes with qualitative exploration of stakeholder experiences. Three questionnaires incorporated the Acceptability of Intervention Measure, Intervention Appropriateness Measure, and Feasibility of Intervention Measure, alongside context-specific items addressing additional outcomes. Three qualitative topic guides supported integration across data sources. Data were collected at time points to capture anticipatory and experience-based perceptions of implementation. The approach aligned implementation outcomes, stakeholder perspectives, trial phases, and mixed-methods data collection without treating the strategy as a fixed or universally applicable instrument.

Conclusions

This study describes a theory-informed, mixed-methods approach for integrating early implementation assessment within clinical trials of complex interventions. Rather than proposing a new standardized instrument, it provides a transparent framework for selecting implementation outcomes, stakeholders, measures, and data collection strategies according to trial stage and objectives. Developed for a palliative rehabilitation intervention, the approach may be adapted to other complex intervention trials requiring implementation assessment alongside effectiveness evaluation.

Keywords
implementation science; complex interventions; hybrid design; mixed methods; implementation outcomes; rehabilitation; early implementation; EPIS; Proctor



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1. Background

Complex interventions in healthcare involve multiple interacting components, diverse professional profiles, individualized care processes, and substantial interactions with the contexts in which they are delivered. The Medical Research Council (MRC) framework emphasizes that the evaluation of such interventions should consider not only their effectiveness but also the contexts in which they are implemented, the processes through which they are delivered, and the mechanisms through which they may generate outcomes.[2–6] The present methodological approach focused specifically on early implementation assessment rather than on the empirical investigation of mechanisms.

Clinical trials remain a central approach for evaluating the effectiveness of healthcare interventions. However, the controlled conditions of a clinical trial may differ substantially from routine healthcare practice.[7] An intervention that demonstrates benefit under trial conditions may therefore face challenges when introduced into routine care, including organizational constraints, differences in professional practices, resource limitations, and variation in patient populations and care pathways.

These challenges are particularly relevant to rehabilitation interventions. Rehabilitation is frequently individualized according to patients' functional abilities, symptoms, priorities, and living environments. Delivery may involve several professional groups and may occur across different healthcare settings. Consequently, implementation is not simply a matter of reproducing a predefined intervention but may involve interactions between intervention characteristics, professionals, patients, organizations, and healthcare systems.

Implementation science has emerged as a field concerned with understanding and improving the uptake, delivery, and sustainability of evidence-based interventions in routine practice.[8] It provides theoretical approaches to examine implementation processes, outcomes, determinants, and contextual influences. Integrating implementation assessment into clinical trials can therefore provide information that complements effectiveness outcomes and may help distinguish between limitations of an intervention itself and limitations related to its delivery or implementation.

However, implementation assessment within clinical trials raises methodological challenges. Implementation science encompasses a wide range of theories, models, and frameworks addressing different questions and levels of analysis.[9] Researchers must therefore determine which theoretical approaches are appropriate for the intervention, the stage of development, the trial design, the outcomes of interest, and the intended use of the findings.

Hybrid effectiveness–implementation designs provide one pragmatic solution by allowing clinical effectiveness and implementation outcomes to be assessed within the same study.[10,11] In particular, hybrid type 1 designs maintain a primary focus on intervention effectiveness while incorporating implementation assessment to provide complementary information and prepare for potential subsequent implementation research.[10–12] In early-stage clinical trials, however, comprehensive implementation assessment may not be feasible or appropriate. Some implementation outcomes, such as adoption or penetration, may be difficult to assess before an intervention has been introduced into routine practice. Conversely, outcomes such as acceptability, appropriateness, feasibility, and fidelity may already provide important information during initial intervention testing.

The challenge is therefore not simply to select an implementation framework, but to develop an assessment strategy that is aligned with the stage of intervention development, the objectives of the clinical trial, the relevant implementation outcomes, and the perspectives of the stakeholders involved.

The objective of this methodological study was therefore to describe the development of a theory-informed, mixed-methods approach for early implementation assessment within clinical trials of complex interventions. The approach was developed and illustrated within the context of INSPIRE, a multinational randomized clinical trial evaluating a personalized palliative rehabilitation intervention for people with incurable cancer. INSPIRE provided the clinical trial context in which the proposed approach was developed and operationalized, while the present paper focuses on the methodological process rather than on the trial results.[13]

2. Methods

2.1 Methodological positioning

The approach was developed and illustrated within INSPIRE, a multinational randomized clinical trial evaluating a personalized palliative rehabilitation intervention in people with incurable cancer.[13]

The trial adopted a hybrid effectiveness–implementation type 1 design, in which the primary research focus remained the evaluation of clinical effectiveness while implementation outcomes were assessed concurrently. The implementation

assessment was therefore designed to provide early evidence regarding how the intervention was perceived and delivered within the participating clinical settings, while generating information that could support interpretation of the clinical trial and inform future implementation research.

The methodological development followed four complementary components:

1. **A process model** to structure implementation according to the temporal phases of the trial;

2. **An implementation framework** to define the implementation outcomes to be assessed;

3. **Stakeholder-specific quantitative and qualitative assessment strategies** to capture multiple perspectives; and

4. **Mixed-methods integration** to compare quantitative assessments with contextualized stakeholder accounts.

The approach was deliberately designed as an adaptable methodological framework rather than as a fixed instrument intended for unchanged replication across studies.

2.2 Selection of implementation theoretical approaches

The first methodological step was to determine which implementation theoretical approaches were appropriate for the clinical trial.

Implementation theories, models, and frameworks address different types of questions and should therefore be selected according to the purpose of the evaluation rather than applied exhaustively.[9,14] Following Nilsen's classification,[9] candidate approaches were considered according to their principal function, including process models, determinant frameworks, implementation theories, and evaluation frameworks.

Three criteria guided selection:

1. The phase of intervention and trial development;

2. The implementation outcomes relevant to this phase; and

3. **The primary objective of the implementation assessment**, namely to complement and contextualize effectiveness evaluation rather than to evaluate large-scale dissemination or system-level implementation.

2.2.1 EPIS as a process model

The Exploration, Preparation, Implementation, Sustainment (EPIS) framework was selected as the primary process model.[15,16] EPIS provides a temporal structure for examining implementation across four phases: Exploration, Preparation, Implementation, and Sustainment. In the present study, EPIS was used primarily to organize when implementation-related questions should be addressed during the development and delivery of the intervention. EPIS was therefore not used as a measurement framework for implementation outcomes. Instead, it provided a temporal structure within which implementation assessment could be positioned. This distinction was important because implementation outcomes such as acceptability, appropriateness, and feasibility require explicit conceptual definitions and measurement strategies.

2.2.2 Determinant frameworks

Determinant frameworks, including the Consolidated Framework for Implementation Research (CFIR), the Theoretical Domains Framework (TDF), and the Promoting Action on Research Implementation in Health Services (PARIHS) framework, were considered as potential approaches for examining determinants that may influence implementation across individual, intervention, organizational, and contextual levels. These frameworks can provide detailed descriptions of determinants operating at individual, organizational, intervention, and contextual levels.[17] However, comprehensive determinant mapping was not the primary objective of the present evaluation. The purpose of the implementation assessment was instead to characterize early implementation outcomes and understand stakeholder perceptions of the intervention within the context of the clinical trial. Determinant-focused frameworks were therefore not selected as the

primary conceptual approach. Their potential contribution was retained as a future extension of the methodology when interventions progress toward implementation and scale-up.

2.2.3 Implementation theories

Implementation theories such as Normalization Process Theory (NPT) were also considered. NPT focuses on the processes through which new practices become embedded and normalized within routine work. It may therefore be particularly relevant when the research question concerns the integration of an intervention into established clinical practices. However, normalization was not the principal question of the present early-stage trial. The intervention was being introduced within a clinical trial rather than evaluated after established integration into routine care. NPT was therefore not selected as the primary theoretical approach.

2.2.4 Evaluation frameworks

Several evaluation frameworks were considered, including RE-AIM and Proctor's taxonomy.

RE-AIM provides a broader evaluation framework encompassing Reach, Effectiveness, Adoption, Implementation, and Maintenance.[18] It can support assessment of intervention impact across multiple dimensions, including implementation and longer-term maintenance. However, several dimensions of RE-AIM were difficult to assess meaningfully at the early stage of intervention development represented by the INSPIRE trial. In particular, adoption and maintenance require sufficient exposure to implementation within routine practice to be interpreted beyond the conditions of the clinical trial. RE-AIM was therefore considered as a broader evaluation framework but was not selected as the primary framework for the present early implementation assessment.

Proctor's taxonomy was considered particularly relevant because it provides conceptual definitions for implementation outcomes including acceptability, appropriateness, feasibility, fidelity, and sustainability.[19,20] The theoretical approaches considered during methodological development, together with their respective functions and rationale for selection or exclusion, are summarized in Supplementary Table 1.

Extended Data 0 presents an overview of the implementation frameworks considered for the INSPIRE project, summarizing their main characteristics and the rationale for their inclusion or exclusion from the study.

2.3 Selection of implementation outcomes

Proctor's taxonomy provides a widely used conceptual framework for defining implementation outcomes and distinguishing them from intervention outcomes.[19,20] Because not all implementation outcomes are equally relevant at every stage of intervention development, outcome selection was guided by the objectives and constraints of the hybrid type 1 clinical trial.

Five implementation outcomes were selected for the present assessment: acceptability, appropriateness, feasibility, fidelity, and sustainability potential.

Sustainability was retained as an early implementation outcome because stakeholders could assess the perceived potential for the intervention, or its core principles, to be maintained beyond the trial, even though actual long-term sustainability could not yet be observed.

Other implementation-related dimensions, including implementation cost, adoption, and penetration, were considered but were not included as implementation outcomes in the present assessment.

The selected outcomes were operationalized for the trial context based on Proctor et al.'s definitions[20] (Table 1).

2.4 Stakeholder groups

Implementation was conceptualized as involving multiple stakeholders rather than being restricted to intervention recipients or intervention providers.

Three stakeholder groups were therefore included:

1. Patients receiving the intervention;

Table 1. Implementation outcomes assessed in the clinical trial.

Implementation outcome	Operational definition adapted to the trial context
Acceptability	The perception that the intervention is agreeable, satisfactory, and acceptable to the stakeholders experiencing or delivering it.
Appropriateness	The perceived fit, relevance, and compatibility of the intervention with patients' needs, clinical circumstances, professional practices, and organizational contexts.
Feasibility	The extent to which the intervention can be successfully delivered within the participating clinical settings.
Fidelity	The degree to which the intervention was delivered according to the predefined intervention procedures and core components of the trial protocol.
Sustainability	The perceived potential for the intervention or its core principles to be maintained within clinical practice beyond the clinical trial.

Table 2. Implementation outcomes assessed by stakeholder group and assessment time point.

Implementation outcome	Patients	Healthcare professionals	Institutional representatives
Acceptability	Baseline/Follow-up	Baseline/Follow-up	Baseline/Follow-up
Appropriateness	Baseline/Follow-up	Baseline/Follow-up	Baseline/Follow-up
Feasibility	Not assessed	Baseline/Follow-up	Baseline/Follow-up
Fidelity	Not assessed	Follow-up	Not assessed
Sustainability potential	Not assessed quantitatively	Follow-up	Follow-up

2. Healthcare professionals delivering or supporting the intervention; and

3. Institutional representatives involved in service organization and management.

The outcomes assessed for each stakeholder group were determined according to their role in the intervention and the type of information they could reasonably provide.

Patients were primarily considered relevant to the assessment of acceptability and appropriateness.

Healthcare professionals were considered relevant to acceptability, appropriateness, feasibility, fidelity, and sustainability potential because of their direct role in intervention delivery.

Institutional representatives were considered relevant to acceptability, appropriateness, feasibility, and sustainability potential because of their involvement in organizational and service-level implementation.

2.5 Development of the mixed-methods assessment strategy

A mixed-methods strategy was selected because standardized quantitative measures and qualitative approaches provide complementary information about implementation.

Quantitative measures allow implementation outcomes to be assessed consistently across participants and time points. Qualitative data provide contextualized accounts of experiences, perceptions, organizational conditions, and issues that may not be adequately captured through standardized questionnaires.[21–24]

The two components were therefore designed in parallel, with the qualitative topic guides structured around the same implementation outcomes assessed quantitatively.

The purpose was not to reproduce quantitative measures qualitatively, but to create conceptual alignment between data sources while preserving the ability of qualitative participants to introduce unanticipated issues.

Table 3. Four-level methodological alignment for implementation assessment.

Methodological level	Role in the assessment
EPIS	When implementation should be considered within the intervention/trial trajectory
Proctor taxonomy	What implementation outcomes should be assessed
Stakeholder-specific assessment	Whose perspective should be captured
Mixed methods	How standardized and contextualized evidence should be generated and integrated

2.5.1 Quantitative assessment

A structured mapping of existing implementation outcome measures was undertaken using the Implementation Outcome Repository developed by the Center for Implementation Science at King's College London, which synthesizes evidence from systematic reviews of implementation outcome measures.[25,26] A total of 56 implementation outcome questionnaires were identified and reviewed during the methodological development process. The questionnaires were classified according to their target implementation outcomes, stakeholder populations and measurement characteristics. The successive steps of identification, classification and selection are presented in Extended Data 1.[1] This mapping highlighted substantial heterogeneity in implementation measurement. A number of available measures were developed for individual studies or contexts, while fewer instruments had undergone psychometric evaluation across settings.

Where appropriate, existing validated measures were therefore prioritized. The Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM) were selected as core measures for the corresponding implementation outcomes.[27] Each measure comprises four items, assessed using a five-point Likert response scale. These validated measures were incorporated into a broader assessment strategy rather than treated as a complete instrument covering all implementation outcomes. Additional items were developed or selected to address implementation outcomes not directly covered by AIM, IAM, and FIM, particularly fidelity and sustainability, as well as stakeholder- and trial-specific dimensions.

Three interdisciplinary workshops involving researchers and clinicians were conducted to refine the assessment strategy.

These workshops focused on:

- Removing redundant items;
- Clarifying wording;
- Ensuring relevance to the intended stakeholder group;
- Maintaining conceptual alignment with the selected implementation outcomes; and
- Minimizing unnecessary trial-specific terminology to facilitate potential adaptation in future studies.

The resulting questionnaires should therefore be considered stakeholder-specific configurations of an implementation assessment approach, rather than a newly validated implementation instrument.

2.5.2 Qualitative assessment

The qualitative component was designed to capture experiential and contextual dimensions of implementation that could not be fully assessed through standardized questionnaires.

Three semi-structured topic guides were developed:

- One for patients;

- One for healthcare professionals; and
- One for institutional representatives.

Guide development followed established methodological principles for semi-structured interviews.[28,29]

Each guide began with a broad, open-ended question allowing participants to describe their overall experience before introducing questions related to predefined implementation outcomes. The guides were structured according to the same implementation outcomes as the quantitative questionnaires. This created conceptual correspondence between the two data sources while maintaining an open-ended qualitative approach. For example, questions related to acceptability explored participants' overall experience and perceptions of the intervention, whereas questions related to appropriateness explored its perceived fit with individual needs, clinical circumstances, professional practice, or organizational context. Questions concerning feasibility, fidelity, and sustainability were adapted according to stakeholder role. Questions addressing equity and access were also incorporated to identify potential differences in the ability of patients or services to access and deliver the intervention. Interviews and focus groups were conducted in participants' native languages where applicable, supporting the expression of context-specific experiences across participating countries of the INSPIRE Project.

2.6 Data collection strategy

Implementation assessment was designed to capture both anticipatory perceptions and experience-based assessments.

Data were therefore collected at two time points:

- Before exposure to the intervention, to capture initial expectations and anticipatory perceptions; and
- After sufficient exposure to the intervention, to capture experience-based assessments.

The timing of assessments was adapted to stakeholder group and trial procedures.

For patients, implementation questionnaires were completed before the first rehabilitation session and after completion of the intervention.

For healthcare professionals and institutional representatives, baseline assessment was conducted before the first patient was included at the participating site, with follow-up assessment after sufficient exposure to the intervention. Follow-up assessment was also used to explore perceptions regarding the future sustainability of the intervention within clinical practice.

This temporal configuration was intended to capture potential changes in perceptions as stakeholders gained experience with the intervention. The approach can be adapted to other trials according to intervention characteristics, implementation phase, and study objectives.

2.7 Data analysis and mixed-methods integration

2.7.1 Quantitative analysis

Questionnaire items were rated using a five-point Likert scale ranging from 1 = completely disagree to 5 = completely agree. Descriptive statistics were used to summarize implementation outcomes at each assessment time point. For the present clinical trial, a score of ≥4 was defined a priori as indicating a favorable assessment of the corresponding implementation outcome. Where paired data were available, changes between assessment time points were examined. Internal consistency was assessed using Cronbach's alpha for the relevant multi-item scales. The quantitative thresholds were used as aids to interpretation rather than as substitutes for qualitative investigation.

2.7.2 Qualitative analysis

Qualitative data were analyzed using reflexive thematic analysis informed by a phenomenological orientation and focused on participants' expressed meanings.[30,31] Coding initially remained close to participants' accounts, with semantic coding used to identify descriptions of experiences, perceptions, and contextual conditions. The predefined implementation outcomes provided an organizing framework for analysis but did not preclude the identification of issues

emerging inductively from participants' accounts. Particular attention was paid to similarities and differences between stakeholder groups and participating countries.

2.7.3 Integration of quantitative and qualitative findings

Integration occurred primarily during interpretation through systematic comparison of quantitative and qualitative findings.

For each implementation outcome, findings were examined for:

- **Convergence**, when quantitative and qualitative findings supported a similar interpretation;
- **Complementarity**, when the two data sources addressed different but compatible dimensions;
- **Divergence**, when findings differed between data sources; and
- **Expansion**, when qualitative findings provided additional dimensions not captured quantitatively.

Where quantitative and qualitative findings diverged, qualitative data were examined to identify contextual or experiential explanations for the observed pattern. This integration strategy was intended to strengthen interpretation of implementation outcomes and to provide contextual information relevant to the interpretation of effectiveness findings.

3. Results

3.1 Development of the methodological approach

The methodological development resulted in an integrated implementation assessment strategy linking the trial phase, implementation outcomes, stakeholder perspectives, measurement methods, and mixed-methods integration. A total of 56 implementation outcome questionnaires were identified and reviewed. Their classification and the successive steps used to assess their relevance and select measurement components are presented in Extended Data 1.[1]

The resulting sequence was:

> Trial phase and objective → selection of process model → selection of implementation outcomes → identification of relevant stakeholders → mapping of existing measures → selection/adaptation of quantitative measures → development of qualitative topic guides → stakeholder- and phase-specific assessment → mixed-methods integration.

Each component retained a distinct function: EPIS structured the temporal positioning of assessment; Proctor's taxonomy defined the implementation outcomes; validated measures were used where appropriate; qualitative methods provided contextualized stakeholder accounts; and mixed-methods integration enabled findings to be interpreted together.

3.2 Quantitative assessment configuration

The mapping of implementation measures identified AIM, IAM, and FIM as appropriate core measures for assessing acceptability, appropriateness, and feasibility. Rather than applying these instruments as a standalone questionnaire, the measures were incorporated into stakeholder-specific questionnaires alongside additional items required to address the implementation outcomes selected for the trial. This resulted in different questionnaire configurations according to stakeholder role. The approach therefore prioritized conceptual consistency across stakeholder groups while allowing measurement content to remain role-specific.

3.3 Qualitative assessment configuration

The qualitative assessment strategy mirrored the implementation outcome structure of the quantitative questionnaires.

For patients, qualitative interviews focused on their overall experience, acceptability, and appropriateness.

For healthcare professionals, interviews and focus groups addressed the full range of implementation outcomes relevant to their role, including feasibility, fidelity, and perceived sustainability potential.

For institutional representatives, qualitative assessment focused on organizational and strategic dimensions of implementation.

The open-ended structure of the topic guides allowed participants to introduce experiences and concerns that were not explicitly represented in the predefined implementation outcomes.

This design supported the identification of contextual dimensions that could subsequently be integrated with quantitative findings.

3.4 Illustrative configuration within the INSPIRE trial

The methodological approach was operationalized in the INSPIRE trial through three stakeholder-specific questionnaires.

The resulting configuration comprised:

- **31 items for patients**, primarily addressing acceptability and appropriateness;
- **62 items for healthcare professionals**, addressing acceptability, appropriateness, feasibility, fidelity, and sustainability; and
- **51 items for institutional representatives**, addressing acceptability, appropriateness, feasibility, and sustainability.

These configurations were tailored to the stakeholder groups and are presented as an illustrative application of the methodological approach rather than as a fixed instrument (Table 2).

For healthcare professionals and institutional representatives, baseline assessment occurred before the first patient was included at the site. Follow-up assessment was conducted after sufficient exposure to the intervention, defined operationally as approximately nine months after trial opening.

In parallel, three qualitative topic guides were developed. The patient guide focused primarily on acceptability and appropriateness. The healthcare professional guide addressed acceptability, appropriateness, feasibility, fidelity, and perceived sustainability potential. The institutional representative guide focused on acceptability, appropriateness, feasibility, and sustainability potential, with fidelity excluded because direct responsibility for intervention delivery did not generally lie with this stakeholder group.

Three stakeholder-specific questionnaires and three corresponding qualitative topic guides were developed as part of the methodological assessment strategy. The questionnaires and topic guides are provided as Extended Data 2–4.[1]

3.5 Alignment between theoretical approaches, outcomes, stakeholders, and methods

The methodological development resulted in a four-level alignment (Table 3):

This alignment was intended to avoid selecting implementation measures independently of the research question or intervention phase.

4. Discussion

4.1 Early implementation assessment as a deliberate methodological positioning

This study describes a methodological approach for assessing implementation early within a clinical trial of a complex intervention. The central premise is that implementation assessment should not necessarily be postponed until an intervention reaches routine practice. Even when a clinical trial is primarily designed to assess effectiveness, early implementation information can provide important insight into whether an intervention is perceived as acceptable and appropriate, whether it can be delivered within the participating settings, whether delivery remains faithful to predefined core components, and what conditions may be relevant to future sustainability.

At the same time, early implementation assessment should not be expected to answer questions that require later stages of implementation. Adoption, penetration, and system-level normalization may be difficult or impossible to assess meaningfully before an intervention has been introduced into routine care.

The methodological approach therefore positions implementation assessment as phase-sensitive and purpose-driven, rather than comprehensive by default. This is particularly relevant to hybrid type 1 designs, where implementation assessment complements rather than replaces the primary effectiveness evaluation.[10,11]

4.2 Combining complementary theoretical approaches

A key methodological contribution of this work is the explicit separation of the functions of different implementation theoretical approaches. Implementation science does not provide a single framework capable of answering all implementation questions. Process models, determinant frameworks, implementation theories, and evaluation frameworks address different dimensions of implementation research.[9]

In the present approach, EPIS was used to structure the temporal positioning of implementation assessment, while Proctor's taxonomy was used to define the implementation outcomes of interest. This distinction avoids treating a process model as a measurement framework. The approach also illustrates that theoretical selection can be driven by the specific stage and purpose of the study rather than by an attempt to incorporate the largest possible number of frameworks.

Determinant frameworks such as CFIR or TDF may become particularly valuable in subsequent implementation phases when the research objective shifts toward identifying barriers and facilitators or designing implementation strategies. Similarly, implementation theories such as NPT may become more relevant when the intervention reaches the stage at which normalization and integration into routine practice can be meaningfully examined. The theoretical approach should therefore evolve with the intervention.

4.3 An adaptable methodological approach rather than a standardized instrument

A second important feature is the distinction between an assessment approach and a standardized measurement instrument.

The present work does not propose a new validated implementation scale. Instead, it provides a transparent process through which researchers can select existing validated measures where available and combine them with context-specific items and qualitative methods according to the objectives of a given trial. This distinction is important because implementation measurement is inherently dependent on the intervention, stakeholder group, context, and implementation phase.

For example, the information required from a patient receiving an intervention may differ from that required from a healthcare professional delivering it or an institutional representative responsible for organizational support. Similarly, feasibility may be interpreted differently at the individual professional and organizational levels. An adaptable methodological approach can therefore preserve conceptual coherence while allowing the content of assessment to remain responsive to the research context.

4.4 The contribution of mixed methods

The use of mixed methods represents another central component of the approach. Quantitative implementation measures can provide standardized information about how stakeholders rate specific outcomes. However, a favorable or unfavorable score does not necessarily explain why participants hold a particular perception. Qualitative data can provide information about the experiences and contextual conditions underlying these assessments.

For example, a relatively low feasibility score may reflect insufficient human resources, limited organizational capacity, scheduling constraints, or difficulties integrating an intervention into existing care pathways. These explanations may not be identifiable from a standardized questionnaire alone. Conversely, qualitative accounts may identify positive experiences that are not fully represented in predefined implementation measures. The integration strategy described here therefore treats quantitative and qualitative findings as complementary sources of evidence rather than as competing forms of data. This is particularly relevant in complex intervention research, where implementation experiences may vary according to intervention characteristics, stakeholder perspectives, professional practices, and organizational conditions.

4.5 Multiple stakeholder perspectives

The inclusion of patients, healthcare professionals, and institutional representatives reflects the multidimensional nature of implementation.

Patients experience the intervention directly and can provide information about whether it is acceptable and appropriate to their needs. Healthcare professionals are directly involved in intervention delivery and can therefore provide information about feasibility, fidelity, and compatibility with clinical practice. Institutional representatives provide a broader

organizational perspective concerning resources, service organization, and the potential for sustainability. These perspectives may converge, but they may also diverge.

Such divergence should not necessarily be interpreted as inconsistency or methodological failure. Rather, it may reflect the fact that implementation outcomes are experienced differently according to stakeholder position. A patient may consider an intervention highly acceptable while professionals perceive substantial organizational barriers to delivering it routinely. Conversely, an organization may consider an intervention feasible while patients experience difficulties related to access or timing.

A multi-stakeholder assessment strategy can therefore provide a more complete representation of implementation than a single stakeholder perspective.

4.6 Implications for effectiveness-focused complex intervention trials

The approach has implications for researchers conducting effectiveness-focused trials of complex interventions. First, implementation assessment can be incorporated without changing the primary objective of a hybrid type 1 study.

Second, early implementation data may contribute to the interpretation of effectiveness findings. For example, if an intervention does not demonstrate the expected clinical effect, implementation data may help determine whether the result occurred despite adequate implementation or whether limitations in delivery, feasibility, fidelity, or exposure may have contributed. Conversely, favorable implementation outcomes may provide evidence that an intervention was acceptable and feasible even when its effectiveness remains uncertain. Implementation assessment can therefore help prevent clinical effectiveness from being interpreted independently of the conditions under which the intervention was delivered.

Importantly, however, implementation outcomes should not be interpreted as substitutes for effectiveness outcomes. They answer different questions.

4.7 Standardization and adaptation in complex interventions

The approach also highlights the methodological tension between standardization and adaptation. Clinical trials require sufficient standardization to ensure that the intervention being evaluated can be defined and interpreted consistently. Complex rehabilitation interventions, however, frequently require adaptation to individual patient needs, clinical circumstances, professional practices, and organizational settings.

Implementation assessment should therefore distinguish between the core components or functions of an intervention and the elements that may reasonably be adapted to context. This distinction is particularly important when assessing fidelity.

Fidelity should not necessarily be understood as rigid replication of every aspect of intervention delivery. Instead, fidelity assessment should be aligned with the elements that are considered essential to the intervention as defined by the trial protocol. At the same time, qualitative assessment can identify adaptations required to make delivery feasible within different contexts.

The combination of quantitative and qualitative methods can therefore help identify where adaptation occurs and whether it is perceived as compatible with the intended intervention.

4.8 Methodological boundaries and future directions

The proposed approach is intentionally limited to early implementation assessment and does not address all questions relevant to later implementation phases. Determinant-focused frameworks, economic evaluations, adoption assessments, and system-level analyses may become relevant as interventions progress toward scale-up. Future research should examine the applicability of the approach across different types of complex interventions, clinical settings, and implementation phases, and investigate how stakeholder-specific measures can be adapted while preserving conceptual comparability across studies.

5. Strengths and limitations

A major strength of this work is the explicit documentation of the methodological reasoning underpinning implementation assessment. Rather than selecting implementation measures opportunistically, the approach links the trial phase, research objectives, theoretical positioning, implementation outcomes, stakeholders, and data collection methods.

A second strength is the integration of validated implementation measures with qualitative methods, allowing standardized assessment to be complemented by contextualized stakeholder accounts.

A third strength is the inclusion of multiple stakeholder groups, which recognizes that implementation is experienced at several levels.

Several limitations should nevertheless be acknowledged. The approach was developed in the context of a single complex rehabilitation intervention and has not yet been formally tested across independent clinical trials. The resulting questionnaires should not be interpreted as a newly validated instrument. Some items were adapted or added to address the specific outcomes and stakeholder groups relevant to the trial, and their psychometric properties require separate evaluation if they are to be used as standardized instruments. In addition, the selection of implementation outcomes was deliberately restricted to those considered relevant to an early-stage hybrid type 1 trial. Consequently, the approach does not address all dimensions of implementation, particularly adoption, penetration, and system-level normalization.

Finally, the methodological approach relies on researchers making context-sensitive decisions regarding theoretical and measurement selection. This flexibility is a strength for complex interventions but may also introduce variability between applications.

6. Conclusion

This study describes a theory-informed mixed-methods approach for assessing early implementation within clinical trials of complex interventions.

The approach combines:

- EPIS to structure the temporal positioning of implementation assessment;
- Proctor's taxonomy to define relevant implementation outcomes;
- Validated measures such as AIM, IAM, and FIM where appropriate;
- Stakeholder-specific quantitative and qualitative assessment; and
- Mixed-methods integration to connect standardized assessments with contextualized experiences.

Rather than proposing a fixed implementation instrument, the approach provides a transparent and adaptable methodological process for aligning implementation assessment with the stage, objectives, intervention characteristics, and stakeholder perspectives of a clinical trial.

Although developed in the context of palliative rehabilitation, this approach may be adapted to other complex intervention trials in which implementation needs to be considered alongside effectiveness.

More broadly, integrating implementation assessment within clinical trials may contribute to a more complete interpretation of complex intervention outcomes by examining not only whether an intervention produces benefit, but also whether it is acceptable, appropriate, feasible, delivered with fidelity, and potentially sustainable within the contexts in which it is intended to be used.

Ethics approval and consent to participate

The INSPIRE protocol was approved by the European Commission (grant no. 101057043), the Health Research Authority (IRAS project ID: 328722; REC reference 23/LO/0991), and the French human protection committee (no. 24.00678.00058).

The ANSPIRE protocol involving healthcare professionals and institutional representatives was approved by the Scientific and Ethics Committee of the Hospices Civils de Lyon (France; no. 23–5238). Healthcare professionals participating in the study completed the implementation questionnaires on a voluntary basis.

For patients, free, informed, and signed consent was obtained for participation in the INSPIRE study, including the rehabilitation intervention and implementation questionnaires, as well as specific consent for participation in the qualitative interviews.

All methods were conducted in accordance with relevant ethical guidelines and regulations.

Availability of data and materials

The methodological materials developed in this study are openly available as Extended Data in Zenodo (Romeyer et al., 2026; https://doi.org/10.5281/zenodo.22764850). The empirical participant-level data generated through the INSPIRE/ANSPIRE study are not publicly available due to ethical and data-governance restrictions. Requests for access may be addressed to the corresponding author, Julia Romeyer, at julia.romeyer20@gmail.com and will be considered subject to the applicable ethical and regulatory requirements.

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