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POSSIBILITIES OF ARTIFICIAL INTELLIGENCE FOR EVALUATING OF MULTIMODAL TREATMENT OF CHRONIC PAIN

RESEARCH PAPER - LITERATURE REVIEW

Author of the Research Paper:
Noora Multala
Student identity card No 042475
/signature/

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Research Supervisor:
Ināra Logina
Professor
RSU Department of Anaesthesiology and Intensive Care

/signature/
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TABLE OF CONTENTS

INTRODUCTION

Chronic pain (CP) is a widespread and multifaceted health problem that affects as much as 30% of people globally, contributing to disability, diminished quality of life, and considerable socioeconomic strain [Cohen et al., 2021; Goldberg & Mcgee, 2011]. CP is recognized not only as a clinical issue but also as a public health challenge due to its association with reduced productivity, high health care costs, and its impact on families and communities. Chronic pain is often compounded with psychiatric comorbidities such as depression, anxiety, and sleep disturbance, forming cycles that complicate management and recovery [Stretanski et al., 2025].

A key difficulty in treating chronic pain lies in the highly subjective nature of pain assessment. Conventional tools, including the visual analogue scale (VAS) and numeric rating scale (NRS), depend on self-reported patient experiences. While these measures are widely used, they provide an incomplete representation of the multidimensional nature of pain and are influenced by individual reporting variability. Moreover, the lack of reliable biomarkers and objective physiological indicators makes it difficult for clinicians to accurately evaluate pain severity and treatment efficacy [Mouraux & Lannetti, 2018; Davis et al., 2020]. The reliance on subjective assessment can delay accurate diagnosis, misguide treatment adjustments, and complicate clinical decision-making.

Standard treatments, such as pharmacological and interventional strategies, can often fall short in providing long-term efficacy. Opioids, although often prescribed in chronic pain treatment, carry risks of misuse, dependence, and adverse effects when used for chronic non-cancer pain [Cai et al., 2021]. Multimodal approaches that combine pharmacological, interventional, psychosocial, and rehabilitative modalities are considered the best practice, but personalization of these strategies remains a persistent challenge due to the heterogeneity of chronic pain presentations [Cohen et al., 2022].

Within this context, artificial intelligence (AI) has emerged as a promising innovation in healthcare. AI systems can synthesize diverse datasets – using clinical, demographic, physiological, imaging, and molecular domains – to uncover hidden patterns and generate predictions that can enhance diagnostic precision, support individualized therapy, and guide resource allocation [Khan et al., 2024; Hagedorn et al., 2024]. By using large-scale data, AI offers a potential solution to the limitations of conventional chronic pain management, in which subjectivity and variability limit treatment success.

The core four aspects reviewed are: 1) To outline methodological foundations of AI and its principal techniques relevant to chronic pain, 2) to describe clinical applications of AI, including predictive modelling, opioid risk assessment, neuromodulation optimization and digital health tools, 3) to assess AI's contribution to precision medicine, particularly through omics, biomarkers, sensors and wearable devices and 4) to discuss existing limitations, ethical challenges and future directions for AI integration into chronic pain management. By addressing these objectives, this review aims to present a comprehensive perspective on how AI may transform chronic pain care, advancing from experimental models toward clinically impactful, patient-centered strategies.

IEVADS

Hroniskas sāpes ir plaši izplatīta un daudzdimensionāla veselības problēma, kas skar līdz pat 30% pasaules iedzīvotāju, veicinot invaliditāti, dzīves kvalitātes samazināšanos un ievērojamu sociālekonomisko slogu [Cohen et al., 2021; Goldberg & Mcgee, 2011]. Hroniskas sāpes tiek atzītas ne tikai par klīnisku problēmu, bet arī par sabiedrības veselības izaicinājumu saistība ar samazinātu produktivitāti, augstām veselības aprūpes izmaksām un negatīvu ietekmi uz ģimenēm un kopienām. Hroniskas sāpes bieži pavada psihiskas komorbiditātes, piemēram, depresija, trauksme un miega traucējumi, kas savukārt apgrūtina ārstēšanu un atveseļošanos [Stretanski et al., 2025].

Viena no galvenajām prolēmam hronisku sāpju ārstēšanā ir sāpju novērtējuma subjektīvā daba.. Tradicionālie instrumenti, piemēram, vizuālā analoga skala (VAS) un numeriskā novērtējuma skala (NRS), balstās uz pacientu pašnovērtējuma datiem. Lai gan šie rīki tiek plaši izmantoti, tie sniedz nepilnīgu priekšstatu par sāpju daudzdimensionālo raksturu un tos ietekmē atškirības individuālajos vērtējumos. Turklāt uzticamu biomarķieru un objektīvu fizioloģisko indikatoru trūkums apgrūtina klīnicistiem precīzi novērtēt sāpju stiprumu un ārstēšanas efektivitāti [Mouraux & Lannetti, 2018; Davis et al., 2020]. Paļaušanās uz subjektīvu novērtējumu var aizkavēt precīzu diagnozi, iētekmēt ārstēšanas izvēles un sarežģīt klīnisko lēmumu pieņemšanu.

Standarta ārtēšanas pieejas, piemēram, farmakoloģiskās un intervencionalās stratēģijas, bieži vien nespēj nodrosināt ilgtermiņa efektivitāti. Opioīdi, lai gan bieži tiek izrakstīti hronisku sāpju ārstēšanai, rada riskus saistībā ar ļaunprātīgu lietošanu, atkarības veidošanos un blaknēm, ja tos lieto hronisku, ar vēzi nesaistītu sāpju gadījumā [Cai et al., 2021]. Multimodālas pieejas, kas apvieno farmakoloģiskos, intervencionālos, psihosociālos un rehabilitacijas aspektus, tiek uzskatītas par labāko praksi, tomēr šo stratēģiju personalizācija joprojām ir izaicinājums hronisku sāpju heterogenitātes dēļ [Cohen et al., 2022].

Šajā kontekstā mākslīgais intelekts (MI) ir kļuvis par daudzsološu inovāciju veselības aprūpē. MI sistēmas spēj apvienot daudzveidīgus datu kopumus – klīniskos, demogrāfiskos, fizioloģiskos, attēldiagnostiskos un molekulāros datus – lai atklātu iespējamos modeļus un izveidotu prognozes, kas var uzlabot diagnostikas precizitāti, veicināt individualizētu terapiju un optimizēt resursu sadali [Khan et al., 2024; Hagedorn et al., 2024]. Izmantojot liela apjoma datus, MI piedāvā potenciālu risinājumu tradicionālās hronisku sāpju aprūpes ierobežojumiem, kur subjektivitāte un mainīgums mazina sekmīgas ārstēšanas rezultātus.

Šajā pārskatā aplūkotas četras galvenās jomas: 1) metodoloģiskie pamati un galvenās MI tehnikas, kas ri nozīmīgas hronisku sāpju kontekstā, 2) MI klīniskie pielietojumi, tostarp prediktīvā modelēšana, opioīdu riska novērtēšana, neiromodulācija un digitālie veselības rīki, 3) MI ieguldījums precīzijas medicīnā, īpaši izmantojot omikas datus, biomrķierus, sensorus un valkājamas ierīces un, 4) esošie ierobežojumi, ētiskie izaicinājumi un nākotnes virzieni MI integrācijai hronisku sāpju aprūpē. Aplūkojot šos uzdevumus, pārskata mērķis ir sniegt visaptverošu skatījumu uz to, kā MI vāretu pārveidot hronisku sāpju ārstēšanu, virzoties no eksperimentāliem modliem uz klīniski nozīmīgām, un pacientu centrētām stratēģijām.

METHODOLOGICAL OVERVIEW

This literature review was conducted by systematically searching peer-reviewed articles in PubMed and Scopus. To reflect the most recent advancements, priority was given to publications from the past decade (2015-2025), through earlier studies were included where relevant. Search terms used in the search strategy included *artificial intelligence, machine learning, deep learning, chronic pain, neuromodulation, precision medicine, biomarkers,* and *opioid risk prediction*. Both original research and review papers were explored.

The final bibliography includes over 50 references covering methodological advances, clinical applications, and broader perspectives on AI in CP management. The analysis was structured to scope AI methodology, clinical areas of application, and broader implementation challenges. Artificial intelligence was used to aid with the structural design and compiling data for the infographic figure and table of this review.

1. ARTIFICIAL INTELLIGENCE IN PAIN MEDICINE: AN OVERVIEW

Chronic pain remains one of the most demanding challenges in modern medicine due to its subjective character, diverse origins, and interaction between biological, psychological, and social factors. These complexities slow down the development of accurate prediction models and personalized treatments [Cohen et. Al., 2021; Stretanski et al., 2025]. Unlike conditions with clear diagnostic biomarkers, pain lacks universally accepted objective measures, underlining the importance of AI's ability to integrate heterogeneous data streams [Mouraux & Lannetti, 2018; Davis et al., 2020].

In medicine, artificial intelligence (AI) encompasses a wide spectrum of computational methods, including machine learning (ML), deep learning (DL), natural language processing (NLP), and large language models (LLMs). These tools allow systems to detect patterns, classify information, and generate predictions that exceed the capabilities of conventional statistical approaches [Hagedorn et al., 2024].

Within pain research, AI has been applied across multiple domains. ML and DL have been used to forecast treatment outcomes, identifying patient subgroups and guiding clinicians toward multimodal therapeutic options [Khan et al., 2024]. Algorithms such as neural networks (NNs) predict whether pain will persist, how the patient will respond to certain drugs, or the risk of opioid misuse, supporting earlier and more targeted interventions [Sun et al., 2023: Ischesco et al., 2021; Chatham et al., 2023]. Integrations of omics data and imaging have facilitated the identification of novel biomarkers linked to pain phenotypes [Curatolo et al., 2024; Miettinen et al., 2022]. In neuromodulation, AI enhances programming of devices such as spinal cord or deep brain stimulators, enabling patient-specific adjustments [Meier et al., 2024; Billet et al., 2024]. Smart device applications and wearable devices, powered by AI, further allow patients to monitor their symptoms and receive personalized feedback [Piette et al., 2022; Nordstoga et al., 2023]. More complex multi-agent systems (MAS) combine behavioural, physiological, and imaging data, advancing automatic pain assessment [Kamal et al., 2023; Cascella et al., 2024].

AI can merge diverse forms of data from neuroimaging and autonomic physiology signals to self-reported experiences, offering a holistic perspective on CP mechanisms [Lee et al., 2018]. However, most AI applications remain at an early stage, with limited validation and restricted generalizability due to reliance on small or single-institution datasets [Antel et al., 2024]. In addition to this, algorithmic bias, lack of transparency, and data privacy highlight the need for strong ethical and regulatory safeguards [El-Tallawy et al., 2024; Casarin et al., 2024].

Overall, AI holds potential to redefine CP management by moving beyond fragmented, subjective assessments toward integrated and patient-tailored care. Success, however, will depend on building robust datasets, interdisciplinary collaboration, and careful clinical implementation.

2. CORE ARTIFICIAL TECHNOLOGIES USED IN PAIN MEDICINE

2.1 Machine learning

Chronic pain management continues to be an area where standard therapies often provide inconsistent results, creating demand for innovative tools that can optimize treatment and improve patient outcomes. Machine learning (ML), a subgroup of AI, offers possibilities by developing algorithms that learn from existing data and make predictions for new cases without explicit programming. ML identifies hidden structures, clusters patients, and predicts outcomes, providing insights that may not be apparent to clinicians [Meier et al., 2024] . Machine learning can be divided into groups based on the amount of information given and the type of learning.

Supervised learning (SL) is a concept of ML where algorithms learn from labelled data. In this model, each training example consists of input variables (e.g., patient weight, clinical history, laboratory values) that are paired with known outcomes (e.g., treatment success or failure). The goal is to learn the relationship between input features and output labels, allowing the algorithm to generalize and make predictions on new, unseen data. For instance, in chronic pain management, SL algorithms can be trained on patient data with labelled pain intensity scores to predict the effectiveness of different treatments or interventions. For example, Nijeme-d'Hollosy et al. study compared 25 ML algorithms on patient-reported low back pain data to model treatment selection. In the study, they evaluated the ability of the model to learn from data and how those demonstrated the feasibility of using ML as a decision-support tool regarding treatment.

Unsupervised learning works with learning patterns and structures from unlabelled data. This method has been applied to uncover patterns or clusters without predefined outcomes. In the context of chronic pain management, this method has been applied to identify hidden subtypes of pain, patient groups with similar symptom patterns, or potential biomarkers. For instance, Kharghanian et al. (2016) used an unsupervised learning approach to analyse facial images for pain detection, achieving almost 95% accuracy.

Reinforcement learning is a model where an agent learns to make decisions by interacting with the environment. It learns through trial and error based on feedback from the environment. In this model, there are no labelled input and output pairs. When it comes to chronic pain management, reinforcement learning can be applied to optimize treatment strategies by adapting to changing patient responses over time. For example, Lopez-Martinez et al. demonstrated this approach by optimizing personalized morphine dosing recommendations in critical care settings.

ML approaches have shown promise in classifying pain phenotypes, tailoring interventions, predicting treatment outcomes, and assisting clinicians with complex decision-making. Supervised learning methods are highly effective with large, annotated datasets, while unsupervised approaches reveal hidden subgrouping of patients that may not be evident to clinicians. Reinforcement learning represents an especially promising avenue for adaptive real-time pain treatment but remains largely experimental. Despite these strengths, most ML studies are retrospective and rely on small, institution-specific cohorts, raising concerns about generalizability. In the future, progress will depend on multicenter collaboration, external validation, and integration of multimodal data sources [Antel et al., 2024].

2.2 Deep learning

Deep learning (DL) has gained more attention in healthcare due to its ability to learn intricate patterns from data. DL is a part of a broader family of ML algorithms based on Artificial Neural Networks (NN), which takes inspiration from networks in the brain. They consist of interconnected nodes or “neurons” organized in layers, comprising an input layer, one or more hidden layers, and an output layer [Meier et al., 2024]. These models are used to recognize patterns, make predictions, and solve complex problems, making them suitable for the multifaceted nature of CP. Information in this model is processed like interconnected brain cells, where the learning can be supervised, semi-supervised, or unsupervised. A suitable algorithm is selected or developed for the application, depending on the available data and the objective. NNs can be used for tasks that involve structured data like electronic health records (EHRs) or physiological signals. It can also be used for image and speech recognition, language processing, and predictive analytics. For example, in the study review of Squarcina et al., they reported promising results of DL in predicting treatment responses in depression, which is a commonly seen comorbidity of chronic pain.

There are different types of DL models, like convolutional neural networks (CNNs) that work by processing grid-like data (e.g., images) by using spatial hierarchies of features. Therefore, CNNs are useful in medical imaging tasks where they can detect abnormalities in scans relating to chronic pain conditions. For example, Fontaine et al. demonstrated in their ResNet-18 convolutional neural network, which analysed facial expressions before and after surgery and achieved a sensitivity of 89.7% for detecting pain, 77.5% for severe pain, and an accuracy of 53% in estimating pain intensity.

Recurrent neural networks (RNNs) can be used for sequential data processing, making them valuable for time-series analysis, which includes longitudinal patient data or physiological signals. In relation to chronic pain, RNNs can capture temporal dependencies and dynamics in pain trajectories, which helps to improve strategies for pain prediction and management. Wang et al. introduced a hybrid RNN (bidirectional long short-term memory (LSTM)) model, which combines auto-extracted and handcrafted features, which help improve the classification of pain intensity more accurately.

Another algorithm that's used is natural language processing (NLP) of clinical text, where DL is used to analyse clinical notes, ICD-codes, genomic sequencing data, and adverse drug effects. NLP can provide insights into patient-recorded outcomes, treatment responses, or sociopsychological factors influencing chronic pain management. An example of using NLP is from the study of Schirle et al., in which they selected relevant terms from clinical notes using term frequency-inverse document frequency (TF-IDF) to identify chronic pain patients with opioid use disorder.

Furthermore, large language models (LMMs) have revolutionized NLP by training on text to capture contextual representations of words or phrases. One model is BERT (bidirectional encoder representations from transformers), which has been used to summarize patient views on chronic pain treatments, drug side effects, and self-medication approaches. In the study of Lituiev et al., social determinants of health were extracted from clinical notes of patients with chronic low back pain. This can show AI's ability to capture non-clinical contextual factors influencing pain. Different LMM-based models enable more accurate and context-aware predictions that can be used to help in disease estimation risk, give guidance for more personalized interventions, and be used in decision support systems [Meier et al., 2024].

Deep learning methods, particularly convolutional and recurrent neural networks, have achieved higher accuracy in detecting pain-related patterns from facial expression, physiological time-series data, and neuroimaging. The ability of deep networks to capture nonlinear and complex interactions makes them especially relevant for the multidimensional nature of pain. However, these models are highly data-dependent, raising issues of feasibility in clinical contexts where large, annotated datasets are scarce. Furthermore, while NLP and LLMs have enabled the extraction of opioid misuse signals and social determinants of health from clinical records, interpretability and potential algorithmic biases raise concerns about trust and usability in clinical practice [Lituiev et al., 2023]. Despite these challenges, DL has demonstrated strong potential in pain detection, treatment prediction, and data integration. Future directions should emphasize explainable AI, transparency in model training processes, and rigorous validation from diverse populations to ensure broader adoption in pain medicine.

3. CLINICAL APPLICATIONS OF AI IN CHRONIC PAIN

In general healthcare, AI tools have demonstrated potential in optimizing clinical outcomes, enabling early disease recognition, reducing cost and time, and enhancing decision-making processes. It can be utilized in drug development and the deployment of large language models to support clinical workflows. Specifically, within pain medicine, AI-driven tools have been developed to support opioid monitoring, reduce associated risks, and improve accessibility to care. These technologies also have potential in optimising outcomes in using neuromodulation devices and assisting clinicians in complex decision-making scenarios. AI-enabled systems can integrate pharmacologic, non-pharmacologic, and interventional modalities to recommend individualised treatment plans.

3.1 Predictive modelling and treatment response

A promising application of AI in chronic pain management is predictive modelling. By processing a large volume of patient data, ML and DL algorithms can anticipate who may develop persistent pain or how many individuals might respond to certain treatments. For example, in the study of Sun et al., it was described how ML could predict patients likely to develop post-surgical chronic pain following breast surgery and help in decision-making of appropriate analgesia to reduce the risk of post-surgical pain. Furthermore, AI models have been developed to determine pharmacological treatment responses, identifying patients likely to benefit from specific analgesic agents. This enhances therapeutic efficacy while minimizing adverse effects and supports the selection of optimal medication regimens. For instance, in an exploratory study of Ichesco et al. used ML to predict which patients with fibromyalgia would be likely to respond to pregabalin therapy.

Beyond pharmacological management, AI predictive effectiveness is being applied to give more targeted, non-pharmacological interventional strategies. For example, AI has been applied to physical and device-based intervention: in the study of Kim et. al, DL algorithms were used to determine which patients suffering from chronic foot pain would benefit from specialized insoles. Also, Knab et al. tested an expert system to recommend treatment regimens including pharmacologic, non-pharmacologic, and interventional modalities for patients with complex chronic pain. In the above studies, there was broad discussion of the tools used, but there exists little evidence of how these tools would work in the environment of clinical practice.

Collectively, AI-driven predictive modelling has demonstrated success in forecasting chronic pain trajectories, surgical outcomes regarding pain, and treatment responses. These applications illustrate AI's potential to enhance clinical decision-making by identifying patients at higher risk of poor outcomes or treatment non-response. Yet, most models are still tested under research conditions, with limited validation in routine clinical practice. To gain clinical credibility, predictive systems must be transparent, user-friendly, and continuously updated with real-world data.

3.2 Opioid risk prediction

Opioids remain a key pharmacological option for CP, but carry serious risks, including misuse and dependency. AI tools are increasingly being developed to be used in opioid-associated risk prediction. ML and NN-based models applied to electronic health records (EHRs) have shown the capacity to flag problematic opioid use earlier than standard clinical observation. Chatham et al. (2023) and Kashyap et al. (2022) reported that these approaches can successfully identify early at-risk individuals based on patient characteristics, clinical, and treatment modalities. Also, in the pilot study of Schirle et al., NLP was used to identify opioid use disorder-related concepts from clinical notes by creating a text-based scoring system. These approaches offer valuable insights and support developing safer and proactive treatment plans regarding chronic opioid therapy. The studies highlighted the need for larger-scale studies and further performance in clinical environments.

The use of AI to stratify patients by opioid misuse risk represents one of the most clinically urgent applications. NLP and DL models analysing EHRs have shown the capacity to detect misuse patterns before they escalate [Chatham et al., 2023; Kashyap et al., 2022]. However, ethical challenges loom large: algorithmic misclassification could lead to undertreatment of pain in vulnerable patients, while privacy concerns arise from analysing sensitive data. Thus, while AI can enhance opioid stewardship, its clinical implementation requires careful balancing of patient safety, ethical responsibility, and equitable access to pain relief.

3.3 Neuromodulation and interventional techniques

In the last few years, there has been a growing interest in using neuromodulation as an alternative treatment method for chronic pain. There are different techniques like spinal cord stimulation (SCS), dorsal root ganglion (DRG) stimulation, deep brain stimulation (DBS), and peripheral nerve stimulation. Studies have been showing promising results in the management of different chronic pain conditions [Head et al., 2019]. There are also studies done about neuromodulation of the autonomic nervous system (ANS) in chronic pain settings showing promise, but systematic reviews have shown inconclusive results for it, needing further research on it [Billet et al., 2024].

A spinal cord stimulator is an implantable device used for chronic pain. It consists of electrodes, connection wires, and a pulse generator. SCS emits electrical pulses to the spinal cord and interrupts the normal transmission of pain signals. With this technique, the sensation of pain can be reduced or blocked [Xing et al., 2024]. For example, this has been used in neuropathic pain and chronic low back pain. In a systematic review of Head et al., they reviewed low- and high-frequency SCS and their effects on pain reduction in the long-term, reporting its efficacy as an alternative treatment method for neuropathic and chronic low back pain. It was noted that future work should be done in investigating the optimal choice of frequency based on pain aetiology and classifying patients who would benefit from it the most. In another study, it was reported that some patients with neuropathic pain continued to experience reduced pain and improved quality of life after years of treatment. It was also found to be cost-effective relative to conventional therapy [O'Connor et al., 2009].

Deep brain stimulation (DBS) is a neurostimulation technique that has been recently explored for chronic pain treatment. It delivers electrical pulses through electrodes implanted in the brain and targets a specific area to modulate abnormal neural signals. In relation to pain treatment, DBS focuses on regions involved in pain signals, like the thalamus and certain deep-brain nuclei. By altering neural activity in these areas, DBS can reduce the perception of pain, therefore offering an analgesic effect. [Alamri & Pereira, 2022]. Using intracranial stimulation as a management of pain is still controversial, since there is a need for well-designed and executed clinical trials. Also, patients used in the research are biased since there has been failure in other pain-control methods. Though studies of DBS give more broader context of AI in neurosurgical pain interventions and encourage scientists and professionals to explore new ways of treatment, allowing for more definitive conclusions on DBS efficacy in chronic pain treatment.

Using the above-mentioned techniques, AI training aids in detecting neural signals associated with pain, provides optimized information to reduce pain signals, and refines device programming for patient-specific intervention. There is also an advancement in employing prospective targets to effectively improve pain relief. Also, ML could further help with the selection of ideal candidates and personalizing stimulation parameters for neuromodulation by using demographics, pain outcome, and physiological data [Meier et al., 2024].

AI technologies are also able to enhance procedural precision in interventional pain management. For instance, advanced AI-assisted ultrasound guidance has been employed in regional anaesthesia to improve the accuracy of nerve blocks and increase procedural success rates, minimize injury to surrounding vascular and neural structures, and reduce the risk of local anaesthetic systemic toxicity. For example, Bowness et al. used an ML model in ultrasound by producing colour overlays on the generated image to identify anatomical structures, which reportedly reduced rates of intervention failure and unwanted needle trauma to surrounding anatomical structures. However, the clinical implementation remains limited and warrants further investigation similar to other applications of AI for pain management.

AI has the potential to revolutionize neuromodulation therapies by enabling more precise patient selection and individualized device programming. Evidence supports the use of AI in optimizing stimulation parameters for spinal cord and deep brain stimulation [Meier et al., 2024]. Similarly, AI-assisted ultrasound guidance can improve procedural accuracy in interventional pain management [Bowness et al., 2022]. Nevertheless, outcomes remain mixed, particularly regarding autonomic nervous system modulation [Billet et al., 2024]. Limitations include small samples, lack of randomized validation, and the technical complexity of integrating AI into implantable systems. Future studies should clarify whether AI-guided neuromodulation and procedural support truly outperform expert-driven programming. Also, future work should be done for creating more in-depth studies and moving towards more clinical practice environments.

3.4 Real-time treatment adaptation and digital health tools

AI can enhance real-time treatment adaptation and self-management. When initiating a treatment regimen, the ability to adequately follow and continuously tailor this regimen could allow for improved outcomes. For example, Coleman et al. used NLP to collect care quality indicators of patients who received pain treatment, and results showed that the co-occurrence of pain care quality indicators describing pain assessment was high. In the realm of physical therapy, case-based reasoning (CBR), which is an ML technique, has been explored to enable real-time adaptation of treatment programs for patients with lower back pain. In the study of Recio-García et al., this method was used to help with the decision-making process of treatment**.** It included tailoring physical therapy regimens for patients with lower back pain based on individual biomechanical measurements and clinical profiles, offering a dynamic and patient-specific therapeutic approach. The study reported a 70% success rate in proposing therapy regimens and highlighted cost-effectiveness in patient treatment using the technique.

Digital health technologies, including smartphone and smartwatch applications, are increasingly integrating AI to support patient self-management of chronic pain. These tools encompass chatbot-based cognitive behavioural therapy (CBT) and electronic medication guidance following hospital discharge [Piette et al., 2022]. One notable example is the selfBACK application, which uses AI to guide decision-making in the self-management of chronic low back pain. It’s a mobile health solution, promising method for delivering tailored evidence-based self-management interventions to patients based on individual characteristics, symptoms, and progression by using CBR [Nordstoga et al., 2023]. In the applications mentioned above was reported high user satisfaction and usability were reported. However, strong data on long-term clinical outcomes are limited and present opportunities for future research.

Digital self-management applications, wearable devices, and case-based reasoning frameworks illustrate how AI can extend pain management beyond the clinic. Such tools better patient engagement, support adherence, and may lower healthcare utilization [Piette et al., 2022; Nordstoga et al., 2023]. Yet evidence regarding their long-term effectiveness and cost-efficiency remains limited. Many digital tools are tested in pilot studies with a narrow population, making generalizability uncertain. For AI-driven digital health to achieve clinical impact, larger randomized trials and regulatory guidance will be essential.

4. PRECISION AND PERSONALIZED PAIN MEDICINE

4.1 Biomarkers and ‘omics integration

The use of precision medicine in healthcare has opened new opportunities for tailoring treatment to the unique biological and clinical features of individual patients. It offers an opportunity to improve outcomes by tailoring treatments to patients, more specifically by using specific genetic variants and metabolic pathways that can lead to different pain states and pain-related phenotypes [Chen et al., 2019]. Pain biomarkers offer biological insights, enabling more objective evaluations of pain severity and characteristics. These markers may be specific molecules, gene expression patterns, or physiological indicators that help signal inflammation, tissue damage, or neural changes. These biomarkers provide an avenue to diagnose more accurately, evaluate disease progression, and optimize therapy [Mouraux et al., 2018; Cai et al., 2022].

Potential field in precision medicine offers large-scale characterization of functional and structural aspects of multiple biological components, including technologies like genomics and transcriptomics, commonly grouped under the term “omics”. Omics methods are used to analyse individual biological systems. Multi-omics methods focus on analysing an environment consisting of multiple organisms. For example, in the study of Curatolo et al., they collected urine and blood samples to analyse different omics that were integrated as data to identify common mechanisms and pathways involved in the pathophysiology of chronic low back pain and fibromyalgia. In another study, Miettinen et al. executed a supervised ML approach to identify key metabolite features that could be implicated in chronic pain, particularly metabolic pathways involved in sleep and obesity, which are often associated with chronic pain states. Omics data is complex, and it naturally lends itself towards ML-based approaches. There is promising work done to differentiate between healthy and disease states and help in generating novel hypotheses about biological mechanisms underpinning CP. There are deep representation learning frameworks like DeepMicro that help effectively represent microbiome profiles. It’s able to reduce dimensionality and extract meaningful representations from microbiome datasets, using ML classification algorithms on the learned representation. While DeepMicro was presented with microbiome data, it could be widely applied to other omics data, like genome and proteome data [Oh & Zhang, 2020]. Different ML methods can be used in supervised or unsupervised capacities for analysis of integrated meta-omics datasets, which allows better understanding of biological systems [Meier et al., 2024].

The application of AI in omics and biomarker research emphasizes the potential for precision pain medicine. Integrating genomic, metabolomic, and microbiomics with ML enables the discovery of novel signatures predictive of pain susceptibility and treatment response [Curatolo et al., 2024; Miettinen et al., 2022]. Yet, despite promising experimental findings, translation into clinical practice is minimal. Biomarker-driven models are often derived from small, homogeneous cohorts and require extensive validation [Davis et al., 2020]. Additionally, the biological complexity of pain means that no single biomarker is likely sufficient; instead, multimodal biomarker panels combined with AI integration may represent the most promising direction.

4.2 Sensors and wearables

Personalised pain medicine approaches tailor pain treatment strategies for more specific needs and characteristics of an individual. This holds potential for improved treatment outcomes, reducing side effects, and better patient satisfaction. There are many ways to make advances in a more personalized approach. There are smart sensors that capture real-time physiological or biochemical markers of pain. Examples are different physical and chemical sensors, biomarkers, imaging devices, intelligent communication devices, and medication pumps [Xing et al., 2024]. These AI technologies offer a continuous and objective method for assessing pain by gathering different data sources, offering clinicians a more complete picture of patient status.

Intelligent physical sensors can monitor physical parameters relevant to pain, such as body temperature, cardiac activity (ECG), blood pressure, muscle activity (EMG), and brain signals (EEG). Studies have evaluated pain by observing individual parameters, like heart rate variability and muscle tension that correlate with pain intensity, but future studies should employ a multisensory perspective to allow more reliable detection and a deeper understanding of causes and effects of pain [Naranjo-Hernández et al., 2020]. Complementing these physical sensors, there are intelligent wearable chemical sensors that analyse changes in bodily chemicals or in examining biological samples. Different pain biomarkers hold value to biological insights and help in a more objective evaluation of pain characteristics [Mouraux et al., 2018; Cai et al., 2022]. These sensors are structured to monitor levels of electrolytes, metabolites, and other biomarkers essential for assessing biochemical conditions. For example, by evaluating specific biomarkers like sweat, chemical sensors can give important insight into the pain status of an individual noninvasively [Ghaffari et al., 2021]. Another example is monitoring biomarkers related to stress responses, like cortisol, can guide physicians to recommend stress- and pain-related management strategies that are effective in managing symptoms in chronic pain patients [Phillips et al., 2008]. Due to subjectivity and complexity of pain, no single parameter can express all its facets, and therefore, integrating multiple parameters with clinical assessment tools holds importance in advancing personalized pain medicine through extensive and accurate pain evaluation [Davis et al., 2020].

In addition to monitoring, wearable devices are being developed for therapeutic purposes. Smart implantable drug pumps, such as programmable micropumps, deliver medication in precise doses through a small catheter implanted in the intrathecal space, which exemplifies how technology can support precise, individualized treatment regimens. This offers a sustained and effective management solution to difficult chronic pain conditions like cancer pain by allowing dosing schedules to adapt dynamically to patient needs [Fallon et al., 2018].

The potential of sensors and wearables lies in their capacity to generate continuous, real-world data outside of clinic visits. Devices capturing physiological or biochemical signals can provide objective indicators of pain states [Naranjo-Hernández et al., 2020; Phillips et al., 2008]. These devices can improve early detection of symptom changes, support adherence, and empower patients in self-management. AI enables the translation of these raw signals into clinically meaningful insights. Also, smart drug delivery systems show how AI can integrate not only monitoring but therapeutic actuation. However, significant barriers remain: usability and comfort for patients, reliability of long-term data collection, integration with healthcare systems, and concerns around privacy. At present, most studies involving wearables remain confined to a research context with limited uptake in routine practice [Davis et al., 2020]. Closing this gap will require not only technical refinement but also clear regulatory pathways and strategies to ensure patient trust in continuous monitoring techniques.

5. SYSTEMS-LEVEL AI APPROACHES

5.1 Multi-agent systems

While much of AI research in pain medicine has focused on discrete applications, systems-level approaches seek to integrate multiple data sources into unified frameworks. Multi-agent systems (MAS) are comprised of multiple autonomous, intelligent agents that interact within a shared environment. Its core concept is to assist communication and cooperation among agents and address diverse challenges. MAS trains models to detect patterns and correlations that humans may not be able to observe, and these systems can identify subtle indicators of pain that may otherwise go unnoticed. Each agent in the MAS system can focus on different dimensions of the pain experience – from physiological signals to behavioural cues – and together they generate a comprehensive representation of the patient's condition [Kamal et al., 2023].

MAS are particularly relevant for automatic pain assessment (APA), where multimodal data are synthesized to provide objective evaluations. Approaches may draw on behavioural features (e.g., facial expressions, speech, body movements), neurophysiological signals (e.g., EEG, ECG, EMG, electrodermal activity), or advanced imaging techniques like functional MRI. These systems can also be combined for wider analysis. Cascella et al. (2023) demonstrated that combining clinical, demographic, and physiological features allowed clustering of cancer patients into groups with distinct pain profiles, treatment responses, and opioid requirements. Similarly, Lee et al. developed ML models to objectively classify pain levels using neuroimaging and autonomic activity data. The study involved patients with chronic back pain and used support vector machine and support vector regression technologies, and the model achieved an accuracy of 92.45% in the classification of pain states.

Practical applications of MAS are also emerging. For example, PainCheck is a digital tool that can help assess pain through facial expressions combined with non-facial expressions of pain like vocalization, movements, and behaviour. For example, it can help in cognitively impaired elderly individuals by using tools to analyse non-verbal cues and physiological signals to provide an objective assessment [Babicova et al., 2021]. Such a tool can highlight the capacity of AI not just to supplement clinical judgement but to extend assessment into populations where self-reporting is unreliable or impossible.

Multi-agent systems and automatic pain assessment models demonstrate AI's potential for systems-level integration. By combining behavioural, physiological, and imaging data, these frameworks can deliver continuous, adaptive, and multimodal pain assessment [Kamal et al., 2023; Cascella et al., 2023]. Although MAS provides a powerful proof-of-concept for holistic pain evaluation, most remain in early research phases, tested on small or highly specific cohorts. Challenges include computational complexity, interoperability with existing electronic health records, and integration into telemedicine infrastructures. To advance, MAS will require rigorous external validation, robust clinical trials, and adaptation for scalability across healthcare systems. Nonetheless, their potential to reduce clinician burden and enhance early detection of complications makes them a compelling frontier in CP management.

Figure 1. Overview of AI methodologies and their applications in chronic pain management

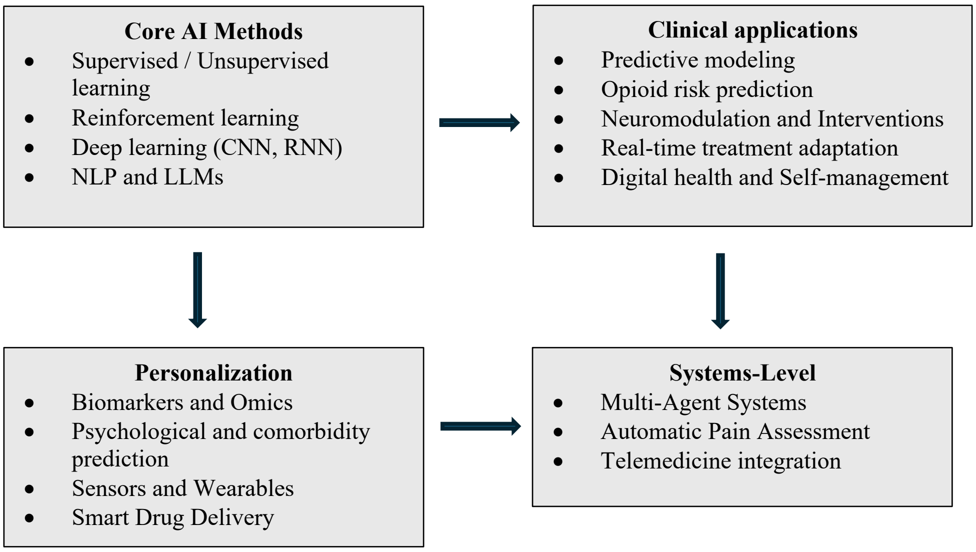

Table 1. Overview of AI methodologies and their applications in chronic pain management

AI method	Data type	Application in Chronic Pain	Example Study	Challenges
Supervised learning	Clinical/demographic data	Predict treatment outcomes, stratify patients	Nijeweme-d'Hollosy et al., 2017	Needs large, labelled datasets
Unsupervised learning	Unlabelled patient data or imaging data	Identify subtypes and biomarkers, patient clustering	Kharghanian et al., 2016	Limited interpretability, validation
Reinforcement learning	Sequential patient feedback/responses	Optimize drug dosing strategies	Lopez-Martinez et al., 2019	Clinical feasibility not yet proven
Deep learning (CNNs)	Medical images, facial expressions	Facial recognition of pain, imaging analysis	Fontaine et al., 2022	Accuracy varies across populations
Deep learning (RNNs)	Time-series physiological data	Pain trajectory prediction, monitoring	Wang et al., 2020	Small datasets limit generalizability
Neural Language Processing (NLP)	Clinical notes, EHR texts	Opioid misuse detection, outcome tracking	Schirle et al., 2021	Dependent on high-quality EHRs
Large Language Models (LMMs)	Large-scale medical text, narratives	Social determinant extraction, opioid risk prediction	Lituiev et al., 2023	Bias, interpretability challenges
Predictive Modelling	Multimodal patient data	Forecast pain prediction and treatment response	Sun et al., 2023; Ichesco et al., 2021	Bias, interpretability challenges
Opioid Risk prediction	EHR and patient characteristics	Identify at-risk opioid users, misuse prevention	Chatham et al., 2023; Kashyap et al., 2022	Privacy/ethical concerns, limited validation
Neuromodulation	Neurostimulation signals, imaging	Optimise SCS, DBS, US-guided interventions	Billet et al., 2024; Bowness et al., 2022	High cost, limited accessibility
Sensors and Wearables	Physiological and biochemical signals, smart drug delivery systems.	Continuous monitoring, biomarker detection	Naranjo-Hernández et al., 2020 Fallon et al., 2018	Integration challenges, long-term data lacking
Multi-Agent systems (MAS)	Behavioural, physiological and imaging data	Automatic pain assessment, subgroup identification	Lee et al., 2018; Cascella et al., 2023	Complexity, infrastructure demands
Digital health and self-management apps	Mobile health data, patient-reported outcomes	Adaptive CBT chatbots, selfBACK app, self-management	Nordstoga et al., 2023; Piette et al., 2022	Limited evidence for long-term outcomes

6. ETCHICAL AND REGULATORY CONSIDERATIONS OF AI IN CHRONIC PAIN

The adoption of AI in chronic pain medicine is not solely a technical matter; it raises pressing ethical, legal, and social issues that must be addressed before large-scale clinical integration. Beyond accuracy and performance, concerns about privacy, fairness, accountability, and patient trust will determine whether these technologies can be safely embedded into health care systems.

6.1 Data privacy and security

AI models in pain medicine often rely on sensitive information from electronic health records, imaging, wearable devices, and even mobile health applications. This may include details about opioid use, psychiatric comorbidities, or biometric data. Without proper safeguards, such data could be exposed or misused. Strategies to mitigate risk include advanced encryption, strict access controls, and ensuring that patients provide fully informed consent before their data is used [El-Tallawy et al., 2024]. Compliance with regulations will be essential to building patient confidence.

6.2 Algorithmic bias and equity

Bias is among the most significant challenges in AI. Models trained on datasets that lack diversity may generate predictions that are less accurate for underrepresented groups. For example, facial recognition systems used for pain assessment may underperform across different ethnicities, while opioid misuse prediction tools may inadvertently reinforce stigma in vulnerable populations [Antel et al., 2024; Chatham et al., 2023]. Addressing these inequities requires deliberate diversification of training data, as well as continuous auditing to ensure fairness and transparency.

6.3 Explainability and clinical trust

AI systems, particularly DL and LLMs, have faced criticism as “black boxes” producing accurate outputs without transparent reasoning. This lack of interpretability undermines clinician confidence, especially in areas like pain medicine, where treatment decisions carry significant consequences for patient quality of life [El-Tallawy et al., 2024]. Explainable AI techniques, such as feature attribution maps or interpretable model architectures, offer one solution. Embedding these into CP research could help clinicians and patients understand why specific recommendations are made, thereby improving adoption.

6.4 Accountability and responsibility

When AI-driven decisions contribute to negative outcomes, questions of liability inevitably arise. If an algorithm misclassifies opioid risk and the patient is undertreated, responsibility may be disputed between clinicians, developers, and healthcare institutions. Clear regulatory frameworks are necessary to define accountability, ensure appropriate oversight, and establish liability protections [Polevikov, 2023]. Professional guidelines and governance structures will play a critical role in clarifying these responsibilities.

6.5 Regulatory and implementation barriers

Despite rapid progress in research, very few AI tools for CP have reached regulatory approval or integration into clinical workflows. Agencies now demand robust evidence of safety, efficacy, and fairness before approving. Implementation also requires technical solutions such as interoperability with existing electronic health systems and training clinicians to effectively use AI-supported tools [Antel et al., 2024]. These barriers highlight the gap between proof-of-concept research and real-world deployment.

6.6 Ethical imperative for patient-centered AI

Ultimately, the goal of AI in pain medicine should not only be efficiency but also the empowerment of patients. Tools such as digital health platforms and wearables can facilitate shared decision making and self-management, but only if they are accessible, understandable, and sensitive to diverse patient needs [Piette et al., 2022]. Without careful design, AI risks reinforcing inequities rather than reducing them. Ethical frameworks that emphasize patient-centeredness, fairness, and inclusivity are therefore indispensable.

In conclusion, the ethical and regulatory dimensions of AI in CP management are as critical as technical performance. Without robust safeguards and frameworks addressing privacy, bias, explainability, and accountability, even the most sophisticated models could fail to earn clinician trust and patient acceptance. By embedding ethical principles into design and ensuring strong regulatory oversight, AI can contribute to equitable, transparent, and trustworthy chronic pain care.

7. POTENTIAL, LIMITATIONS, AND FUTURE DIRECTIONS OF AI FOR CHRONIC PAIN MANAGEMENT

7.1 Potential of artificial intelligence in chronic pain management

The reviewed literature demonstrates that AI holds considerable promise as a transformative tool for chronic pain management. Its greatest strength lies in its capacity to combine heterogeneous data sources - including clinical, imaging, physiological signals, and molecular profiles – and translate them into individualized predictions [Khan et al., 2024; Hagedorn et al., 2024]. Predictive models can help clinicians anticipate which patients are likely to transition from acute to chronic pain, while DL applied to neuroimaging or sensor data provides more objective means of pain detection and assessment [Wang et al., 2020; Fontaine et al., 2022].

AI has also shown potential to optimize treatment strategies. Examples include neuromodulation programming tailored to individual physiology, as well as adaptive self-management apps that provide real-time feedback [Meier et al., 2024; Nordstoga et al., 2023]. At the systems level, multi-agent frameworks suggest new possibilities for continuous, multimodal monitoring and decision support that could shift CP management towards more dynamic and personalized care [Kamal et al., 2023; Cascella et al., 2023].

AI has immense potential to transform the evaluation and delivery of multimodal treatment strategies for chronic pain. Current efforts are increasingly focused on establishing comprehensive AI-integrated systems that span the entire continuum of patient care from diagnosis and assessment to treatment and long-term monitoring. These systems aim to optimize treatment outcomes, improve clinical decision-making, and streamline care processes in a complex and often subjective field of pain medicine.

7.2 Current limitations and barriers to implementation

Despite these promising applications, significant obstacles constrain the field. A recurring limitation is the narrow scope of datasets, often derived from single institutions with limited sample sizes. This undermines external validity and restricts the generalizability of models

[Antel et al., 2024]. Another challenge is methodological: many studies are retrospective and lack prospective validation in clinical settings.

Technical integration also presents barriers. Data often exists in incompatible formats across health systems, leading to challenges in interoperability. At the same time, implementation requires not only technological infrastructure but clinician training and workflow adaptation, both of which demand great investment [Polevikov, 2023].

Evidence of long-term benefit, cost-effectiveness, and scalability is still sparse. While pilot studies show feasibility, few provide evidence of long-term clinical benefit, cost effectiveness, or scalability [Casarin et al., 2024]. Finally, ethical concerns such as bias, privacy, and explainability are increasingly acknowledged but seldom systematically addressed, further widening the gap between experimental research and clinical adoption.

7.3 Future directions

Future progress will depend on addressing different methodological and translational gaps. Key priorities include: 1) data expansion and harmonization could be addressed by building multicenter, multimodal, and standardized datasets to enhance external validity and minimize bias. 2) Embedding AI tools into randomized controlled trials and real-world clinical studies to generate evidence of clinical benefit. 3) By developing explainable models to improve clinician confidence and support decision-making. 4) Systems integration to ensure interoperability across electronic health records, digital health tools, and wearable devices for seamless implementation. 5) Extending AI applications to early detection of high-risk patients to prevent pain chronification. 6) Lastly, making an effort to foster interdisciplinary collaboration by bringing together clinicians, data scientists, ethicists, and regulators to co-create clinically meaningful tools.

In summary, AI for chronic pain management is advancing rapidly but remains largely at the experimental stage. Its potential to enable personalized, objective, and adaptive care is well supported by preliminary findings, yet widespread clinical translation will require methodological rigor, robust datasets, and stronger integration into real-world healthcare systems.

CONCLUSION

Chronic pain remains a challenging condition in healthcare, owing to its high prevalence, significant socioeconomic burden, and the impact on quality of life [Cohen et al., 2021; Goldberg & McGee, 2011]. Traditional assessment methods heavily rely on subjective patient reporting and conventional treatments, often characterized by variable efficacy and risks such as opioid misuse, highlighting the need for innovative approaches [Mouraux & Lannetti; 2018; Cai et al., 2022].

Artificial intelligence offers a promising pathway to address these challenges. By enabling the integration of diverse data sources, detecting hidden patterns, and generating predictive insights, AI can support more accurate diagnosis, individualized treatment planning, and adaptive care. Applications across predictive modelling, biomarker discovery, neuromodulation optimization, opioid risk assessment, and digital self-management illustrate the extent of AI's potential [Sun et al., 2023; Meier et al., 2024; Nordstoga et al., 2023].

Nevertheless, most current evidence remains preliminary. Models are frequently based on narrow datasets, tested retrospectively, and lack validation in clinical environments. Technical barriers such as interoperability, as well as ethical concerns around bias, privacy, and explainability, further limit translation into clinical adoption [Antel et al., 2024; El-Tallawy et al., 2024]. Moreover, while experimental results are encouraging, clear evidence of scalability, cost-effectiveness, and real-world benefit is still limited [Casarin et al., 2024].

Looking forward, the successful integration of AI into chronic pain management will require a transition from proof-of-concept models to clinically validated, ethically grounded, and interoperable systems. Building large, representative datasets, fostering interdisciplinary collaboration, and developing appropriate regulatory frameworks will be key to success.

If these challenges can be addressed, AI has potential, not to replace clinical expertise, but to augment it, enabling earlier detection, more personalized treatment, and continuous support throughout the patient journey. In this way, AI represents not only a technological innovation but also a catalyst for reimagining chronic pain care as a dynamic, adaptive, and patient-centered discipline.

Bibliography

Alamri, A., & Pereira, E. A. (2022). Deep brain stimulation for chronic pain. *Neurosurgery Clinics of North America*, *33*(3), 311–321. https://doi.org/10.1016/j.nec.2022.02.013

Antel, R., Whitelaw, S., Gore, G., & Ingelmo, P. (2024). Moving towards the use of artificial intelligence in pain management. *European Journal of Pain*. https://doi.org/10.1002/ejp.4748

Babicova, I., Cross, A., Forman, D., Hughes, J., & Hoti, K. (2021). Evaluation of the Psychometric Properties of PainChek® in UK Aged Care Residents with advanced dementia. *BMC Geriatrics*, *21*(1). https://doi.org/10.1186/s12877-021-02280-0

Billet, B., Goudman, L., Rigoard, P., Billot, M., Roulaud, M., Verstraete, S., Nagels, W., & Moens, M. (2024). Effect of neuromodulation for chronic pain on the autonomic nervous system: a systematic review. *BJA Open*, *11*, 100305. https://doi.org/10.1016/j.bjao.2024.100305

Bowness, J. S., Laurent, D. B., Hernandez, N., Keane, P. A., Lobo, C., Margetts, S., Moka, E., Pawa, A., Rosenblatt, M., Sleep, N., Taylor, A., Woodworth, G., Vasalauskaite, A., Noble, J. A., & Higham, H. (2022). Assistive artificial intelligence for ultrasound image interpretation in regional anaesthesia: an external validation study. *British Journal of Anaesthesia*, *130*(2), 217–225. https://doi.org/10.1016/j.bja.2022.06.031

Cai, H., Ao, Z., Tian, C., Wu, Z., Kaurich, C., Chen, Z., Gu, M., Hohmann, A. G., Mackie, K., & Guo, F. (2022). Engineering human spinal microphysiological systems to model opioid-induced tolerance. *Bioactive Materials*, *22*, 482–490. https://doi.org/10.1016/j.bioactmat.2022.10.007

Cascella, M., Leoni, M. L. G., Shariff, M. N., & Varrassi, G. (2024). Artificial Intelligence-Driven diagnostic processes and comprehensive multimodal models in pain medicine. *Journal of Personalized Medicine*, *14*(9), 983. https://doi.org/10.3390/jpm14090983

Cascella, M., Di Gennaro, P., Crispo, A., Vittori, A., Petrucci, E., Sciorio, F., Marinangeli, F., Ponsiglione, A. M., Romano, M., Ovetta, C., Ottaiano, A., Sabbatino, F., Perri, F., Piazza, O., & Coluccia, S. (2024). Advancing the integration of biosignal-based automated pain assessment methods into a comprehensive model for addressing cancer pain. *BMC Palliative Care*, *23*(1). https://doi.org/10.1186/s12904-024-01526-z

Casarin, S., Haelterman, N. A., & Machol, K. (2024). Transforming personalized chronic pain management with artificial intelligence: A commentary on the current landscape and future directions. *Experimental Neurology*, *382*, 114980. https://doi.org/10.1016/j.expneurol.2024.114980

Chatham, A. H., Bradley, E. D., Schirle, L., Sanchez-Roige, S., Samuels, D. C., & Jeffery, A. D. (2023). Detecting problematic opioid use in the Electronic Health Record: Automation of the Addiction Behaviors Checklist in a Chronic Pain population. *medRxiv (Cold Spring Harbor Laboratory)*. https://doi.org/10.1101/2023.06.08.23290894

Chen, R., & Snyder, M. (2012). Promise of personalized omics to precision medicine. *WIREs Systems Biology and Medicine*, *5*(1), 73–82. https://doi.org/10.1002/wsbm.1198

Cohen, S. P., Vase, L., & Hooten, W. M. (2021). Chronic pain: an update on burden, best practices, and new advances. *The Lancet*, *397*(10289), 2082–2097. https://doi.org/10.1016/s0140-6736(21)00393-7

Coleman, B. C., Finch, D., Wang, R., Luther, S. L., Heapy, A., Brandt, C., & Lisi, A. J. (2023). Extracting Pain Care Quality Indicators from U.S. Veterans Health Administration Chiropractic Care

Using Natural Language Processing. *Applied Clinical Informatics*, *14*(03), 600–608. https://doi.org/10.1055/a-2091-1162

Curatolo, M., Chiu, A. P., Chia, C., Ward, A., Johnston, S. K., Klein, R. M., Henze, D. A., Zhu, W., & Raftery, D. (2024). Multi-Omics Profiles of chronic low back pain and Fibromyalgia - Study protocol. *Research Square (Research Square)*. https://doi.org/10.21203/rs.3.rs-4669838/v1

Davis, K. D., Aghaeepour, N., Ahn, A. H., Angst, M. S., Borsook, D., Brenton, A., Burczynski, M. E., Crean, C., Edwards, R., Gaudilliere, B., Hergenroeder, G. W., Iadarola, M. J., Iyengar, S., Jiang, Y., Kong, J., Mackey, S., Saab, C. Y., Sang, C. N., Scholz, J., . . . Pelleymounter, M. A. (2020). Discovery and validation of biomarkers to aid the development of safe and effective pain therapeutics: challenges and opportunities. *Nature Reviews Neurology*, *16*(7), 381–400. https://doi.org/10.1038/s41582-020-0362-2

D'Antoni, F., Russo, F., Ambrosio, L., Bacco, L., Vollero, L., Vadalà, G., Merone, M., Papalia, R., & Denaro, V. (2022). Artificial intelligence and Computer aided diagnosis in Chronic Low back Pain: A Systematic review. *International Journal of Environmental Research and Public Health*, *19*(10), 5971. https://doi.org/10.3390/ijerph19105971

El-Tallawy, S. N., Pergolizzi, J. V., Vasiliu-Feltes, I., Ahmed, R. S., LeQuang, J. K., El-Tallawy, H. N., Varrassi, G., & Nagiub, M. S. (2024). Incorporation of "Artificial Intelligence" for Objective Pain Assessment: A Comprehensive Review. *Pain and Therapy*, *13*(3), 293–317. https://doi.org/10.1007/s40122-024-00584-8

Fallon, M., Giusti, R., Aielli, F., Hoskin, P., Rolke, R., Sharma, M., & Ripamonti, C. (2018). Management of cancer pain in adult patients: ESMO Clinical Practice Guidelines. *Annals of Oncology*, *29*, iv166–iv191. https://doi.org/10.1093/annonc/mdy152

Fontaine, D., Vielzeuf, V., Genestier, P., Limeux, P., Santucci-Sivilotto, S., Mory, E., Darmon, N., Lanteri-Minet, M., Mokhtar, M., Laine, M., & Vistoli, D. (2022). Artificial intelligence to evaluate postoperative pain based on facial expression recognition. *European Journal of Pain*, *26*(6), 1282–1291. https://doi.org/10.1002/ejp.1948

Goldberg, D. S., & McGee, S. J. (2011). Pain as a global public health priority. *BMC Public Health*, *11*(1). https://doi.org/10.1186/1471-2458-11-770

Ghaffari, R., Yang, D. S., Kim, J., Mansour, A., Wright, J. A., Model, J. B., Wright, D. E., Rogers, J. A., & Ray, T. R. (2021). State of Sweat: Emerging wearable systems for Real-Time, noninvasive sweat sensing and analytics. *ACS Sensors*, *6*(8), 2787–2801. https://doi.org/10.1021/acssensors.1c01133

Hagedorn, J. M., George, T., Aiyer, R., Schmidt, K., Halamka, J., & D'Souza, R. S. (2024). Artificial Intelligence and Pain Medicine: An Introduction. *Journal of Pain Research*, *Volume 17*, 509–518. https://doi.org/10.2147/jpr.s429594

Head, J., Mazza, J., Sabourin, V., Turpin, J., Hoelscher, C., Wu, C., & Sharan, A. (2019). Waves of Pain relief: A systematic review of clinical trials in spinal cord stimulation waveforms for the treatment of chronic neuropathic low back and leg pain. *World Neurosurgery*, *131*, 264-274.e3. https://doi.org/10.1016/j.wneu.2019.07.167

Ichesco, E., Peltier, S. J., Mawla, I., Harper, D. E., Pauer, L., Harte, S. E., Clauw, D. J., & Harris, R. E. (2021). Prediction of differential pharmacologic response in chronic pain using functional neuroimaging biomarkers and a support vector machine algorithm: an exploratory study. *Arthritis & Rheumatology*, *73*(11), 2127–2137. https://doi.org/10.1002/art.41781

Kamal, M. A., Ismail, Z., Shehata, I. M., Djirar, S., Talbot, N. C., Ahmadzadeh, S., Shekoohi, S., Cornett, E. M., Fox, C. J., & Kaye, A. D. (2023). Telemedicine, E-Health, and Multi-Agent systems for chronic pain management. *Clinics and Practice*, *13*(2), 470–482. https://doi.org/10.3390/clinpract13020042

Kashyap, A., Callison-Burch, C., & Boland, M. R. (2022). A deep learning method to detect opioid prescription and opioid use disorder from electronic health records. *International Journal of Medical Informatics*, *171*, 104979. https://doi.org/10.1016/j.ijmedinf.2022.104979

Khan, M. A., Koh, R. G., Rashidiani, S., Liu, T., Tucci, V., Kumbhare, D., & Doyle, T. E. (2024). Cracking the Chronic Pain code: A scoping review of Artificial Intelligence in Chronic Pain research. *Artificial Intelligence in Medicine*, *151*, 102849. https://doi.org/10.1016/j.artmed.2024.102849

Kharghanian, R., Peiravi, A., & Moradi, F. (2016). Pain detection from facial images using an unsupervised feature learning approach. *Pain Detection From Facial Images Using Unsupervised Feature Learning Approach*, 419–422. https://doi.org/10.1109/embc.2016.7590729

Kim, J. K., Yoo, J. C., In, S. P., Jin-Woo, C., Park, D., & Chang, M. C. (2023). Deep-Learning Algorithms for Prescribing Insoles to Patients with Foot Pain. *Applied Sciences, 13*(4), 2208. https://doi.org/10.3390/app13042208

Knab, J. H., Wallace, M. S., Wagner, R. L., Tsoukatos, J., & Weinger, M. B. (2001). The use of a Computer-Based decision support system facilitates primary care physicians’ management of chronic pain. *Anesthesia & Analgesia*, *93*(3), 712–720. https://doi.org/10.1097/00000539-200109000-00035

Lee, J., Mawla, I., Kim, J., Loggia, M. L., Ortiz, A., Jung, C., Chan, S., Gerber, J., Schmithorst, V. J., Edwards, R. R., Wasan, A. D., Berna, C., Kong, J., Kaptchuk, T. J., Gollub, R. L., Rosen, B. R., & Napadow, V. (2018). Machine learning–based prediction of clinical pain using multimodal neuroimaging and autonomic metrics. *Pain*, *160*(3), 550–560. https://doi.org/10.1097/j.pain.0000000000001417

Lituiev, D. S., Lacar, B., Pak, S., Abramowitsch, P. L., De Marchis, E. H., & Peterson, T. A. (2023). Automatic extraction of social determinants of health from medical notes of chronic lower back pain patients. *Journal of the American Medical Informatics Association*, *30*(8), 1438–1447. https://doi.org/10.1093/jamia/ocad054

Lopez-Martinez, D., Eschenfeldt, P., Ostvar, S., Ingram, M., Hur, C., & Picard, R. (2019). Deep Reinforcement Learning for Optimal Critical Care Pain Management with Morphine using Dueling Double-Deep Q Networks. *Deep Reinforcement Learning for Optimal Critical Care Pain Management With Morphine Using Dueling Double-Deep Q Networks*, 3960–3963. https://doi.org/10.1109/embc.2019.8857295

Meier, T. A., Refahi, M. S., Hearne, G., Restifo, D. S., Munoz-Acuna, R., Rosen, G. L., & Woloszynek, S. (2024). The role and applications of artificial intelligence in the treatment of chronic pain. *Current Pain and Headache Reports*, *28*(8), 769–784. https://doi.org/10.1007/s11916-024-01264-0

Miettinen, T., Nieminen, A. I., Mäntyselkä, P., Kalso, E., & Lötsch, J. (2022). Machine Learning and Pathway Analysis-Based discovery of metabolomic markers relating to chronic pain phenotypes. *International Journal of Molecular Sciences*, *23*(9), 5085. https://doi.org/10.3390/ijms23095085

Mouraux, A., & Iannetti, G. D. (2018). The search for pain biomarkers in the human brain. *Brain*, *141*(12), 3290–3307. https://doi.org/10.1093/brain/awy281

Naranjo-Hernández, D., Reina-Tosina, J., & Roa, L. M. (2020). Sensor Technologies to manage the Physiological traits of Chronic Pain: a review. *Sensors*, *20*(2), 365. https://doi.org/10.3390/s20020365

Nijeweme-d'Hollosy, W. O., Van Velsen, L., Poel, M., Groothuis-Oudshoorn, C. G., Soer, R., & Hermens, H. (2017). Evaluation of three machine learning models for self-referral decision support on low back pain in primary care. *International Journal of Medical Informatics*, *110*, 31–41. https://doi.org/10.1016/j.ijmedinf.2017.11.010

Nordstoga, A. L., Aasdahl, L., Sandal, L. F., Dalager, T., Kongsvold, A., Mork, P. J., & Nilsen, T. I. L. (2023). The role of pain duration and pain intensity on the effectiveness of App-Delivered Self-Management for low back pain (SelfBACK): secondary analysis of a randomized controlled trial. *JMIR Mhealth and Uhealth*, *11*, e40422. https://doi.org/10.2196/40422

Oh, M., & Zhang, L. (2020). DeepMicro: deep representation learning for disease prediction based on microbiome data. *Scientific Reports*, *10*(1). https://doi.org/10.1038/s41598-020-63159-5

O'Connor, A. B. (2009). Neuropathic pain. *PharmacoEconomics*, *27*(2), 95–112. https://doi.org/10.2165/00019053-200927020-00002

Phillips, K. M., Antoni, M. H., Lechner, S. C., Blomberg, B. B., Llabre, M. M., Avisar, E., Glück, S., DerHagopian, R., & Carver, C. S. (2008). Stress management intervention reduces serum cortisol and increases relaxation during treatment for nonmetastatic breast cancer. *Psychosomatic Medicine*, *70*(9), 1044–1049. https://doi.org/10.1097/psy.0b013e318186fb27

Piette, J. D., Newman, S., Krein, S. L., Marinec, N., Chen, J., Williams, D. A., Edmond, S. N., Driscoll, M., LaChappelle, K. M., Kerns, R. D., Maly, M., Kim, H. M., Farris, K. B., Higgins, D. M., Buta, E., & Heapy, A. A. (2022). Patient-Centered pain care using artificial intelligence and mobile health tools. *JAMA Internal Medicine*, *182*(9), 975. https://doi.org/10.1001/jamainternmed.2022.3178

Polevikov, S. (2023). Advancing AI in healthcare: A comprehensive review of best practices. *Clinica Chimica Acta*, *548*, 117519. https://doi.org/10.1016/j.cca.2023.117519

Recio-García, J. A., Díaz-Agudo, B., Kazemi, A., & Jorro, J. L. (2021). A data-driven predictive system using Case-Based Reasoning for the configuration of device-assisted back pain therapy. *Journal of Experimental & Theoretical Artificial Intelligence*, *33*(4), 617–635. https://doi-org.db.rsu.lv/10.1080/0952813X.2019.1704441

Schirle, L., Jeffery, A., Yaqoob, A., Sanchez-Roige, S., & Samuels, D. C. (2021). Two data-driven approaches to identifying the spectrum of problematic opioid use: A pilot study within a chronic pain cohort. *International Journal of Medical Informatics*, *156*, 104621. https://doi.org/10.1016/j.ijmedinf.2021.104621

Squarcina, L., Villa, F. M., Nobile, M., Grisan, E., & Brambilla, P. (2020). Deep learning for the prediction of treatment response in depression. *Journal of Affective Disorders*, *281*, 618–622. https://doi.org/10.1016/j.jad.2020.11.104

Stretanski, M. F., Kopitnik, N. L., Matha, A., & Conermann, T. (2025, June 23). *Chronic pain*. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK553030/

Sun, Y., Kang, J., Brummett, C., & Li, Y. (2023). Individualized risk assessment of preoperative opioid use by interpretable neural network regression. *The Annals of Applied Statistics*, *17*(1). https://doi.org/10.1214/22-aoas1634

Wang, R., Xu, K., Feng, H., & Chen, W. (2020). Hybrid RNN-ANN Based Deep Physiological Network for Pain Recognition. *Annual International Conference of the IEEE Engineering in Medicine and*

Biology Society. IEEE Engineering in Medicine and Biology Society. Annual International Conference, *2020*, 5584–5587. https://doi.org/10.1109/EMBC44109.2020.9175247

Xing, Y., Yang, K., Lu, A., Mackie, K., & Guo, F. (2024). Sensors and devices guided by AI for personalized pain medicine. *Cyborg and Bionic Systems*, *5*. https://doi.org/10.34133/cbsystems.0160

Declaration

I, __Noora Multala_______, certify that this Research Paper on the topic

„Possibilities of artificial intelligence for evaluating of multimodal treatment of chronic pain”

(Title of the Research Paper in Latvian)

„Mākslīgā intelekta iespējas hronisku sāpju multimodālās ārstēšanas novērtēšanāi ”

(Title of the Research Paper in English)

This is my own independent research. All other sources of data, definitions, and quotations in my Research Paper are referenced accordingly. The text of this Research Paper has never been submitted in any way to any other National Examination Commission for evaluation in its entirety or parts, and has never been published in its entirety.

__________________ /___Noora Multala____/
(Student’s signature) (Name, surname)

21.10. 2025