References

Barta, J. A., Erkmen, C. P., Shusted, C. S., Myers, R. E., Saia, C., Cohen, S., Wainwright, J., Charnita Zeigler-Johnson, Farouk Dako, Wender, R., Kane, G. C., Anil Vachani, & Rendle, K. A. (2023). The philadelphia lung cancer learning community: A multi–health-system, citywide approach to lung cancer screening. *JNCI Cancer Spectrum*, *7*(5). https://doi.org/10.1093/jncics/pkad071

Berge, G. T., Granmo, O. C., Tveit, T. O., Munkvold, B. E., Ruthjersen, A. L., & Sharma, J. (2023). Machine learning-driven clinical decision support system for concept-based searching: A field trial in a norwegian hospital. *BMC Medical Informatics and Decision Making*, *23*(1). https://doi.org/10.1186/s12911-023-02101-x

- Natural language processing clinical decision support systems can extract information from EHRs to facilitate important decision-making tasks, but they have received limited attention (Berge et al., 2023).
- A clinical decision support system (CDSS) with rule-based algorithms for clinical concept-based searching can identify and classify allergies; semi-supervised machine learning can help automatically annotate medical concepts in a narrative (Berge et al., 2023).
- The CDSS studied by Berge et al. had high acceptance with positive attitude and increased patient allergy detection (Berge et al., 2023).
- The machine-learning and rule-based approach improved system performance, efficiency, and interpretability (Berge et al., 2023).
- Recommendations for further improvements include reducing alarm quantities, more clinical concepts in the system, closer EHR integration, and more available care point work stations (Berge et al., 2023).

Botsis, T., Spiker, J., Kreimeyer, K., Fatteh, M., Wehr, J., Najjar, M., Tao, J., Xian, R., Imamovic, N. L., Pindzola, A., Dobs, A., Canzoniero, J., & Anagnostou, V. (2024). A precision oncology platform to support genotype-tailored therapy selection. *Studies in Health Technology and Informatics*. https://doi.org/10.3233/shti240792

- There is a need to identify genotype-matched individuals for enrollment into clinical trials and targeted therapies.
- Integrating diverse molecular data sources remains a challenge in current methodologies.
- The list of genomic alterations for FDA-approved therapies is expanding, but there is a lack of interoperability or end-to-end information technology.
- There's a need to link targeted therapies to precision medicine delivery.
- This study integrated electronic health records (EHRs; external knowledge bases) and annotated standardized genomic data to visualize it in an interactive user interface. A molecular tumor board (MTB) could then review the annotations for decision-making support.
- The platform this study used was installed on an IRB-approved web-based environment to manage standardized data.

Craddock, S. J., Lee, J., Zhu, H., Chen, P. M., Wahid, U., Hamann, H. A., Bhalla, S., Rodrigo Catalan Cardenas, Vijaya Subbu Natchimuthu, Johnson, D. H., Santini, N. O., Patel, H. R., & Gerber, D. E. (2023). Assessing barriers and facilitators to lung cancer screening: Initial findings from a patient navigation intervention. *Population Health Management*, *26*(3), 177–184. https://doi.org/10.1089/pop.2023.0053

- Fewer than 5% undergo low-dose computed tomography (LDCT)-based lung cancer screening for lung cancer in the United States (Lee et al., 2023).
- For those who adhere to screening, over 90% are white, educated, former smokers, and received care in a controlled environment for clinical trials (Lee et al., 2023).
- Patient navigators found that provider-related barriers to recall a clinician discussion about screening accounted for 45% of noted patient intake calls (Lee et al., 2023).
- Personal barriers associated with health-related social needs, such as a lack of transportation, accounted for 48% of all reported barriers (Lee et al., 2023).
- LDCT cannot be performed in the office setting (Lee et al., 2023).

Czerw, A., Deptała, A., Partyka, O., Pajewska, M., Wiśniewska, E., Sygit, K., Wysocki, S., Cipora, E., Konieczny, M., Banaś, T., Małecki, K., Grochans, E., Grochans, S., Cybulska, A. M., Schneider-Matyka, D., Bandurska, E., Ciećko, W., Drobnik, J., Pobrotyn, P., & Grata-Borkowska, U. (2024). Lung cancer screening—trends and current studies. *Cancers*, *16*(15), 2691. https://doi.org/10.3390/cancers16152691

- 80% of lung cancer deaths are associated with smokers; 85% of lung cancer cases are associated with smoking (Czerw et al., 2024).
- Smoking and advanced age are the main risk factors for lung cancer (Czerw et al., 2024).
- Screening using low-dose computed tomography (LDCT) reduces mortality as a lung cancer developing result by 20% compared to chest X-rays and 24% by a control group that did not receive testing; nevertheless, LDCT has robust results but is not a 100% effective method for screening patients for lung cancer (Czerw et al., 2024).
- The literature review found a study that examined the sensitivity and specificity of PCR-based tests in lung cancer diagnoses relative to computed tomography results; another study is working on an artificial intelligence model to estimate lung cancer risk on computed tomography and blood biomarker (micro-RNA and C-reactive protein) results (Czerw et al., 2024). The literature review mentioned a study developing an information technology tool that analyzes patients' medical records to determine whether the patient meets the criteria for screening using LDCT (Czerw et al., 2024).
- The literature review lamented that studies conducted in the screening and early diagnoses area are disappointingly small (Czerw et al., 2024).

Hussein, R., Balaur, I., Burmann, A., Ćwiek-Kupczyńska, H., Yojana Gadiya, Ghosh, S., Prabath Jayathissa, Florian Katsch, Kremer, A., Jaakko Lähteenmäki, Meng, Z., Morasek, K., Rancourt, R. C., Venkata Satagopam, Sauermann, S., Scheider, S., Stamm, T., Muehlendyck, C., & Gribbon, P. (2024). Getting ready for the 2uropean health data space (EHDS): IDERHA's plan to align with the latest EHDS requirements for the secondary use of health data. *Open Research Europe*, *4*, 160–160. https://doi.org/10.12688/openreseurope.18179.1

- European Health Data Space 2 (EHDS2) aims for standardization with the following: data discoverability, enabling semantics interoperability, and health data exchange (Hussein et al., 2024).
- EU participants aim to accelerate policy development by building consensus recommendations for heterogeneous data (Hussein et al., 2024).
- Participants have identified four cases of lung cancer to demonstrate value for health data integration by developing artificial intelligence and machine learning tools in a federated environment and personalized remote monitoring applications: 1) risk profiling, 2) diagnosis, 3) prognosis, 4) well-being and patient engagement (Hussein et al., 2024).
- Consortium partners can participate (e.g., institutions, services, repositories, etc.) (Hussein et al., 2024).
- The standardized infrastructure should be a federated data infrastructure with participatory governance and shared datasets can be analyzed using federated machine learning algorithms (FML).
- Public and private sources, including patient-reported outcome measures (PROM) and patient-reported experiences measures (PREM) (Hussein et al., 2024), can be aggregated for secondary use; PROMs inform clinicians on symptoms for clinical management, while PREMs inform providers on the care process patient experience (Hussein et al., 2024).
- The vision is to establish a data quality framework, generate results that can be assessed by a clinical advisory board, and support healthcare data standards and models for interoperability that facilitate findability, accessibility, interoperability, and reusability (Hussein et al., 2024).
- Communication channels should be established to foster networking among stakeholders, and piloting provides a framework for gathering forces for standardization (Hussein et al., 2024).
- The framework for federated access and processing anonymized and pseudo-anonymized health data ensures data protection and sovereignty through privacy-preserving technologies (Hussein et al., 2024).

Kreimeyer, K., Canzoniero, J. V., Fatteh, M., Anagnostou, V., & Taxiarchis Botsis. (2024). Using retrieval-augmented generation to capture molecularly-driven treatment relationships for precision oncology. *Studies in Health Technology and Informatics*. https://doi.org/10.3233/shti240575

Kukhareva, P. V., Li, H., Caverly, T. J., Fagerlin, A., Del Fiol, G., Hess, R., Zhang, Y., Butler, J. M., Schlechter, C., Flynn, M. C., Reddy, C., Choi, J., Balbin, C., Warner, I. A., Warner, P. B., Nanjo, C., & Kawamoto, K. (2024). Lung cancer screening before and after a multifaceted electronic health record intervention: A nonrandomized controlled trial. *JAMA Network Open*, *7*(6), e2415383. https://doi.org/10.1001/jamanetworkopen.2024.15383

- Healthcare systems across the US are starting to implement clinical decision support (CDS), such as clinician-facing reminders and an electronic health record-integrated shared decision-making (SDM) tool (Kukhareva et al., 2024). These types of EHR

prompts are associated with increased lung cancer screening orders (Kukhareva et al., 2024).

- Kukhareva et al.'s primary goal was to offer a more holistic understanding of a multifaceted, EHR-based CDS intervention with lung cancer screening (LCS) care gap closure; the secondary goal was to evaluate whether patient portal reminders for LCS-eligible patients were associated with additional improvements in care gap closure (Kukhareva et al., 2024).
- Multifaceted EHR integration improved LCS care gap closure in academic healthcare systems, where clinician-facing interventions and patient-facing reminders were associated with improvement (Kukhareva et al., 2024).
- Several areas further need research and improvement, such as improving EHR smoking history documentation and patients following through after screening orders (Kukhareva et al., 2024).

Lajmi, N., Alves-Vasconcelos, S., Tsiachristas, A., Haworth, A., Woods, K., Crichton, C., Noble, T., Salih, H., Várnai, K. A., Branford-White, H., Orrell, L., Osman, A., Bradley, K. M., Bonney, L., McGowan, D. R., Davies, J., Prime, M. S., & Hassan, A. B. (2024). Challenges and solutions to system-wide use of precision oncology as the standard of care paradigm. *Cambridge Prisms: Precision Medicine*, *2*, e4. https://doi.org/10.1017/pcm.2024.1

- The NIH reported a projected $246 billion in total cancer costs based on the US population (Lajmi, 2024).
- Better outcomes are achieved when cancer treatments are personalized, but oncology precision medicine has been challenging to scale (Lajmi et al., 2024).
- Heterogenous data from disparate sources can result in variable patient outcomes; structured digital innovation can lead to integrating more relevant data streams (Lajmi et al., 2024).
- 80% of medical data remain unstructured; while natural language processing is a possible solution, NLP is not cost-effective for scalability (Lajmi et al., 2024). Streamlining how data is structured and pre-processed through data standardization must be considered for a cost-effective standard of care (SOC) (Lajmi et al., 2024).
- While there are no international patient data privacy laws, data anonymization, cryptography, and access control were recommended to keep patient data anonymous and dissociated from patients; patient data ownership through blockchain technology is a proposed novel approach that gives patients control over their data (Lajmi et al., 2024).
- Clinical workflow inefficiencies, reimbursement, and regulatory procedures are barriers that contribute to and exacerbate the ability to scale oncology precision medicine (Lajmi et al., 2024).
- Data integration platforms, in combination with clinical decision support systems and molecular tumor board integration with standard-of-care multidisciplinary treatment teams and cloud-based platforms, can collectively support scaling clinical support technologies (Lajmi et al., 2024).
- Clinical trial matching is a challenging process that should be automated, but proprietary software makes widespread adoption difficult (Lajmi et al., 2024).
- Patient-reported outcomes (PRO) apps for patients and providers help improve patient outcomes, and CMS Innovation suggested that ePRO should be the standard for quality of care (Lajmi et al., 2024).

- While financing and reimbursement are major barriers to any implementation for oncology precision medicine, establishing international research consortia and collaborative platforms for research sharing between academia and industry, establishing a standardized legal framework, utilizing financial agreements, and improving transparency in pricing and reimbursement could help solve health economic challenges for oncology precision medicine (Lajmi et al., 2024).

Ni, Y., Bermudez, M., Kennebeck, S., Liddy-Hicks, S., & Dexheimer, J. (2019). A real-time automated patient screening system for clinical trials eligibility in an emergency department: Design and evaluation. *JMIR Medical Informatics*, *7*(3), e14185. https://doi.org/10.2196/14185

- There has historically been a lack of efficient methods for identifying subjects that meet clinical trial eligibility criteria.
- The large EHR data volume is labor-intensive for screening relevant information for patient recruitment.
- Ni et al. developed an NLP and ML-based system, the Automated Clinical Trial Eligibility Screener (ACTES), to analyze structured data with unstructured narratives to determine patient sustainability for clinical trial enrollment.
- Manual screening by clinical research coordinators (CRCs) was reduced by 34%, and subject screening, approach, and enrollment numbers were improved.
- Barriers to clinical trial patient recruitment include high labor intensity, insufficient timeliness, and poorly efficacious translational research conduct. These factors create a significant financial burden and hinder successful clinical study completions.
- ML rule-based triggers have accuracy challenges, but automated matching methods relying on NLP improve accuracy for subject identification.
- Integrating the ML model into the institutional workflow, leveraging NLP matching methods, reduced screening efforts by less than 50%. Automated screening was more beneficial for clinical trials with multiple conditions and a vague eligibility description.'
- Some features that are or will be helpful in the model are a continual 24-hour screening service, easy-to-learn screener, full integration, developed regular expressions bag-of-phrases matching for the NLP component of the model, and better functionalities for the dashboard.

Patel, S., Goldsack, J. C., Cordovano, G., Downing, A., Fields, K. K., Geoghegan, C., Grewal, U., Nieva, J., Patel, N., Rollison, D. E., Sah, A., Said, M., Keere, I. V. D., Way, A., Wolff-Hughes, D. L., Wood, W. A., & Robinson, E. J. (2023). Advancing digital health innovation in oncology: Priorities for high-value digital transformation in cancer care. *Journal of Medical Internet Research*, *25*(1), e43404. https://doi.org/10.2196/43404

- Oncology has fallen behind in healthcare delivery digital innovation compared to other therapeutic areas despite the complex data and biomarker volumes. Lack of infrastructure is one of the primary limitations to oncology digital innovation.
- Patient survival is varied by zip code, race, socioeconomic status, sex, and site of care; disparate data sources and systems exacerbate these disparities.
- Integrated digitization and streamlined administrative tasks could help facilitate efficiencies in payor reimbursements and claims.

- Effective cancer care coordination demands easy data information exchange and data standardizations for unstructured data.
- Opportunities for digital innovation in oncology include defining and optimizing core digital measures, standardizing methodological approaches, automating and streamlining clinical operations, proposing implementation parameters, aggregating and streamlining various datasets for data integration, and approaches to access hard-to-reach and underserved populations.

Santiago Ponce Aix, Núñez-Benjumea, F. J., Cervera-Torres, S., Flores, A., Arnáiz, P., & Fernández-Luque, L. (2023). Data-Driven personalized care in lung cancer: Scoping review and clinical recommendations on performance status and activity level of patients with lung cancer using wearable devices. *JCO Clinical Cancer Informatics*, *7*. https://doi.org/10.1200/cci.23.00016

- 5-year OS rates remain low in NSCLC. Many clinical decisions in lung cancer rely on health indicators and subjective assessments (Santiago et al., 2023).
- Electronic Activity Monitoring (EAM) has been used in oncology to gather more objective patient-generated health data (PGHD) information.
- EAMs were sued to study sleep or physical activity, and the devices in the studies were typically paired with a mobile app to deliver feedback and electronic patient-reported outcomes (ePROs).
- Increased immobility was associated with worse lung cancer patient survival (Santiago et al., 2023).
- Patients with cancer present high levels of sleep-related burdens (Santiago et al., 2023).
- The study identified several drawbacks and limitations. Patients may not adhere to wearing EAM devices, and their growing use in applications will require refining how to combine heterogeneous patient-generated data. There will be concerns for equity and accessibility to technology, and patient registries or the integration of clinical guidelines should be created (Santiago et al., 2023).

van der Aalst, C. M., ten Haaf, K., & de Koning, H. J. (2021). Implementation of lung cancer screening: What are the main issues? *Translational Lung Cancer Research*, *10*(2), 1050–1063. https://doi.org/10.21037/tlcr-20-985

- About 70% of lung cancers are in the advanced stage at the time of diagnosis, leading to a 5-year survival rate of 15% (van der Aalst et al., 2021).
- Personalized risk for lung cancer screening can have a less intensive regimen based on methods such as biomarker outcomes amongst individuals identified as high risk for developing lung cancer (van der Aalst et al., 2021).

Wu, J. T., Wakelee, H. A., & Han, S. S. (2023). Optimizing lung cancer screening with risk prediction: Current challenges and the emerging role of biomarkers. *Journal of Clinical Oncology*, *41*(27), 4341–4347. https://doi.org/10.1200/JCO.23.01060

- There is previous evidence that risk-prediction model-based screening eligibility could improve sensitivity to detecting lung cancer cases, and recent advances in lung cancer biomarkers have enhanced risk prediction performance for identifying lung cancer cases (Wu et al., 2023).

- CMS requires shared decision-making for reimbursement (Wu et al., 2023).
- Biomarkers, including DNA, proteins, and hormone levels, are potentially useful tools for detecting cancer and may serve as a useful adjunct to risk-prediction models based on clinical factors; nevertheless, biomarker risk prediction models for lung cancer currently lack validation (Wu et al., 2023).
- Incorporating a circulating protein biomarker panel can improve lung cancer mortality prediction (Wu et al., 2023).
- Wu et al. discussed one study where a circulating biomarker panel improved sensitivity, specificity, and positive predictive value for lung cancer death (2023).
- Bio-marker-based stratification, or risk-based screening, may be implemented independently by interpreting a single blood test instead of collecting multiple clinical data elements from patient histories (Wu et al., 2023).
- Given the significance of smoking as a lung cancer risk factor, incorporating biomarkers with other key risk factors will allow risk prediction to be more accurate (Wu et al., 2023).
- Decision aids based on risk prediction models are infrequently used in clinical practice, and prediction tools alone are unlikely to address the challenge of low screening uptake (Wu et al., 2023).
- Risk-based screening strategies should use comprehensive metrics, such as life-years gained versus lung cancer aversion numbers (Wu et al., 2023).
- On a population level, cost-effectiveness and population smoking prevalence may drive threshold selection (Wu et al., 2023).
- The current primary clinical use for risk prediction models is for shared decision-making contexts, and lung cancer benefits are reaped in reliable settings with a patient who is fit enough to receive treatment and will adhere to follow-ups (Wu et al., 2023).