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ALTERNATIVE TREATMENTS FOR PAIN MEDICINE (C ROBINSON, SECTION EDITOR)

# The Ethical Stewardship of Artificial Intelligence in Chronic Pain and Headache: A Narrative Review

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## Abstract

**Purpose of Review** As artificial intelligence (AI) and machine learning (ML) are becoming more pervasive in medicine, understanding their ethical considerations for chronic pain and headache management is crucial for optimizing their safety.

**Recent Findings** We reviewed thirty-eight editorial and original research articles published between 2018 and 2023, focusing on the application of AI and ML to chronic pain or headache. The core medical principles of beneficence, non-maleficence, autonomy, and justice constituted the evaluation framework. The AI applications addressed topics such as pain intensity prediction, diagnostic aides, risk assessment for medication misuse, empowering patients to self-manage their conditions, and optimizing access to care. Virtually all AI applications aligned both positively and negatively with specific medical ethics principles.

**Summary** This review highlights the potential of AI to enhance patient outcomes and physicians' experiences in managing chronic pain and headache. We emphasize the importance of carefully considering the advantages, disadvantages, and unintended consequences of utilizing AI tools in chronic pain and headache, and propose the four core principles of medical ethics as an evaluation framework.

**Keywords** Artificial intelligence · Machine learning · Medical ethics · Chronic pain · Chronic headache

## Introduction

Recent years have seen substantial advances in artificial intelligence (AI) that have impacted the lives of millions of people. The repercussions and applications of these advances, however, extend far beyond the technical field. Applications of AI in healthcare offer new possibilities for patients ranging from early cancer diagnosis [1] to empowering physicians to develop more personalized treatment plans [2]. The field of chronic pain is no exception, as AI applications have been developed to better support patients and clinicians. AI has the potential to improve the lives of the estimated 50.2 million American adults who live with chronic pain [3]. Reviews of the pain medicine literature

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indicate a growing relevance of technologies such as virtual reality (VR), machine learning (ML), and AI in recent years [4]. However, the promise of AI for chronic pain and headache treatment also raises ethical concerns that demand careful consideration [5]. As such, how we weigh AI's benefits and costs could dramatically affect the lives of patients with chronic pain and headache. Therefore, considering the risks, benefits, and unintended consequences of using any new AI technology and employing measures that ensure its net benefit are crucial.

Although often overlooked in the technical world, ethics allow people to consider the potential outcomes—both positive and negative—of their actions. The foundations of principle-based medical ethics comprise four fundamental principles: beneficence, non-maleficence, autonomy, and justice. Beneficence underscores a physician's obligation to promote the patients' well-being, striving to improve health and quality of life. Non-maleficence refers to a foremost commitment not to cause harm and suffering for patients. Autonomy emphasizes physicians' obligations to empower patients to make informed decisions regarding their healthcare that are free of coercion. Lastly, justice refers to physicians' obligations to treat individual patients and patient groups fairly and equitably, ensuring appropriate and timely access to medical treatments and other healthcare resources for all [6]. These four guiding principles of medical ethics offer a valuable framework for examining the potential benefits and drawbacks of integrating AI into healthcare settings.

This narrative review addresses the relevant advancements in AI for chronic pain and headache-specific applications over the past five years, while simultaneously highlighting their ethical considerations. To select the appropriate literature, we performed a search query of all PubMed-indexed entries between 2018 and 2023, specifically focusing on the mention of AI and chronic pain or headache in either the title or abstract. Our query yielded 155 articles, of which 52 met this initial screening criteria. The list of articles was further refined to exclude prior reviews, leaving primarily original research articles or editorial/opinion pieces. We then excluded articles that primarily addressed topically adjacent fields, such as acute pain or non-AI-powered digital tools. In the end, we incorporated 38 articles into this review.

The included AI applications are organized according to the primary ethical principle with which they most clearly align based on our best judgment, while acknowledging that articles often encompass multiple principles. After briefly summarizing the applications, we perform an ethical analysis of the potential positive and negative effects associated with integrating AI-based technology into healthcare settings. Discussions are separated by relevance to either chronic pain or headache under each of the four ethical principles.

## Beneficence

### Chronic Pain

Enabling patients to predict future pain states may help them more accurately prioritize their pain management. With the smartphone-based app cliexa-EASE [7], which relies on user-inputted bodily sensation maps and reports of current emotions, patients can predict their pain two weeks into the future with 65 – 72% accuracy when discriminating between low and high pain intensity. Such predictions also have utility for guiding, for example, clinicians' post-treatment follow-up periods with their patients, if their patients are willing and able to share these data.

Similarly, advancements that uncover novel or more precise relationships among seemingly coincident patient factors can enable clinicians to predict a patient's risk of developing additional symptoms related to their chronic pain. Elgendi et al. [8] utilized unsupervised learning techniques, specifically an ensemble of three clustering algorithms and principal component analysis, within a cohort of 656 subjects with chronic pelvic pain who had other conditions including endometriosis and irritable bowel syndrome. The subjects' 0–10 ratings of their pelvic pain intensity were correlated with 24 other patient factors and the researchers found that chronic pelvic pain scores and quality-of-life measures correlated with depression, anxiety, and pain catastrophizing scales; intriguingly, the diagnosis of endometriosis itself was found not to directly correlate with chronic pelvic pain—a finding that appeared to contradict the researchers' prior analysis of the data using non-AI approaches.

Moreover, multiple published studies have demonstrated AI's potential to either provide an objective marker for chronic pain or aid in the diagnosis of a patient's specific chronic pain etiology. Regarding the former, several studies have discussed the promise of using structural and functional magnetic resonance imaging (MRI), as well as electroencephalogram (EEG) data, to train AI models to recognize and characterize imaging-based cortical or parenchymal markers of chronic pain states [9–11]. Notably, Yang et al. [10] applied a hierarchical clustering algorithm to resting-state functional MRI (RS-fMRI) scans of 159 chronic pain patients and identified an association between the severity of patients' depression and sleep disturbances with higher signal connections in specific brain areas on RF-fMRI scans. While intriguing, these imaging-based AI studies raise the question of whether training AI algorithms on costly and resource-intensive imaging and encephalography data for the purposes of characterizing chronic pain states is ethically just, since not all patients can afford such studies. Regarding the latter, Soin et al. [12] employed a decision-tree algorithm trained on 85 clinical features across 246 consecutive patients with back pain, showing a 72% accuracy for predicting a clinician's specific back pain diagnosis. The algorithm addressed what the authors consider an inherent challenge to diagnosing back pain conditions, as almost all patients presented with an ensemble of clinical findings without any single clinical test being pathognomonic. Nevertheless, nearly 20% of patients were not easily categorized into a mainstream diagnostic category and because the diagnostic "gold standard" was decided by a specific clinician, the algorithm is susceptible to diagnostic bias.

All the AI applications outlined above could offer chronic pain patients and their clinicians greater consistency, insight, and even predictive abilities. However, none of them provide an explanatory framework that would allow either the patient or the clinician to construct an actionable management model of the pain condition at hand. The "explainability" of AI has been referenced in prior ethics discussion by Cascella et al. [5] as being broadly important to the goals of multiple stakeholders including the patient and the clinician. In accordance with this concern across AI applications for chronic pain, Janevic et al. [4] observed that information technology-geared pain research up through 2020 had placed significant effort into pain "measurement…as opposed to management"—potentially in an attempt to minimize that technology's risk of unintentionally harming patients and thereby violating the principle of non-maleficence. To enable AI-powered tools' further alignment with the principle of beneficence through clinical management support, while also mitigating the risks of patient harm, other authors have highlighted the crucial role of tool validation and long-term, post-deployment monitoring on a widespread basis [13]. Nonetheless, achieving this goal may be particularly challenging in pain medicine, which as a field has yet to conform to clear-cut algorithmic standards when it comes to clinical decision-making [14••].

## Headache

Clinicians' abilities to help headache patients and promote their welfare can be increased with AI. While accurate headache diagnoses have historically required patients to be seen by headache specialists, AI now offers an alternative.

Extremely Randomized Trees have been developed to predict migraine diagnoses using questionnaire data for children and adolescents, which can help patients access appropriate treatment early in their courses. This advancement is particularly helpful considering that migraine is believed to be a progressive disease [15]. Researchers also use AI models to predict whether patients have different headache types using questionnaire data [16–18], and some of the models are sufficiently small to be distributed through a smartphone app [18]. Other classifiers rely on more sophisticated types of data. For example, experts have used MRI data to distinguish healthy individuals from those with migraine, as well as to further distinguish between simple and complex migraine with aura [19]. MRI data have also been employed to predict average Migraine Aura Complexity Score, which can help better delineate the biological markers of migraines [20].

Alternative models can be used to better understand the effectiveness of EMG-biofeedback as migraine treatment and identify specific variables that may affect Migraine Disability Assessment Scores (MIDAS) [21]. With such information, clinicians can better identify patients who can benefit from such biofeedback therapy and tailor their treatment in the best fashion possible. Some devices, such as the Relivion, are already available to the public and can help people self-administer treatment for their migraines and have AI-enabled personalized treatment recommendations sent to physicians. [22].

While all the diagnostic tools have the potential to help patients get faster, more tailored, and more effective treatments, considering their potential drawbacks is vital. If algorithms were to make the wrong prediction, patients might not receive the appropriate treatment, potentially leading to adverse health outcomes in the long-term and violation of the principle of non-maleficence—not dissimilar to an instance of misdiagnosis by a human physician. Moreover, most such models were trained using a unique physician's diagnosis as the gold standard, which may or may not be correct. Thus, expert review of the algorithms' output is still needed. Lastly, while the more complex data types can provide important additional information, considering the cost of performing studies such as MRIs or EMGs is vital from a justice standpoint, as not every headache patient has the financial resources to afford them. Nonetheless, clarifying that the presence of a resource burden does not automatically render the development of a new technology impermissible is crucial. Failing to develop tools that could enhance the lives of a segment of the pain patient population could itself be construed as a violation of the beneficence principle. Instead, our aim is to underscore the nuanced implications of decisions in AI for healthcare, which often extend beyond initial considerations.

Other experts rely on unstructured natural language to study headaches. For example, one study evaluated the usage of physicians' notes to identify headache concepts and symptoms [23]. Other models used physicians' notes to measure outcomes of migraine treatment and prevention [24], or headache frequency [25]. Such models can offer valuable insights into patients' conditions that would have been lost had they used only self-reported questionnaire data. The additional information contributes to a more accurate diagnosis of the condition and more tailored and effective treatment strategies. On the other hand, physicians are subject to biases that can guide their notetaking and the interpretation of patients' symptoms, and notes for the same physician–patient interaction may vary widely among physicians. All these considerations should be kept in mind when using models that rely on subjective input.

## Non-Maleficence

### Chronic Pain

Given the well-established risks of respiratory depression, overdose, and death with opioid use, AI can be valuable for the assessment and management of opioid misuse risk in vulnerable patient populations. Piette et al. [26] evaluated the adaptability and effect of PowerED, a reinforcement learning tool for guiding opioid misuse interventions based on patients' self-reported risk, assigning 228 patients to counseling sessions over 12 weeks according to their modified Current Opioid Misuse Measure scores. The study revealed a decreased requirement for live counseling and improvements in scores for high-risk patients, showing how reinforcement learning can minimize harm and promote patient well-being. Additionally, the study supports the principle of justice by optimizing the allocation of limited healthcare resources, as evidenced by the fact that only 22% of therapeutic encounters ended up necessitating a live counselor's time. That said, patient adherence and engagement was a concern with these types of interventions—a critique that we will return to later in this review. Moreover, the selection and monitoring of patients based on sensitive self-reported parameters related to substance misuse risk raises privacy concerns and implications for patient autonomy and future access to healthcare services. Additionally, self-reported data are inherently biased, which may impact the accuracy and reliability of the interventions and subsequent outcomes.

Adams et al. [14••] noted relevant concerns regarding accountability in case of unintended patient harm. Suppose a physician utilizes an AI-powered substance use risk stratification tool such as PowerED or some hypothetical AI-powered procedural guidance tool to mitigate risk. If doing so ultimately results in unintended harm, how accountable is the physician? What about the developers of the tool? Should clinicians have "known better?" Should they have known exactly how the tool works to have a more nuanced understanding of the risks involved? While these concerns do not neatly fall under the four guiding principles regarding the patient, we posit that they fall under the principle of autonomy for the clinician and the technology developers involved with the application. Namely, a clinician's ability to make an informed decision about whether to utilize an AI-powered procedure aide or a particular clinical decision tool for patient safety may be compromised due to a lack of model explainability as expressed by Cascella et al. [5]. One solution involves expanding the transparency and explanatory power of how these AI tools work, so that the physician has an informed understanding of the tools' designs, biases, and limitations. However, such an alternative poses challenges due to technical complexities, the current lack of focus on this area, and the difficulty in effectively communicating these intricacies to non-technical individuals.

### Headache

Applications of AI for headache have the potential for concordance with the non-maleficence principle. For example, researchers have used a random forest algorithm that relies on patients' drawings depicting pain locations to predict their surgical outcomes. With such information, physicians can assess the potential benefits and drawbacks of surgery on an individualized basis and advise against performing surgeries when there is little expected improvement, thus preventing potential unnecessary harm to patients [27]. However, such patient drawings may be inaccessible for individuals with other conditions such as visual or mobility impairments, which limits the model's generalizability to the entire headache patient population and may be at odds with the justice principle. Yet, striking a balance between the considerations of generalizability and accessibility, as dictated by the principle of justice, and promoting patient well-being rooted in the principle of beneficence, remains critical even if the benefits may not extend to the entire pain patient population.

While AI has been studied as a diagnostic tool for headaches, it also can help individuals in other headache-related areas. For example, algorithms can predict medication overuse (MO) in migraine by using demographic, clinical, and biochemical data, which can help medical experts prevent the harmful outcomes associated with MO such as migraine chronification and the development of secondary headaches [28]. Specifically, physicians may be able to identify patients at risk for medication overuse early in their treatments and tailor treatment plans accordingly to avoid negative outcomes, thus preventing additional harm to patients. However, considering the potential for someone to be misclassified as having a high risk of MO should be considered, as doing so may unfairly exclude some patients from optimal treatment, thereby interfering with the justice principle.

## Autonomy

### Chronic Pain

Literature on patient autonomy-aligned applications of AI for chronic pain centers on empowering patients to play a more active, independent, and positive role in their pain management. Inductive thematic analysis of mental health app users with chronic pain has determined that pain management concerns coincide with general health and socioeconomic concerns, and that patients with chronic pain demonstrate a strong need for psychosocial support [29]. Therefore, any advancements toward enhancing independence and autonomy hold the potential for transformative outcomes. In addition to the previously discussed, smartphone-based app cliexa-EASE [7], another AI-powered app, PainDrainer, was designed to engage the patient in acceptance and commitment therapy (ACT). A prospective, single-arm, multi-center clinical trial of 43 patients by Barreveld et al. [30] assessed the impact of engagement with PainDrainer over a 12-week study period specifically on pain interference as the primary outcome. The authors noted that 57.5% of subjects had clinically significant improvement over the study period. Considering that both apps can function independently without clinician guidance, that the patient is free to engage with them however he or she chooses, and that the cost of accessing them is small when compared to other medical or interventional therapies, further development and utilization of such apps is encouraging for patients' autonomy and self-actualization.

That said, using the apps does presume a degree of digital literacy to which patients with either more limited means or technological exposure may not be accustomed, which raises a concern in the domain of justice: for people who remain locked out of access to these tools, what equitable options would be available? Moreover, there is a decline in patient engagement with the apps over time. For example, for PainDrainer, the authors reported compliance rates of 65% and 52% at six- and 12-weeks follow-up, respectively. Because the efficacy of therapies such as cognitive behavioral therapy (CBT) has been shown to wane over time once the therapy is discontinued [31], protecting against user disengagement from these and other digital therapeutic apps may be crucial for perpetuating therapeutic effect [4, 29]. Frustratingly, this concern also appears to positively correlate with increased severity of patients' depressive symptoms [32, 33]. Rather than expressing criticism, we hope that these findings translate to mindful design of future AI-powered apps that would make the delivery of the intended therapy more equitable. Notably, developers have already started looking into ways to increase user retention. For example, in the case of the Wysa for Chronic Pain app, a secondary survival analysis of user retention revealed that automatic morning check-ins with patients help stave off disengagement over time [34].

### Headache

AI has enormous potential to enhance the autonomy of headache patients. Diagnostic tools that operate without direct medical intervention empower patients to self-educate regarding their conditions. For example, researchers have developed an algorithm that allows the app to ask questions in a screening questionnaire only if doing so would change the current diagnostic impression, thus reducing patients' burden and increasing the speed of diagnoses [35]. However, we must acknowledge the potential shortcomings of the algorithm; the combined influence of multiple questions might shape the diagnostic impression, so excluding individual questions may directly impact patients' diagnoses and treatments.

Moreover, several studies have focused on using AI to empower patients to make informed life decisions based on their conditions. For example, using ECG data, researchers have identified migraine with aura as an independent risk factor for paroxysmal atrial fibrillation [36]. Such knowledge enables patients to proactively adopt preventive measures to try to mitigate the likelihood of developing the condition. Additionally, the ability to predict a future migraine attack can substantially improve patients' quality of life. Studies have focused on predicting headaches using data such as weather forecasts [37], or diary entries with biofeedback sessions [38]. Other studies have identified differences in the interictal and preictal phases of migraine using EEG and questionnaire data [39]. The prediction of future headaches provides patients with the autonomy to adjust their daily schedules to engage in preemptive treatment, thus giving them more control over their migraine management. Yet, as previously mentioned, while these studies can help migraine patients, they also risk exacerbating disparities between people of different socioeconomic statuses, as well as exacerbating the urban–rural divide.

Large language models (LLMs) have also been studied in medical applications. An example of such would be physicians receiving assistance in explaining conditions to patients by creating materials that are easy to understand for a specific target audience [40]. Patients can further use LLMs such as ChatGPT to obtain information regarding treatment possibilities such as medications for migraine. However, while this practice would allow people to quickly obtain responses, LLMs often output incorrect information and even cite imaginary papers [41], which could impact patients' abilities to make rational decisions based on their condition, thus necessitating experts' review of LLM outputs.

## Justice

### Chronic Pain

Our literature review suggests that AI developments in chronic pain management have had perhaps the most compelling positive alignment with the principle of justice by either helping to increase access to scarce therapeutic resources, expanding pain monitoring modalities to groups that are otherwise poorly engaged or disengaged with the mainstream healthcare system, or promising for more equitable representation of chronic pain patients in either the broader society and the healthcare community.

In terms of increasing access, Piette et al. [42•] tested the application of CBT supported by reinforcement learning (AI-CBT) for chronic pain, with the goal of decreasing patients' reliance on scarce human therapist session time. Results over 10 weeks demonstrated AI-CBT's non-inferior outcomes relative to standard care, and a significant reduction in therapist time, offering promise for expanding access to mental health treatments while efficiently allocating resources. A similar promise has been put forth by the AI-supported CBT app, Wysa for Chronic Pain, as well as for the broader category of "asynchronous" tele-health tools that allocate various sorts of healthcare resources according to patient needs [13, 32]. As much as the goal of efficient healthcare resource allocation speaks to the foundations of the principle of justice, Li et al. [13] have also expressed the crucial concern that the long-term efficacy of these platforms must be thoroughly monitored and studied on wide scale post-deployment. A hypothetical worst-case scenario entails certain patients being repeatedly "triaged out" of needed therapy based on flawed modeling.

Pain assessment and monitoring is complex, particularly when it comes to cognitively-impaired, non-verbal, home-bound, or otherwise incapacitated patients [5]. Fritz et al. [43] explored using "smart home" sensors and machine learning to predict pain episodes in home-bound patients. They used non-video, non-audio sensor data from 11 older adults' homes, training a random-forest classifier to distinguish pain-related events. The algorithm achieved 70% accuracy, with decreased grooming behavior predictive of future pain episodes. These findings demonstrate that AI tools are promising not only for out-of-hospital monitoring of patients' pain courses, but also for anticipating pain episodes based on data that do not rely on cogent patient engagement and communication with the AI system itself. That said, smart home monitoring technology introduces patient privacy concerns, even without the use of video or audio data. If patient privacy at home is breached, this could constitute a violation of the principle of non-maleficence.

With regard to increased representation of chronic pain communities, Monaco et al. [44] suggested open access to digital data streams from chronic pain patients and caregivers, advocating for its potential in accelerating research, community-building, and resilience. This data could come from online platforms and wearable sensors, and it may improve the visibility of chronic pain patients in society, allow patients and their caregivers greater control in helping to generate AI-powered solutions, and offer a sense of broader community that in itself could be healing. While the concept of open chronic pain data is thought-provoking for all of the mentioned reasons, we anticipate concerns regarding patient privacy violation and the impact that this could have on patient autonomy. Concerns regarding privacy violation and data bias exist, as patients engage with data acquisition platforms, risking targeted advertising and data transfer.

Finally, we would be remiss not to echo several concerns raised by Adams et al. [14••] in their editorial regarding the implications of AI in pain medicine that we feel are also relevant to the principle of justice. First, AI-based clinical decision support tools that summarize formidable amounts of past data regarding a complex chronic pain patient would help clinicians deliver the same type of timely care that a less complex patient would receive. Second, using AI for the purpose of making decisions regarding insurance coverage of a given therapy for a given patient may hinder appropriate therapy access if such decisions are based on biased AI models. Third, the authors more broadly highlight the concern of data bias in the training of AI models, and how these biases can perpetuate and potentially exacerbate existing healthcare delivery disparities among under-represented and minority groups.

### Headache

The lack of healthcare professionals specializing in headaches is a problem around the world. However, AI can help increase the access of headache diagnoses to more patients. For example, using a diagnostic tool to determine the type of headache that patients have can help people gain access to better care, and research has suggested how non-expert diagnoses improve when they have access to accurate AI predictions [45•]. Such tools can help more people, particularly in remote areas, gain access to potentially more accurate diagnoses. Yet, one must be aware of the potential for the AI model diagnoses to be incorrect, which could impact a larger number of individuals if widely deployed, in contrast to the traditional patient-doctor interaction. If clinicians overly rely on such incorrect diagnoses, patients can get hurt, and those patients who do not have access to headache specialists who can validate or contradict the AI diagnosis would suffer most.

## Moving Forward

As we consider the future of AI applications in healthcare, addressing some of the main challenges that impede the path to further innovation and collaboration is crucial. In particular, the limited discussion of technical details in most papers on ML models for medical applications, which only mention model type, directly affects the reproducibility of models and inhibits collaboration among experts seeking to build upon existing research. While not delving deep into technical details can lift barriers to entry for nontechnical people to engage in the AI community, this also hinders progress and innovation. Thus, a more thorough description of the models employed, either within the same analysis or in a more technically detailed version, should be considered to foster collaboration, reproducibility, and advancement in the field of AI-driven healthcare.

## Conclusion

AI undoubtedly has the potential to improve the lives of millions of patients around the world. However, it is fundamental that both clinicians and technical experts carefully consider the potential negative consequences of a technology prior to its widespread adoption, enabling proactive measures to mitigate risks. Perpetuating existing societal biases, the potential for erroneous AI predictions, and the potential exacerbation of disparities in access to care among different socioeconomic and geographical groups highlight the critical need for cautious implementation. Yet, the potential positive implications of AI applications in healthcare offer sufficient incentive to justify exploring the AI field with appropriate care, physician oversight, and system-wide post-deployment analysis. Improving diagnostic speed and accuracy, removing barriers to treat remote populations of lower socioeconomic status, allowing for personalized treatment, and alerting patients prior to an incoming pain attack or crisis to take proactive measures can certainly help patients better cope with their chronic pain. While embracing AI as a supportive tool for clinicians and patients holds immense promise, prioritizing ethical considerations on an ongoing basis is essential in order to ensure its responsible and equitable integration into healthcare practice.

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### Compliance with Ethical Standards

**Conflict of interests** MEM: No relevant conflicts to disclose. EB: No relevant conflicts to disclose. MES: Syneos Health (AdComm). CG: No relevant conflicts to disclose. CJG: No relevant conflicts to disclose. RJY: No relevant conflicts to disclose.

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- • Of importance
- •• Of major importance


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