Scientific report: Ekhaga 2016-61

Integrated Outcomes for Integrated Care
– *Evidence-based assessment of integrated healthcare interventions for pain*

Tobias Sundberg, PhD

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FOREWORD

Stockholm, Mars 2018

This scientific report summarizes the research project *Integrated outcomes for integrated care – Evidence-based assessment of integrated healthcare interventions for pain*, which was supported by grant 2016-61 from Ekhagastiftelsen.

The research work of this project has been conducted in three phases, each with a specific objective and a related sub-study, which have been reported in full in three separate research reports: a systematic literature review (Appendix 1), an international congress report (Appendix 2), and a clinical outcomes toolkit (Appendix 3). Accordingly, to provide an overview of the whole project, this scientific report summarizes the research of each project phase in an aggregated format providing excerpts from the three main reports. Please see the appendixes for the full project reports including comprehensive details of the methods and results as well as the discussions and conclusions of each of the three project phases (Appendix 1-3).

We thank Ekhagastiftelsen for the valuable support that enabled this research.

Sincerely,

Tobias Sundberg, PhD
Project leader

BACKGROUND

Pain rehabilitation

Pain is common, disabling and costly for persons and society. Rehabilitation strategies might be challenging to formulate, implement and evaluate. The use of multiple-components care strategies such as integrated or multimodal rehabilitation, also known as complex health care interventions, have shown promising results and have been advocated in health technology assessment recommendations. The Swedish Council on Health Technology Assessment, in their report "Rehabilitation of chronic pain" (1) defines multimodal rehabilitation as:

> *"Multimodal rehabilitation involves a combination of psychological interventions and physical activity / exercise, manual and physical treatment methods."*

It can be concluded that multimodal rehabilitation improves conditions for the patient to return to work, compared with no or less extensive efforts. In addition to actual return to work, decreased sick leave and that the patient believes that their work ability has increased can also be counted as such improvement. The scientific evidence, however, is insufficient in terms of what type of multimodal rehabilitation is best in these respects.

Knowledge gaps

There are a number of identified knowledge gaps and prioritized areas in healthcare that need further attention to improve complex and multimodal rehabilitation strategies for patients suffering from chronic pain. Some of these knowledge gaps include:

- Better definition and description of patients that receive pain rehabilitation, e.g. regarding: pain status (duration, intensity), physical functioning (level of activities of daily living), emotional/cognitive/psychological functioning (depression, anxiety, anger and irritability), symptoms and negative experiences, patients' own evaluation of improvements and satisfaction of care, participant characteristics in clinical rehabilitation programs.

- Detailed descriptions of different types of integrated health interventions and clinical multimodal pain rehabilitation programs to improve interpretability and replication of successful care strategies in the management of chronic pain patients. This includes better details about professional healthcare providers and organizational stakeholders that are responsible for different rehabilitation programs/models.

- Information about adverse events and complications following treatment and rehabilitation of pain are currently rarely reported in clinical research targeting multimodal rehabilitation of pain patients.

- Healthcare organizations processes and clinical care routines in clinical practice. Notably, there is almost a complete lack of studies that illustrate how health care organization and health care practices affect the outcome of various treatment strategies for people with chronic pain.

- Health economy. The availability of health economic studies in this field is very limited. There is a need for health economic studies concerning the costs and effects of various non-pharmacological methods for the treatment of chronic pain.

- Practice (praxis). Further analysis is needed of the causes of common practice variations for the care of patients with chronic pain. Although the impact of these variations, as well as barriers and opportunities to influence practices are important areas for future study.

➔ *Importantly, in order to investigate many of these knowledge gaps there is a need for implementing a range of different and relevant clinical outcomes.*

Integrated healthcare

We have previously conducted a number of research studies in the area of integrated healthcare interventions, notably in part with the generous support of Ekhaga foundation. In particular, we have explored multiple-components care strategies in terms of the integration of conventional and complementary therapies in the rehabilitation of patients with various pain disorders and used different kinds of outcomes in the evaluations processes. For example, we have gained valuable experiences targeting different types of rehabilitation in different health care settings, such as primary care management of patients with chronic back and neck pain (2–6); the use integrative care in health promotion of nursing staff in emergency care (7); the integration of massage as an adjunct therapy in the emergency care management of patients with pain following motor vehicle injuries (8); assessed the feasibility of using hospital data and routines to evaluate anthroposophic integrative care management of patients with chronic pain and stress (9) and used registry data to explore drug utilization following that type of multimodal rehabilitation for pain and stress (10,11).

Development and improvement of current rehabilitation strategies

In essence, to continue fostering a positive development and improvement of rehabilitation strategies of patients with chronic pain there is an urgent need for more systematic research and longer-term evaluation of intervention programs. So far, most research initiatives targeting the rehabilitation of chronic pain patients have focused on the effects of one type of treatment vs. no treatment or other types of selected treatments. However, there is also an important need to develop and implement other types of assessment and evaluations of pain rehabilitation programs. A number of additional research questions might therefore be appropriate (1), such as:

1. What are the treatment components that contribute to the effect?
2. What other treatments / components can be added to optimize power?
3. What parameters can be varied to affect the outcome positive?
4. How effective is one treatment strategy compared with other treatment strategies for the current state of pain?
5. What characteristics of the patients, the situation and the environment affects the outcome (moderators)?
6. What processes or mechanisms in the treatment conveys change (mediators)?
7. To what extent are treatment effects generalized to other states, health care providers and care levels?

➔ *Again, in order to investigate such research questions there is a need for implementing a range of different and relevant clinical outcomes.*

Integrated outcomes for integrated care

Considering the currently identified knowledge gaps and the research questions initiatives relating to multimodal pain rehabilitation research, we believe it is highly important to not only disseminate research that have investigated single types of treatments with selected single outcomes. Rather, we believe that there are increasingly important needs to foster an evidence-informed understanding about evaluation strategies that target the integration of multiple relevant clinical outcomes, which may further improve the evidence-based assessments of integrated healthcare interventions for pain.

A step toward achieving such improved understanding of outcome assessment is to synthesize and share the best available evidence and expert opinions in the field, i.e. how to integrate, analyze and interpret apparently different but potentially synergistic outcomes in the assessment and evaluation of pain rehabilitation strategies such as integrated care. Importantly, such efforts will be of relevance not only for the Swedish healthcare system and stakeholders, but also for an international audience of healthcare providers, patients, policy and decision makers wishing to close the gap between research and practice in the field of integrated and multimodal healthcare interventions for pain.

AIM AND OBJECTIVES

The overall aim of this project was to gather best available evidence and expert opinions on integrating outcomes for integrated care, i.e. the evidence-based assessment of integrated healthcare interventions for pain. The research project was conducted in three phases, each with a specific objective and a related sub-study:

Specific objectives and project phases

Phase 1: *Reviewing the literature*
Objective: To identify key scientific outcomes used for evidence-based assessment of integrated pain rehabilitation interventions.

Phase 2: *Gathering expert opinions*
Objective: To gather stakeholders' expert opinions of integrating outcomes in the assessment of integrated pain rehabilitation interventions.

Phase 3: *Synthesizing outcomes*
Objective: To synthesize scientific outcomes and export opinions into a proposed clinical "outcomes toolbox" for evidence-based assessment of integrated healthcare interventions for pain.

MATERIALS AND METHODS

Please see the appendixes for the full project reports including comprehensive details of the methods used in each of the different project phases (Appendix 1-3).

Phase 1: A systematic literature review

A systematic literature review of randomized controlled trials was conducted to identify key scientific outcomes. The following four electronic databases were used: CINAHL (12), EMBASE (13), PEDro (14), and PubMed/MEDLINE (15). The searches was limited to articles written in English, detailing an adult population with non-specific chronic pain, and published over the last ten years (Jan 2008 to Dec 2017).

The specific literature searches were modified according to the particular interface of each electronic database, whereby combinations of the below main key words and search strings were employed.

1. Pain [Title/Abstract] AND Chronic [Title/Abstract]
2. "Non-specific" [Title/Abstract] OR "Non specific" [Title/Abstract]
3. 1 AND 2
4. Care* [Title/Abstract] OR Treatment [Title/Abstract] OR Rehabilitation* [Title/Abstract]
5. "Randomized Controlled Trial" [Publication Type] OR "controlled clinical trial" [Publication Type] OR randomized [Title/Abstract] OR randomized [Title/Abstract] OR random* [Title/Abstract] OR trial [Title/Abstract] OR group* [Title/Abstract]
6. 3 AND 4 AND 5

The subsequent selection of scientific articles was conducted in a stepwise approach, first screening the titles and abstracts, then the full text peer-reviewed articles, in order to identify the reported scientific outcomes. Clinical trial and outcome measure data was gathered based on the Cochrane handbook for data extraction (16). Thematic analysis was used to categorize the identified outcome measures into domains based on clinical features.

Phase 2: An international research symposium

An international research symposium, i.e. a focused meeting with national and international stakeholders in the field of researching pain rehabilitation and integrated care, was arranged in order to gather expert opinions. The research symposium took place at the World Congress Integrative Medicine and Health in Berlin 5th May 2017, which was also the 10th European Congress for Integrative Medicine and the 12th International Congress on Complementary Medicine Research sponsored by the International Society for Complementary Medicine Research.

The invitation of stakeholders to the symposium panel was made to represent a wide and relevant spectrum of panellists with different professional backgrounds and clinical expertise so that any given perspective would dominate the panel. The panel would thus intentionally be comprised of experts from several fields of relevance for multimodal rehabilitation of pain patients. Notably, the panel tried to combine "in-house" research experts from Sweden with external experts and international leaders each from different academic and clinical healthcare disciplines. Additionally, the invited stakeholders would represent different

clinical and academic organizations, e.g. the European Society of Integrative Medicine (ESIM) and the Academic Consortium for Integrative Medicine and Health (ACIMH) in North America. Detailed information about each expert in the final panel is given in the full congress report (Appendix 1).

A medical journalist and media researcher (DF) observed and documented the symposium. The symposium moderator, who was also one of the presenters (TS), took field notes detailing the types of outcome measures that was presented and discussed. The aggregated symposium documentation and field notes data were used to derive a list of identified outcome measures. Thematic analysis was used to categorize the identified outcome measures into different domains based on their clinical features (17). The final set of outcomes were analysed descriptively and tabulated using aspects of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines as a template (18).

Phase 3: Synthesizing scientific outcomes and export opinions

The scientifically derived outcomes and the outcomes reported by international stakeholders were synthesized in the form of a clinical "outcomes toolkit" guideline report.

Data of outcome measures from the first two project phases, i.e. from the systematic literature review (n=61), and from the international research symposium (n=90), in total 151 types of outcome measures or outcome areas, were merged. Following the removal of duplicates, the remaining outcomes measures were thematically analysed and categorized into domains and sub-domains. The final sets of outcomes were descriptively tabulated into "toolkit tables" detailing different types of clinical outcomes.

RESULTS

Please see the appendixes for the full project reports including complete figures, tables and supplementing information of the results from each of the different project phases (Appendix 1-3).

Phase 1: Outcomes from the scientific literature

The electronic database searches resulted in an initial pool of 64 records, of which 37 records were excluded after screening the titles and abstracts. Following the removal of duplicates from the remaining 27 records, a sample of 13 articles was eligible for full-text assessment. Two papers were excluded for not fulfilling the inclusion criteria, which resulted in a final sample of 11 articles to be included in the systematic review (19-28).

In total there were 61 different outcome measures identified in the scientific literature, which were categorized into three domains: patient reported outcome measures (n=30), outcome measures of physical function (n=13), and outcome measures of resource utilization, costs and cost-effectiveness (n=18).

The patient reported outcomes measures ranged from different types of single rating scales for pain intensity and severity of pain, to more complex questionnaires targeting outcomes such as pain-related disability, depression and health-related quality of life. Physical function outcome measures included many different types of tasks, for example lifting, walking, or climbing stairs in standardized forms. There were a variety of utilization and cost measures

including direct and indirect costs relating to different kinds of health care resources, as well as more theoretical constructs such as quality-adjusted life years gained, cost-effectiveness acceptability curves, and incremental cost effectiveness ratios.

Phase 2: Outcomes from expert opinions

The title of the research symposium was "Evidence-based assessment of integrative care for pain". Eight experts participated as panellists at the research symposium in Berlin. Together the panellists represented five countries, at least eight universities, and several hospitals and clinics internationally.

The panellists presented and discussed a wide range of different types of outcomes (n=90) and outcome domains (n=7) during the stakeholder symposium. Seventy-one of the outcome measures were categorized into the following three domains, which were similar to the domains that emerged in the systematic literature review: patient reported outcome measures (n=54), outcome measures of physical function (n=2), and different outcome measures of resource utilization, costs and cost-effectiveness (n=15).

In addition to the previously identified outcome domains, the panellists presented an additional nineteen (n=19) types of outcomes that were categorized into four new outcome domains, which had not been covered in the systematic literature review. These domains comprised qualitative (n=6), public health/social (n=7), biomarker (n=2), and other (n=2) outcomes.

Phase 3: The outcomes toolkit

A total of 124 clinical outcomes were identified and reported in 4 toolkit tables, each representing different outcomes, domains and sub-domains. The final set of outcomes were categorized into 7 domains and 7 sub-domains:

Toolkit table 1:	Domain:	Patient reported outcome measures (n=62)
	Sub-domains:	Pain (n=9)
		Quality of life or health status (n=12)
		Efficacy or disability (n=8)
		Depression or anxiety (n=9)
		Functional or other (n=24)
Toolkit table 2:	Domain:	Outcome measures of physical function (n=15)
Toolkit table 3:	Domain:	Resources, costs and cost-effectiveness outcomes(n=28)
	Sub-domains:	Specific cost analysis outcomes (n=7)
		Direct and indirect costs (n=21)
Toolkit table 4:	Domain:	Qualitative outcomes (n=6)
	Domain:	Public health/social outcomes (n=7)
	Domain:	Biomarker outcomes (n=2)
	Domain:	Other outcomes (n=4)

The complete toolkit tables are presented in the full outcomes report (Appendix 3).

DISCUSSION

Please see the appendixes for the full project reports including the discussions and conclusions from each of the different project phases (Appendix 1-3).

The main aim of the systematic literature review was to identify and summarize outcomes measures currently reported in the scientific assessment and evaluation of multi-component pain rehabilitation interventions. Sixty-one different outcome measures were identified in total, which could be categorized into the three main domains: patient reported outcome measures, physical function outcome measures, and resource utilization and cost-related outcome measures. The domain with the highest number of outcome measures was patient reported outcome measures that had 30 different outcome measures. The clinical use of patient reported outcome measures was much more common than the use of either physical function outcome measures or cost-related outcome measures. One possible explanation to this finding is that most patient reported outcome measures consists of single rating scales, or short forms or questionnaires that are easy to administrate, takes little time to complete and can be carried out at the patients' choice of place including in their home or over the phone. The targeted and specific pain-related questions of patient reported outcome measures might also have a high degree of face validity to the responding patients making them relevant in the clinical context. Among the most popular patient reported outcome measures that were identified in the analysis were the numerical rating scales (NRS, 0-10) and visual analogue scales (VAS, 0-100) of e.g. pain intensity or pain severity. Notably, both of these scales are similar single-item outcome measures that are, if not the most, very commonly used clinical tools in the assessment of pain. As these outcome measures have been found to be responsive to change in pain patients, they should be strongly considered for continued use in clinical practice.

During the international research symposium, the panellist presented and discussed numerous clinically relevant outcome measures and outcome areas, both generally as well as going into details about certain specific instruments. Accordingly, in comparison to the systematic literature review (Appendix 1), the symposium session entailed an overall larger number of types of outcomes and outcome areas. This was to be expected since reports of randomized clinical trials need to be limited by nature and only include the specific outcome measures that were used in each specific study. Seventy-one (n=71) of the types of outcomes that were discussed by the panellists could be categorized into the similar three domains as the outcomes identified in the systematic literature review, which include: patient reported outcome measures, outcome measures of physical functioning, and resources, costs and cost-effectiveness outcomes. Similar to the literature review, the vast majority of outcomes were relating to the patient reported outcomes (n=54), secondly to cost-related types of outcomes (n=15). Surprisingly, very few, only two, types of outcome measures or areas relating to physical function were addressed. The reason for this is unclear, but perhaps the panellists were less familiar with the use of physical function outcomes. Notably, albeit several of the panellists had clinical backgrounds from different health care professions, few had a clinical background in physical rehabilitation specifically, which may help to explain the low prevalence of such types of outcomes in the symposium presentations.

The objective of the third project phase was to synthesize outcomes from the scientific literature and outcomes identified from expert opinions to develop an evidence-informed structured overview or guideline of different clinical outcomes, i.e. a proposed outcomes toolkit. A total of 124 final clinical outcomes were identified and reported in 4 different

toolkit tables, 7 domains and 7 sub-domains. The patient reported outcomes were the most the frequent types of identified outcomes (n=62). To be expected this was the same quantitative pattern that was found in the previous two project phases, i.e. from the systematic literature review (Appendix 1), and from the research symposium gathering the international stakeholders' expert opinions (Appendix 2). From a clinical perspective it was clear that the numerous types of identified patient reported outcomes would benefit from further categorization to aid clinical decision-making in the selection of outcomes. The thematic analysis resulted in 5 different sub-domains of patient reported outcome measures. Four of the sub-domains entailed clearly defined clinical areas of evaluation: pain, quality of life or health status, efficacy or disability, and depression or anxiety (Appendix 3, Toolkit table 1). These were represented by 38 different types of clinical outcomes, which can be measured by instruments such as numerical rating scales for pain intensity or pain severity, health-related quality of life questionnaires, self-efficacy or back pain disability indexes, or anxiety and depression inventories. The patient reported outcome measures that could not be categorized into the first four sub-domains were gathered in a fifth sub-domain described by functional or other outcomes. The identified functional or other outcomes could be exemplified by various types of outcomes including perceived effects of recovery from complaints, pain catastrophizing, sleep quality, postural awareness, or satisfaction with care. Albeit these types of outcomes may be less commonly used in regular evaluation of pain rehabilitation interventions, they may nonetheless be relevant clinical outcomes and worth considering in certain types of rehabilitation contexts or for certain sub-groups of pain patients, for example those with sleep disorders or perceived low body awareness. Taken together the toolkit tables may be used as a starting point by clinicians and researches to aid clinical decision-making, selection, use and uptake of relevant outcomes in the evidence-based assessment of integrated multi-component interventions for patients with chronic pain.

Methodological considerations

There are several limitations to this research project. For example, only outcomes that were reported in randomized clinical trials were investigated in the systematic literature review. However, as randomized clinical trials are generally considered to be the gold standard in clinical research, it may be reasoned that the outcomes reported in such trials are of generally high standard and accepted by the authors as clinically and scientifically meaningful in the area of investigation. Although beyond the scope of this study, it is possible that a broadening of the inclusion criteria to also include studies with other types of research designs may have resulted in additional and different outcome measures. Further, the current research project focused on identifying different types of outcome measures that had been used in scientific studies and that was presented by a select group of international stakeholders. It did not investigate whether each instrument had been tested for validity, reliability and responsiveness within the selected target group of patients with non-specific chronic pain. Nonetheless, several of the identified outcome measures, such as the patient reported rating scales for pain and the pain disability questionnaires, are very common in clinical practice and have previously been researched in these regards, and even if an outcome measure has not been previously tested for validity it may not necessarily be interpreted as "invalid", and may thus this still be relevant for use in clinical treatment evaluation.

Lastly, a major strength of the current research project was the inclusion of three specific objectives and related sub-studies, which taken together provided a rich basis for identifying and synthesizing the most relevant and current clinical outcomes for evidence-based assessment of healthcare interventions for pain.

CONCLUSIONS

The use of relevant clinical outcomes is important in order to understand the effects of pain treatment and rehabilitation.

Considering the findings of the current systematic literature review it may be recommended to use a combination of key outcomes from three main outcome domains including patient reported outcome measures, physical function outcome measures, and cost-related outcome measures. By doing so a relevant and broad understanding of the impact of multi-component pain rehabilitation interventions in clinical practice may be more easily achieved. Notably, the integrated use of different outcomes may facilitate clinical assessment and decision-making as well as health technology assessment and policy decisions in chronic pain management, which is ultimately of benefit for individual patients and society alike.

The panellists of the international research symposium provided numerous examples of different types of outcomes measures, in multiple outcome domains, that can be used in the evidence-based assessment of complex health care interventions for patients with chronic pain. Considering the large number of outcomes that are available, it is clear that the assessment of multiple factors and perspectives can be attained and specifically tailored to different caring models and contexts. By using complementing outcome measures from different domains the understanding of the evidence-base for multi-component chronic pain management can continue to improve to the benefits of patients and society.

The proposed outcomes toolkit, derived from data of a scientific literature review and expert opinions from international stakeholders, presents an evidence-informed structured overview of 124 final clinical outcomes reported in 4 toolkit tables covering 7 domains and 7 sub-domains. The outcomes toolkit compilation should provide ample support and guidance to aid clinicians and researchers in their selection of relevant outcomes for evidence-based assessment of integrated and complex pain rehabilitation interventions.

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APPENDIX 1:
Scientific article manuscript

Ekhaga 2016-61
Research report phase 1

Scientific article manuscript:
Integrated outcomes for integrated care for pain
– A systematic literature review

Tobias Sundberg, PhD

Scientific article manuscript

Integrated outcomes for integrated care for pain – A systematic literature review

Tobias Sundberg

ABSTRACT

Background and objectives
Managing chronic pain conditions is complex and challenging for both the individual sufferers and society. Multi-component interventions are recommended in the rehabilitation of chronic pain. In order to understand the impact of different types of pain treatment and rehabilitation, there is a need to use relevant outcome measures. The objective of this study was to identify and summarize currently reported outcomes measures used in the scientific assessment and evaluation of multi-component chronic pain rehabilitation interventions.

Methods
A systematic literature review of randomized controlled trials was conducted using the following electronic databases: CINAHL, EMBASE, PEDro, and PubMed/MEDLINE. The searches was limited to articles written in English, detailing an adult population with non-specific chronic pain, and published over the last ten years (Jan 2008 to Dec 2017). The selection of articles was conducted in a stepwise approach, first screening the titles and abstracts, then the full text peer-reviewed articles, in order to identify the reported outcome measures. Clinical trial and outcome measure data was gathered based on the Cochrane handbook for data extraction. Thematic analysis was used to categorize the identified outcome measures into domains based on clinical features.

Results
In total there were 61 different outcome measures identified in the literature. The outcome measures could be categorized into three main domains, whereby we identified 30 different patient reported outcome measures, 13 outcome measures of physical function, and 18 different outcome measures of resource utilization, costs and cost-effectiveness. The patient reported outcomes measures ranged from different types of single rating scales for pain intensity and severity of pain, to more complex questionnaires targeting outcomes such as pain-related disability, depression and health-related quality of life. Physical function outcome measures included many different types of tasks, for example lifting, walking, or climbing stairs in standardized forms. There were a variety of utilization and cost measures including direct and indirect costs relating to different kinds of health care resources, as well as more theoretical constructs such as quality-adjusted life years gained, cost-effectiveness acceptability curves, and incremental cost effectiveness ratios.

Conclusions
Considering the current findings it may be recommended to use a combination of key outcomes from patient reported outcome measures, physical function outcome measures, and cost-related outcome measures, in order to achieve a relevant and broad understanding of the impact of multi-component chronic pain rehabilitation interventions in clinical practice.

BACKROUND

Pain is common, disabling and costly for persons and society. Rehabilitation strategies might be challenging to formulate, implement and evaluate. The use of multiple-components care strategies such as integrated or multimodal rehabilitation, i.e. also known as complex health care interventions, have shown promising results and have been advocated in health technology assessment recommendations. The Swedish Council on Health Technology Assessment, in their report "Rehabilitation of chronic pain" (1), concludes that multimodal rehabilitation improves conditions for the patient to return to work, compared with no or less extensive efforts. However, there are a number of identified knowledge gaps and prioritized areas in healthcare that need further attention to improve multi-components rehabilitation and clinical care of patients suffering from chronic pain. Such highlighted areas include better definition and description of the patients that receive pain rehabilitation, and also strategies to improve the interpretability and the replication of successful care strategies in the management of chronic pain patients. In order to address this, i.e. to provide detailed and relevant descriptions of pain patients, and equally important, to investigate the impact of different pain interventions and pain rehabilitation programs, there is a need to implement relevant outcome measures. Arguably, an appropriate selection of outcome measures might facilitate not only the understanding of the effects of treatment on individual patient recovery, but may also help informing decision-making and broader societal perspectives on pain rehabilitation such as potential health economy implications of different treatment strategies.

We have previously conducted a number of research studies in the area of multi-component or integrated healthcare interventions, notably in part with the generous support of Ekhaga foundation. In particular, we have explored care strategies in terms of the integration of conventional and complementary therapies in the rehabilitation of patients with various pain disorders. Here, we have gained valuable experiences targeting different outcomes and aspects of the rehabilitation processes in different health care settings, e.g. in the primary care management of patients with chronic back and neck pain (2–6); the use integrative care in health promotion of nursing staff in emergency care (7); the integration of massage as an adjunct therapy in the emergency care management of patients with pain following motor vehicle injuries (8); assessed the feasibility of using hospital and registry data to evaluate integrative care management of patients with chronic pain and stress (9,10,11). In essence, to continue fostering a positive development and improvement of rehabilitation strategies of patients with chronic pain there is an urgent need for more systematic research and longer-term evaluation of intervention programs. Considering previous research initiatives and identified knowledge gaps of multimodal pain rehabilitation research we believe that it is of high importance to not only disseminate research by means of single scientific reports of selected single outcomes. Rather, there is an equally imperative need to foster understanding and consensus of research and evaluation strategies, especially targeting the integration of different types of outcomes in evaluation, that may further improve the evidence-based assessments of complex healthcare interventions for pain. Notably, such efforts will be of importance not only for the Swedish healthcare system and stakeholders, but also for an international audience of healthcare providers, patients, policy and decision makers wishing to close the gap between research and practice in the field of integrated healthcare interventions for pain.

Aim and objectives

The overall aim of this project was to gather best available evidence on integrating outcomes for integrated care, i.e. the evidence-based assessment of integrated healthcare interventions for pain. Accordingly, the specific objectives of this report were to identify and describe the key outcomes used for evidence-based assessment of integrated pain rehabilitation interventions.

METHODS

Study design

A systematic literature review.

Databases and search strategy

The searches of was conducted using the following electronic databases:

- CINAHL (12),
- EMBASE (13),
- PEDro (14), and
- PubMed/MEDLINE (15).

The specific literature searches were modified according to the particular interface of each electronic database, whereby combinations of the below main key words and search strings were employed.

1. Pain [Title/Abstract] AND Chronic [Title/Abstract]
2. "Non-specific" [Title/Abstract] OR "Non specific" [Title/Abstract]
3. 1 AND 2
4. Care* [Title/Abstract] OR Treatment [Title/Abstract] OR Rehabilitation* [Title/Abstract]
5. "Randomized Controlled Trial" [Publication Type] OR "controlled clinical trial" [Publication Type] OR randomized [Title/Abstract] OR randomized [Title/Abstract] OR random* [Title/Abstract] OR trial [Title/Abstract] OR group* [Title/Abstract]
6. 3 AND 4 AND 5

Inclusion criteria

The searches were limited to randomized controlled trials, articles written in English, detailing adult populations with non-specific chronic pain, and published over the last ten years (1st of January 2008 to 31st of December 2017).

Types of interventions: The interventions had to be within the area of pain rehabilitation and involve multi-component management, i.e. at least two different types of treatments, therapies, or care. Any kind of therapy could be included, including any conventional and/or complementary therapy procedures.

Comparator(s)/control: There was no restriction regarding the type of control intervention.

Types of outcome measures: There was no restriction on the type of outcome measures, as the main objective of this review was to investigate reported outcomes.

Data extraction and analysis

The titles and abstracts of each retrieved record were screened according to the inclusion criteria. Following the initial screening, the full text articles of the records that appeared to meet the inclusion criteria were obtained and further assessed for eligibility. The full text was also assessed if there was any doubt regarding the potential suitability of the study. Thus, the selection of the final articles for review was conducted in a stepwise approach, first screening the titles and abstracts, then the full text peer-reviewed articles, in order to identify records that complied with the stipulated inclusion criteria. Subsequently, data targeting the clinical trial and the reported outcome measures was gathered using a template adapted from the Cochrane handbook for data extraction (16) for the purposes of this review.

Outcome measures reported in each of the randomized clinical trial articles were identified and tabulated. Thematic analysis (17) was used to categorize the identified outcome measures into domains based on clinical features. Additional clinical trial data, including country of origin, clinical setting, target diagnosis, sample size and age of the study population, details about the types of interventions, and type/s of comparators/controls were descriptively analyzed and tabulated. The results were reported using aspects of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines as a template (18).

RESULTS

Search and retrieval of articles

The electronic database searches resulted in an initial pool of 64 records of randomized controlled trials, of which thirty-seven records could be excluded from screening the titles and abstracts (Figure 1). Removing duplicates from the remaining 27 articles resulted in a sample of 13 articles eligible for full-text assessment (Figure1). Two additional papers were excluded for not fulfilling the inclusion criteria resulting in a final sample of 11 articles (19-28) to be included in the review (Figure 1). A detailed list of the records from each database, including data on the first author, publication year, title, and reasons for exclusion, is reported in the attached article supplement (Supplement 1).

Flow Diagram of Paper Search and Retrieval

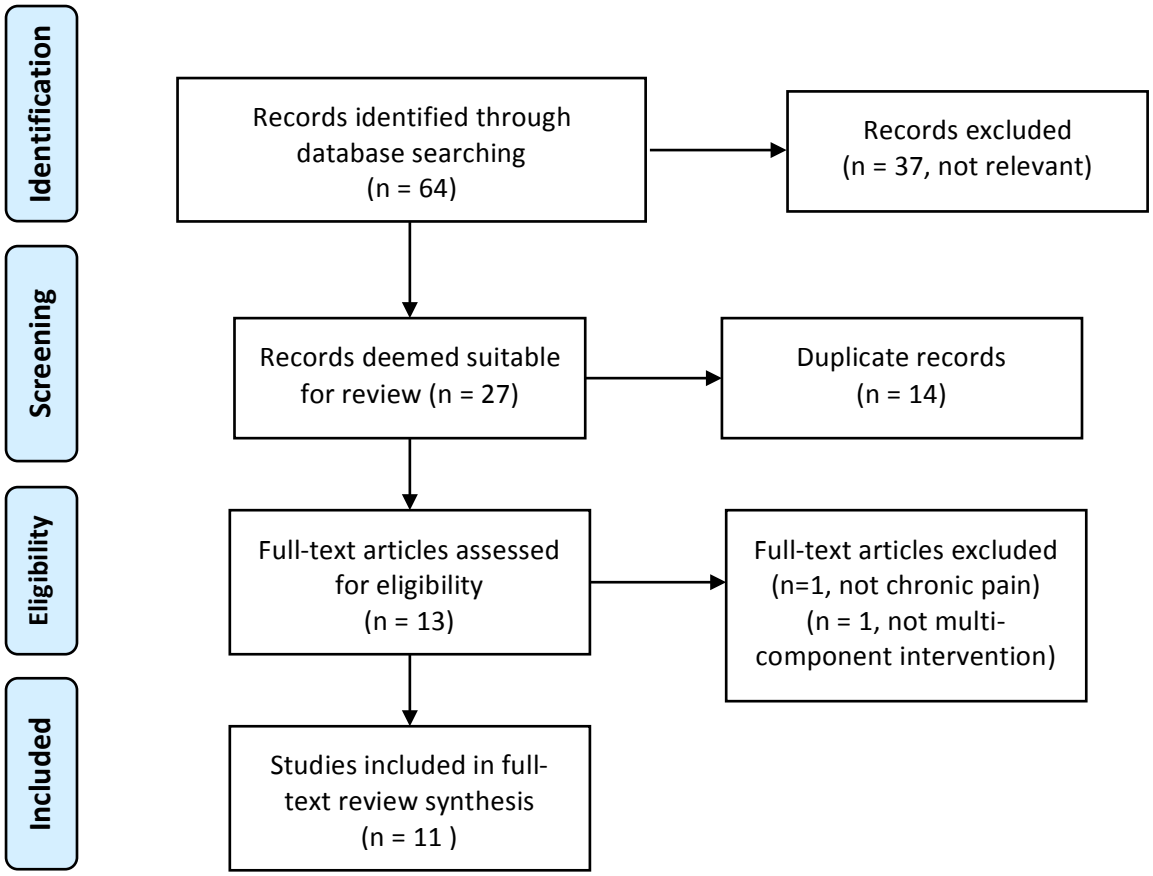

Figure 1. PRISMA flow diagram over the search and retrieval of scientific papers for inclusion in the literature review.

Characteristics of randomized controlled trials

The characteristics of the randomized controlled trials, including the interventions and outcome measures reported in the articles, are presented in in detail in article supplement 2. Most studies had been conducted in European countries, although other countries were also represented including Japan, Iran, Turkey and Taiwan, and the most common diagnosis across the trials was non-specific low back pain of chronic duration. The clinical trial interventions mostly targeted physical therapy oriented interventions with combinations of conventional or usual care procedures, albeit complementary therapies such as massage or acupuncture were also included in some trials (Supplement 2).

Outcomes

In total, 61 different outcome measures were identified in the retrieved sample of clinical studies (Table 1), which could be categorized into three main domains:

- Patient reported outcome measures (PROMs) (n=30);
- Outcome measures of physical function (n=13);

- Outcome measures of resource utilization, costs and cost-effectiveness (n=18).

The PROMs ranged from different types of single rating scales for pain intensity and severity of pain, to more complex questionnaires targeting outcomes such as pain-related disability, depression and health-related quality of life (Table 1).

Physical function outcome measures included many different types of tasks, for example lifting, walking, or climbing stairs in standardized forms, but also more rare physical measures such as pelvic floor muscle assessment, and sensory acuity (Table 1.

There were a variety of utilization and cost measures including direct and indirect costs relating to different kinds of health care resources, as well as more theoretical constructs such as quality adjusted life years gained (QALY), cost-effectiveness acceptability curves (CEAC), and incremental cost effectiveness ratios (ICER) (Table 1).

Table 1. Overview of outcome measures and domains.

	Patient reported outcome measures (n=30)	**Outcome measures of physical function (n=13)**	**Resourses, costs and cost-effectiveness outcomes (n=18)**
1	Bothersomeness of back pain (Bothersomeness)	1-min stair climbing (number of stairs)	Help from partner or friends (hours)
2	Beck Depression Inventory (BDI)	5-min walking (m)	Absenteeism from paid work (hours)
3	Center for Epidemiologic Studies Depression scale (CES-D, 0–60)	50 foot walking (s)	Alternative therapist (no of visits)
4	Chronic Pain Self-efficacy Scale (CPSS), PSEQ (0–100), PSE: pain self-efficacy, FSP: functional self-efficacy, CSE: coping self-efficacy	6-Minute Walk Test (6MWT)	Cost-effectiveness acceptability curves (CEAC)
5	Fear Avoidance Beliefs Questionnaire (FABQ)	Five times sit to stand (s)	General practice (no of visits)
6	Global perceived effect (GPE): GPE for recovery from complaints, GPE for recovery of functioning in daily activities	Forward reaching by holding a stick with a weight of 4.5 kg at shoulder height (cm)	Hospital admission including medical procedure (costs)
7	Hannover functional ability questionnaire (HFAQ)	Functional capacity evaluation (FCE)	Incremental cost effectiveness ratio (ICER)
8	Health-related quality of life (EuroQol, EQ-5D)	Movement control impairment (MCI) was measured by means of six movement control tests	Indirect costs due to absence of paid work (cost diaries and treatment attendance lists)
9	Health-related quality of life Short-Form 36 questionnaire (SF-36)	Pelvic Floor Muscle strength and endurance were assessed using perineometer (Bø and Finckenhagen, 2001).	Medical specialist care (no of visits)
10	Hospital anxiety and depression (HAD)	Progressive isoinertial lifting evaluation	Non-prediscribed medication (costs)
11	Keele Start Back Tool (KSBT)	Sensory acuity of the lower back by measuring the two-point-discrimination threshold	Occupational physician (no of visits)

12	McGill pain questionnaire (MPQ)	Single-Leg Balance Test	Paid housekeeping (hours)
13	Mean pain intensity over the prior 7 days (NRS, 0-10)	Timed-up and go Test (TUG)	Prescribed medication (costs)
14	Minnesota Mutiphasic Personality Inventory-II (MMPI-II)		Psychologist (no of visits)
15	Multi Dimensional Pain Inventory – Dutch Language Version (MPI-DLV)		Quality adjusted life years gained (QALY) by using the EuroQol-5D
16	Neck Disability Index (NDI, 0–100)		Radiology (no of visits)
17	Nottingham Health Profile (NHP)		Therapist (physiotherapy, manual therapy, Cesar or Mensendieck therapist; no of sessions)
18	Oswestry Disability Index (ODI)		Total costs, existing of direct health and non-health costs (cost diaries and treatment attendance lists)
19	Pain Catastrophizing Scale (PCS)		
20	Pain severity (NRS, 0–10)		
21	Patient perceived satisfactory improvement (PPSI)		
22	Patient-Specific Functional Scale (PSFS)		
23	Patients' severity of 3 main main complaints (VAS, 0-100)		
24	Rating of impairment associated with back pain (NRS, 0-10)		
25	Roland Morris Disability Questionnaire (RMDQ)		
26	Self-perceived improvement of disability (7-point Likert scale)		
27	Severity of main complaint (NRS, 0–10)		
28	Tampa Scale for Kinesiophobia (TSK, 17–68)		
29	Visual Analogue Scale for pain intensity (VAS, 0-100)		
30	Waddell Disability Index (WI)		

DISCUSSION

The main aim of the current literature review was to identify and summarize outcomes measures currently reported in the scientific assessment and evaluation of multi-component pain rehabilitation interventions. Sixty-one different outcome measures were identified in total, which could be categorized into the three main domains: patient reported outcome measures, physical function outcome measures, and resource utilization and cost-related outcome measures.

The domain with the highest number of outcome measures was patient reported outcome measures that had 30 different outcome measures. The clinical use of patient reported outcome measures was much more common than the use of either physical function outcome measures or cost-related outcome measures. One possible explanation to this finding is that most patient reported outcome measures consists of single rating scales, or short forms or questionnaires that are easy to administrate, takes little time to complete and can be carried out at the patients' choice of place including in their home or over the phone. The targeted and specific pain-related questions of patient reported outcome measures might also have a high degree of face validity to the responding patients making them relevant in the clinical context. Among the most popular patient reported outcome measures that were identified in the analysis were the numerical rating scales (NRS, 0-10) and visual analogue scales (VAS, 0-100) of e.g. pain intensity or pain severity. Notably, both of these scales are similar single-item outcome measures that are, if not the most, very commonly used clinical tools in the assessment of pain. Considering that these outcome measures have been found to be responsive to change in pain patients, they should be strongly considered for continued use in clinical practice (30).

In comparison to self-administered patient reported outcome measures, tests of physical function were less commonly reported. Possibly due to that such outcomes would typically require specifically trained personnel to administering and conducting the testing of the patients. Additionally, physical tests might require special equipment, allocated space and facilities, and adequate time. Not all clinics have these resources available, and not all patients may have the time nor be willing to come in for extra testing procedures. Such factors may thus be important to consider when selecting what tests to possibly include in clinical practice. Nevertheless, measures of physical function can be very satisfying and provide clear benchmarks of what a patient can and cannot do. Accordingly, such aspects may therefore be very important in order to observe and track clinical progress in rehabilitation and training of patients with chronic pain. Physical tests can sometimes also be easily transferred into specific exercises and training protocols, which may further facilitate their use by pain patients and add to the relevance of using these outcome measures in clinical practice and evaluation of rehabilitation programs.

Outcome measures covering resource utilization and different types of direct and indirect costs will often require that the patient, or a family member or someone else that is close to the patient, devotes energy and time to keep detailed track of direct and indirect expenses relating to their chronic pain, for examples by writing a cost diary. Hence, due to the potential cumbersomeness involved, this is typically not requested from pain patients receiving care in routine clinical practice outside of a clinical trial. Thus, other ways of tracking costs may be considered and preferred. Recent advances in electronic record keeping and related reporting of data to local or national registries have facilitated the use of patient records, prescription data or sick leave in the analysis of resource utilization and costs. In the current review there were few such outcomes. Potential barriers to using these types of outcomes include the need to have staff with special training and knowledge on how to obtain, validate and analyze such data, and also to make sure to plan the use of these kinds of outcomes far in advance, as there may be long waiting periods to get access to such data. However, once such matters have been ensured there are likely interesting possibilities to get clinical as well as more theoretical perspectives on different types of costs relating to pain rehabilitation. For example, broader perspectives on resource utilization relevant for individuals and society, like quality adjusted life years gained (QALY), cost-effectiveness acceptability curves

(CEAC), and incremental cost effectiveness ratios (ICER) that are cornerstones in health economic evaluations. The latter outcomes currently have high impact on policy and decision making in all of health care, and especially in prioritized and costly areas like chronic pain management (1).

The majority of the retrieved randomized clinical trials had investigated interventions for patients with non-specific chronic low back pain. Perhaps not surprisingly this also reflects clinical practice where this type of low back pain is among the most common and disabling disorders for which patients seek health care (1). Interestingly, most types of chronic low back pain do not have an identified pathology that can be treated to cure the pain. Rather there are multiple and complex bio-psycho-social interactions that need to be addressed in order to effectively manage the patient's low back pain, and hence the apparent relevance for multi-component interventions in order to address the bio-psycho-social complexity (1). Most interventions reported in the current literature review detailed different types of physical therapy treatment and usual care interventions. Albeit massage and acupuncture were incorporated in some study interventions, complementary therapies were generally not included in most studies. This finding aligns with previous research that concludes there is a severe scarcity of investigations, especially randomized clinical trials, of multi-component interventions involving both complementary and conventional therapies (31). Albeit there are policy and research reports suggesting that integrated models of conventional and complementary care may be relevant from several perspectives, including clinical and safety measures (32-33), the non-academic tradition of the vast majority of complementary therapies may help explain the very low integration of these treatments in conventional care rehabilitation and research.

Most of the reviewed articles used patient reported outcome measures, some in combination with physical function outcomes and/or cost-related outcome measures. However, and in agreement with the Swedish Council on Health Technology Assessment (1), information about adverse events and complications following treatment and rehabilitation of pain were rarely reported in clinical research targeting multi-component pain rehabilitation. The reason for this is unclear, but may relate to underreporting, or that the administered pain treatments are considered to be safe. Nonetheless, adverse events are important both in terms of their potential interference with the clinical effects of the treatments, and also in relation to costs. Hence, it is recommended that adverse events from clinical treatment should routinely be reported in all randomized controlled trials as well as in routine clinical practice.

Further, none of the retrieved trials included specific biological or biomarker outcomes. Perhaps this was to be expected considering that biological measures are currently unusual as outcomes in the clinical management of non-specific low back pain. Nonetheless, building on the identified knowledge gaps in this area, our research group has, in another project with financial support from Ekhaga foundation, recently launched a prospective clinical trial in pain rehabilitation called "Exigence" that for the first time will describe and contrast two multimodal pain programs, one conventional university hospital based and one integrated private hospital based, by a range of different outcomes including biomarker and genomic outcomes to explore the value of such assessments. The Exigence study is ongoing and will be reported in a different project.

Methodological considerations

There are limitations to this systematic review. First, only outcomes that were reported in randomized clinical trials were investigated. However, as randomized clinical trials are generally considered to be the gold standard in clinical research, it may be reasoned that the outcomes reported in such trials are of generally high standard and accepted by the authors as clinically and scientifically meaningful in the area of investigation. Although beyond the scope of this study, it is possible that a broadening of the inclusion criteria to also include studies with other types of research designs may have resulted in additional and different outcome measures. Secondly, the current study only investigated which different types of outcome measures that had been used in the retrieved studies; it did not investigate whether each instrument had been tested for validity, reliability and responsiveness within the selected target group of patients with non-specific chronic pain. Nonetheless, several of the identified outcome measures, such as the patient reported rating scales for pain and the pain disability questionnaires, are very common in clinical practice and have previously been researched in these regards, and even if an outcome measure has not been previously tested for validity it may not necessarily be interpreted as "invalid" (30), and may thus this still be relevant for use in clinical treatment evaluation. Lastly, the current review only investigated the selected databases over the last ten years. It is possible that including additional databases and employing a longer search period may have resulted in the identification of additional outcome measures.

Conclusions

Considering the findings of the current systematic literature review it may be recommended to use a combination of key outcomes from three main outcome domains including patient reported outcome measures, physical function outcome measures, and cost-related outcome measures. By doing so a relevant and broad understanding of the impact of multi-component pain rehabilitation interventions in clinical practice may be more easily achieved. The integrated use of such outcome measures may facilitate clinical assessment and decision-making as well as health technology assessment and policy decisions in chronic pain management, which is ultimately of benefit for individual patients and society alike.

Acknowledgements

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Database records CINAHL

Database	Record	Author year	Title	Included for full text review	Reason for exkl
CINAHL	1	Itoh 2009	A pilot study on using acupuncture a	INKL	
CINAHL	2	Vonk 2009	Effectiveness of a behaviour graded	INKL	
CINAHL	3	Glazov 2009	Laser acupuncture for chronic non-s	EXKL	Not multi
CINAHL	4	Smeets 2009	More is not always better: cost-effe	INKL	
CINAHL	5	Mohseni-Bandpei 2011	The effect of pelvic floor muscle exe	INKL	
CINAHL	6	Tsauo 2009	The effectiveness of a functional tra	INKL	
CINAHL	7	Glazov 2010	The influence of baseline characteris	EXKL	Not multi
CINAHL	8	Ryan 2010	The relationship between psycholog	EXKL	Not randomized
CINAHL	9	Wand 2009	The self-reported aggravating activit	EXKL	Not randomized
List of exkluded papers n=4					
CINAHL	3	Glazov 2009	Laser acupuncture for chronic non-s	EXKL	Not multi
CINAHL	7	Glazov 2010	The influence of baseline characteris	EXKL	Not multi
CINAHL	8	Ryan 2010	The relationship between psycholog	EXKL	Not randomized
CINAHL	9	Wand 2009	The self-reported aggravating activit	EXKL	Not randomized
List of papers for full text review n=5					
CINAHL	1	Itoh 2009	A pilot study on using acupuncture a	INKL	
CINAHL	2	Vonk 2009	Effectiveness of a behaviour graded	INKL	
CINAHL	4	Smeets 2009	More is not always better: cost-effe	INKL	
CINAHL	5	Mohseni-Bandpei 2011	The effect of pelvic floor muscle exe	INKL	
CINAHL	6	Tsauo 2009	The effectiveness of a functional tra	INKL	

Database records EMBASE

Database	Record	Author year	Title	Included for full text review	Reason for exkl
EMBASE	1	Gedin 2017	Effectiveness, costs and cost-effecti	EXKL	Study protocol
EMBASE	2	Yilmaz Yelvar 2017	Is physiotherapy integrated virtual w	INKL	
EMBASE	3	Zhang 2016	Randomised controlled trial of contr	EXKL	Not multi
EMBASE	4	Lauche 2016	Efficacy of the Alexander Technique	EXKL	Not multi
EMBASE	5	Jacobs 2016	Effects of low back pain and of stabi	INKL	
EMBASE	6	Petrozzi 2015	Does an online psychological interve	EXKL	Study protocol
EMBASE	7	Ritchie 2015	StressModEx--Physiotherapist-led St	EXKL	Study protocol
EMBASE	8	Luedtke 2015	Effectiveness of transcranial direct c	INKL	
EMBASE	9	Wälti 2015	Short-term effect on pain and functi	INKL	
EMBASE	10	O'Keeffe 2015	Individualised cognitive functional th	EXKL	Study protocol
EMBASE	11	Seo 2014	Bee venom acupuncture, NSAIDs or	EXKL	Study protocol
EMBASE	12	Petit 2014	Effectiveness of three treatment stra	EXKL	Study protocol
EMBASE	13	Haller 2014	Credibility of a comparative sham cc	EXKL	Not multi
EMBASE	14	Lauche 2013	Effectiveness of home-based cuppin	EXKL	Not multi
EMBASE	15	Hofmann 2013	Effects of behavioural exercise thera	EXKL	Study protocol
EMBASE	16	Paolucci 2012	Psychological features and outcome	INKL	
EMBASE	17	Morone 2011	Quality of life improved by multidisc	INKL	
EMBASE	18	Berenguera 2011	Study protocol of cost-	EXKL	Study protocol
EMBASE	19	Lauche 2011	The influence of a series of five dry c	EXKL	Not multi
EMBASE	20	Rodriguez-Blanco 2010	Study protocol of effectiveness of a	EXKL	Study protocol
EMBASE	21	Perez-Palomares 2010	Percutaneous electrical nerve stimu	EXKL	Not multi
EMBASE	22	Itoh 2009	A pilot study on using acupuncture a	INKL	
EMBASE	23	Smeets 2008	Chronic low back pain: physical train	INKL	

List of exkluded papers n=15

EMBASE	1	Gedin 2017	Effectiveness, costs and cost-effecti	EXKL	Study protocol
EMBASE	3	Zhang 2016	Randomised controlled trial of contr	EXKL	Not multi
EMBASE	4	Lauche 2016	Efficacy of the Alexander Technique	EXKL	Not multi
EMBASE	6	Petrozzi 2015	Does an online psychological interve	EXKL	Study protocol
EMBASE	7	Ritchie 2015	StressModEx--Physiotherapist-led St	EXKL	Study protocol
EMBASE	10	O'Keeffe 2015	Individualised cognitive functional th	EXKL	Study protocol
EMBASE	11	Seo 2014	Bee venom acupuncture, NSAIDs or	EXKL	Study protocol
EMBASE	12	Petit 2014	Effectiveness of three treatment stra	EXKL	Study protocol
EMBASE	13	Haller 2014	Credibility of a comparative sham cc	EXKL	Not multi
EMBASE	14	Lauche 2013	Effectiveness of home-based cuppin	EXKL	Not multi
EMBASE	15	Hofmann 2013	Effects of behavioural exercise thera	EXKL	Study protocol
EMBASE	18	Berenguera 2011	Study protocol of cost-	EXKL	Study protocol
EMBASE	19	Lauche 2011	The influence of a series of five dry c	EXKL	Not multi
EMBASE	20	Rodriguez-Blanco 2010	Study protocol of effectiveness of a	EXKL	Study protocol
EMBASE	21	Perez-Palomares 2010	Percutaneous electrical nerve stimu	EXKL	Not multi

List of papers for full text review n=8

EMBASE	2	Yilmaz Yelvar 2017	Is physiotherapy integrated virtual w	INKL	
EMBASE	5	Jacobs 2016	Effects of low back pain and of stabi	INKL	
EMBASE	8	Luedtke 2015	Effectiveness of transcranial direct c	INKL	
EMBASE	9	Wälti 2015	Short-term effect on pain and functi	INKL	
EMBASE	16	Paolucci 2012	Psychological features and outcome	INKL	
EMBASE	17	Morone 2011	Quality of life improved by multidisc	INKL	
EMBASE	22	Itoh 2009	A pilot study on using acupuncture a	INKL	
EMBASE	23	Smeets 2008	Chronic low back pain: physical train	INKL	

Database records PEDro

Database	Record	Author year	Title	Included for full text review	Reason for exkl
PEDro	1	Wälti 2015	Short-term effect on pain and functi	INKL	
PEDro	2	Beinert 2015	Cervical joint position sense in neck	EXKL	Not multi
PEDro	3	Smeets 2008	Chronic low back pain: physical train	INKL	
PEDro	4	Yilmaz Yelvar 2017	Is physiotherapy integrated virtual w	INKL	
PEDro	5	Lauche 2016	Efficacy of the Alexander technique	EXKL	Not multi
PEDro	6	Jacobs 2016	Effects of low back pain and of stabi	INKL	
PEDro	7	Lee 2013	Managing psychosocial contributors	INKL	
PEDro	8	Morone 2011	Quality of life improved by multidisc	INKL	
PEDro	9	Perez-Palomares 2010	Percutaneous electrical nerve stimu	EXKL	Not multi
PEDro	10	Paolucci 2012	Psychological features and outcome	INKL	
List of exkluded papers n=3					
PEDro	2	Beinert 2015	Cervical joint position sense in neck	EXKL	Not multi
PEDro	5	Lauche 2016	Efficacy of the Alexander technique	EXKL	Not multi
PEDro	9	Perez-Palomares 2010	Percutaneous electrical nerve stimu	EXKL	Not multi
List of papers for full text review n=7					
PEDro	1	Wälti 2015	Short-term effect on pain and functi	INKL	
PEDro	3	Smeets 2008	Chronic low back pain: physical train	INKL	
PEDro	4	Yilmaz Yelvar 2017	Is physiotherapy integrated virtual w	INKL	
PEDro	6	Jacobs 2016	Effects of low back pain and of stabi	INKL	
PEDro	7	Lee 2013	Managing psychosocial contributors	INKL	
PEDro	8	Morone 2011	Quality of life improved by multidisc	INKL	
PEDro	10	Paolucci 2012	Psychological features and outcome	INKL	

Database records PubMed

Database	Record	Author year	Title	Included for full text review	Reason for exkl
PubMed	1	Berenguera 2011	Study protocol of cost-	EXKL	Study protocol
PubMed	2	Buselli 2011	Effectiveness evaluation of an integr	EXKL	Study protocol
PubMed	3	Cuesta-Vargas 2015	Changes in disability, physical/ment	EXKL	Not RCT
PubMed	4	Eardley 2013	Professional kinesiology practice for	EXKL	Not multi
PubMed	5	Haller 2014	Credibility of a comparative sham cc	EXKL	Not multi
PubMed	6	Hofmann 2013	Effects of behavioural exercise thera	EXKL	Study protocol
PubMed	7	Itoh 2009	A pilot study on using acupuncture a	INKL	
PubMed	8	Jacobs 2016	Effects of low back pain and of stabi	INKL	
PubMed	9	Lauche 2016	Efficacy of the Alexander Technique	EXKL	Not multi
PubMed	10	Lauche 2013	Effectiveness of home-based cuppin	EXKL	Not multi
PubMed	11	Lauche 2012	My back has shrunk: the influence o	EXKL	Not multi
PubMed	12	Luedtke 2015	Effectiveness of transcranial direct c	INKL	
PubMed	13	Morone 2011	Quality of life improved by multidisc	INKL	
PubMed	14	O'Keeffe 2015	Individualised cognitive functional th	EXKL	Study protocol
PubMed	15	Paolucci 2012	Psychological features and outcome	INKL	
PubMed	16	Petit 2014	Effectiveness of three treatment stra	EXKL	Study protocol
PubMed	17	Ritchie 2015	StressModEx--Physiotherapist-led St	EXKL	Study protocol
PubMed	18	Rodriguez-Blanco 2010	Study protocol of effectiveness of a	EXKL	Study protocol
PubMed	19	Seo 2014	Bee venom acupuncture, NSAIDs or	EXKL	Study protocol
PubMed	20	Wälti 2015	Short-term effect on pain and functi	INKL	
PubMed	21	Yilmaz Yelvar 2017	Is physiotherapy integrated virtual w	INKL	
PubMed	22	Zhang 2016	Randomised controlled trial of contr	EXKL	Not multi

List of exkluded papers n=15

PubMed	1	Berenguera 2011	Study protocol of cost-	EXKL	Study protocol
PubMed	2	Buselli 2011	Effectiveness evaluation of an integr	EXKL	Study protocol
PubMed	3	Cuesta-Vargas 2015	Changes in disability, physical/ment	EXKL	Not RCT
PubMed	4	Eardley 2013	Professional kinesiology practice for	EXKL	Not multi
PubMed	5	Haller 2014	Credibility of a comparative sham cc	EXKL	Not multi
PubMed	6	Hofmann 2013	Effects of behavioural exercise thera	EXKL	Study protocol
PubMed	9	Lauche 2016	Efficacy of the Alexander Technique	EXKL	Not multi
PubMed	10	Lauche 2013	Effectiveness of home-based cuppin	EXKL	Not multi
PubMed	11	Lauche 2012	My back has shrunk: the influence o	EXKL	Not multi
PubMed	14	O'Keeffe 2015	Individualised cognitive functional th	EXKL	Study protocol
PubMed	16	Petit 2014	Effectiveness of three treatment stra	EXKL	Study protocol
PubMed	17	Ritchie 2015	StressModEx--Physiotherapist-led St	EXKL	Study protocol
PubMed	18	Rodriguez-Blanco 2010	Study protocol of effectiveness of a	EXKL	Study protocol
PubMed	19	Seo 2014	Bee venom acupuncture, NSAIDs or	EXKL	Study protocol
PubMed	22	Zhang 2016	Randomised controlled trial of contr	EXKL	Not multi

List of papers for full text review n=7

PubMed	7	Itoh 2009	A pilot study on using acupuncture a	INKL
PubMed	8	Jacobs 2016	Effects of low back pain and of stabi	INKL
PubMed	12	Luedtke 2015	Effectiveness of transcranial direct c	INKL
PubMed	13	Morone 2011	Quality of life improved by multidisc	INKL
PubMed	15	Paolucci 2012	Psychological features and outcome	INKL
PubMed	20	Wälti 2015	Short-term effect on pain and functi	INKL
PubMed	21	Yilmaz Yelvar 2017	Is physiotherapy integrated virtual w	INKL

APPENDIX 1:

Supplement 2

Characteristics of the included studies and the reported outcome measures.

Reference Author year (n=11)	**Origin** Country; Setting.	**Participants** Type of pain; Sample size; Age.	**Intervention details** The reported treatment arms and types of interventions. Integrated/combined treatments, therapies or care in bold.	**Outcomes** Reported outcome measures (primary/secondary as reported), name and brief description, e.g. pain intensity, pain disability, quality of life, functional measures etc.
Itoh 2009	Japan; Meiji University of Oriental Medicine Hospital.	LBP >= 6 months; N=32 (20 women, 12 men); 16-81 years.	4 treatment groups: 1) Control group no treatment 2) Acupuncture group 3) Transcutaneous electrical nerve stimulation group **4) Acupuncture and transcutaneous electrical nerve stimulation (A&T) group**	Primary outcome measures: • Pain intensity, quantified with a 10 cm visual analogue scale (VAS, 0–100 mm) • Pain disability measured with the Roland Morris Questionnaire (RDQ, 0– 24 points).
Luedtke 2015	Germany; Interdisciplinary chronic pain centre.	LBP >= 12 weeks; N=135; 18-65 years.	**Anodal transcranial direct current stimulation** (identical electrode position) for five consecutive days immediately before **cognitive behavioural management** (four week multidisciplinary programme of 80 hours). **Sham transcranial direct current stimulation** (identical electrode position) for five consecutive days immediately before **cognitive behavioural management** (four week multidisciplinary programme of 80 hours).	Primary outcome measures: • Pain intensity (0-100 visual analogue scale) • Oswestry disability index Secondary outcome measures: • Hannover functional ability questionnaire • "Bothersomeness" • RAND SF-36-item health survey; • Fear avoidance beliefs questionnaire; • Hospital anxiety and depression (HAD); • Patient perceived satisfactory improvement
Mohseni-Bandpei 2011	Iran; University clinic(?)	Chronic LBP; N=20 (all women); 20-50 years.	Control group: traditional physiotherapy treatment for LBP including electrotherapy and general exercises. The experimental group was given **traditional physiotherapy treatment for LBP** (same as control group) and **pelvic floor muscle (PFM) exercise** in addition.	• Visual analogue scale (VAS) • Oswestry Disability Questionnaire • Pelvic Floor Muscle strength and endurance were assessed using perineometer (Bø and Finckenhagen, 2001).
Morone 2011	Italy; Rehabilitative specialized centre.	Chronic LBP; N=74 (final sample 70 patients; 25 male, 45 women); 18-80 years	• **Multidisciplinary professional healthcare back school program** (theory, obstacle course simulation, exercise protocol, ergonomics, activities of daily living, specific exercises to re-educate breathing, self-stretching, erector spinae reinforcement, postural exercises) **+ usual care** • Usual care only (medical/pharmacological assistance as needed "…like analgesics, miorelaxants, and NSAIDs…".	• Quality of Life SF-36 • Visual analogue scale for pain (VAS) • Waddell Disability Index (WI) • Oswestry Disability Index (ODI)
Paolucci 2012	Italy; Ambulatory rehabilitative university centre.	Chronic LBP; N=50; 18-80 years.	• **Multidisciplinary professional healthcare back school program** (theory, obstacle course simulation, exercise protocol, ergonomics, activities of daily living, specific exercises to re-educate breathing, self-stretching, erector spinae reinforcement, postural exercises) **+ medical treatment** same as below for the control group. • Control group medical treatment (NSAIDs and myorelaxant) self administered under physician supervision.	• Minnesota Mutiphasic Personality Inventory-II (MMPI-II) is one of the most commonly used self-report instrument in the psychological evaluation • Quality of Life SF-36 • Visual analogue scale for pain (VAS) • Waddell Disability Index (WI) • Oswestry Disability Index (ODI)

APPENDIX 1: Supplement 2

Smeets 2008	The Netherlands; Three outpatient rehabilitation centres.	Chronic LBP (>= 3 months); N=172; 18-65 years.	• **Combination treatment (a *active physical treatment* and an operant-behavioral graded activity with problem solving training)** • Active physical treatment (physical training of aerobic capacity and muscle reconditioning) • Operant-behavioral graded activity with problem solving training	Primary outcome measure: • Roland Disability Questionnaire Secondary outcome measure: • Patients' severity of 3 main main complaints (VAS 0-100) • Back pain intensity (VAS 0-100) • McGill pain questionnaire • Self-perceived improvement of disability (7-point Likert scale), • Beck Depression Inventory • Six physical performance tasks: (1) 5-min walking (m), (2) 50 foot walking (s), (3) five times sit to stand (s), (4) forward reaching by holding a stick with a weight of 4.5 kg at shoulder height (cm), (5) 1-min stair climbing (number of stairs), (6) progressive isoinertial lifting evaluation; the patient lifts a box with a weight four times within 20 s from floor up to a 75 cm high table. After each cycle of four lifting movements, the weight is increased in a standardized way (completed cycles.
Smeets 2009	The Netherlands; Three outpatient rehabilitation centres.	Chronic LBP (>= 3 months); N=172; 18-65 years.	• **Combination treatment (a *active physical treatment* and an operant-behavioral graded activity with problem solving training)** • Active physical treatment (physical training of aerobic capacity and muscle reconditioning) • Operant-behavioral graded activity with problem solving training	• Total costs, existing of direct health and non-health costs (cost diaries and treatment attendance lists) • Indirect costs due to absence of paid work (cost diaries and treatment attendance lists) • Type of utilization: General practice (no of visits), Medical specialist care (no of visits), Radiology (no of visits), Occupational physician (no of visits), Psychologist (no of visits), Therapist (physiotherapy, manual therapy, Cesar or Mensendieck therapist; no of sessions), Hospital admission including medical procedure (costs), Alternative therapist (no of visits), Prescribed medication (costs), Non-prediscribed medication (costs), Paid housekeeping (hours), Help from partner or friends (hours), Absenteeism from paid work (hours) • Roland Disability Questionnaire • Quality adjusted life years gained (QALY) by using the EuroQol-5D • Incremental cost effectiveness ratio (ICER) • Cost-effectiveness acceptability curves
Tsauo 2009	Taiwan; Rehabilitation clinic .	Chronic LBP (>=3 months); N=37 (final sample 25); Mean age 49 and 46 in the two intervention groups respectively.	• Training group (**individualised functional training programme** with specific trunk stabilisation training for patients with LBP "The training intensity and time increased to a maximum of 3 h per day as the patients' endurance improved. In all, patients would spend 100 h over a period of 2–3 months in training.") **+ current treatment** • Control group (current treatment) Both groups maintained their current treatment, and the training group participated in the additional programme for 100 h over a period of 2-3 months.	• Rating of impairment associated with back pain (0-10) • Oswestry disability index (ODI) • Functional capacity evaluation (FCE): Reaching (cm) Walking 1 min (m) Balance beam (s) Stair climbing 1 min (steps) Ladder climbing 3-step for five repetitions (level) Bilateral carrying 5 m (kg) Pushing 3 m (kg) Pulling 3 m (kg) Floor to knuckle lifting (kg) Knuckle to shoulder lifting (kg) Shoulder to overhead lifting (kg) Power grip, left (kg) Power grip, right (kg)

				Lateral pinch, left (kg) Lateral pinch, right (kg) Complete Minnesota Dexterity Test – Placing (s) Complete Minnesota Dexterity Test – Turning (s) Complete Minnesota Dexterity Test – deposition (s) Complete Minnesota Dexterity Test – One hand turning and placing (s) Complete Minnesota Dexterity Test – Two hand turning and placing (s) Purdue pegboard, right (piece) Purdue pegboard, left (piece) Purdue pegboard, both hand (piece) Purdue pegboard, assembly (piece) Repetitive crouching, 24 times (s) Repetitive stooping, 24 times (s) Sustained stooping 3 min (level) Sustained crouching 3 min (level) Sustained kneeling 3 min (level) Sustained sitting (level) Sustained standing (level)
Vonk 2009	The Netherlands; General practice, outpatient setting	Chronic neck pain >=3 months (mean duration 60 months); N=139; 18-70 years (mean age 46 years).	• **Conventional exercise** decided by participating physiotherapists (treatment guided by the patient's pain experience, strong focus on exercise but additional techniques allowed were **massage**, thoracic treatment up to thoracic 9, localized 3-d **mobilization** within the physiological boundaries of the joint capsule, mobilization in all directions, **traction**, and non-manipulative techniques of **Mulliken or McKenzie** (manipulative techniques, acupuncture and other (alternative) techniques were excluded, as were physical applications such as ultrasound or diathermy). • Graded activity programme (The treatment was according to a biopsychosocial model, which implies that it is guided by the patient's functional abilities and that time-contingent methods are used to increase the activity level of the patient).	Primary outcome: • Global perceived effect (GPE) with two parts: GPE for recovery from complaints, and GPE for recovery of functioning in daily activities (7-point Likert scale, ranging from completely recovered (1) to worse than ever (7)). Secondary outcome measures: • Severity main complaint (0–10) • Pain severity (0–10) • Impediment (0–10) • Neck Disability Index (NDI) (0–100) • Multi Dimensional Pain Inventory – Dutch Language Version (MPI-DLV): activities (0–6) • Chronic Pain Self-efficacy Scale (CPSS), PSEQ (0–100), PSE: pain self-efficacy, FSP: functional self-efficacy, CSE: coping self-efficacy • Tampa Scale for Kinesiophobia (TSK) (17–68) • Pain Catastrophizing Scale (PCS) (0–52) • Center for Epidemiologic Studies Depression (CES-D) scale (0–60) • Health-related quality of life (EQ-5D) (0–1)
Wälti 2015	Switzerland; Centre for health care.	Chronic LBP (>=3 months) N=28; 18-60 years.	• **Multimodal treatment** (MMT) for patients with moderate to severe disability and medium risk of poor outcome. MMT includes a) **neurophysiological education** on the perception of pain to decrease self-limitation due to catastrophizing believes about the nature of NSCLBP, b) **sensory training** of the lower trunk because these patients predominantly show poor sensory acuity of the trunk, and c) **motor training** to regain definite movement control of the trunk. Treatment was aimed at reducing pain and disability and, potentially, addressing associated abnormal cortical processing in NSCLBP. • Usual physiotherapy	Primary outcome measure: • Mean pain intensity over the prior 7 days (NRS 0-10) Secondary outcome measures: • Roland and Morris Disability Questionnaire (RMDQ) • Keele Start Back Tool (KSBT) • Patient-specific disability measured with the Patient-Specific Functional Scale (PSFS) • Fear avoidance beliefs were measured using the Fear Avoidance Beliefs Questionnaire (FABQ) • Catastrophizing thoughts measured with the Pain Catastrophizing Scale (PCS) • Movement control impairment (MCI) was measured by means of six movement control tests, • Sensory acuity of the lower back by measuring the two-point-discrimination threshold • Sick leave during the last seven

				days • Analgesic intake during the last seven days • Adherence to treatment
Yilmaz Yelvar 2017	Turkey; University Hospital Department of Physical Therapy and Rehabilitation	Subacute and chronic LBP (>=2 months) N=44;	• Physical therapy (hot pack (15 min), TENS (15 min), deep heat with ultrasound (5 min), and therapeutic exercises (extension exercise, posterior pelvic tilt, cat–camel exercise, and stretching of the lumbar extensor muscle). • **Physical therapy + virtual walking** (passively watch virtual walking video clip in a sitting position (Vita Digital Productions, NC, USA) played via an iPod (Apple Inc., CA, USA) with video glasses (Wrap920, Vuzix Coorporation, NY, USA) at each therapy session during hotpack application. For the virtual walking task, a video clip was taken by a cameraman who was naturally walking down Ireland forest at the speed of approximately 1.0 km/h. The patients were asked to imagine as if they were actually walking, while they were watching the video clip.)	• Visual Analog Scale (VAS) • TAMPA Kinesiophobia Scale (TKS) • Oswestry Disability Index (ODI) • Nottingham Health Profile (NHP) • Timed-up and go Test (TUG) • 6-Minute Walk Test (6MWT) • Single-Leg Balance Test

APPENDIX 2:
Research congress report

Ekhaga 2016-61
Research report phase 2:

Research congress report:
Integrated outcomes for integrated care for pain
– Expert opinions from an international research symposium

Tobias Sundberg, PhD

Research congress report

Integrated outcomes for integrated care for pain – Expert opinions from an international research symposium

Tobias Sundberg, David Finer

ABSTRACT

Background and objectives
Outcomes reported in randomized clinical trials may not be the only relevant outcomes for measuring the effects of multi-component interventions for patients suffering from chronic pain. Therefore, a team of international stakeholders, representing a broad range of professions and research expertise in the field of pain and integrated care rehabilitation, were invited to an international research symposium to share their expert opinions about the use of outcomes in pain management evaluation from different perspectives.

Methods
Eight international panellists participated in the symposium that took place at the World Congress Integrative Medicine and Health in Berlin, May 2017. A medical journalist and media researcher (DF) observed and documented the symposium. The symposium moderator, who was also one of the presenters (TS), took field notes detailing the types of outcome measures that was presented and discussed. The aggregated symposium documentation and field notes data were used to derive a list of identified outcome measures. Thematic analysis was used to categorize the identified outcome measures into different domains based on their clinical features. The final set of outcomes were analysed descriptively and tabulated.

Results
There was a wide range of different types of outcome measures (n=90) and outcome domains (n=7) that were presented and discussed during the stakeholder symposium. Seventy-one of the outcome measures were categorized into the following three domains: patient reported outcome measures (n=54), outcome measures of physical function (n=2), and different outcome measures of resource utilization, costs and cost-effectiveness (n=15). Nineteen additional types of outcomes were categorized into the following four domains: qualitative outcomes (n=6), public health/social outcomes (n=7), biomarker outcomes (n=2), and other outcomes (n=4).

Conclusions
The stakeholders presented numerous clinically relevant outcome measures that can be used in the evidence-based assessment of multi-component interventions for patients with chronic pain. Considering the vast range of identified outcomes and domain categories that emerged from the symposium, it is clear that there are ample possibilities for clinicians and researchers to identify clinically relevant outcomes measures, and to specifically tailor different combinations of outcomes, for appropriate evaluation of different chronic pain management models, interventions and target groups of patients.

BACKGROUND

In the systematic literature review conducted in the first phase of this project (please see the scientific article manuscript reported in Appendix 1) if was found that a combination of key outcomes from the three main domains of patient reported outcome measures, physical function outcome measures, and cost-related outcome measures may be recommended in order to attaining a comprehensive understanding of the effects of combined treatment strategies for patients with non-specific chronic pain. Among the 61 different outcome measures that were identified in the scientific literature, the patient reported outcome measures were the most common types of outcomes, and some studies combined these with physical function measures or cost-related outcomes. However, adverse events and biomarker outcomes were not reported in the retrieved articles. Importantly, there may also be a range of additional outcomes that can be of clinical relevance for multi-component pain rehabilitation assessment that have not been identified. In order to explore this matter further a team of leading stakeholders and researchers were invited to an international research symposium.

Aim and objective

The general aim of the second project phase was to gather stakeholders' expert opinions about the use of outcomes in clinical pain management. Specifically, the objective was to explore outcomes for evidence-based assessment of complex healthcare interventions for patients with chronic and non-specific pain.

METHODS

Gathering stakeholder expert opinions – An international research symposium

An international research symposium, i.e. a focused meeting with national and international stakeholders in the field of researching pain rehabilitation and integrated care, was arranged in order to gather expert opinions.

Setting

The research symposium took place at the World Congress Integrative Medicine and Health in Berlin 5th May 2017, which was also the 10th European Congress for Integrative Medicine and the 12th International Congress on Complementary Medicine Research sponsored by the International Society for Complementary Medicine Research (Figure 1).

Figure 1. http://www.ecim-iccmr.org/2017/

Participants

The invitation of stakeholders to the symposium panel was made to represent a wide and relevant spectrum of panellists with different professional backgrounds and clinical expertise so that any given perspective would dominate the panel. The panel would thus intentionally be comprised of experts from several fields of relevance for multimodal rehabilitation of pain patients. Notably, the panel tried to combine "in-house" research experts from Sweden with external experts and international leaders each from different academic and clinical healthcare disciplines. Additionally, the invited stakeholders would represent different clinical and academic organizations, e.g. the European Society of Integrative Medicine (ESIM) and the Academic Consortium for Integrative Medicine and Health (ACIMH) in North America. Detailed information about each expert in the final panel is given in the results section below.

Additionally, participants were also the attending audience in the symposium auditorium, which was open for all congress delegates, researchers, educators, policy makers and providers with interests in pain rehabilitation.

Research panel agenda

Dr Sundberg chaired the symposium, together with Dr Falkenberg, and moderated the presentations. Figure 2 details an overview of the panellists and their presentation topics. Dr Sundberg opened the research symposium by presenting first. To ensure proper time and focus for each panellist to present their selected outcome topics, the panel of stakeholders took turn sharing their experiences and expert opinions. Highlighting the need for integrated perspectives and analyses, emphasize was made to include different types of outcomes measures as part of the presentations. Dr Sundberg moderated the questions and discussion that followed, where the stakeholder participants as well as members of the audience interacted. The discussions were monitored to make sure that all participants who wanted to had the opportunity to speak. Once all questions had been answered the symposium session was closed.

Data gathering and analysis

A medical journalist and media researcher (DF), external to the symposium group, attended, observed and documented the symposium session at the congress in Berlin, whereby a written "symposium summary" of each stakeholder's contribution was detailed in report form. Additionally, the moderator (TS) took field notes detailing identified outcome measures from the stakeholders' presentations and discussions. The aggregation of the symposium documentation and field notes data was used to derive a list of identified outcome measures. Thematic analysis was used to categorize the identified outcome measures into different domains based on their clinical features. The findings were analysed and tabulated descriptively alongside the symposium summaries of the panellists and their presentations.

RESULTS AND DISCUSSION

The World Congress Integrative Medicine & Health, Berlin 2017

Congress overview

The first World Congress on Integrative Medicine and Health in Berlin, Germany, May 3-5, 2017 was unique. With some 800 participants from over 50 countries, the quality and quantity of research was unprecedented. Also, for the first time a joint statement, the historic Berlin Agreement, was agreed upon, calling for self-responsibility and social action in practicing and fostering integrative medicine and health globally. The congress – formally a combination of the 10th ECIM (European Society of Integrative Medicine) and 12th ICCMR (International Society for Complementary Medicine Research) Congresses – was opened by Hermann Gröhe the Federal Minister of Health Germany, and the Head of WHO Margaret Chan. The theme was ”The Future of Comprehensive Patient Care – Strengthening the Alliance of Researchers, Educators and Providers”.

Several participants remarked on the high quality and quantity of research contributions, both oral presentations and posters. For example, professor David Eisenberg (who was one of the stakeholders at the symposium), and a veteran of integrative medicine research in the USA, in rounding up the conference, told the plenary:

> *"I cannot remember a conference with so many high-quality posters and good presentations."*

Kathrin Wode, PhD, a Swedish researcher and oncologist voiced similar sentiments:

> *"The scientific level is generally speaking very high. Apart from the focus on evidence, participants also question themselves in a critical, self-reflective way, which I find very refreshing. I found the complex discussions on placebo particularly interesting. And the oncology presentations, of course."*

The research symposium

The title of the research symposium was "Evidence-based assessment of integrative care for pain". Figure 2 presents an overview of the eight experts that participated as panellists at the research symposium in Berlin. Together the panellists represented five countries, at least eight universities, and several hospitals and clinics internationally (Figure 2).

It was difficult to achieve an exact number of the audience, as congress delegates came and left for other parallel sessions during the one and a half hour long symposium, but an estimate was that approximately 80 delegates attended the symposium.

Program

Friday, May 5, 2017

14:30 - 16:00 Saal A, B	Symposium **Evidence-based assessment of integrated care for pain** Chair: Sundberg T, Falkenberg T (Stockholm/SE)
14:30 - 14:40	Evidence-based assessment of integrated chronic pain - How do we best integrate different outcomes? Sundberg T (Stockholm/DE)
14:40 - 14:50	Perspectives on health economic research outcomes in Integrative Medicine for chronic pain Baars E (Leiden/NL)
14:50 - 15:00	Public health outcomes in researching Integrative Medicine for pain Steel A (Melbourne/AU)
15:00 - 15:10	Psychological outcomes in researching Integrative Medicine for pain Lauche R (Ultimo/AU)
15:10 - 15:20	Provider's and patient's experiences in integrative care for pain Andermo S (Huddinge/SE)
15:20 - 15:30	Outcome measures used in mind-body interventions for pain Cramer H (Essen/DE)
15:30 - 15:40	Integrative care for low back pain - results of a Harvard study Eisenberg D (Boston/US)
15:40 - 15:50	Existential genomics - a prospective clinical observational study Falkenberg T (Stockholm/SE)
15:50 - 16:00	Questions and wrap-up Sundberg T (Stockholm/DE)

Figure 2. List of participants and presentation topics at the Berlin symposium.

The outcomes

During the symposium, the panellist presented and discussed numerous clinically relevant outcome measures and outcome areas, both generally as well as going into details about certain specific instruments. Accordingly, in comparison to the systematic literature review (Appendix 1), the symposium session entailed an overall larger number of types of outcomes and outcome areas. This was to be expected since reports of randomized clinical trials need to be limited by nature and only include the specific outcome measures that were used in each specific study.

Seventy-one (n=71) of the types of outcomes that were discussed by the panellists could be categorized into the similar three domains as the outcomes identified in the systematic literature review. These are presented in Table 1 and include: patient reported outcome measures, outcome measures of physical functioning, and resources, costs and cost-effectiveness outcomes. Similar to the literature review, the vast majority of outcomes were relating to the patient reported outcomes (n=54), secondly to cost-related types of outcomes (n=15). Surprisingly, very few, only two, types of outcome measures or areas relating to

physical function were addressed. The reason for this is unclear, but perhaps the panellists were less familiar with the use of physical function outcomes. Notably, albeit several of the panellists had clinical backgrounds from different health care professions, few had a clinical background in physical rehabilitation specifically, which may help to explain the low prevalence of such types of outcomes in the symposium presentations.

Table 1. Patient reported, physical function, and cost-related outcomes, and outcome areas, presented by the panellists.

	Patient reported outcomes (n=54)	**Outcome measures of physical function (n=2)**	**Resources, costs and cost-effectiveness outcomes (n=15)**
1	Aberdeen back pain scale (ABPS)	Endurance	Cost-benefit analysis
2	Arthritis Self Efficacy Scale	Exercise activity	Cost-effectiveness analysis
3	Avoidance Endurance Questionnaire (KPI-AEQ)		Cost-minimization analysis
4	Back-specific disability		Cost-utility analysis
5	Beck Anxiety Inventory (BAI)		Direct costs
6	Beck depression inventory (BDI)		Drug dispensing at pharmacies, over the counter
7	Body awareness		Indirect costs
8	Body function (SF-36)		Minimal number of clinical encounters to achieve the optimal clinical outcome
9	Bothersomeness of pain		Not being able to work
10	Brief pain inventory (BPI)		Medication other than analgesics
11	Center for Epidemiologic Studies Depression Scale (CESD)		Physician visits
12	Chronic Pain Acceptance Questionnaire (CPAQ)		Prevalence of use of care
13	Chronic Pain Self Efficacy Scale (CPSS)		Registered drug prescriptions
14	Depression Anxiety Stress Scale (DASS)		Use of over the counter analgesics
15	Disease specific quality of life, e.g. EORTC (cancer)		Use of prescription analgesics
16	Effortless awareness and connectedness		
17	Fear Avoidance Belief Questionnaire (FABQ)		

18	Fibromyalgia impact questionnaire (FIQ)		
19	Forced awareness		
20	Freiburg Mindfulness Inventory (FMI)		
21	Generalized Anxiety Disorder (GAD)		
22	Generic quality of life (SF-12)		
23	Generic quality of life (SF-36)		
24	Geriatric Depression Scale (GDS)		
25	Hamilton Anxiety Rating Scale (HAM-A)		
26	Hamilton Depression Scale (HAM-D)		
27	Headache-Specific Locus of Control Scale		
28	Health Locus of Control Scale		
29	Hospital Anxiety and Depression Scale (HADS)		
30	McGill pain questionnaire (MPQ)		
31	Mental health (SF-36)		
32	Multidimensional Health Locus of Control		
33	Multidimensional pain inventory (MPI)		
34	Numerical rating scale for pain intensity (NRS)		
35	Oswestry Disability Index (ODI)		
36	Pain Catastrophizing Scale (PCS)		
37	Pain disability index (PDI)		
38	Pain locus of control		
39	Pain Self Efficacy Questionnaire (PSEQ)		
40	Patient global impression of change		
41	Patient Health Questionnaire (PHQ-9)		
42	Patient Perspective Survey (PPS)		

43	Perception of body posture		
44	Pittsburgh Sleep Quality Index (PSQI)		
45	Postural awareness scale		
46	Quality of life (EQ-5D)		
47	Quality of life (WHO-QOL-BREF)		
48	Roland Morris Disability Questionnaire (RMDQ)		
49	Satisfaction of care		
50	Satisfaction with health/life		
51	Spielberger State-Trait Anxiety Inventory (STAI)		
52	Visual analogue scale for pain intensity (VAS)		
53	Vitality		
54	Wellbeing		

However, and interestingly, in addition to the previously identified and familiar outcome domains, the panellists presented an additional nineteen (n=19) types of outcomes that were categorized into four new outcome domains, which had not been covered in the systematic literature review. These outcomes are presented Table 2.

Particularly, these additional types of outcomes areas may be considered either "up-and-coming" in the clinical trial research arena, such as biomarker outcomes investigating DNA breakage/repair by telomerase enzyme activity, or outcomes that are less commonly part of randomized clinical trials or routine clinical pain management, such as qualitative or public health related outcomes, or other perhaps more theoretically driven outcomes such as long term model feasibility or outcomes derived from discourse analytics (Table 2).

Another outcome area that emerged at the symposium, especially during the discussions and interactions with participants of the audience, was relating to the family's or the spouses' perspectives on living with persons suffering from chronic pain (Table 2). Exploring such types of outcomes may contribute with important information to further the understanding of the broader individual and social impacts that may follow from living with chronic pain, for example barriers and facilitators to engaging in participatory activities with the family, at work, during leisure time or other activities.

Table 2. Qualitative, public health/social, biomarker, and other outcomes, and outcome areas, presented by the panellists.

	Qualitative outcomes (n=6)	**Public health/social outcomes (n=7)**	**Biomarker outcomes (n=2)**	**Other outcomes (n=4)**
1	Empowerment from care	Family or spouses perspectives/implications of living with someone who has chronic pain	DNA breakage/repair, i.e. telomerase enzyme activity	Duration perspectives, both in terms of follow-ups of outcomes but also in terms of suitable intervention lengths to achieve optimal results (dose response)
2	Patient experiences	Health promotion, eg by CAM use	Glycaemic control	"Model feasibility" as an outcome in clinical care, sustainability.
3	Patient perspectives	Mortality		Spirituality
4	Provider experiences	National surveys, eg use of resources/services/self-care		Interpretation of disease/illness
5	Provider perspectives	Preventive medicine, eg contributions by naturopaths to aid individuals risk factors for cardiovascular disease		
6	Self-care and self-management strategies	Scope of health conditions treated in a "model of care"		
7		Social implications of pain		

The presentations – symposium summaries

A highlight of the final day's proceeding was the international research panel on Evidence-based Assessment of Integrated care for Pain, chaired by Tobias Sundberg, PhD and Torkel Falkenberg, PhD, Karolinska Institutet, Sweden.

The summary of each panellist's research presentation that was delivered at the international stakeholder symposium session is presented below.

* * *

Presentation:	***Evidence-based assessment of integrated care for chronic pain***
Panellist:	*Tobias Sundberg, PhD, Karolinska Institutet, Stockholm, Sweden.*
About:	*Dr Sundberg has a clinical background in physical therapies and functional rehabilitation with a special interest in chronic back and neck pain.*

Dr Sundberg started off by thanking Ekhagastiftelsen (the Ekhaga Foundation) for support, then after introducing the international panel members he started the his presentation by asking the panellists and the auditorium:

> *"How do we best integrate different outcomes?"*

Dr Sundberg then talked about different outcomes identified in the literature and possible ways to approach and research outcomes in clinical practice. One illustration he gave was a pilot project that he managed in Sweden and which explored a consensus-based integrative medicine model for back and neck pain in primary care adhering to multiple stakeholders' perspectives. The team of providers included a GP, an administrator and a range of CAM providers (acupuncture, massage, spinal mobilization/manipulation, shiatsu, yoga and qigong).

> *"The diversity of providers made it hard to agree on outcomes, especially since the team emphasized consensus decisions, but this was achieved after a range of meetings during more than half a year", said Dr Sundberg.*

Ultimately, the team of providers agreed on the following outcome areas for the developed model of integrative medicine for back and neck pain:

- Patient-reported outcome measures including pain intensity
- Measures of body function, mental health, quality of life outcomes
- Outcomes by means of patient/provider experiences and perspectives
- Cost-effectiveness outcomes

Accordingly, the project design synthesized evidence from health services research, randomized control trials, focus group discussions and cost utility analysis. The findings of the project were that patients did better on both integrative medicine and conventional treatment. But the team did not stop there. After all, why bother with integrative medicine, if there is no difference in outcomes? On further analysis, it was revealed that there were also clinical trends in terms of less use of analgesics, improved quality of life, vitality, empowerment and self-care strategies in favour of integrative medicine.

Dr Sundberg's conclusion was that the understanding of integrated care rehabilitation had benefitted from integrated outcome evaluation.

* * *

Presentation:	***Perspectives on health economic research outcomes in Integrative Medicine for chronic pain***
Panellist:	*Erik W. Baars, MD, MSc Epidemiology, PhD, University of Applied Sciences Leiden, The Netherlands,*
About:	*Dr Baars holds a professorship in anthroposophic healthcare and has a background as an anthroposophic physician.*

Professor Baars spoke on perspectives on health economic research outcomes. The term health economic evaluation refers to a study which includes both the comparative costs associated with two or more health care interventions, and the comparative clinical effects, measured either in clinical units, health preferences or monetary benefit.

A full health economic evaluation includes the following types of analyses:

- Cost-minimization analysis, where there are two similar alternatives; this type of analysis is not very common in the literature
- Cost-effectiveness analysis, e.g., for patients with chronic renal failure, who receive a transplant or dialysis, so we are looking at the same outcome but with different costs, as measured by cost per unit of effect (e.g., amount of euros spent per life-year gained) or effects per unit of cost (e.g., life-years or mm Hg reduction gained per euro spent):
- Cost-utility analysis, including units of overall impact on length and quality of life such as Quality-adjusted life-years (costs per QALY gained) or Healthy years equivalent (cost per healthy year gained)
- Cost-benefit analysis, including monetary units, either as a ratio (e.g. euro cost/euro benefits in a functioning market), net benefit (loss) of one program over another, or willingness-to-pay (with no available functioning market)

Measures of health effects used in health economic evaluations may relate to outcomes or costs.

- Outcomes can be measured as:
  Intermediate or final outcomes, e.g., glycaemic control or clinical symptoms of diabetes, where final outcomes may be measured along single dimensions or multiple dimensions (e.g., mortality rate or attributes/ domains of health), and where – in turn - multiple dimensions may be e.g., disease specific or generic, e.g. cancer-specific (EORTC) or Quality of Life (QoL: SF-36).
- Costs may be measured as:
  Direct costs (e.g., costs of pain medication or physician visists) or indirect costs (e.g., costs of not being able to work) in the short or long term. Here it is particularly important to make sure that all such costs are included and calculated.

Moving to the topic of integrative medicine interventions, he discussed health promotion interventions. Their aim is typically to strengthen and/or support the ability of the individual to self-manage and adapt. They typically entail a large investment in therapy at the start but are cost effective in the long term, as they achieve lasting symptom reduction without treatment. Importantly, the relevance of this fact for health economic outcome evaluations on

integrated treatment is that interventions should cover a long period. In his presentation, Beers mentioned in particular a 2012 review by Patricia M Herman et al from 2012 on lower back pain (LBP) (Are complementary therapies and integrative care cost-effective? A systematic review of economic evaluations, BMJ Open 2012; 2(5): e001046. In summary, the review showed that complementary therapies may be more effective for some disorders in the long term than conventional treatment. A summary of results of complementary and integrative medicine economic evaluations that met five study-quality criteria (31 articles representing 28 studies) was made for e.g., patient populations with low back pain (LBP), painful rheumatic disorders, headache and dysmenorrhoea. The higher-quality studies indicate potential cost-effectiveness, and even cost savings across a number of complementary therapies and populations. However, while there were a number of cost-effective analyses and cost-utility analysis in the material, cost-benefit analyses were absent. Furthermore, measurement periods in some of the studies, e.g., for dysmenorrhea (3-6 months) and headache (up to 15 treatments/3 months) may have been too short, dr Baars concluded.

* * *

Presentation:	***Integrative care for low back pain – results of a Harvard study***
Panellist:	*Prof David Eisenberg, MD, Harvard University T.H. Chan School of Public Health, USA.*
About:	*Prof Eisenberg has a clinical background as a physician and is one of the pioneers in researching complementary and integrative medicine in the US*

Professor Eisenberg presented the results of a Harvard study on integrative care for low back pain (LBP), taking two decades and involving many colleagues. He said:

> *"From a health services research perspective, we may study people with a common condition who get usual care without complementary and alternative medicine (CAM), people who use usual care and a single CAM option or people who use usual care together with multiple CAM Rx, i.e. an "integrative care team" (including nurses and physicians). I am excited that we were able to evaluate the last option, representing a best-case scenario option in my opinion."*

The researchers received a National Institutes of Health (NIH) grant about 15 years ago for work published in April 2012 in the Journal of Alternative and Complementary Therapy by Eisenberg et al as "A model of integrative care for low-back pain". The goal was to determine if such team care is more effective than usual care alone in decreasing symptoms and improving function for adults with chronic LBP. The training of the team took 6-12 months and involved:

- Establishing and maintaining an atmosphere of mutual respect, collegiality, and shared appreciation
- Providing didactic presentations and demonstrations
- Experiential learning by all team members (e.g. a neurologist who receives massage and acupuncture)
- A professional facilitator and medical anthropologist to guide communications and break down professional barriers

- Mindful listening and formal Mindfulness based stress reduction instruction for all team members
- Volunteer study subjects recruited for team evaluation (diagnosis) and treatment “in a fish bowl”
- Awareness of the unexpected; openness to transformational experiences
- Trans-disciplinary training applied to subjects in randomized pilot study

After that a pilot randomized controlled trial was done with employees from Brigham and Women’s Hospital in Boston and HMO (health maintenance organization) subjects. Six patients received usual care, and 14 integrative team care. All were evaluated at 2, 5, 12 and 26 weeks in terms of symptoms, functional status and when they could return to work. Already after 2-5 weeks the groups diverged, with people getting integrative care feeling better. Once the initial symptomatic relief achieved (usually via passive CAM Rx), patients were referred for more participatory/educational self-care instruction (e.g., Mindfulness Based Stress Reduction, occupational therapy, physical therapy, movement exercises, nutrition and/or psychological counselling). Increased self-awareness was regarded as a synergistic intervention. The goal was to determine the minimal number of clinical encounters to achieve the optimal clinical outcome during the 12 weeks the treatment lasted. The conclusions of the pilot study were that it was feasible for a multidisciplinary, outpatient integrative care team to deliver coordinated, individualized intervention to patients with sub acute lower back pain. Results showed a promising trend for benefit of treating patients with persistent lower back pain with this model, and warranted evaluation in a full-scale study, which was made possible at the The Osher Center at Harvard Medical School (OCC) which was created in 2001, with support from the Bernard Osher Foundation, of which professor Eisenberg was the founding director.

> *"Every patient has individual “fingerprinting”, no two were exactly the same, and the unit of intervention was a trained team, not simply access to these modalities, professor Eisenberg explained."*

He went on to present unpublished results of a larger NIH-funded follow-up study 2010-2015, in which observational integrative care was compared with usual care for LBP Patients (looking at 150 enrolled patients for usual care and 150 enrolled patients for usual and team care). Follow-up was very high, with an average of 94% at both 6 and 12 months. For both disability and bothersomeness of pain, there were clinically meaningful improvements at 6 months, and these changes were significantly greater than the control group changes. Of note, these group differences appear to increase over time. But we have not yet seen results of longitudinal models testing for group by time interactions). Similar patterns were seed of measures of pain intensity, and we observed a slightly greater improvement in exercise activity in the OCC, with group differences being statistically different 6 months.

Figure 3. Professor David Eisenberg.

Professor Eisenberg drew three conclusions from the preliminary presentation: 1. First, in the real world setting of an academic hospital, significant socio-demographic differences (e.g., education, income, race) exist between those who do and do not utilize a complementary and integrative medicine for chronic LBP. Surprisingly, this was not true for other characteristics of the LBP group, e.g., chronicity, injection use and surgeries. 2. After controlling for a number of major confounders, the OCC integrative model exhibited statistically greater improvements at 6 months in disability and pain; positive effects were sustained, if not greater, at 12 months. 3. Positive trends were also observed in multiple secondary outcomes. Cost-effectiveness analyses are pending, but as we move from a fee for service payment model to a capitated care model, integrative care teams may become clinical and financial "assets", professor Eisenberg concluded.

* * *

Presentation:	***Public health outcomes in researching integrative medicine for pain***
Panellist:	*Amie Steel, PhD, University of Technology Sydney, Australia.*
About:	*Dr Steel has a clinical background in naturopathy.*

Dr Steele spoke on public health outcomes and started her presentation with three questions:

- What are the public health impacts of pain?
- How can public health research contribute to the body of evidence about pain management in integrative medicine?
- How can clinical practice based research networks (PBRNs) be used to undertake public health research about pain management in integrative medicine?

Pain is a public health challenge due to factors such as high prevalence, disparity across population groups, the impacts of uncontrollable external factors, the contribution of pain to other public health issues, the huge economic burden involved, and the need for appropriately educated health professionals. Dr Steel warned of the danger of tying complementary research exclusively to the issue of efficacy. Methods and perspectives were needed from neighbouring traditions such as public health, health services research and social science. There is, she continued, also an urgent need for research initiatives built on: A critical, non-partisan approach; Rigorous methods and designs; A coordinated, broad and multidisciplinary focus; Inclusivity and network building, i.e., facilitating and promoting already existing networks and promoting research activity elsewhere as necessary. The most established and well-recognised mechanism for this is the practice-based research networks, or PBRN. It allows the clinician to combine a primary focus on community care with strong links to the research community. Not having to do the research (unless you want to) but having a say in how the research is done. In Australia there are three such networks in the complementary and integrative medicine field:

- PRACI (Practitioner research and Collaboration Initiative),
- ACORN Australian Chiropractic Research Centre and
- ORION (Osteopathy Research and Innovation Network).

One of the things that makes these organisations unique in terms of their research approach is, according to Dr Steel, that - rather than taking "a big data approach", they focus on sub-studies, using a combination of basic science, clinical trials, epidemiological and sociological methods. A survey of almost 500 practitioners in the PRACI network e.g., shows that across 14 types of complementary and integrative practitioners from acupuncturists to yoga practitioners, over half had a special interest in pain management. A health services perspective on the same survey showed that chiropractors, osteopaths, physiotherapists and counsellors were the most likely to share their primary clinical practice with another profession. Figures for GPs, nurses, midwives etc were considerably lower. From a health economics viewpoint, figures, which show that practitioners spend most of their time on pain patients, can be used to justify funding for integrative pain research. PRACI sub-studies are now underway to show in detail the:

- Prevalence of use, e.g., an exploration of complementary and integrative medicine for managing acute respiratory tract infections in children
- Scope of health conditions treated, e.g., medical conditions and symptoms presented to complementary and integrative medicine practitioners in Australia.
- Managing national health priority areas, e.g., studying the perceptions of traditional Chinese medicine practitioners on treating people with arthritis
- Health promotion, e.g., a national survey on various types of complementary and integrative medicine practitioners and gluten-free diets
- Preventive medicine, e.g., exploring the contribution made by Australian naturopaths to the management of individuals with cardiovascular disease and/or known cardiovascular disease risk factors

Meanwhile, ACORN has studied socio-demographics, occupational roles, practice characteristics and clinical management among its members, e.g., chiropractic treatment approaches to headache, their provision of nutritional advice and to what extent they implement evidence-based practice principles

"Public health research contributes important insights to the larger body of research within integrative medicine of pain management, Dr Steel concluded. PBRNs can be structured to afford IM researchers an opportunity to explore a diverse range of research questions of significance."

* * *

Presentation:	***Psychological outcomes in researching integrative medicine for pain***
Panellist:	*Dr Romy Lauche, Chancellors postdoctoral research fellow, University of Technology Sydney.*
About:	*Dr Lauche has a degree in psychology and is also well acquainted with naturopathy and complementary therapies.*

Dr Lauche spoke about psychological outcomes and her presentation covered three main issues: Why include psychological outcomes in pain research? What psychological outcomes are available? How to chose optimal outcomes?

Many of the root factors for chronic low back pain are physical, based in neurophysiology, muscles/connective tissue and movement patterns. However, many psychosocial factors involved are also involved, not least in the chronification of low back pain. These include learning, attitudes and beliefs, endurance, and psychological distress. Some of these are predictive of treatment outcome. With the caveat, that she was not presenting a complete overview, Dr Lauche quoted studies showing that:

- Baseline anxiety and depression had small to moderate predictive value for low back pain
- Decrease in pain catastrophizing mediates outcomes
- Fear avoidance can be a as moderator of treatment efficacy
- Increases in self-efficacy predicts improvements of pain intensity in chronic pain patients after a 10-week lifestyle modification program (unpublished)

In general, there is a paucity of trials that include psychosocial outcomes; the randomized controlled trials that do exist have low external validity, while at the same time, there are limitations associated with observational study designs. There are many aspects to consider in choosing the optimal outcome measures. Is the study theoretically driven or explorative (qualitative)? What depth of investigation is aimed at, and what is feasible? In terms of properties of outcome measures, one must consider: Prevalence of use; Available languages; Validity; Reliability; Long version, short version; Selected scale; Disease specific vs. general outcomes. In designing the study, decisions must be taken as to the duration of the intervention as well as when and how often the outcomes are to be assessed. In terms of which characteristics to sample, there are also choices to be made, such as including age and diagnosed mental health conditions vs. subclinical problems, whether outcomes should be patient- or clinician-reported, the cost of using various measurement instruments, and their licensing, as well as the comparability between various studies. Which instruments should be chosen? For depression there are more than six commonly used scales, and the same applies for measuring anxiety. And there are many more, e.g., scales, questionnaires or other instruments to measure chronic pain acceptance, pain catastrophizing, fear avoidance, avoidance endurance, locus of control, pain self-efficacy, and so on.

"You have to choose your instruments with care based on your special needs, and the patients", said Dr Lauche, advising the audience to "be creative, have ideas, but also compare with the literature".

In summary, Dr Lauche said that most pain conditions are associated with mental health and psychological factors, that psychological instruments can guide the use of interventions in different patients, and that there are a variety of psychological measurement instruments available for this purpose, allowing for a tailored study design.

* * *

Presentation:	***Providers' and patients' experiences in integrative care for pain***
Panellist:	*Susanne Andermo PhD, Karolinska Institutet, Stockholm, Sweden.*
About:	*Dr Andermo has a background in public health and anthropology and is also well acquainted with complementary therapies.*

Dr Andermo talked about her research for her doctoral dissertation on the previously mentioned randomized clinical trial integrative medicine pilot project in Stockholm, run by Dr Sundberg. Andermo's focus was on both patients and providers explored by utilizing outcomes derived from qualitative research. The patients reported their experiences of conventional and integrative care for back and neck pain and their experiences of changes in health, and the providers their experiences of the process of collaboration in the integrative medicine project. The data for her first paper was collected using 11 focus group discussions with 26 participants and analysed with latent content analysis. The results were presented under the overarching theme of "integrative care, combining valuable conventional medical diagnosis with empowering self-help strategies." Sub-themes were management characteristics as well as care strengths and weaknesses of the different modalities (integrative vs. conventional care).

Patients experienced strengths of conventional care in terms of specialisation and valuable diagnostic support but saw weaknesses being its reductionist approach and lack of accessibility, time, and guidance. Integrative care on the other hand was seen as taking account of them as whole people. They also experienced an increased treatment response and less need for analgesics, as well as individual support, empowerment, and self-help strategies. However, patients also identified collaborative and financial problems with integrative care. In summary, results showed that integrative care was described as a valuable combination of biomedical diagnostics and empowering strategies for self-care.

In another research paper in her thesis, Andermo used discourse analysis to analyse statements by providers, participating in a series of patient conferences, in terms of their collaboration and interaction in the integrative care team. Results showed how participants discursively constructed the collaborative process and developed a shared vision of the integrative care. The results of the second paper were described in terms of three themes, reflecting the discursive constructions of a collaborative process where the practitioners learned to capitalize on the synergies of their collaboration and developed a shared vision of integrative health care. The themes were:

- Building consensus-based decision-making: At first, the group was dominated by biomedicine, as evidenced e.g. in the use of discourse/language and also in the

impact of physicians on the patients´ treatment plans. However, over time, the caregivers developed the ability to make consensus-based decisions.

- Building a team: Positions of the caregivers shifted discursively from subject positions to members of a team.
- The evolving role of integrative health care: This theme described how caregivers developed their vision of the goal of their work, so that they were strengthened by the team collaboration while simultaneously positioning themselves as a marginal practice in relation to conventional care.

In summary, by utilizing qualitative outcomes it was found that the patients valued the whole person perspective of integrative care, characterized by a valuable combination of biomedical diagnostics and empowering self help strategies, and where integrative providers' collaboration and shared understanding were understood as a means to understand and encounter the whole person.

* * *

Presentation:	***Outcome measures used in mind-body interventions for pain***
Panellist:	*Holger Cramer, PhD, Research Director at the Outcome Department of Internal and Integrative Medicine, Kliniken Essen-Mitte Faculty of Medicine, University of Duisburg-Essen, Essen, Germany.*
About:	*Dr Cramer has a clinical background in phychology and also in naturopathy and heilpractice.*

Dr Cramer spoke about measuring outcomes in mind-body interventions for pain. NCCAM defines mind-body interventions as "A variety of techniques designed to enhance the capacity of the mind to affect bodily function and symptoms." Data from the NIH show that yoga, deep breathing, meditation, progressive relaxation are among the top ten most used modalities of complementary and integrative medicine in the US. There are recommendations for these modalities, which are disease-specific, focusing on pain symptoms, physical functioning, quality of life, wellbeing etc.

Cramer's group has performed several systematic reviews, showing that e.g., in measuring the effects of yoga on low back pain, 80% of studies used pain symptom ratings and 90% used back-specific functioning as primary outcome measures. However, only some 30% of studies measured wellbeing, which dr Cramer found surprising. Indeed, he said, it appears that yoga has effects on disease-specific outcomes. On the other hand, all trials on Mind Body Mindfulness-Based Stress Reduction for low back pain used pain symptoms or disability as measures and 85% used back-specific disability and 71% wellbeing. For pain, there was also a positive effect. Proposed mechanisms of action for these effects were – for mindfulness-based interventions - mindfulness/acceptance, whereas for yoga and tai chi, the proposed mechanism was increased body awareness. Interestingly however, no effects were seen in studies of MBSR on mindfulness and acceptance. Hence the effects on pain may not actually go via mindfulness-based stress reduction but rather via yoga as the most active component.

For fibromyalgia, however, only changes in mindfulness were associated with changes in clinical outcomes so perhaps there is only a fit between certain diseases and certain intervention-specific outcome measures. For yoga, it seems there are differences in mechanisms between different effects of yoga. Dr Cramer´s group looked at yoga-postural awareness for chronic neck pain. It seemed that yoga classes themselves were not so

important as a change in the perception of body posture, e.g., lowering the shoulders. The group constructed a 12-point postural awareness scale, and carried out a 10-week postural awareness study. They also compared the effects of effortless awareness and connectedness vs. forced awareness, finding the latter more effective on pain. So postural awareness seems to be a mechanism for pain reduction. Conversely, Dr Cramer said, quoting the previous researcher Dr Lauche, for postural awareness and tai chi, less awareness and connectedness seem to be relatively strong predictors of changes in pain intensity. In short, different ways of increasing postural awareness might be strong mechanisms of action for those mind-body interventions.

In summary, primary outcomes for mind-body interventions for pain are mainly clinical and disease-specific, and thus comparable to other types of interventions such as drugs. Secondary outcomes often test (hypothesized) mechanisms and are thus intervention-specific, said Dr Cramer, mentioning hypnosis as an example.

* * *

Presentation:	***Existential genomics - a prospective clinical observational study***
Panellist:	*Dr Torkel Falkenberg, PhD, Accociate professor and head of the Unit for Integrative Care, Karolinska Institutet, Stockholm, Sweden.*
About:	*Dr Falkenberg has a background in molecular biology and public health and is also well acquainted with nursing and complementary therapies.*

Dr Falkenberg was the last speaker on the panel. He gave a brief overview of some of the projects of his research unit, mentioning in passing the updated WHO Traditional and Complementary Medicine strategy for the period 2014–2023 that devotes more attention than its predecessors to prioritizing health services and systems, including traditional and complementary medicine products, practices and practitioners.

Previously, Dr Falkenberg led a research project using trained actors as would-be patients to study to what extent staff at private-for-profit pharmacies in Thailand and Vietnam sold antibiotics and other Rx drugs over the counter. Researchers found that only 4% did not dispense drugs. Dr Falkenberg also supervised the previously presented projects of Dr Sundberg and Dr Andermo, showing that IM models for back pain compared to conventional care showed benefit that were cost effective within the standards set by the Swedish health care system. More recently, Falkenberg's group has used other methods, e.g. Swedish health registries, to compare outcomes of pain management in integrative care and conventional care in Stockholm County Council. The results have suggested e.g. that the use and cost of analgesics may be lowered after integrated care but may increase after conventional care. In a new prospective clinical trial the possible mechanisms of such “black-box” effects will be explored, and the team has consulted with Nobel Prize winner Professor Elizabeth Blackburn to investigate to what extent treatment effects might be mediated via DNA breakage/repair, i.e. activity of the enzyme telomerase. Meditation and eating habits have already been shown to be linked to telomerase activity, so this might be a possible outcome to see if integrative care actually contributes to the sustainability of the chromosomes. If so, there is hard evidence for considering integrative care to be good medicine, Dr Falkenberg said.

* * *

Auditorium discussions

After the panel member had given their presentations and answered questions there were additional questions from the audience for all of the panellists leading to discussions. However, as these did not typically cover the use of specific outcomes, only some of these are briefly covered here to provide context. For example, one question regarded whether patients were included in the team approach presented by Dr Andermo and Dr Sundberg. Dr Andermo replied that there had been many perspectives to account for that, and that the team had discussed the possibility to include patients to the case conference sessions. However, it was logistically much more efficient for the patients to interact directly with their therapists than in the team case conferences. Another question referred to whether participants in the Australian practice-based networks received compensation? Dr Steel answered that arrangements are made and collaborating researchers in sub-studies are encouraged to make accommodations for this. Such aspects can be important to consider as they may have a potential impact on for example attrition rates and provider contributions, which ultimately is of importance for the sustainability and success of PBRNs.

Additionally, there was one member of the audience, a wife of someone with back pain, who asked if the psychosocial approach to low back pain included taking families or spouses into account, as patients may be "in a bubble", and there are much wider ripple effects of both disease and treatments than mentioned. This led to discussions relating to a broader use of outcomes in research and clinical practice, where Dr Steel agreed that indeed the wider public health perspective was important, but that she had been alluding to such effects in discussing the social implications of pain. Commenting on the roll-out of public health interventions, Dr Falkenberg said that while the question was important, "we have not been that translational yet". Following the ending of the symposium there were additional individual talks and discussions both within the group of panellists and with members of the audience. However, as these could not be covered they are not reported here.

Conclusions

In conclusion the panellists provided numerous examples of different types of outcomes measures, in multiple outcome domains, that can be used in the evidence-based assessment of complex health care interventions for patients with chronic pain. Considering the large number of outcomes that are available, it is clear that the assessment of multiple factors and perspectives can be attained and specifically tailored to different caring models and contexts. By using complementing outcome measures from different domains the understanding of the evidence-base for multi-component chronic pain management can continue to improve to the benefits of patients and society.

Acknowledgements

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APPENDIX 3:
Outcomes toolkit

Ekhaga 2016-61
Research report phase 3:

Outcomes toolkit:
Integrated outcomes for integrated care for pain
– A proposed "toolkit" for evidence-based assessment of integrated healthcare interventions for pain

Tobias Sundberg, PhD

Outcomes toolkit

Integrated outcomes for integrated care for pain – A proposed "toolkit" for evidence-based assessment of integrated healthcare interventions for pain

Tobias Sundberg

ABSTRACT

Background and objectives
To appreciate the effects of different types of pain treatments and rehabilitation programmes, there is a need to use relevant clinical outcomes. To guide clinicians and researchers in their selection of different clinical outcomes, the objective of the third project phase was to develop an evidence-informed structured overview of different clinical outcomes, i.e. a proposed "outcomes toolkit".

Methods
Data of outcome measures from the first two project phases, i.e. from the systematic literature review (n=61), and from the international research symposium (n=90), in total 151 types of outcome measures or outcome areas, were merged. Following the removal of duplicates, the remaining outcomes measures were thematically analysed and categorized into domains and sub-domains. The final sets of outcomes were descriptively tabulated into "toolkit tables" detailing different types of clinical outcomes.

Results
A total of 124 clinical outcomes were identified and reported in 4 toolkit tables. The final set of outcomes were categorized into 7 domains and 7 sub-domains: Patient reported outcome measures (n=62) [sub-domains: pain (n=9); Quality of life or health status (n=12); Efficacy or disability (n=8); Depression or anxiety (n=9); Functional or other (n=24)]; Outcome measures of physical function (n=15); Resources, costs and cost-effectiveness outcomes (n=28) [sub-domains: Specific cost analysis outcomes (n=7); Direct and indirect costs (n=21)]; Qualitative outcomes (n=6); Public health/social outcomes (n=7); Biomarker outcomes (n=2); Other outcomes (n=4).

Conclusions
The proposed outcomes toolkit comprised 4 toolkit tables providing an evidence-informed structured overview of 124 clinical outcomes in 7 main domains and 7 sub-domains. The toolkit tables may be used as a starting point by clinicians and researches to aid clinical decision-making, selection, use and uptake of relevant outcomes in the evidence-based assessment of integrated multi-component interventions for patients with chronic pain.

Keywords: Toolkit, outcomes, chronic pain, assessment, patient-reported, multi-component, multi-disciplinary, integrated, evidence-informed, evidence-based

BACKGROUND

To comprehend the effects of different types of interventions directed towards patients suffering from chronic pain, there is a need to use relevant clinical outcomes that can be used to measure change over time. However, it might not be an easy task to select appropriate outcomes to implement in clinical practice, especially in integrated multi-component interventions that may be expected to impact multiple aspects of a patient's pain, health and wellbeing. Therefore, in order to facilitate clinical decision-making, selection, use and uptake of relevant outcomes in chronic pain rehabilitation, this project set out to gather the best available evidence and expert opinions on the use different types of clinical outcomes in integrated healthcare interventions for pain.

Accordingly, in the first phase of this research project, a systematic literature review was conducted to identify clinical outcome measures reported in randomized clinical trials of multi-component pain interventions. Then, in the second phase of the research project, an international stakeholder research symposium was arranged to gather expert opinions on different outcomes in pain rehabilitation. The results of the first two project phases have been reported in separate research reports, please see Appendix 1 and Appendix 2 respectively.

The specific objective of this third phase was to synthesize the scientific outcomes identified in the systematic literature review and the outcomes gathered from the stakeholders' export opinions, in order to develop a structured overview of different clinical outcomes, i.e. a proposed "outcomes toolkit".

METHODS

Design

Clinical guideline report, synthesizing scientifically derived outcomes and outcomes reported by international stakeholders, in the form of a clinical "outcomes toolkit".

Data collection and analysis

Data on outcomes from the first two project phases, i.e. from the systematic literature review (n=61) and from the international research symposium (n=90), in total 151 types of outcome measures or outcome areas were merged. Following the merge, quantitative content analysis was used to identify and remove duplicate outcomes in the aggregated data. The remaining outcomes measures were analysed thematically and categorized into domains and sub-domains. The final sets of outcomes were descriptively tabulated into "toolkit tables" where each toolkit table detailed a specific set of domains/sub-domains of clinical outcomes.

RESULTS

Outcomes, domains and sub-domains

The developed toolkit tables presents 124 different types of clinical outcomes categorized into 7 domains and 7 sub-domains:

Toolkit table 1:	Domain:	Patient reported outcome measures (n=62)
	Sub-domains:	Pain (n=9)

		Quality of life or health status (n=12) Efficacy or disability (n=8) Depression or anxiety (n=9) Functional or other (n=24)
Toolkit table 2:	Domain:	Outcome measures of physical function (n=15)
Toolkit table 3:	Domain:	Resources, costs and cost-effectiveness outcomes(n=28)
	Sub-domains:	Specific cost analysis outcomes (n=7) Direct and indirect costs (n=21)
Toolkit table 4:	Domain:	Qualitative outcomes (n=6)
	Domain:	Public health/social outcomes (n=7)
	Domain:	Biomarker outcomes (n=2)
	Domain:	Other outcomes (n=4)

The outcomes toolkit

The developed outcomes toolkit comprised of four toolkit tables, each representing different outcomes, domains and sub-domains. The toolkit tables are presented below (Tables 1-4).

Toolkit table 1. Patient reported outcome measures.

Sub-domains:	**Domain:** **Patient reported outcome measures (n=62)**
Pain (n=9)	Bothersomeness of back pain (Bothersomeness)
	Brief pain inventory (BPI)
	Chronic Pain Acceptance Questionnaire (CPAQ)
	Fibromyalgia impact questionnaire (FIQ)
	McGill pain questionnaire (MPQ)
	Multidimensional pain inventory (MPI)
	Numerical rating scale for pain intensity (NRS)
	Numerical rating scale for pain severity (NRS)
	Visual Analogue Scale for pain intensity (VAS, 0-100)
Quality of life or health status (n=12)	Aberdeen back pain scale (ABPS)
	Body function (SF-36)
	Disease specific quality of life, e.g. cancer (EORTC)
	Health-related quality of life (SF-12)
	Health-related quality of life (SF-36): Mental health component; Physical health component
	Health-related quality of life (EuroQol, EQ-5D)
	Nottingham Health Profile (NHP)
	Patient Health Questionnaire (PHQ-9)
	Quality of life (EQ-5D)
	Quality of life (WHO-QOL-BREF)
	Vitality
	Wellbeing

Efficacy or disability (n=8)	Arthritis Self Efficacy Scale (ASES)
	Chronic Pain Self-efficacy Scale (CPSS)
	Neck Disability Index (NDI)
	Oswestry Disability Index (ODI)
	Pain disability index (PDI)
	Pain Self Efficacy Questionnaire (PSEQ): PSE: pain self-efficacy, FSP: functional self-efficacy, CSE: coping self-efficacy
	Roland Morris Disability Questionnaire (RMDQ)
	Waddell Disability Index (WI)
Depression or anxiety (n=9)	Beck Depression Inventory (BDI)
	Center for Epidemiologic Studies Depression scale (CES-D)
	Depression Anxiety Stress Scale (DASS)
	Generalized Anxiety Disorder (GAD)
	Geriatric Depression Scale (GDS)
	Hamilton Anxiety Rating Scale (HAM-A)
	Hamilton Depression Scale (HAM-D)
	Hospital Anxiety and Depression Scale (HADS)
	Spielberger State-Trait Anxiety Inventory (STAI)
Functional or other (n=24)	Avoidance Endurance Questionnaire (KPI-AEQ)
	Body awareness scale (BAS)
	Fear Avoidance Beliefs Questionnaire (FABQ)
	Freiburg Mindfulness Inventory (FMI)
	Global perceived effect (GPE): GPE for recovery from complaints, GPE for recovery of functioning in daily activities
	Hannover functional ability questionnaire (HFAQ)
	Headache-Specific Locus of Control Scale (HSLC)
	Keele Start Back Tool (KSBT)
	Minnesota Mutiphasic Personality Inventory-II (MMPI-II)
	Multi Dimensional Pain Inventory - Dutch Language Version (MPI-DLV)
	Multidimensional Health Locus of Control Scale (MHLC)
	Pain Catastrophizing Scale (PCS)
	Pain locus of control (PLOC)
	Patient global impression of change
	Patient perceived satisfactory improvement (PPSI)
	Patient Perspective Survey (PPS)
	Patient-Specific Functional Scale (PSFS)
	Pittsburgh Sleep Quality Index (PSQI)
	Postural awareness scale; Effortless awareness and connectedness; Forced awareness
	Rating of impairment associated with back pain (NRS,

	0-10)
	Satisfaction of care
	Satisfaction with health/life
	Self-perceived improvement of disability (7-point Likert scale)
	Tampa Scale for Kinesiophobia (TSK, 17-68)

Toolkit table 2. Outcome measures of physical function.

Domain: Outcome measures of physical function (n=15)
1-min stair climbing (number of stairs)
5-min walking (m)
50 foot walking (s)
6-Minute Walk Test (6MWT)
Endurance (eg. local muscular, or central cardiovascular)
Exercise activity (eg. step counter)
Five times sit to stand (s)
Forward reaching by holding a stick with a weight of 4.5 kg at shoulder height (cm)
Functional capacity evaluation (FCE)
Movement control impairment (MCI) was measured by means of six movement control tests
Pelvic Floor Muscle strength and endurance (perineometer)
Progressive isoinertial lifting evaluation
Sensory acuity of the lower back by measuring the two-point-discrimination threshold
Single-Leg Balance Test
Timed-up and go Test (TUG)

Toolkit table 3. Resources, costs and cost-effectiveness outcomes.

Sub-domains:	**Domain:** **Resources, costs and cost-effectiveness outcomes (n=28)**
Specific cost analysis outcomes (n=7)	Cost-benefit analysis (CBA)
	Cost-effectiveness acceptability curves (CEAC)
	Cost-effectiveness analysis (CEA)
	Cost-minimization analysis (CBA)
	Cost-utility analysis (CUA)
	Incremental cost effectiveness ratio (ICER)
	Quality adjusted life years gained (QALY), e.g. by using the EuroQol-5D (EQ-5D) instrument
Direct and indirect costs (n=21)	Absenteeism from paid work (hours)
	Alternative therapist (no of visits)
	Drug dispension frequency at pharmacies (over the counter)
	General practice (no of visits)
	Help from partner or friends (hours)
	Hospital admission including medical procedure (costs)

	Indirect costs due to absence of paid work (cost diaries and treatment attendance lists)
	Medical specialist care (no of visits)
	Medication other than analgesics
	Minimal number of clinical encounters to achieve the optimal clinical outcome
	Occupational physician (no of visits)
	Paid housekeeping (hours)
	Physician visits (no of visits)
	Prevalence of use of care
	Psychologist (no of visits)
	Radiology (no of visits)
	Registered drug prescriptions
	Therapist (physiotherapy, manual therapy, Cesar or Mensendieck therapist; no of sessions)
	Total costs, existing of direct health and non-health costs (cost diaries and treatment attendance lists)
	Use of over the counter analgesics (costs)
	Use of prescription analgesics (costs)

Toolkit table 4. Qualitative, public health/social, biomarker, and other outcomes.

Domain: Qualitative outcomes (n=6)	**Domain: Public health/social outcomes (n=7)**	**Domain: Biomarker outcomes (n=2)**	**Domain: Other outcomes (n=4)**
Empowerment from care	Family or spouses implications of living with someone who has chronic pain	DNA breakage/repair, i.e. telomerase enzyme activity	Duration perspectives, both in terms of follow-ups of outcomes but also in terms of suitable intervention lengths to achieve optimal results (dose response)
Patient experiences	Health promotion, eg by using complementary therapies	Glycemic control, blood sugar values	"Model feasibility" as an outcome in clinical care, sustainability.
Patient perspectives	Mortality		Spirituality
Provider experiences	National surveys, eg use of resources/services/self-care		Interpretation of disease/illness

Provider perspectives	Preventive medicine, eg contributions by naturopaths to aid individuals risk factors for cardiovascular disease		
Self-care and self-management strategies	Scope of health conditions treated in a "model of care"		
	Social implications of pain		

DISCUSSION

The objective of this project phase was to develop an evidence-informed structured overview or guideline of different clinical outcomes, i.e. a proposed outcomes toolkit. A total of 124 final clinical outcomes were identified and reported in 4 different toolkit tables, 7 domains and 7 sub-domains.

Patient reported outcomes

The patient reported outcomes were the most the frequent types of identified outcomes (n=62). To be expected this was the same quantitative pattern that was found in the previous two project phases, i.e. from the systematic literature review (Appendix 1), and from the research symposium gathering the international stakeholders' expert opinions (Appendix 2). From a clinical perspective it was clear that the numerous types of identified patient reported outcomes would benefit from further categorization to aid clinical decision-making in the selection of outcomes. The thematic analysis resulted in 5 different sub-domains of patient reported outcome measures. Four of the sub-domains entailed clearly defined clinical areas of evaluation: pain, quality of life or health status, efficacy or disability, and depression or anxiety (Toolkit table 1). These were represented by 38 different types of clinical outcomes, which can be measured by instruments such as numerical rating scales for pain intensity or pain severity, health-related quality of life questionnaires, self-efficacy or back pain disability indexes, or anxiety and depression inventories (Toolkit table 1). The patient reported outcome measures that could not be categorized into the first four sub-domains were gathered in a fifth sub-domain described by functional or other outcomes. The identified functional or other outcomes can be exemplified by various types of outcomes including perceived effects of recovery from complaints, pain catastrophizing, sleep quality, postural awareness, or satisfaction with care (Toolkit table 1). Albeit these types of outcomes may be less commonly used in regular evaluation of pain rehabilitation interventions, they may nonetheless be relevant clinical outcomes and worth considering in certain types of rehabilitation contexts or for certain sub-groups of pain patients, for example those with sleep disorders or perceived low body awareness.

Outcomes of physical function

The outcomes of physical function (Toolkit table 2) were less frequent than the patient reported outcomes, but may be worthwhile considering if there are specific concerns about

patients physical health and performance. While tests of physical function may require additional resources, for example in the form of special training of staff and specific apparatus to collect data, several of the identified outcomes also included simpler tests and modes of evaluation such as different types of walking, sit-to-stand, reaching, or balance tests (Toolkit table 2). Hence, the integration of some form of physical function outcomes may still be feasible even if clinical rehabilitation or research resources are scarce.

Cost-related outcomes

Regarding resource utilization, there were three identified sub-domains in this outcome area (Toolkit table 3). That meant the cost-related outcomes could be categorized into either direct costs, indirect costs, or into specific types of cost-effectiveness analysis outcomes. Direct costs are costs that occur due to direct personal expenses on different types of health resources, for example visits to the family physician, physiotherapy treatments, or the costs of drugs. Indirect costs are costs that may be described occurring as a consequence to the disease, for example costs relating to not being able to work and sick leave. Detailed measures of direct and indirect costs may require lengthy data collection procedures, for example having patients log all their expenses, health care visits, sick leave days, and use of other resources in a cost diary. Albeit it may look simple on paper, the real world use of such data collection procedures may be challenging, for example due to logistics, recall bias and time constrains. Hence, the use of outcomes that rely on auto-generated modes of data collection, such as registry data, may be preferred. However, the decision to use registry based outcomes must also take into account the need for potential lengthier data collection periods, and higher project costs, as there may be a delay from when a specific resource is used by the patient, such as a sick leave period, to when that resource use is reported first locally then in the registry, and to when it is subsequently available to order for data extraction and analysis. Nonetheless, integrating different outcomes of direct and indirect costs can help inform the bigger picture about the effects of pain rehabilitation. Particularly, the specific types of cost-effectiveness analysis, as detailed in Toolkit table 3, may be used to provide outcomes of not only patient related consequences, but also societal impacts, of different pain management and pain rehabilitation strategies. Notably, resources, costs and cost-effectiveness outcomes are increasingly recommended and used in the evaluation of pain rehabilitation programmes, informing health technology assessments and health economic policy.

Qualitative outcomes

There were a number of additional outcomes that were categorized into for four final domains (Toolkit table 4). One of these domains targeted the use of qualitative outcomes. Importantly, qualitative research methods may be used to identify specific outcomes and outcome areas that have not been previously recognized, i.e. employing an inductive approach, to understand the effects of different pain interventions. Qualitative procedures may also be used deductively, for example to confirm hypothesis or verify results from previous quantitative investigations or other groups of patients. Example of general qualitative outcomes included patients' and providers' experiences and perspectives of care, and examples of specific qualitative outcomes included patient empowerment and self-care strategies. Typically data for exploring qualitative outcomes will be gathered from participatory research such as interviews or focus group discussions. Individual interview can be appropriate when sensitive information sharing may be expected, whereas focus group discussions can be favourably used to gather multiple individuals' interaction and

communications about a given topic. The latter mode of investigation may also be efficient in terms of logistics and time, which may be important to consider in clinical practice or busy research projects.

Public health/social outcomes

The area of public health/social outcomes may also be explored by participatory research methods, although such data may also be collected by questionnaires or through large population surveys. Predominantly, public health/social outcomes will target broader perspectives of the potential impacts of chronic pain, such as implications for the family or spouses living with a person suffering from pain. Other identified public health/social outcomes related to wider public concerns including prevention, promotion or mortality relating to pain. These types of outcomes may be especially important to consider when more comprehensive evaluations of pain management are warranted, for example involving organisations or community based interventions.

Biomarker outcomes

Perhaps surprisingly, only two identified outcomes related to the use of biomarkers. One was relating to using telomerase enzyme activity to investigate DNA breakage and repair as a measure to understand critical biological effects of pain and pain rehabilitation. This type of outcome has gained increased recognition within the scientific community over the last decade since Professor Elisabeth Blackburn and colleagues were awarded the 2009 Nobel Prize in Medicine or Physiology for its discovery. However, using telomerase and similar biomarker outcomes is currently very expensive and only possible through invasive testing procedures and advanced laboratory analysis, thus probably not feasible to implement as a standard outcome in most clinical pain rehabilitation settings. Nonetheless, in select studies this type of biological outcome, especially when combined and correlated with other types of outcomes, may be able to provide a more detailed interpretation of the effects of pain and different pain rehabilitation programs. The other biological outcome that was identified was relating to glycaemic control, which was brought up during the stakeholder research symposium as an example of a biomarker that can be used as one measure to investigate the effects of treatments in patients with diabetes. Notably, diabetic patients may develop something called diabetic nerve pain, or painful diabetic peripheral neuropathy, which is a common long-term complication of diabetes. One of the most common causes of diabetic nerve pain is poorly controlled blood sugar over time. Hence, this biomarker outcome may be of particular relevance to integrate when evaluating treatment for this target group of chronic pain patients.

Additional outcomes

Lastly, outcome areas directed towards other aspects of pain evaluation, including the feasibility different treatment models, duration and dose-response perspectives, or spirituality, or interpretations of disease, were categorized into a final mixed outcomes domain. These types of outcomes are less often used than many of the other identified outcomes, but may be valuable to consider in selected target groups of pain patients and rehabilitation contexts (Toolkit table 4).

Methodological considerations

The clinical outcomes toolkit presents a structured overview of 124 identified outcomes in seven main areas. Albeit the outcomes were informed by evidence from a systematic literature review, and international stakeholders' expert opinions, it is possible that there are additional outcomes and outcome areas that may be of clinical relevance for evaluating pain treatment and rehabilitation. Nonetheless, the outcomes presented in the current outcomes toolkit compilation should provide ample support and guidance to aid clinicians and researchers in their selection of relevant outcomes for evidence-based assessment of integrated and complex pain rehabilitation interventions. Future studies are warranted to further contribute to the compilation of recommended clinical outcomes in this area.

Conclusions

The use of relevant clinical outcomes is important in order to understand the effects of pain treatment and rehabilitation. The proposed outcomes toolkit, derived from data of a scientific literature review and expert opinions from international stakeholders, presents an evidence-informed structured overview of 124 final clinical outcomes reported in 4 toolkit tables covering 7 domains and 7 sub-domains. Clinicians and researches may use the outcomes toolkit as a starting point to facilitate the clinical selection, use and uptake of relevant outcomes for evidence-based assessment of integrated multi-component rehabilitation interventions for patients with chronic pain.

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