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Harnessing AI for Precision Oncology: Transformative Advances in Non-Small Cell Lung Cancer Treatment

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Abstract This systematic review examines the emerging role of Artificial Intelligence (AI) in planning and optimizing treatment for Non-Small Cell Lung Cancer (NSCLC). Focusing on patient-tailored therapy planning and enhancing treatment efficacy through advanced deep learning algorithms, we meticulously selected and analyzed thirteen high-quality research studies demonstrating AI's integration in NSCLC management. These studies show the ability of AI to process complex clinical, radiomic, and genomic data to provide personalized therapy plans.
AI technologies, such as deep learning models and machine learning, have shown exceptional promise in predicting immune responses to initial treatments, potentially revolutionizing the management of NSCLC. This review highlights AI's transformative impact on predicting treatment outcomes, optimizing therapy regimens, and improving decision-making processes in NSCLC treatment. The collective findings from these studies reveal a significant trend towards personalized medical approaches, showcasing AI's remarkable capacity to handle extensive datasets and forecast individual patient reactions. This reassures us about the efficiency of AI in managing complex information, thereby increasing treatment efficacy and improving patient health outcomes. However, this review also underscores the pressing need for further research and development in AI applications, highlighting the urgency and importance of this field. Integrating AI into NSCLC treatment marks a new era of precision cancer care, paving the way for more accurate, efficient, and patient-centered care. The challenges and limitations identified in this review serve as a call to action, urging the oncology community to continue pushing the boundaries of AI in cancer care.
This review aims to identify the most advanced and effective technologies, enabling oncology researchers and healthcare professionals to utilize these tools without having to search through various available sources. This approach aims to streamline access to crucial information, allowing practitioners to focus on recent advancements. For this reason, the study concentrates on the last two years, which have been marked by significant integration of AI into precision medicine.

Keywords Lung cancer, NSCLC, Treatment, Artificial Intelligence

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1. Introduction

Artificial intelligence is making significant inroads in healthcare, and its role in the fight against lung cancer is particularly noteworthy. Lung cancer is a powerful argument for the incorporation of AI-driven solutions because it is the leading cause of cancer-related deaths worldwide [1, 2]. AI can revolutionize the field, impacting diagnosis, treatment, and patient outcomes. In this discussion, we explore the transformative impact of AI in lung cancer, delving into key areas such as early detection, image analysis, predictive modeling, treatment planning, and monitoring, all of which contribute to the evolving landscape of lung cancer care.

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1.1. Lung cancer statistics

Lung cancer is a significant public health issue, and its statistics can provide insight into its prevalence, risk factors, and impact on society.

Lung cancer is one of the most frequently diagnosed cancers globally, marked by disturbingly high rates of incidence and mortality [3]. In 2020 alone, it was estimated that there were 2.2 million new cases of lung cancer worldwide [4], making it the most widespread type of cancer. Moreover, lung cancer accounted for approximately 12% of all cancer cases, but it represented 21% of all cancer deaths, highlighting its significance as a global health concern [5].

The mortality rate associated with lung cancer is distressingly high, primarily due to frequent diagnosis in an advanced stage when treatment options are limited. In 2020, lung cancer remained the leading cause of cancer-related deaths worldwide, claiming an estimated 1.8 million lives [6]. According to the World Cancer Research and Fund International organization, ten countries have the highest lung cancer incidence rates in 2020. There were 2,206,771 cases globally, with an age-standardized rate (ASR) of 22.4 per 100,000 individuals. Hungary topped the list with 10,274 cases and an ASR of 50.1, followed by Serbia with 8,048 cases at an ASR of 47.3.

France (including New Caledonia) and French Polynesia reported significantly lower absolute numbers (166 and 144 cases) but had high ASRs of 42.9 and 40.4. Turkey presented a more significant number of cases (41,264) with an ASR of 40.0. Montenegro, Belgium, Bosnia and Herzegovina, North Korea, and Denmark also featured on the list, with cases ranging from a few hundred to over ten thousand. However, all had high ASRs, indicating a significant impact on lung cancer in these countries [7]. Historically, lung cancer has exhibited gender disparities, primarily affecting men. However, changes in smoking habits have led to a narrowing of this gap. In some regions, lung cancer incidence in women has even surpassed that in men, highlighting the changing dynamics of this disease. Worldwide, 15,124,771 people have been affected by lung cancer, including 14,353,943 men and 770,828 women. Figure 1 displays the incidence of lung cancer in the two countries with the highest rates, Hungary and Serbia, for both men and women.

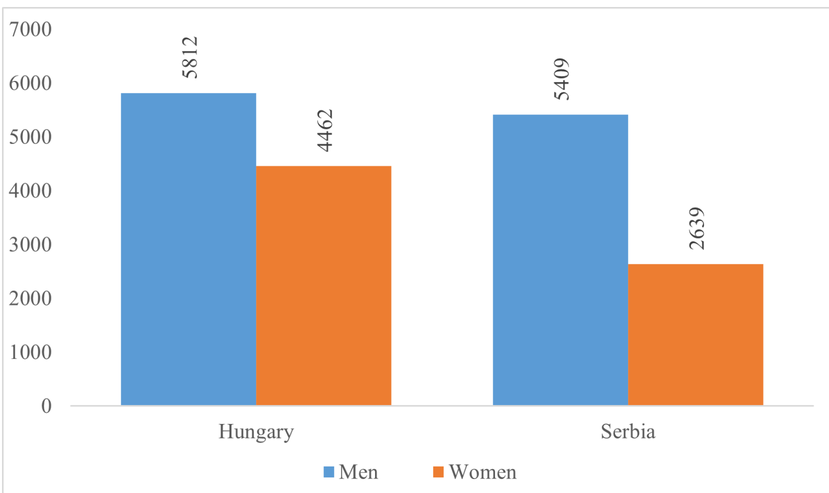


Figure 1. Incidence of lung cancer in Hungry and Serbia for both men and women.

The data in Table 1 depicts lung cancer incidence and mortality rates in different regions, broken down by age and gender (female and male). Rates vary significantly from one region to another, and some regions show substantially higher rates than others. For instance, Oceania, encompassing Australia, New Zealand, and Micronesia, exhibit some of the highest rates, while Western Africa and Southeast Asia have lower rates. Overall, lung cancer incidence and mortality rates tend to be higher in men than in women. However, it is essential to note that in certain regions, female rates are significantly elevated, possibly due to smoking habits and other risk factors.

Lung cancer development is significantly influenced by age. The likelihood of contracting this disease increases with age; most cases are diagnosed in people 65 years or older. This age-related risk underscores the importance of early detection and prevention, particularly among older populations. Smoking is the main risk factor for lung cancer [8]. An estimated 85% of lung cancer cases are believed to be caused by smoking [9]. The carcinogens and toxins present in tobacco smoke can lead to genetic mutations and cellular damage, increasing the likelihood of cancer development. Additionally, exposure to secondhand smoke poses a significant risk, making smoking cessation crucial for not only smokers but also those in close contact with them. Occupational exposure to carcinogens, such as asbestos and radon, can also contribute to lung cancer. Workers in specific industries, such as construction and mining, are at increased risk due to their exposure to these hazardous substances.

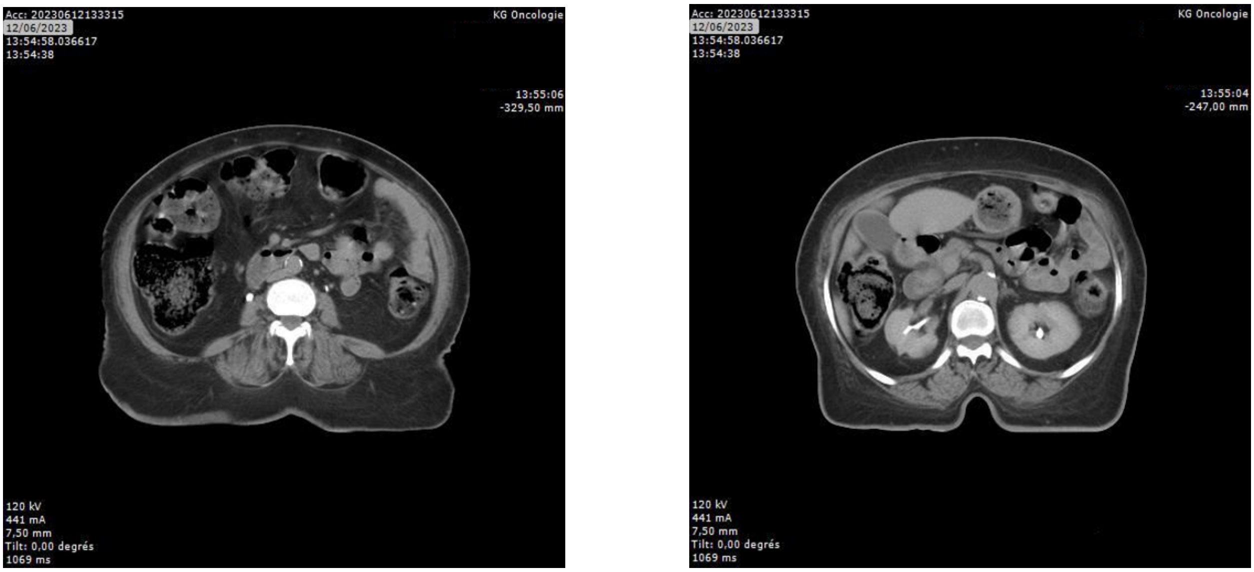
Table 1. Estimated age-standardized (per 100 000 persons) mortality rates (World) in 2020, lung cancer, both sexes, all ages[7].

	Female					Male				
Age	0-14	15-29	30-44	45-59	60+	0-14	15-29	30-44	45-59	60+
Australia and New Zealand	0	0.03	1.1	17.9	98.6	0	0.03	0.86	20.6	143.9
Caribbean	0	0.18	1.4	14.5	78.8	0.06	0.19	2.1	24.0	157.0
Central America	0.02	0.13	0.82	4.7	24.3	0.02	0.26	0.69	6.1	47.6
Central and Eastern Europe	0.00	0.11	1.5	15.7	61.9	0.01	0.25	3.2	67.1	284.4
Eastern Africa	0.00	0.08	0.56	4.6	17.5	0.01	0.11	0.75	6.0	25.4
Eastern Asia	0.01	0.22	2.9	24.1	123.3	0.00	0.36	4.7	50.7	283.5
Melanesia	0	0	0.49	9.7	58.6	0	0.13	0.84	19.9	110.8
Micronesia	0	0	0	31.2	164.0	0	0	6.8	50.4	375.7
Middle Africa	0	0.03	0.46	3.3	9.8	0	0.09	0.84	4.7	20.9
Northern Africa	0.01	0.18	0.87	5.7	18.5	0.01	0.17	2.4	33.2	109.6
Northern America	0.02	0.05	0.62	22.1	122.3	0.01	0.08	1.5	23.4	167.4
Northern Europe	0	0.06	1.3	18.7	131.7	0	0.08	0.56	22.8	178.8
Polynesia	0	0	4.6	28.9	130.6	0	0	1.7	61.4	316.2
South America	0.04	0.17	1.2	14.0	60.9	0.03	0.26	1.5	16.8	113.9
South-Central Asia	0.01	0.19	1.2	6.2	17.6	0.02	0.21	1.8	17.5	52.3
South-Eastern Asia	0.01	0.11	1.7	12.9	55.4	0.01	0.22	4.1	35.5	159.6
Southern Africa	0.03	0.12	0.98	12.2	55.1	0.04	0.34	2.4	41.3	153.8
Southern Europe	0.01	0.05	1.5	24.0	72.1	0	0.16	1.8	43.2	245.2
Western Africa	0.00	0.04	0.21	2.6	10.9	0.01	0.04	0.48	4.1	17.5
Western Asia	0	0.18	1.6	12.0	50.1	0.00	0.22	1.9	44.5	283.3
Western Europe	0.01	0.02	2.0	30.9	106.1	0.01	0	1.6	52.3	217.6

Thus, workplace safety measures and regulations are essential for reducing these risks. The development of lung cancer may be influenced by genetic factors [10]. Some individuals may have genetic predispositions that make them more susceptible to the disease. Genetic research is ongoing to identify specific genes associated with lung cancer, which could aid in early detection and personalized treatment strategies [11]. Small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) represent the two primary subtypes of lung cancer, with NSCLC being the more common of the two, accounting for approximately 85% of all lung cancer cases [12].It encompasses several subtypes, each with its unique characteristics and treatment options. Although less common, SCLC is often more aggressive and has a higher likelihood of spreading to other body parts.

The provided CT scan images shown in Figure 2 display cross-sectional views of the abdomen of a patient diagnosed with non-small cell lung cancer (NSCLC). A clear presence of ascites indicates an abnormal fluid accumulation within the peritoneal cavity. This finding is often associated with advanced malignancies and suggests metastatic progression of lung cancer. The images also show changes in soft tissue density, consistent with tumor involvement, which further supports the diagnosis of advanced-stage cancer. Various abdominal organs, including the liver and kidneys, are visible in the scans, but a detailed evaluation would be necessary to identify specific metastatic involvement in these organs.

Table 2 illustrates lung cancer incidence and mortality rates in various regions, revealing significant disparities. High incidence and mortality rates are evident in several Pacific Island nations, Central and Eastern Europe, and parts of Asia, emphasizing the substantial burden of lung cancer in these areas. In contrast, some regions, such as Southern and Northern Europe, North America, Australia, and New Zealand, exhibit comparatively lower rates. These variations can be attributed to a complex interplay of factors, including smoking prevalence, occupational exposures, healthcare infrastructure, and public health interventions. These statistics underscore the need for comprehensive strategies to control lung cancer, including prevention and early detection measures, as well as effective anti-smoking campaigns, to mitigate the impact of this major contributor to cancer-related morbidity and mortality.



(a) Axial CT Scan of the Abdomen Showing Ascites and Intestinal Structures

(b) Axial CT Scan of the Abdomen Highlighting Ascites and Abdominal Structures

Figure 2. Comprehensive CT Imaging of the Thoracic and Abdominal Regions in a Patient with NSCLC and Associated Ascites

The stage at which lung cancer is diagnosed has a significant impact on survival rates. Early stage lung cancer has a much higher chance of successful treatment and long-term survival. Unfortunately, most cases are diagnosed at advanced stages, leading to lower survival rates.

For localized lung cancer (confined to the lungs), the 5-year survival rate is 56% [13]. If the cancer has spread regionally (to nearby lymph nodes or tissues), the survival rate drops to 31%. When lung cancer has reached a distant stage (spread to other organs), the 5-year survival rate is a stark 6%.

Table 2. Estimated age-standardized (per 100 000 persons) incidence and mortality rates (World) in 2020, lung cancer, all ages[7].

Region	Male		Female	
	Incidence	Mortality	Incidence	Mortality
Polynesia	53.0	44.3	21.7	19.5
Micronesia	51.3	50.1	24.6	22.7
Central and Eastern Europe	49.0	42.0	11.6	9.5
Eastern Asia	48.1	39.7	22.1	17.8
Southern Europe	43.1	33.8	16.4	11.8

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Table 2 – Continued from previous page

Region	Male		Female	
	Incidence	Mortality	Incidence	Mortality
Western Asia	41.7	38.3	8.7	7.6
Western Europe	41.7	32.1	25.0	16.7
Northern America	35.7	22.2	30.1	16.9
Northern Europe	33.3	23.2	26.8	17.5
World	31.5	25.9	14.6	11.2
Australia and New Zealand	28.1	19.1	22.7	13.7
Southern Africa	27.5	23.6	9.3	8.1
South-Eastern Asia	26.4	23.7	9.6	8.4
Caribbean	23.0	21.3	13.0	11.1
Northern Africa	19.5	17.5	3.5	3.1
South America	17.8	15.4	10.3	9.1
Melanesia	17.4	15.4	9.2	8.0
South-Central Asia	9.7	8.8	3.5	3.1
Central America	6.7	6.4	4.0	3.6
Eastern Africa	4.2	3.9	3.0	2.7
Middle Africa	3.4	3.2	1.8	1.7
Western Africa	2.8	2.6	1.8	1.6

These statistics underscore the importance of early detection and the need for improved screening and diagnostic methods. The statistics surrounding lung cancer underscore the urgency of addressing this disease through prevention, early detection, improved treatment options, and support for those affected.

The flowchart, illustrated in Figure 3, delves into the comprehensive treatment process tailored to address these challenges. By mapping out each phase of treatment, from initial diagnosis to recurrence management, this flow chart provides a systematic approach to improving patient outcomes in light of the complex statistical backdrop. It presents a structured, sequential overview from the initial diagnosis to managing disease recurrence or progression. Initial Diagnosis: This stage includes the imaging and biopsy procedures necessary to establish an initial diagnosis. Staging and Assessment: Following the initial diagnosis, further detailed evaluations using techniques such as Computed Tomography (CT), Positron Emission Tomography (PET), and Magnetic Resonance Imaging (MRI) are performed to determine the cancer's stage. Treatment: Depending on the stage and individual characteristics of the cancer, treatment may include surgery, chemotherapy, radiotherapy, and AI-assisted interventions. Follow-Up: Patients enter a follow-up phase after initial treatment to monitor side effects and treatment response. Beneath each primary step, specific processes are detailed: Genetic and Molecular Testing: Performed post-initial diagnosis to identify specific biomarkers and mutations. Personalized Treatment Planning: Utilizing AI and clinical trials to tailor treatment to the patient's characteristics. Treatment Optimization: AI-based adjustments to treatment plans to maximize efficacy and minimize side effects. Response Evaluation: Imaging and lab tests are used to assess treatment response. The diagram continues with second-level processes, emphasizing ongoing care: Multidisciplinary Review: Discussion of cases within a tumor board for collegiate decision-making. Treatment Execution: Ongoing implementation and evaluation of the treatment plan. Remission or Disease Control: Regular scans and check-ups to monitor for remission or disease control. Recurrence or Progression: Management of treatment options in case of disease recurrence or progression.

By mapping out each phase of the treatment, from initial diagnosis to management of recurrence, this flowchart provides a systematic approach to improving patient outcomes in light of the complex statistical backdrop. It presents a structured, sequential overview from the initial diagnosis to managing disease recurrence or progression.

1. Initial diagnosis: This stage includes the imaging and biopsy procedures necessary to establish an initial diagnosis.
2. Staging and Evaluation: Following the initial diagnosis, further detailed evaluations using different techniques to determine the cancer's stage.

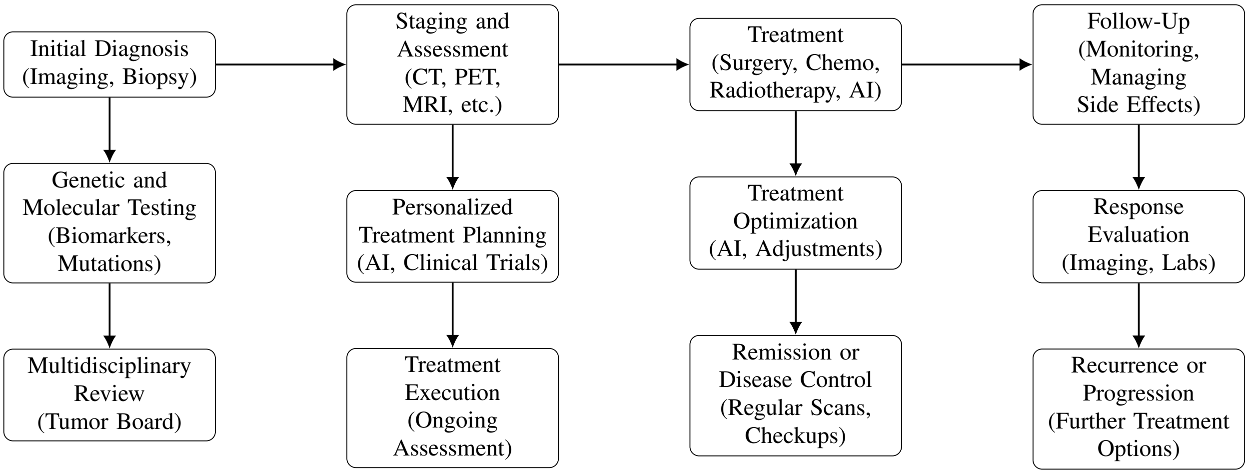

Figure 3. Comprehensive Treatment Process Flowchart for Non-Small Cell Lung Cancer.

3. Treatment: Depending on the stage and individual characteristics of the cancer, treatment can include surgery, chemotherapy, radiation therapy, and AI-assisted interventions.
4. Follow-Up: Patients enter a follow-up phase after initial treatment to monitor side effects and treatment response.

Below each primary step are detailed specific processes.

- Genetic and Molecular Testing: Performed post-initial diagnosis to identify specific biomarkers and mutations.
- Personalized Treatment Planning: Using artificial intelligence and clinical trials to tailor treatment to the patient's characteristics.
- Optimization of Treatments: AI-based adjustments to treatment plans to maximize efficacy and minimize side effects.
- Response Evaluation: Imaging and laboratory tests are used to assess treatment response.

The diagram continues with second-level processes, emphasizing ongoing care:

- Multidisciplinary Review: Discussion of cases within a tumor board for collegiate decision-making.
- Treatment Execution: Ongoing implementation and assessment of the treatment plan.
- Remission or Disease Control: Regular scans and checkups to monitor for remission or disease control.
- Recurrence or Progression: Management of treatment options in case of disease recurrence or progression.

1.2. Using artificial intelligence in lung cancer treatment

With the potential to completely transform disease detection, diagnosis, and treatment, the impact of artificial intelligence on healthcare care has attracted a lot of attention recently. One of the main causes of cancer-related death worldwide is lung cancer, which makes a strong case for the use of AI technologies [14]. This systematic review aims to assess the influence of AI on lung cancer mortality rates by synthesizing the existing body of literature. This review identifies and analyzes research focused on integrating AI into lung cancer care through a comprehensive search for peer-reviewed articles and studies. Key areas of investigation include AI-driven early detection, image analysis for tumor identification and staging, predictive modeling, treatment planning, and assessment of treatment response. In addition, we evaluate the quality of evidence and the methodologies employed in these studies. Preliminary findings suggest that AI has the potential to enhance lung cancer outcomes by enabling more accurate and timely diagnosis [15], individualized treatment plans, and real-time monitoring of disease progression. AI-driven algorithms have shown promise in improving the sensitivity and specificity of radiological imaging [16], thus helping to early diagnose. Additionally, AI can assist clinicians in identifying optimal treatment regimens while facilitating therapeutic response assessment through image analysis and predictive modeling. Nevertheless, implementing AI in clinical practice is challenging, including issues related to data privacy, integration into healthcare workflows, and the need for robust validation in diverse patient populations. This review addresses these barriers and discusses potential solutions and future directions in AI research for lung cancer. The synthesis of available evidence will shed light on the evolving landscape of AI applications in lung cancer care and its potential impact on reducing mortality rates. By examining the current state of AI-driven innovations in lung cancer management, this systematic review seeks to inform healthcare professionals, researchers, and policymakers about the implications of AI for improved patient outcomes. Ultimately, a thorough understanding of AI's benefits, limitations, and future prospects in lung cancer care is essential to guide its effective integration into clinical practice and advance the fight against this deadly disease.

2. Materials and Methods

2.1. Study design

This systematic review focused on examining the influence of AI on the treatment of NSCLC, drawing on online articles published in reputable journals.

2.2. Search strategy

Between October 2, 2023, and November 8, 2023, a comprehensive and extensive search of the literature was carried out on the following electronic databases: ”PubMed”, ”Elsevier”, ”Springer”, and ”Web of Science” for quality studies in journals indexed Q1 according to the Journal Citation Reports (JCR) classification system between the period 2021 and 2023 using the search strategy (impact) AND (artificial Intelligence) OR (machine learning) OR (deep learning) AND (Lung cancer). The choice of databases was guided by the accessibility of free access, which led to the exclusion of certain databases such as Embase and CINAHL (Cumulative Index to Nursing and Allied Health Literature). Additionally, BioRxiv and Arxiv were excluded from the search as the articles published on these platforms are not peer-reviewed and therefore not indexed as Q1. The Directory of Open Access Journals (DOAJ) was the only database included to complement the study due to its inclusion of open access, peer-reviewed journals.

2.3. Inclusion and exclusion criteria

This systematic review encompasses studies focusing on the significant integration of artificial intelligence in lung cancer treatment, particularly in the management of NSCLC. No language restrictions were applied; however, the search results yielded articles published exclusively in English or French.
The systematic review included studies that involved outpatient clinic visits, diagnostic and prognostic tests, treatment processes, and case referrals. However, it excluded studies that investigated other diseases in NSCLC patients or analyzed the impact of mental health issues and the COVID-19 pandemic on the progression of the disease.

2.4. Data extraction

Following the initial selection process, thirteen articles were ultimately selected for inclusion in this review. We used the PRISMA 2020 Statement [17] to conduct systematic data interrogation to maintain methodological integrity. Figure 4 shows the PRISMA flow diagram for this systematic review along with the study selection process.
Searching only on PubMed with the exact keywords was insufficient to obtain all the articles before screening. Although most of the articles were published on PubMed, one study was not published in this database. Each database relies on different search algorithms, which means that using the same keywords may not yield the same articles, even if they are published in the same databases.

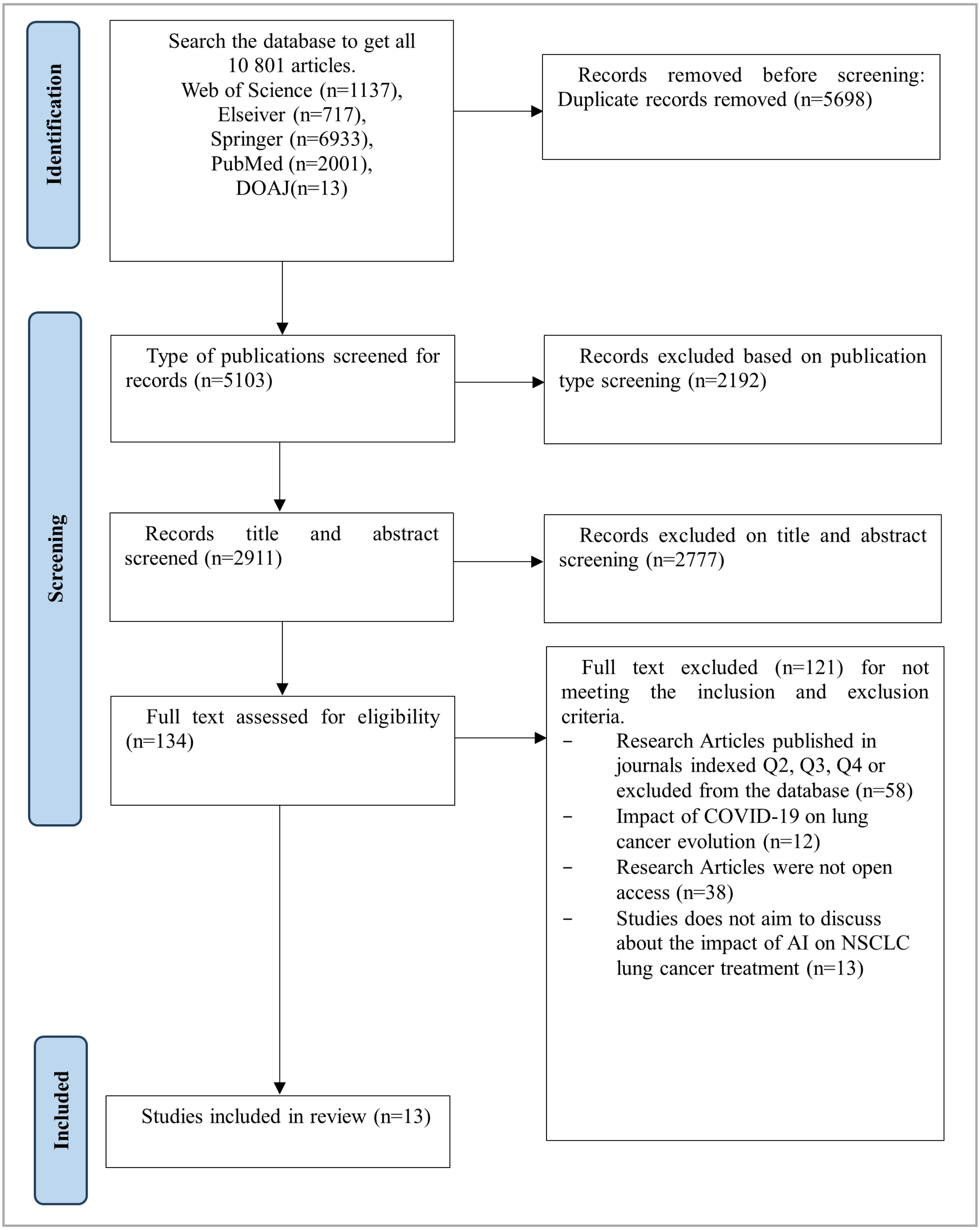

Figure 4. PRISMA flow diagram of the systematic review.

Two of the thirteen articles selected were found in the Springer database, hence the importance of diversifying databases.
By creating an MS Excel spreadsheet, the following information was extracted from some chosen articles: study title, objectives, methodology, main findings, PubMed reference number, and study goals.

A summary of all the articles included in this systematic review is presented in Table 3.

Table 3. Summary of included studies.

S. No.	PMID	Title of the study	Objective of the study	Study design	Major finding
1	37773123	Machine learning prediction models for different stages of non-small cell lung cancer based on tongue and tumor marker: a pilot study	Exploring the feasibility of developing predictive models for non-small cell lung cancer (NSCLC) at various stages by analyzing tongue characteristics and tumor markers.	Exploratory pilot study	Tongue characteristics and tumor markers were significantly more pronounced in the advanced NSCLC group compared to the non-advanced NSCLC group. Neural Network, Random Forest, and Naive Bayes demonstrated superior classification efficiency when applied to the tongue feature, tumor marker, and baseline data sets.
2	36395737	Deep learning for predicting the major pathological response to neoadjuvant chemotherapy in non-small cell lung cancer: A multi-center study	Developing a deep learning model using computed tomography to predict the main pathological response (MPR) to neoadjuvant chemoimmunotherapy.	Multicentre study	A high deep learning score was linked to the downregulation of pathways that mediate tumor proliferation and the enhancement of antitumor immune cell infiltration in the microenvironment.
3	35813093	A deep learning-based system for survival benefit prediction of tyrosine kinase inhibitors and immune checkpoint inhibitors in stage IV non-small cell lung cancer: A multicenter, prognostic study	Using pre-therapy computed tomography (CT) scans, estimate the survival benefit of EGFR-TKIs and ICIs in patients with stage IV non-small cell lung cancer (NSCLC).	Multicentre study	With ESBP support, the precision of the physician's diagnosis increased from 47. 91% to 66. 32% for those with two years of experience and 53. 12% to 61. 41% for those with five years of experience.

4	35572597	A Machine Learning Model Based on PET/CT Radiomics and Clinical Characteristics Predicts Tumor Immune Profiles in Non-Small Cell Lung Cancer: A Retrospective Multicohort Study	Create, test, and use a machine learning model that uses clinical characteristics and 18F-FDG PET / CT radiomics to predict TIME patterns in non-small cell lung cancer (NSCLC).	Retrospective Multicohort Study	The CD8-high projected group had considerably higher immunological scores and more active immune pathways than the CD8-low predicted group, according to TCGA data, suggesting that CD8 expression might signify TIME profiles in NSCLC.
5	37497221	Short-term outcomes of robot-assisted versus video-assisted thoracoscopic surgery for non-small cell lung cancer patients with neoadjuvant immunochemotherapy: a single-center retrospective study	Evaluating the advantages of Robotic-Assisted Thoracic Surgery (RATS) over Video-Assisted Thoracic Surgery (VATS) in terms of short-term outcomes for treating NSCLC patients with neoadjuvant immunochemotherapy.	Single-center retrospective study	A single-center retrospective study found that 30-day mortality rates were 0% in the RATS group and 3.23% in the VATS group.
6	36028289	Clinical validation of deep learning algorithms for radiotherapy targeting non-small cell lung cancer: an observational study	Segregating primary non-small cell lung cancer (NSCLC) tumors and related lymph nodes on CT images using deep learning algorithms that have been clinically validated.	Observational study	The tested models generated target volumes with radiation dose coverage comparable to the experts'. In addition, we found no discernible variations between expert-performed and AI-assisted de novo segmentations.
7	37268451	Predicting benefit from immune checkpoint inhibitors in patients with non-small cell lung cancer by deep learning based on CT: a retrospective study	Investigating the use of deep learning in thoracic CT scans to identify an imaging hallmark of the immune checkpoint inhibitor response and evaluate its additional value in a therapeutic setting.	Retrospective study	When the Deep-CT model was combined with traditional risk indicators, testing revealed a considerable improvement in prediction accuracy, with the overall survival C-index rising from 0-70 (clinical model) to 0-75 (composite model).

8	34061904	Prediction of outcome in patients with non-small cell lung cancer treated with second-line PD-1 / PDL-1 inhibitors based on clinical parameters: Results from a prospective, single institution study	Examination of the impact of clinical and laboratory factors on treatment outcomes in patients receiving second-line PD-1/PD-L1 inhibitors for metastatic non-small cell lung cancer (NSCLC).	Prospective study	With an AUC = 0.806 [95% CI: 0.714-0.889], the algorithm developed predicted the likelihood of stabilization of the disease (PR or SD) in a single person.
9	37718448	Development and validation of a risk model with variables related to non-small cell lung cancer in patients with pulmonary nodules: a retrospective study	Developing a novel predictive nomogram utilizing a design dataset of 515 lung nodules is to be designed using a secondary dataset of 140 nodules and a separate dataset of 237 nodules for external validation.	Retrospective study	The therapeutic utility of this predictive nomogram was validated by decision curve studies when used at a probability threshold 18% for NSCLC.
10	36505920	Computerized tumor-infiltrating lymphocytes density score predicts survival of patients with resectable lung adenocarcinoma	Development of an artificial intelligence-based pathology scoring system to evaluate TILs on H&E-stained whole slide LUAD images	Retrospective Cohort Study	The prognostic prediction model, combined with the WELL score in all four cohorts, outperformed the clinicopathological model in terms of discrimination, as indicated by a higher AUC at most time points (0.597 for the validation cohort) compared to the reference model (0.575).

11	36106060	What is the optimal input information for deep learning-based pre-treatment error identification in radiotherapy?	Development of a deep learning model for error identification in pre-treatment quality assurance	Comparative study	The normalization of mean and standard deviation particularly improved the classification of level 2 (error magnitude). Increasing image resolution improved error identification for volumetric modulated arc therapy (VMAT), although for SBRT a lower image resolution was also sufficient.
12	35705792	Usability of deep learning and H&E images predict disease outcome-emerging tool to optimize clinical trials	Using a weakly supervised survival convolutional neural network (WSS-CNN) with a visual attention mechanism	Multicentre study	The approach used provides a better understanding of the tumor microenvironment and has important implications for using computational pathology algorithms to predict prognosis and improve the efficacy of clinical trial studies.
13	-	Potential added value of an AI software with prediction of malignancy for the management of incidental lung nodules	Evaluation of the effects of an AI program that predicts cancer on the treatment of lung nodules that are unintentionally found	Retrospective study	The AI software using deep learning algorithms demonstrated a high negative predictive value (NPV) of 100% (with a 95% confidence interval of 82% to 100%), suggesting its potential use in reducing the need for follow-up in nodules categorized as benign. Specifically, adding an AI score to the initial CT scan could have avoided the recommended follow-up in 50% of benign pulmonary nodules (6 out of 12).

3. Results

In this systematic review that covers thirteen studies, three focus on personalized treatment, while six aim to optimize treatment in NCSLC using AI.

AI and Classification Models in NSCLC Treatment

Four out of the thirteen studies focused on using AI to improve the classification and diagnosis of NSCLC by integrating linguistic characteristics, tumor markers, and basic patient data (e.g., gender and age). These studies found that models incorporating a combination of these data points significantly outperformed those relying on single data types. For instance, Shi et al. employed logistic regression, Support Vector Machine (SVM), Random Forest, Naive Bayes, and Neural Network classifiers. Their findings indicated that combined features improved classification accuracy and reduced missed diagnoses. In their study, Shi et al.[18] employed five classifiers: logistic regression, support vector machine (SVM), random forest, naive Bayes and neural network, utilizing a combination of language characteristics, tumor markers, and basic patient data (gender, age) to develop classification and diagnostic models for NSCLC at various stages.
The results indicated that classifiers that relied solely on language characteristics or tumor markers independently produced inadequate classification results and a high rate of missed diagnoses. However, the performance of the models significantly improved when language characteristics were combined with tumor markers and basic patient data. This finding suggests that the use of a single language feature or tumor marker for NSCLC classification at different stages may need to be revised or influenced by the sample size.

AI in Radiotherapy Planning

Radiation planning is a one-time, high-cost investment that significantly impacts the efficiency of radiation therapy in terms of both time and money. To maximize radiation delivery to cancerous tissues while minimizing exposure to healthy tissues, precise radiotherapy planning is essential. After acquiring medical images, the subsequent planning steps include image registration, target and surrounding organ segmentation, and dose distribution calculation. One of the most labor-intensive tasks performed by radiation oncologists is the manual segmentation of the target, which includes the primary tumor and affected lymph nodes. This precise task requires voxel-by-voxel image analysis to accurately define the target volume. Despite advancements in modern radiotherapy techniques, such as intensity-modulated radiotherapy and image-guided radiotherapy, which allow for lower radiation doses to surrounding organs, these methods still demand a high degree of accuracy. With the support of AI, the segmentation time, the amount of time it takes to define or outline specific regions of interest (ROI), was reduced by 65% (5.4 minutes; $p < 0.0001$) and a 32% reduction in interobserver variability (SD; $p = 0.013$) [19].This improvement demonstrates AI's potential to streamline radiotherapy planning, making it more efficient and accurate by reducing the manual labor required and enhancing consistency across different observers [20].

Advanced Imaging and Predictive Systems for Survival Benefits

The use of a combined radiomic-clinical 18F-FDG PET/CT model accurately predicted tumor immune status in NSCLC, outperforming traditional clinical and radiomic models. The nomogram in the study by Zufang Liao et al. [21], integrating hypertension status and lung nodule size, reliably predicted NSCLC, with significant net reclassification improvement (NRI) and integrated discrimination improvement (IDI). The expression of CD8, a marker used to determine tumor immune microenvironment profiles (TIME), was examined in the study by Haipeng Tong et al. [22]. This study revealed that a combined radiomic-clinical 18F-FDG PET/CT model can accurately predict tumor immune status in non-small cell lung cancer (NSCLC), outperforming existing clinical models and radiomic models alone. This combined approach exploits both imaging data and clinical information to provide a more comprehensive assessment of the tumor's immune environment. The study by Yunlang She et al. [23] demonstrated that integrating radiomic features with clinical data improves the accuracy of predicting the immune status of non-small cell lung cancer tumors. The improved predictive ability of the model is crucial for tailoring personalized immunotherapy treatments, as it enables the identification of patients who are more likely to respond to immune checkpoint inhibitors (ICIs). These results suggest that advanced imaging techniques, when combined with clinical parameters, offer oncologists a powerful tool to better understand the immune context of the tumor. This comprehensive assessment is essential to optimize treatment strategies and improve outcomes for patients with non-small cell lung cancer.

The Efficient Survival Benefit Prediction System (ESBP) utilizing the EfficientNetV2 model significantly enhanced diagnostic accuracy among healthcare professionals. This system effectively predicted survival benefits of EGFR-TKI and ICI therapies in advanced-stage NSCLC [24]. Clinicians with two years of experience saw diagnostic accuracy improvements from 47.91% to 66.32%, while those with five years of experience improved from 53.12% to 61.41%. The study by Michelin et al. [25] demonstrated that adding an AI score to the initial CT scan to better manage incidentally discovered tumors could have avoided a guideline-recommended follow-up in 50% of benign pulmonary nodules (6/12 nodules), thereby avoiding these costs and burdens for patients and healthcare professionals.

Clinical Features and Predictive Signatures

Only 20 to 30% of NSCLC patients derive lasting benefits from immune checkpoint inhibitors, but a deep learning model on pre-treatment CTs (Deep-CT) showed better performance than conventional risk factors. It's crucial to emphasize that relying on Body Mass Index (BMI) and albumin levels alone falls short in providing a complete assessment of a patient's nutritional health, especially in the context of cancer patients receiving immunotherapy. To fully grasp the effects of body composition on these patients, a more in-depth and multifaceted analysis is necessary. This approach ensures a more accurate understanding of their overall health and how it may influence the effectiveness of their immunotherapy treatment [26]. These findings underscore the importance of considering multiple clinical factors in predictive models to improve treatment personalization and outcomes for NSCLC patients [27]. In the Rounis et al. study [28], patients with metastatic Non-Small Cell Lung Cancer (NSCLC) who lacked EGFR mutations or ALK translocations and had progressed following platinum-based chemotherapy were treated with Immune Checkpoint Inhibitors (ICIs). The study utilized JADbio, which identified four vital clinical features to develop a predictive signature. This signature demonstrated an 81% accuracy rate in forecasting disease stabilization post-ICI treatment, marking a significant advancement in personalized cancer care. These characteristics are prolonged antibiotic administration, bone metastases, liver metastases, and a BMI $< 25\,\text{kg/m}^2$.

Deep Learning Models and Immunotherapy

A comparison of video-assisted and robot-assisted thoracoscopic surgery was conducted on forty-six patients with NSCLC undergoing neoadjuvant immunochemotherapy [29]. With no discernible variations in surgical outcomes, pathological outcomes, or postoperative complications, baseline clinical features and induction-related adverse events were similar in both groups (RATS and VATS). RATS analyzed more N1 lymph nodes (LNs) and LN stations than VATS, which was linked to a shorter ICU stay. The one-year recurrence-free survival rates attained by VATS and RATS were similar. The 30-day mortality in the RATS and VATS groups was 0% and 3.23%, respectively ($p = 1.000$). The clinical validation of deep learning algorithms for radiotherapy targeting of NSCLC showed a significant reduction in segmentation time and interobserver variability, highlighting the efficiency of AI in this field. This meticulous task of manual target segmentation, crucial in radiotherapy planning, has benefited from advanced planning and administration techniques, demanding high segmentation precision. The studies collectively illuminate the evolving diagnostic and treatment methods for NSCLC, marking an increasing integration of advanced technologies in the medical field. All the studies included in this review have confirmed that the strength of machine learning prediction models lies in considering multiple factors (baseline data, clinical characteristics, etc.). The correlation between these factors leads to more effective treatment by considering all parameters impacting the progression of the disease. Studying the effects of different parameters helps confirm concerns about treatment, such as the use of $> 10\,\text{mg}$ prednisone equivalent in patients receiving ICIs [30] or, conversely, identifying effective treatments for specific categories of patients with particular diagnoses.

Based on these studies, routinely available variables may be used to distinguish between people who can control the course of the disease and people who are likely to worsen while receiving treatment. The latter group is advised to participate in clinical trials, try different treatment plans, or be subjected to closer observation.

4. Discussion

Numerous global initiatives and research projects support the ongoing fight against lung cancer, which is dedicated to understanding the disease, enhancing treatment options, and increasing survival rates. Scientists are continually exploring new therapeutic approaches, including targeted therapies and immunotherapies, which aim to tailor treatments to individual patients based on their genetic profiles and the specific characteristics of their cancer. Significant advances in lung cancer treatment have been achieved through clinical trials. These trials evaluate novel medications, therapies, and treatments, offering hope to patients who have exhausted traditional care options. Participation in clinical trials is crucial for developing innovative therapies that could become standard treatments in the future. This research aims to explore the effects of AI on NSCLC treatment through a systematic review methodology guided by specific eligibility criteria. The process involved thoroughly screening relevant literature, culminating in selecting thirteen pertinent articles aligned with the study's objectives. The final analysis was meticulously prepared, drawing insights from these selected studies. The findings presented in this article underscore the significant contribution of AI in enhancing the accuracy of NSCLC detection and advancing treatment approaches. Notably, AI has been instrumental in facilitating personalized medicine strategies, which accommodate individual patients' medical histories and treatment preferences, thereby improving overall treatment efficacy in NSCLC management. The studies included in this systematic review highlight the transformative potential of AI in reshaping the management of non-small cell lung cancer. Insights from the literature emphasize the profound implications of AI-based approaches in facilitating earlier detection, refining predictive prognostic models, and customizing treatments for individual patients. Moreover, optimizing treatment strategies through AI interventions appears promising, indicating a future where technological advancements significantly enhance therapeutic outcomes for patients battling this form of lung cancer. As indicated in all the studies, AI is a decision-support tool that predicts outcomes, identifies cancer stages, and tailors treatment—an approach known as personalized medicine. AI is not intended to replace oncologists but to support them by enhancing diagnostic accuracy and treatment planning. Healthcare professionals' involvement extends beyond treatment prescription to emotional support and ongoing mental health follow-up, positively impacting the patient's care trajectory. A patient-centric approach, which includes raising awareness and engaging patients in their care, is essential. This principle is mirrored in palliative care, which aims to enhance the quality of life for patients with severe, often advanced illnesses by alleviating associated symptoms. Palliative care focuses on relieving physical pain while addressing the psychological, social, and spiritual aspects of the patient [31]. Palliative care is not exclusively for terminally ill patients; it can be provided at any stage of a severe illness alongside curative or life-prolonging treatments. Its goal is to help patients live as comfortably and thoroughly as possible, considering their needs, preferences, and values and those of their families. AI provides healthcare professionals with a decision-support tool that enables faster and more accurate diagnoses, facilitating the prescription of appropriate treatments. In chemotherapy, for instance, localizing and identifying the tumor size and adapting the injected dose help restrict cancer progression and prevent mutations. Despite advancements in the knowledge and management of lung cancer, significant obstacles remain. Many lung cancer patients continue to experience unfavorable outcomes due to late-stage diagnoses, a lack of treatment options for advanced cases, and disparities in access to healthcare. To overcome these challenges, a multifaceted approach is required. This includes boosting funding for lung cancer research, increasing public awareness of smoking risks, improving access to early screening and diagnostic tools, and providing comprehensive support to lung cancer patients and their families. Additionally, health organizations must implement robust security measures to ensure patient confidentiality when using AI in lung cancer treatment. Concerns about patient data privacy and security are paramount, highlighting the importance of high-quality data when training AI algorithms to prevent biases and incomplete datasets and ensure inclusive and accurate outcomes for patient care. Evolving legal frameworks and ethical standards are crucial for regulating AI applications and prioritizing patient care. Ensuring that AI-driven advancements are affordable for all patients, regardless of their financial situation, is a formidable challenge. With its potential for earlier detection, precise diagnosis, personalized treatments, and improved progress monitoring, AI represents a revolutionary leap in lung cancer treatment. Its integration significantly improves patient outcomes while also increasing healthcare efficiency.

Limitations and Challenges of AI Applications

While the potential of AI in NSCLC treatment is significant, several limitations and challenges must be addressed. One of the main concerns is data privacy. Figure 5 presents the main limitations for the use of AI applications in NSCLC treatment, but these limitations are not exhaustive and extend to other socio-economic aspects, which are detailed subsequently.

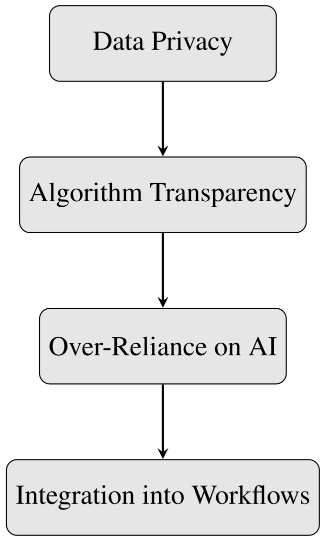

Figure 5. Limitations of AI Applications in NSCLC Treatment.

The use of patient data in AI models raises significant privacy concerns. Ensuring that data is anonymized and securely stored is crucial to protect patient confidentiality and comply with regulations such as GDPR(General Data Protection Regulation) and HIPAA(Health Insurance Portability and Accountability Act)[32, 33].
Robust data governance frameworks are needed to manage the collection, storage, and sharing of sensitive health information [34]. Another challenge is the transparency of the algorithm. Many AI algorithms function as "black boxes," making it difficult to understand how decisions are made. This opacity can hinder the trust and adoption of AI in clinical settings. Efforts to increase transparency, such as explainable AI (XAI) techniques shown in Figure 6, are essential to gain the trust of the clinician and the patient.

Explainable AI aims to make the "black-box" nature of many AI models more transparent. This means providing clear, understandable insights into how the AI system reaches its decisions or predictions. By making AI models more interpretable, XAI helps build trust among users. When clinicians and patients understand how an AI model comes to its conclusions, they are more likely to trust and adopt these technologies in clinical practice. Some regulations and standards require transparency and accountability in many fields, including healthcare. XAI helps ensure that AI systems comply with these regulations by providing explanations that can be audited and verified. Explainable AI allows users to better evaluate the recommendations made by AI systems. This can lead to improved decision-making as users can understand the strengths and limitations of the AI's outputs. Furthermore, when AI models are interpretable, it is easier to identify and correct errors or biases. These techniques aim to make the decision-making process of AI models more interpretable and understandable [35].

There is also a risk of over-relying on AI-generated recommendations without sufficient clinical oversight. This can lead to suboptimal patient care if healthcare professionals follow the AI system's recommendations without critical evaluation. It is essential to maintain a balance where AI serves as a decision-support tool rather than a replacement for human judgment [36]. Integrating AI systems into existing healthcare workflows poses practical challenges. These include training staff to use new technologies, ensuring interoperability with current systems, and adapting existing processes to incorporate AI tools. Successful integration requires careful planning, adequate resources, and ongoing support to address these challenges [37].

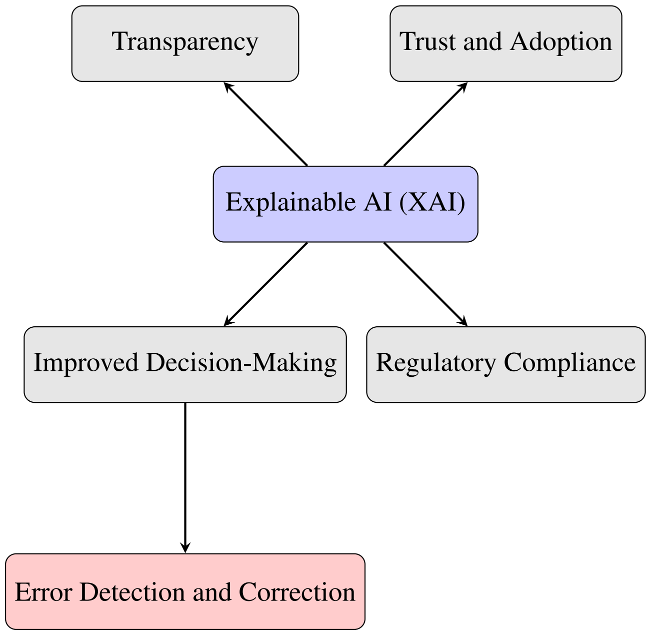

Figure 6. Concept of Explainable AI (XAI).

Ethical and Privacy Concerns

The implementation of AI in healthcare raises several ethical and privacy concerns. It is essential to ensure that patients are fully informed and provide consent for their data to be used in AI models. This involves clear communication about how their data will be used, the potential risks, and the benefits. Informed consent is a cornerstone of ethical medical practice and must be defended using AI [38]. Implementing robust data security measures to protect patient information is critical. This entails encryption, secure access controls, and regular audits to prevent unauthorized access and data breaches. Data security measures must evolve continuously to counter emerging threats [39]. Developing guidelines for the ethical use of AI, including addressing potential biases in AI decision-making, is crucial. Bias in AI models can arise from biased training data, leading to unfair treatment recommendations. Establishing ethical standards and continuously monitoring AI systems for bias can help mitigate these issues [40].

Economic implications

The adoption of AI technologies in treating NSCLC has several economic implications. Analyzing the cost-effectiveness of AI systems compared to traditional methods is vital to justify investing in AI technologies. AI can potentially reduce healthcare costs by improving diagnostic accuracy and treatment efficiency, but comprehensive cost-benefit analyses are necessary [41].

Ensuring that AI technologies are accessible to patients in different healthcare settings, including low-resource environments, is a significant challenge. Efforts must be made to develop affordable AI solutions that can be widely implemented, ensuring equitable access to advanced healthcare technologies [42]. AI technologies not only promise long-term savings, but also have the potential to significantly improve patient outcomes [43]. By enabling early detection and preventive care, AI can lead to better health for patients. However, economic barriers, such as the high initial costs of AI implementation, must be addressed to prevent exacerbating healthcare inequalities [44]. Practical training for healthcare professionals and patient education is essential to ensure that these technologies are effectively integrated into clinical practice, maximizing their benefits and reassuring patients about the quality of care they can expect [45]. AI can assist in creating personalized treatment plans, increasing treatment efficacy, and reducing the trial-and-error approach often associated with cancer treatment, potentially lowering costs. AI can also streamline administrative tasks and reduce the time of healthcare professionals on routine tasks, improving efficiency and reducing operational costs. Better diagnostic and treatment processes can improve patient outcomes, reducing long-term healthcare costs associated with extended hospital stays, complications, and palliative care. The expenses of treating cancer in its later stages can be greatly decreased by using AI to aid in early identification and prevention. However, ensuring that AI technologies are accessible to patients in different healthcare settings, including low-resource environments, remains a significant challenge.

AI-powered telemedicine can provide access to expert consultations for patients in remote or underserved areas, reducing the need to travel and making specialized care more accessible. Using AI in cancer treatment can enable a more widespread distribution of advanced diagnostic tools and treatment plans, allowing smaller healthcare facilities to offer high-quality care. Although AI technologies may reduce long-term costs, initial costs can be high. Ensuring that these technologies are covered by insurance or subsidized by governments is crucial for making them accessible to all patients. There is a risk that high initial costs could widen the gap between high-income and low-income patients unless measures are taken to ensure equitable access.

Ensuring patients understand and trust AI technologies is essential. This involves educating patients on how AI can benefit their treatment and addressing concerns or misconceptions. Adequate training for healthcare professionals is necessary to integrate AI effectively into treatment protocols and ensure that they can assist patients in understanding and accessing these technologies.

Future Research Directions

Future research should address the following areas to further enhance the application of AI in NSCLC treatment:

- **Improving Data Quality**: Developing methods to ensure high-quality, unbiased data for training AI models is crucial. This includes standardizing data collection processes and curating diverse datasets to prevent bias [46].
- **Enhancing Algorithm Transparency**: Creating more transparent AI algorithms that can provide interpretable results is essential. Research in explainable AI (XAI) should be prioritized to make AI decisions more understandable to clinicians and patients [47].
- **Integrating AI with Clinical Practice**: Studying the best practices for integrating AI systems into clinical workflows without disrupting existing processes is vital. Pilot studies and implementation research can provide insights into the most effective ways to incorporate AI into healthcare settings [48].

The limitations of this literature review include the exclusion of studies that focus on other diseases in patients with NSCLC, as well as those that analyze the impact of mental health issues and the COVID-19 pandemic on disease progression. Additionally, the review did not include research from paid databases, potentially limiting access to some high-quality, peer-reviewed studies. We are working on future research to address these gaps, with the aim of incorporating interactions between other diseases and the progression of NSCLC, as this directly impacts treatment. Collaborating with medical institutions such as Cheikh Zaid Hospital to access paid databases and oncology experiences will allow us to include a comprehensive range of high-quality published articles, thereby avoiding omissions in the analysis and recommendations. This approach will enable us to later build a predictive model for cancer treatment based on machine learning, informed by treated cases.

5. Conclusion

Lung cancer remains a global health issue with profound implications for both individuals and communities. The high incidence and mortality rates associated with non-small cell lung cancer (NSCLC) underscore the urgent need for comprehensive strategies encompassing preventive measures, early diagnosis, advanced treatment options, and robust support systems for those affected. Current data on lung cancer emphasize the critical need to address this disease through multifaceted approaches. Preventive strategies, such as smoking cessation programs and public health campaigns, are essential to reduce the incidence of lung cancer. Early diagnostic techniques, including low-dose computed tomography (CT) scans, can significantly improve survival rates by identifying tumors at more

treatable stages.
The treatment landscape for NSCLC is evolving rapidly, with ongoing research and global initiatives paving the way for better patient outcomes. Innovations in targeted therapies and immunotherapies have already shown promise in extending survival and improving the quality of life of patients. Furthermore, comprehensive support systems, including psychological, social, and palliative care, are essential to address the multifaceted needs of lung cancer patients and their families. Artificial intelligence (AI) has emerged as a transformative force in the battle against lung cancer. Its impact spans various facets of care, from early detection and accurate tumor identification to predictive modeling, treatment planning, and real-time monitoring. AI algorithms, trained in vast datasets, can identify subtle patterns in imaging and genomic data that human eyes might miss, thus enhancing the precision of diagnoses. The role of AI in predictive modeling is particularly noteworthy.
By analyzing diverse data points, AI can forecast disease progression and treatment responses, enabling personalized treatment plans tailored to individual patient profiles. This personalized approach promises more effective treatments and a reduction in adverse effects, thereby improving overall patient outcomes. In treatment planning, AI assists clinicians in designing optimal therapeutic strategies, integrating data from various sources to recommend the most effective interventions. Real-time monitoring through AI-driven tools ensures that patients receive timely adjustments to their treatment regimens, maximizing efficacy, and minimizing complications. Despite AI's significant promise, several challenges remain in integrating these technologies seamlessly into healthcare systems. Issues such as data privacy, algorithm transparency, and the need for rigorous clinical validation must be addressed to build trust among healthcare providers and patients. Additionally, training healthcare professionals to utilize AI tools effectively is crucial for their successful implementation.
Looking ahead, the future of NSCLC care is bright, marked by continuous innovation and the potential to significantly reduce the global burden of this disease.
AI stands at the forefront of this revolution, promising more effective treatments, personalized care, and better patient outcomes. As we overcome the challenges associated with AI integration, we move closer to a future where lung cancer is more manageable and potentially curable.

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REFERENCES

1. M. A. Thanoon, M. A. Zulkifley, M. A. A. Mohd Zainuri, and S. R. Abdani, "A Review of Deep Learning Techniques for Lung Cancer Screening and Diagnosis Based on CT Images," *Diagnostics*, vol. 13, no. 16, p. 2617, Jan. 2023, number: 16 Publisher: Multidisciplinary Digital Publishing Institute. [Online]. Available: https://www.mdpi.com/2075-4418/13/16/2617
2. M. Liu, J. Wu, N. Wang, X. Zhang, Y. Bai, J. Guo, L. Zhang, S. Liu, and K. Tao, "The value of artificial intelligence in the diagnosis of lung cancer: A systematic review and meta-analysis," *PLoS One*, vol. 18, no. 3, p. e0273445, Mar. 2023. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10035910/
3. R. El Sabrouty, A. Elouadi, and M. A. S. Karimoune, "Care Pathway Model for Patients with Localized Lung Adenocarcinoma," in *International Conference on Advanced Intelligent Systems for Sustainable Development (AI2SD'2023)*, M. Ezziyyani, J. Kacprzyk, and V. E. Balas, Eds. Cham: Springer Nature Switzerland, 2024, pp. 344–354.
4. C. Li, S. Lei, L. Ding, Y. Xu, X. Wu, H. Wang, Z. Zhang, T. Gao, Y. Zhang, and L. Li, "Global burden and trends of lung cancer incidence and mortality," *Chinese Medical Journal*, vol. 136, no. 13, p. 1583, Jul. 2023. [Online]. Available: https://journals.lww.com/cmj/fulltext/2023/07050/global_burden_and_trends_of_lung_cancer_incidence.10.aspx
5. D. A. Siegel, S. A. Fedewa, S. J. Henley, L. A. Pollack, and A. Jemal, "Proportion of Never Smokers Among Men and Women With Lung Cancer in 7 US States," *JAMA Oncol*, vol. 7, no. 2, p. 302, Feb. 2021. [Online]. Available: https://jamanetwork.com/journals/jamaoncology/fullarticle/2773380
6. "World Lung Cancer Day 2023: Know the Types and Treatment of Lung Cancer," Aug. 2023. [Online]. Available: https://www.timesnownews.com/health/world-lung-cancer-day-2023-know-the-types-and-treatment-of-lung-cancer-article-102301347
7. "Lung cancer statistics | World Cancer Research Fund International." [Online]. Available: https://www.wcrf.org/cancer-trends/lung-cancer-statistics/
8. B. Audelan, "Probabilistic segmentation modelling and deep learning-based lung cancer screening."

9. "Lung cancer." [Online]. Available: https://www.who.int/news-room/fact-sheets/detail/lung-cancer
10. M. B. Lebrett, E. J. Crosbie, M. J. Smith, E. R. Woodward, D. G. Evans, and P. A. J. Crosbie, "Targeting lung cancer screening to individuals at greatest risk: the role of genetic factors," *J Med Genet*, vol. 58, no. 4, pp. 217–226, Apr. 2021. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8005792/
11. C. Chouaïd, S. Gendarme, and J.-B. Auliac, "Artificial intelligence to finally enable precision medicine for the management of resected non-small-cell lung cancer," *Ann Oncol*, vol. 34, no. 7, pp. 565–566, Jul. 2023.
12. L. Xiong, C. Zhu, Y. Lu, M. Chen, and M. Li, "Serum THBS2 is a potential biomarker for the diagnosis of non-small cell lung cancer," *J Cancer Res Clin Oncol*, vol. 149, no. 17, pp. 15 671–15 677, Nov. 2023. [Online]. Available: https://doi.org/10.1007/s00432-023-05330-9
13. "Time to Treatment Impacts on Early-Stage Lung Cancer Surgery Outcomes," Mar. 2022. [Online]. Available: https://www.jons-online.com/lung-cancer-monthly-minutes/4466-time-to-treatment-impacts-on-early-stage-lung-cancer-surgery-outcomes
14. J. M. Archer, M. T. Truong, G. S. Shroff, M. C. B. Godoy, and E. M. Marom, "Imaging of Lung Cancer Staging," *Semin Respir Crit Care Med*, vol. 43, no. 6, pp. 862–873, Dec. 2022, publisher: Thieme Medical Publishers, Inc. [Online]. Available: http://www.thieme-connect.de/DOI/DOI?10.1055/s-0042-1753476
15. Y. Kl, T. Ys, Y. Hc, L. Cj, K. Pc, L. Mr, H. Ct, K. Lc, W. Jy, H. Cc, S. Jy, and Y. Cj, "Deep learning with test-time augmentation for radial endobronchial ultrasound image differentiation: a multicentre verification study," *BMJ open respiratory research*, vol. 10, no. 1, Aug. 2023, publisher: BMJ Open Respir Res. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/37532473/
16. M. Cellina, M. Cè, G. Irmici, V. Ascenti, N. Khenkina, M. Toto-Brocchi, C. Martinenghi, S. Papa, and G. Carrafiello, "Artificial Intelligence in Lung Cancer Imaging: Unfolding the Future," *Diagnostics (Basel)*, vol. 12, no. 11, p. 2644, Oct. 2022.
17. M. J. Page, J. E. McKenzie, P. M. Bossuyt, I. Boutron, T. C. Hoffmann, C. D. Mulrow, L. Shamseer, J. M. Tetzlaff, E. A. Akl, S. E. Brennan, R. Chou, J. Glanville, J. M. Grimshaw, A. Hróbjartsson, M. M. Lalu, T. Li, E. W. Loder, E. Mayo-Wilson, S. McDonald, L. A. McGuinness, L. A. Stewart, J. Thomas, A. C. Tricco, V. A. Welch, P. Whiting, and D. Moher, "The PRISMA 2020 statement: an updated guideline for reporting systematic reviews," *BMJ*, vol. 372, p. n71, Mar. 2021.
18. Y. Shi, H. Wang, X. Yao, J. Li, J. Liu, Y. Chen, L. Liu, and J. Xu, "Machine learning prediction models for different stages of non-small cell lung cancer based on tongue and tumor marker: a pilot study," *BMC Medical Informatics and Decision Making*, vol. 23, no. 1, p. 197, Sep. 2023. [Online]. Available: https://doi.org/10.1186/s12911-023-02266-5
19. A. Hosny, D. S. Bitterman, C. V. Guthier, J. M. Qian, H. Roberts, S. Perni, A. Saraf, L. C. Peng, I. Pashtan, Z. Ye, B. H. Kann, D. E. Kozono, D. Christiani, P. J. Catalano, H. J. W. L. Aerts, and R. H. Mak, "Clinical validation of deep learning algorithms for radiotherapy targeting of non-small-cell lung cancer: an observational study," *Lancet Digit Health*, vol. 4, no. 9, pp. e657–e666, Sep. 2022.
20. T. Qaiser, C.-Y. Lee, M. Vandenberghe, J. Yeh, M. A. Gavrielides, J. Hipp, M. Scott, and J. Reischl, "Usability of deep learning and h&e images predict disease outcome-emerging tool to optimize clinical trials," *npj Precision Oncology*, vol. 6, no. 1, 2022, cited by: 16; All Open Access, Gold Open Access. [Online]. Available: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85132160474&doi=10.1038%2fs41698-022-00275-7&partnerID=40&md5=b178ab643abc60b416606c148319e655
21. H. Tong, J. Sun, J. Fang, M. Zhang, H. Liu, R. Xia, W. Zhou, K. Liu, and X. Chen, "A Machine Learning Model Based on PET/CT Radiomics and Clinical Characteristics Predicts Tumor Immune Profiles in Non-Small Cell Lung Cancer: A Retrospective Multicohort Study," *Front Immunol*, vol. 13, p. 859323, 2022.
22. Z. Liao, R. Zheng, N. Li, and G. Shao, "Development and validation of a risk model with variables related to non-small cell lung cancer in patients with pulmonary nodules: a retrospective study," *BMC Cancer*, vol. 23, p. 872, Sep. 2023. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10506295/
23. Y. She, B. He, F. Wang, Y. Zhong, T. Wang, Z. Liu, M. Yang, B. Yu, J. Deng, X. Sun, C. Wu, L. Hou, Y. Zhu, Y. Yang, H. Hu, D. Dong, C. Chen, and J. Tian, "Deep learning for predicting major pathological response to neoadjuvant chemoimmunotherapy in non-small cell lung cancer: A multicentre study," *EBioMedicine*, vol. 86, p. 104364, Dec. 2022.
24. K. Deng, L. Wang, Y. Liu, X. Li, Q. Hou, M. Cao, N. N. Ng, H. Wang, H. Chen, K. W. Yeom, M. Zhao, N. Wu, P. Gao, J. Shi, Z. Liu, W. Li, J. Tian, and J. Song, "A deep learning-based system for survival benefit prediction of tyrosine kinase inhibitors and immune checkpoint inhibitors in stage IV non-small cell lung cancer patients: A multicenter, prognostic study," *EClinicalMedicine*, vol. 51, p. 101541, Sep. 2022.
25. B. Michelin, A. Labani, P. Bilbault, C. Roy, and M. Ohana, "Potential added value of an ai software with prediction of malignancy for the management of incidental lung nodules," *Research in Diagnostic and Interventional Imaging*, vol. 8, p. 100031, 2023. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S2772652523000108
26. M. B. Saad, L. Hong, M. Aminu, N. I. Vokes, P. Chen, M. Salehjahromi, K. Qin, S. J. Sujit, X. Lu, E. Young, Q. Al-Tashi, R. Qureshi, C. C. Wu, B. W. Carter, S. H. Lin, P. P. Lee, S. Gandhi, J. Y. Chang, R. Li, M. F. Gensheimer, H. A. Wakelee, J. W. Neal, H.-S. Lee, C. Cheng, V. Velcheti, Y. Lou, M. Petranovic, W. Rinsurongkawong, X. Le, V. Rinsurongkawong, A. Spelman, Y. Y. Elamin, M. V. Negrao, F. Skoulidis, C. M. Gay, T. Cascone, M. B. Antonoff, B. Sepesi, J. Lewis, I. I. Wistuba, J. D. Hazle, C. Chung, D. Jaffray, D. L. Gibbons, A. Vaporciyan, J. J. Lee, J. V. Heymach, J. Zhang, and J. Wu, "Predicting benefit from immune checkpoint inhibitors in patients with non-small-cell lung cancer by CT-based ensemble deep learning: a retrospective study," *Lancet Digit Health*, vol. 5, no. 7, pp. e404–e420, Jul. 2023.
27. C. J. Wolfs and F. Verhaegen, "What is the optimal input information for deep learning-based pre-treatment error identification in radiotherapy?" *Physics and Imaging in Radiation Oncology*, vol. 24, p. 14 – 20, 2022, cited by: 4; All Open Access, Green Open Access. [Online]. Available: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85137304627&doi=10.1016%2fj.phro.2022.08.007&partnerID=40&md5=45cf92be4c3e621cb74ea3052fa15254
28. K. Rounis, D. Makrakis, C. Papadaki, A. Monastirioti, L. Vamvakas, K. Kalbakis, K. Gourlia, I. Xanthopoulos, I. Tsamardinos, D. Mavroudis, and S. Agelaki, "Prediction of outcome in patients with non-small cell lung cancer treated with second line PD-1/PDL-1 inhibitors based on clinical parameters: Results from a prospective, single institution study," *PLoS One*, vol. 16, no. 6, p. e0252537, 2021.
29. H. Pan, N. Zou, Y. Tian, H. Zhu, J. Zhang, W. Jin, Z. Gu, J. Ning, Z. Li, W. Kong, L. Jiang, J. Huang, and Q. Luo, "Short-term outcomes of robot-assisted versus video-assisted thoracoscopic surgery for non-small cell lung cancer patients with neoadjuvant

immunochemotherapy: a single-center retrospective study," *Front Immunol*, vol. 14, p. 1228451, 2023.
30. B. Ricciuti, S. E. Dahlberg, A. Adeni, L. M. Sholl, M. Nishino, and M. M. Awad, "Immune Checkpoint Inhibitor Outcomes for Patients With Non–Small-Cell Lung Cancer Receiving Baseline Corticosteroids for Palliative Versus Nonpalliative Indications," *JCO*, vol. 37, no. 22, pp. 1927–1934, Aug. 2019, publisher: Wolters Kluwer. [Online]. Available: https://ascopubs.org/doi/10.1200/JCO.19.00189
31. R. E. Sabrouty, A. Elouadi, and M. A. S. Karimoune, "Remote palliative care: A systematic review of effectiveness, accessibility, and patient satisfaction," *International Journal of Advanced Computer Science and Applications*, vol. 15, no. 5, p. 502 – 513, 2024, cited by: 0; All Open Access, Gold Open Access. [Online]. Available: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85195048466&doi=10.14569%2fIJACSA.2024.0150550&partnerID=40&md5=de6314402a7a1fa698056ee1d5aea15c
32. E. Union, "Regulation (eu) 2016/679 of the european parliament and of the council of 27 april 2016," *Official Journal of the European Union*, vol. L119, pp. 1–88, 2016.
33. U.S. Department of Health and Human Services, "Health insurance portability and accountability act of 1996 (hipaa)," 1996, public Law 104-191.
34. H. Rao, J. Rees, and C. Minnick, "Data privacy and security issues in healthcare," *Journal of Medical Internet Research*, vol. 22, no. 5, p. e18991, 2020.
35. A. B. Arrieta *et al.*, "Explainable artificial intelligence (xai): Concepts, taxonomies, opportunities and challenges toward responsible ai," *Information Fusion*, vol. 58, pp. 82–115, 2020.
36. E. Topol, "Deep medicine: How artificial intelligence can make healthcare human again," 2019.
37. F. Wang *et al.*, "Healthcare ai: Applications and challenges," *IEEE Journal of Biomedical and Health Informatics*, vol. 22, no. 5, pp. 1531–1537, 2018.
38. B. D. Mittelstadt *et al.*, "The ethics of algorithms: Mapping the debate," *Big Data & Society*, vol. 4, no. 2, p. 2053951717722352, 2017.
39. S. Kastner *et al.*, "Security and privacy in healthcare computing," *IEEE Journal of Biomedical and Health Informatics*, vol. 23, no. 2, pp. 854–865, 2019.
40. I. Chen *et al.*, "Ethical machine learning in health care," *Annual Review of Biomedical Data Science*, vol. 3, pp. 123–144, 2020.
41. T. Davenport and R. Kalakota, "The potential for artificial intelligence in healthcare," *Future Healthcare Journal*, vol. 6, no. 2, p. 94, 2019.
42. S. Whitelaw *et al.*, "Applications of artificial intelligence in emergency medicine," *The Lancet Digital Health*, vol. 2, no. 12, pp. e667–e676, 2020.
43. Z. Obermeyer and E. J. Emanuel, "Predicting the future-big data, machine learning, and clinical medicine," *New England Journal of Medicine*, vol. 375, no. 13, p. 1216 – 1219, 2016, cited by: 1902; All Open Access, Green Open Access. [Online]. Available: https://www.scopus.com/inward/record.uri?eid=2-s2.0-84990046464&doi=10.1056%2fNEJMp1606181&partnerID=40&md5=ac19ca8a440810873860c6ade70f0a55
44. E. J. Topol, "High-performance medicine: the convergence of human and artificial intelligence," *Nature Medicine*, vol. 25, no. 1, p. 44 – 56, 2019, cited by: 2896. [Online]. Available: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85059811921&doi=10.1038%2fs41591-018-0300-7&partnerID=40&md5=7e94ff9df8df70571e2c2a8e98d5cfba
45. F. Jiang, Y. Jiang, H. Zhi, Y. Dong, H. Li, S. Ma, Y. Wang, Q. Dong, H. Shen, and Y. Wang, "Artificial intelligence in healthcare: Past, present and future," *Stroke and Vascular Neurology*, vol. 2, no. 4, p. 230 – 243, 2017, cited by: 1958; All Open Access, Gold Open Access, Green Open Access. [Online]. Available: https://www.scopus.com/inward/record.uri?eid=2-s2.0-85050483912&doi=10.1136%2fsvn-2017-000101&partnerID=40&md5=ed7e04ae9b08ac22e581ecd3c611d2fa
46. B. Norgeot *et al.*, "Minimum information about clinical artificial intelligence modeling: the mi-claim checklist," *Nature Medicine*, vol. 26, pp. 1320–1324, 2020.
47. F. Doshi-Velez and B. Kim, "Towards a rigorous science of interpretable machine learning," *arXiv preprint arXiv:1702.08608*, 2017.
48. T. M. Maddox *et al.*, "The ethical implications of ai in clinical practice," *Journal of the American College of Cardiology*, vol. 73, no. 10, pp. 1310–1316, 2019.