Tampere University

LINDA NIEMINEN

Decision Support for Tailored Biopsychosocial Rehabilitation

In Non-specific Low Back Pain

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Decision Support for Tailored Biopsychosocial Rehabilitation

In Non-specific Low Back Pain

ACADEMIC DISSERTATION
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To my family and other decision supporters

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The challenges of finding effective solutions for non-specific low back pain has been on the global research agenda for many years. Therefore, when I had the chance to face this when working in the Department of Physical Medicine and Rehabilitation, I felt that I wanted to play my part in ensuring that patients and health care professionals would no longer feel so powerless. I knew, however, that this was not a task for one person, and the time has now come to thank all those people who made this dissertation a reality.

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Tampere, February 2023

Linda Nieminen

ABSTRACT

Low back pain is globally the most burdensome symptom causing disability. It is most commonly defined as non-specific, which means no pathoanatomical cause can be demonstrated as the cause. Different biopsychosocial factors are widely related to the experience and prolongation of pain and disability. Some of these factors can be affected by targeting timely interventions and decreasing the risk for pain chronicity. Pain related biopsychosocial factors and their connections can be understood more profoundly with the help of the International Classification of Functioning, Disability, and Health (ICF) framework developed by the World Health Organization (WHO), which describes disability from a wide biopsychosocial perspective.

The main aim of this dissertation was to develop methods to support the decision-making in the tailored biopsychosocial rehabilitation of patients with non-specific LBP. The secondary aims were to produce a topical summary of the known biopsychosocial risk factors for low back pain chronicity, and to find methods to recognize those factors as well as support the assessment and execution of tailored interventions targeted to the individually recognized factors.

A systematic literature review was compiled from the results of 25 different studies on the risk factors associated with low back pain chronicity. The studies had to evaluate the possible risk factor before the chronic phase of pain (3 months) in order to be regarded as a preceding factor for pain. To help the recognition of biopsychosocial factors at the individual level, an artificial intelligence algorithm application was developed that identifies disability information from electronic health records in accordance with the ICF framework. The results of the application were compared to the findings of a domain expert. The processes of patients with low back pain in primary and occupational health care were developed to more comprehensively assess possible risk factors and better tailor interventions to the individuals. A multidisciplinary team was formed from primary, occupational, and special health care professionals for the process design. For the purposes of developing new methods, a patient population of 93 patients with chronic low back pain were gathered. The data comprised free text from electronic health records and quantitative information from medical history forms.

According to the systematic review, 45 different factors were identified as being associated with low back pain chronification. The factors were divided into demographical and medical history related factors, biomechanical factors, symptom related factors, psychological and psychosocial factors, and lifestyle factors. The factors were interrelated with the description of disability in the ICF framework, with the exception of the demographic and medical history related factors. The applied artificial intelligence algorithm was able to recognize disability information from the electronic health records with a sensitivity of 83.1% and specificity of 99.84% compared to the results of the domain expert. The rehabilitation process design was presented in a logic model that guides the needed professionals into the process according to the patients' needs, clearly states the activities of the professionals, and comprehensively exploits a multidisciplinary community over sector boundaries.

The findings of this dissertation open new research possibilities in the areas of low back pain and the exploitation of disability information. The results of the systematic review will help clinicians to better understand the biopsychosocial entity of low back pain more competently and researchers to extend their intervention study designs. In future, a feasibility study on the rehabilitation process should be executed before a larger intervention. The benefits of the artificial intelligence algorithm application are planned to be expanded to other patient groups and languages.

TIIVISTELMÄ

Alaselkäkipu on maailman yleisin toimintakyvyn haittaa aiheuttava oire. Suurin osa alaselkäkivusta on niin sanottua epäspesifiä, eikä sille ole osoitettavissa aukottomasti patoanatomista taustaa. Kivun ja toimintakyvyn haitan kokemukseen ja kroonistumiseen liittyy laajasti erilaisia biopsykososiaalisia tekijöitä, joista osaan voidaan vaikuttaa kohdentamalla interventioita oikea-aikaisesti oikealle potilaalle, ja täten vähentää kivun pitkittymisen riskiä. Kipuun liittyviä biopsykososiaalisia tekijöitä ja niiden välisiä yhteyksiä voidaan ymmärtää paremmin maailman terveysjärjestö WHO:n kansainvälisen toimintakyvyn, toimintarajoitteiden ja terveyden luokituksen (ICF-viitekehys) avulla, joka kuvaa toimintakykyä laaja-alaisena biopsykososiaalisena kokonaisuutena.

Tämän artikkeliväitöskirjan päätavoitteena oli kehittää menetelmiä tukemaan yksilöllisen biopsykososiaalisen kuntoutuksen suunnittelua ja toteutusta selkäkipupotilailla. Alatavoitteina oli tuottaa ajankohtaista tietoa tunnistetuista alaselkäkivun kroonistumisen riskitekijöistä, sekä löytää uusia menetelmiä biopsykososiaalisten tekijöiden tunnistamiseen ja näiden tekijöiden avulla sopivan intervention valintaan yksilöllisesti.

Alaselkäkivun kroonistumisen riskitekijöistä tehtiin systemaattinen kirjallisuuskatsaus, jossa tutkittiin 25 tutkimuksen tuloksia. Tutkimusten tuli arvioida mahdollista riskitekijää ennen kivun kroonistumisen alkamista (3kk), jotta riskitekijää voitiin pitää ennakoivana tekijänä kroonistumiselle. Biopsykososiaalisten tekijöiden tunnistamiseen kehitettiin sovellus tekoälyalgoritmista, jonka tarkoituksena on tunnistaa toimintakykyyn liittyvää tietoa potilaskertomusteksteistä ICF-viitekehyksen mukaisesti. Sovelluksen tuloksia verrattiin alan asiantuntijan tekemään tunnistamiseen. Selkäpotilaan prosesseja perusterveydenhuollossa ja työterveydessä kehitettiin paremmin tunnistamaan kroonistumisen riskitekijöitä sekä valitsemaan sopivat interventiot yksilöllisesti. Prosessin kehittämisessä oli mukana moniammatillinen työryhmä perusterveydenhuollosta, työterveydestä sekä erikoissairaanhoidosta. Uusien menetelmien kehityksen tueksi kerättiin 93 kroonisen alaselkäkipuisen potilaan aineisto. Aineisto sisälsi vapaata tekstiä potilaskertomusteksteistä sekä numeerista dataa esitietolomakkeiden muodossa.

Systemaattisen kirjallisuuskatsauksen mukaan yhteensä 45 erilaista riskitekijää on tunnistettavissa selkäkivun kroonistumisen riskitekijäksi. Riskitekijät jaoteltiin demografisiin ja sairaushistoriaan liittyviin tekijöihin, biomekaanisiin tekijöihin, oireiden ominaisuuksiin liittyviin tekijöihin, psykologisiin ja psykososiaalisiin tekijöihin, sekä elintapatekijöihin. Tunnistetut riskitekijät olivat yhdistettävissä ICF-viitekehyksen toimintakyvyn kuvauksiin, lukuun ottamatta demografisia ja sairaushistoriaan liittyviä tekijöitä. Kehitetty tekoälyalgoritmin sovellus tunnisti toimintakykytietoa potilaskertomusteksteistä 83.1 % herkkyydellä ja 99.84 % tarkkuudella verrattuna alan asiantuntijan tekemään tunnistukseen. Selkäpotilaan prosessin kehityksen tuotoksena syntyi vuokaavio, jonka avulla oikeat ammattilaiset ohjautuvat mukaan prosessiin potilaan tarpeiden mukaisesti, tietävät omat tehtävänsä, sekä pystyvät hyödyntämään paremmin moniammatillista ja monisektorista yhteisöä yksilöllisesti potilaan hyväksi.

Tämä artikkeliväitöskirja luo uusia tutkimusmahdollisuuksia sekä selkäpotilaiden että toimintakykytiedon hyödyntämisen alueilla. Kirjallisuuskatsauksen tulokset auttavat kliinikoita paremmin ymmärtämään selkäkivun biospykososiaalista kokonaisuutta ja tutkijoita laajentamaan interventiotutkimusasetelmiaan. Tulevaisuudessa kuntoutusprosessista voidaan tehdä soveltuvuustutkimusta ennen laajempaa interventiota, ja tekoälyalgoritmin sovelluksen hyödyntämistä muille potilasryhmille ja kielille suunnitellaan.

CONTENTS

1 Introduction 19

2 Review of the literature 23

2.1 Low back pain 23

2.1.1 Definitions and epidemiology 23

2.1.2 Chronification of low back pain 26

2.1.2.1 Physiology of pain chronification 27

2.1.2.2 Risk factors for pain chronicity 28

2.1.3 Biopsychosocial perspective of low back pain 29

2.1.4 Main strategies in the treatment of low back pain 31

2.1.4.1 At the individual level 31

2.1.4.2 At the system level 33

2.1.5 Rehabilitation in low back pain 35

2.1.5.1 Different rehabilitation approaches 36

2.1.5.2 Rehabilitation according to individual biopsychosocial factors 37

2.2 International Classification of Functioning, Disability, and Health (ICF) 38

2.2.1 Structure of the ICF 39

2.2.2 Applying the ICF to rehabilitation medicine 40

2.3 Decision support in health care 42

2.3.1 Decision support tools in the treatment of low back pain 43

2.3.2 Artificial intelligence in health care decision support 44

2.3.2.1 Artificial intelligence in clinical decision-making 44

2.3.2.2 Artificial intelligence in system level decision support 47

2.3.2.3 Artificial intelligence in low back pain decision support 48

2.3.2.4 Artificial intelligence and the ICF for decision support 49

2.4 Summary of the literature review 50

3 Aims of the study 52

4 Data and methods 53

4.1 Study settings 53

4.1.1 Systematic review (I) 53

4.1.2 Development of an AI application (II, IV) 53

4.1.3 Development of a rehabilitation process (III) 54

4.2 Collection of data and resources 55
4.2.1 Literature material (I, III) 55
4.2.2 Population data (II, III, IV) 58
4.2.3 Multidisciplinary team (III) 60
4.3 Measurements 61
4.4 Analysis 61
4.4.1 Literature material (I, III) 61
4.4.2 Population data (II, III, IV) 62
4.4.3 Algorithm (II, IV) 62
4.5 Ethical considerations 66

5 Summary of the Results 67
5.1 Systematic review (I) 67
5.1.1 Studies included in the systematic review 67
5.1.2 Prognostic factors for pain chronicity in low back pain 67
5.2 Population data (II, III, IV) 70
5.3 Development of the AI application (II, IV) 73
5.3.1 Analysis of the algorithm 73
5.4 Development of the rehabilitation process (III) 75

6 Discussion 79
6.1 Factors associated with low back pain chronicity (I) 79
6.2 Applying the AI algorithm in health care decision support (II, IV) 81
6.3 Development of the tailored rehabilitation process (III) 82
6.4 Strengths and limitations 83
6.5 Usefulness of the results and implications for future research 86
6.6 Summary of the discussion 89

7 Conclusions 90

List of Figures

Figure 1. Clinical classification of low back pain. Adopted from the studies of O'Sullivan et al.[29,33]. 24

Figure 2. The biopsychosocial model, adopted from the articles by Fillingim[68] and Mescouto[69] 30

Figure 3. The resources for LBP management according to Pirkanmaa Hospital District's regional care program. CBT= Cognitive behavioral therapy........ 34

Figure 4. The structure of the ICF. Adopted from ICF Beginner's guide[17]. (Reprinted with permission)........ 40

Figure 5. Artificial intelligence and its subfields........ 45

Figure 6. Flow chart of the study selection process for the systematic review........ 57

Figure 7. Flow chart of the study population selection. VAS= Visual analog scale........ 60

Figure 8. Simplified example of the semantic network model of EHR notes made by Graphmind. Preprint from study IV........ 63

Figure 9. The data architecture of the algorithm. EHR= Electronic health record, MESH= Medical subject heading, MD= Medical doctor. Preprint from study IV[168]........ 64

Figure 10. The treatment process of patients with LBP in primary health care (PHC) and occupational health care (OHC) in the Pirkanmaa region........ 76

Figure 11. The logic model of the tailored rehabilitation process. (Reprinted with permission)........ 78

List of Tables

Table 1. Treatment strategies in the Finnish current care guideline for non-specific low back pain[23]. NSAID= Non-steroid anti-inflammatory drug, CBT= Cognitive behavioral therapy, TENS= Transcutaneous electrical nerve stimulation. [a] Combined with physical exercise and advice, [b] Graded exposure, exercises aiming at enhancing physical endurance, [c] Stratification according to psychosocial factors and movement classification........ 32

Table 2. Different rehabilitation approach examples divided according to the underlying strategy........ 36

Table 3. Design for the development process in study III........ 55

Table 4. The PICO search strategy for study III. MSK= Musculoskeletal........ 58

Table 5. Inclusion and exclusion criteria for the study population. SBT= Start Back Tool, VAS= Visual Analog Scale. 59

Table 6. The setups used for the algorithm-ontology configuration in study II. (Reprinted with permission). MeSH= Medical subject headings, ME= Medical expert. 65

Table 7. Prognostic factors for pain chronicity in low back pain. HDL= high-density lipoproteins, MCV= motor vehicle collision. Categorical variable measured yes/no or in larger categories; continuous variable measured by continuous scale. Risk=statistically significant risk factor, protective=statistically significant protective factor, NS= not significant statistically, IE= inconclusive evidence...............68

Table 8. Population characteristics. BMI= Body Mass Index, NSAID= non-steroid anti-inflammatory drug, VAS= Visual Analog Scale, SBT= STarT Back Tool. SBT Q3= I have walked only short distances because of my back pain, Q4=In the last two weeks, I have dressed more slowly than usual because of my back pain. Preprint from study IV[168] 71

Table 9. ICF core set of the evaluation dataset (20 patients). The domains are presented in the chapter level. The numbers in brackets represent the number of findings. Preprint from study IV[168]..72

Table 10. The results of study II. Body structures and functions (b and d codes) are combined. (Reprinted with permission)..73

Table 11. The results of the factor recognition. Preprint from study IV[168]....................74

ABBREVIATIONS

AI	Artificial intelligence
ANN	Artificial neural networks
AUC	Area under the curve
BDI-21	Beck Depression Inventory
BDNF	Brain-derived neurotrophic factor
BMI	Body mass index
BPS	Biopsychosocial
CBT	Cognitive behavioral therapy
CNS	Central nervous system
COHERE	Council of Choices in Healthcare
CPU	Central processing unit
DigiHTA	Health technology assessment framework for digital healthcare services
DNN	Deep neural network
DST	Decision support tool
EBMEDS	Evidence-based medicine electronic decision support
EHR	Electronic health record
FinCCHTA	Finnish Coordinating Center for Health Technology Assessment
GAD-7	Generalized Anxiety Disorder Questionnaire
GDPR	General data protection rule
HADS	Hospital Anxiety and Depression Scale
HDL	High-density lipoproteins
ICD	International Classification of Diseases and related health problems
ICF	International Classification of Functioning, Disability, and Health
ICF-CY	ICF for children and youth
ICHOM	International Consortium for Health Outcomes Measurement
LBP	Low back pain
MeSH	Medical subject headings

ML	Machine learning
MRC	Medical Research Council
MRI	Magnetic Resonance Imaging
MSK	Musculoskeletal
MVC	Motor vehicle collision
NIH	National Institute of Health
NLP	Natural language processing
NSAID	Non-steroidal anti-inflammatory drug
PDI	Pain Disability Index
PROMs	Patient Reported Outcome Measures
PSEQ	Pain Self-Efficacy Questionnaire
PSWQ	Penn State Worry Questionnaire
RMDQ	Roland-Morris Disability Questionnaire
ROC	Receiver operating characteristics
SBT	STarT Back Tool
SOM	Self-organizing map
TENS	Transcutaneous electrical nerve stimulation
TSK	Tampa scale for Kinesiophobia
VAS	Visual Analog Scale
WHO	World Health Organization
WHOQOL	WHO Quality of Life
YLD	Years lived with disability

LIST OF ORIGINAL PUBLICATIONS

This dissertation is based on the following original publications referred to in the text by the Roman numerals I-IV:

I Nieminen, L. K., Pyysalo, L. M., & Kankaanpää, M. J. (2021). Prognostic factors for pain chronicity in low back pain: a systematic review. Pain reports, 6(1), e919.

II Nieminen, L., Vuori, J., Ketamo, H., & Kankaanpää, M. (2022). Applying Semantic Computing for Health Care Professionals: The Timing of Intervention is the Key for Successful Rehabilitation. In S. Balandin, & T. Shatalova (Eds.), *Proceedings of the 31st Conference of Open Innovations Association FRUCT, FRUCT 2022* (pp. 201-206). (Conference of Open Innovation Association, FRUCT; Vol. 2022-April). IEEE.

III Nieminen, L., Vuori, J. & Kankaanpää, M. (2022). An early biopsychosocial intervention design for the prevention of low back pain chronicity: a multidisciplinary empirical approach. J Rehab Med 2022 Oct 21;54:jrm00338.

IV Nieminen L., Ketamo H., Vuori J., & Kankaanpää, M (2022). A holistic perspective on disability with graph machine learning. Manuscript, submitted

AUTHOR'S CONTRIBUTION

The author of this dissertation was the first writer in all the included studies. The author was responsible for designing the studies, gathering the data, analyzing the data, writing the manuscripts, and acting as the corresponding author for the publications. In study I, the author acted as one of two researchers who analyzed the quality of the included articles. In study III, the author organized meetings for the multidisciplinary team and acted as a chairperson throughout the design process. In studies II and IV, the author worked as the domain expert and analyzed the results of the algorithm. The author also produced the setups that included information from the vocabulary used by clinicians (referred to as "real life"). The manuscripts were prepared by all the writers mentioned in the publications.

1 INTRODUCTION

Although much research and resources have been devoted to the treatment of low back pain (LBP) during the past decades[1], the burden of LBP has increased, making it the most burdensome health problem affecting years lived with disability (YDL) in high- and middle-income countries[2]. Moreover, LBP is one of the costliest illnesses in the industrialized countries, causing major economic burden on both individuals and societies[3–5]. Indeed, the higher the daily limitation and disability is, the higher the health care costs are. At present, indirect costs (loss of productivity, sickness benefits) make up half of the costs, with only one fourth used to treat and rehabilitate the individuals. [5]

Why is the health care system treating the consequences of the problem but not trying to prevent the prolongation of this pandemic? There are several reasons why the "holy grail" for LBP has not been found. First, the most common cause of LBP is non-specific LBP, where there is no pathoanatomical cause of the pain[6]. Thus, the traditional biomedical approach (find the cause; treat the cause; problem solved) does not work. We, therefore, need a more complex approach, such as a biopsychosocial (BPS) way of thinking[7]. Second, at present, there is lack of knowledge and expertise of how to apply such a broad approach to current health care systems, the resources needed are scattered or absent, there are not enough tools that fit into the busy clinical workflow to help clinicians, and the current system does not support the biopsychosocial approach. Third, there is criticism about the whole BPS approach[8], and the neurophysiological processes of pain are somewhat outside the scope of such an approach. Even though BPS rehabilitation has shown promising results in the treatment of patients with LBP[4,9], it is unknown how well it is applied by caregivers[10], or how well it is implemented in the health care system.

Obviously, the BPS approach will not solve the entire global dilemma of LBP. Nonetheless, it will help us to take a step back from the musculoskeletal and neurophysiological processes[11,12], which are closely related to back pain, and to see the bigger picture. Furthermore, it will help us to better understand why some individuals develop chronic pain and disability.[13] This approach might also give us the construction materials needed for building preventive, tailored solutions in medicine.

As previously stated, there is a need to raise awareness of the nature of LBP among those health care professionals and other stakeholders who are dealing with LBP, policymakers, and patients. Additionally, the implementation of a BPS model needs to be well-fitted with the current health care system.

There are numerous recognized biopsychosocial factors that can affect the chronicity of LBP[14], but their early detection is often missed due to inoperative clinical pathways. With the unsustainable age pyramid and the rising costs of health care, there is an urgent need for long-term solutions that will ease the upward pressure on health care costs and the disability of individuals. Although the transition from acute pain to chronic pain is not fully understood, it is known that the longer the pain persists, the harder it is to treat. For example, long-term disability is correlated with work absence lasting for one month[15]. The leading authorities in the field of LBP state that strategies that ensure the early identification of patients who are at risk for persistent pain and disability should be developed and implemented and, furthermore, strategies that addresses such risk factors should be promoted[16].

Since the complexity of factors related to LBP and their timely recognition are challenging, even for experienced health care professionals, there is a necessity for new tools and systems that would help decision-making and the construction of tailored rehabilitation interventions in busy outpatient clinics. To this end, the World Health Organization (WHO) has developed the International Classification for Functioning, Disability, and Health (ICF) as a standard language and framework to describe the biopsychosocial aspects of health and health-related states[17]. However, it has not reached its full potential for the benefit of individuals, health care professionals, and health care systems due to the implementation difficulties posed by its complex structure[18].

Compared to humans, artificial intelligence (AI) applications have the potential to provide solutions to complex dilemmas and harness relevant data from massive data pools in a matter of seconds. Indeed, there is an ever-growing number of AI solutions available that can be easily applied in health care systems. To be embedded in health care, these solutions must bring benefits in the form of better outcomes for patients and lower costs for the health care system. Therefore, they must be applicable, secure, useful, and well-fitted to the clinical flow. More importantly, they must convince regulators and funders of their benefits.[19,20]

In this dissertation, I aim to provide solutions to fill the knowledge gaps in the recognition of the broad view in LBP, and how we can use it for the good of individuals and society.

2 REVIEW OF THE LITERATURE

2.1 Low back pain

2.1.1 Definitions and epidemiology

Low back is defined as the area on the posterior aspect of the body from the lower margins of the 12th ribs to the lower gluteal folds[21]. Low back pain (LBP) is defined as pain, muscular tension, or stiffness that is localized to the low back, with or without leg pain[22]. LBP can be divided into acute (less than 6 weeks), subacute (6 to 12 weeks), and chronic (over 12 weeks) pain with respect to duration[23]. LBP is a symptom, not a disease, and hence can be the result of several different known and unknown reasons[3].

Furthermore, LBP can be divided into three distinct categories according to symptoms and clinical features: specific spinal pathology, radicular syndrome, and non-specific LBP. The rarest cause of LBP is specific spinal pathologies (<1% of cases in primary care), which include vertebral fracture, malignancy, spinal infection, axial spondyloarthritis, and cauda equine syndrome [24,25]. A range of clinical features or red flags have been proposed for the identification of spinal pathologies. However, only a small subset of red flags (i.e., older age, prolonged corticosteroid use, severe trauma, and the presence of a contusion or abrasion) are informative for the detection of fracture, and a history of malignancy alone increases the likelihood of other spinal pathologies.[6,24,26] In radicular syndrome (5%-10% of cases in primary care), there are three subsets of nerve root involvement, each with distinctive symptoms: radicular pain (neuralgia), radiculopathy (nerve root dysfunction, sensory and/or motor defect with or without neuralgia), and spinal stenosis (clinical features of lumbar myelopathy)[24,25].

Non-specific LBP is the most common cause of LBP (approximately 90%)[6,27]. Although several innervated lumbar structures are plausible explanations for non-specific LBP (annulus fibrosus, facet joints, muscles, ligaments), there is no clinical test available to determine a definitive link between a pain-sensitive structure and the pain felt by the patient[6,24,25]. Furthermore, the discussion of structural abnormalities and non-specific LBP can be continued further with studies that indicate a strong association between LBP and Modic type 1 changes, disc bulge, disc eruption, and spondyloarthritis seen in Magnetic Resonance Imaging (MRI). These findings are, however, also common in pain-free individuals, and the evidence is insufficient for predicting the course of LBP. Thus, the importance of these findings will remain a source of debate until stronger evidence becomes available.[3,28]

A variety of clinical LBP classification systems are described in the literature to help in diagnostics and treatment choices[29]. Since non-specific LBP is the most common cause for LBP, an effort has been especially made to divide it into homogenous subgroups[30]. Most classifications divide non-specific LBP into mechanically driven and non-mechanically driven pain (figure 1)[29–31]. Moreover, mechanical pain is referred to as nociceptive, pain with peripheral sensitization, whereas non-mechanical pain has characteristics from central sensitization[32].

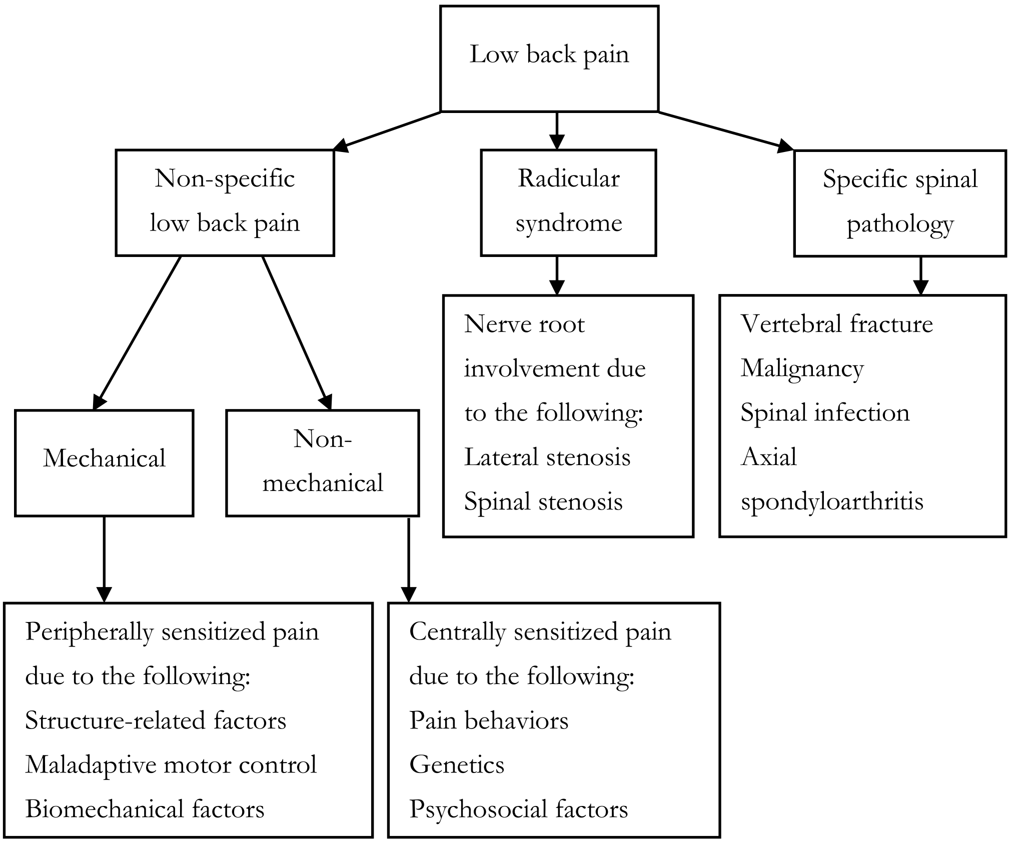

Figure 1. Clinical classification of low back pain. Adopted from the studies of O'Sullivan et al.[29,33].

Low back pain is a major public health problem and the most common musculoskeletal problem globally[21,34]. Furthermore, LBP is the leading cause for years lived with disability (YLD)[2]. According to the Finterveys 2017 study, 44% of men and 48% of women in Finland have suffered from back pain during the past 30 days. Although there was some indication of a reduction in the prevalence of LBP in Finland between the current study and a nation-wide health survey conducted in 2000[35], international studies indicate a rise in prevalence. According to Global Burden of Disease Studies, there was a rise of 17.3% in chronic LBP reported between 2005 and 2015[36]. As there is some heterogeneity among LBP epidemiological studies, it is difficult to combine data to form precise estimates. For example, estimates of the 1-year incidence of a first-ever episode of LBP range from 6.3% to 15.4%, whereas estimates of the 1-year incidence of any episode of LBP range from 1.5% to 36%.[37]

Women are more frequently affected by diseases that cause pain than men[38], and LBP is no exception. In a global prevalence study[37], the mean point prevalence and 1-month prevalence were higher among females, but no significant difference was found between sexes in 1-year or lifetime prevalence. Age is also a factor that affects the prevalence of LBP. Indeed, age-specific point prevalence increases progressively from childhood until the age of 80 to 89 and declines thereafter. Interestingly, YLDs peak at the age 40 to 49 before decreasing. Both sexes have similar age-dependent trends.[34] The differences between the prevalence of LBP and LBP-induced disability may be partly due to high occupational and domestic exposures in middle-aged groups[39].

Low back pain causes a major economic burden on society and individuals. Disability caused by LBP is the highest in the working-age groups[3]. Typically, indirect costs are much higher than direct costs[6] . The majority of the societal and economic costs are used to treat patients with chronic LBP [4,40,41]. In Finland, a substantial portion of disability pensions are granted to persons with chronic LBP problems[42]. In 2019, 31% of disability pensions were granted on the grounds of musculoskeletal disorder[43]. For the individual, the economic effects are direct causing a loss of income and often forcing early retirement. These problems seem to accumulate with the number of comorbidities.[44]

2.1.2 Chronification of low back pain

Chronic pain affects every fifth European; meaning approximately 95 million Europeans are living with chronic pain. It has been that the estimated financial burden of chronic pain in Europe is €300 billion.[45] As previously stated, chronic LBP accounts for most of the cost of LBP [4,40–42]. The economic burden is attributed to increased use of health care resources and medication therapies, disability pensions and sickness benefits, and indirect causes such as loss of work productivity[6,42,46].

Chronic pain is described as pain lasting for more than the expected healing period, most commonly three months[23,47]. It has its own characteristic mechanisms related to the neurophysiological processes, which is described in the next chapter. Chronic pain is not only a burden on society, with direct and indirect costs, but also on the individual with prolonged suffering. It has also been reported that the longer the pain continues, the harder it is to treat. This can be due to many reasons, such as preceding individual factors, initial causes of the acute pain, or the neurophysiological processes of pain in the individual.[47,48]

Estimates of the transition from acute to chronic LBP differ among studies and countries. A global prevalence study reported a range between 4% and 25%, chronic LBP increasing between 30 to 60 years of age, and chronic LBP being more prevalent in women[39]. Regional studies describe a wide variability in the development of chronic LBP problems. In high-income countries, for example, the prevalence of all LBP ranges between 2% and 48%[39,40,49], whereas in low- and middle-income countries, chronic LBP makes up a larger proportion of all LBP cases while mean lifetime prevalence is lower[50].

To prevent pain chronification at the system level, the recommendations given by experts in the field suggest that local services should be organized to promote healthy lifestyles across the whole life cycle to prevent and effectively treat diseases causing pain. In addition, risk factors for pain chronification should be assessed as a part of organized health check-ups. To achieve these goals, the efficient treatment of acute pain should be promoted using a multidisciplinary approach, Acute Pain Service clinics should be established, prevention of pain should be guided by prognostic factors, education of health care professionals and citizens on prognostic factors and treatment possibilities should be enhanced, and timely treatment and rehabilitation services should be promoted. [51]

2.1.2.1 Physiology of pain chronification

The pain perception pathway in the nervous system can be divided into four sections: transduction (activation of the nociceptors), transmission (pain message to the central nervous system), modulation, and perception[11].

Pain sensation is mediated via nociceptors that transmit acutely painful feelings as a warning that body tissue is being damaged or at risk of being damaged. Nociceptors are free nerve endings that are widely distributed throughout the body. There are selective nociceptors for mechanical, thermal, and chemical stimuli. Additionally, polymodal nociceptors are sensitive to different combinations of stimuli. Nociceptive axons include both Aδ fibers that mediate sensations of sharp, burning pain and C fibers that mediate more persistent feelings of dull, burning pain.[12] After transduction, the pain message is mediated from the periphery to the spinal cord, where the primary afferent neuron communicates with a projection neuron. Information is transferred in spinothalamic tracts to the nuclei of the thalamus. From here, it is passed further on to the frontal cortex and the somatosensory cortex.[11]

Pain sensation can be modulated in a variety of ways. For example, inhibitory tracts in the CNS can prevent pain stimuli mediation in the spinal cord. The frontal cortex and hypothalamus activate the inhibitory tracts of the middle brain and medulla oblongata which, in turn, modulate the spinal cord. The modulatory interneurons in the spinal cord can be either inhibitory or excitatory. The modulation of pain by efferent tracts from the CNS partly explains why psychological factors can affect our pain sensation. The effect of different neurotransmitters can either increase or decrease the pain. [11] In addition, the periphery has its own modulation tracts. Damaged tissue releases a variety of chemicals (including neurotransmitters, peptides, lipids, proteases, neurotrophins, cytokines, chemokines, and others) that trigger a local inflammation. As a result, capillary permeability increases. Additionally, substance P, released from nerve endings, causes nearby mast cells to release histamine which, in turn, activates nociceptor endings resulting in hyperalgesia (peripheral sensitization). Another example of pain modulation is called the axon reflex. Action potentials from the site of an injury can propagate into the side branches of the same axon that innervates the neighboring areas. As a final example of pain modulation, pain can be modified by non-painful sensory input. By the simultaneous activation of low threshold mechanoreceptors (Aα and Aβ fibers), the pain evoked by the activity of nociceptors can be reduced.[12]

The transition from acute to chronic pain is not fully understood. While acute pain has an adaptive purpose, chronic pain is a paradoxical phenomenon[52]. Although there is no consensus on the mechanisms of pain chronification, studies suggest that peripheral and central sensitization, genetic priming, gliopathy[53] and other inflammatory responses, and alterations in the corticolimbic circuitry ("emotional brain")[54] are involved[55]. In addition, sleep deprivation, stress, and other psychosocial factors, as well as lifestyle and environmental factors play an important role in the transition from acute to chronic pain[14,56].

Central sensitization can be described as "facilitated excitatory synaptic response and depressed inhibition, causing amplified responses to noxious and innocuous inputs"[57]. It can be triggered by neuronal, immune, or glial-related activation. The heightened synaptic transmission causes a reduction in the pain threshold, an amplification of pain responses, and the spread of pain to non-injured areas. Central sensitization increases the sensitivity of spinal neurons so that neurons generate action potentials to stimuli that would normally be ineffective. The long-term maintenance of chronic pain involves late-onset central sensitization, which requires the activation of transcription. Brain-derived neurotrophic factor (BDNF) release plays a key role in the long-term maintenance of central sensitization, as this pathway can modulate transcriptional processes in the cell.[52] There are hundreds of genes that play a part in pain sensitization[52,56], and it seems that chronic pain also shares a genetic predisposition with depression and fatigue[58], along with other pain-related diseases[56].

2.1.2.2 Risk factors for pain chronicity

Although many risk factors for the onset of LBP have been studied, there is no strong evidence on the causality of such factors[23]. According to meta-analyses, lifting at work[59], smoking[60], obesity[61], and depressive symptoms[62] increase the risk for a first episode of LBP by a modest amount.

On the other hand, there is much more evidence on the prognostic factors for pain chronification. A systematic review by the author and colleagues[14] (Study I) found that a total of 45 statistically significant factors concerning personal factors and medical history, symptom characteristics, biomechanical factors, psychological and psychosocial factors, and lifestyle factors were either protective of or risk factors for LBP chronicity. Higher pain intensity, higher body weight, carrying heavy loads at work, difficult working positions, and depression were the most frequently observed prognostic risk factors for chronic LBP. Moreover, maladaptive behavioral strategies, general anxiety, functional limitation during the episode, smoking, and physical work were also explicitly predictive of chronicity. The most frequently observed protective factors were physical exercise and higher blood pressure.[14]

The expectations behind the identification of risk factors are that tailored interventions, according to the underlying risk factors, would be beneficial to the healing process. These interventions are more closely discussed in section 2.1.5.2.

2.1.3 Biopsychosocial perspective of low back pain

The current consensus considers non-specific LBP a complex condition in which biological, psychological, and social factors have an impact on both the experience of the pain as well as the pain-related disability[3,63]. This explains why interventions that have no effect on biomedical processes (e.g., psychological therapies) can still have profound effects on pain and quality of life[64]. The basic principle is to treat people, not spines[13].

The model for the biopsychosocial (BPS) perspective on pain (figure 2) is derived from studies conducted by Melzack and Kasey [65] in 1968, where they posited that pain is not only a central nervous system's (CNS) response to a sensory input, but rather a complex sequence of behavior that is determined by sensory, motivational, and cognitive processes. Each individual, therefore, experiences pain uniquely as a result of a mixture of different biopsychosocial factors that can interact with physical pathology to modulate the individual's symptoms and subsequent disability[66]. The BPS model was proposed in its current form by G.L. Engel in 1977 with a statement that since the biomedical approach is not having a sufficient impact on health care, it must additionally consider the patient, the social context in which the patient lives, and the complementary system devised by society to deal with the disruptive effects of the patient's illness[67]. In relation to LBP, G. Waddell stated in 1987 that the BPS model should be applied to LBP and that there is a need for a fundamental change in previous clinical practice led by the biomedical model[7].

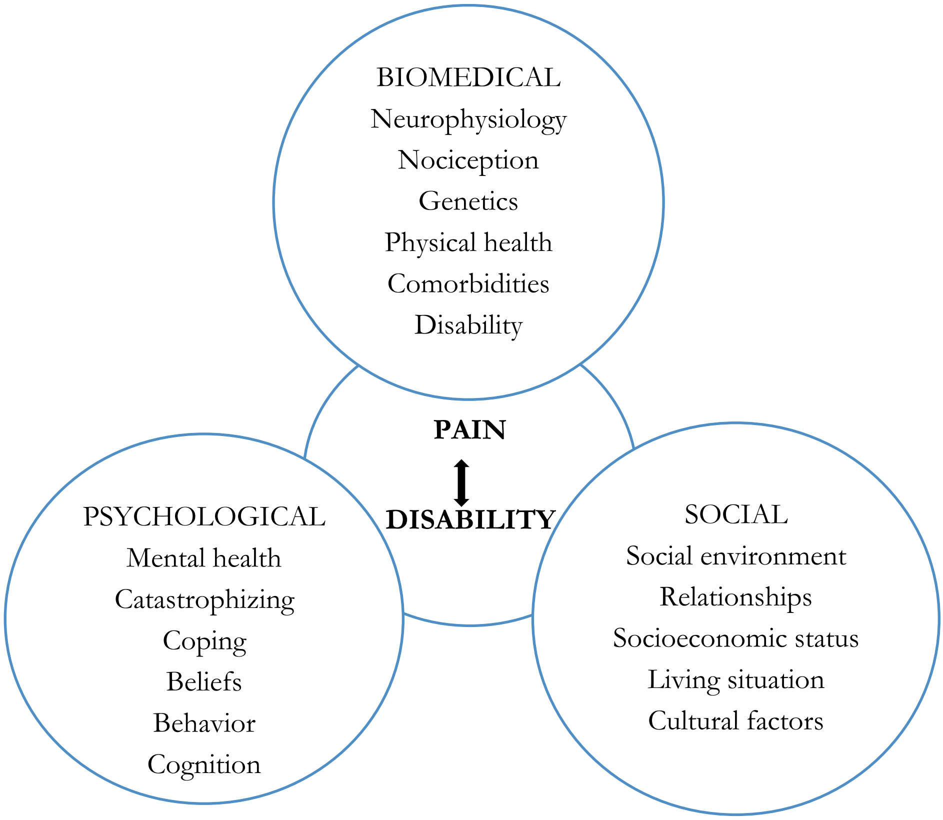

Figure 2. The biopsychosocial model, adopted from the articles by Fillingim[68] and Mescouto[69].

The basic disease model, where there is an assumption that if we cure the pain, the disability will resolve, works quite well for diseases with clear pathology (such as spinal fractures), but it fails for non-specific LBP. This failure is due to many reasons: non-specific LBP is a symptom without a known pathoanatomical cause rather than a disease, the neurophysiology of pain is complex, and, as we can see, the traditional biomedical approach has not solved the problem.[13]

The BPS model has been adapted to serve as a foundation for an ever-growing number of interventions in LBP care. There has, however, been criticism of the narrow or even misuse of the term "biopsychosocial". Even though the term is used as a base for an intervention, it can be underpinned by biomedical concepts. Unfortunately, there is a notable narrow focus on some psychological dimensions of LBP and little consideration of the social dimensions and other important dimensions of LBP care, such as cultural considerations and institutional power. Moreover, current interventions may over-emphasize the psychological aspect, leading to the "psychologization" of chronic pain.[69] When dealing with patients with

LBP, a lack of the requisite skills and confidence to deal with psychosocial factors may also lead to stigmatization[10]. In contrast, those interventions that especially focus on psychosocial factors, such as understanding pain, unhelpful thoughts, coping styles, and goal setting, seem to be effective when dealing with chronic LBP[70].

With recent criticism in mind, some researchers have begun to re-conceptualize the BPS model. For example, Stilwell and Harman[8] state that the boundaries between the biological, psychological, and social are artificial, and this leads to a fragmentation of applications, i.e., social interventions with no connection to the person's biology. On the contrary, pain experience is an interconnected, dependent process between the brain, the body, and the world.

2.1.4 Main strategies in the treatment of low back pain

2.1.4.1 At the individual level

Since no pathoanatomical cause for non-specific LBP has been determined, treatment focuses on reducing pain and its consequences[6]. The main strategies in the treatment of LBP include education and advice, pharmacological management, and non-invasive management. In most cases, invasive management is rarely recommended. Rehabilitation is embedded in the treatment pathway and is discussed more extensively in its own chapter (see 2.1.5). Although recommendations differ according to national guidelines, there is a similarity in the ground rules. Table 1 presents the Finnish national current care guidelines[23] for LBP management.

Table 1. Treatment strategies in the Finnish current care guideline for non-specific low back pain[23]. NSAID= Non-steroid anti-inflammatory drug, CBT= Cognitive behavioral therapy, TENS= Transcutaneous electrical nerve stimulation. [a] Combined with physical exercise and advice, [b] Graded exposure, exercises aiming at enhancing physical endurance, [c] Stratification according to psychosocial factors and movement classification.

	Education and advice	Pharmacological management	Non-invasive management	Invasive management
Acute pain	Avoid bed rest Continue daily chores and return to work as soon as possible Hard physical exercise is not recommended	Paracetamol NSAIDs Tramadol Muscle relaxants	Light exercise, e.g., walking Superficial heat Manipulation or traction are not recommended	
Subacute pain	Encouragement to take an active role in the rehabilitation	Paracetamol NSAIDs Weak opioids	Rehabilitation and work ability assessment Active rehabilitation Superficial heat Massage[a]	
Chronic pain	Encouragement to take an active role in the rehabilitation	Paracetamol NSAIDs Weak opioids Duloxetine Transdermal buprenorphine	Exercise therapy[b] Multidisciplinary biopsychosocial rehabilitation Institutional rehabilitation Stratified rehabilitation[c] CBT TENS Massage[a] Acupuncture Manipulation, traction, or laser therapy are not recommended	Epidural injections or facet joint injections are not recommended

National guidelines vary to some extent in their recommendations for different treatment modalities. Some differences that are worth mentioning include pharmacological treatment, more precisely the use of paracetamol as a first-line drug. NICE guidelines[71] do not recommend paracetamol as a single drug therapy. The Canadian guidelines from 2015[72] still recommend paracetamol, but a newer guideline by the Canadian OPTIMa Collaboration[73] states that the use of paracetamol is challenged by new evidence. This is a reference to the studies, including a Cochrane review from 2016[74], where it was found that paracetamol is no better than a placebo when treating LBP. The American College of Physician guidelines[75] also exclude paracetamol. Instead, NSAIDs and muscle-relaxants are seen as first-line drugs if pharmacological treatment is needed. The same guideline recommends superficial heat, massage, acupuncture, or spinal manipulation for the non-invasive management of acute or subacute LBP. Furthermore, for chronic LBP, it is recommended that initially non-pharmacological treatment choices are selected that include exercise, multidisciplinary rehabilitation, acupuncture, mindfulness-based stress reduction, tai chi, yoga, motor control exercises, progressive relaxation, electromyography biofeedback, low-level laser therapy, operant therapy, cognitive behavioral therapy, or spinal manipulation. In the NICE guidelines[71], radiofrequency therapy is recommended for chronic LBP if the main source of the pain is thought to come from structures supplied by the medial branch. A Cochrane review from 2015[76] does not, however, support this procedure on the grounds that high-quality evidence is lacking.

Patient education is the cornerstone of LBP management. To support evidence-based patient education and advice, all university hospital districts in Finland created Health Village as a joint project in 2016-2018 supported by the Ministry of Health and Social Affairs. This globally unique data source offers reliable health information for the public and health care professionals via the Internet. Health Village also includes digital care pathways on a physician's referral, and a HealthVillagePRO service portal for professionals.[77]

2.1.4.2 At the system level

In Finland, the public sector is responsible of organizing health services. According to the Constitution of Finland, the public authorities shall guarantee for everyone adequate social, health and medical services. The treatment of a patient is provided in either primary health care or specialized medical care, depending on the level of care they require.[78] In Finnish health care, the service choices include disease prevention, examinations to detect illness, treatment, and rehabilitation. The aim is to only use methods that are effective, safe, and reasonable in terms of cost.[79]

The Finnish current care guidelines are independent, evidence-based clinical practice guidelines intended to form the basis of treatment decisions. Furthermore, they also form the basis for compiling regional care programs.[80] Depending on local resources, a group of relevant stakeholders decide the regional treatment and rehabilitation pathways for LBP patients. In the Pirkanmaa Hospital District, the regional care program (figure 3)[81] recommends direct access to a physiotherapist as the first contact for LBP patients, if no red flags are identified during treatment needs assessment. Timely check-ups are at 1-2 weeks and at 3-6 weeks after the first contact. Occupational health care is recognized as a relevant participant in the treatment pathway from the beginning. Physiotherapists' resources are used mainly for advice and guidance in the acute phase, and a more active exercise therapy is initiated in the subacute phase. Consultation with a physiatrist is recommended in complicated cases. Moreover, a multidisciplinary approach is advisable in cases of prolonged pain, as is the early recognition of psychosocial factors and the use of cognitive behavioral therapy (CBT) approaches. The treatment pathway leads to special health care when prolonged pain problems show no signs of healing over a period of 6-12 weeks. In special health care (Tampere University Hospital), staff in the Spine center, which includes physiatrists, orthopedists, and neurosurgeons, evaluate and treat patients with LBP in collaboration with different diagnostic disciplines. In the rehabilitation outpatient clinic, the effect of the patient's diseases and injuries on their professional ability and functional capacity are evaluated and possibilities for rehabilitation are explored.[82] The need for the medical and occupational rehabilitation services provided by Kela (the Social Insurance Institution of Finland) and others should be evaluated during the chronic phase at the latest.[81]

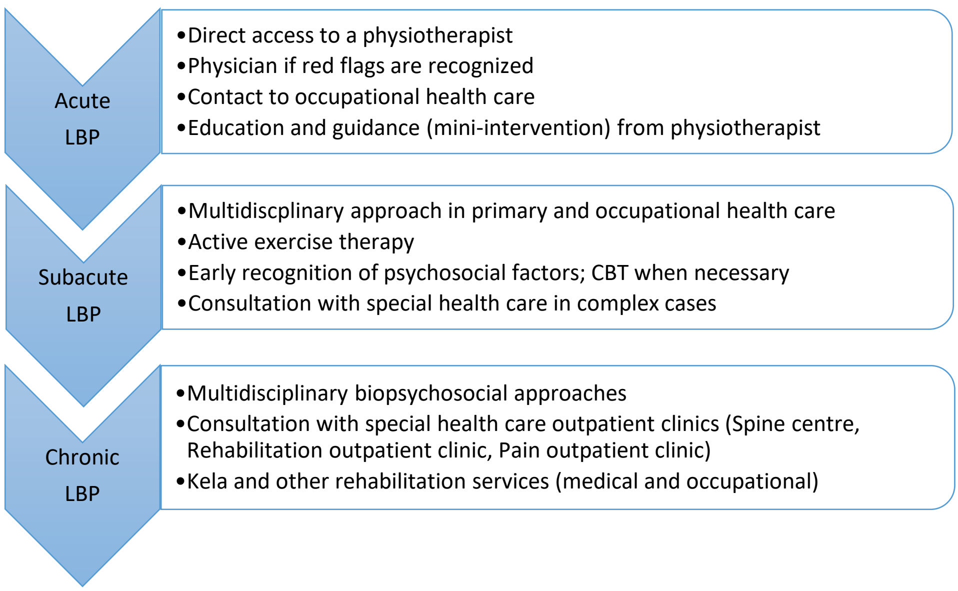

Figure 3. The resources for LBP management according to Pirkanmaa Hospital District's regional care program. CBT= Cognitive behavioral therapy.

2.1.5 Rehabilitation in low back pain

Rehabilitation is defined as a multimodal, patient-centered, collaborative process in a health care context that includes interventions targeting a patient's capacities and/or contextual factors related to performance. The goal of rehabilitation is to optimize the functioning of a patient with health conditions who is currently experiencing disability, is likely to experience disability, or is a person with disability.[83]

In Finland, rehabilitation for patients with LBP is primarily organized by primary health care and occupational health care. Special health care serves mainly as a place for rehabilitation assessment where recommendations on the intensity and contents of the rehabilitation are given. Kela, the Social Insurance Institution of Finland, operates institutional rehabilitation and adaption training courses, mainly for working age patients with LBP. In addition, multidisciplinary individual rehabilitation and intensive medical rehabilitation are both options for patients who have a broad range of symptoms causing a variety of disabling problems and major difficulties in coping with daily life.[84] In case of a preceding injury, the Insurance companies may organize the rehabilitation services. Overall, there is a great variation in the criteria and availability of rehabilitation across the country. Moreover, the financial issues concerning the rehabilitation processes are often unclear when the patient changes from one service provider to another. This lack of clarity may lead to delays in the rehabilitation, increasing the number of patients with chronic pain.[51] As a result, patient processes in the rehabilitation pathways have been developed to avoid these types of problems. For example, Pirkanmaa Hospital District updated their treatment and rehabilitation process for patients with neck and back pain in 2018 [81]. In addition, the Ministry of Social Affairs and Health has established a Council for Choices in Healthcare (COHERE Finland) that recommends which service choices, including rehabilitation, should be available publicly[79]. The council has considered the burden LBP places on resources in primary and occupational health care. It justifies the need to move from the biomedical model of care to the biopsychosocial model with the present understanding of LBP chronification.[85] Thus, a recommendation concerning biopsychosocial rehabilitation in prolonged or recurrent LBP is available[86], whereas other recommendations for LBP rehabilitation concentrate on post-surgical rehabilitation (disc herniation[87], spinal stenosis[88], and arthrodesis[89]).

2.1.5.1 Different rehabilitation approaches

There are numerous approaches to LBP rehabilitation that range from pilot phase intervention studies to widely used guidelines. In a broader context, different rehabilitation approaches can be divided into stepped, stratified, or tailored rehabilitation strategies, as described in table 2[90].

Table 2. Different rehabilitation approach examples divided according to the underlying strategy.

Stepped rehabilitation		
Approach	Provides basic rehabilitation for all, progresses gradually to more complex interventions when lower level does not work	
Examples	Current care guidelines[23]	Basic rehabilitation in acute stage, progression to a wider perspective when pain is prolonged
	Stepped-care approach[91]	Three steps of intervention, chronological progress guided by observed outcome
Stratified rehabilitation		
Approach	Categorizes patients into subgroups and provide different levels of comprehensiveness or approaches accordingly	
Examples	STarT Back Tool[92]	Three subgroups with different levels of treatment-modifiable prognostic indicators (physical and psychosocial)
	Örebro Musculoskeletal Pain Questionnaire[93]	Identifies workers at risk of failing to return to work due to personal and environmental factors (low risk--high risk)
	Treatment-based classification[94]	Three levels of classification based on historical information, behavior of symptoms, and clinical signs
	McKenzie classification[95]	Three levels of classification according to the symptomatic and mechanical response to repeated movements and sustained positions
Tailored rehabilitation		
Approach	Individualizes the rehabilitation based on the patient's personal needs	
Examples	Pain and disability driver management model[96]	Model that encompasses all domains within the ICF to form a patient profile for individualized rehabilitation
	Individually tailored behavioral medicine intervention[97]	Intervention is individually tailored according to patient's behavioral treatment goals and functional behavioral analyses

Additionally, LBP rehabilitation can also be divided according to the contents of the intervention into exercises, back schools (pain education with or without exercise), cognitive behavioral approaches (psychoeducation), and manual therapy[63]. Exercise is the most common modality of LBP rehabilitation. However, to date, there is no clear evidence that a certain approach is superior to any other. Therefore, many different types, ranging from specific to mixed methods, are used.[63] Though the content of back schools varies widely, they were first introduced as a concept of a therapeutic program given to groups of people that included both education and exercise. Systematic reviews, however, suggest that back schools are ineffective for LBP in all its stages.[98,99] Cognitive behavioral approaches, such as cognitive functional therapy, focus on changing a patient's beliefs, confronting their fears, educating them about pain mechanisms, enhancing mindfulness of the control of their body during pain provocative functional tasks, training them to reduce excessive trunk muscle activity, and to change behaviors related to pain provocative movements and postures[100]. Different guidelines[23,71,73,101] recommend a variety of manual therapies for LBP but mainly in combination with other modalities such as exercise.

2.1.5.2 Rehabilitation according to individual biopsychosocial factors

Leading authorities in the field of LBP have identified challenges in the prevention of persistent LBP-associated disability. Actions should, therefore, include the development and implementation of strategies to address the modifiable risk factors for disabling LBP.[16] There is consistent evidence that a "wait and see" approach to LBP rehabilitation is no longer advisable. Early screening of the prognostic factors of pain chronification provides valuable information for identifying those who are at risk for delayed recovery and for formulating an individual treatment strategy earlier along the treatment pathway. The stratified and tailored approaches for rehabilitation (see table 2) share the assumption that those at risk for pain prolongation can be identified and treated early so that chronic pain is prevented.[90]

As an example of an intervention on recognized risk factors, the stratification of the treatment according to the STarT Back Tool (SBT) has shown promising results. In 2014, a randomized trial[102] found that Roland-Morris Disability Questionnaire (RMDQ) scores were significantly higher in the intervention group than in the control group at four-month follow-up. In addition, economical value was achieved from the stratified care. Another cohort study[103] found that the group receiving stratified care according to the risk level had shorter sick absences from work in addition to a small but significant difference in RMDQ.

In the work-related context, a Danish research group[104] identified subgroups of patients who would benefit more from a multidisciplinary approach than a brief intervention. Multidisciplinary interventions seemed more effective on patients reporting low job satisfaction, having no influence on work planning, and feeling at risk of losing their jobs due to their sick leave.

Rehabilitation approaches that mainly focus on biomechanical stratification, such as treatment-based classification, have also recognized the need to also address more holistically the psychosocial issues related to LBP disability. In an updated version of the above-mentioned classification, regardless of the rehabilitation approach (symptom modulation, movement control, functional optimization), patients with a medium-to-high psychological risk profile are recognized as also requiring psychologically informed rehabilitation[105].

2.2 International Classification of Functioning, Disability, and Health (ICF)

While mortality and diagnostic data are important, they do not adequately capture the health outcomes of individuals or populations. Diagnosis alone does not explain what individuals can and cannot do, what they need in order to improve their quality of life, what their prognosis will be, or what the cost of their treatment will be.[106]

The International Classification of Functioning, Disability and Health (ICF) is a framework developed by the World Health Organization (WHO) to form a conceptual basis for the definition, measurement, and policy formulations for health and disability. It provides a standard language and framework for the description of health and health-related states. The ICF works as a complementary framework for ICD-10/11 (the International Classification of Diseases and related health problems). Whereas the ICD gives a classification on diagnosis and disease, the ICF classifies functioning and disability associated with health conditions.[17] The ICF sees the person's functioning as an interaction between health status and both personal attributes and environmental influences, rather than merely a consequence of a disease[107]. Functioning, as described in the ICF, is introduced as the third health indicator complementing the established indicators mortality and morbidity[108]. The ICF was developed with the following underlying principles: universality (classification should be applicable to all people irrespective of the underlying health condition), parity (the content of the classification's structure should not be differentiated by etiology), and neutrality (the content of the classification should be worded in neutral language to express both positive and negative aspects)[17]. The universal, interdisciplinary language of the ICF has the capability to be applied globally in different health care settings, and by different professions for a broad biopsychosocial understanding of health[18].

2.2.1 Structure of the ICF

The descriptions of disability and functioning are viewed as outcomes of the interaction between health conditions and contextual factors[17]. The components of the model comprise the following:

1) body structures, as the anatomical parts of the body
2) body functions, as the physiological and psychological functions of the body
3) activities, referring to the execution of tasks or actions by individuals
4) participation, implying the involvement in a life situation
5) environmental factors, referring to physical, social, and attitudinal situations in which people live
6) personal factors, that are the background of an individual's life and living situation comprising features that are not part of a health condition.

The components of the model are classified to a hierarchy of chapters and categories. Different levels offer either a general or more specific description of different domains.[17,107] Moreover, all descriptions are labeled with an individual code. There are three to four levels in the classification of different components, which is reflected in the coding (Figure 4). For example, in body functions, chapter level: b2 sensory functions and pain, 2nd level: b280 sensation of pain, 3rd level: b2801 pain in body part, and 4th level: b28013 pain in back. Individual factors are not coded because of the wide variability among cultures.[17,109]

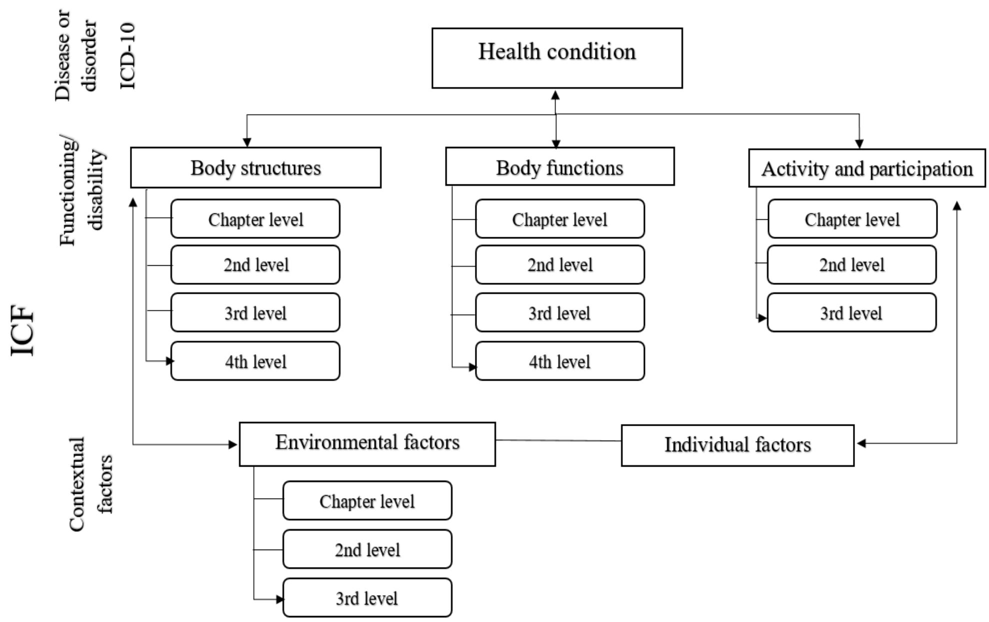

Figure 4. The structure of the ICF. Adopted from ICF Beginner's guide[17]. (Reprinted with permission)

In addition to the different levels of describing the components of the model, there are qualifiers to record the presence and severity of a problem in functioning at the body, person, and societal levels. In body functions and structures, the qualifier indicates the presence of an impairment and the degree of the impairment on a five-point scale. In activity and participation, two different qualifiers are provided: the performance qualifier and the capacity qualifier. The first describes what individuals do in their current environment, and the latter describes the ability of individuals to execute a task or action. Finally, in the environmental factor's domain, a generic qualifier is given with a negative and positive scale to denote the extent of the barriers and facilitators, respectively.[17]

2.2.2 Applying the ICF to rehabilitation medicine

The ICF was developed to be used to answer a wide range of questions involving clinical, research, and policy development issues. With regard to rehabilitation medicine at the system level, the ICF can be used as a framework for eligibility criteria for state entitlements, social policy development, needs assessment at a societal level, management and outcome evaluation, and resource planning and development. At the individual level, applications of the ICF include the assessment of individuals, individual treatment planning, evaluation of treatment and other interventions, communication using a common language in multidisciplinary communities, and the self-evaluation of individuals. Additionally, the ICF is a universally applicable tool that provides a framework for research purposes to make research results comparable. [17]

The implementation of the ICF has been limited on an operational level due to its exhaustive nature[18,110]. To facilitate the more comprehensive use of the ICF in clinical settings, the WHO has developed a series of instruments, including the ICF Checklist[111], the ICF Core Sets[112], and the WHO Disability Assessment Schedule 2.0 (WHODAS 2.0)[113].

Several intervention studies have applied the ICF in rehabilitation settings. In a Japanese convalescent rehabilitation ward, intervention included the serial assessment and discussion of the ICF rehabilitation set with patients. A multidisciplinary rehabilitation approach combined with serial assessment and discussion using the ICF rehabilitation set was associated with favorable recovery.[114]A Norwegian study used the ICF for goal setting with patients with chronic disabilities. Goal setting was guided by health care professional to emphasize activities and participation domains rather than the body function domain. Goal setting predicted long-term mental functioning following rehabilitation.[115]

In addition, several studies have investigated means to implement and the success of the implementation of the ICF to rehabilitation medicine. Improvements in communication, enhancing the clarity of team roles, helping to structure the service provision, and aiding clinical reasoning were all reported as benefits when using the ICF in a stroke rehabilitation unit[116]. Another study from neurorehabilitation reported positive effects on the daily work of rehabilitation professionals, including improvement in the quality of interdisciplinary teamwork, sharing of the rehabilitation processes with the patient and their family, and reducing the time needed to complete tasks[117]. A Swedish longitudinal, multicenter study[118] concluded that the use of the ICF-CY (ICF for children and youth) provided a common framework for professionals and enhanced the awareness of a child's participation in everyday life. However, the implementation was seen as time consuming, and the complexity of the framework might be perceived as a barrier to implementation.

2.3 Decision support in health care

Health care should deliver safe, evidence-based care that takes individual preferences into account when selecting treatments[119]. There is a need, therefore, for strategies to support the changes in the structure, process, and organization of care[120]. Decision support tools (DST) or decision support systems are designed to aid in clinical decision-making, where the characteristics of individual patients are matched with evidence-based knowledge to generate patient-specific assessments or recommendations[121]. From a wider perspective, all systems that enhance clinical decision-making can be categorized as aiding in decision support. These include clinical guidelines, condition-specific flow charts, focused patient data reports and summaries, computerized diagnostic support applications in electronic health records, and contextually relevant reference information, among other tools. These tools and systems are designed to address the growing information overload faced by clinicians, and to provide a platform for integrating evidence-based knowledge into the delivery of care.[122] In addition, they represent a possibility for tailored treatment decisions and can increase patient engagement and knowledge using personalized aids for patient education[120].

The most quickly evolving type of DST are computer-assisted tools, where large sets of data can be synthetized to perform complex evaluations[121]. The data input can include the genetic, sociodemographic, or clinical characteristics of an individual to improve the delivery of personalized care[120].

Although systems for decision support provide several benefits for health care professionals, challenges in implementation are recognized. There are, for example, misperceptions on the usefulness of DST, as well as the belief that professionals are more accurate in risk estimation. Additionally, tools should be fully integrated into the care processes without disrupting the clinical workflow.[120]

Research-based decision support is also crucial at the macro-level of health care, where governmental health policymakers must allocate scarce resources to reflect the general needs of the population. At the policy development level, problem-solving processes follow the same principals as in clinical settings, only the scope and impact are in different perspectives. Decision support can be enhanced with research-derived information at many levels of policymaking:

1. Assessment:
    a. identifying and defining the problem
    b. previous options to address the problem

    c. new options and their applicability (long-term outcomes, cost-effectiveness, implementation to the current system, unintended effects)
2. Planning:
    a. refining the plan in a cost-effective manner, with minimal negative effects and the greatest impact as wide as possible
    b. problem solving for unintended effects, implementation pathway problems, etc.
3. Implementation and evaluation
    a. monitoring of short- and long-term outcomes
    b. evaluation of intended effects, unintended effects, accessibility, etc.[123]

2.3.1 Decision support tools in the treatment of low back pain

Various methods have been proposed to strengthen clinical decision-making in LBP. Different classifications can help to identify variables that predict the prognosis and could thus be used to prioritize patients for a certain intervention. In addition, some classifications aim to inform treatment selection. For example, when certain patient profiles are more likely to benefit from a certain treatment. The STarT Back Tool (SBT) is a validated example of stratified care for LBP based on the patients' prognosis. [124]

SBT is a brief questionnaire that identifies possible psychosocial risk factors for LBP. The tool includes nine items: referred leg pain, comorbid pain, disability (two items), bothersomeness, catastrophizing, fear, anxiety, and depression. These prognostic factors were chosen by the developers on the assumption that they could potentially be modified by treatment options in primary care. Analysis of the prognostic factors was made from a secondary analysis of two populations. Poor outcome was defined as 12-month follow-up Roland Morris Disability Questionnaire (RMDQ) scores above the median. The first population consisted of 402 patients who participated in a randomized controlled trial[125] (329 at the end of follow-up) and the other consisted of 447 patients in a cohort follow-up study[126]. Patient acceptability of the screening tool was assessed using feedback from a small sample (n = 12) of patients. [92]

The predictive validity of the instrument can be analyzed with receiver operating characteristic (ROC) curve analysis, where the area under the curve (AUC) provides an overall measure of the discriminative ability of the instrument[127]. In a systematic review by Karran and colleagues[127], the discriminative performance of SBT in pain as an outcome measure was "non-informative" (pooled AUC=0.59). This carries the risk of misclassification of the patient. In another study, the accuracy of clinicians' predictions compared to SBT was comparable and low[128].

The Orebro musculoskeletal pain screening questionnaire (OMPSQ) was created to determine the risk of long-term absenteeism from work due to LBP[129]. The questionnaire screens for the psychosocial factors affecting work absenteeism. The initial version distinguished two sub-groups ("at risk"/" not at risk") but several cut-offs have been proposed since[130]. The original version has 25 items and a shortened version with 10 items has been developed for easier clinical use with similar predictive properties as the initial version[131].

2.3.2 Artificial intelligence in health care decision support

2.3.2.1 Artificial intelligence in clinical decision-making

From a historical point of view, health care was recognized early on as a promising field of application for artificial intelligence (AI). In the past 50 years, many applications have been developed to support clinical decision-making, ranging from supporting the diagnostics of acute abdominal pain[132] to mortality prediction in the intensive care unit (ICU)[133].

It is difficult to define AI with a single definition, since the field is constantly redefined with new topics[134]. One definition describes AI as follows: "the capacity of computers or other machines to exhibit or simulate intelligent behavior; and the field of study concerned with this"[135]. Artificial intelligence, a branch of computer science, is a heading for its subfields, including machine learning (ML), natural language processing (NLP), expert systems, robotics, speech, planning, and computer vision[136]. The subfields are more closely described in figure 5.

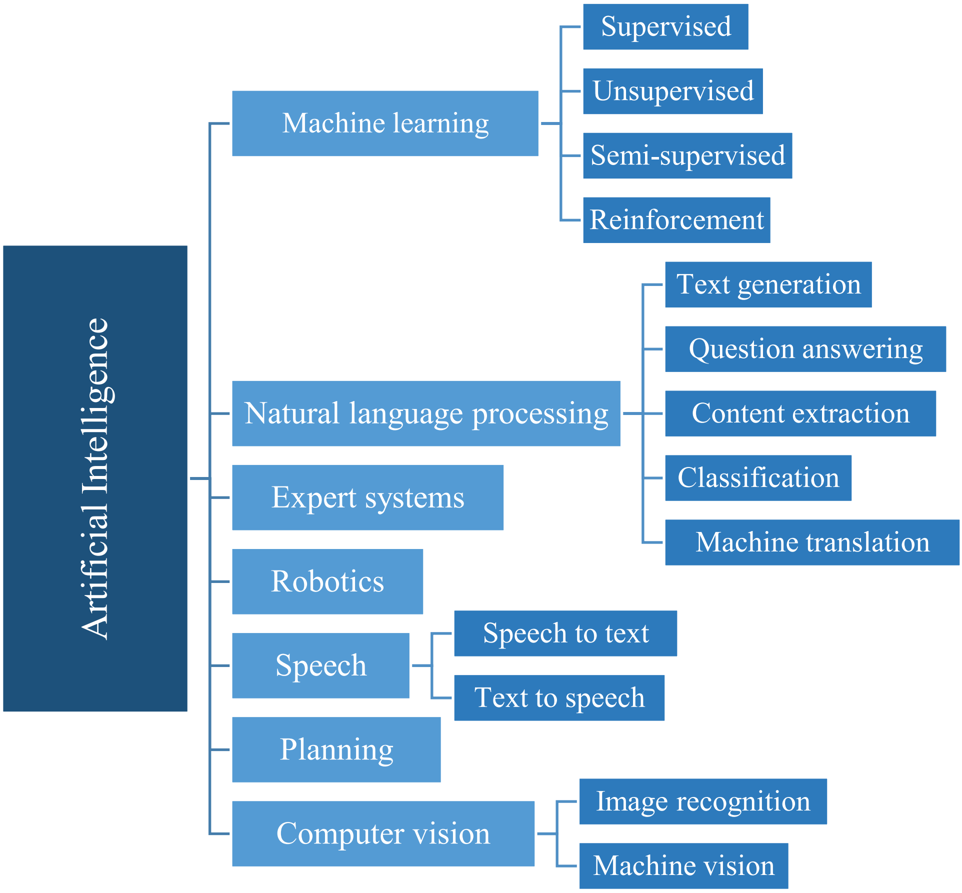

Figure 5. Artificial intelligence and its subfields.

Some AI techniques are of great importance in health care and decision support contexts, and some examples of these techniques are presented below.

Rule-based expert systems based on collections of "if-then" rules have been widely used in the past for health care purposes in clinical decision support. These systems require domain experts to construct a series of rules. An example of such a system is the Evidence-Based Medicine Electronic Decision Support (EBMEDS) application developed by Duodecim Medical Applications in Finland. The system retrieves relevant structured data from electronic health records (EHR) and returns reminders, guideline links, and alarms when appropriate.[137] However, when the number of rules begins to exceed several thousands, the rules begin to conflict with one another, and the systems tend to break down. As a result, they are replaced by more sophisticated approaches based on data and machine learning algorithms.[19]

The field of natural language processing (NLP) includes applications such as speech recognition, text analysis, translation, and other goals. In health care, NLP systems are used, for example, for analyzing unstructured clinical notes on patients, preparing reports, transcribing patient interactions, and conducting conversational AI.[19]

Various machine learning (ML) models have been developed for different decision support purposes. These models include choosing appropriate musculoskeletal management[138], predicting ventilator admission in the ICU[139], and making patient stratification easier in organ transplantation[140]. In addition, genome and biomarker interpretation using ML methods can identify certain types of components related to clinical phenotypes, which can, in turn, predict the status of several diseases. The successful deployment of these methods has implications for both clinical decision-making and trial design.[141] A research team from Cambridge University has developed a ML framework called Autoprognosis that includes automated ML pipelines for creating prognostic models for health care use. The framework uses either raw or curated medical datasets, completes the data with different imputation methods, decides which ML pipelines are used for a given function, explains how the chosen model came to its conclusion, and finally gives an illustrative interface of the results. The tool is available as an open-source package that researchers can use in their work.[142]

Currently, the most widely used and most successful field of medical AI applications is automated medical-image detection. The results of applications using medical-imaging modalities (such as x-rays, MRIs, Computed Tomography), dermatology samples, histopathological slides, and fundus pictures in ophthalmology can be translated for clinicians to use in decision making.[141]

Many AI solutions have embedded different AI subtypes in their algorithms. For example, IBM Watson has as set of cognitive services that include speech and language, vision, and machine learning-based data analysis programs[19]. Microsoft also has its own health care ecosystem (Microsoft Cloud for Healthcare) with a set of different AI solutions for improving data utilization from the perspective of patients, clinicians, and health care providers[143].

The embedding of AI solutions in electronic health record (EHR) systems for clinical decision support may allow real-time risk prediction. According to a recent systematic review, the most common clinical tools are related to thrombotic disorders and sepsis. Since many of the studies are published in medical journals, the components of the algorithms are not always fully explained even though most EHR systems seem to use ML techniques. [144]

AI solutions face similar implementation problems as other DSTs, i.e., integration to the clinical workflow and EHR systems is challenging. Formulating therapeutic plans in complex settings is difficult because a gold standard in not always available[20]. In addition, AI systems must be approved by regulators, and sufficient funding should be available[19]. As most medical AI applications are conducted on retrospective data[145], prospective studies are needed to show the real-world applicability of such systems[141]. Moreover, the trust of health care professionals is crucial for successful implementation. Therefore, the systems must address a real, clinical problem, the scientific background must be strong, they must be developed in co-operation with health care professionals, and the models must be explainable and transparent for the end users.[20]

2.3.2.2 Artificial intelligence in system level decision support

During the past few decades, policymaking has shifted from making decisions based on personal experience and observations to data and empirical evidence driven decisions[146]. AI can support the core objectives of health policy such as preventive strategies, equitable health and social services, secondary prevention of long-term diseases and disabilities, and the promotion of healthy lifestyles with patient-centered approaches[147]. AI could also support policymakers when making decisions about service choices and delivery by adapting to the local needs of citizens[148]. It could forecast disease outbreaks and give timely warnings to the population to prepare[149]. For example, some AI algorithms anticipated the impact of Covid-19 before many countries and the WHO released a report on the outbreak[150].

At present, the data stored in silos and legislative regulations (e.g., the European Union's general data protection regulation GDPR) do not enable seamless decision-making in health policy powered by AI. However, the Nordic countries[151] and the European Union[152] are working to create spaces for safe data-sharing to produce innovative solutions for improved health outcomes.

When implementing AI in health policy decision-making, it is important to recognize sources of bias, as bias can lead to discrimination and other unintended effects. At worst, bias could increase existing health and social inequities and decrease inclusion.[153] Additionally, challenges with legislative frameworks, as mentioned above, and procurement systems act as a barrier to implementation[149].

2.3.2.3 Artificial intelligence in low back pain decision support

AI could improve LBP outcomes by enhancing the ability to detect patterns of clinical characteristics and guide treatment. The benefits of such systems should be at least two-sided: to help patients with improved outcomes and to help the health care system with reduced costs and burden of diseases.[154]

An artificial neural network (ANN) approach was developed to predict the incidence and severity of LBP in industrial workers. The model contained information on personal, occupational, and psychosocial factors collected via interviews, questionnaires, and assessments in occupational health care. The accuracy of the model (both training and testing phase) was 96%. The researchers concluded that the results of prediction could be suitable for developing preventive strategies and corrective interventions.[155] Another ANN approach predicted the risk of pain chronicity and severity 6 months after hospitalization in patients with LBP, using 28 yellow flags as inputs. The strongest neurons predicting long-term pain intensity were depression, pain-related suppressive behavior, and pain-related thoughts of suppression.[156]

Three different supervised machine learning models (decision tree, random forest, and boosted tree) were trained on fictive cases of patients with LBP in order to design a clinical decision support system to support patients in their self-referral to primary care. The system supported receiving the right interventions at the right moment, i.e., referral to a general practitioner, referral to a physiotherapist, or self-care. The boosted tree model performed best in the intervention classification with an accuracy of 72%. In the test dataset containing real-life cases, the accuracy was 71%.[157]

Another study from the United Kingdom compared three different models (ANN, latent class analysis, and logistic regression) for decision support in allocating patients with LBP to the cognitive behavioral approach. The aim was to recognize those patients who would benefit from the treatment using seven predictor variables collected from the Roland-Morris Disability Questionnaire (RMDQ): fear avoidance beliefs questionnaire, pain self-efficacy, Hospital Anxiety and Depression Scale (HADS), and patient-reported troublesomeness. The ANN model showed the best combination of overall error rate and log score for decision support.[158]

A ruler-based system was developed to support the diagnostics of LBP. In this system, 14 different, mainly structure-related, categories were presented after 13 to 15 pages of questions related to demographics, clinical history, and current symptoms, among other things. The average accuracy of the system was 73% when compared with the domain expert's opinion.[159]

A clinical decision tool that helps refer a patient for consultation to a spine surgeon or a non-surgical spine care specialist (Nijmegen Decision Tool for Chronic Low Back Pain) consists of a web-based screening questionnaire and a provisional decision algorithm. The screening questionnaire includes indicators regarding sociodemographic, pain, somatic, psychologic, functioning, and quality of life status.[160]

A fuzzy inference system (process of formulating input/output mappings using fuzzy logic[161]) considers age, sex, pain intensity parameters, metabolic rate, mobility parameters, such as range of motion, and disability level while determining the appropriate treatment plan for patients with intervertebral disc degeneration and LBP (surgery, medication with exercise, or no action needed)[162].

2.3.2.4 Artificial intelligence and the ICF for decision support

The ICF can be used for decision support in many ways and is described in more detail in section 2.2.2.

An automatic translation algorithm was developed to link Patient Reported Outcomes (PROMs), i.e., RMDQ and the Pain Disability Index (PDI), to the ICF codes for the standardization of functioning and health information. The data were collected from 244 patients with chronic LBP, and the random forest model predicted the presence or absence of ICF codes presented in the brief core set for LBP.[163]

A Dutch research team was interested in the functioning data of patients with Covid-19. The unstructured text data from EHR were searched for nine categories from the ICF framework, representing relevant information on functioning. A support vector machine model was used to classify the information into the relevant ICF categories and logistic regression model to classify the level of assigned category.[164]

As part of the redesign of an Italian regional health and social information system, an application was designed that was able to describe the functioning information of individuals in the form of the ICF and to provide suggestions for customized intervention plans [165].

To map functioning information from free text health records, an automated NLP system was developed to code the ICF domains from the mobility and self-care/domestic life domains (thirteen and sixteen second-level categories, respectively) using both classification (comparing each sample to each other, previously seen samples) and candidate selection (directly comparing a sample to the ICF categories). The patient documents pertained to disability benefit claims. A support vector machine that used word embedding features as an input was used as a classification model and deep neural network (DNN) for candidate selection. The training of the model was conducted with three linguistic corpora, i.e., data concerning critical care admissions, physical and occupational therapy encounters, and data associated with disability benefit claims.[166]

2.4 Summary of the literature review

Non-specific LBP is a symptom without known pathoanatomical cause[3,24,25,27,28]. It is benign, yet complex condition where various biopsychosocial aspects impact the experienced pain and disability[3,63]. When the pain persists over 3 months, it is described as chronic pain[23,47]. The transition from acute to chronic pain is not fully understood. Studies suggest that sensitization in the nervous system, genetics, inflammatory responses, as well as sleep deprivation, stress, and other psychological aspects, lifestyle, and environmental factors play a part in the pain chronification.[14,52-56]

Treatment of non-specific LBP focuses on reducing pain and its consequences[6]. Patient education and advice about the nature of symptoms play the main role. Additionally, pharmacological treatment, and rehabilitation interventions, preferably according to underlying individual factors, are encouraged[23].

The International Classification of Functioning, Disability, and Health (ICF) classifies functioning and disability with interactions with health conditions. The classification includes descriptions of body structures and functions, activities, and participation, and contextual factors, such as environmental factors. ICF can e.g., assist decision-making in the assessment of individuals, individual treatment planning, and evaluation of treatment and other interventions.[17,107]

Decision support tools are designed to aid in clinical decision-making, where the characteristics of individual patients are matched with evidence-based knowledge to generate patient-specific assessments or recommendations[121]. In LBP, stratification questionnaires such as STarT Back Tool (SBT) are currently used[124]. When taking into account the complex nature of non-specific LBP, solutions such as artificial intelligence (AI) that can solve complex tasks, could enhance outcomes by e.g., detecting clinical patterns or guiding treatment[154]. AI is a branch of computer science, and the use of AI solutions in health care is quickly evolving[135,136].

3 AIMS OF THE STUDY

This study discusses the challenges and new possibilities of decision support and the implementation of tailored biopsychosocial rehabilitation for patients with non-specific low back pain in current healthcare. However, at present, the knowledge, expertise, and tools that would facilitate such an implementation are lacking. The hypothesis of this dissertation is that new methods can be developed to increase the holistic understanding of disability induced by LBP and to support the timely, tailored rehabilitation of LBP. When implemented, these methods would have the potential to ease the burden of LBP at both the individual and healthcare system level. Furthermore, the results of this dissertation will raise awareness of the complexity of LBP and, at the same time, demonstrate that there are solutions already available in the healthcare system as well as technological solutions that can be used, with some adjustments, for the benefit of patients with LBP and their caregivers. The main aim of this dissertation is, therefore, to develop methods to support the decision-making for the tailored biopsychosocial rehabilitation of patients with non-specific LBP.

The specific aims of this study are as follows:

1. To determine what are the biopsychosocial factors leading to LBP chronicity (Study I)
2. To help the recognition of these biopsychosocial factors using a new tool based on artificial intelligence algorithm (Studies II, IV)
3. To support the tailored biopsychosocial rehabilitation interventions at the healthcare system level. (Study III)

4 DATA AND METHODS

4.1 Study settings

The individual studies on which this dissertation is based were carried out using population data collected from Tampere University Hospital. The AI algorithm was developed by Headai Ltd. (Pori, Finland). The multidisciplinary, multisector team included professionals from Tampere, Valkeakoski, and Kangasala social and health services, Pirte occupational healthcare services, Tampere University, and Tampere University hospital. The studies were retrospective and registry-based in nature and included no interventions. The biopsychosocial model[7] acted as a theoretical background and the ICF[17] as a framework for the studies.

4.1.1 Systematic review (I)

The purpose for conducting a systematic review was to strengthen the theoretical knowledge of the prognostic factors for LBP chronicity, thus building a solid background for creating novel methods for the recognition of and the interventions on such factors. There was also a gap in the literature for an up-to-date literature review, since the previous comprehensive review on risk factors for LBP chronicity was conducted in 1997 by Valat and colleagues[167]. Since then, several studies have been conducted on the subject. Another comprehensive literature review on the subject conducted in 2010 focused on "yellow flag" risk factors[49].

Furthermore, following the biopsychosocial approach, the systematic review considered the biomedical, psychological, and social aspects of pain chronification.

4.1.2 Development of an AI application (II, IV)

A comprehensive view on disability and health is practical when assessing rehabilitation needs at both the individual and population level. The ICF works as a framework for such information, and the data in EHR systems contain this information in an unstructured way. The aim of studies II and IV was to develop an AI application that could retrieve ICF-formed information from the free text in the EHR. Study II worked as a preliminary study for the feasibility study (study IV).

The AI method chosen in the studies was a semantic network-based ML engine called Headai Graphmind (by Headai Ltd., Pori, Finland). The method has the capability to imitate human reading and processing of texts. It has previously been applied for making overviews of skill demands in the labor market, assessing curriculum gaps in educational institutions, and forecasting future skills needs for technology industries.[168–170] To our knowledge, our studies (II and IV) are the first to apply this type of method in the field of healthcare.

4.1.3 Development of a rehabilitation process (III)

The aim for study III was to develop a comprehensive tailored intervention for non-specific LBP suitable for primary and occupational health care in the Pirkanmaa Hospital District, Finland. Although there is an ever-growing number of interventions targeted at reducing LBP chronicity, very few interventions are truly comprehensive when the multiple risk factors driving pain and disability and their interactions (in accordance with the ICF framework) are considered[96]. Therefore, the aim of the study was to address the key problems concerning the effective rehabilitation of patients with LBP regarding the correct timing of risk stratification and the tailoring of interventions. More specifically, rehabilitation processes were developed in order to recognize which resources and clinical pathways were needed for the early recognition of the prognostic factors of LBP chronicity and the activities that follow their recognition. Multidisciplinary teams were formed to take part in the design process.

The design of the intervention followed the development phase of the Medical Research Council's (MRC) complex interventions framework[171]. Additionally, the optimization of the design was adopted from a framework application by Bleijenberg and colleagues[172] to strengthen the value and future implementation of the intervention. Interestingly, an update of the MRC complex interventions framework[173], which quite closely reflected the ideas behind Bleijenberg's application, was published at the end of the design process.

The design was divided into the following phases: identifying the problem, identifying the evidence, identifying the theory, identifying the needs, examining the current context, and modeling the theory, and is described in more detail in table 3.

Table 3. Design for the development process in study III.

I. Problem identification	A systematic review (I) about the risk factors for LBP chronicity is examined and compared to the experience of professionals. The factors that initiate the intervention are identified, as well as the road map to the intervention.
II. Identifying the evidence	A review of previous interventions is conducted, and their applicability to the new design is scrutinized. Their effectiveness and feasibility of the identified problem are studied at the intended implementation site.
III. Identifying the theory	Psychological theories of health behavior and behavioral change techniques are studied to form the theoretical basis for the intervention. A theoretical framework provides information on how the intervention influences the causal chain that would lead to pain chronicity.
IV. Identifying the needs	Following the ICF framework, a retrospective population study of chronic LBP is analyzed to identify the specific difficulties in everyday functioning. With the help of the study, the intervention's intended targets are recognized. The ICHOM patient-centered outcome measures for LBP are examined to identify those outcomes that matter the most to patients.
V. Examining current context	Existing resources are identified as well as any possible gaps and weaknesses that could challenge the implementation of the intervention. Different ways that are needed to enhance the multidisciplinary collaboration in the intervention are considered. The facilitators and barriers to the intervention among providers and recipients are identified.
VI. Modeling the theory	The active components of the intervention are modeled by synthesizing the knowledge gathered from the previous phases. Questions regarding timing, dose, and intensity (how, what, when, where, and by whom) are answered. As a result of the intervention design, a logic model is produced.

4.2 Collection of data and resources

4.2.1 Literature material (I, III)

Study I (Systematic review)

The literature search strategy was developed in collaboration with an information specialist. The primary target of the search was articles concerning predictive risk and protective factors for chronic, nonspecific LBP, with or without pain radiation, in the working-age population (18 to 65 years). A chronic condition was defined as persistent pain in the lower back for a period of 3 months or longer, and the studies included must have assessed the predictive factors before that period.

The following databases were searched for articles in the English and Finnish languages without any date restriction: MEDLINE (PubMed), Cochrane Database, and Medic, which was used to identify articles in the Finnish language. From PubMed, both the Medical Subject Headings (MeSH) and title or abstract search in all fields were used. The search terms "low back pain", "chronic disease OR chronic pain OR chronic", and "risk factors OR prognosis OR prognostic risk factor OR prognostic factor" were used. Publication types with the following MeSH terms were included: systematic review or review or cohort studies. A title or abstract search was conducted in the search for the following publication types: systematic review, or review or cohort or prospective, or retrospective, or longitudinal or follow up/follow-up. The MeSH terms humans, English, and adults were included. From the Cochrane Database, title, abstract, and keyword search in all fields were used. We used similar search terms as used in the PubMed search. Medic (Terkko, National Health Sciences Library, Helsinki, Finland) was searched for Finnish articles with the following search terms: "alaselkäki*", "krooninen*", and riskitekij*" together and separately.

The study types included in the literature search were cohort studies, follow-up studies, and reviews. The reviews were only used to search for additional articles to avoid duplication. Randomized controlled trials were not included, as the effect of the intervention on the outcome (chronic LBP) could not be excluded and observing only the group without intervention could create bias. However, studies with interventions could be included when the intervention concerned the whole followed population, or its impact could be considered in some other way. The references of the studies that met the inclusion criteria were searched for additional articles. Articles that dealt only with operative treatment were also excluded, since the systematic review was conducted to serve as background information for a rehabilitation intervention.[14]

In total, 25 articles met all the inclusion criteria and were included in the systematic review. Figure 6 presents the study selection process.

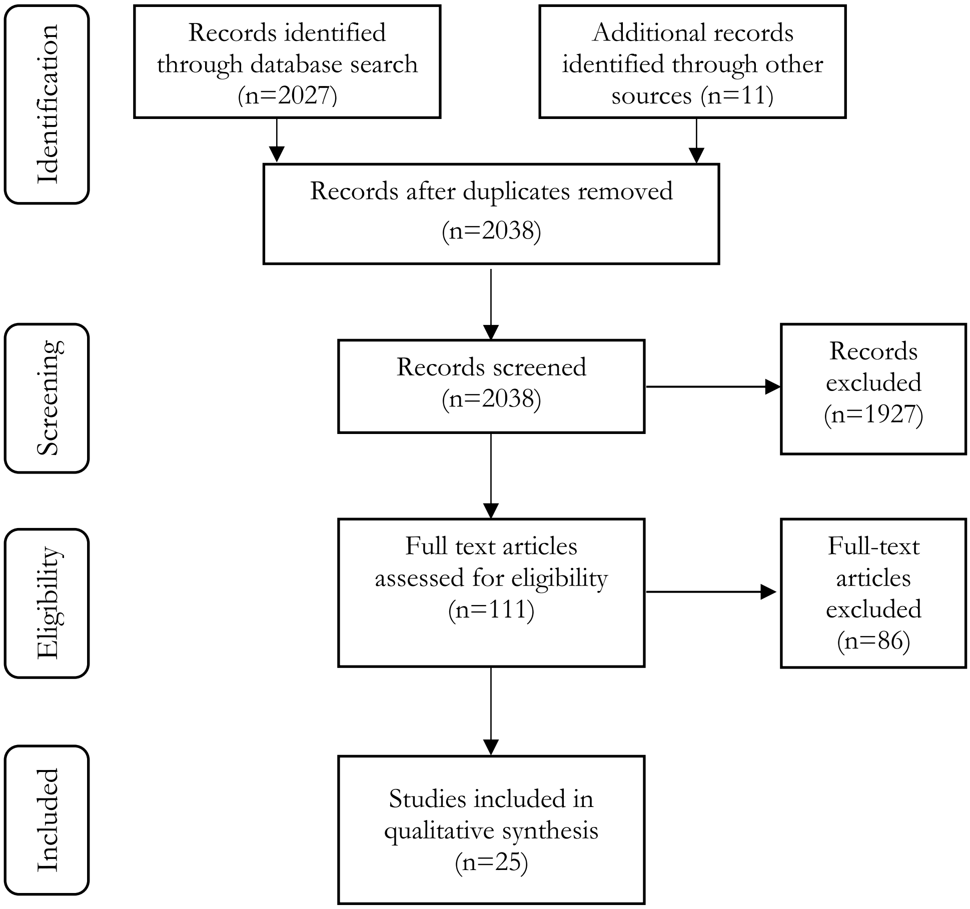

Figure 6. Flow chart of the study selection process for the systematic review.

Study III (Rehabilitation process)

A literature review of the previous interventions concerning any of the aspects from the biopsychosocial perspective was conducted in order to increase the understanding of previous successes and failures and their applicability to the Pirkanmaa Hospital District. The aim was to provide a representative picture of the current literature for the multidisciplinary team rather than execute a comprehensive systematic review. PubMed and Google Scholar were used as databases, and the references of suitable articles were searched for additional articles.[174] The PICO (patient, intervention, control, outcome) search strategy is described in table 4.

Table 4. The PICO search strategy for study III. MSK= Musculoskeletal.

	Patient	Intervention	Control	Outcome
Biomechanical	Working-age adults with back pain, or other painful MSK disorder	Workplace interventions, mainly targeted to biomechanical factors	Not specified, e.g., natural course	Reduction in pain or work disability
Psychological	Working-age adults with back pain	Intervention targeted to psychological factors and/or included a psychological component	Not specified, e.g., natural course	Reduction in pain, disability, or psychological symptoms
Social and environmental	Working-age adults with back pain, other painful MSK disorder, and/or social factors associated with LBP chronicity	Intervention targeted to social or environmental factors	Not specified, e.g., natural course	Reduction in pain or disability
Lifestyle and personal	Working-age adults with back pain, other painful MSK disorder, or lifestyle factors associated with LBP chronicity	Intervention targeted to lifestyle or personal factors	Not specified, e.g., natural course	Reduction in pain, disability or outcome on the lifestyle/personal factor

4.2.2 Population data (II, III, IV)

The population data were collected from Tampere University Hospital, Finland between October 2019 and February 2021. The main complaint of the study population was chronic non-specific LBP. Chronic LBP was defined as pain in the anatomical region between the costal margins and the inferior gluteal folds, with or without radicular pain, lasting for 3 months or longer. The medical forms of the patients visiting the Physiatry Outpatient Clinic were collected in order to find suitable patients for data collection. The medical forms were used to examine the inclusion and exclusion criteria and to collect quantitative data from the study population. The EHR of the included patients were read to make sure the inclusion criteria were still met (see table 5). Finally, the free text of the physician's notes from the EHR concerning the patients' visit to the Physiatry Outpatient Clinic was collected and stored in the Hospital's own secure cloud storage system (Lokero).

Tampere University Hospital was the data controller. Further, a written permission and data transfer contract was signed between the author, Headai Ltd, and Tampere University Hospital. Since the study was registry-based and the integrity of the patients was maintained throughout, review by a formal ethics committee and informed written consent from the patients were not required. Furthermore, the legislation for the secondary use of social and health information (552/2019) was applied.

Table 5. Inclusion and exclusion criteria for the study population. SBT= Start Back Tool, VAS= Visual Analog Scale.

Inclusion criteria
Age 18 to 65 years
LBP symptoms ≥ 3 months
SBT questionnaire completed
Pain chart completed
Social security number available
VAS ≥ 3
Exclusion criteria
Malignancy
Recent traumatic fracture to the pain region
Osteoporotic fracture
Infection (i.e., epidural abscess)
Ankylosing spondylitis
Modic 1 changes
Unstable spondylolisthesis
Anomaly of the bone in the pain region
Severe scoliosis (>45°)
A nerve root disorder with apparent dermatomal and/or myotomal radiculopathy (pain, numbness, paresthesia, tingling, muscle weakness)
Any other obvious specific reason for LBP

In total, the medical forms of 1569 patients were screened to obtain a study population that fulfilled the criteria. A study population comprising 93 patients was gathered to investigate the difficulties in the functioning of chronic non-specific LBP patients. Figure 7 presents the flow chart of the study population selection.

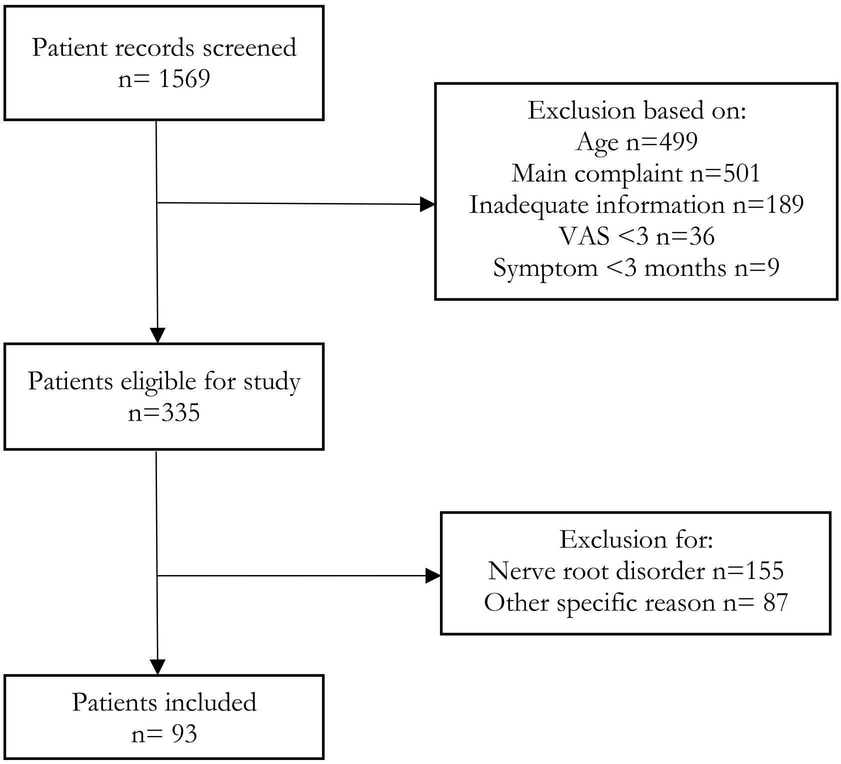

Figure 7. Flow chart of the study population selection. VAS= Visual analog scale.

4.2.3 Multidisciplinary team (III)

In study III, a multidisciplinary team was formed to design the rehabilitation processes. To be included, the health care professional had to have extensive knowledge of treating patients with LBP. In addition, at least several years of work experience and the will and vision to advance the management of patients with LBP in their working environment were also needed. Considering the theoretical, biopsychosocial background of the design, it was necessary to have professionals who represented different aspects of the approach, including physicians, physiotherapists, mental health physiotherapists, nurses, psychologists, social workers, and rehabilitation counselors.[174]

4.3 Measurements

The main topic of interest in the population data was retrieval of the ICF codes and disability information from the free text of the EHR. All the domains (body functions, body structures, activity and participation, and environmental factors) were retrieved from the free texts collected from the EHR in a manner described in more detail in section 4.4.2.

Other variables collected from the study population were in the form of quantitative data in the medical forms. These included demographic data (age, sex), other diseases, information on pain intensity (VAS[175] in rest and in motion) and duration, use of pain medication, SBT[92] scores, information on sick leave, the self-reported work ability in 2 years, and information on previous physiotherapy, institutional rehabilitation, or imaging studies. Since the medical forms included no disability questionnaire, the SBT questions concerning daily functioning (question 3: I have walked only short distances because of my back pain, and question 4: In the last two weeks, I have dressed more slowly than usual because of back pain) were removed for a separate inspection in addition to questions 5-9 concerning the psychosocial factors.[168]

4.4 Analysis

4.4.1 Literature material (I, III)

In the systematic review[14], study quality was assessed using the National Institute of Health's (NIH) study assessment tool[176]. Two independent reviewers evaluated all the included articles according to the assessment tool criteria. The methodological quality criteria included elements from the study population, measured exposures, measured outcomes, and study characteristics. If the ratings differed, the reviewers discussed the article to reach consensus. If consensus was not achieved, a third reviewer was consulted. Each study was judged as good, fair, or poor by evaluating the potential risk of bias resulting from the existing flaws. The prognostic factors described in the chosen articles were categorized according to the biopsychosocial framework into subsections. Additionally, the previous systematic reviews[49,167] were studied to direct the contents of the subsections. In study III, the literature review was used as a scientifical background for the multidisciplinary teamwork and the applicability to the designed process was discussed in the teams.

4.4.2 Population data (II, III, IV)

For studies II and IV, the free texts of the population data were annotated to the ICF codes. The linking of the ICF to the EHR applied the principals of the proposed ICF linking rules[177]. In study II[178], the author acted as a domain expert and analyzed the longitudinal free text datasets of five patients to compare the matching done by the expert to the semantic matching done by the algorithm. The codes and the free text in question were listed as the annotation proceeded so that similar settings would be coded iteratively. In study IV[168], a random data sample of the EHR notes of 20 patients was selected to form a training data set for Headai Graphmind. The annotation proceeded in a similar fashion as in study II. Additionally, the results of Headai Graphmind were analyzed using another random sample of 20 patients. Once again, the author annotated the free texts to the ICF codes, which were then compared with the algorithm's results. Both random samples were obtained by computer aided randomization. The quantitative findings of the annotations and the algorithm's matching were synthetized to gain understanding of the factors found and the reliability of the algorithm on the semantic matching. In study III, the disability information retrieved from the EHR was used to understand the disabilities patients with LBP face. Additionally, when designing the different intervention processes (biomechanical, social, psychological, and lifestyle factors) the outcomes were targeted to provide solutions to the difficulties identified from the population data.

4.4.3 Algorithm (II, IV)

At the heart of Headai Graphmind technology is a general language model which has a pre-trained semantic understanding of language. The model is based on gigabytes of generic data taken from research and policy papers, labor market information, and professional news.[168] This semantic network of language is based on a self-organizing map (SOM) type of unsupervised machine learning[170]. Graphmind adds, modifies, and reasons according to conceptual learning theories[179]. By processing the natural language of the training data, Graphmind learns what words are meaningful, when the words form a compound word (also called n-grams in linguistics), what is the relation between them, and eventually the context where the words and n-grams are used. In our studies, Graphmind turned EHR notes into similar semantic networks as the pre-trained language model (figure 8).

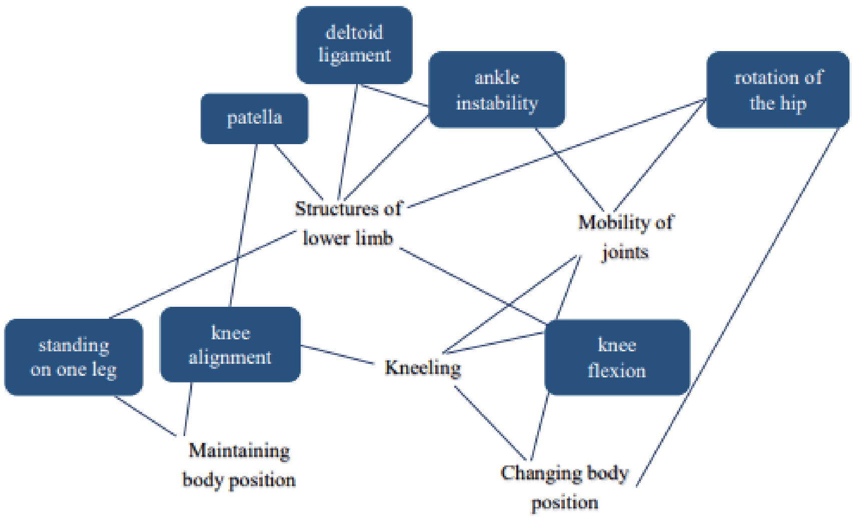

Figure 8. Simplified example of the semantic network model of EHR notes made by Graphmind. Preprint from study IV.

Thereafter, it started to fit the ICF descriptions to the model and used the general language model to understand the particles of the data better, e.g., synonyms, neighboring concepts, and so forth. Each patient's semantic network is analyzed against each ICF definition (1610 codes) separately with the chosen setups (described below). This resulted in, for example, 36 000 analyses per patient in study IV. The architecture of the algorithm is illustrated in more detail in figure 9.

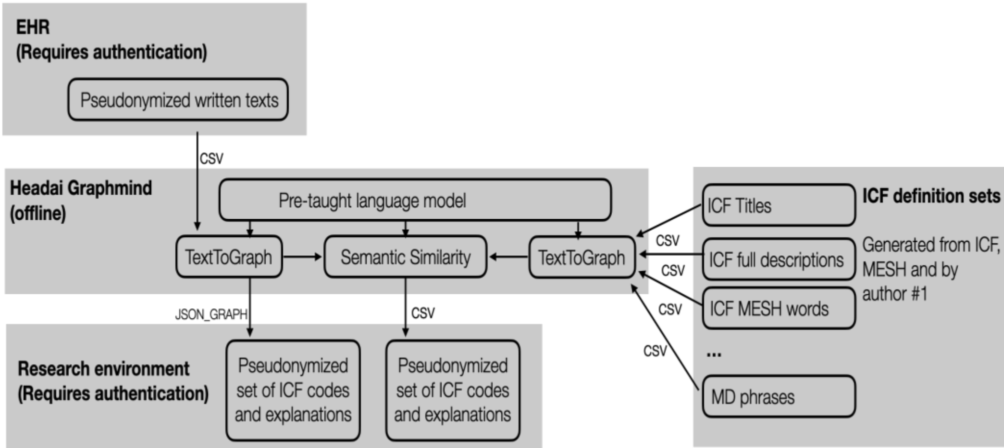

Figure 9. The data architecture of the algorithm. EHR= Electronic health record, MESH= Medical subject heading, MD= Medical doctor. Preprint from study IV[168].

Because Graphmind uses shallow neural networks, the analysis of the data of one patient takes about 2-10 seconds on a CPU (central processing unit) core, depending on the data volume and complexity.[168]

In study II, the purpose was to test different setups for the algorithm-ontology configuration in order to find the most functional setups for the proceeding studies (called ICF definition sets in figure 8). These setups and their explanations are presented in table 6.

In study IV, the setups used for the algorithm-ontology configuration were the "ICF title" and "ICF real life", with the extension of fuzzy logic. The "ICF Real life" input was extended from study II using the random data sample of 20 patients (described in the previous section). In addition, MeSH (Medical Subject Heading) was still carried out as an option for the analysis. However, since it proved to be too vague, it was not used for further analysis by the domain expert.

Table 6. The setups used for the algorithm-ontology configuration in study II. (Reprinted with permission). MeSH= Medical subject headings, ME= Medical expert.

Setup abbreviation	Setup name	Explanation of the input/algorithm-ontology configuration
a	ICF title	The ontology of the ICF (title level)
b	ICF title fuzzy	The ontology of the ICF (title level) analyzed with fuzzy logic
c	ICF description	The ontology of the ICF (description level)
d	ICF description fuzzy	The ontology of the ICF (description level) analyzed with fuzzy logic
e	ICF real life	The ontology of the ICF was extended with the language used by physicians from ME point of view, e.g., b1342 onset of sleep= to fall asleep
f	ICF real life fuzzy	The ontology of the ICF was extended with the language used by physicians from ME point of view, and analyzed with fuzzy logic
g	MeSH-ICF	The ontology of the ICF (title level) was extended with MeSH vocabulary
h	MeSH-ICF fuzzy	The ontology of the ICF (title level) was extended with MeSH vocabulary, and analyzed with fuzzy logic
i	MeSH-ICF description	The ontology of the ICF (description level) was extended with MeSH vocabulary
j	MeSH-ICF description fuzzy	The ontology of the ICF (description level) was extended with MeSH vocabulary, and analyzed with fuzzy logic
k	MeSH-ICF real life	Setup e. was further extended with MeSH vocabulary
l	MeSH-ICF real life fuzzy	Setup e. was further extended with MeSH vocabulary, and analyzed with fuzzy logic

The results of the algorithm were analyzed by comparing the retrieved codes to the codes found by the domain expert. A code was defined as a correct finding (true positive) if the algorithm found the same code from the free text of one patient as the domain expert. False positives (in study II stated as “found something”) were the codes that the domain expert did not find and, after reappraisal, were still regarded as false findings. Codes were defined as false negatives or not found if a code was found by the domain expert but not by the algorithm. Additionally, some codes were found first by the algorithm and, after reappraisal, were found by the domain expert as well (algorithm found better than expert).

4.5 Ethical considerations

The Helsinki declaration and Finnish legislation were followed during the individual studies. Since the integrity of patients was preserved and the study was registry-based, the Ethical Board of Tampere University Hospital waived the need for their consent or written informed consent from the patients. Additionally, the Finnish legislation on the secondary use of social and health care data allowed the use of the EHR data for research purposes, although it was originally stored for the purposes of health care activities[180]. The data were utilized within the research group following the data protection rules of the European Union and Finland and the guidelines for the responsible conduct of research issued by the Finnish National Board on Research Integrity (TENK)[181].

The data architecture of the AI algorithm, Headai Graphmind, was built to meet high data and security requirements. The data was transferred to Graphmind as a pseudonymized encrypted csv. file on a memory stick. All the matching analyses performed by Graphmind were run in off-line mode. The anonymized results were then transferred to the research environment with authenticated network access.[168]

The developed AI solutions can be seen as an enabler of faster and more tailored clinical and system level decision-making, leaving the decision-making to health care professionals and policymakers. Likewise, the developed rehabilitation process acts as an enabler to make more tailored decisions in mutual agreement with the patient.

Shared decision-making with the stakeholders and end-users during the planning and design phase is essential, since it has profound effects on the quality of health care through the person-centered approach[182]. Patients were considered during the design of both methods to enhance the decision-making processes. In study II, the shift from health care professional driven planning to the reciprocal roles of the individual, the professional, and the algorithm was described. Additionally, in study III, the design phase was introduced to the LBP patient forum (experts by experience) for feedback and refinement of the design before designing the pilot intervention study.

5 SUMMARY OF THE RESULTS

5.1 Systematic review (I)

5.1.1 Studies included in the systematic review

From the 2038 studies identified, 25 studies were included in the systematic review. When comparing the included articles to previous systematic reviews on the subject[49,167], 68% (17) of the included studies were published in 2010 or thereafter[183–199].

According to the National Institute of Health's assessment tool[176] the methodological quality of the studies was as follows: one study was rated good quality[200], 19 studies were rated fair quality[183–191,195,196,198,199,201–206], and five were rated poor quality[192,193,197,207,208]. The main reasons to exclude the articles were differing definitions of chronic pain, and the study population being chronic at baseline. In some articles, the baseline information was inadequate regarding the duration of pain.

5.1.2 Prognostic factors for pain chronicity in low back pain

In total, 80 prognostic factors were found from the 25 articles, and 45 of those were regarded as statistically significant.

The personal factors and medical history factors that were most studied were body weight, female sex, and age. Higher body weight and female sex were regarded as risk factors, whereas the evidence about age was inconsistent (age was found to be both a risk factor and a protective factor). Other statistically significant factors that were studied in more than one article included smoking or nicotine dependence and a previous episode of LBP. According to two studies, higher blood pressure was a protective factor[190,200].

The symptom characteristics that were seen as statistically significant risk factors were higher pain intensity and longer duration, pain radiating to the upper back, pain worse on standing, and higher disability or functional limitation.

The biomechanical factors that were statistically significant were strongly associated with physical work characteristics. The risk factors recognized by more than one article were particularly physical work, difficult working positions, and carrying heavy loads or lifting at work. Other significant factors were self-reported work-related back pain, physical intensity of work being vigorous and/or moderate, and vibrations or jolts at work.

Many of the psychological and psychosocial factors were comparable with the findings of the previous systematic review[49]. The most studied significant factors were depression, general anxiety, somatization, and perceived risk of persistence. Furthermore, post-traumatic stress disorder or any other psychiatric diagnosis, catastrophizing, perceived stress, low tolerance of pain, coping by ignoring pain, and non-recognition of work were risk factors for pain chronicity. Support at work, good quality of life, and coping by listening to music or watching television were recognized as protective factors. All the found factors are listed in table 7.

Table 7. Prognostic factors for pain chronicity in low back pain. HDL= high-density lipoproteins, MCV= motor vehicle collision. Categorical variable measured yes/no or in larger categories; continuous variable measured by continuous scale. Risk=statistically significant risk factor, protective=statistically significant protective factor, NS= not significant statistically, IE= inconclusive evidence.

Category	Prognostic factor	Categorical (1) or continuous variable (2)	Predictive value overall	Study quality (n)		
				Good	Fair	Poor
Personal factors and medical history	Age	1,2	IE		7	1
	Female gender	1	Risk		5	1
	Body weight	1,2	Risk		7	
	Body height	1	Risk		1	
	Body measures	1	Risk		1	
	Diabetes	1	Risk		1	
	Rheumatological event ≥1	1	Risk		1	
	Blood pressure	1	Protective	1	1	
	Pulse pressure	1	Protective		1	
	High cholesterol	1	NS		1	
	High HDL cholesterol	1	NS		1	
	High triglycerides	1	NS		1	

	Smoking, nicotine dependence	1	Risk		4	
	Alcohol dependence	1	NS		1	
	Psychoactive substance dependence	1	NS		1	
	Previous back surgery	1	NS		1	
	Previous episode of LBP	1	Risk		1	1
	Low back injured in MVC	1	Risk		1	
	Baseline disability prior to LBP	2	Risk		2	
	Baseline general health poor	2	Risk		1	
	Physical well-being	1	Protective		2	
	Physical exercise	1	Protective		5	1
	Level of education	1	NS			2
	Former productivity-related income	1	Risk		1	
	Disability compensation	1	Risk		2	1
	Occupational status	1	NS		2	1
	Number of different jobs held	1	Protective		1	
	Back pain in parents	1	NS			1
Symptom characteristics	Pain intensity	1,2	Risk		4	1
	Pain duration	1	Risk		3	1
	Pain radiation	1	NS		2	
	leg pain		NS		1	1
	to upper back		Risk			1
	multiple pain sites		NS		1	
	Pain requiring medication	1	NS		2	1
	Days of reduced activity due to LBP	1	Protective		1	
	Affective pain	1	NS		1	
	Pain interfering sleeping	1	NS			1
	Pain worse on standing	1	Risk			1
	Pain worse on lying	1	NS			1
	Disability and functional limitation	1,2	Risk		4	3
Biomechanical factors	Spinal mechanical load	2	NS		1	
	Work-related back pain	1	Risk			1
	Particularly physical work	1	Risk		2	1
	Physical intensity of work	1				
	moderate or vigorous		Risk			1
	vigorous only		Risk			1
	Frequent rest breaks from work	1	NS		1	
	Difficult working positions	1	Risk		2	2
	Repetitive short movements	1	NS			1
	Carrying heavy loads/lifting at work	1	Risk		3	2
	Arms elevated at work	1	NS			1

	Bending and twisting trunk	1	NS			1
	Working kneeled/squatted	1	NS			1
	Vibration and jolts at work	1	Risk		1	1
	Working with animals	1	NS			1
	Working while tired	1	NS			1
Psychological and psychosocial factors	Good quality of life	1	Protective		1	
	Mental well-being	1	NS		1	
	Depression	1,2	Risk		5	1
	General anxiety	1	Risk		2	1
	Post-traumatic stress disorder	1	Risk		1	
	Antisocial personality disorder	1	NS		1	
	Any psychiatric diagnosis	1	Risk		1	
	Somatization	1	Risk		1	1
	Fear avoidance	1				
	in general		NS		1	
	of work activity		NS		1	1
	of physical activity		NS		1	1
	Perceived risk of persistence	1	Risk		1	1
	Catastrophizing	1	Risk		1	1
	Perceived stress	1	Risk			1
	Low tolerance of pain	1	Risk		1	1
	Coping by ignoring pain	1	Risk			1
	Coping by music or tv watching	1	Protective			1
	Non-recognition of work	1	Risk		1	
	Job satisfaction/control	1	NS		1	
	Work absenteeism	1	NS		1	
	Support at work	1	Protective		2	1
	Support at home		NS		1	
	High psychological job demands	1	NS		4	
	Difficulty communicating	1	NS		1	

5.2 Population data (II, III, IV)

The population data formed the basis for the development of the AI algorithm application and were also used in the development of the rehabilitation process. A study population of 93 patients with chronic non-specific LBP were collected in a manner described in the Methods section. Population characteristics were collected from the medical forms (table 8). The majority of the population were females (n=63, 68%) with a mean age of 45 years. Over a third of the population had had LBP for over 10 years (n=33, 36%), and another third for between 1 and 5 years (n=32, 34%).

Table 8. Population characteristics. BMI= Body Mass Index, NSAID= non-steroid anti-inflammatory drug, VAS= Visual Analog Scale, SBT= STarT Back Tool. SBT Q3= I have walked only short distances because of my back pain, Q4=In the last two weeks, I have dressed more slowly than usual because of my back pain. Preprint from study IV[168]

Variable	Population (n=93)
Male (n/%)	30/32%
Age (mean)	45 years (95% CI ±2 years)
BMI (mean)	28.3 (95% CI ± 2,7)
Duration of LBP (n/%)	
3-6 months	6/6%
6-12 months	14/15%
1-2 years	15/16%
2-5 years	17/18%
5-10 years	8/9%
>10 years	33/36%
On pain medication (n/%)	86/92%
NSAID	69/74%
Paracetamol	42/45%
Opiate	30/32%
Neuropathic pain medication	25/27%
VAS in motion (mean)	6.3 (95% CI ±0.6)
VAS in rest (mean)	5.5 (95% CI ±0.5)
SBT score	
total score (mean)	7 (95% CI ± 0.3)
sub score Q5-9 (mean)	4 (95% CI ±0.2)
Yes to Q3	64/69%
Yes to Q4	51/55%
On sick leave due to LBP	61/66%
less than 30 days	11/18%
1-3 months	24/39%
4-6 months	5/8%
over 6 months	17/28%
N/A	4/7%
"I can work in the same profession in 2 years' time despite my health"	
Most definitely	13/14%
I'm not sure	42/45%
Probably not	31/33%
N/A	7/8%
Has had physiotherapy	76/82%
Has been in institutional rehabilitation	15/16%
Has had imaging studies done	83/89%

Almost every patient was on pain medication during the outpatient visit (n=86, 92%). When asked about future work ability, a third of patients thought they probably could not work in the same profession after 2 years (n=31, 33%). More patients had their imaging studies done than had received physiotherapy (n=83, 89%; n=76, 82%, respectively). According to SBT scoring, the patient population would be regarded as a high-risk group, since the total score was over 4 and the sub score (questions 5 -9) was 4[92]. The information on patients' functioning was extracted from the EHR in the manner described in section 4.4.2. The ICF core set of the population (table 9) differed minimally from the ICF core set described by the WHO[209]. The words or phrases related to occupational factors and the ones related

Table 9. ICF core set of the evaluation dataset (20 patients). The domains are presented in the chapter level. The numbers in brackets represent the number of findings. Preprint from study IV[168]

Body	
Function	Structure
Sensory functions and pain (366) Neuromusculoskeletal and movement related functions (349) Mental functions (99) Functions of the digestive, metabolic, and endocrine systems (62) Genitourinary and reproductive functions (12) Functions of the cardiovascular, hematological, immunological, and respiratory systems (8)	Structures related to movement (1364) Structures of the nervous system (73) Structures related to the digestive, metabolic, and endocrine systems (7)
Activities and participation	
Mobility (310) Community, social, and civic life (103) Major life areas (89) Self-care (44) Domestic life (16) Interpersonal interactions and relationships (7)	
Environmental factors	
Services, systems, and policies (298) Products and technology (253) Support and relationship (137) Natural environment and man-made changes to the environment (4)	

to mood were the most difficult to annotate, since there are overlapping ICF domains in those areas (occupational factors: d845 Acquiring, keeping and terminating a job, d850 Remunerative employment, d859 Work and employment, other specified and unspecified; mood related factors: b126 Temperament and personality functions, b152 Emotional functions).

5.3 Development of the AI application (II, IV)

5.3.1 Analysis of the algorithm

The algorithm's ability to analyze free text from the EHR and match the text to the ICF codes was compared and evaluated to the domain experts' findings, which were regarded as the gold standard.

In study II, the dataset of five patients consisted of 15 EHR notes. The free text included referrals, physical appointments, contacts by phone call and by letter. In total, the algorithm found 182 ICF codes from the dataset, whereas the domain expert (referred in study II as the medical expert, ME) found 173 codes. The algorithm and ME agreed in 56% of the codes. The main results of study II are presented in table 10.

Table 10. The results of study II. Body structures and functions (b and d codes) are combined. (Reprinted with permission)

<table>
<tr><td rowspan="3">ICF DOMAINS (N=355)</td><td colspan="7">FINDINGS OF HEADAI GRAPHMIND (HGM) AND THE MEDICAL EXPERT (ME)</td></tr>
<tr><td colspan="2">(1) Graphmind found the same as ME</td><td colspan="2">(2) Graphmind found something</td><td colspan="2">(3) Graphmind found better</td><td>Total</td></tr>
<tr><td>ME n (%)</td><td>HGM n (%)</td><td>ME n (%)</td><td>HGM n (%)</td><td>ME n (%)</td><td>HGM n (%)</td><td>n (%)</td></tr>
<tr><td>Body structures and functions*</td><td>106 (29.9)</td><td>72 (20.3)</td><td rowspan="3">N/A</td><td>34 (9.6)</td><td rowspan="3">N/A</td><td>10 (2.8)</td><td>222 (62.5)</td></tr>
<tr><td>Activity/ participation</td><td>46 (13.0)</td><td>9 (2.5)</td><td>14 (3.9)</td><td>9 (2.5)</td><td>78 (22.0)</td></tr>
<tr><td>Environmental factors</td><td>21 (5.9)</td><td>16 (4.5)</td><td>13 (3.7)</td><td>5 (1.4)</td><td>55 (15.5)</td></tr>
<tr><td>Total</td><td>173 (48.7)</td><td>97 (27.3)</td><td></td><td>61 (17.2)</td><td></td><td>24 (6.8)</td><td>355 (100)</td></tr>
</table>

The environmental factor domains were the most accurate, with agreement found in 76% of the codes, and the poorest in activity and participation, where the findings were in agreement in 20% of the codes. In table 10, the second column presents those findings (61 codes in total) that could not be interpreted as correct findings after several reappraisals. The algorithm also found correct codes that the ME did not. A total of 24 codes were regarded as correct findings after reappraisal. These cases can be explained by human error and more accurate interpretations of the text.

The main results of the study IV are presented in table 11. In this study, the algorithm reached a sensitivity of 83.1% (95% CI 79.9-86.3). The sensitivity was the highest in both environmental factors (E codes) and body structures (S codes, 85.2%) and the lowest in activity and participation (D codes, 77.7%). The specificity of the algorithm reached 99.84% (99.80-99.89), being the lowest in the body functions (B codes, 99.74%) and the highest in body structures (99.95%). When comparing the content of the codes, the domain expert found 119 distinct codes (30 s codes, 35 b codes, 40 d codes, and 14 e codes) from the evaluation dataset, whereas the algorithm found 112 codes (30 s codes, 35 b codes, 35 d codes, and 12 e codes).

Table 11. The results of the factor recognition. Preprint from study IV[168]

	S	B	D	E	TOTAL
Expert found	423	311	226	112	1072
Algorithm found					
Codes in total	371	312	208	100	991
True positives	368	285	195	94	942
False positives	3	27	13	6	49
False negatives	63	53	55	20	191
Codes better than expert	4	14	12	1	31
Correct codes in total	427	325	238	113	1103
Sensitivity % (95% CI)	85.2% (82.3-88.0)	84.4% (80.9-87.8)	77.7% (71.7-83.8)	85.2% (76.0-94.4)	83.1% (79.9-86.3)
Specificity % (95% CI)	99.95% (99.90-100)	99.74% (99.65-99.82)	99.86% (99.80-99.92)	99.89% (99.81-99.97)	99.84% (99.80-99.89)

5.4 Development of the rehabilitation process (III)

The multidisciplinary team worked via remote meetings following the phases of the design described in table 3. The systematic review (Study I) worked as a basis for problem identification, and the team discussed those risk factors that in their opinion play a crucial role in pain chronification. Additionally, the timing of risk factor identification was discussed and the patient's pathway towards the rehabilitation process was identified (illustrated in figure 10).

A literature review on the previous studies, including interventions concerning the identified risk factors for LBP chronicity, was conducted using the PICO search strategy (table 4). The findings of the review were used as a background for the intervention design. The review included the Finnish National Current Care Guideline for treating LBP[23], previous systematic reviews considering the prolongation of pain and disability[210,211], an article explaining the development of chronic pain[56], the reviews used to support the development of the national public rehabilitation guidelines organized by the Social Insurance Institution of Finland[212,213], and the Cochrane review on multidisciplinary biopsychosocial rehabilitation[4]. Additionally, 26 previous interventions[70,92,103,104,214–235] were studied to evaluate their applicability to the designed rehabilitation process (appendix of study III).

The psychological theories of health behavior were examined in terms of the desired change that the intervention would produce. The theory of planned behavior, social-cognitive theory, and self-regulation theories[236] were found suitable to support the theoretical background for those techniques already used in the daily workflow. The following health behavior techniques were regarded as applicable:

1. Goals should be timely, realistic, concrete, with graded tasks, and meet with the recipient's resources.
2. Provider's support, monitoring and feedback are important, concrete exercises with the provider.
3. Activities should be planned beforehand (what, where, when, how, and with whom).
4. Positive beliefs and self-efficacy should be amplified, discrepant views should be confronted.
5. Motivation and positive changes should be amplified from the recipient's perspective, and providers should only support the recipient's own remarks.

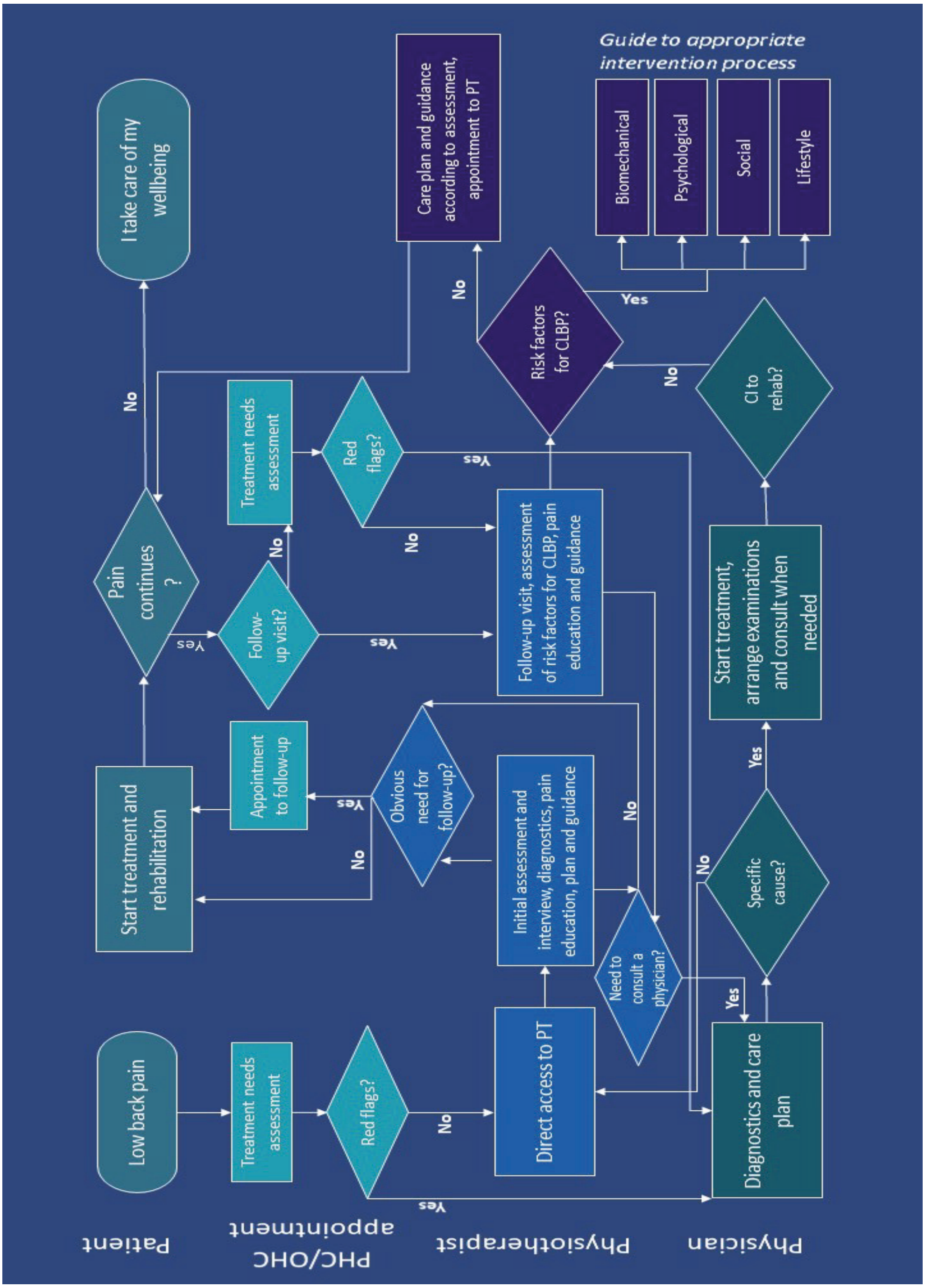

Figure 10. The treatment process of patients with LBP in primary health care (PHC) and occupational health care (OHC) in the Pirkanmaa region.

6. Recipient's limitations and strengths should be recognized and empowering resources cherished.
7. Self-monitoring with the recording of thoughts both verbally and literally should be used to increase cognitive learning.
8. Techniques based on self-belief (mental rehearsal, self-talk) as well as distraction should be used.
9. The social and physical environment should be examined and opportunities for change should be created with the necessary services.
10. Feelings of pain and discomfort should be encountered and normalized.
11. Communality and reward systems should be benefitted.

The target of the intervention was examined through the population data and, more precisely, the ICF core set of the data. The problems in the functioning and health of the chronic LBP population were examined beforehand to reflect the intervention design in addressing the problems. Furthermore, to understand the patient's need for the rehabilitation process, the International Consortium for Health Outcomes Measurement (ICHOM) standard set[237] was examined, as no patients were involved in the design phase.

Since the multidisciplinary team members were currently working in the context where the designed process was supposed to be implemented, the current resources, multidisciplinary collaboration, and weaknesses in the current system were discussed without further examination. The facilitators and barriers to the intervention among the providers and recipients were identified using the experience gained from daily work.

The main result of study III, the design of a new rehabilitation intervention process, was introduced in a logic model (see figure 11). The model gives a graphic presentation of the needed resources, their activities and intended effects, as well as the assumptions and contextual factors where the intervention operates[238].

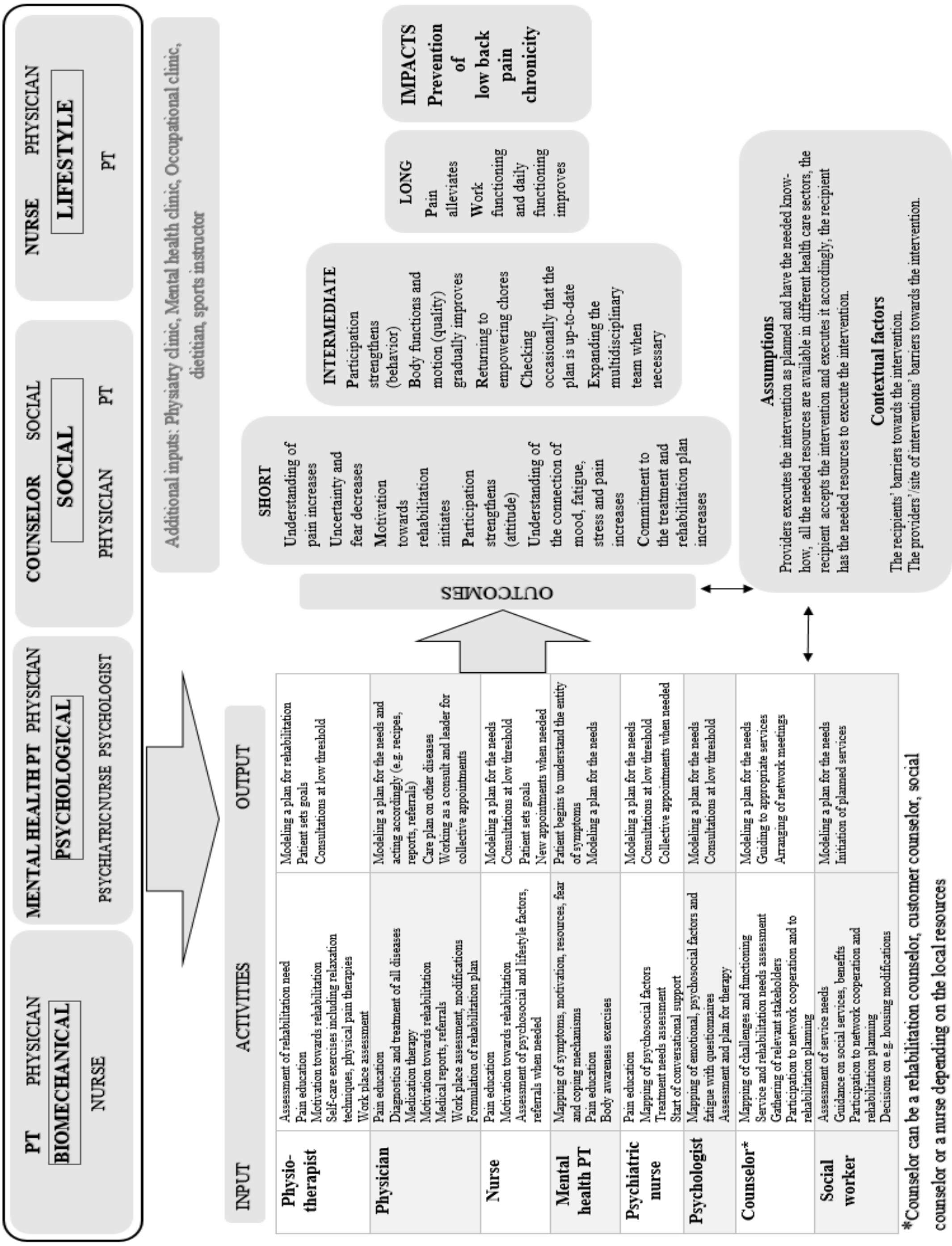

Figure 11. The logic model of the tailored rehabilitation process. (Reprinted with permission)

6 DISCUSSION

The aim of this dissertation was to understand the biopsychosocial factors related to LBP chronicity and to develop new methods for the decision support of tailored biopsychosocial rehabilitation interventions for patients with non-specific LBP. Experts in the field have urged that solutions should be found to meet the challenges associated with the prevention of disabling LBP. This dissertation, therefore, aimed to find solutions to a number of challenges: to develop strategies to ensure early identification of the persistence of LBP, to develop strategies to address modifiable risk factors, to move away from the emphasis on the biomedical model of care, to develop clear care pathways in which the right person is treated in the right way at the right time, and to promote active multidisciplinary rehabilitation to support return to work.[16]

In order to consider all the relevant factors regarding the patients' biopsychosocial functioning and to have a solid basis for the development of the methods, a systematic review was conducted (study I). The new methods for decision support included the application of an AI algorithm to retrieve disability information in the ICF framework from the EHR that could be used for clinical and system-level purposes (studies II, IV). Another method was the design of a tailored biopsychosocial rehabilitation process to be used in primary and occupational care, with the emphasis on early timing (study III).

6.1 Factors associated with low back pain chronicity (I)

To our best knowledge, the previous comprehensive review on the factors associated with LBP chronicity was published in 1997[167], and another review concentrating on psychosocial factors in 2010[49]. Our systematic review (study I) produced a topical summary on the subject. Compared to the previous reviews[49,167], our systematic review presented new factors associated with LBP chronicity. The most evident of these were obesity, smoking, higher pain intensity, and occupational factors, such as difficult working positions, vibrations, and jolts at work. Interestingly, 68% of the chosen articles were published in 2010 or thereafter.

The findings of the review were in line with the factors associated with pain chronicity in general[239]. For example, the protective nature of high blood pressure in LBP chronicity is consistent with theories about hypertension-associated hypoalgesia, where pain sensitivity decreases while blood pressure increases [190]. The phenomenon is not fully understood, but studies suggest an interaction between the cardiovascular and pain regulatory systems, along with a role of baroreceptors and neurotransmitters[200]. Some factors associated with LBP chronicity were, however, missing or understudied. Other possible explanation for the missing information may have been the frames given by inclusion and exclusion criteria. It is suggested that older patients have more chronic pain than younger patients[240], whereas our review found that the evidence about older age being a risk factor for LBP chronicity was inconsistent. Sleeping disorders are related to chronic pain, and the relation seems bidirectional, i.e., poor sleep induces pain and pain induces poor sleep[241]. The same connection has been studied between the intensity of LBP and sleep disturbances[242]. However, our search yielded no results on sleep disturbances being a risk factor for LBP chronicity.

We decided to concentrate our systematic review precisely on the chronicity of pain rather than the chronicity of disability. In LBP and pain in general, these two factors are strongly associated. We found, however, that in studies concerning the chronicity of LBP-induced disability, other factors related to the field of disability were not clearly stated. Disability and functioning are broad entities in LBP, as described by the ICF[243]. Therefore, by concentrating the search on those studies where the main outcome was pain chronicity, we tried to minimize this confounding factor. Interestingly, it was also noted that factors associated with pain chronicity could be widely described using the descriptions included in the ICF.

Another confounding factor is the artificial boundaries of time concerning pain chronicity. It is known from long-term studies, for example, that people with chronic pain can have pain-free periods, periods of continuous mild pain with a low impact, or periods of severe pain with a large impact on their lives[244]. We excluded the articles where the long-standing pain was measured by point prevalence at three months or thereafter. Our view was that the experience of long-standing pain reported by the patient (continuous pain for three months or more), even with variations in the intensity of the pain, is more likely to be persistent pain, with all the typical neurophysiological changes, than pain measured with point prevalence.

The National Institute of Health's (NIH) assessment tool for observational cohort and cross-sectional studies[176] was selected to assess the quality of the included studies. The tool was chosen, as it covered all the article types included in the review, and thus the results of the qualitative assessment were easier to compare. Another widely used assessment tool could also have been chosen, for example, the STROBE checklist for case-control, cohort, and cross-sectional studies[245]. However, we found that the guidance on the chosen tool was clearer, and the division of the questions was also in our opinion more suitable for our requirements.

6.2 Applying the AI algorithm in health care decision support (II, IV)

To facilitate the integration of biopsychosocial assessments and the ICF framework to the current healthcare systems, new tools are needed that fit the clinicians' workflow, help personalize the treatment pathways, and help allocate resources in a more cost-effective way. For the first time, we applied a semantic network-based ML algorithm to retrieve disability information from the EHR texts of patients with LBP in accordance with the ICF framework with convincing results. Previously, similar studies[164,166] using different methods have only been able to match a fraction of the codes compared to the matching abilities of our application (112 codes versus 29 and 9 codes). Since the other studies used different characteristics to describe the results, the sensitivity and specificity of the results are not directly comparable. However, it seems that the algorithm was able to perform conceptual reasoning in challenging domains, without any known procedural rules. It must be noted that the algorithm performed best with the definition sets prepared by the domain expert. Therefore, collaboration between computational, linguistic, and health care expertise will still be needed in future to further develop the algorithm and to make it a more usable interface for health care professionals and policy makers.

The reason we chose Graphmind as the algorithm was solely due to the collaboration opportunity provided. Within the scope of this dissertation, it is not possible to compare whether another method would have produced different results. Usually, the development process of a new working algorithm can take years, and since we were given the opportunity to use an already working algorithm, we were able to overcome many obstacles. Since the algorithm had previously been used for the benefit of technology industries and for educational purposes, there is no baseline with which to compare the results. However, the sensitivity and specificity of the results imply that the chosen algorithm is functionable for the purposes of our studies. Furthermore, as Graphmind uses shallow neural networks, the speed of this technology and the low energy consumption that comes with it (compared to deep learning models), allow repeated, large-scale analyses to be conducted, enabling time series analysis. When it comes to data security issues, the algorithm runs the matching offline, and can be used as a plug-in without needing software integration to the current computing architectures.[168]

The ICF was developed 20 years ago for various purposes, where information on functioning, disability, and health is needed[17]. Due to the complexity of the framework's taxonomy, different tools have been developed to facilitate its use [111,113,243]. However, the implementation of the ICF and its full potential has only been partially achieved. With the developed application of an AI algorithm, information on disability from individuals and communities can be extracted for multiple purposes.

6.3 Development of the tailored rehabilitation process (III)

As previously stated, experts in the field find the present biomedical model insufficient to meet the needs of an ever-growing LBP patient population. There is, therefore, a need for timely, efficient ways to implement the biopsychosocial model, and use the recognized, modifiable risk factors as a basis for treatment and rehabilitation[16]. We developed a tailored biopsychosocial rehabilitation process suitable for primary and occupation health care in the Pirkanmaa Hospital District. The design team included experts from various health care facilities, sectors, and occupational groups. Methodologically, the design followed the MRC complex intervention framework's[171,173] design phase with an enrichment used for the framework's application[172] to increase the value of the intervention.

The MRC framework was chosen for the approach used in the design process for many reasons. For example, it has been developed for complex interventions in healthcare, where the intervention has complex properties[173]. It is both theory and evidence-based, and thus provides a strong scientific background for the intervention[246]. The same framework can be used all the way from the design phase to the implementation evaluation. Furthermore, the framework is widely used and cited for health care interventions[246]. However, the MRC framework was found to lack the details needed in the design phase. Consequently, the enrichment for the design phase was used, and the application proposed by Bleijenberg's research team[172] was found suitable. According to the researchers, studying the implementation context, the providers and the recipients, as well as assessing the likelihood of effectiveness provide valuable information that will help determine whether the intervention is ready to proceed to the next phase. Additionally, following the proposed steps will help optimizing the intervention to be well-adopted, fit for the context, add effectiveness, and be ready for piloting.

There are only a few comprehensive tailored models that consider the holistic perspective when designing treatment and rehabilitation for patients with non-specific LBP. In the Cochrane reviews of multidisciplinary biopsychosocial rehabilitation for subacute[4] and chronic[9] LBP, the tailoring of interventions is scarce. Furthermore, the word biopsychosocial is often misused, since the interventions may only involve a physical exercise program and a work-place assessment. National guidelines, such as the Finnish current care guideline[23] and NICE guideline[71] recommend assessing the patient more comprehensively in the subacute stage using questionnaires (such as SBT[92]), workplace assessments, and so forth. However, the current pathways in primary and occupational care do not support such assessment, and what should be done if modifiable risk factors are found.

In 2017, a Canadian research group published a theoretical model for tailored biopsychosocial rehabilitation with the ICF model used in the assessment[96]. Unfortunately, there are no intervention studies that use this theoretical model to evaluate the feasibility or effectiveness of the model. Although our tailored rehabilitation process used the risk factors identified from the systematic review (study I) and from daily work as the guideline for tailoring instead of the ICF model, the activities of the intervention were allocated to meet the disabilities of real patients with LBP described in the form of the ICF. In this way, the designed rehabilitation process would more accurately meet the needs of actual patients. It should be noted, however, that the data used concern patients with chronic LBP, and the needs might, therefore, be different in the subacute stage. Thus, this topic needs further investigation in the form of a feasibility study.

6.4 Strengths and limitations

All the studies included in this thesis followed the guidelines for the responsible conduct of research by the Finnish National Board on Research Integrity (TENK)[181]. Two new methods were developed: an AI algorithm application with convincing sensitivity and specificity, and a rehabilitation process with solid methodological quality resulting from the use of a high-quality framework and top health care professionals.

The applied AI algorithm is, to our best knowledge, the first attempt to automatize the harnessing of disability information in the Finnish language from the EHR. Moreover, the algorithm has shown the most promising results when compared to other algorithms used in similar settings[163,164,166].

The use of a complex intervention framework means the designed rehabilitation process has an advantage over previously published LBP interventions, since the use of the framework helps the interventions to be more acceptable, implementable, cost effective, scalable, and transferable across contexts[173]. Additionally, the described process provides an example of how clinical pathways in other patient groups could be updated in future to increase their effectiveness.

There were some limitations regarding the studies that should be mentioned. First, the systematic review had several limitations: according to the quality assessment, only one high-quality study was found. The main reason for a study to be regarded as fair quality instead of high quality was the loss of patient population during the follow-up (greater than 20%). A further limitation was the use of valid questionnaires for the outcome. Pain as an outcome is hard to validate, since it is always self-reported. Many studies have tried to minimize this bias by using validated questionnaires. The scarcity of high-quality studies can be also due to the chosen assessment tool and the parameters used for making judgements.

Second, nine of the studies used the same population (HUNT studies). However, in our opinion, the risk of bias from the studies can be regarded as low, since both the sample size and follow-up time in these studies were large. The Nord-Trøndelag Health Studies (HUNT studies) were population-based health surveys conducted in the years 1984 to 1986, 1995 to 1997, and 2006 to 2008. All legal residents of Trøndelag county in Norway aged 20 years and older were invited to take part in these large surveys.[191]

Third, the systematic review did not comment on the importance of the factors: is one more important than another, or does a combination of factors pose a bigger risk than one sole risk? Another methodological approach would be needed to explore this subject in more detail.

In the preliminary (study II) and feasibility studies (study IV) of the development of the AI algorithm application, the data used posed some limitations. The EHR data consisted of only physicians' notes, and the notes of other relevant health care professionals were absent. Thus, the results can only be generalized to the texts of physicians. The study population was patients with chronic non-specific LBP, which ensured that the texts were rich with varied information about disability. In this way, we were able to develop an application that semantically recognizes and matches the

ICF definitions as widely as possible. However, the results can only be generalized to the LBP patient population, and further annotation is needed to understand disability information in other patient groups. Moreover, the annotation and analysis were done by only one expert (the author), which can be regarded as a limitation as well as a strength. The annotation and the analysis of the algorithm's results proceeded in a homogenous fashion, but other experts could have brought different and perhaps more versatile interpretations of the texts. This would have possibly enhanced the sensitivity and prepared the algorithm to better understand other patient and health care professional groups.

The application of the algorithm was not developed to recognize the ICF qualifiers. However, some ideas on how to detect the qualifiers were considered. The annotation process can be extended to longer phrases (n-grams), so that different nuances of the text can be annotated to the qualifiers. If a visual network is produced for the end-users, they are then able to define the quality of the impairment. Also, the quantitative cumulation of the codes could act as a trigger to define the qualifier. Nonetheless, the application must be tested on the end-users before deciding which idea seems the most suitable for helping in the decision support.

In the design of the tailored rehabilitation process, the team planned where and when the risk factors directing the intervention would be recognized, but not how they would be recognized. There was a discussion whether different questionnaires, such as SBT[92], could be used. Additionally, the team members used the following tools in their daily work: Pain Self-Efficacy Questionnaire (PSEQ)[247], Tampa scale for Kinesiophobia (TSK)[248], Penn State Worry Questionnaire (PSWQ)[249], Generalized Anxiety Disorder Questionnaire (GAD-7)[250], WHO Quality of Life (WHOQOL)[251], and the Beck Depression Inventory (BDI-21)[252]. There are, however, some complications in these questionnaires that need to be discussed. First, they all concentrate on psychological and psychosocial issues and ignore the biomedical and lifestyle-related factors of the biopsychosocial model. Second, they are time consuming. The strength of these questionnaires is that they are validated and have been proven to reflect the patient's current state. In conclusion, the team decided that questionnaires can be beneficial if one is used to working with them. However, there is still a need for further discussion with the patient about their life situation. The team found the developed application of the AI algorithm (studies II, IV) to be a welcomed tool for future clinical use.

Patient involvement is encouraged in the design processes of the interventions. There are several recognized benefits of patient involvement in the design processes that include knowledge of conditions, interventions, and the expanding of perspectives on both sides (the patients and the researchers). Additionally, the resultant study designs are more pragmatic and transparent. Patient involvement may also help in recruitment and funding issues. According to a review of the reviews on the subject, in most studies, patients were asked for feedback rather than actively participating in the design process.[253] Our study was presented to an LBP patient forum (10 experts by experience), where the intervention received mainly positive feedback. The exploitation of current resources on behalf of patients with LBP, the structure of the intervention, and low thresholds between professionals were mentioned as a positive improvement on current practice. As development targets, the education of professionals, especially in patient encounters, the availability of resources in terms of time, and skilled professionals were listed. Since the next step towards an intervention study is the feasibility phase, patient involvement can be augmented to identify weaknesses and barriers to ensure the greater acceptance and effectiveness of the intervention.

As the involved team members were working in the supposed target of the intervention, a larger study on the current context was not conducted. Another reason for not conducting a larger study was that there are currently changes made in the Finnish healthcare system. The public health and social care sector in Finland are currently undergoing reform, and the organization of these services will be transferred from municipalities to wellbeing services counties from 2023[254]. The LBP patients' pathway will be standardized in the wellbeing services county of Pirkanmaa so that the direct access physiotherapist will be the first contact for the patient and physicians will be consulted only when needed. This will open possibilities for the designed process to conduct a large intervention study and, if proved effective, implemented in a catchment population of over 500 000.

6.5 Usefulness of the results and implications for future research

The results of the studies included in this dissertation will be beneficial for all stakeholders who are involved in the treatment and rehabilitation pathways, as caregivers, patients, or policymakers, to enhance the tailored assessment and execution of biopsychosocial rehabilitation in non-specific LBP.

The main purpose of this dissertation was to develop new methods to enhance decision support for tailored biopsychosocial rehabilitation, and trials with prospective data were not conducted due to limited time resources. The results are nonetheless already useful for the scientific community. The developed AI algorithm application is the first developed on such a large scale to obtain disability information from the EHR. Other similar methods[164,166] have not achieved such convincing results when it comes to the number of the ICF codes and contents. The potential benefits of embedding the developed application for tailoring and timing rehabilitation for chronic diseases can produce results in a short period of time. Cost-effectiveness can be achieved in many ways by allocating time and health care professional resources better and by preventing the prolongation of disability. The benefits for the patient are in the tailoring of the rehabilitation and treatments, leading to better quality of life and less disability.[255]

Furthermore, the developed rehabilitation process is one of the few holistic processes developed. It is hoped that other research groups, which are based on similar health care systems, would develop their own local biopsychosocial interventions so that benchmarking analysis would be possible in future.

Since a "wait and see" approach is no longer advisable, and tailored solutions are needed to formulate new strategies to minimize the risk of delayed recovery[16,90], the findings of the systematic review can be helpful for researchers in the planning of future interventions and in clinical use for health care professionals to detect those patients at risk for chronic pain.

For future research, the developed methods open new research opportunities for many studies to come. A feasibility study should be conducted as the next step towards the implementation of the tailored rehabilitation process. The feasibility phase should involve patients to maximize the reception in the patient population and to ensure greater effectiveness. Additionally, economic considerations must be made with a cost-benefit analysis to evaluate the cost-effectiveness of the process. When proceeding to the intervention study, a case-control study is recommended to minimize the confounding factors caused by local phenomena. When proceeding to implementation, a team of professionals must be formed to define the outcome measures of the implementation as well as to continuously develop and monitor the process. At present, there is a lack of information on how well, for example, local guidelines or clinical pathways are implemented. Therefore, it is important to gain such knowledge and to create more concrete ways to ensure the continuity of care for patients with LBP. There are already nominated nurses for patients with asthma and diabetes in Finnish primary care, and similar ways could be implemented in the care pathways of patients with LBP.

When assessing new digital technologies for health care, issues concerning safety, data security, feasibility, clinical evidence, cost-effectiveness, and fluent integration are often mentioned[255]. To implement a new health technology, the technology must go through rigorous assessment. Every country has its own health technology assessment model that systematically evaluates the positive and unintended effects of new technologies[255,256]. In Finland, Finnish Coordinating Center for Health Technology Assessment (FinCCHTA) uses the digi-HTA process (health technology assessment framework for digital healthcare services) to evaluate the feasibility of new technologies in health care. If the technology is classified as a medical device, as the AI application developed here would be, it must fulfill all the requirements of the Medical Device Regulation[255,257].

The challenges of implementing AI in health care include those aspects concerning the data, the target, and the usage environment. The data silos are one obstacle in many health care systems. However, in Finland, the unified patient care records make data standardization possible. By breaking the data silos, AI can be used more efficiently. At present, there are initiatives towards unified health care records in the Nordic countries[151] as well as in the European Union[152]. The AI method applied here is fluent in several languages[168], and future international collaboration is welcome not only for language translations and access to health care records but also for understanding local contextual factors, which can differ between different cultures.

The embedding of AI architecture into current traditional computing architectures requires tools for the transition, which can pose problems regarding data protection[258]. However, the AI method used in this study can work as a plug-in, without needing any integration into the computing architecture, and can thereby bypass the problem[168].

The usage environment, i.e., the health care professionals and the patients, the regulators and policy makers, and hospitals and other health care facilities need to benefit from the implementation with minimum disturbance to the workflow. The health care sector is usually slow in making changes to their ecosystem, and different stakeholders might have totally different interests when embedding new policies[259]. Therefore, national decision-making should encourage the integration of new methods nation-wide instead of making local decisions on solutions that are designed to ease the burden on the economy and patients. Naturally before such decisions, critical assessment on the effectiveness of the methods should be made[255].

The developed methods are most importantly developed with the benefit of individuals in mind. To empower individuals to take action on their own health, they need a broader view of the health challenges as well as their own strengths. The engagement of patients is crucial because without the involvement and trust of the population, these healthcare solutions are useless. The future aim is to have a healthier population with fewer long-term disabilities and, at the same time, to ease pressure on healthcare systems and their budgets.

6.6 Summary of the discussion

The main arguments of this discussion are that the factors affecting the chronicity of low back pain are biopsychosocial. Therefore, as the pathoanatomical mechanisms do not solidly explain non-specific LBP, guidelines and clinical pathways should embed this thinking more strongly in future updates.

The ICF is an important framework in all patient groups, and we need to benefit better from the disability information. The developed application of the AI algorithm can help us to understand the phenomena of diseases and disability more comprehensively. In developing the application, the primary purpose was clinical use, but perhaps an even more higher purpose was to understand the disability of the population better. This would enable us to perform Global Disability Studies in a similar fashion to the Global Disease Studies that have been executed since 1990[260].

The clinical pathways of patients with LBP need reforming so that the right person is treated in the right way at the right time. There are already solutions, knowledge, and expertise available, but they are not being exploited reasonably. The designed tailored rehabilitation process gives an example of how we can meet the challenges that the prolongation of LBP poses.

7 CONCLUSIONS

In conclusion, this dissertation found that the developed AI application is a feasible method for the recognition of the biopsychosocial factors related to non-specific low back pain. Therefore, it has the capability to support the decision-making for tailored rehabilitation solutions. In addition, the developed rehabilitation process can facilitate decision-making for the assessment and execution of tailored biopsychosocial rehabilitation interventions for patients with non-specific low back pain. Finally, this dissertation synthetized the present knowledge of the biopsychosocial factors for pain chronicity in low back pain. With a holistic view on disability, tailored assessments together with other health parameters and patient engagement, there is an opportunity to decrease the economic and physical burden of non-specific low back pain.

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Prognostic factors for pain chronicity in low back pain: a systematic review

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Abstract

Low back pain is the leading cause for years lived in disability. Most people with acute low back pain improve rapidly, but 4% to 25% of patients become chronic. Since the previous systematic reviews on the subject, a large number of new studies have been conducted. The objective of this article was to review the evidence of the prognostic factors behind nonspecific chronic low back pain. A systematic literature search was performed without date limitation from the MEDLINE, Cochrane library, and Medic databases. Specific inclusion criteria were used, and risk factors before the onset of chronic symptoms were searched. Study quality was assessed by 2 independent reviewers. One hundred eleven full articles were read for potential inclusion, and 25 articles met all the inclusion criteria. One study was rated as good quality, 19 studies were rated as fair quality, and 5 articles were rated as poor quality. Higher pain intensity, higher body weight, carrying heavy loads at work, difficult working positions, and depression were the most frequently observed risk factors for chronic low back pain. Maladaptive behavior strategies, general anxiety, functional limitation during the episode, smoking, and particularly physical work were also explicitly predictive of chronicity. According to this systematic review, several prognostic factors from the biomechanical, psychological and psychosocial point of view are significant for chronicity in low back pain.

Keywords: Nonspecific, Low back pain, Risk factors, Prognostic factors, Chronic pain

1. Introduction

Low back pain (LBP) is the leading cause of years lived in disability in high-income and middle-income countries.[39] Moreover, a similar increase has also been seen in low-income countries.[68] In 2015, LBP was responsible for approximately 60.1 million years lived in disabilities, an increase of 54% since 1990.[39] For industrialized countries, LBP is a very costly illness[21,138] and indirect costs (work absenteeism, productivity loss) account for more than half of the total costs.[9] In many patients, the specific nociceptive source of LBP cannot be identified and those affected are often classified as having so-called "nonspecific low back pain."[84] Nonspecific LBP represents 90% to 95% of cases, with other causes being specific spinal pathology (<1% of cases) and radicular syndrome (approximately 5%–10% of cases).[7] The global point prevalence of activity-limiting LBP lasting more than 1 day is estimated to be 12%.[69] Although most patients with acute LBP show rapid improvements in pain and disability within 1 month,[106] between 4% and 25% of patients drift to chronicity.[92] The prevalence of chronic low back pain (CLBP) increases linearly from the third decade of life until the age of 60 years, with CLBP being more prevalent in women.[92]

The prognosis of nonspecific LBP is greatly influenced by factors not related to the spine.[115] In 1987, a biopsychosocial model for understanding LBP was first introduced by George Waddell.[136] The idea behind the model is based on how psychologic and social influences modulate an individual's perception of symptoms. An overemphasis on pain alone and a dependence on only mechanical, nominal diagnosis can lead to more disability. Therefore, when treating patients with LBP, clinicians should consider all aspects (biomechanical, psychological, and psychosocial) of the illness.

To date, few comprehensive reviews have studied the risks of chronicity in patients with LBP. A review by Valat et al. in 1997[133] concluded that CLBP is more closely related to demographic, psychosocial, and occupational factors than to the medical characteristics of the disorder itself. A 2010 systematic review of "yellow flag" risk factors for developing CLBP[15] concluded that maladaptive pain coping behaviors, lower functional impairment at baseline, nonorganic signs referring to somatization, worse general health status before the onset of pain, and the presence of psychiatric comorbidities were significant in terms of chronicity.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Since then, a large number of studies have focused on revealing the risk factors behind this global problem.

The aim of this systematic review is to identify the prognostic factors for pain chronicity in patients with LBP and to provide an update on the existing data.

2. Materials and methods

2.1. Literature search

Systematic literature searches from computerized databases were conducted until March 30, 2020. The search strategy was developed in collaboration with an information specialist. The following databases were searched without any date restriction: MEDLINE (PubMed), Cochrane Database, and Medic specifically for articles in the Finnish language. The primary target of the search was articles concerning predictive risk factors for chronic, nonspecific LBP. The full search strategy is presented in Appendix 1 (available at http://links.lww.com/PR9/A99).

2.2. Study selection and inclusion criteria for selection of studies

The study types included in the literature search were cohort studies, follow-up studies, and reviews. The reviews were used only to search for additional articles to avoid duplication. Randomized controlled trials were not included because the effect of the intervention on the outcome (CLBP) could not be excluded and observing only the group without intervention could create bias. However, studies with interventions could be included if the intervention concerned the whole followed population or its impact could be taken into account in some other way. The references of the studies that met the inclusion criteria were searched for additional articles. There was no time limit for the search. Studies in the English or Finnish languages that focused on working population (aged 18–65 years) were included. If older individuals were recruited, the mean age with SD had to be no more than 65 years. The main outcome was nonspecific CLBP with or without pain radiation, but specific nerve root disorders were excluded. Articles that dealt only with operative treatment were also excluded. Chronic pain is most commonly described as lasting longer than 3 months.[129] Therefore, studies must have assessed the predictive risk factors before that period to be included in the search. A chronic condition was defined as persistent pain in the lower back for a period of 3 months or longer.

2.3. Quality assessment

Study quality was assessed using the National Institute of Health study assessment tool.[94] Two independent reviewers evaluated all the included articles according to assessment tool criteria. If the ratings differed, the reviewers discussed the article in an effort to reach consensus. If consensus was not achieved, a third reviewer was consulted. Each study was judged as good, fair, or poor by evaluating the potential risk of bias resulting from the existing flaws.

3. Results

3.1. Results of the search

A Prisma flow chart of the study selection is presented in **Figure 1**. A total of 2,028 articles were identified. The first exclusion round was based on inappropriate titles or abstracts. We then read the full text of 111 articles, and 25 articles met all the inclusion criteria. Characteristics of the included studies are presented in **Table 1**. Of these 25 articles, 17 68% were published in 2010 or thereafter.[32,56–63,83,88,89,97,99,103,119,122] Two articles were found from the references of included articles.[46,55] The excluded articles and the reasons for exclusion are listed in **Table 2**. Most of the

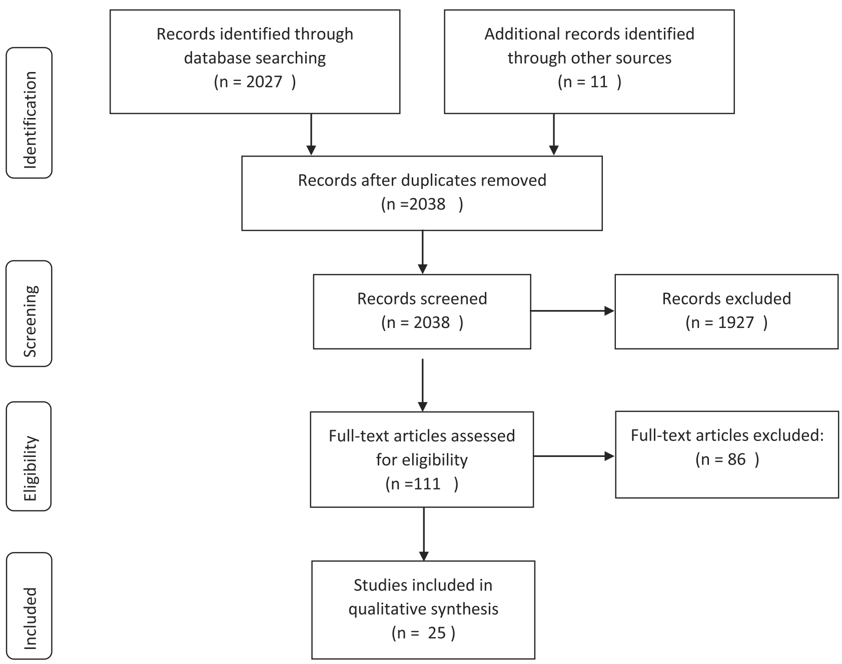

Figure 1. Prisma flow diagram[93] of the study selection process.

Table 1
Characteristics of included studies.

Author, year of publication, country	Study design	Study objective	Follow-up time	Population at follow-up	Inclusion and exclusion criteria	Participant characteristics	Chronic LBP after follow-up	Prognostic risk factors with significant *P*
Bakker et al. 2007,[6] the Netherlands	Prospective inception cohort study	To assess the prognostic value of spinal mechanical load and influence on the course of acute LBP	6 mo	n = 88	Nonspecific LBP less than 6 wk, exclusion: pathologic and sciatica syndrome, not understanding Dutch language, previous episode of LBP in the past 12 mo, significant trauma, pregnancy, and spinal surgery	Age 15–82 y (mean 41, SD 13.5), 56% male, and mean duration of symptoms 11.8 d	n = 53 (60%)	Smoking OR 4.41 95% CI 1.50–12.95, age OR 0.96 95% CI 0.93–0.99
Coste et al. 2003,[18] France	Inception cohort study	To investigate various biologic and psychosocial factors in the natural history of acute LBP	3 mo	n = 111	18 y or older, primary complaint of LBP, and pain duration <72 h without radiation below the gluteal fold. Exclusion: malignancy, infection, spondyloarthropathy, vertebral fracture, neurologic signs, or episode of LBP during the previous 3 mo, illiteracy, or unable to speak French	Age ≥18 y (mean 44.3, SD 13.7), 49% male, and mean duration of symptoms 1.1 d	n = 6 (5%)	Poorer disability at baseline recovery HR 0.97 95% CI 0.93–1.00 (P = 0.05) and poorer general health at baseline recovery HR 0.89 95% CI 0.80–0.99 (P = 0.03)
Coste et al. 1994,[19] France	Inception cohort study	To identify clinical, psychological, and sociodemographic prognostic factors for recovery from acute LBP	3 mo	n = 92	18 y and over, primary complaint back pain, and duration <72 h without radiation below gluteal fold. Exclusion: malignancies, infections, spondyloarthropathies, vertebral fractures, neurological signs, or episode of LBP during the previous 3 mo, illiteracy, or unable to speak French	Age ≥18 y (mean 46.5, SD 14.3), 60% male, and mean duration of symptoms 26 h	n = 2 (1.9%)	Previous chronic episode of LBP HR for recovery 0.21 95% CI 0.07–0.60 (P = 0.0004) and pain worse on standing 0.49 95% CI 0.30–0.77 (P = 0.003)
Esquirol et al. 2016,[32] France	Prospective cohort study (VISAT study)	To determine the impact of a wide range of occupational factors on the incidence and persistence of chronic LBP	5 y	n = 1560	Workers born in 1934, 1944, 1954, and 1964	Age 32–52 y, 52% male	n = 255 (22.6%)	Older age 42 y OR 1.44 95% CI 1.02–2.03 and 52 y 1.46 95% CI 0.99–2.15, history of rheumatological events ≥1 OR 2.34 95% CI 1.69–3.25, former productivity-related income 2.03 95% CI 1.18–3.50, number of different jobs held ≥2 OR 0.70 95% CI 0.51–0.95, carrying heavy loads at work OR 1.54 95% CI 1.09–2.18, and nonrecognition of work OR 1.76 95% CI 1.21–2.56
Hagen et al. 2005,[46] Norway	Public health study (HUNT studies)	To evaluate the relationship between blood pressure and prevalence of chronic MSCs	11 y	n = 46901	All residents of the county 20 y and older	Age ≥20 y	n = 8182 (17.5%)	Higher blood pressure OR 0.7 95%CI 0.6–0.7

(*continued on next page*)

Table 1 (*continued*)

Characteristics of included studies.

Author, year of publication, country	Study design	Study objective	Follow-up time	Population at follow-up	Inclusion and exclusion criteria	Participant characteristics	Chronic LBP after follow-up	Prognostic risk factors with significant *P*
Heneewer et al. 2007,[54] Belgium	Prospective cohort study	To evaluate the association between psychosocial factors and the transition from acute to subacute LBP to chronicity	3 mo	n = 56	New episode of nonspecific LBP less than 12 wk, pain-free period at least 3 mo, age between 21–60 years, and able to understand the Dutch language. Exclusion: suspicion of specific cause, pregnancy, and coexisting major medical disease.	Age (mean) 41.95 y, 61% male, and duration of symptoms <4 wk 52%, 4–6 wk 27%, 7–12 wk 21%	n = 25 (45%)	Higher pain intensity OR 1.787 95% CI 1.677–1.916 (P = 0.002)
Henschke et al. 2008,[55] Australia	Cohort study	To estimate 1-y prognosis and identify prognostic factors in cases of recent-onset LBP managed in primary care	1 y	n = 944	Low back pain 24 hours—2 wk, at least 14 years old, able to speak and read English. Exclusion: serious pathology, radiculopathy	Age (mean) 43.3 y (SD 14.4), 54.8% male, and mean duration of symptoms 4.9 d	n = 388 (41%)	Age recovery HR 0.99 95% CI 0.99–1.00 (P = 0.004), pain intensity recovery HR 0.86 95% CI 0.77–0.96 (P = 0.009), depression recovery HR 0.94 95% CI 0.91–0.97 (P < 0.001), risk of persistence recovery HR 0.92 95% CI 0.89–0.95 (P < 0.001), compensable LBP recovery HR 0.59 95 %CI 0.47–0.74 (P < 0.001), days of reduced activity recovery HR 1.04 95% CI 1.00–1.008 (P = 0.033), and duration of episode recovery HR 0.97 95% CI 0.94–1.0 (P = 0.033)
Herin et al. 2014,[56] France	Longitudinal prospective epidemiological survey (ESTEV)	To assess the impact of work-related factors according to sex on the development of regional and multisite MSP	5 y	n = 12591	Workers born in 1938, 1943, 1948, and 1953, random selection from patients under the supervision of volunteer physicians	Birth year 1938 16.9%, 1943 27%, 1948 28.4%, 1953 27.7%, male 64.8%, BMI ≥25 43.4%, blue collar workers 25.4%, clerks 26.5%	n = 1206 (9.6%)	Forceful effort at work HR 1.20 95% CI 1.01–1.44 men, awkward postures HR 1.19 95% CI 1.01–1.39 men, HR 1.33 95% CI 1.07–1.64 women, and exposure to vibration HR 1.73 95% CI 1.01–3.01 women
Heuch et al. 2019,[57] Norway	Follow-up study (HUNT studies)	To explore the association between diabetes and subsequent risk of chronic LBP	11 y	n = 18972	All residents of the county 20 y and older, study was restricted to respondents aged 30–69 y, and without chronic LBP at baseline and with known information about diabetes	Age 30–69 y	n = 3380 (17.8%)	Diabetes men RR 1.43 CI 95% 1.04–1.96 (P = 0.043)

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Table 1 (*continued*)

Characteristics of included studies.

Author, year of publication, country	Study design	Study objective	Follow-up time	Population at follow-up	Inclusion and exclusion criteria	Participant characteristics	Chronic LBP after follow-up	Prognostic risk factors with significant *P*
Heuch et al. 2017,[58] Norway	Prospective cohort study (HUNT studies)	To study association between physical activity level at work and risk of chronic LBP	11 y	n = 14915	All residents of the county 20 y and older, study was restricted to respondents aged 30–69 y. Study included participants without chronic LBP at baseline, with information about physical activity at work, education, physical activity in leisure time, smoking, and BMI. Exclusion: not employed or did not perform professional work	Age 30–69 y, 49% male	n = 2501 (16.8%)	Particularly strenuous physical work men RR 1.22 95% CI 1.01–1.49 ($P = 0.041$) and work involving walking and heavy lifting women RR 1.21 95% CI 1.06–1.38 ($P = 0.006$))
Heuch et al. 2015a,[59] Norway	Cohort study (HUNT studies)	To compare relationships with LBP for several measures of body size	11 y	n = 25329	All residents of the county 20 y and older, study was restricted to respondents aged 30–69 y, with information whether they suffered from chronic LBP and had measurements of height, weight, waist, and hip	Age 30–69 y, 50% male, and 74% without LBP at baseline	NA	Body weight (kg): RR 1.087 95% CI 1.039–1.138 women ($P < 0.001$), RR 1.091 95% CI 1.030–1.157 men ($P = 0.003$), BMI: RR 1.075 95% CI 1.023–1.128 women ($P = 0.004$), RR 1.091 95% CI 1.027–1.158 men ($P = 0.004$), higher hip and waist circumference; waist RR 1.078 95% CI 1.025–1.134 women ($P = 0.004$), 1.064 95% CI 1.001–1.131 men ($P = 0.05$), hip: RR 1.073 95% CI 1.024–1.123 women ($P = 0.003$), 1.060 95% CI 1.00–1.123 men ($P = 0.05$)
Heuch et al. 2015b,[60] Norway	Prospective cohort study (HUNT studies)	To study associations between body height and chronic LBP	11 y	n = 25329	Cohort of population aged 30–69 y with or without LBP	Age 30–69 y, 45% male, and 74% without LBP at baseline	n = 3230 (17%) of those without chronic LBP at baseline	Women height per 10 cm RR 1.09 95% CI 1.01–1.17 ($P = 0.03$)
Heuch et al. 2014a,[61] Norway	Prospective cohort study (HUNT studies)	To study relation between levels of cholesterol, HDL, and triglycerides to chronic LBP	11 y	n = 25450	Cohort of population aged 30–69 y with or without LBP	Age 30–69 y, 45% male, and 74% without LBP at baseline	n = 3254 (17%) of those without chronic LBP at baseline	All results not significant statistically after complete adjustment for confounding variables

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Table 1 (*continued*)

Characteristics of included studies.

Author, year of publication, country	Study design	Study objective	Follow-up time	Population at follow-up	Inclusion and exclusion criteria	Participant characteristics	Chronic LBP after follow-up	Prognostic risk factors with significant *P*
Heuch et al. 2014b,[62] Norway	Prospective study (HUNT studies)	To investigate associations between blood pressure and chronic LBP	11 y	n = 22949	Cohort of population aged 30–69 y with or without LBP	Age 30–69 y,45% male, and 75% without LBP at baseline	n = 2936 (17%) of those without chronic LBP at baseline	Higher systolic pressure OR 0.95 95% CI 0.92–0.99 women (*P* = 0.005) and pulse pressure OR 0.93 95% CI 0.89–0.98 women (*P* = 0.007)
Heuch et al. 2013,[63] Norway	Prospective cohort study (HUNT studies)	To determine whether elevated BMI increase chronic LBP	11 y	n = 25450	Cohort of population aged 30–69 y with information available on height, weight, and with or without chronic LBP at baseline	Age 30–69 y, 45% male, and 74% without LBP at baseline	n = 3254 (17%) of those without chronic LBP at baseline	BMI ≥30 vs BMI ≤25 OR 1.34 95% CI 1.08–1.67 men (*P* = 0.006), OR 1.22 95% CI 1.03–1.46 women (*P* = 0.008)
Machado et al. 2016,[83] Australia	Case crossover study	To investigate the association of transient exposures to physical and psychosocial activities with the development of nonpersistent and persistent LBP	12 mo	n = 832	Sudden-onset LBP with or without leg pain, preceded by a period of at least 1 mo without LBP. Must comprehend English, presented within 7 d from pain onset, and pain at least moderate intensity. Exclusion: serious spinal pathology	Mean age 45.3 y, 54% male	n = 352 (42.3%)	Moderate or vigorous physical activity OR 2.4 95% CI 1.2–4.8, vigorous only OR 2.8 95% CI 1.0–7.8, manual tasks involving heavy loads OR 8.0 95% CI 2.8–22.6, awkward postures OR 16.0 95% CI 5.0–51.4
Mehling et al. 2015,[88] USA	Prospective cohort study	To investigate the prognosis of acute LBP	2 y	n = 436	Age 18–70, pain less than 1 mo, no other episodes preceded in the past year, speaking English, no red flags, fibromyalgia, chronic pain conditions, disabling psychiatric disease, or prescription for narcotics	Average age 50.5(±12.6) years, 44% male, 61% with a college degree, 59% employed full time, and median duration of pain at baseline 14 d	n = 66 (13%) at 6 months, n = 84 (19%) at 2 y	At 6 mo: perceived risk that pain will persist OR 1.13 95% CI 1.01–1.27, catastrophizing OR 1.12 95% CI 1.01–1.24, coping with pain by ignoring OR 1.11 95% CI 1.01–1.21, coping with TV or music OR 0.90 95% CI 0.82–0.98, pain spreading to the upper back OR 6.06 95% CI 2.98–12.31; at 2 y: perceived stress OR 1.12 95% CI 1.02–1.24, low willingness to tolerate pain OR 1.17 95% CI 1.00–1.36
Melloh et al. 2013,[89] Australia	Inception cohort study	To evaluate risk factors and protective factors of persistent LBP	6 mo	n = 168	Cohort consecutively recruited by health practitioners. Ability to read and write English, 18–65 y. Exclusion: LBP free at baseline, chronic LBP at baseline, specific LBP, osteoarthritis of knee or hip, pregnancy, and age older than 65 y	Mean age 36.0 y (±13.1), 48% male, mean BMI 28 (±6)	n = 38 (23%)	Social support at work OR 0.67 95% CI 0.45–0.99 (*P* = 0.045), somatization OR 1.08 95% CI 1.01–1.15 (*P* = 0.022)

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Table 1 (*continued*)

Characteristics of included studies.

Author, year of publication, country	Study design	Study objective	Follow-up time	Population at follow-up	Inclusion and exclusion criteria	Participant characteristics	Chronic LBP after follow-up	Prognostic risk factors with significant *P*
Nilsen et al. 2011,[97] Norway	Prospective study of longitudinal data (HUNT studies)	To investigate the association between physical exercise, BMI, and risk of chronic MSP	11 y	n = 32417	All residents of the county 20 y or older, patients who participated at baseline and follow-up, had all relevant baseline information available. Exclusion: MSP for 10 y or more, physically impaired at baseline	48% male, mean BMI 24.9 (±27.7)	n = 3314 (10.2%)	Physical exercise ≥2 h/wk RR 0.92 95% CI 0.79–1.07 women (P = 0.02), RR 0.75 95% CI 0.64–0.88 men (P < 0.001), and obesity RR1.21 95% CI 1.04–1.41 women (P < 0.001)
Nolen et al. 2017,[99] Canada	Population-based cohort study	To investigate the association between a lifetime history of LBP injury in a motor vehicle collision and future troublesome LBP	12 mo	n = 509	Saskatchewan residents 20–69 years old with a valid health services card. Age-stratified random sample of 0%. 4% from eligible individuals	Mean age 40,4 y (SD 12.5), 58% male, and history of low back injury 6.1%	n = 45 (at 6 mo, 7.6%) and n = 39 (at 12 mo 7.7%)	History of low back injury in a motor vehicle collision HRR = 2.20, 95% CI 1.04–4.68
van Oostrom et al. 2012,[103] the Netherlands	Prospective cohort study	To explore long-term associations between physical load exposure and chronic LBP	10 y	n = 4378	Inhabitants of Doetinchem, 20–60 y, were examined in population-based study every 5 y for 15 y, this study used population from the second examination onward	Age 25–65 y, 46.6% male, at paid job 61.8%, smokers 31.1%, and BMI ≤25 49.3%	n = 3196–3230 (20%)	Awkward postures OR 2.51 95% CI 1.25–5.07
Poiraudeau et al. 2006,[110] France	Longitudinal descriptive survey	To assess the outcome of subacute LBP, identify characteristics related to outcome of patients and physicians	3 mo	n = 440 (patients). n = 266 (physicians)	Random selection of rheumatologists from national database, each enrolled 1–4 consecutive patients. Exclusion: ≤18 y, had pain less than 4 or more than 12 wk, sciatica, subacute LBP during the past 12 mo, unemployed, pregnancy, infection, tumor, of inflammatory disease, and had consulted another physician for the same episode	Patients: mean age 42.8 y (±9.5), 58.4% male, and duration of back pain 6.1 wk (±1.6)	n = 178 (40%)	Anxiety OR 2.41 95% CI 1.44–4.09 (<0.001), female sex OR 2.03 95% CI 1.30–3.18 (P = 0.0033), work-related back pain OR 3.37 95% CI 1.08–5.17 (P = 0.0028), patients' beliefs about work-related back pain OR 1.02 95% CI 1.00–1.05 (<0.001)
Shaw et al. 2010,[119] USA	Prospective cohort study	To assess whether pre-existing psychiatric diagnoses increase the likelihood of transitioning from subacute to chronic LBP	12 mo	n = 122	First episode of LBP lasting 6–10 wk, age 18–50 y. Exclusion: major medical illness, pain disorder, taking medications to affect mood, major surgery 12 mo earlier, back pain from neoplastic disease, and osteomyelitis or fracture	Average age 30 y (±7.19),59% psychiatric disorder, 46% back pain without radiation, 16% had neurological signs (weakness, reflex, or sensory abnormality)	n = 49 (40%)	Depression OR 4.99 95% CI 1.49–16.76 (P < 0.01), general anxiety OR 2.45 95% CI 1.06–5.68 (P < 0.05), post-traumatic stress disorder OR 3.23 95% CI 1.11–9.44 (P < 0.05), nicotine dependence OR 2.49 95% CI 1.15–5.40 (P < 0.05), and psychiatric comorbidity 3.21 95% CI 1.29–7.99 (P < 0.05)

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Table 1 (*continued*)

Characteristics of included studies.

Author, year of publication, country	Study design	Study objective	Follow-up time	Population at follow-up	Inclusion and exclusion criteria	Participant characteristics	Chronic LBP after follow-up	Prognostic risk factors with significant *P*
Sihawong et al. 2016,[122] Thailand	Prospective study	To identify predictors for chronic neck and LBP	1 y	n = 615	18–55 y working full time. Exclusion: Symptoms 3 mo before baseline, pregnancy, history of trauma in the spinal region, surgery 12 mo before baseline, and had diagnosis for specific disease of the spine	Mean age 35.7 (±8.3), 25% male, history of LBP 78.5%, and BMI 23.4 (±4.9)	n = 28 (26.7%)	History of LBP OR 4.54 95% CI 1.02–20.21 (P = 0.04), high initial pain intensity OR 1.82 95% CI 1.46–2.28 (P < 0.01)
Wand et al. 2009,[140] United Kingdom	Prospective observational study	To evaluate which patient profile offers the most useful guide to long-term outcome in acute LBP	6 mo	n = 54	Nonspecific LBP less than 6 wk, 20–55 y, pain free at least 3 mo. Exclusion: specific low back pathology, nerve root pain, pregnancy or less than 3-mo postpartum, involvement in litigation, coexisting major medical disease, currently in physiotherapy, and previous spinal surgery	Mean age 35 y, range 21%–55%, 48% male, duration 2.9(±1.4) wk, and 93% employed	NA	LBP-related disability, RMDQ correlation coefficient 0.48 (P < 0.01), higher pain intensity correlation coefficient 0.40 (P < 0.01), quality of life, EQ5D correlation coefficient −0.42 (P < 0.01), physical well-being, PCS correlation coefficient −0.36 (P < 0.01)

BMI, body mass index, EQ5D, Euro-Qol health transition score, ESTEV study, French epidemiological survey, Health, Work, and Ageing investigation, HUNT study, Nord-Trondelag Health Study, LBP, low back pain, MSC, musculoskeletal complaint, MSP, musculoskeletal pain, PCS, Short Form-36 physical component score, RMDQ, Roland– Morris Disability Questionnaire, VISAT study, Viellissement Santé Travail study

excluded articles did not meet the criteria concerning the prospective information before the onset of chronic pain, the chronic pain was defined as lasting less than 3 months/12 weeks, or the pain was already chronic at baseline. In some articles concerning the working population, the chronic disease was only defined according to the time spent on sick leave without explaining whether the sick leave was due to LBP or to some other medical condition. In many of the excluded articles, the outcome was defined as timely pain during the follow-up contact compared with persistent symptoms for at least 3 months.

3.2. Quality assessment

The methodological quality of the studies was evaluated. Only 1 study was rated as good quality,[46] 19 studies were rated as fair quality,[6,18,32,54–63,89,97,99,119,122,140] and 5 articles were rated as poor quality.[19,83,88,103,110] Those studies that met the criteria according to the National Institute of Health assessment tool[94] are categorized as study population, measured exposures, measured outcomes, and study characteristics in **Table 3**.

3.3. Prognostic risk factors

All prognostic factors are presented in **Table 4**. In total, 80 prognostic factors were found from the studies.

3.4. Personal factors and medical history

Three fair-quality studies found higher body weight to increase the risk of CLBP.[59,63,97] Females seemed to be more at risk of developing chronicity according to 5 fair-quality studies[32,55,89,122,140] and 1 poor-quality study,[110] although statistical significance was achieved only in the latter. There was inconclusive evidence about age as a risk factor, although 2 fair-quality studies[32,55] had a statistically significant result about age being a risk of chronicity. In 2 fair-quality studies, smoking and/or nicotine dependence was statistically significant risk factor.[6,119] The only study rated as good quality found a statistically significant association between higher blood pressure and lower chronicity.[46]

3.5. Symptom characteristics

Higher pain intensity seemed to increase the risk of CLBP according to 6 studies,[54,55,89,110,122,140] from which statistical significance was achieved in 4.[54,55,122,140] Longer duration of symptoms before the onset of entering the studies (less than 3 months) was found to be predictive for chronicity in 1 fair-quality study.[55] Seven studies investigated functional limitation and disability because of LBP as a risk factor,[19,54,55,88,89,110,140] from which statistical significance was achieved in 1 study.[140]

3.6. Biomechanical factors

Carrying heavy loads at work was the most studied biomechanical risk factor for chronicity in 3 fair-quality studies[32,56,58] and 2 poor-quality studies,[103,110] and statistically significant in 3.[35,58,83] Other significant factors predicting chronicity with statistical significance according to more than 1 study included particularly physical work[56,58] and difficult working positions.[56,83,103] Furthermore, vibrations and jolts at work significantly increased the risk of chronicity in 1 fair-quality study[56] and nonsignificantly in 1 poor-quality study.[103]

Table 2

Excluded articles with reasons for exclusion.

Article	Reason for exclusion
Amorim et al.[3]	Only chronic population at baseline
Andersen et al.[5]	Baseline information inadequate
Andersen et al.[4]	Different definition for chronic pain; >30 days during last year
Ashworth et al.[2]	Including chronic population at baseline
Beneciuk et al.[8]	Including chronic population at baseline
Bohman et al.[10]	Different definition for chronic pain; no persistent pain
Burton et al.[11]	Including chronic population at baseline
Campbell et al.[12]	Including chronic population at baseline
Carey et al.[13]	Different definition for chronic pain; RMDQ
Cats-Baril and Frymoyer[14]	Baseline information inadequate
Chou and Shekelle[15]	Review
Costa et al.[17]	Only chronic population at baseline
Currie and Wang[20]	Different definition for chronic pain; no time frame, including adolescents
Dario et al.[22]	Baseline information inadequate
Diamond and Borenstein[23]	Dissertation
Dunn et al.[26]	Including chronic population at baseline
Edmond et al.[27]	Different definition for chronic pain; maximal pain over the past week
El-Metwally et al.[29]	Only chronic population at baseline
Endo et al.[30]	Baseline information inadequate
Esteve et al.[31]	Multiple pain sites
Fishbain et al.[33]	Only chronic population at baseline, multiple pain sites
Fransen et al.[35]	Baseline information inadequate
Friedman et al.[36]	Different outcome; Roland Morris disability questionnaire
Gatchel et al.[37]	Different definition for chronic pain; return to work status at follow-up
Gatchel et al.[38]	Different definition for chronic pain; return to work status at follow-up
Green et al.[40]	Including chronic at baseline
Grotle et al.[43]	Different definition for chronic pain; pain during the past week at follow-up
Grotle et al.[42]	Different definition for chronic pain; RMDQ at 12 mo
Gurcay et al.[44]	Different definition for recovery; assessed after 2 wk of follow-up
Hagen et al.[45]	Baseline information inadequate
Haglund et al.[47]	Only chronic population at baseline
Hasue and Fujiwara[48]	Baseline information inadequate
Hayden et al.[49]	Including chronic population at baseline
Hayden et al.[50]	Review (the part discussing population)
Heitz et al.[51]	Review
Helmhout et al.[52]	Including chronic population at baseline
Heneewer et al.[53]	Only chronic population at baseline
Heymans et al.[64]	Including chronic population at baseline
Holtermann et al.[66]	Different definition for chronic pain; >30 d during last year
Hussain et al.[70]	Baseline information inadequate
Imagama et al.[71]	Study on elderly
Jegan et al.[72]	Only chronic population at baseline
Jones et al.[73]	Including chronic population at baseline
Kardouni et al.[74]	Baseline information inadequate
Klenerman et al.[77]	Different definition for outcome; information on the chronic group inadequate
Kopec et al.[78]	Different definition for chronic pain; diagnose for back problems
Kovacs et al.[79]	Including chronic population at baseline
Lagersted-Olsen et al.[80]	Baseline information inadequate

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Table 2 (*continued*)

Excluded articles with reasons for exclusion.

Article	Reason for exclusion
Matsuda et al.[85]	Only chronic population at baseline
Matsudaira et al.[87]	Baseline information inadequate
Matsudaira et al.[86]	Baseline information inadequate
Melloh et al.[90]	Different definition for chronic pain; >6 wk, measured by oswestry
Mercado et al.[91]	Baseline information inadequate, multiple pain sites
Neubauer et al.[95]	Including chronic population at baseline
Nisenzon et al.[98]	Baseline information inadequate
Noormohammadpour et al.[100]	Only chronic population at baseline
Nordstoga et al.[101]	Only chronic population at baseline
Oliveira et al.[102]	Only chronic population at baseline
Pagé et al.[104]	Only chronic population at baseline
Picavet et al.[107]	Baseline information inadequate
Pinheiro et al.[108]	Only chronic at baseline
Pinto et al.[109]	Only chronic population at baseline
Popescu and Lee[111]	Dissertation
Rabey et al.[112]	Only chronic population at baseline
Ramond et al.[113]	Review
Reis et al.[114]	Baseline information inadequate
Rodeghero et al.[116]	Baseline information inadequate
Schiøttz-Christensen et al.[117]	Different definition for chronic pain: sickleave and functional recovery
Shiri et al.[121]	Review and meta-analysis
Shultz et al.[118]	Baseline information inadequate
Smedley et al.[123]	Baseline information inadequate
Swinkels-Meewisse et al.[126]	Different definition for chronic pain; point prevalence at follow-up
Thomas et al.[127]	Baseline information inadequate
Traeger et al.[128]	Duplicate
Trinderup et al.[130]	Only chronic population at baseline
Urquhart et al.[131]	Prevalence study, does not have a follow-up
Wahlgren et al.[137]	Different definition for chronic pain; point prevalence at follow-up
Valat et al.[132]	Different definition for chronic pain; 7 wk
Walton et al.[139]	Multiple pain sites
van der Hoogen[67]	Including chronic population at baseline
van der Weide et al.[141]	Different definition for chronic pain; functional disability, return to work
Verkerk et al.[134]	Only chronic population at baseline
Werneke et al.[142]	Different definition for chronic pain; pain during the past week at follow-up
Wilkens et al.[143]	Only chronic population at baseline
Villafañe et al.[135]	Only chronic population at baseline
Williams et al.[144]	Different definition for chronic pain; point prevalence at follow-up
Yosef et al.[146]	Including chronic population at baseline

3.7. Psychosocial factors

Numerous psychosocial factors were identified. Depression was the most studied factor predicting chronicity with statistically significant results in 2 studies[55,119] and nonsignificantly in 4.[32,89,110,140] Psychological risk factors that were investigated in more than 1 study included fear avoidance,[54,89,110] general anxiety,[55,110,119] somatization,[88,89] pain catastrophizing,[88,89] low tolerance of pain,[55,88] patients' perceived risk of persistence of the symptoms,[55,88] high psychological job demands,[32,56,89,122] and finally support at work[32,88,89] as a protective factor.

Compared with previous reviews,[15,133] new factors were found to be predictive of CLBP. Of these, the most evident were obesity, smoking, higher pain intensity, and occupational factors, such as difficult working positions, vibrations, and jolts at work.

4. Discussion

The main findings in this review are that higher pain intensity, higher body weight, carrying heavy loads at work, difficult working positions, and depression are the most frequently observed prognostic risk factors for CLBP. Moreover, maladaptive behavior strategies, general anxiety, functional limitation during the episode, smoking, and particularly physical work are also explicitly predictive of chronicity. Most frequently observed protective factors were physical exercise and higher blood pressure.

According to the findings of this review, lifestyle-related factors, such as smoking and obesity, are major risk factors for pain chronicity. Odd ratios for smoking differed between 2.49 (95% confidence interval [CI] 1.15–5.40)[119] and 4.41(95% CI 1.50–12.95).[6] In obesity, odd ratios varied between 1.075 (95% CI 1.023–1.128)[59] and 1.21 (95% CI 1.04–1.41)[97] in women and between 1.091 (95% CI 1.027–1.158)[59] and 1.16 (95% CI 1.05–1.29)[63] in men. In general, the findings about the risk factors of pain chronicity are similar.[120,145] Baseline personal factors concerning poorer general health[18] and functionality[18] were found to be significant risk factors for chronic pain in this review. Conversely, physical well-being[140] and physical exercise[97] were found to protect against chronicity. Poor general health and functionality are coherently interrelated to multimorbidity, which is a major risk factor for general pain chronicity.[24] The same nonmodifiable risk factors, such as age and female sex, found in this review are also found to be risk factors for other chronic pain conditions.[28,41]

LBP-induced disability and functional limitation were significant risk factors according to the findings of this review.[140] A study by Wand et al.[140] reported that the correlation coefficient between Roland–Morris Disability Questionnaire and CLBP was 0.48. A similar finding about functional impairment at baseline was reported in a previous review.[15] The lower levels of functionality might be a continuum of a person's lifestyle and behavioral factors. Therefore, avoiding bed rest despite the pain seems even more important.

The physical intensity of work, particularly strenuous physical work, carrying heavy loads, and working in difficult working positions, was related to higher chronicity in this review.[32,56,58,83,103] In a study by Machado and colleagues,[83] the carrying of heavy loads was predictive for CLBP with an odds ratio of 8.0 (95% CI 2.8–22.6). It is possible therefore that the physical work itself is preventing workers from getting back to work in a timely fashion[125] and thereby contributing to the prolongation of the symptoms.

There is previous strong evidence that cognitive factors, such as attitudes, cognitive style, and fear-avoidance beliefs, are related to the development of pain and disability in patients with back pain.[82] Maladaptive behaviors, such as perceived risk of persistence,[55,88] pain catastrophizing,[88] somatization,[88,89] and coping by ignoring pain,[88] were found to be risk factors in a total of 3 studies. It is not always the case that maladaptive behavior is the first step on the road to chronicity. The prospective designs included in this review would, however, implicate such causality, but one might suggest that fear avoidance, eg, is the immediate result of the pain in the acute phase of LBP, as Linton[82] discussed in his review. Low tolerance of pain was a significant risk factor in this review.[88] The low pain threshold is a complex concept and combines both genetic[124] and psychological aspects. In a study of pain thresholds in patients with chronic pain, there was a correlation between lower pain threshold and depressive tendency and hypochondriac concerns.[75]

A previous history of LBP substantially increases the risk of a subsequent new episode.[105] In this review, it was found to be a risk factor in 2 studies.[19,122] Interestingly, we found no evidence of sleep disturbances being a risk factor for chronicity. However, since there is a bidirectional relationship between the intensity of LBP and sleep disturbances,[1] one might assume it would also be a risk factor for CLBP. This would be an interesting hypothesis to study in the future.

So-called "yellow flags" is an umbrella term used to describe psychological risk factors and social and environmental risk factors for prolonged disability and failure to return to work as a consequence of musculoskeletal symptoms.[76] Many of the risk factors for chronicity identified in this review fall under this category. The interest in yellow flags originates from the concept that early interventions might avert the development of disability. When patient selection is performed accurately and when an intervention known to address these factors is competently applied, good outcomes are to be expected.[96]

4.1. Limitations of this review

A major limitation of this review was that only 1 high-quality study was detected in our literature search. Loss to follow-up was significant in many fair-quality studies, and this reduced the

Table 3

Criteria for methodological quality.

Criteria for methodological quality	All articles n = 25 [n (%)]	Good n = 1 [n (%)]	Fair n = 19 [n (%)]	Poor n = 5 [n (%)]
Study population				
Description of population	20 (91)	1 (100)	17 (89)	4 (80)
Participation of eligible participants ≥50%	18 (82)	1 (100)	16 (84)	3 (60)
Inclusion criteria precise	21 (96)	1 (100)	19 (100)	4 (80)
Loss to follow-up ≤20%	7 (32)	0 (0)	7 (37)	1 (20)
Measured exposures				
Exposures measured before outcome	22 (100)	1 (100)	19 (100)	5 (100)
Levels of exposure examined	13 (59)	1 (100)	12 (63)	3 (60)
Exposure measures valid	10 (45)	1 (100)	9 (47)	0 (0)
Exposures assessed more than once	10 (45)	1 (100)	8 (42)	1 (20)
Measured outcome				
Sufficient timeframe to detect outcome	22 (100)	1 (100)	19 (100)	5 (100)
Outcome measures valid	8 (36)	1 (100)	7 (37)	1 (20)
Study characteristics				
Research question clearly stated	19 (86)	1 (100)	18 (95)	3 (60)
Sample size justification	3 (14)	1 (100)	2 (11)	0 (0)
Outcome assessors blinded	1 (5)	0 (0)	1 (5)	0 (0)
Confounding variables adjusted	14 (64)	1 (100)	14 (74)	1 (20)

Table 4

Prognostic factors.

Category	Prognostic factor	Categorical (1) or continuous variable (2)	Evaluated in the study as [ref. number]			Predictive value in overall	Study quality (n)		
			Risk factor	Protective factor	Not significant statistically		Good	Fair	Poor
Personal factors and medical history	Age	1, 2	32,55	6	56,89,110,122,140	IE		7	1
	Female sex	1	110		32,55,89,122,140	Risk		5	1
	Body weight	1, 2	59,63,97		32,56,89,122	Risk		7	
	Body height	1	60			Risk		1	
	Body measures	1	59			Risk		1	
	Diabetes	1	57			Risk		1	
	Rheumatological event ≥1	1	32			Risk		1	
	Blood pressure	1		46,62		Protective	1	1	
	Pulse pressure	1		62		Protective		1	
	High cholesterol	1			61	NS		1	
	High HDL cholesterol	1			61	NS		1	
	High triglycerides	1			61	NS		1	
	Smoking and nicotine dependence	1	6,119		32,56	Risk		4	
	Alcohol dependence	1			119	NS		1	
	Psychoactive substance dependence	1			119	NS		1	
	Previous back surgery	1			18	NS		1	
	Previous episode of LBP	1	19,122			Risk		1	1
	Low back injured in MVC	1	99			Risk		1	
	Baseline disability before LBP	2	18		122	Risk		2	
	Baseline general health poor	2	18			Risk		1	
	Physical well-being	1		140	89	Protective		2	
	Physical exercise	1		97	32,56,89,110,122	Protective		5	1
	Level of education	1			88,110	NS			2
	Former productivity-related income	1	32			Risk		1	
	Disability compensation	1	55		18,19	Risk		2	1
	Occupational status	1			19,32,140	NS		2	1
	Number of different jobs held	1		32		Protective		1	
	Back pain in parents	1			110	NS			1
Symptom characteristics									
	Pain intensity	1, 2	54,55,122,140		89,110	Risk		4	1
	Pain duration	1	55		89,110,140	Risk		3	1
	Pain radiation	1			89,140	NS		2	
	Leg pain				55,88	NS		1	1
	To upper back		88			Risk			1
	Multiple pain sites				55	NS		1	
	Pain requiring medication	1			55,110,140	NS		2	1
	Days of reduced activity because of LBP	1		55		Protective		1	
	Affective pain	1			89	NS		1	
	Pain interfering sleeping	1			88	NS			1
	Pain worse on standing	1	19			Risk			1

(continued on next page)

Table 4 (*continued*)

Prognostic factors.

	Pain worse on lying	1			19	NS		1
	Disability and functional limitation	1, 2	140		19,54,55,88,89,110	Risk	4	3
Biomechanical factors								
	Spinal mechanical load	2			6	NS	1	
	Work-related back pain	1	110			Risk		1
	Particularly physical work	1	56,58		110	Risk	2	1
	Physical intensity of work	1						
	Moderate or vigorous		83			Risk		1
	Vigorous only		83			Risk		1
	Frequent rest breaks from work	1			122	NS	1	
	Difficult working positions	1	56,83,103		32	Risk	2	2
	Repetitive short movements	1			103	NS		1
	Carrying heavy loads/lifting at work	1	32,58,83		56,103	Risk	3	2
	Working arms elevated	1			103	NS		1
	Bending and twisting trunk	1			103	NS		1
	Working kneeled/squatted	1			103	NS		1
	Vibration and jolts at work	1	56		103	Risk	1	1
	Working with animals	1			83	NS		1
	Working tired	1			83	NS		1
Psychological and psychosocial factors								
	Good quality of life	1		140		Protective	1	
	Mental well-being	1			89	NS	1	
	Depression	1, 2	55,119		32,89,110,140	Risk	5	1
	General anxiety	1	110,119		55	Risk	2	1
	Post-traumatic stress disorder	1	119			Risk	1	
	Antisocial personality disorder	1			119	NS	1	
	Any psychiatric diagnosis	1	119			Risk	1	
	Somatization	1	88,89			Risk	1	1
	Fear avoidance	1						
	In general				54	NS	1	
	Of work activity				89,110	NS	1	1
	Of physical activity				89,110	NS	1	1
	Perceived risk of persistence	1	55,88			Risk	1	1
	Catastrophizing	1	88		89	Risk	1	1
	Perceived stress	1	88			Risk		1
	Low tolerance of pain	1	88		55	Risk	1	1
	Coping by ignoring pain	1	88			Risk		1
	Coping by music or TV watching	1		88		Protective		1
	Nonrecognition of work	1	32			Risk	1	
	Job satisfaction/control	1			89	NS	1	
	Work absenteeism	1			89	NS	1	
	Support at work	1		88,89	32	Protective	2	1
	Support at home				89	NS	1	

(*continued on next page*)

Table 4 (*continued*)

Prognostic factors.

	High psychological job demands	1	32,56,89,122	NS	4
	Difficulty communicating	1	32	NS	1

Categorical variable measured yes/no or in larger categories, continuous variable measured by continuous scale. Reference number of the studies evaluating each prognostic factor presented in brackets. The number of studies (sum) presented in quality categories.

HDL, high-density lipoprotein; IE, inconclusive evidence; LBP, low back pain; MCV, motor vehicle collision; NS, not significant statistically; protective, statistically significant protective factor; risk, statistically significant risk factor.

number of good-quality studies. Furthermore, chronic low back pain as an outcome is hard to validate since it is always more or less self-reported. Many studies have tried to minimize this bias by using validated questionnaires.

Nine of the studies (36%) used the same population data from HUNT studies.[46,57–63,97] The results that were only observed from HUNT studies were body height[60] and measures,[59] diabetes,[57] blood pressure,[46,62] and pulse pressure.[62] However, the risk of bias in this particular study population can be assessed as low because of the large sample size and long follow-up period. The Nord-Trondelag Health Studies (HUNT studies) were population-based health surveys conducted in 1984 to 1986, 1995 to 1997, and 2006 to 2008. All residents older than 20 years of the entire Norwegian county were invited to take part in these large surveys.[63]

Some risk factors that seemed similar and were detected in multiple studies differed nonetheless to some extent in definition or measurement choice. To avoid too much heterogeneity inside 1 risk factor, they were intentionally not combined. Thus, it was difficult to reach a strong conclusion about the significance of several risk factors because they were only evaluated by a small number of studies.

Defining CLBP as persistent pain for at least 3 months is an artificial means of controlling the heterogenic population with LBP symptoms. Evidence from long-term studies indicates that people with long-term problems can have pain episodes separated by periods that are pain free, periods of continuous mild pain with low impact, or periods of severe pain with a large impact on their lives.[25]

When finding a potential association between a prognostic factor and an outcome, one must not assume that the effect is direct and isolated. Nonspecific low back pain is a multifactorial and complex condition with the impact of different factors changing over time.[32] This review simply identifies the factors related to chronicity; it does not, however, study whether the presence of 1 factor is sufficient or whether a certain mix of factors is required. Therefore, when developing more comprehensive models that include connections between these factors, it is essential to consider which factors are truly important.

4.2. Usefulness of results and recommendations

A "wait and see" approach is no longer advisable because early screening provides reliable and valuable information for identifying those at risk of delayed recovery and for formulating a treatment strategy from the start.[81] The subgrouping of patients with nonspecific LBP and finding tailored treatments and management strategies are the main research priorities in the field of LBP.[16] It is therefore important to detect those patients at risk of developing chronicity in the early phases of the symptoms and to offer tailored treatment according to the risks in question. Especially stratification according to psychosocial risk factors has achieved promising results,[34,65] but the disadvantage is the lack of work-related items, socioeconomic variables, and symptom factors. Then, additional steps may be needed to identify the specific problems of patients to improve outcomes.[81]

The findings of this review may be helpful in the planning of future studies concerning the prevention of CLBP and to aid clinicians detect patients at risk of chronicity.

Disclosures

The authors have no conflicts of interest to declare.

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Appendix A. Supplemental digital content

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PUBLICATION
II

Applying Semantic Computing for Health Care Professionals: The Timing of Intervention is the Key for Successful Rehabilitation.

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Applying Semantic Computing for Health Care Professionals: the Timing of Intervention is the Key for Successful Rehabilitation

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Abstract—**This study aims to apply Graph Machine Learning, a subset of artificial intelligence, in labeling electronic health records. The theoretical approach of the study stems from the studies of AI, machine learning, health policy, and physical medicine and rehabilitation.**

The data of chronic low back pain patients (n=93) were collected from electronic health records in form of a free text. The comparative analysis between the AI and medical expert was executed with the data of randomly selected patients (n=5).

The International Classification of Functioning, Disability, and Health was used as a scientifical frame to identify the factors affected by a patient's medical status. A medical expert identified the factors stated in the electronic health records. Data was analyzed and labeled with the graph (semantic networks) based machine learning engine, Headai Graphmind. Headai Graphmind automatically converted the findings to a readable map of factors, which are relevant concerning the timing of rehabilitation.

Headai Graphmind found 56% of identical factors in relation to the medical expert. In future studies, the analyses of mutuality between Headai Graphmind, the health care professional and the patient are crucial to set the right timing for rehabilitation.

I. Introduction

It has become tremendously obvious that the authority of artificial intelligence (AI) technologies will challenge the digital world of healthcare in the future. Advocates of critical scrutiny such as Bartlett [1] are taking a pioneering roles in Armageddon. They are convinced that the technologies of AI, big data, mobile and social media will even destroy democracy in the world of technology companies that scale fast but do not question anything. This raises a question in a global setting: is embraced "big tech" a real threat to effective, equitable, and personalized health service delivery [2]? Perhaps, but are we a bigger threat to ourselves than tech if we are not able to ensure that we control our machines, rather than the other way around [3]?

Admittedly, this trend is daunting to healthcare, but both AI data and evidence based current care guidelines are still in many diseases general and indefinite in terms of personalized medical decisions. Likewise, allegorically it makes sense to argue according to Karl Polanyi's [4] paradox: "me medical expert know more than I can tell and document". Specifically, medical experts know how to treat patients tacitly but cannot tell all of it to colleagues. Due to machine learning the investigation of the paradox proceeds rapidly [5]. On the other hand, AI and Machine Learning (ML) are umbrellas of thousands of algorithms, methods, and setups, all performing well in certain areas and poorly in other areas, thus making the selection of AI/ML algorithm difficult. For example, Deep Learning algorithms perform well in categorizing tasks when the task is well defined and the training material is big enough. Nevertheless, Deep Learning cannot perform well in cases where the task is ill-defined and requires humankind of reasoning to work with unknown factors. At present, as Panch et al [2] put it, the algorithms that feature prominently in the research literature are not very much, if at all, executable at the frontlines of clinical practice. On the other hand, Graph/Semantic Networks based Machine Learning seems to perform well [6], [7].

In this study, the semantic network based machine learning engine, Headai Graphmind (HGM), does, at its best, reasoning to supply best guess answers where formal procedural rules are unknown. The biggest difference between Headai Graphmind and common Graph Machine Learning is in the fundamentals of how Graph (detailed Semantic Network) is processed. HGM adds, modifies, and reasons according to conceptual learning theories [8] and Semantic Network is a storage structure for all the leaned data. I.e. HGM's Semantic Network include only processed data with explanations, not just nodes and edges. This is promising in a frame of patients with multiple morbidities and where the steps needed to achieve adequate health services are considered exceptionally highly complex.

The fact is that physicians and other health care professionals cannot be replaced with machines and robots as fast as the "optimistic hypers of AI" promise. That does not necessarily follow so far as machines can mainly be assistants in heavy lifting and logistics. Currently, approximately only 9 % of the worktime of an expert can be automated compared with 78 % of worktime in predictable physical work [9].

But cynical arguments against AI in healthcare are not very well articulated either. Conversely, according to the opponents, the real benefit will be realized in a continuous move in the managed health value chain from a labour-driven and technology-enabled model to a digital-driven and human-enabled one [10]. Most importantly, however, transforms toward personalized medicine do not happen only with simple decision support systems driven by AI and data. Likewise, in a rehabilitation process, successful personalization presupposes both right timing in the intervention and a specific profile produced most effortlessly by AI. Therefore, this paper highlights the importance of timing in the rehabilitation process in the frame of individual and societal, professional needs for rehabilitation (see Fig. 1).

A. Research design

In Fig. 1 is described the research design of the study. At the beginning of rehabilitation (T [1]) an individual's need for rehabilitation and its intensity is almost always higher than the need for rehabilitation by health care professional/ societal expertise (HP). Logically, human beings suffer first and society, in this case, health care professionals with medical experts start the treatment and rehabilitation much later along the clinical pathway.

Nevertheless, even if an active approach toward rehabilitation is taken at the beginning of the process, the intensity is quite low and close to non-existent, if professionals have adopted a "wait and see approach" [11](see Fig. 1, HP/ T[1]). This causes a dilemma in which individuals are not always taken care of at the right time, at the right place, and the right intensity. In some cases, time delay in rehabilitation leads to individuals' frustrations and other symptoms (e.g. psychosocial). The dilemma manifests itself usually in the phase of T [3]or later. In these cases, rehabilitation becomes more ineffective if individuals are not motivated to self-manage themselves anymore for many reasons (e.g. unemployment, isolation, depression, etc.) [12].

On this basis, it makes sense to believe that by applying Headai Graphmind (HGM) at T [1] in a very profiled way, health care professionals can obtain knowledge more quickly and thus, begin the rehabilitation planning (T [2] at the latest). This multidisciplinary knowledge is based on theoretical and scientific knowledge of machine learning, health policy, and physical medicine and rehabilitation.

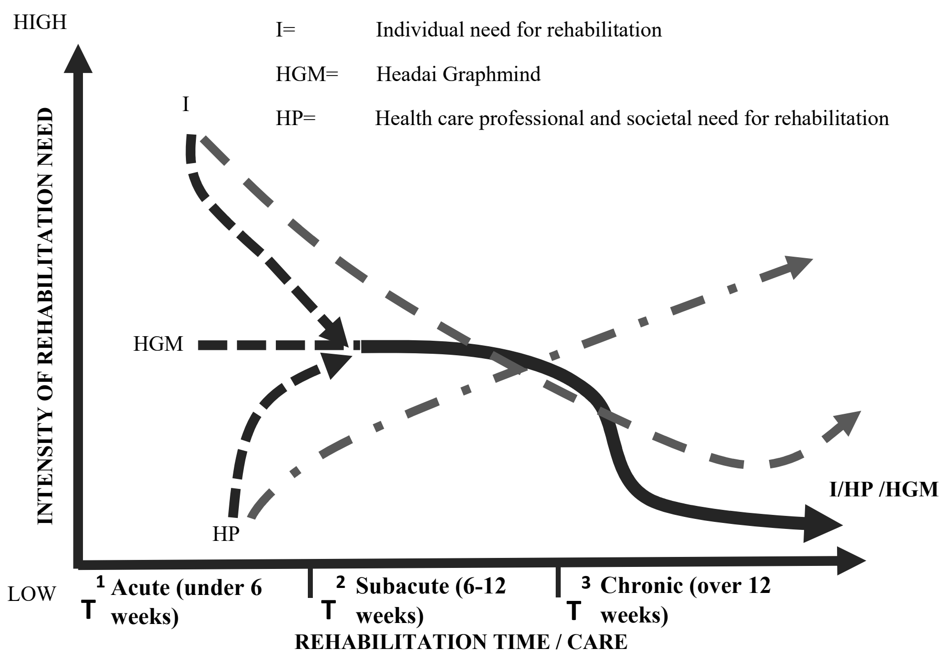

Fig. 1. The research design of rehabilitation processes embedded in patient involvement (I), Headai Graphmind (HGM) and medical expertise (HP)

B. Aims of the study

Low back pain (LBP) is the most burdensome medical condition worldwide in terms of disability [13] and when reaching the chronic stage (> 12 weeks), it comes with enormous individual and societal burden, let alone economic burden [14], [15]. There are numerous identified risk factors for developing LBP chronicity [16], but their early detection is often missed at the latest for the sake of inoperative clinical pathways. The timely recognition and targeted rehabilitation would help in the prevention of pain chronicity, but achieving such a plan can be a difficult task even for experienced health care professional. This study aims to apply a semantic network based machine learning engine, Headai Graphmind, in physical medicine and rehabilitation. The free text from electronic health records (EHR) is automatically converted into a readable map of factors, which are relevant to the timing of rehabilitation. To our knowledge, this form of method has not been used to date. The research questions are:

a) do the findings of a medical expert (ME) differ from Headai Graphmind's findings?

b) what is the potential impact of Headai Graphmind's findings on the timing of the rehabilitation process?

II. Data And Methods

Overall, 1569 patient records were screened. Inclusion and exclusion criteria were used to form an eligible patient sample. The included patients were adults (18 to 65 years) suffering from chronic LBP (duration over 12 weeks). Specific reasons for LBP, such as nerve root disorders, or fractures of the spine were excluded. 93 patients fulfilled the criteria. These patients were suffering from non-specific LBP, where a specific biomechanical reason for the pain could not be identified. The data was collected in form of a free text from EHR between October 2019 and February 2021. The data was in the Finnish language. A longitudinal dataset of five patients was used for the result comparison (n=15 EHR notes) between medical expert and Headai Graphmind. The data was retrieved under a data transfer contract from Tampere University Hospital (Finland), where patients had been visiting the unit of Rehabilitation and Psychosocial support for their prolonged back pain. At the data collection time, there were 10 physicians (specialists and residents of physical medicine and rehabilitation) working in the unit, who were responsible for producing the EHR notes.

The International Classification of Functioning, Disability and Health (ICF) by World Health Organization (WHO) [17] was used as a scientifical frame to identify the factors affected by their medical status (Fig.2). A medical expert identified the factors stated in the patient's EHR produced by physicians. The ME was one of the physicians working in the unit of data retrieval, which minimized the misunderstanding of the data's medical content. The data was analyzed with HGM that imitates human reading and processing of the texts. HGM automatically converted the findings to a readable map of factors, which are relevant concerning the timing of rehabilitation.

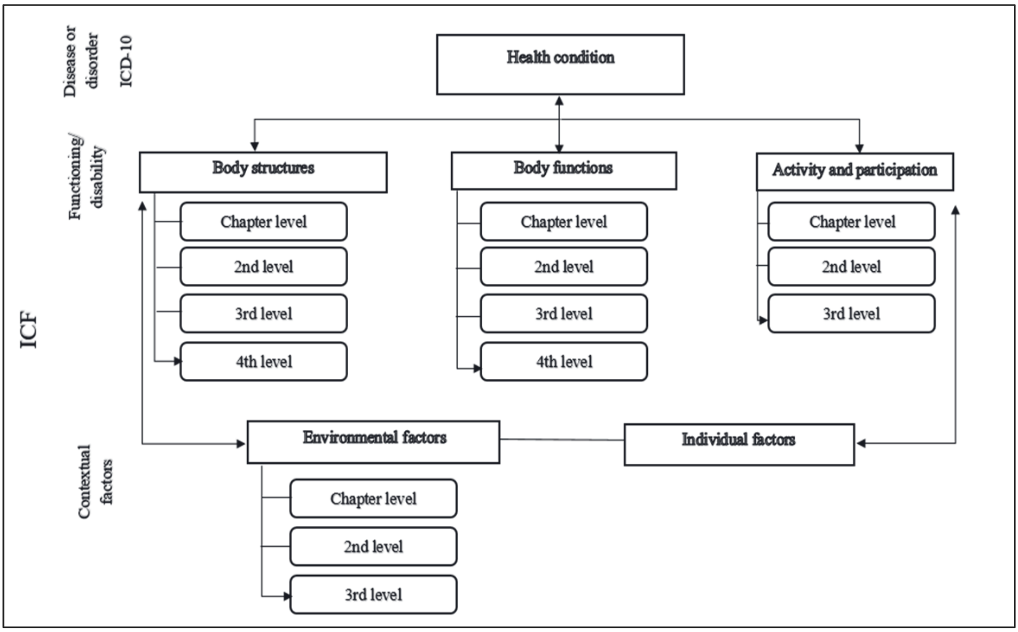

Fig. 2. The structure of International Classification of Functioning, Disability and Health (ICF). Different domains (e.g. body functions) are divided to three to four levels, which represent the ontology of the coding. For example in body functions, chapter level: b2 sensory functions and pain, 2nd level: b280 sensation of pain, 3rd level: b2801 pain in body part, and 4th level: b28013 pain in back. Individual factors are not coded because of the wide variability among cultures. Adopted from WHO Beginner's guide

The automated conversion of known LBP factors from EHR to ICF codes was executed with the cognitive text analyses, using natural language processing algorithms and semantic networks based machine learning.

Overall, 12 different setups were tested within the algorithm (Table I). The inputs included the ICF ontology, Medical Subject Headings (MeSH, a hierarchical vocabulary for life sciences), and medical experts' view of the language used by physicians in their texts.

The abilities of the algorithm to detect and convert the known factors were tested on a longitudinal dataset of five patients. A medical expert (ME) read the free texts of physicians (n=15 EHR notes) several times and searched for words, terms, and short sentences that could have a link to the ICF codes. The codes and the free text in question were listed as the reading went along so that the similar words and terms would be coded iteratively. The results of Headai Graphmind's different setups were compared to the codes converted by the ME. This comparative analysis was made by the same ME who had done the conversion. The matching results, the false conversions of the algorithm, and the results that were detected by the algorithm but not by the medical expert were listed.

III. Results

The dataset of each patient consisted of two to five notes in their EHR (n=15), that were entered during their period of treatment. The notes consist of referrals from primary health care, occupational health care, or private sector (n=4), physical appointments (n=6), contacts by phone call (n=4), or by letter (n=1).

The semantic networks based machine learning engine, HGM, and the ME found ICF domains (n=355) differently from five patients' EHRs (Table II). First, HGM and ME found partially the same codes in all the domains. In category 1 from body functions and structures domains, HGM found 68% of the ME's findings (20,3% of total findings), 76% from environmental domains (4,6% of total findings), but in the activity and participation domain the findings were in line in only 20% of the codes (2,5% of total findings). HGM found also codes that the ME did not. In category 3 there were 24 codes (6,8% of total findings) that HGM found better than the ME; these are explained by human error and different (but logical) interpretations of the text. For example, the ME coded "walking on different surfaces" and HGM "moving around in different locations", which both suited to the context. In addition, 61 code findings (17,2% of total findings) in all domains were not to be interpreted as correct findings after several appraisals of the data. Headai Graphmind missed 44% (n=76, 21,4% of total findings) of the findings of the ME's (category 1), and vice versa, ME missed 20% (n=24, 6,8% of total findings) of correct findings of HGM (category 3).

The most promising setups (Table I) were "ICF title" and "ICF real life fuzzy", where the relation of the correct findings to the false conversions was the highest. As far as the information and medical scientist's collaboration are concerned, it seems, that ICF codes combined with medical expert's view on the medical language will lead to intriguing results. The most important implication for AI scientists is that interdisciplinary research cooperation with medical experts should be encouraged. First, the prediction of risk scenarios in complex services might become easier in the future. Second, information scientists can innovate novel research designs with a better terminological understanding of medical counterparts. Finally, the research collaboration will lead to better applications also in other health care services.

TABLE I. The Explanation Of Different Setups. ICF= International Classification Of Functioning, Disability And Health; MeSH= Medical Subject Headings (A Hierarchical Vocabulary For Life Sciences)

Setup abbreviation	Setup name	Explanation of the input/algorithm-ontology configuration
a	ICF title	The ontology of the ICF (title level)
b	ICF title fuzzy	The ontology of the ICF (title level) analyzed with fuzzy logic
c	ICF description	The ontology of the ICF (description level)
d	ICF description fuzzy	The ontology of the ICF (description level) analyzed with fuzzy logic
e	ICF real life	The ontology of the ICF was extended with the language used by physicians from ME point of view, e.g. b1342 onset of sleep= to fall asleep
f	ICF real life fuzzy	The ontology of ICF was extended with the language used by physicians from ME point of view, and analyzed with fuzzy logic
g	MESH-ICF	The ontology of ICF (title level) was extended with MeSH vocabulary
h	MESH-ICF fuzzy	The ontology of ICF (title level) was extended with MeSH vocabulary, and analyzed with fuzzy logic
i	MESH-ICF description	The ontology of ICF (description level) was extended with MeSH vocabulary
j	MESH-ICF description fuzzy	The ontology of ICF (description level) was extended with MeSH vocabulary, and analyzed with fuzzy logic
k	MESH-ICF real life	Setup e. was further extended with MeSH vocabulary
l	MESH-ICF real life fuzzy	Setup e. was further extended with MeSH vocabulary, and analyzed with fuzzy logic

TABLE II. HEADAI GRAPHMIND VS. THE MEDICAL EXPERT: THE COMPARISON OF THE CONVERSION FROM LOW BACK PAIN PATIENT'S ELECTRONIC HEALTH RECORDS TO ICF DOMAINS. *BODY STRUCTURE AND BODY FUNCTION CODES COMBINED

ICF DOMAINS (N=355)	FINDINGS OF HEADAI GRAPHMIND (HGM) AND THE MEDICAL EXPERT (ME)						
	(1) Graphmind found the same as ME		*(2) Graphmind found something*		*(3) Graphmind found better*		*Total*
	ME n (%)	**HGM n (%)**	**ME n(%)**	**HGM n (%)**	**ME n(%)**	**HGM n (%)**	**n (%)**
Body structures and functions*	106 (29.9)	72 (20.3)	*N/A*	34 (9.6)	*N/A*	10 (2.8)	222 (62.5)
Activity/ participation	46 (13.0)	9 (2.5)		14 (3.9)		9 (2.5)	78 (22.0)
Environmental factors	21 (5.9)	16 (4.5)		13 (3.7)		5 (1.4)	55 (15.5)
Total	173 (48.7)	97 (27.3)		61 (17.2)		24 (6.8)	**355 (100)**

IV. DISCUSSION

This paper introduces the principles of applying Semantic Network based Machine Learning engine Headai Graphmind to the framework of functioning, disability, and health (ICF), which can help our health care professionals in co-operation with the individuals plan the rehabilitation processes needed in a personalized healthcare fashion. In precise, the study highlights the correct timing in rehabilitation in minimizing the time of disability and waste of resources. The future key should be in the combination of knowledge of individuals, health care professionals, and advanced machine learning.

In Fig. 1. were described the potential shift from individual (I) or health professional (HP) driven planning and rehabilitation process to the more effective process constructed by the semantic fields of the texts habituated into reciprocal roles played by the individual, the health professional and HGM (I/HP/HGM) [18]. The described results of data analysis (Table II.) give arguments for the shift within the categories 2 and 3. The categories are highly promising for the inquiries of a new ontology of ICF domains. At its worst, health professionals only maintain, modify, and reconstruct the reality of unquestionable ICF domains. However, the category 2 findings go in line with the fuzzy logic and are not ontologically based on the ICF domains, therefore offering health professionals new ways to approach LBP patients in general. The findings of category 3 challenge the health professionals as well. Fictionally, HGM can define better the status of the patient following the ontology of ICF domains and could easily ask a physician: "you didn't change new sunglasses to see the whole picture and specific needs of individuals in the rehabilitation process, did you?" The applications of supervised machine learning (e.g. Deep Learning) in this case would have not produced the findings described in categories 2 and 3. Therefore, HGM promises a lot in a frame of risk analysis for preventive rehabilitation. In addition, these findings may pave the way for new interesting studies of fuzzy logic in risk analysis and scenarios, particularly in information sciences.

HGM reached identical conclusions in 56% of the ME's results. Different reasons for this can be that HGM was not yet learned well, or data was too limited and not rich enough for a more precise conversion. Further development of the most functional setups should lead to higher accuracy of HGM in relation to the medical experts and can even give discoveries on the individual's functioning and disability.

V. CONCLUSIONS

This paper underlines the importance to provide profiled knowledge of patients with managed machine learning to create a more effective rehabilitation process from the beginning. The first research question concerned the difference between a medical expert and the machine. Table II answered the question simply with the existence of categories 2 and 3. These categories remind readers of the classical learning curves that are more often non-linear than linear. The second research question was exploring the potentiality of HGM's effectiveness in the right timing of rehabilitation. Answering this question comprehensively is not possible with this pilot study. First, we must test HGM with a prospective and larger data, and conduct a study with a reasonable follow-up time. Second, the questions of timing and time need to be considered carefully in this kind of analysis. In the work of health professionals it is dynamic, and the issues of the right timing in treatments prior in many cases the question of duration of the treatments.

It seems promising that the Semantic Network based Machine Learning engine Headai Graphmind is capable to do conceptual reasoning in challenging domains. However, it must be highlighted that Headai Graphmind's performance was at its best in two cases: with training data based on ICF titles and with training data based on domain professional's short explanations of the ICF code written in professional language. When applying MeSH vocabulary or too generic definitions as training data, the results were not that good. Furthermore, this is nothing unexpected. In fact, this is aligned with earlier studies on semantic computing: the smaller the training data is, the more critical the quality of the data is, no matter what the algorithm is. Finally, semantic computing cannot solve ICF coding alone, but it can be exploited wisely by experienced health care professionals.

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PUBLICATION III

An early biopsychosocial intervention design for the prevention of low back pain chronicity: a multidisciplinary empirical approach.

Nieminen, L., Vuori, J. & Kankaanpää, M.

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ORIGINAL REPORT

AN EARLY BIOPSYCHOSOCIAL INTERVENTION DESIGN FOR THE PREVENTION OF LOW BACK PAIN CHRONICITY: A MULTIDISCIPLINARY EMPIRICAL APPROACH

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Objective: **Comprehensive intervention models for prevention of chronification of low back pain, in which the early identification of holistic risk factors is considered are needed. The aim of this study is to design a tailored biopsychosocial intervention for patients with low back pain to prevent pain chronicity.**
Design: **A multidisciplinary empirical approach.**
Methods: **A multidisciplinary team designed a biopsychosocial intervention following an application from the Medical Research Council's complex intervention framework. The methods used included problem identification, identification of the evidence, theory, and needs, examination of the current context and modelling of the theory. Biomechanical, psychological, social and environmental, and lifestyle and personal risk factors were taken into account.**
Results: **The intervention process was introduced in a logic model. The model presents all the required resources, their activities and outputs, as well as the outcomes and impacts of the intervention. The intervention was tailored according to the underlying risk factors for pain chronification in patients with low back pain.**
Conclusion: **A comprehensive tailored intervention may decrease the risk of pain chronicity. Further studies are needed to obtain information on the feasibility, effectiveness and cost-effectiveness of such interventions.**

Key words: low back pain; chronic pain; biopsychosocial model; rehabilitation; multidisciplinary research.

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LAY ABSTRACT

Low back pain is the leading cause of years lived with disability worldwide. In cases of non-specific low back pain, a specific structural reason for the pain cannot be identified. It is recognized, however, that individual factors, such as biomechanical, psychological, social, environmental, lifestyle, and personal factors, can increase the risk of pain chronicity. Therefore, a multidisciplinary intervention was designed to address these individual factors in addition to traditional treatment methods. The intervention was also designed to improve the timing of the rehabilitation to prevent pain chronification. This study presents the background, the different phases of the design process, and the model for the intervention. Further studies will be conducted to determine the applicability and effectiveness of the design.

Public health requires immediate global intervention actions (1) for the early identification of risk factors associated with chronicity of low back pain (LBP) (2). In terms of disability, LBP is the most burdensome global health problem (3). To date, many LBP interventions have been introduced, but, in many cases, the knowledge of key professionals has not been exploited holistically enough. Likewise, very few interventions are truly comprehensive mutualistic models in which the multiple risk factors driving pain and disability and their interactions are considered (4). Furthermore, there is a scarcity of usage of intervention frameworks that increase the validity of the design and decrease resource waste (5). The key problems concerning the effective rehabilitation of patients with LBP are mostly related to the correct timing of risk stratification, the tailoring of interventions, and the mutuality between healthcare professionals and patients.

Achieving the correct timing of rehabilitation is difficult, especially in patients with multiple morbidities where the steps involved are considered highly complex. In particular, the problems associated with LBP should be explored in more detail regarding the timing and shared decision-making for rehabilitation in rapidly ageing populations of people with biased health information. Therefore, to scrutinize the health problems associated with LBP, the following questions should be answered: how can healthcare professionals identify the relevant factors that affect the risk of chronicity in patients with LBP in a comprehensive and timely manner? How can healthcare professionals proceed effectively in the rehabilitation process with colleagues if this data is unavailable at the beginning of the process?

With the increasing costs of healthcare, new interventions should aim to add effectiveness to the margins of the available resources. Although not all patients with LBP need comprehensive, multidisciplinary rehabilitation, the delayed detection of patients at risk of chronicity can result in excessive costs, not to mention the burden for the patient in terms of decreased quality of life and functioning. The foundations of new interventions should be based on value clarifications (where the patient's values and preferences are heard during the decision-making process) (6) and value-based healthcare (VBHC). Thus, the interventions should be equitable, sustainable, and transparent, while using the resources available to achieve better outcomes and experiences for all patients. The aim should be to deliver the best possible outcome for patients individually with the resources available (7).

This study develops a comprehensive intervention for non-specific LBP suitable for primary and occupational healthcare. The effective healthcare policy aim is to prevent chronicity of pain and disability by considering the whole spectrum of disability and health in accordance with the International Classification of Functioning, Disability, and Health (ICF). A secondary aim is to identify the individualized needs of patients according to the underlying risk factors in the rehabilitation process using the following research questions:

- Which healthcare professionals and stakeholders are needed in primary healthcare for the effective prevention of LBP chronicity?
- What are the roles of different healthcare professionals in the intervention processes of patients with risk factors for LBP?

METHODS

The design of the intervention (Table I) followed the development phase of United Kingdom Medical Research Council's (MRC) complex interventions framework (8), which is the most cited guidance using an iterative approach (5). A new update of the framework came at the end of the design process, and the intervention design reflected the most recent implications (9). The optimization of the design was adopted from a framework application, which enriches the development phase of the MRC framework. The approach adds crucial elements to the development phase to strengthen the internal and external validity, to minimize research waste, and to add value to healthcare research (5). The rehabilitation design was divided into 4 sections to represent those risk factors affecting patients with non-specific LBP: biomechanical, psychological, social and environmental, and lifestyle and personal.

Table I. Study methods

Intervention design	
I. Problem identification	Review of the literature
	Identifying the problem in different risk factors
II. Identifying the evidence	Review of the literature
	Identifying the existing interventions and evaluation of their usefulness in this context
III. Identifying the theory	Research on different health psychology theories
	Identifying the theoretical framework and behaviour change techniques
IV. Identifying the needs	Retrospective population study
	Identifying the specific needs within the ICF framework
	Exploring the ICHOM standard set for LBP
V. Examining current context	Identifying existing resources, identifying the gaps
	Barriers, and facilitators of providers and recipients
VI. Modelling the theory	Modelling the intervention design to a logic model

ICF: International Classification of Functioning, Disability and Health; ICHOM: International Consortium for Health Outcomes Measurement; LBP: low back pain.

Multidisciplinary professional teams involving different stakeholders were gathered to design the intervention. To be included in the team, participants had to have strong knowledge of treating patients with LBP, at least several years of work experience, and the will and vision to advance the management of patients with LBP in their working environment. The teams included physicians, physiotherapists, mental health physiotherapists, nurses, a psychologist specialized in pain management, a social worker, and a rehabilitation counsellor (Table II). The teams worked via remote meetings between April 2021 and February 2022. Before the collaborative discussion, the chairperson gave an introduction based on scientific literature concerning the subject of the meeting.

At the beginning of the design process of the intervention (phases I and II, Table I), a previous systematic review of the risk factors for LBP chronicity (2) was examined and compared with the experience the professionals in the current study encountered in their daily work. Another review of the literature was performed to increase our understanding of previous interventions. The aim was to provide a representative picture of the literature rather than execute a comprehensive systematic review. The previous interventions were discussed in the teams in terms of their usefulness for the design. The search (Table III) was made with an advanced search (query from title/abstract with LBP, intervention, and hypernym of different risk factors, e.g. psychological) from PubMed and Google Scholar, and the references of suitable articles were searched for additional articles. The principal patient group was patients with back pain; however, due to the lack

Table II. The professionals and their working experience

Team	Biomechanical	Psychological	Social	Lifestyle
Professionals (*n*)				
PT	3	1	1	1
Mental health PT	–	3	–	–
General physician	1	–	2	–
Occupational consultant	1	1	–	1
PMR consultant	1	1	1	1
Psychologist	–	1	–	–
Nurse	1	–	1	1
Rehabilitation counsellor	–	–	1	–
Social worker	–	–	1	–
Work experience				
Years (mean)	19	17	15	14
Sectors, at present (*n*)				
Primary healthcare	3	2	4	1
Special healthcare	1	3	2	1
Occupational healthcare	3	2	1	2
Sectors, overall (*n*)				
Primary healthcare	6	5	5	4
Special healthcare	4	4	2	2
Occupational healthcare	3	3	3	3
Duties, overall (*n*)				
Clinical experience	7	7	7	4
Development	4	5	1	1
Management	3	1	–	–
Research	1	1	2	1
Teaching	–	–	2	–

PT: physiotherapist; PMR: physical medicine and rehabilitation.

of articles that would be applicable to the healthcare system in question, a few articles from patients with other painful musculoskeletal disorders were also included. In addition, systematic reviews with other patients groups could also be accepted. In the search for articles concerning social or lifestyle factors associated with back pain, articles with interventions targeting the risk factors associated with LBP chronicity (LBP was excluded from the query) were also accepted.

The psychological theories of health behaviour were studied and their applicability for the intervention was discussed. Behaviour change techniques were examined in terms of the desired change, and were reflected in the chosen psychological theories (phase III). The main challenges for patients with LBP in functioning and health within the ICF framework were examined from a secondary analysis of a retrospective population study of patients with chronic LBP (10). The ICF framework was used to further discuss the domains where the intervention was to be targeted (phase IV). In addition, current resources were discussed as well as the problems in the clinical pathways of patients with complex LBP. The facilitators of, and barriers to, the intervention givers and receivers were identified (phase V). In the final phase of the intervention design (phase VI), the implementation road map was planned.

RESULTS

Problem identification

A systematic review was used as a basis to identify the risk factors for LBP chronicity (2). The teams discussed those factors that, in their opinion, play a crucial role in LBP chronicity (Table IV). A flow chart of patients with non-specific LBP from primary contact to the intervention was identified. The primary contact is a direct access physiotherapist (PT) when red flags or specific reasons for LBP are not identified during the treatment needs assessment. In cases where red flags are identified, the primary contact is a physician. A healthcare professional (direct access PT or physician) then performs an initial assessment and interview, excludes mechanical and specific reasons for LBP (11), gives pain education and plans the treatment and rehabilitation needs. Assessment of the risk factors for chronic LBP will be conducted during the follow-up visits (2–3 weeks from initial visit) and, if these factors are recognized, a broader multidisciplinary team will be contacted according to the factors identified.

Identifying the evidence

In the literature review, an introduction consisted of the Finnish National Current Care Guideline for treating LBP (12), previous systematic reviews considering the prolongation of pain and disability (2, 13, 14), and an article explaining the development of chronic pain (15). The reviews used to support the development of the na-

Table III. Patient/Population, Intervention, Comparison, Outcomes (PICO) search strategy for previous interventions in different risk factor groups for back pain chronicity

	Biomechanical	Psychological	Social and environmental	Lifestyle and personal
Patient	Working-age adults with back pain, or other painful MSK disorder	Working-age adults with back pain	Working-age adults with back pain, other painful MSK disorder, and/or social factors associated with LBP chronicity	Working-age adults with back pain, other painful MSK disorder, or lifestyle factors associated to LBP chronicity
Intervention	Workplace interventions, mainly targeted to biomechanical factors	Intervention targeted to psychological factors, and/or included a psychological component	Intervention targeted to social or environmental factors	Intervention targeted to lifestyle or personal factors
Control	Not specified, e.g. natural course	Not specified, e.g. natural course	Not specified, e.g. natural course	Not specified, e.g. natural course
Outcome	Reduction in pain or work disability	Reduction in pain, disability, or psychological symptoms	Reduction in pain or disability	Reduction in pain, disability or outcome on the lifestyle/personal factor

MSK: musculoskeletal; LBP: low back pain.

Table IV. Identified risk factors targeted by the intervention from the clinical experts' point of view, compared with findings from a systematic review (2)

Psychological factors		Social and environmental factors	
Clinical experience	Systematic review	Clinical experience	Systematic review
Depression	Depression	Difficulties in social affairs	Good quality of life (protective)
Anxiety	General anxiety	Challenging family obligations	–
Traumatic experiences	Post-traumatic stress disorder	Difficulties in work adaption	Support at work (protective)
Fatigue	Any psychiatric diagnosis	Workload too excessive	Work-related back pain
Catastrophizing	Catastrophizing	Returning to work after long sickness leave	–
Certain personality disorders	Somatization	Contradictions in the workplace	Non-recognition of work
Prolonged stress	Perceived stress	Financial problems	Disability compensation
Pain-related fear behaviour	Low tolerance of pain	Cultural background and age	–
Low self-efficacy, resources	Perceived risk of persistence	Level of education	–
Addictions	Coping by ignoring pain	Form of residence	–
Sleep disorders	–		
Biomechanical factors		**Lifestyle and personal factors**	
Clinical experience	Systematic review	Clinical experience	Systematic review
Physically heavy work	Particularly physical work	Multimorbidity	–
Inactive lifestyle	Physical exercise (protective)	Smoking	Nicotine dependence
Disabilities in the musculoskeletal system	Baseline disability	Diabetes	Diabetes
Unhealthy lifestyle combined	Physical wellbeing (protective)	Obesity	Obesity
–	Difficult working positions	Inactive lifestyle	Poor health
–	Carrying heavy loads	Disability	Baseline disability
–	Vibrations and jolts	Previous LBP episodes	Previous episode of LBP
		Sleep disorders	–
		–	Female sex

tional public rehabilitation guidelines organized by the Social Insurance Institution of Finland were introduced. The first review concerned the rehabilitation of musculoskeletal disorders as a whole (16), and the latter the rehabilitation of patients with subacute back pain with biopsychosocial aspects and patient stratification (17). In addition, the Cochrane review on multidisciplinary biopsychosocial rehabilitation was presented (18).

In addition to the preface, 26 studies were found suitable for strengthening the scientific foundation of the design (19–44). Details of the studies and the comments of the teams are shown in Appendix I.

Identifying the theory

The perception of different behaviour change theories was initiated with the COM-B system (45). This system works as an umbrella theory to understand different aspects of how a theory works on capability, opportunity, and motivation. Behaviour change techniques were explored to increase the understanding of the theoretical background of the techniques already used in everyday practice (46, 47). Finally, different theories were studied more closely. The theory of planned behaviour, social-cognitive theory and self-regulation theories were found suitable to form a base for the intervention (48). From the basis of the theories, the chosen behavioural change techniques were as follows:

- Goals should be timely, realistic, concrete, with graded tasks, and meet with the recipient's resources.
- Provider's support, monitoring and feedback are important, concrete exercises with the provider.
- Activities should be planned beforehand (what, where, when, how and with whom).
- Positive beliefs and self-efficacy should be amplified, discrepant views should be confronted.
- Motivation and positive changes should be amplified from the recipient's perspective, and providers should only support the recipient's own remarks.
- Recipient's limitations and strengths should be recognized, and empowering resources cherished.
- Self-monitoring with the recording of thoughts verbally and literally should be used to increase cognitive learning.
- Techniques based on self-belief (mental rehearsal, self-talk) as well as distraction should be used.
- The social and physical environment should be examined and opportunities for change should be created with the necessary services.
- Feelings of pain and discomfort should be encountered and normalized.
- Communality and reward systems should be benefitted.

Identifying needs

A secondary analysis of a retrospective population study of patients with chronic LBP (10) was examined to identify the main aspects of disability in the ICF framework. The recognition of the population's difficulties in functioning and health was used to theoretically reflect the domains targeted by the intervention. During the design phase, the recipients were not included in the team. Instead, the ICHOM (International Consortium for Health Outcomes Measurement) standard set for LBP was followed (49) This is the reference for ICHOM to identify those outcomes that matter the most to patients.

Table V. Facilitators and barriers of recipients and providers

Facilitators of recipients	The fulfilment of the need to be heard
	Individualized treatment from the beginning
	Fluent flow of the process among different intervention providers
	Working towards the essential outcomes: pain, disability, work status, quality of life and the need for medications
	Understanding increases
	Good biopsychosocial resources to participate
Facilitators of providers	Positive feedback, recipients positive progress
	Sensibleness in one's work
	True interest in the recipient
	Finding the right help for the right patient at the right time
	Small acts can make great changes
	Early interventions produce better results
	Better use of resources, low thresholds between professionals
Barriers of recipients	Mixed information from different professionals
	Nocebo, negative feedback
	Lack of understanding, approval is in progress
	The intervention does not meet with the recipients resources
	Weak biopsychosocial resources
	Previous negative experiences of interventions
	Accumulation of problems, too many comorbidities
Barriers of providers	Shortage of staff or time resources
	Inflexible timetables, to be used for the recipients in need of more time
	Difficulty in recognizing the risk factors for chronicity
	Providers negative attitudes and morale
	Sense of inadequacy

Examining current context

The facilitators and barriers of the recipients and intervention givers were discussed (Table V). Clinical experience was used to identify the facilitators and barriers of the recipients. The themes were in line with previous studies on the subject (50). Some healthcare units have the required resources and, according to the team members, their availability is adequate. The mental health resources (mental health PT, psychiatric nurse and psychologist) were seen as the most vulnerable members of the multidisciplinary team. The time resource for risk recognition was also discussed as a possible dilemma. Different aspects to increase multidisciplinary collaboration were discussed through the team members' previous experiences from their working environment.

Modelling the theory

The intervention was introduced in a logic model (Fig. 1). The model graphically represents the needed resources, their activities and intended effects, and the assumptions and contextual factors where the intervention operates (51). The healthcare professionals needed depend on the patient's personal needs and the underlying risk factors. When certain risk factors are recognized, the process owner (e.g. in the biomechanical group PT; bold text in Fig. 1) will take charge of the multidisciplinary assessment and invite all the required professionals to the process. Additional inputs are principally contacted via a referral from the physician.

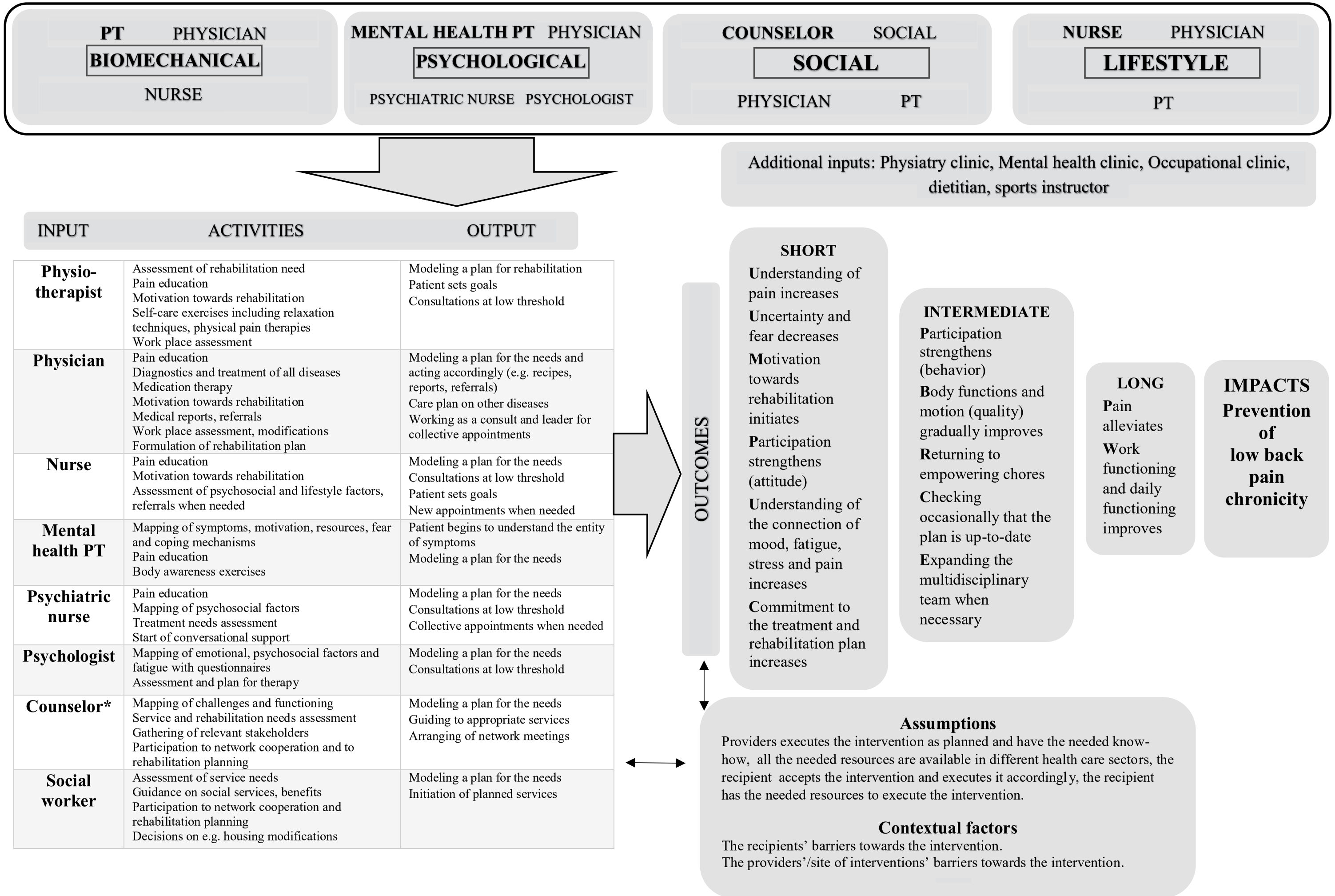
DISCUSSION

This study outlines the design process of a multidisciplinary, tailored biopsychosocial intervention for the prevention of LBP chronicity. The design process was conducted using an iterative approach, since the elements have reciprocal relations (5). In future, a new reflection on the design elements will be collected from a feasibility study. Furthermore, economic considerations will be conducted with a cost-benefit analysis before a larger intervention study.

Adequate resources in the primary and occupational care for the early recognition of LBP chronicity should lead to cost-effective clinical pathways. At present, the prevalent clinical pathways in high-income countries are costly, and the financial burden is projected to increase in the coming decades (52). Global disability caused by LBP is highest among the working-age populations. In Europe, LBP is one of the most common causes of medically certified sick leave and early retirement (52). In addition, there is a correlation between longer-term disability and work absence extending beyond 1 month (53). These findings should encourage healthcare providers to find functional solutions to the primary contact site of patients with LBP.

Local resources may vary, which may complicate the implementation of the intervention. It is, therefore, desirable that the feasibility study should verify the resource needs identified in this design. Other implementation challenges are related to the reception of the intervention. To be accepted by the recipients, sufficient resources must be allocated for patient education before the intervention process begins. With limited time resources, the use of high-quality patient material (54) is strongly suggested. In addition, healthcare professionals must have adequate skills to recognize specific reasons for LBP, which might need different treatment approaches, such as interviews and examinations. In case the feasibility study, cost-benefit analysis, and larger intervention study find the designed intervention superior to present clinical practice, a strategy and evaluation protocol for the implementation should be created. A team of professionals is needed to define widely the outcome measures of the implementation (e.g. use of valid questionnaires such as Determinants of Implementation Behavior Questionnaire) (55), to monitor, as well as continuously develop, the process.

In this study, multidisciplinary teams brought their clinical experience to common use and the conversation was enriched with current scientific knowledge. Healthcare professional teams embedded within a



INPUT	ACTIVITIES	OUTPUT
Physio-therapist	Assessment of rehabilitation need Pain education Motivation towards rehabilitation Self-care exercises including relaxation techniques, physical pain therapies Work place assessment	Modeling a plan for rehabilitation Patient sets goals Consultations at low threshold
Physician	Pain education Diagnostics and treatment of all diseases Medication therapy Motivation towards rehabilitation Medical reports, referrals Work place assessment, modifications Formulation of rehabilitation plan	Modeling a plan for the needs and acting accordingly (e.g. recipes, reports, referrals) Care plan on other diseases Working as a consult and leader for collective appointments
Nurse	Pain education Motivation towards rehabilitation Assessment of psychosocial and lifestyle factors, referrals when needed	Modeling a plan for the needs Consultations at low threshold Patient sets goals New appointments when needed
Mental health PT	Mapping of symptoms, motivation, resources, fear and coping mechanisms Pain education Body awareness exercises	Patient begins to understand the entity of symptoms Modeling a plan for the needs
Psychiatric nurse	Pain education Mapping of psychosocial factors Treatment needs assessment Start of conversational support	Modeling a plan for the needs Consultations at low threshold Collective appointments when needed
Psychologist	Mapping of emotional, psychosocial factors and fatigue with questionnaires Assessment and plan for therapy	Modeling a plan for the needs Consultations at low threshold
Counselor*	Mapping of challenges and functioning Service and rehabilitation needs assessment Gathering of relevant stakeholders Participation to network cooperation and to rehabilitation planning	Modeling a plan for the needs Guiding to appropriate services Arranging of network meetings
Social worker	Assessment of service needs Guidance on social services, benefits Participation to network cooperation and rehabilitation planning Decisions on e.g. housing modifications	Modeling a plan for the needs Initiation of planned services

Fig. 1. Logic model for the intervention. The first contact in the different risk factor groups is shown in **bold** text.
*Rehabilitation counsellor, customer counsellor, social counsellor or nurse, depending on local resources.

complex system enabled team members to understand that rehabilitation as a complex system is not unitary, but an interdisciplinary concept constructed by different scientific terms. The teams explored answering "what if" questions to avoid the traps of rehabilitation defined solely by one discipline or profession. By doing this they were able to evaluate how alternative rehabilitation plans might be developed.

Although accurate plans for the recognition of the risk factors associated with pain chronicity were not in the scope of the intervention design phase, they were discussed within the teams. Different questionnaires (see Appendix I for team's comments) were found to be suitable, going through the health records before the appointment was seen as important, as were bringing up the issues of mood, social situation, and lifestyle factors in the assessment conversation. In addition, evaluation of the outcomes was considered. The ICHOM working group (49) recommends using the Numerical Pain Rating Scale (NPRS), the Oswestry Disability Index (ODI), and EuroQol-5D for the evaluation of pain, disability and quality of life. 15D for health-related quality of life and Net Promoter Score (NPS) for patient satisfaction were also found to be suitable for the evaluation.

In future, artificial intelligence (AI) will help scientists to find answers for risk recognition. Moreover, AI technologies (10) could fill the gap in tailored solutions and help to achieve successful clinical pathways. However, AI cannot be exploited successfully until a mutual holistic understanding between all key healthcare professionals involved in the rehabilitation process is achieved.

This study has some limitations. The facilitators and barriers of the implementation site were not listed, as the exact site for the study was not decided during the design phase. However, the barriers connected to the resources, and the agreement regarding the possible variations were discussed, so that the intervention can still maintain the integrity of the core components while varying across different contexts (9). The absence of the recipients during the design phase was a weakness of this study. However, the completed intervention design was introduced to a LBP patient forum (10 experts by experience), where the intervention received mainly positive feedback. The exploitation of current resources on behalf of patients with LBP, the structure of the intervention, and low thresholds between professionals were mentioned. Education of professionals, especially regarding the patient encounters, the availability of resources in terms of time, and skilful professionals were listed as development targets. In addition, patient satisfaction, and their overall opinion on the intervention will be collected during the feasibility study before larger intervention. The intervention will be conducted as a case-control study to avoid the confounding factors of local phenomena.

In the near future, it is hoped that more biopsychosocial primary healthcare interventions from similar healthcare systems will be developed, so that benchmarking analyses can be conducted. It would also be beneficial to find an agreement on the evaluation of implementation and outcomes for an effective comparison.

In conclusion, this study developed a multidisciplinary rehabilitation for non-specific LBP, which holistically considers the entities of functioning, disability, and health in accordance with the ICF framework. The design has the potential to broaden our understanding of disability, lower the threshold for collaboration between different healthcare professionals and healthcare sectors, move the rehabilitation pathway towards preventive services, and decrease the risk of pain chronicity.

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PUBLICATION IV

A holistic perspective on disability with graph machine learning.

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Submitted.

A holistic perspective on disability with graph machine learning

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Abstract

Introduction: A comprehensive perspective on disability is useful when making assessments for treatment and rehabilitation. World Health Organizations' International Classification for Functioning, Disability, and Health (ICF) has been developed for such a purpose. However, its complex structure poses a problem for wider implementation.

Objective: The main aim of this feasibility study is to test the semantic matching abilites of a graph machine learning engine application, Headai Graphmind, to recognize ICF codes from the free text of electronic health records written in the Finnish language.

Methods: The dataset of 93 patients aged 18 to 65 years with chronic low back pain was collected. The data of 20 randomly selected patients were used as a training set. Graphmind was tested on a second randomly selected sample of 20 patients.

Results: Headai Graphmind reached a sensitivity of 83.1% and specificity of 99.8% when compared to the results of a domain expert. The application was able to find 112 distinct ICF codes compared to 119 codes found by the domain expert.

Conclusions: The presented application seems applicable for gaining holistic perspective on disability. In future studies, the validity and reliability of the application will be further tested on new datasets and graph networks extended to enable feasibility in other medical fields and time series analysis. Furthermore, preparations for international collaboration are being made to enable the utilization of the application in other languages.

1 Introduction

How can we comprehensively treat a patient who has prolonged pain, so that the onset pain chronicity becomes preventable? What are the obstacles preventing this patient with multiple morbidities from returning-to-work? The answers to the holistic perspective on disability and health can usually be found in the health records of individual patients or in group-specific clusters (1). However, exploring the answers to these questions is a challenge that cannot be achieved by evaluating diagnosis codes alone. For example, two patients with the same low back pain diagnosis can have completely different disability levels, with the first patient coping at work, whereas the second patient has major difficulties coping and low quality of life (2).

To better understand disability holistically, the World Health Organization (WHO) has developed the International Classification of Functioning, Disability, and Health (ICF) framework (3). When used as part of disability assessment, the ICF can create not only a broader and more complete picture of the disability but can also reflect the patients' self-reported problems more closely than a typical medical assessment (4). Previously, different approaches have been used to integrate the ICF with electronic health records (EHR) (1), predominantly in rehabilitation settings, and in some cases where the ICF is embedded in health information systems (5). However, the optimal implementation of the ICF, including structured documentation conducted by health care professionals has been slow. This delay has been mainly due to its complex structure of the ICF taxonomy that comprises more than 1600 codes representing different domains of disability (1,6). There is, therefore, an urgent need for efficient and reliable methods to enhance the wider implementation of the ICF in health care settings.

The use of artificial intelligence (AI) techniques shows promise in the implementation of ICF, since they have the capability to solve complex tasks. Likewise, AI techniques could also serve to promote a broader understanding of those factors concerning the disability of the patients (7). It should, however, be noted that AI and machine learning (ML) are umbrella terms for thousands of algorithms, methods, and setups with varying degrees of performance in the execution of different tasks. Therefore, the selection of a suitable AI/ML algorithm is complicated. For example, deep learning algorithms perform well in categorizing tasks when the task is well defined and training material is large enough. In contrast, deep learning cannot perform well in cases where task is ill defined and requires human reasoning to work with unknown factors (8). In a previous study on the subject, Newman-Griffis and colleagues used natural language processing (NLP) technique for linking free text to 29 ICF-based categories (9).

A semantic network -based ML engine, Headai Graphmind, which has the capability to imitate human reading and processing of texts, has been applied to forecast future skill needs in the labor market and to optimize learning paths for the future workforce using curriculum gap assessment (10,11). In previous studies graph-based machine learning or semantic network -based setups have shown promise in different complex settings (12–14). Graphmind adds, modifies, and reasons natural language according to conceptual learning theories (15), whereas semantic network (graph) serves as a structure for all the data learned. This type of technology, which can operate with unstructured data and in a context where formal procedural rules for matching are unknown, has the potential to fully utilize EHR information and harness crucial data for further analysis conducted by health care professionals ((14).

A good example of the applicability of the application is in the risk recognition of patients with low back pain (LBP). Although much research and resources have been devoted to LBP during the last decades (16), the burden of LBP has increased making it the most burdensome global health problem affecting years lived with disability (YDL) (17). However, not all patients with LBP go on to develop a chronic pain problem (18). Indeed, the increased use of health care resources and the rise in costs related to LBP are driven more by chronic than acute cases (19). Therefore, strategies that ensure the early identification of those patients at risk for persistence of pain and disability should be developed and implemented (20). At present, questionnaires such as the STarT Back Screening Tool (SBT) (21) and the Örebro Musculoskeletal Pain Screening Questionnaire (ÖMPSQ) (22) are used to identify psychosocial factors related to prolonged pain and disability. The main drawback with these questionnaires is that they are not comprehensive enough to recognize all the relevant factors (23) for a holistic decision-making. Thus, new approaches should be developed for the identification of a broader range of biopsychosocial factors concerning disability and health (7), along with the contextual and health system-related issues that affect the content of the intervention (24). The findings of our preliminary study (14) suggest that Graphmind could have the potential to facilitate the timing and tailoring of interventions in the LBP patient population. The exploration of this potential may provide a crucial turn for understanding disability and health of individuals in ageing societies.

In this feasibility study, the electronic health records of chronic LBP patients are used to generate natural language definitions of the ICF. The main aim of the study is to test the internal validity of Headai Graphmind applied to determine semantically best matches between the ICF code definitions and natural language of the EHR. The reliability of Graphmind is tested against the findings of a domain expert, who has profound understanding on the EHR in question, on disability of LBP patients, and the ICF. Our research questions were as follows: What factors of disability can be found from the electronic health records of patients? Can an AI method perform factor recognition reliably enough to support health care decision-making when compared to a domain expert?

2 Methods

2.1 Data architecture and data processing

The generic idea behind Graphmind is that it has a pre-trained semantic understanding of language. This understanding is based on gigabytes of generic data from research papers (open journals), policy papers (such as the European Union's archive), labor market information (e.g. job ads) and professional news (technology, business, medical, and so forth). The training data have been selected from sources that are widely used and trusted, as it affects the semantic behavior of the engine. When reading this training data Graphmind learns what words are meaningful, when the words establish a compound word (also called n-grams in linguistics), what is the relation between the words and n-grams and eventually the context of the used words and n-grams. This semantic network is applied when starting to perform reasoning between ICF code descriptions and real-world texts from the EHR. Graphmind turns the EHR texts into a similar type of semantic network as the pre-trained language model (figure 1). After that, it starts to fit the ICF descriptions to the EHR semantic network and applies the pre-trained language model to understand the small data, such as synonyms, neighboring concepts, similar meanings, and so forth, better. This two-layer approach enables matching between two small datasest without getting stacked into a lack of structured data or non-matching words.

The data architecture (figure 2) from the EHR to Graphmind to the research environment was built to meet high data security and privacy requirements. All the data from the EHR were provided as an encrypted pseudonymized csv. -file on a memory stick that was extracted offline on Graphmind's side. In a preliminary study (14), 12 different ICF definition sets were studied to find the most functionable setups. The best performing candidates that were chosen for this study (called ICF title, ICF real life, ICF real life fuzzy, MesH words, MeSH-ICF title), were also imported to Graphmind before the analysis. However, because these datasets were not GDPR (General Data Protection Regulation) -data, they were imported directly from the csv. -file without encryption.

The matching between the EHR data and the ICF definition sets were run in offline mode and the results with pseudo-identifier were copied into the research environment with authenticated network access. The offline nature of the Graphmind process means that all the data and computing are done outside the network-accessible directories of the Headai Graphmind computing infrastructure, and Graphmind itself is connected to the network and only few directories are accessible via the network.

The Graphmind semantic matching process is described in more detail in figure 3. The written texts in the EHR are turned into semantic networks / knowledge graphs. Each patient's semantic network is analyzed against each of the more than 1600 ICF definitions in the chosen definition sets, meaning that approximately 36 000 analyses were performed per patient in this study. Graphmind's semantic matching is based on shallow neural networks, so this analysis only took between 2 to 10 seconds in one CPU core per patient, depending on data volume and data complexity. In this study the stored patient's semantic network (JSON_GRAPH in figure 3) was only used to support the domain expert's evaluation.

2.2 Population data

This study used patient data gathered between October 2019 and February 2021. The natural language data were free text (Finnish language) consisting of the EHR of patients with low back pain who attended the department of Physical Medicine and Rehabilitation at Tampere University Hospital, Finland. Additional information was collected in the form of quantitative data, which were retrieved from medical history forms. The quantitative data were used for the data selection process (the fulfillment of the inclusion and exclusion criteria, table 1). The data were collected retrospectively after the treatment period had ended and the patient had returned to primary or occupational care. Since the study was registry-based and the integrity of the patients was maintained, the ethical committee of Tampere University Hospital waived the need for an ethical approval or an informed consent from the patients for this study. Additionally, Finnish research legislation on the secondary use of health and social data (legislation no. 552/2019) (25) allowed the retrieval of the retrospective data from the EHR for research purposes without an informed consent from the patients. In the present study, since the data was gathered from a single data source, a data transfer contract was drawn up between the researchers and the data controller, Tampere University Hospital, Finland. All methods were carried out in accordance with relevant guidelines and regulations.

Low back pain was defined as pain in the anatomical region between the costal margins and the inferior gluteal folds with or without radicular pain. Multifocal pain was not an exclusion criterion. Inclusion and exclusion criteria are presented in table 1.

The electronic health records datasets of 20 patients were randomly selected to form a training set for Graphmind. The free text annotation, being the linking of the ICF to the EHR, applied the principals of proposed ICF linking rules (26). A domain expert searched the EHR texts of the training dataset for suitable words and n-grams that represent the contents of the ICF. These words and n-grams were further annotated with the ICF codes. In addition, the developed vocabulary was enriched with the domain expert's perspective on the language used by professionals ("jargon") in case some words or n-grams were missing from the training dataset. For example, code b4550 “general physical endurance” was labeled with words such as physique, basic physical health, and fitness.

Another twenty randomly selected electronic health records datasets were used for the quality analysis of Graphmind. The same domain expert who assembled the training data also evaluated the Graphmind results. Both samples of the study population were obtained using computer-based randomization. The search of the contents and further annotation with the ICF codes repeated the method of the training set compilation. The disability information gathered from the free texts was synthesized quantitatively to gain understanding of the ICF factors found (table 2). The results were analyzed by the domain expert between the original EHR data end results in the research environment. Only the author, who had access to both systems, participated in this part of the study.

The results were interpreted by the domain expert in the following manner. The finding was defined as true positive if the algorithm found the same code as the domain expert from the free text of one patient. False positives were the codes that the domain expert did not find and, after reappraisal, were still regarded as false findings. Codes were defined as false negatives if a code was found by the domain expert but not by the algorithm. Additionally, there were codes that were first found by the algorithm and, after reappraisal, found by the expert as well.

The population data were analyzed with IBM SPSS Statistics for Windows, Version 28.0, for mean and 95% confidence intervals.

3 Results

3.1 Study population

The flow diagram (figure 4) presents the selection of the patient sample. The EHR of 93 patients were collected for the purposes of this and the preliminary research (14). In total, the EHR comprised 312 physicians’ notes in total, including texts of referrals, physical appointments, and contacts by phone and letter. The characteristics of the patient population are presented in table 3.

The ICF core set of the population data differed only minimally from the core set assembled by the WHO (27). Table 2 presents the quantitative findings of the domain expert from the evaluation dataset (EHR from 20 patients, 63 EHR notes). The mention of body structures was the highest (n=1,444), which was not unexpected, as “low back” can be repeated several times in the notes. Interestingly, the notes also contained versatile information on other domains related to disability, such as neuromusculoskeletal and movement -related functions (n=349), information on joint and bone mobility and muscle endurance, information on products and technology (n=253), information on medication, and the mobility aids the patients used. Additionally, mental functions (n=99) contained information on sleep quality, mental and personality disorders, emotions, and mental energy levels. Social factors were available from community, social, and civic life (n=103) or major life areas (n=89) where work-related factors are described.

3.2 Headai Graphmind

Graphmind was analyzed for its semantic matching abilities of factor recognition in the four domains of ICF: body structures (S codes), body functions (B codes), activities and participation (D codes), and environmental factors (E codes) (table 4). Graphmind performed the matching on the data of the whole population (93 patients, 312 EHR notes). In addition, to obtain an estimate of Graphmind’s reliability, the evaluation of the factor recognition was performed on a random sample of the EHR of 20 patients (63 EHR notes) due to the exhaustive nature of the evaluation process.

The algorithm reached a sensitivity of 83.1% (95% CI 79.9 to 86.3) and specificity of 99.84% (95% CI 99.80 to 99.89). Sensitivity was the highest in both the environmental factor and body structure domains (85.2%) and the lowest in the activity and participation domain (77.7%), whereas specificity was the highest in the body structure domain (99.95%) and the lowest in the body function domain (99.74%). Furthermore, when comparing the content of the codes, the domain expert found 119 distinct codes (30 s codes, 35 b codes, 40 d codes, and 14 e codes) from the evaluation dataset, whereas the algorithm found 112 codes (30 s codes, 35 b codes, 35 d codes, and 12 e codes).

4 Discussion

The main finding of this feasibility study was that the selected AI method, Headai Graphmind, performed the factor recognition of ICF information from EHR of patients with low back pain with convincing sensitivity and specificity when compared to the results of the domain expert. Concerning the first study question, the EHR notes of individuals with chronic LBP were expressive, containing holistic information about the individuals' disability. Compared to a previous study on the subject (9), a wider selection of ICF-based categories was obtained. Gaining this information from the patient population makes it possible to holistically support the decision-making in the treatment and rehabilitation assessments of individuals.

Furthermore, these results offer the promise of a new functionable application for the benefit of personalized medicine, where an individualized model of the patients' history can be used to take preventative actions (28). The ICF frameworks' perspective identified from the EHR can broaden our understanding of those factors affected by the patients' medical condition, and the kind of obstacles that can emerge in the healing process. Interestingly, the universal, interdisciplinary language of the ICF can be applied globally in different health care settings and by different health care professions to produce a broader biopsychosocial understanding of disability (1). Additionally, when individuals have a broader view of the health challenges as well as their strengths, they can be empowered to the necessary steps to care of their own health.

EHR combined with the ICF framework can act as a support tool for health care professionals in decision-making, and it can decrease the time spent browsing through the EHR. Thus, the health care professionals can then use their time and effort making more comprehensive care and rehabilitation plans as well as developing high-quality patient- health care professional relationships. At the population level, we can examine, for example, the older population or a specific disease group. For example, those factors associated with pain and disability prolongation in patients with LBP can be linked with ICF definitions. Therefore, the developed application can be beneficial both for patients with LBP and stakeholders involved in the rehabilitation decision-making process for making timely, personalized decisions. In particular, health care policy makers can better see what themes of disability and health arise from the community, so that resources can be allocated more efficiently.

Since Graphmind is based on shallow neural networks, the speed (and resulting low energy consumption) enables large scale analysis in e.g. monthly analysis. Likewise, it takes approximately 15 days to analyze 1 000 000 patient records with 8 core computing setups, which, at the moment, can be regarded as a very low requirement. Concerning data safety issues and the embedding of AI architecture to current computing architectures (29), Graphmind can work as a plug-in and does not require any software integration. In future, the graph will be extended with the ICF codes and visualized as a network, which could be an effective interface for health care professionals who wish to read the reasoning of the matching and codes in a few seconds.

When using AI-derived information for decision support, it is important to make sure that noise in the health care data does not drive the decision-making. Consequently, it is up to the end-user to make sure that the information does not lead to unintended effects, such as discrimination, increased inequities, and decreased inclusion (30).

The data used in this present study had some limitations. The data consisted of only the medical notes of physicians, and other relevant professional groups were missing. Therefore, the results of the present study can only be generalized to physicians' notes and patients with low back pain. A further analysis of construct validity will, therefore, be needed to study the sensitivity and specificity of Graphmind with the notes of other health care professionals and patient groups.

Another question that was not answered within the scope of the present study regards the detection of ICF qualifiers. The purpose of the qualifiers is to indicate the extent and quality of the impairment (6). However, some possible solutions for the problem did emerge during the study. First, the annotation can be extended to separate the negative and positive phrases, and their nuances to distinguish the qualifiers. Second, the recognition of the extent of the impairment can be left to the end-users by visualizing the words and n-grams from where the ICF code was retrieved. Third, a quantitative cumulation of the codes could act as a trigger for notification. And finally, the notes of professionals usually state the problems that patients are struggling with, so that ICF codes alone, without the qualifiers, already provide a lot of information to work with.

The presence of only one domain expert doing the annotation and the analysis can be regarded as both a strength and weakness in this study. On the one hand, the annotation and analysis proceeded in a homogenous way, but on the other multiple experts would have brought different interpretations of the text and results, thereby strengthening the study, especially for future applicability. In the future validation process, inter rater reliability will be tested.

A semantic network-based ML engine is capable of conceptual reasoning in challenging domains. However, it must be noted that Graphmind's performance was at its best in two cases: with training data based on ICF titles and with training data based on the domain expert's short explanations of the ICF code written in professional language. When applying Medical Subject Headings (MeSH) vocabulary or too generic definitions as training data, the results were not that good (which was expected). Indeed, this finding agrees with the results of earlier studies on semantic computing, i.e., the smaller the training data are, the more critical the quality of the data is. Thus, although semantic computing cannot solve ICF coding alone, it can be applied effectively when there is enough computational, linguistic, and health care expertise involved.

Several future implications emerged during our study. As part of the study, only one semantic network was performed per patient to study the quality of the process. In future, however, yearly networks can be performed per patient to enable time series analysis. Furthermore, new studies on the validity and reliability of the developed application must be conducted with texts unrelated to chronic pain. At present, Graphmind performs fluently in English, Swedish, Estonian, and Finnish, has beta versions available in Spanish and German, and prototypes in 17 other languages. This will enable the global use of the application in new electronic health record settings. It should be noted, however, that data silos pose a problem for efficient data processing in many health care ecosystems. In Finland, there is a centralized archive of electronic patient data, making data standardization possible (31). There are also initiatives towards unified health care records in the Nordic countries (32) as well as in the European Union (33).

In conclusion, this feasibility study suggests that the method developed here has the capability to be used as an interface in the current computing architectures of health care facilities for making personalized decisions in rehabilitation settings as well as in acute environments.

5 Conflict of Interest

Authors H.K. and J.V. are employed by Headai. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

6 Author Contributions

All the authors contributed to designing the study. L.N. worked as the domain expert, collected the data, generated the training and evaluation datasets, annotated the texts, and analyzed the algorithm's results. H.K. developed the algorithm, the data architecture, and controlled the data procession. L.N. and H.K. wrote the manuscript, with inputs and critical appraisals from J.V. and M.K.

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9 Data Availability Statement

The original patient data in this study were used under a data transfer contract and are not publicly available due to General Data Protection Regulations. However, data are available from the corresponding author upon reasonable request and with permission of Tampere University Hospital, Finland. Headai Graphmind is a commercial semantic computing infrastructure. It can be licensed and run in Linux and Azure clouds and servers in isolated mode (as done in this study). Furthermore, Graphmind REST-API is available for cases where data can be transferred to internet.

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Table 1. Inclusion and exclusion criteria. LBP= low back pain, SBT= STarT Back Screening Tool, VAS= Visual Analog Scale.

Inclusion criteria	Exclusion criteria
Age 18 to 65 years LBP symptoms ≥ 3 months SBT questionnaire fulfilled Pain chart fulfilled Social security number available VAS ≥ 3	Malignancy Recent traumatic fracture to the pain region Osteoporotic fracture Infection (i.e., epidural abscess) Ankylosing spondylitis Modic 1 changes Unstable spondylolisthesis Anomaly of the bone in the pain region Severe scoliosis (>45°) A nerve root disorder with apparent dermatomal and/or myotomal Radiculopathy (pain, numbness, paresthesia, tingling, muscle weakness) Any other obvious specific reason for LBP

Table 2. The quantitative findings of ICF chapter level domains in the EHR of the evaluation dataset (20 patients). The number of findings is presented in brackets. Chapter domains with only one or no findings are excluded.

<table>
<tr><th colspan="2">Body</th></tr>
<tr><th>Function, B (n=896)</th><th>Structure, S (n=1444)</th></tr>
<tr><td>Sensory functions and pain (366)
Neuromusculoskeletal and movement related functions (349)
Mental functions (99)
Functions of the digestive, metabolic and endocrine systems (62)
Genitourinary and reproductive functions (12)
Functions of the cardiovascular, hematological, immunological and respiratory systems (8)</td><td>Structures related to movement (1364)
Structures of the nervous system (73)
Structures related to the digestive, metabolic and endocrine systems (7)</td></tr>
<tr><th colspan="2">Activities and participation, D (n=569)</th></tr>
<tr><td colspan="2">Mobility (310)
Community, social, and civic life (103)
Major life areas (89)
Self-care (44)
Domestic life (16)
Interpersonal interactions and relationships (7)</td></tr>
<tr><th colspan="2">Environmental factors, E (n=692)</th></tr>
<tr><td colspan="2">Services, systems, and policies (298)
Products and technology (253)
Support and relationship (137)
Natural environment and human-made changes to environment (4)</td></tr>
</table>

Table 3. Characteristics of the study population. BMI= Body Mass Index, LBP= Low back pain, NSAID= non-steroid anti-inflammatory drug, VAS= Visual Analog Scale, SBT= STarT Back Tool. SBT Q3= I have walked only short distances because of my back pain, Q4=In the last two weeks, I have dressed more slowly than usual because of my back pain.

Variable	Population (n=93)
Male (n/%)	30/32%
Age (mean)	45 years (95% CI ±2 years)
BMI (mean)	28.3 (95% CI ± 2.7)
Duration of LBP (n/%)	
3-6 months	6/6%
6-12 months	14/15%
1-2 years	15/16%
2-5 years	17/18%
5-10 years	8/9%
>10 years	33/36%
On pain medication (n/%)	86/92%
NSAID	69/74%
Paracetamol	42/45%
Opiate	30/32%
Neuropathic pain medication	25/27%
VAS in motion (mean)	6.3 (95% CI ±0.6)
VAS in rest (mean)	5.5 (95% CI ±0.5)
SBT score	
total score (mean)	7 (95% CI ± 0,3)
sub score Q5-9 (mean)	4 (95% CI ±0,2)
Yes on Q3	64/69%
Yes on Q4	51/55%
On sick leave due to LBP	61/66%
less than 30 days	11/18%
1-3 months	24/39%
4-6 months	5/8%
over 6 months	17/28%
N/A	4/7%
"I can work in the same profession in 2 years' time despite my health"	
Most definitely	13/14%
I'm not sure	42/45%
Probably not	31/33%
N/A	7/8%
Has had physiotherapy	76/82%
Has been in institutional rehabilitation	15/16%
Has imaging studies done	83/89%

Table 4. Results of the factor recognition. S= body structures, B= body functions, D= activities and participation, E= environmental factors.

	S	B	D	E	Total
Expert found	**423**	**311**	**226**	**112**	**1072**
Graphmind found					
codes in total	371	312	208	100	**991**
true positives	368	285	195	94	**942**
false positives	3	27	13	6	**49**
false negatives	63	53	55	20	**191**
codes better than expert	4	14	12	1	**31**
Correct codes in total	427	325	238	113	**1103**
Sensitivity %	85.2%	84.4%	77.7%	85.2%	**83.1%**
(95% CI)	(82.3-88.0)	(80.9-87.8)	(71.7-83.8)	(76.0-94.4)	**(79.9-86.3)**
Specificity %	99.95%	99.74%	99.86%	99.89%	**99.84%**
(95% CI)	(99.90-100)	(99.65-99.82)	(99.80-99.92)	(99.81-99.97)	**(99.80-99.89)**

Figure 1. Simplified and cleaned example of the semantic network model after Graphmind has read the EHR texts.

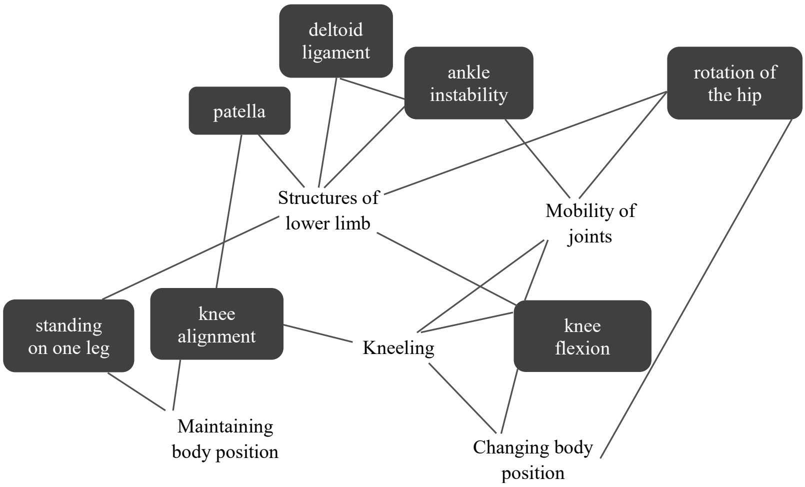

Figure 2. Data architecture and components.

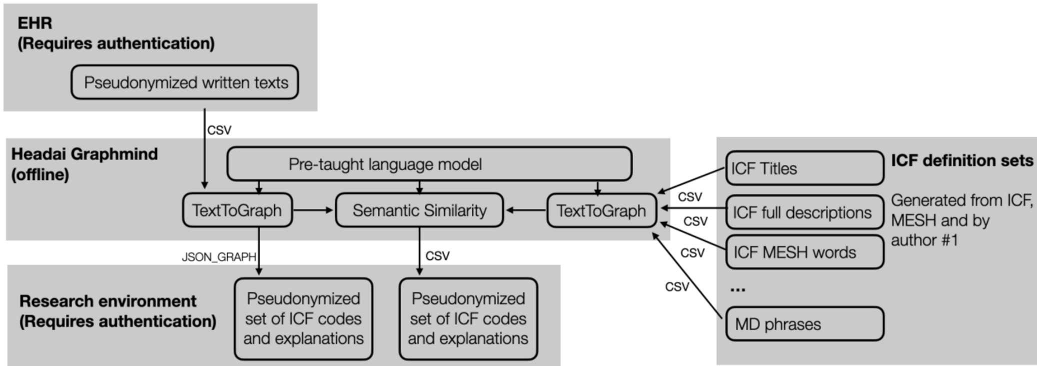

Figure 3. Graphmind's semantic matching process in the current study. MD= Medical doctor.

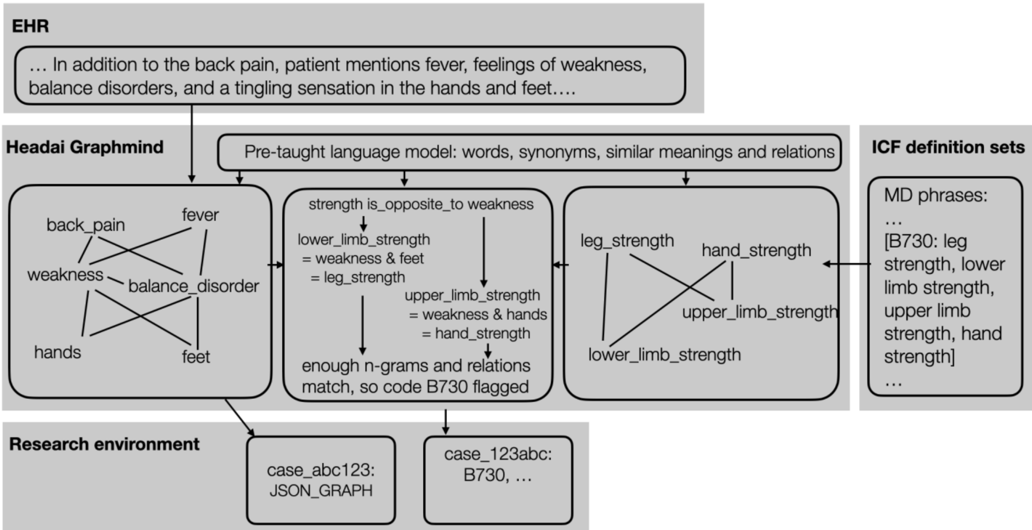

Figure 4. The flow diagram of the patient selection.