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# Ανασκόπηση

## Artificial Intelligence (AI) in Palliative Care: Ethical Challenges

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### Abstract

Palliative Care (PC), which has recently become a more prominent field in healthcare, focuses on providing patients quality of life, relief from pain and other symptoms of serious illnesses, regardless of the diagnosis or stage of the disease. Even though several studies have reported the development of Artificial Intelligence (AI) in medicine, AI in the field of PC is still in early progress. The application of AI technologies in PC raises many ethical challenges which this paper will attempt to highlight. To achieve this, a literature review was conducted, scientific studies were gathered and were critically examined. It was observed that current AI applications in PC include Mortality risk prediction, Data annotation and Morbidity prediction. Ethical dilemmas and the legal framework will be investigated to emphasize the rights of patients, as well as the responsibilities and obligations healthcare professionals carry. Furthermore, directions for trustworthy AI in PC will be proposed. Finally, since PC requires a close doctor-patient relationship, healthcare professionals should focus on developing AI algorithms that align with the patients' needs and the goals of PC.

**Keywords:** artificial intelligence, AI, deep learning, machine learning, palliative care, ethical challenges, ethics.

## Η Τεχνητή Νοημοσύνη (TN) στην παροχή Παρηγορητικής Φροντίδας: Ηθικές προκλήσεις

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### Περίληψη

Η Παρηγορητική Φροντίδα, η οποία τελευταία αναδεικνύεται ως πιο σημαντικός τομέας στην υγειονομική περίθαλψη, επικεντρώνεται στην παροχή ποιότητας ζωής και στην ανακούφιση από τον πόνο ή από άλλα συμπτώματα σοβαρών ασθενειών, ανεξαρτήτως διάγνωσης ή σταδίου της νόσου. Παρόλο που αρκετές μελέτες έχουν αναφέρει την ανάπτυξη της Τεχνητής Νοημοσύνης (TN) στην Ιατρική, η TN στον τομέα της Παρηγορητικής Φροντίδας βρίσκεται ακόμα σε πρώιμα στάδια. Η εφαρμογή τεχνολογιών TN στην Παρηγορητική Φροντίδα εγείρει πολλά ηθικά διλήμματα, τα οποία θα συζητηθούν μέσω αυτής της εργασίας. Για να επιτευχθεί αυτό, πραγματοποιήθηκε ανασκόπηση της βιβλιογραφίας, συγκεντρώθηκαν επιστημονικές μελέτες, οι οποίες εξετάστηκαν κριτικά. Παρατηρήθηκε ότι οι τρέχουσες εφαρμογές TN στην Παρηγορητική Φροντίδα περιλαμβάνουν την πρόβλεψη της θνητότητας, τον σχολιασμό δεδομένων και την πρόβλεψη νοσηροτήτων. Τα ηθικά διλήμματα και το νομικό πλαίσιο θα διερευνηθούν για να δοθεί έμφαση στα δικαιώματα των ασθενών, καθώς και στις ευθύνες και υποχρεώσεις των επαγγελματιών υγείας. Επιπλέον, θα προταθούν κατευθύνσεις για δημιουργία αξιόπιστης TN στην Παρηγορητική Φροντίδα. Τέλος, δεδομένου ότι η Παρηγορητική Φροντίδα απαιτεί στενή σχέση γιατρού-ασθενούς, οι επαγγελματίες υγείας θα πρέπει να επικεντρωθούν στην ανάπτυξη αλγορίθμων TN που να ευθυγραμμίζονται με τις ανάγκες των ασθενών και τους στόχους της Παρηγορητικής Φροντίδας.

**Λέξεις κλειδιά:** τεχνητή νοημοσύνη, TN, παρηγορητική φροντίδα, μηχανική μάθηση, ηθικές προκλήσεις, ηθική.

## INTRODUCTION

Palliative Care (PC) is explicitly and inseparably linked to the human right to health. This can be easily understood from its purpose and definition. PC is an approach that improves the quality of life of patients, both adults and children, and their families who are facing problems associated with life-threatening illness. It prevents and relieves suffering through the early identification, correct assessment and treatment of pain and other problems, whether physical, psychosocial or spiritual.<sup>1</sup> Its main purpose is to offer a support system in order to help patients live as actively as possible until death. Despite the crucial importance of palliative care and its inseparable nature from human rights, it is not being successfully applied in the medical care of patients. According to WHO, each year, an estimated 56.8 million people are in need of palliative care. Worldwide, only about 14% of people who need palliative care currently receive it. The global need for palliative care will continue to grow as a result of the aging of populations and the rising burden of noncommunicable diseases and some communicable diseases. Regardless of the unmet need for palliative care, national health policies and systems often do not include palliative care at all and training on palliative care for health professionals is often limited or non-existent.

Within this context, the reality of Artificial Intelligence (AI) is unfolding, with its use spreading more and more in healthcare. The use of AI in medicine has stood at the center of interdisciplinary scientific research, political debate, and social activism. With the increasing availability of health-care data and the rapid progress in analytics techniques, AI has the potential to transform the health sector. It can offer health professionals the ability to reduce errors and costs of care, to increase their engagement with their patients, to enable research in clinical settings, to provide timely intervention, predictive analytics and as much informed patient care as possible.<sup>2</sup> All the above suggest that artificial intelligence could address the growing need for Palliative Care

and potentially enhance its applications and benefits for patients. However, one should not overlook the considerations discussed in the health sector about the use of AI in medicine, and by extension in palliative care, but also the possible ways that this use could be harmful.<sup>3,4</sup>

To maintain a common understanding with readers regarding AI and its related terms, it is essential to clarify the main terms and concepts in medical AI used throughout this report. The historical definition of AI talks about a machine that is able to mimic human intelligence or even surpass it to perform a given task such as prediction or reasoning. However, dominant in healthcare is actually a subfield of AI called Machine Learning (ML) which uses methods that learn to perform given tasks, such as prediction or classification or tasks automation, based on existing data. Accordingly, a subfield of ML is Deep Learning (DL), which refers to the use of large Neural networks (NNs) and big data to better solve complex problems. It is important to note that DL and NN demand sufficiently large data samples, so when this condition cannot be applied other techniques are used such as decision trees or support vector machines.<sup>5</sup>

In this literature review it is considered important to highlight dilemmas that may be caused by AI applications in PC, such as Mortality Risk prediction, Data annotation, Morbidity prediction and Response prediction under PC settings. It should be noted that current literature does not adequately cover this problem and the ethical challenges that arise from these applications.

## METHODS

The study aims to understand the areas of Palliative Care in which AI techniques have been implemented and to critically examine the ethical challenges that occur from this application. In order to examine the ethical challenges of AI use in PC, scientific studies were gathered from various databases and journals (PubMed, Google Scholar, ResearchGate, UpToDate etc.). Examples of AI applications in PC are provided and examined based on ethical dimensions and

values. The following keywords were used: artificial intelligence, AI, deep learning, machine learning, palliative care, ethical challenges, ethics

## RESULTS

The relevant studies that were identified in the literature are briefly presented in Section A, whereas the studies referring to the ethical challenges are presented in Section B. A more extensive analysis of the ethical challenges that may occur through AI applications in PC is presented in Section C.

### A. STUDIES REGARDING THE APPLICATION OF AI IN PALLIATIVE CARE

#### A1. Improving Palliative care with Deep Learning<sup>6</sup>

In this study, scientists described a method using DL and Electronic Health Record (EHR) data of patients, to predict all-cause 3-12 month mortality of patients as a proxy for those who could benefit from palliative care. The EHR data of admitted patients were automatically evaluated by an algorithm, which brings patients who are likely to benefit from palliative care services to the attention of the Palliative Care team. These predictions enable the Palliative Care team to take a proactive approach in reaching out to such patients, rather than relying on referrals from treating physicians, or conduct time consuming chart reviews of all patients. They used the following proxy problem statement: “Given a patient and a date, predict the mortality of that patient within 12 months from that date, using EHR data of that patient from the prior year”. They were also separately interested in the model performance on a subproblem — the ability to predict mortality of patients who are currently admitted. This is because it is much easier for the palliative care staff to intervene with admitted patients. The model eventually was a little under-confident in its probability estimates. Although some patients did not pass away within 12 months from their prediction dates, they were often

diagnosed with terminal illness and/or were high utilizers of healthcare services. They also demonstrated a novel method of generating explanations from complex deep learning models that helps build confidence of practitioners to act on the recommendations of the system.

#### A2. Machine Learning-based model to predict delirium in patients with advanced cancer treated with palliative care: a multicenter, patient-based registry cohort<sup>7</sup>

This study aimed to present a machine learning model that predicted delirium in patients in palliative care and to identify the significant features that influenced the model. The study dataset included 165 patients with delirium among 2314 patients with advanced cancer admitted to the acute palliative care unit. Seven machine learning models, including extreme gradient boosting, adaptive boosting, gradient boosting, light gradient boosting, logistic regression, support vector machine, and random forest, were evaluated. The study revealed that the combination of XBoost and RF delivered the most optimal performance. Additionally, they identified that sex was the primary contributor in predicting delirium, followed by a history of delirium, chemotherapy, smoking status, alcohol consumption, and living with family. Furthermore, the machine learning model was successfully deployed on a public website (<http://ai-wm.khu.ac.kr/Delirium/>) to provide public access to delirium prediction results in patients with advanced cancer. The plan is to securely store the user-entered information with their consent, facilitating a real-time learning process to enhance the machine learning model.

#### A3. Novel method for predicting nonvisible symptoms using machine learning in cancer palliative care<sup>8</sup>

This study aimed to create a model to predict non-visible symptoms from visible symptoms and basic patient characteristics using machine learning. They performed a retrospective clinical survey involving 213 patients with cancer (no children included) by

dividing the reported symptoms into two groups-visible and nonvisible symptoms. They used decision tree analysis as an analytical machine learning method. The machine learning model used patient background data and visible symptoms to predict nonvisible symptoms: pain, dyspnea, fatigue, drowsiness, anxiety, delirium, inadequate informed consent, and spiritual issues. Although the proposed application is unlikely to be an absolute replacement for palliative care specialists, it is expected to help improve the quality of palliative care provided by healthcare professionals. The results can help better assess and manage symptoms in patients with cancer.

#### **A4. Development and Validation of a Deep Learning Algorithm for Mortality Prediction in Selecting Patients With Dementia for Earlier Palliative Care Interventions<sup>9</sup>**

The aim of this study was to develop a deep learning algorithm using longitudinal electronic health records to predict mortality risk as a proxy indicator for identifying patients with dementia who may benefit from palliative care. This retrospective cohort study, used patient demographic information and topics generated from clinical notes, to conduct 6-month, 1-year, and 2-year mortality prediction models with recurrent neural networks. They chose the long short-term memory (LSTM) network, given LSTM's ability to model longitudinal EHR data, in conjunction with an appropriate gradient-based learning algorithm. The models were trained using a data set of 24,229 patients and validated using another data set of 2,692 patients. The top-ranked latent topics associated with 6-month and 1- and 2-year mortality in patients with dementia include palliative and end-of-life care, cognitive function, delirium, testing of cholesterol levels, cancer, pain, use of health care services, arthritis, nutritional status, skin care, family meeting, shock, respiratory failure, and swallowing function. The model proved that clinical notes along with patient demographics are informative, and the deep learning neural

network structure can successfully capture short- and long-range longitudinal patterns.

#### **A5. Identifying Connectional Silence in Palliative Care Consultations: A Tandem Machine-Learning and Human Coding Method<sup>10</sup>**

This study is a cross-sectional analysis of 354 audio-recorded inpatient palliative care consultation conversations to evaluate the reliability, efficiency and sensitivity of a tandem ML-HC (Machine Learning-Human Coding) approach to identify Connectional Silence. The codebook included three types of Connectional Silences: Emotional, Compassionate and Invitational. Connectional Silences were rare (5.5%) among all two-second or longer pauses in palliative care conversations. Tandem ML-HC demonstrated strong reliability. HC alone required 61% more time than the Tandem ML-HC method. No Connectional Silences were missed by the ML screening algorithm. According to the authors tandem ML-HC method meets the purpose for which it was created in serious illness conversations.

#### **A6. Applications of Machine Learning in Palliative Care: A Systematic Review<sup>11</sup>**

In this study they systematically searched for published research papers that used different kinds of machine learning in palliative care for different use cases. In total, 22 publications using ML for mortality prediction (n=15), data annotation (n=5), predicting morbidity under palliative therapy (n=1), and predicting response to palliative therapy (n=1) were included. The studies used a variety of different supervised and unsupervised models such as neural networks, (boosted) tree-based classifiers, support vector machines, and hierarchical clustering. This review found mortality prediction as the most frequent use case of ML in palliative care. According to the authors, in an ideal world, models that recommend patients for palliative care referral should not only predict mortality but also try to predict the time to clinical deterioration, which is usually the much more relevant event to determine when palliative



care is needed. In conclusion, machine learning in palliative care is mainly used to predict mortality, but recent publications indicated its potential for other innovative use cases such as data annotation and predicting complications.

#### **A7. Improving palliative care with machine learning and routine data: a rapid review [version 2; peer review: 3 approved]<sup>12</sup>**

In this study they conducted a rapid review including peer-reviewed studies that used ML approaches on routine data to improve palliative care for adults. The specified outcomes were survival, quality of life (QoL), place of death, costs, and receipt of high-intensity treatment near the end of life. The database search identified 426 citations. One paper predicted six-month mortality, one paper predicted 12-month mortality and one paper cross-referenced predicted 12-month mortality with healthcare spending. ML-informed models outperformed logistic regression in predicting mortality where data inputs were relatively strong, but those using only basic administrative data had limited benefit from ML. Identifying poor prognosis does not appear effective in tackling high costs associated with serious illness. While ML can help to identify those at risk of adverse outcomes and inappropriate treatment, applications to policy and practice are formative. Future research must not only expand scope to other outcomes and longer timeframes, but also engage with individual preferences and ethical challenges of this emerging field. According to the authors, most important is to recognise that improving clinical decision-making will require more than simply improving the predictive power of mortality models.

### **B. STUDIES ABOUT ETHICAL CHALLENGES IN THE USE OF AI IN PC**

After a brief review of the literature, it appears that there are not many references to the ethical dilemmas that may arise from the use of artificial intelligence in palliative care.

#### **B1. Ethical challenges of artificial intelligence technology in palliative care<sup>13</sup>**

This project aimed to identify the ethical challenges of AI in palliative care. Ethical challenges for AI in palliative care were identified and summarized into themes, using the four ethical principle framework (Autonomy, Beneficence, Non-maleficence, Justice). AI may limit individual autonomy to choose who has access to their data, where, how and for what purposes. It may not be possible for the individual to be fully aware of what is involved in the analysis (autonomy). The individual may not benefit directly; privacy for their data may need to be sacrificed to benefit wider society (Beneficence). AI may amplify pre-existing biases in the data set and/or in society (Non-maleficence). Resource poor areas and individuals and groups with limited data (e.g. homeless) are least likely to benefit from data driven medicine (Justice).

#### **B2. Ethical Considerations Related to Using Machine Learning-Based Prediction of Mortality in the Pediatric Intensive Care Unit<sup>14</sup>**

This study discusses ethical challenges associated with applying ML technology in pediatric intensive care unit (PICU) patients by considering the benefits and risks related to the technology and to care delivery, as well as organizational and legal issues. Pediatric patients differ from adults because children generally do not have legal control over their data or legal authority to give or withhold consent. Because data can be tracked across a longer proportion of their lives, the implications for privacy harms extend through the lifespan. Firstly, regarding technical considerations, ML relies on “learning” from comprehensive datasets. Lack of diversity or inaccuracy in datasets becomes reflected in predictions. Also, some prediction algorithms are so complex that one cannot determine how decisions are made (the “black box” phenomenon). This lack of transparency can lead to or contribute to mistrust and may affect clinician and patient acceptance and use of such technology if the models are not properly checked for their safety and effectiveness.

Secondly, regarding care delivery considerations, for the patients who are predicted to live, the perceived objectivity of ML could substantiate decisions about using high-risk or resource-, time-, and labor-intensive therapies. When decisions involve therapies with high side effect profiles impacting future quality of life, such as an organ or hematopoietic stem cell transplant, families and clinicians would be better informed to make such choices. One might argue that such models could reduce the decision-making burden on families who are now sometimes asked to contribute to life and death decisions about their child's care with limited data. However, mortality prediction models could also limit the advancement of medical knowledge and family engagement. If clinicians avoid therapies with unknown efficacy for patients predicted to die, we could lose opportunities to learn. Third, regarding organizational considerations, healthcare organizations may be interested in the financial impact of using ML. The initial cost for hospitals purchasing AI technology ranges from \$75,000 to \$120,000. Despite the importance of transparency, hospitals currently use many prediction models as part of "quality improvement efforts" without necessarily disclosing their use to patients. This practice reflects the blurry line between hospital operations and medical research. Fourth, regarding legal considerations, AI also introduces liability questions. Under current law, physicians may be liable for harm to patients if they follow AI recommendations to use nonstandard approaches to care delivery. Current law likely only shields physicians from liability when they follow the standard of care. However, if AI becomes part of the standard of care, physicians will likely avoid liability when following (even incorrect) AI recommendations and patient harm occurs.

### C. ETHICAL CHALLENGES OF AI APPLICATIONS IN PALLIATIVE CARE

As the applications of AI in medicine keep rising and developing, they require compliance both with scientific and ethical rules, in order to produce benefit for the patients,

notwithstanding safety and effectiveness of medical care. Palliative care is a sensitive field of AI as its applications directly impact the quality of life, the mental and physical distress or discomfort and the comfort care of patients<sup>1</sup>. With the intention of focusing on the ethical challenges that arise, the use of AI will be approached on the basis of fundamental human rights, which are defined by the EU charter of fundamental rights<sup>4</sup>. These rights include respect for human dignity, freedom of the individual, solidarity, equality, citizens' rights, justice, respect for democracy and the law. The parallels that unite these rights can be reflected by what has been described as an "anthropocentric approach". In addition, they are legally binding rights and they ensure the compliance of the AI applications with the law. This approach for AI applications is necessary to promote health for everyone and everywhere by accelerating the development and adoption of appropriate, accessible and affordable person-centric digital healthcare<sup>15</sup>. The following analysis will be based on a set of 5 principles (autonomy, beneficence, non-maleficence, justice, data privacy) that could conflict with applications of AI in palliative care.

Firstly, it should be taken under consideration if the AI applications in PC maintain respect for human autonomy, which surrounds the idea that every human being should never be degraded, violated, or suppressed by new technologies such as AI systems. Briefly, end-users of those systems must have meaningful opportunities for choice over who accesses their data, where, when and for what purpose. Each patient or end-user must have their own voice and they should make decisions not only about their treatment but also the services they will receive<sup>16</sup>. This patients' right inevitably leads the health professionals to what is described as Transparency. Transparency and explainability are increasingly recognized as critical to ethical AI, leading the PC providers to fully inform the patients' or their caregivers of what is involved, meaning the goals, benefits and possible risks<sup>15,17</sup>. Without such information, a decision cannot be duly contested. An



explanation as to why a model has generated a particular output or decision is not always possible (“black box” phenomenon). This task is rather easy for clinicians since it raises the question of whether the patients will be able to understand the function of AI, how it will affect their treatment or their data privacy, keeping in mind the complexity of those systems. This difficulty should definitely not stand in the way of clinicians informing patients and families about the function-purpose-risks, since the trust between patients and clinicians would be shattered.<sup>12</sup> The degree to which explicability is needed is highly dependent on the context and the severity of the consequences and risks that AI applications can produce. For example, the results from Mortality Risk Prediction can potentially affect clinical decisions according to PC treatment and influence the patients’ psychological burden.<sup>11</sup> On the other hand AI models, that are used safely and with shared decision making, may provide more opportunities for patients to access PC or make decisions for their treatment.<sup>13</sup>

The following considerations are raised by the principle of Beneficence, which supports that AI applications should be designed and implemented for the common good to benefit humanity by some measure. Patient safety and quality of care are priorities when designing and implementing AI models in PC, hence its connected to PCs values and goals. The benefit for the patients must be emerged by all different “layers” of AI applications, which include the reliable and reproducible design, accuracy of performance, ecological validation, quality evaluation, proper implementation and training of clinicians. Such considerations could apply for patients whose data have been used to train AI algorithms. These patients may not benefit directly from these applications. Though, their data is used for the common good if the AI algorithm meets the rest of the criteria. For example, data has been used to identify the patients who are in need of PC, but not all patients are. This can lead to the fact that privacy of data might be sacrificed to benefit wider society. On the other hand, AI

applications in PC can lead to improvements of provided healthcare and more access to evidence-based, updated Palliative Care.<sup>13</sup>

Furthermore, as far as the principle of Non-maleficence is concerned, AI systems should neither cause nor exacerbate any harm or affect humans negatively. This entails the protection of human dignity, as well as mental and physical integrity. AI systems and the environments in which they operate should be secure and protected. They should be technically robust while ensuring that they are not open to malicious use. An example of such consideration could be the ML-based model that predicts delirium in patients with cancer treated with PC.<sup>7</sup> This model is deployed on a public website to provide public access to its results while it uses the data to enhance the ML model and train it. It has to be clarified that the research team ensures security of data and proper information of patients. Vulnerable people should be given more attention and included in the development and deployment of AI systems. For example, there are studies and ML models, from those mentioned above, that exclude children from the input data. In the AI models that refer to PC there are either not enough models trained over childrens’ data or children are not adequately represented in the data for training these AI models.<sup>18</sup> Particular attention should also be given to situations where AI systems are likely to cause or exacerbate negative effects due to power or information asymmetry, such as between employers and employees, businesses and consumers, or governments and citizens. Harm prevention also involves consideration of the natural environment and all living things.

In addition, the principle of Justice is concerned as far as the AI applications in PC, meaning that the development and implementation of AI systems should be done in a fair manner. The main factors that contribute to inequalities, inequities and injustice include sex/gender, age, ethnicity, income, education and geography<sup>19</sup>. The main problem that threatens societies following the development of AI is the social gap issue. In all countries around the world, with every development, discovery and invention, people

face greater social inequality and less social justice. Although AI improves the accessibility to more information about science and technology, it exacerbates social inequality with a greater gap between developing and advanced countries. These are also strengthened by the fact that almost all studies were conducted based on data from Western countries, mostly from the USA. Other countries included Canada, the UK, France, Denmark, Germany, Spain, and Australia. One study collected data from both North America and Asia, and another study included data from three European countries (Switzerland, Germany, and Italy). One study used data from nine Western countries. Two non-Western countries/regions appeared in the collection of studies: sub-Saharan Africa and India.<sup>11</sup> Consequently, resource poor areas and individuals or groups with limited data in PC are least likely to benefit from data driven medicine. Such systematic biases and missing data in training data sets (such as electronic health records (EHRs) and insurance claims) are likely to perpetuate existing health disparities and they contribute to the disparity in AI performance among different demographic groups. While some of these inequities are systemic due to socioeconomic differences and discrimination, human biases also play an important role. For example, in the United States, existing research has demonstrated that doctors do not take Black patients' complaints of pain as seriously nor do they respond to them as quickly as they do for their White counterparts.<sup>20</sup> Another example of common bias embedded in healthcare systems is gender-based discrimination. Once again, in the domain of pain management, studies have pointed to the increased invisibilisation of female patients when reporting pain<sup>21</sup>. Though, there is not enough research and data around the biases in Palliative Care settings. It is widely argued that the most common cause for unfairness in medical AI is the bias in the data used to train the machine learning models. Besides that, another dimension that AI systems should imply commitment to, is that justice entails the ability to contest and provides effective legal protection against

decisions taken by the systems and by the people who operate them. In order to do this, the entity that is responsible for the decision should be identifiable and the decision-making processes should be explained. As far as the AI in PC settings is concerned, the so far applications of AI models are either for training algorithms or aiding clinicians as simple prognostic tools with none crucial decision-making responsibility.

Lastly, yet another concerning principle is that of Data Privacy. Informed consent is a crucial and integral part to the patient's experience in healthcare and it is linked to protection from harm, respect for autonomy and privacy protection. The risks that may arise from poor data privacy of patients could be using and sharing patients' data without informed consent, repurposing them without their knowledge, exposing data as a result of thefts or frauds and potential cyberattacks on AI models<sup>4</sup>. Not informing patients and families about these risks could result in loss of their trust in both their clinicians and the health care system<sup>17</sup>. Such an example is the use of EHR data in an AI algorithm that can detect possible patients who are in need of PC. Further considerations are born regarding children. Childrens' data exists and thus can be tracked across a longer proportion of their lives, which creates severe considerations and potential implications of privacy harms that extend through their lifespan.<sup>14</sup>

## DISCUSSION

At first glance, while the need for PC has grown exponentially, current research about applications of AI in PC, even though not nonexistent, remain low compared to the actual needs for patients and caregivers<sup>12</sup>. The results suggest that there has been an effort of applying AI models in PC, most of which have been training models and some have been provided for public access. The use of AI in PC can be summarized as all cause 3-12 months Mortality risk prediction as a proxy for those who could benefit from PC, Morbidity prediction under PC (dementia, delirium, non visible symptoms) and Data annotation

(Identifying Connectional Silence in Palliative Care Consultations). The majority of research suggests that the AI models should not be used as an automated clinical decision, rather than a tool to make the workflow of a human more efficient. In any case, the clinician is always in the loop to make the decision after having a closer look at patients' history. In addition, most of ML models are accompanied with limitations such as low data heterogeneity with imbalance in the number of patients in each groups,<sup>7,8,9</sup> limited sample size datasets<sup>7,8</sup>, use of assessments and tools that differ from clinical trials and might exclude confusing results<sup>7</sup>. Furthermore, while the timing of offering PC to a patient is certainly an important aspect that could benefit from AI, it is far from being the only one.<sup>22</sup> Every decision where the clinician has to weigh the benefits of an intervention and the consequences of performing it, could benefit from more precise predictions.

The limitations and ethical dilemmas are evidently challenging for both clinicians and researchers. The difficulty is accompanied by lack of regulations regarding AI applications in PC. The European Union (EU) has been at the forefront of medical AI innovation and has explicitly recognized the challenges AI presents for existing liability regimes. To provide legal certainty, the European Commission has proposed one of the first legal frameworks specific to AI, the *Artificial Intelligence Act*. This framework aims to promote the safe use of AI in high impact sectors, such as healthcare, while also strengthening technological innovation<sup>23</sup>. Research and implementation should be in accordance with general regulations regarding AI in healthcare and medicine. Most importantly, it is crucial to assess the risk of the AI application or development early in the design process. The Risk assessment should be performed according to the EU AI-ACT Risk Classification. It sets out four risk levels for AI systems: unacceptable, high, limited, and minimal (or no) risk. So far, AI applications in PC mainly concern models for mortality or comorbidities prediction. However, they do not contribute to the decision-making process

but they are used as tools to support and assist clinical decisions, meaning that the clinician makes the final decision after critical examination. Therefore, the so far applied AI models in PC can be classified as minimal risk. As stated by the AI-ACT, minimal risk AI models do not have any restrictions or mandatory obligations. Nevertheless, it is suggested to follow general principles such as human oversight, non-discrimination and fairness. If these models functioned as decision-makers, the risk would be classified as limited or high. This is explained by the potential for significant damage if these models fail or are misused. For example, if decisions about who receives palliative care were determined solely by such models, many patients could be deprived of the care they need. Some examples of limited risk AI in PC could potentially be the use of deepfakes as patient data in order to create larger databases and better train algorithms, or the use of biometric systems to recognize emotions such as anxiety or fatigue to improve the provision of PC. AI-ACT states that AI systems of limited risk must be transparent, meaning any deepfakes should be donated as such and humans should be informed about their interaction with the AI. An example of high risk AI in PC could be the risk assessment by insurance companies of whether a candidate will need PC or not. AI systems in this risk-class must meet certain requirements in order to be put on the market and operate in the EU.<sup>23</sup>

The overall conclusion drawn from these facts is that risk assessment is of utmost and mandatory importance for the development of an AI model, both in the field of healthcare and specifically in PC. A helpful self-assessment checklist exists in the FUTURE-AI guidelines for trustworthy AI in medicine.<sup>24</sup> These guidelines are organized according to six principles (Fairness, Universality, Traceability, Usability, Robustness, Explainability) and comprise concrete recommendations and a self-assessment checklist to enable AI designers, developers, evaluators and regulators to develop

trustworthy and ethical AI solutions in medicine and healthcare.

It is certainly understood that the existence of a common axis is necessary for the development of algorithmic models and their application in PC, in order to have reproducible and repeatable results. For the time being, researchers should develop their models in accordance with National Regulations, such as the assessment checklist for trustworthy AI called ALTAI.<sup>15</sup> The checklist is structured along seven categories: 1) human agency and oversight, 2) technical robustness and safety, 3) privacy and data governance, 4) transparency, 5) diversity, non-discrimination and fairness, 6) environmental and societal well-being and 7) accountability.<sup>15</sup> Consequently, the ethical challenges are not insurmountable. Health care professionals have the capability and obligation to act in the best interest of the patients and to ensure that the use of AI meets safeguards for mitigating these ethical risks.

## CONCLUSION

In summary, AI applications in palliative care are ushering in a new era for the field, though they are still in a premature stage of development. As mentioned, current applications include Mortality risk prediction, Data annotation and Morbidity prediction under PC settings. AI, ML and DL technologies are drastically advancing, offering healthcare greater possibilities, while becoming more and more popular every day. However, this potential is accompanied by significant ethical challenges that cannot be ignored. First and foremost, AI applications in PC must incorporate patient needs and ensure patients have control over their data and treatment decisions. In addition, transparency is crucial, requiring healthcare providers to fully inform patients about the goals, benefits, and risks of AI technologies. This should be accompanied by informed consent in order to maintain patients' trust and protect against potential risks. AI must be designed for the common good, prioritizing patient safety and quality care. Healthcare professionals must

develop AI systems fairly, avoiding biases that exacerbate social inequalities. Legally, it is not yet clear how civil liability should apply to AI and who would be liable, due to ongoing debates about whether human or product liability should be applied. Nonetheless, AI systems should be developed in accordance with the ethics guidelines for trustworthy AI, presented by HLEG. Finally, it's important to mention that PC requires a close doctor-patient relationship, which means that AI should be used alongside traditional palliative care methods. AI in PC is not just about Mortality prediction, but also about developing algorithms that can identify patient needs and lead to beneficial interventions.

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