

## RESEARCH ARTICLE

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# ARTIFICIAL INTELLIGENCE IN CLINICAL LABORATORY MEDICINE: APPLICATIONS IN BIOMARKER INTERPRETATION, DIAGNOSTIC PREDICTION, AND CANCER SCREENING



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## Abstract

The increasing complexity of clinical laboratory data has led to the growing research and investigation of the use of artificial intelligence (AI) to aid in the interpretation of such data and to support diagnostic decision-making. With increasing availability of biochemical, hematological, molecular, proteomic, and image-based laboratory information, machine learning (ML) and deep learning (DL) approaches have provided opportunities to uncover clinically relevant patterns that may not be easily detected by traditional methods. In this review, the uses of AI in clinical laboratory medicine are discussed, focusing on the interpretation of biomarkers, the prediction of diagnosis, optimization of laboratory workflows, and cancer screening. AI-based methods can help to combine multiple biomarkers to capture multivariable signatures, aid in disease classification and risk prediction, and enable the analysis of high-dimensional molecular and proteomic datasets. AI has been explored in cancer screening for the interpretation of circulating biomarkers, liquid biopsies, and digital pathology to aid in early cancer detection and risk assessment. In addition to its role in the preanalytical stage of laboratory testing, AI can also help with the analytical phase and the postanalytical stage by performing quality control, detecting anomalies, interpreting tests automatically, and providing clinical decision support. Despite all these opportunities, implementation in the clinic is limited by data quality, missing information, varying measurements, class imbalance, selection bias, limited external validation, model interpretability, and differences between laboratories. In addition to these considerations, ethical issues related to patient privacy, data security, algorithmic biases, and accountability play a role in responsible AI implementation. Standardization and representativeness of the datasets, multicenter and prospective validation, proper calibration, assessment of usefulness in clinical practice, incorporation in laboratory information and health records, and ongoing monitoring following implementation are necessary for successful translation into routine use. In conclusion, AI shows great promise to not only revolutionize the way clinical laboratory medicine is practiced but also to serve as an integral element in a multivariable and increasingly individualized diagnostic process, with human oversight as a crucial part of the clinical decision-making process.

**Keywords** Artificial intelligence, machine learning, deep learning, clinical laboratory medicine, biomarker interpretation, diagnostic prediction.

## INTRODUCTION

Clinical laboratory medicine is an essential part of

modern medical care, which gives information on a quantitative and qualitative basis that helps the

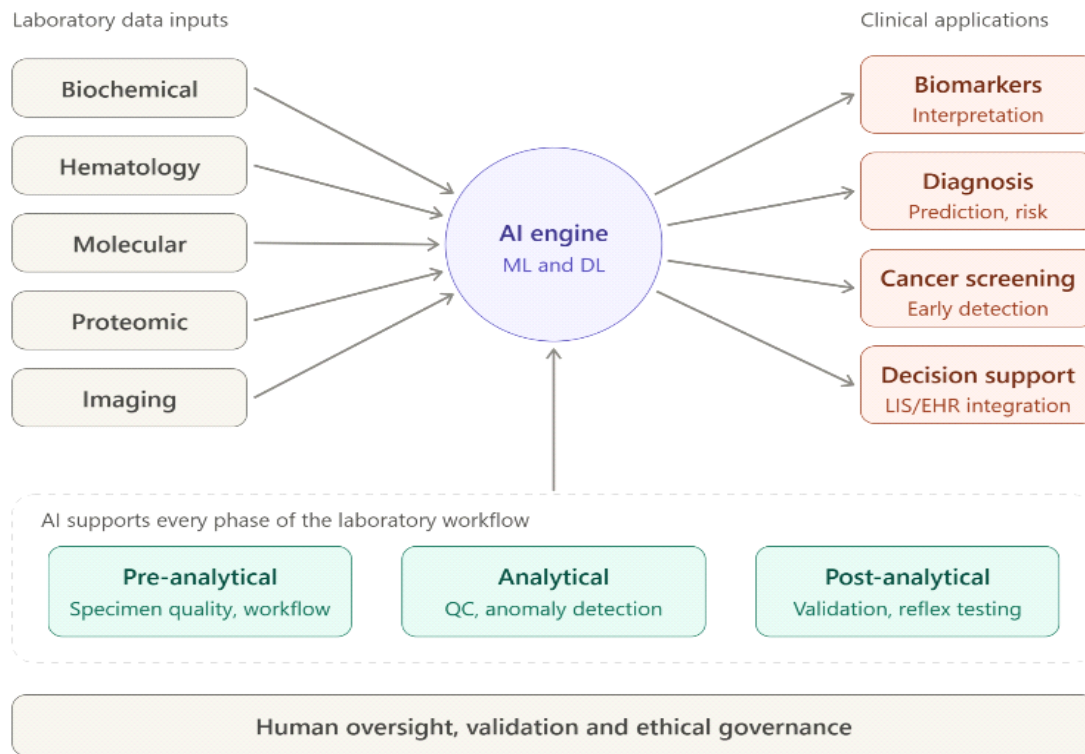
detection of diseases and their diagnosis, prognosis, selection of treatment, and monitoring of patients. Laboratory investigations produce a growing and varied amount of information, such as biochemical data, hematological indices, immunological markers, molecular profiles, and pathological information [1]. Laboratory data sets have become very large and complex due to new technologies like high-throughput technologies and electronic health records. This expansion would have the benefit of allowing for more detailed characterization of the disease but would also create some challenges with the standard method of interpretation in the lab. When considered individually, the relationships between some of the laboratory variables may not be linear, subtle, or easily identified. Thus, greater interest has been shown in developing computational methods that can be used to detect clinically relevant patterns in complex laboratory data [2].

The tradition of laboratory medicine has been founded on the idea of well-defined reference intervals, well-established statistical relationships, clinical algorithms, and interpretation of the individual or small groups of laboratory test results. These methods are still employed in everyday lab work, but, as the amount of multidimensional laboratory data increases, novel analytical techniques are needed, which go beyond the scope of traditional methods. Patient-related, disease-related, biological, analytical, and pre-analytical factors can affect the laboratory measurement and make diagnostic interpretation more challenging [3]. Furthermore, in many diseases, there are overlapping biochemical, hematological, and molecular signatures, and diagnosis purely based on one of these markers is not adequate in many clinical scenarios.

Therefore, clinical laboratories are now a significant source of structured clinical information with the introduction of automated analyzers, laboratory information systems, EHRs, and HT molecular technologies. These advances have provided an opportunity to move beyond a single laboratory measurement to the use of patterns of biomarkers and relationships between variables.

However, the advent of artificial intelligence (AI), in particular machine learning (ML) and deep learning (DL), has shown to be a way to extract clinically relevant information from complex data sets [4]. While classical statistical models are generally built based on a specific set of assumptions regarding the relationship between different variables, ML algorithms can learn the complex relationship among the variables in multidimensional data. It may be possible to assign a disease state based on supervised learning or to predict a disease state based on supervised learning; unsupervised learning may find new patterns or patient subgroups. These capabilities are further extended by deep-learning methods, which automatically learn the hierarchical representation from more complex laboratory and molecular and image data.

Therefore, AI can be applied to different levels when it comes to clinical laboratory medicine: in data processing in the laboratory, analyzing biomarkers, predicting results for diagnostics, and assisting with clinical decision-making [5]. It's worth highlighting that AI should not be used to replace the role of lab specialists but rather be used alongside them. Its value is only as useful as its input, as well as how well the analytical technique matches the data and how well the computed data can be converted to clinically useful information.



- **Conceptual overview of artificial intelligence applications across the clinical laboratory medicine workflow.**

The potential applications of AI extend across the pre-analytical, analytical, and post-analytical phases of laboratory practice, including data-quality assessment, automated pattern recognition, biomarker interpretation, diagnostic classification, and clinical risk prediction. This broad integration provides a framework for understanding AI as part of an interconnected laboratory workflow rather than as an isolated diagnostic technology.

AI can be used in the pre-analytical, analytical, and post-analytical phases of the lab, including in data quality, automated pattern recognition, biomarker interpretation, diagnostic classification, and clinical risk prediction [6]. This broad integration

provides a holistic view of AI in the entire lab workflow rather than as a point-of-care diagnostic tool.

Part of the reason for using AI in laboratory medicine is due to the intricate relationships between biomarkers. Some biochemical, hematological, molecular, or protein markers could be slightly sensitive or specific for various diseases, while certain markers might be only slightly sensitive or specific. The variables can be used in conjunction with AI-based models to gauge the model and, in certain cases, can also uncover patterns that would not be obvious from a traditional interpretation [7]. These could include improved ability to detect disease at an earlier stage, improved discrimination of disease, and improved ability to stratify for clinical disease by estimating the probability of a clinical disease based on laboratory data.

One of the most promising is cancer screening.

During the early stages of malignancies, there may be subtle changes in the molecular or biochemical makeup of the disease, which may be difficult to interpret by using only one biomarker [8]. Laboratory-derived features like circulating nucleic acids, proteins, and hematological parameters, and many more, can be analyzed using AI to discover disease signatures. Likewise, digital pathologists and molecular data could be used for automated classification and screening strategies with the help of AI.

The review focuses on the potential and actual use of AI in the field of clinical laboratory medicine, specifically in the interpretation of biomarkers, diagnostic prediction, processing of laboratory data, and cancer screening. It explores the potential of the analysis of laboratory data from biochemical, hematological, molecular, protein, and image data and the ability to detect clinically relevant patterns using ML and DL methods. Additionally, important topics for clinical translation, including data quality, model interpretability, validation, generalizability, lab integration, and limitations, are discussed. To provide a holistic perspective on the opportunities and challenges of AI in clinical laboratories, this review will focus on these elements.

- **Artificial Intelligence Approaches in Clinical Laboratory Medicine**

Artificial Intelligence (AI) is an umbrella term that describes the ability of a computing system to learn, recognize patterns, predict, and make decisions. AI is becoming more applicable in clinical laboratory medicine, generating systems with vast amounts of structured and high-dimensional data in the laboratory environment. One of the largest fields of AI is machine learning (ML), which enables the computational models to learn relationships between the input variables and clinical outcomes without having to have rules written by hand [9]. Deep learning (DL), a sub-branch of machine learning (ML) that makes use of multi-layer ANNs, is

learning increasingly complex representations from increasingly huge amounts of data. These techniques can be used to help interpret clinical measurements in a laboratory, classify diseases, analyses biomarkers, and make clinical predictions.

- **Fundamentals of Artificial Intelligence and Machine Learning**

Generally, ML approaches are classified into three types: supervised, unsupervised, or semi-supervised. In supervised learning, the datasets have a known outcome, e.g., disease status or response to a treatment, whose association with laboratory variables is known. It is therefore very appropriate for diagnostic classification and prediction [10]. Unsupervised learning is the study of data sets with no predetermined output labels and may discover clusters, patterns, or patient subgroups. Semi-supervised learning also uses labelled and unlabeled data and can be used when it is hard to get a lot of clinically annotated laboratory data.

Clinical and laboratory datasets have been analysed using several conventional ML algorithms. Some of the traditional ML algorithms were applied to clinical and laboratory data sets. Logistic regression is a relatively interpretable method for estimating the probability of a clinical outcome, while decision trees and random forests can identify nonlinear relationships and interactions between variables. Support vector machines (SVMs) are especially important for classification problems with high-dimensional biomarker datasets; k-nearest neighbors (k-NN) classify observations by comparing them with neighboring data points, and gradient-boosting methods stack several weak predictive models to gain better classification or regression accuracy.

The deep-learning techniques offer further capabilities in cases where a laboratory dataset is very

complex [11]. ANNs can model complex relationships between several laboratory variables. CNNs are particularly useful in image-based applications, such as in digital pathology and cellular morphology, as they can automatically extract the spatial features from images. Recurrent neural networks

(RNNs) are used for sequential or longitudinal data and autoencoders can learn low-dimensional representations of high-dimensional data and can be used in dimensionality reduction and anomaly detection.

### 1. Major AI/ML approaches used in clinical laboratory medicine and their principal applications

| AI approach         | Typical laboratory input      | Major application              | Key strength                        | Major limitation                   |
|---------------------|-------------------------------|--------------------------------|-------------------------------------|------------------------------------|
| Logistic regression | Clinical/laboratory variables | Diagnostic prediction          | High interpretability               | Limited nonlinear modelling        |
| Random forest       | Multivariable laboratory data | Classification/risk prediction | Handles complex interactions        | Reduced interpretability           |
| SVM                 | Biomarker/molecular data      | Disease classification         | Effective for high-dimensional data | Parameter-sensitive                |
| Neural networks     | Multimodal laboratory data    | Prediction/classification      | Nonlinear pattern recognition       | Data-intensive                     |
| CNN                 | Digital pathology/images      | Image-based diagnosis          | Automated feature extraction        | Requires substantial training data |

#### • AI Inputs in Laboratory Medicine

The laboratory inputs could be biochemical data, blood markers, immunologic markers, molecular markers, molecular markers derived from genome and transcriptome, and proteome data, etc. [12],

which are all varying types of data that can be processed by the AI model. DL can also be applied to analyses image-based information, such as from

digital pathology, cytology, and blood-cell morphology. The inclusion of these diverse forms of data enables multimodal analysis where multiple modes of complementary biological information may be combined for enhanced diagnostic discrimination and disease characterization.

- **AI Model Development and Prediction Workflow**

Typically, the first step in developing an AI model in the laboratory is to gather and preprocess data, which may involve quality control, normalization, imputation of missing values, and feature selection. Then feature selection and feature extraction are carried out to select those which contribute to prediction. Selected data is then used to train the model, and the model is then internally validated by methods like cross-validation or independent testing data sets. Generalizability is especially critical and is best determined by external validation with data from other populations and/or institutions. Lastly, model products should be clinically interpreted and appraised in terms of utility in the laboratory workflow. Therefore, to implement AI successfully, it is not enough to deliver predictive performance; it needs to have reliable data, right validation, be easy for clinicians to interpret and ideally be easy for clinicians to use.

- **AI for Biomarker Interpretation**

Biomarkers can be used to measure biological information which can help in diagnosis, prognosis, and treatment monitoring of diseases [13]. Most commonly, laboratory interpretation is done on a biomarker-by-biomarker basis or in small clusters of analytes using reference ranges. This is still the primary way that disease is diagnosed and treated in clinical medicine, but complex diseases may manifest changes in several biological pathways, and these changes may be too subtle to be detected by a single biomarker for most clinical uses. AI, specifically machine learning (ML), offers the chance to examine several laboratory parameters at once and determine combinations or patterns of these that correlate with clinical situations. These are new opportunities for biomarker interpretation, discovery, and development of multianalyte diagnostic models with the ability of ML to process high-

dimensional datasets.

- **Conventional Challenges in Biomarker Interpretation**

Each of these biomarkers has value in the clinical setting, but this value is dependent on the characteristics of the biomarker, including biological variability, prevalence of the target condition, analytical precision, sensitivity, and specificity. One biomarker can show significant overlap between healthy and diseased populations and thus not be very informative for diagnosis. In addition, biomarker levels may be different for age, gender, races, physiological status, presence of comorbidities, medications, and disease stage. Therefore, reference ranges and cut-off values might not reflect the biological variability of the entire patient population.

Pre-analytical and analytical factors also affect laboratory biomarkers. Measured concentrations and subsequent interpretation may be influenced by the collection, transport, storage, analytical method, instrument characteristics, and variability involved in analysis. A further drawback of biomarkers is that they are rarely used singly. Various molecular features, such as inflammatory markers, blood-cell indices, metabolic parameters, proteins, nucleic acids and other molecular features can be affected simultaneously by a pathological process. It is, therefore, important to consider conventional methods that assess each measure individually and might not capture clinically meaningful interactions among measures.

These restrictions justify the use of computation models that can be used to quantify several biomarkers at the same time. The ML models can uncover nonlinear relationships and interactions among the lab variables and clinical outcomes, which could provide a more complete account of biological patterns associated with the disease.

- **Machine Learning for Multibiomarker Analysis**

The great benefit of these methods is that many biochemical markers are already routinely generated in clinical laboratories, and thus large datasets are available for the development of the models [14]. AI-based interpretation could thus be integrated into existing laboratory platforms, without the need for new analytical platforms. Clinical chemistry applications, which have been explored, showed the potential of AI in various areas of laboratory testing, such as predicting the laboratory results, assisting in diagnosis and automating the interpretation of laboratory results.

- **Biochemical Biomarkers**

Clinical chemistry provides a substantial source of routinely available data for AI-based biomarker interpretation. Liver and renal function markers, glucose-related measurements, lipid parameters, enzymes, hormones, and inflammatory biomarkers can be evaluated individually or as integrated profiles. AI models can identify combinations of routine biochemical measurements associated with specific diseases or clinical outcomes, potentially extracting diagnostic information that is difficult to recognize from individual results.

The advantage of these approaches is that many biochemical measurements are already generated routinely in clinical laboratories, providing large datasets for model development. AI-based interpretation may therefore be incorporated into existing laboratory workflows without necessarily requiring entirely new analytical platforms. Applications in clinical chemistry before 2024 demonstrated the potential of AI across different phases of laboratory testing, including prediction of laboratory results, diagnostic support, and automated interpretation.

- **Hematological Biomarkers**

Another important source of information for the AI models is the hematological parameters. Derived variables derived from the CBC as well as inflammatory ratios can be used to accentuate disease-associated patterns in addition to the CBC variables for leukocytes, erythrocytes, and platelets. Indirect markers of systemic inflammation and immune responses, such as neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio, may be useful.

ML can make use of multiple blood-cell parameters and other lab measurements, instead of just a single hematological parameter [15]. This is especially true for disease classification and risk stratification, where small variations in several routine parameters may be predictive of a disease outcome as a group more than as individuals.

- **Molecular and Genetic Biomarkers**

As molecular laboratory technologies have improved, data from genomic molecular structures, such as DNA, RNA, microRNA, methylation profile, etc., is becoming increasingly multidimensional. They are ideal for computational analysis, as they can include thousands of features, many of which are biologically redundant and/or correlated.

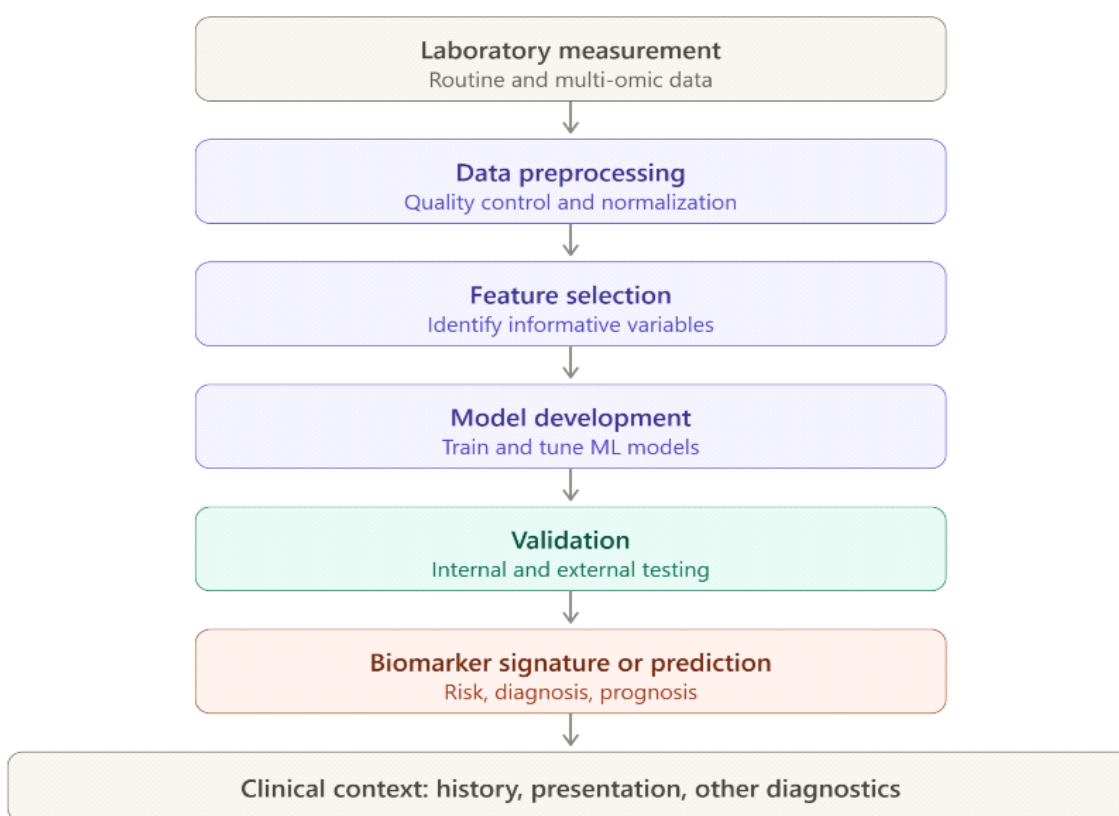
ML can help to identify informative molecular properties and to create signatures linked to disease phenotypes. Cancer research is an area where AI and deep-learning techniques have been explored to incorporate genomic and transcriptomic information along with other molecular data to derive predictive biomarkers and disease sub-classes. These methods are especially useful when the interactions of the molecules involved are complex and cannot be well described by linear models.

- **Protein and Proteomic Biomarkers**

Proteomic technologies provide a large amount of data on the abundance, modification, and interaction networks of proteins [16]. High-throughput proteomics allows for the measurement of many proteins simultaneously, whereas traditional biomarker studies measure individual proteins. AI can help identify patterns in these sets of data and choose which sets of proteins are linked to disease conditions.

A major application of mass-spectrometry-based

proteomics is that large data sets can have thousands of measurements of molecular properties. The analysis of multivariate molecular signatures, therefore, rather than searching for a single molecule to act as a biomarker, can be achieved with the help of AI. However, some technical variation, sample preparation, differing platforms, and independent clinical validation are significant challenges for implementing proteomic signatures in a clinical lab setting.



- AI-assisted biomarker interpretation workflow

The overall process can be conceptualized as a sequence beginning with laboratory or molecular

measurements, followed by data preprocessing, quality assessment, feature selection, model development, and validation. The final model produces a

biomarker signature or prediction that can be interpreted within the relevant clinical context. This framework emphasizes that AI-based biomarker interpretation is not simply an algorithmic process; reliable clinical implementation depends on the quality and representativeness of the biological data entering the model.

### • AI-Based Biomarker Discovery

In addition to the interpretation of existing biomarkers, AI can be used to identify and propose potential new biomarkers. A variety of feature selection algorithms can determine variables that contribute significantly to prediction ability, and an

unsupervised approach can identify a new molecular or clinical subpopulation [17]. An important feature of AI is that it is especially appealing for biomarker discovery since contemporary omics technologies produce data sets with a lot more features measured than clinical samples.

### 2. applications of AI for interpretation of biochemical, haematological, molecular, and protein biomarkers

| Biomarker/data type         | Disease/clinical condition          | AI method                | Main objective                                   | Key findings/applications                                         | Validation approach                | Clinical relevance                      |
|-----------------------------|-------------------------------------|--------------------------|--------------------------------------------------|-------------------------------------------------------------------|------------------------------------|-----------------------------------------|
| Biochemical biomarkers      | Various diagnostic conditions       | ML/classification models | Multivariable interpretation                     | Identification of combinations of routine laboratory measurements | Internal/external model validation | Automated diagnostic support            |
| Hematological parameters    | Hematological and systemic diseases | ML, ensemble methods     | Disease classification and risk prediction       | Integration of CBC-derived features and inflammatory indices      | Cross-validation/test datasets     | Low-cost use of routine laboratory data |
| Genomic/transcriptomic data | Cancer and molecular diseases       | ML/DL                    | Molecular classification and biomarker discovery | Identification of disease-associated molecular signatures         | Independent molecular cohorts      | Precision diagnosis and stratification  |
| microRNA/RNA signatures     | Cancer and other diseases           | ML/classification        | Signature identification                         | Combination of multiple RNA features                              | Training/test cohort validation    | Potential early-detection biomarkers    |
| Proteomic data              | Cancer and                          | ML/DL                    | Protein-                                         | Identification of                                                 | Independent                        | Candidate                               |

|                  | systemic diseases |                   | pattern recognition            | multivariate protein signatures                                                   | validation where available         | bi-omarker panels                          |
|------------------|-------------------|-------------------|--------------------------------|-----------------------------------------------------------------------------------|------------------------------------|--------------------------------------------|
| Multi-omics data | Cancer            | ML/DL integration | Integrated biomarker discovery | Joint analysis of genomic, transcriptomic, proteomic and other molecular features | Cross-validation/external datasets | Precision medicine and molecular subtyping |

- But there are methodological risks associated with biomarker discovery with ML. Flexible models have the power to recognize patterns that are only present in their training set but are not repeatable biological signals. Thus, overfitting is a significant worry, especially for large molecular datasets and small numbers of patients. Before the features identified by computation could be said to be clinically relevant biomarkers, they must be validated and biologically interpreted independently.

#### • Multimodal Biomarker Interpretation

A key advancement in the field of AI-powered biomarker analysis is the ability to incorporate diverse data modalities. Laboratory markers can be correlated with demographic data, clinical features, and molecular markers and features of imaging to provide a broader picture of disease [18]. These multimodal approaches may be especially useful if there is no single biomarker that is able to reliably diagnose the condition.

The ability to correlate molecular changes with clinical phenotypes using multi-omics approaches that integrate information from the genome, epigenome, transcriptome, proteome and other biological layers is possible with AI. With AI, multi-omics approaches can be used to correlate molecular

changes with clinical phenotypes, enabling the simultaneous investigation of

relationships between changes in the genome, epigenome, transcriptome, proteome and other biological layers. In oncology, these have been investigated for cancer classification, discovering biomarkers, risk stratification, prognosis setting and precision medicine.

Multimodal biomarkers also provide a potential route to the more personalized interpretation of diagnosis. Theoretically, an AI model can calculate a patient-specific probability using the combination of the biomarker measurements and all the clinical information, rather than relying on a single threshold in one measurement. However, the models must be thoroughly validated for various populations, laboratories, analytical platforms, and disease stages before being able to be adopted in routine practice. AI has a lot of promises to revolutionize how biomarker interpretation goes from a single measurement evaluation to a multivariable and potentially personalized evaluation.

#### • AI for Diagnostic Prediction and Clinical Decision Support

The use of artificial intelligence (AI) in interpreting laboratory findings into actionable information for

diagnosis and prognosis has garnered increasing interest. In the conventional laboratory interpretation, the results of a single laboratory test are compared with a set of laboratory reference intervals, clinical decision limits or a combination of preselected laboratory test results [19]. All these methods are relevant to clinical practice; however, they might not have very good performance on characterizing multiple laboratory variables that may have complicated nonlinear relationships. Machine learning (ML) and deep learning (DL) can be used to predict the probability of disease, classify disease conditions, and forecast disease outcomes by utilizing combinations of laboratory, demographic and clinical data. Therefore, the era of AI-based diagnostic prediction is a crucial shift from the use of individual laboratory markers to a more comprehensive and data-driven approach to clinical decision-making [20].

- **From Laboratory Results to Diagnostic Prediction**

The traditional interpretation of the diagnosis relies on the clinical setting where laboratory tests are drawn. Some biomarkers may be more sensitive or specific, and a series of laboratory abnormalities may be more indicative of a specific disease. Yet, it becomes more difficult to handcraft several more variables as the dimension of the data grows. Relationships between laboratory features and predefined diagnostic outcomes can be learned and can be used to solve this problem with the help of AI models.

Lab datasets, where the disease status is known, can be used to train supervised ML methods. The models created can be used to make diagnoses and can also provide estimates of the probability of a given condition. Probabilistic models can be used to generate continuous risk estimates which might inform clinical decisions. as opposed to a binary diagnosis. These are important for situations where

lab results can be similar for diseased and non-diseased populations.

- **AI-Based Prediction Using Routine Laboratory Data**

Routine laboratory investigations are an appealing source of data for AI-based diagnostic prediction models, as they are routinely ordered during care, are easily available, and are relatively cheap. Various laboratory variables, including complete blood count (CBC) parameters, biochemical measurements, inflammatory markers, liver and renal function tests and others, can be included in ML models.

Hematological parameters can provide information about inflammation, infection, malignancy and physiological changes throughout the body. A combination of certain biochemical variables can also reflect patterns that reflect organ dysfunction or metabolic abnormalities. Laboratory variables may be combined with demographic and clinical data to provide better prediction than laboratory measurements alone, and variables related to inflammatory markers may be helpful to provide additional information about systemic responses.

One of the key benefits of models depending on regular lab data is their scalability. Routine tests are a type of test that can be performed in multiple healthcare environments, whereas specialized molecular assays are limited to certain healthcare settings. As such, existing laboratory infrastructure could largely remain unchanged, and validated AI models based on routinely measured variables may be able to help identify risks at an earlier stage [21].

- **Disease Classification**

Laboratory models based on artificial intelligence have been studied to differentiate various clinical conditions, such as non-infectious and infectious diseases, benign and malignant conditions, and

disease subtypes. Multiple variables can be included in the classification models, and combinations of these variables can be used to discriminate disease.

For instance, in oncology, a combination of lab tests can be useful to differentiate patients who have cancer from those who do not. In the context of infectious disease diagnosis, for example, inflammatory and hematological markers could present similar but distinct patterns in the different infections, as explored in the lab through ML models. The molecular laboratory data can also be used to further disease classification by including genetic, transcriptomic or other disease-specific signatures.

The biggest benefit of these methods is that they may detect multivariable patterns and not only the single diagnostic threshold. Better classification performance, however, must be taken with a grain of salt, as differences in patient populations, prevalence of the disease, laboratory testing method, and reference standards can significantly affect model performance.

- **Prognostic and Risk Prediction**

AI can not only identify a disease, but it can also utilize lab data to predict disease progression, mortality, treatment response or risk of recurrence. Longitudinal laboratory measurements can be incorporated into prognostic models to detect changes prior to clinically significant deterioration. This is especially true for chronic diseases and cancer, as the laboratory profile may vary according to the disease's progression.

Risk stratification can also help with clinical prioritization to help direct patients for closer monitoring or further diagnostics. Combinations of laboratories, molecular and clinical parameters have been studied in oncology to find out whether they can

predict response to therapy or patient prognosis [22]. Despite this, for prognostic models it is important to take care of calibration and external validation, as a well-calibrated model that discriminates well between high-risk and low-risk patients can result in poorly calibrated absolute risk estimates.

- **Based Diagnostic Support in Specialized Laboratory Areas**

AI is used in various areas of the lab. In hematology, ML and DL techniques can be used to classify diseases and detect abnormalities in blood cell counts, morphologies and their derived indices. In clinical chemistry, AI can be used to analyse biochemical data and identify patterns that could indicate organ dysfunction and systemic diseases.

AI has found applications in microbiology for microorganism classification, lab data and image interpretation, and the prediction of antimicrobial resistance. Immunological profiles of antibodies, immune markers and serological profiles can be processed and analysed using computational tools. Another application of molecular diagnostics is the high dimensionality of the features contained in the genomic and transcriptomic data sets, their suitability for computational classification and prediction [23].

- **Combining Laboratory and Clinical Data**

The diagnostic potential of AI can be used and amplified with other clinical data from clinical sources. Laboratory values can be influenced by demographic variables like age and sex, and the clinical history and symptoms give context to the laboratory values.

the

**3. Examples of AI-based diagnostic prediction using clinical laboratory data**

| <b>Disease/condition</b> | <b>Dataset/sample type</b> | <b>Laboratory variables</b>                  | <b>AI algorithm</b>             | <b>Performance</b>                                | <b>Validation</b>                   | <b>Potential clinical application</b>  |
|--------------------------|----------------------------|----------------------------------------------|---------------------------------|---------------------------------------------------|-------------------------------------|----------------------------------------|
| Cancer                   | Blood/serum/plasma         | Biochemical and/or molecular biomarkers      | ML classification               | Reported using AUROC, sensitivity and specificity | Internal/external validation        | Early detection and diagnostic support |
| Hematological disease    | CBC/blood samples          | CBC parameters and derived indices           | Random forest/SVM/NN            | Accuracy/AUROC                                    | Cross-validation/test cohort        | Automated disease classification       |
| Infectious disease       | Blood/serum                | Inflammatory and hematological markers       | ML classification               | Sensitivity/specificity                           | Independent test dataset            | Infection prediction                   |
| Organ dysfunction        | Routine laboratory data    | Liver/reneal/metabolic markers               | Logistic regression/ensemble ML | AUROC/calibration                                 | Internal validation                 | Risk stratification                    |
| Cancer prognosis         | Blood + clinical data      | Laboratory biomarkers and clinical variables | ML/DL                           | Risk prediction metrics                           | External validation where available | Prognosis and treatment planning       |

- Laboratory data, diagnosis, medications, vital signs, clinical notes, patient history and other data can be integrated into AI systems with electronic health records (EHR). Imaging data can also be combined into multimodal models where the lab and imaging data can complement each other and make a prediction for diagnosis. In the diagnosis of cancer, the

integration of these is particularly relevant, as each of these can provide complementary information.

Yet multimodal models face also some other challenges regarding missing data, data format differences, temporal alignment and differences between healthcare institutions. Therefore, strong data infrastructure and robust validation are

needed to ensure successful implementation.

- **Performance of AI Diagnostic Models**

There are several complementary measures of evaluation of AI-based diagnostic models. Specificity is the ability to correctly identify those who don't have the target condition, while sensitivity is the ability to correctly identify those who do. Accuracy is the percentage of correctly classified observations and can be misleading when the datasets are imbalanced. Precision (or PPV in suitable cases) represents the percentage of positive cases that were correctly predicted, and the F1 score is a trade-off between precision and recall.

Different decision thresholds can be evaluated based on the area under the receiver operating characteristic curve (AUROC) [24]. However, a high AUROC is not enough to ensure clinical usefulness. There is also a need for calibration, as predicted probability should match appropriately the observed frequencies. For instance, a model that estimates a 20% probability of disease should be able to select a group where about 20% of the patients have the disease under the same conditions.

In conclusion, in addition to statistical performance, the clinical utility, generalizability, interpretability and impact of AI diagnostic prediction should be assessed. External validation in independent populations is especially critical since some models may be accurate in the development population but fail to be as accurate when applied to other institutions or patient populations. As such, establishing computational model validation for a clinically relevant decision support system involves strict validation, proper calibration and incorporation of existing laboratories and clinical workflows.

- **Artificial Intelligence in Cancer Screening and Early Detection**

Cancer screening is designed to detect cancer at an earlier stage, before symptoms will appear, and when the chances of curing the cancer are usually higher and the treatment may be more effective. Reductions in mortality for certain cancers have been made to a significant extent through traditional screening methods, but test sensitivity, specificity, access, patient uptake and the nature of the disease all affect the success of the screening. Cancer in its early stages may cause only mild biological changes, and there may be a significant variation in the level of biomarkers detected due to tumor heterogeneity. To this end, the implementation of Artificial Intelligence (AI) can be used to overcome some of these issues by combining several laboratory data, molecular, clinical and image-derived features and by identifying patterns related to early malignancy. Machine learning (ML) and deep learning (DL) were found to be promising approaches for cancer detection and analysis of liquid biopsies, digital pathology and personalized cancer risk assessment and had been extensively [25].

- **Challenges in Conventional Cancer Screening**

An important hurdle in cancer screening is the ability to pick up cancer in the early stages, when the tumor burden is low. A few molecules of malignancy might be present in circulation and be difficult to distinguish from normal biological variation in the early stages of malignancy. Biomarkers, therefore, which work well in advanced diseases, may not be as sensitive as early diseases.

One other limitation is false-positive and false-negative results. The false-positive results may result in invasive testing, patient anxiety and higher healthcare expenses, while the false-negative results can cause a delay in diagnosis. Additionally, screening can be complicated by tumor heterogeneity, which refers to the fact that a cancer that

develops in a different tissue, molecular subtype or stage of disease may have different biomarkers. This restriction has sparked interest in minimally invasive methods that can detect multiple molecular signals at a time.

This is where the relevance of AI becomes prominent since the computational models can analyze combinations of weakly informative or moderately informative features, instead of relying on a single biomarker. These methods may enhance the performance of the ability to define cancer-associated patterns and to differentiate these from biological variation, but improvements in the performance of such models do not necessarily lead to a clinical screening benefit.

- **AI-Based Analysis of Cancer-Associated Biomarkers**
- **Blood-Based Biomarkers**

Blood is one of the easiest biological samples to obtain for cancer screening, which can be done in a minimally invasive manner. The study of circulating proteins, tumor-associated antigens, cell-free DNA (cfDNA), circulating tumor DNA (ctDNA), circulating RNA and microRNAs, among others, as cancer biomarkers have been explored. But the amount of tumor-derived material may be very low, especially at an early stage of the disease.

However, this can be overcome using AI and ML techniques, which can integrate several circulating biomarkers into predictive signatures. Rather than having to be able to detect a pattern in a single variable, algorithms can detect patterns in multiple variables. Protein-based models can consider several proteins that circulate bloodstream, and molecular models can include genetic, epigenetic and RNA characteristics.

cfDNA and ctDNA are especially appealing since

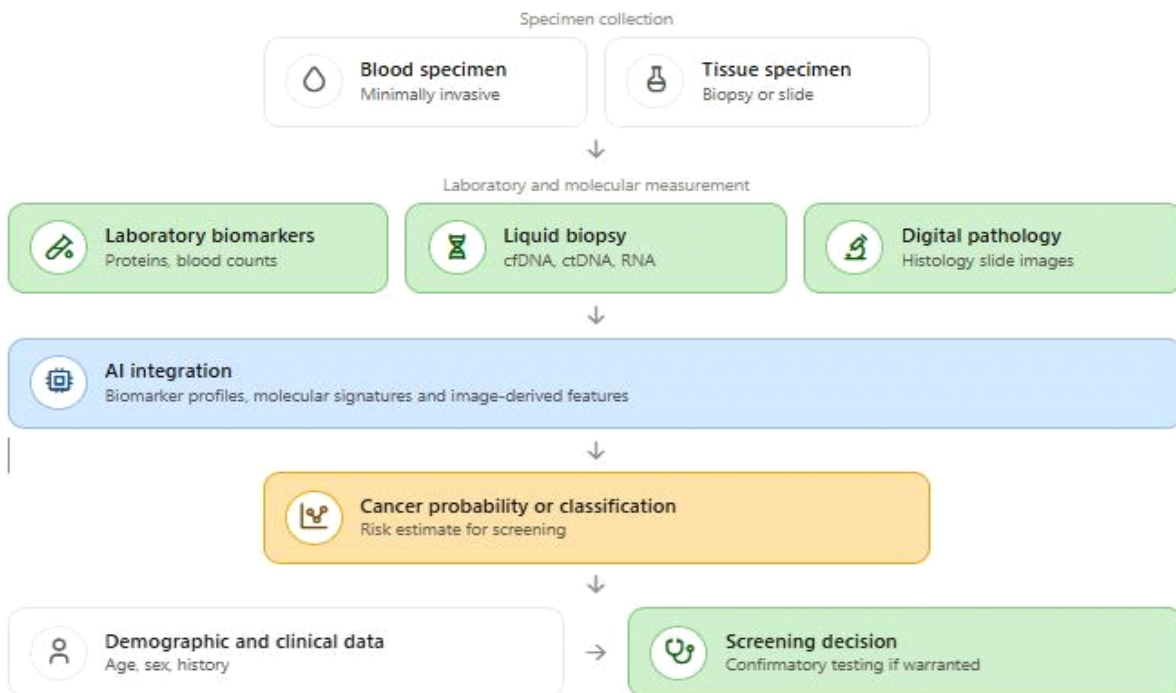
DNA from a tumor may harbor genetic and epigenetic changes that are linked to malignancy. But separating out the signals from the far greater amount of non-tumor cfDNA is difficult. Computational methods can help to pinpoint patterns that are associated with cancer, methylation patterns, fragment characteristics and combinations of molecular features [26].

- **Multi-Biomarker Cancer Signatures**

One of the most significant use cases of AI in cancer screening is the creation of Multi biomarker signatures. In the case of ML algorithms, they can consider many candidate features and find combinations that are linked to the cancer status. Feature-selection techniques can eliminate redundant features and provide the most informative biomarkers; classification techniques can then take the marker signatures obtained from the feature-selection process and classify the cancer and non-cancer samples.

Multi-cancer detection is an added development of this strategy. Instead of creating a specific model for each type of malignancy, scientists have investigated whether molecular patterns can help detect cancer and, in some instances, help determine the anatomical source of the cancer. These methods are especially appealing because they might be able to test for multiple types of cancer by just a single blood test.

But the use of multi-cancer prediction poses significant methodological challenges. They may release different levels of biomarkers in the blood, and the prevalence of different cancers, along with their molecular features, may vary. It is important to judiciously assess models for each cancer disease and each stage of cancer to make sure that the differences between study populations are not responsible for the apparent performance.



- Integration of AI with laboratory biomarkers, liquid biopsy, and digital pathology for cancer screening and early detection.

A conceptual cancer-screening workflow begins with the collection of blood or tissue specimens, followed by laboratory or molecular measurement. AI algorithms can then integrate biomarker profiles, molecular signatures, and image-derived features to generate a cancer probability or classification. When appropriate, the output can be combined with demographic and clinical information to support screening decisions and determine whether confirmatory diagnostic testing is warranted.

#### • AI and Liquid Biopsy

Liquid biopsy is increasingly recognized as a valuable tool for cancer detection, as it allows for molecular analysis of material released from the

tumor in the body fluids, especially in the blood. Liquid biopsy may yield data on ctDNA, cfDNA, CTCs, cRNA, EVs, proteins and others, depending on the analytical platform used.

The high dimensionality of molecular assays in liquid biopsy lends itself well to the use of AI. A combination of mutations, methylation patterns, fragmentomic features, RNA signatures, or protein measurements relevant to malignancy can be identified by ML algorithms. Molecular data sets can also contain complex representations that can be identified using deep-learning methods.

AI can do more than just identify cancer vs. non-cancer patients; it can be used to help predict a patient's outcome. The potential use of AI-assisted liquid biopsy is not limited to cancer vs. non-cancer diagnosis; it can also be used to predict a patient's outcome. A model can help determine cancer subtypes, predict cancer stages, identify high-risk

patients, and/or give information about tissue of origin. However, early detection can be difficult, as the level of tumor-derived material in the blood can be very small. The performance of the model can be affected by analytical sensitivity, biological variation, sequencing errors, and variations between assay platforms.

- **AI in Digital Pathology and Laboratory Imaging**

AI-driven cancer screening doesn't have to be limited to blood markers. A new and important field in which DL methods can be used to aid cancer detection is digital pathology. Histopathological slides can have significant amounts of morphological information, which may be hard to consistently and quickly assess at scale. Convolutional neural networks (CNNs) can acquire the features of the image and classify tissue regions, identify malignant cells, and help to grade or classify tumor subtypes.

Analogous studies have been conducted in cytology, where analysis of abnormal cellular morphology can be performed automatically. AI image analysis could also be useful for interpreting blood-cell morphology and for assisting in the diagnosis of hematology, adding value to laboratory blood measurements.

In digital pathology, AI has the potential to decrease manual evaluation and assist pathologists with identifying suspicious areas for additional analysis. But image-based models are still limited by the quality of the images, staining protocols, characteristics of scanned images, and training sets that are representative. Thus, models based on a set of images from one lab or institution may not be equivalent when used to analyse images generated by different laboratory or imaging procedures.

- **AI for Cancer Risk Stratification**

AI can also help to detect those who might have a higher risk of contracting or even existing with cancer. Laboratory biomarkers can be used in combination with age, sex, family history, clinical characteristics, previous diagnosis and other available information in risk-stratifying models.

Rather than using a one-size-fits-all approach to screening, risk prediction may enable screening resources to be used more efficiently for individuals at higher predicted risk. AI models can also deliver ongoing probability estimates that can assist in deciding on the need for further testing.

Linking with population-level screening programmed may then be able to generate a more personalized screening programmed. Risk-based approaches, however, need to be carefully assessed since there may be systematic variations in access to health care, demographics, disease prevalence, and data quality, which can lead to bias. The real clinical value of risk stratification is whether having the ability to identify a high-risk group results in earlier diagnosis and better patient outcomes [27].

- **Challenges in AI-Driven Cancer Screening**

While AI shows great promise in cancer screening, there are still some drawbacks. The overall prevalence of cancer in most general screening populations is significantly lower than in many research populations, resulting in an extreme class-imbalanced situation. If a good model in the case-control design yields a lot of false-positive results in the low-prevalence screening population, then care must be taken in interpreting its performance parameters. If the model performs well in the case-control population, it can yield significantly more false-positive results in the low-prevalence screening population, and care must be taken when interpreting the performance parameters of the model.

One additional important consideration is for

spectrum bias. Advanced or clinically evident diseases may be present in research datasets but not in real-world screening, where they are asymptomatic and biologically diverse. Therefore, the sensitivity reported can overestimate performance in the target population for screening.

The significance of false-positive results is especially great when millions may undergo testing, as any small decrease in specificity can lead to a huge false alarm rate of unnecessary investigations. There is also the danger of overdiagnosis when the AI systems detect low-risk conditions that might not ever have clinched a diagnosis.

So, it is crucial to have external validation. The evaluation of models should be conducted with independent populations of various demographics, disease stages, healthcare systems, and laboratory platforms. Specimen processing, assay technologies, sequencing platforms, imaging systems and data preprocessing can all influence the performance of the model.

In conclusion, AI can enhance current cancer screening methods by combining multiple

laboratory and molecular markers and aid in the identification of patients who need additional diagnostic testing. But the leap from promises to practice for screening in the general population demands careful prospective validation, external validation, clinical utility, and proof of meaningful patient outcomes through AI-driven detection.

#### • AI Across the Clinical Laboratory Workflow

Artificial intelligence (AI) in clinical laboratory medicine far reaches beyond diagnostic prediction and biomarker interpretation. AI has the potential to help address several points within the laboratory testing pathway, such as pre-analytical, analytical and post-analytical. This wider application is crucial, as mistakes and inefficiencies can arise during the various steps of the laboratory process, and improvements in one stage may not benefit the rest of the process. AI can help enhance laboratory efficiency, quality, and consistency by combining automated data analysis, pattern recognition, anomaly detection, and decision support functionalities [28].

#### 4. AI applications in cancer screening and early cancer detection using laboratory-derived biomarkers and diagnostic data

| Cancer type       | Bi-marker/data source                        | AI method | Study population           | Diagnostic objective   | Reported performance           | Validation                | Limitations                               |
|-------------------|----------------------------------------------|-----------|----------------------------|------------------------|--------------------------------|---------------------------|-------------------------------------------|
| Lung cancer       | Blood-based biomarkers/molecular data        | ML/DL     | Cancer and control cohorts | Early cancer detection | AUROC, sensitivity/specificity | Internal/external cohorts | Population and stage differences          |
| Colorectal cancer | cfDNA/ctDNA, proteins or combined biomarkers | ML        | Screening/cancer cohorts   | Cancer detection       | Classification metrics         | Training/test cohorts     | Low tumor-derived signal in early disease |

|                  |                                            |        |                                |                                                  |                                |                                        |                                           |
|------------------|--------------------------------------------|--------|--------------------------------|--------------------------------------------------|--------------------------------|----------------------------------------|-------------------------------------------|
| Breast cancer    | Protein, molecular and/or imaging data     | ML/DL  | Cancer and control populations | Detection/classification                         | AUROC, sensitivity/specificity | Cross-validation/independent cohorts   | Biological heterogeneity                  |
| Prostate cancer  | PSA-related and other laboratory variables | ML     | Screening/clinical cohorts     | Risk classification                              | AUROC/calibration              | Internal validation                    | Dependence on clinical population         |
| Multiple cancers | Multi-biomarker/liquid biopsy data         | ML/DL  | Multi-cancer cohorts           | Cancer detection and tissue-of-origin prediction | Sensitivity/specificity/AUROC  | Independent validation where available | Disease prevalence and stage effects      |
| Various cancers  | Digital pathology                          | CNN/DL | Histopathology cohorts         | Tumor detection/classification                   | Accuracy/AUROC                 | Test/validation datasets               | Image and laboratory workflow variability |

### • Pre-Analytical Applications

Preamerical activities consist of any work carried out prior to analysis in the laboratory, such as patient identification, collection of samples, transportation of samples, sample preparation and evaluation of sample suitability. This stage is especially prone to errors, as problems with the collection, such as incorrect identification, inappropriate collection, an insufficient quantity, transportation time or storage conditions, can adversely affect the laboratory sample.

AI systems can help identify potentially inappropriate samples and look for patterns that may indicate pre-analytical issues. If appropriate imaging data is provided, automated image-analysis methods can aid in the recognition of sample properties such as hemolysis, for example. Predictive models can also detect conditions that cause specimen rejection or specimen testing delays.

AI can also help optimize workflow by forecasting sample volumes, prioritizing lab resources and samples for quick delivery, and assisting with resource allocation. This could help to minimize the

amount of manual effort required and speed up turnaround time in such applications. But for implementation, there are requirements to ensure reliable integration with the laboratory information system and proper protection to prevent accidental degradation of specimen identification and patient safety with automated recommendations.

### • Analytical Applications

In the analytical stage, AI can aid in automated result interpretation, quality control, anomaly detection, and monitoring of instrument performance. Laboratory instruments produce high volumes of measurements, and computational models can detect strange patterns that could signal out-of-range or unusual patient results, instrument

abnormalities, or analytical errors.

Traditional quality-control processes might be complemented with the help of machine learning techniques that are able to detect complex patterns in several analytical variables. AI models can identify correlations among measurements that can be used to identify systematic shifts in instrument performance or assay behavior, rather than evaluating each measurement separately. The results may also be found using anomaly-detection techniques, which could uncover results that vary significantly from the anticipated patterns and thus warrant further examination.

Another important application is automated interpretation. AI can combine several test data and identify the patterns of various diseases or physiological conditions. This type of system can help with reflex testing or can alert you to the need for a professional evaluation. However, AI-powered analytical systems should be used alongside existing laboratory quality management processes and not in place of them.

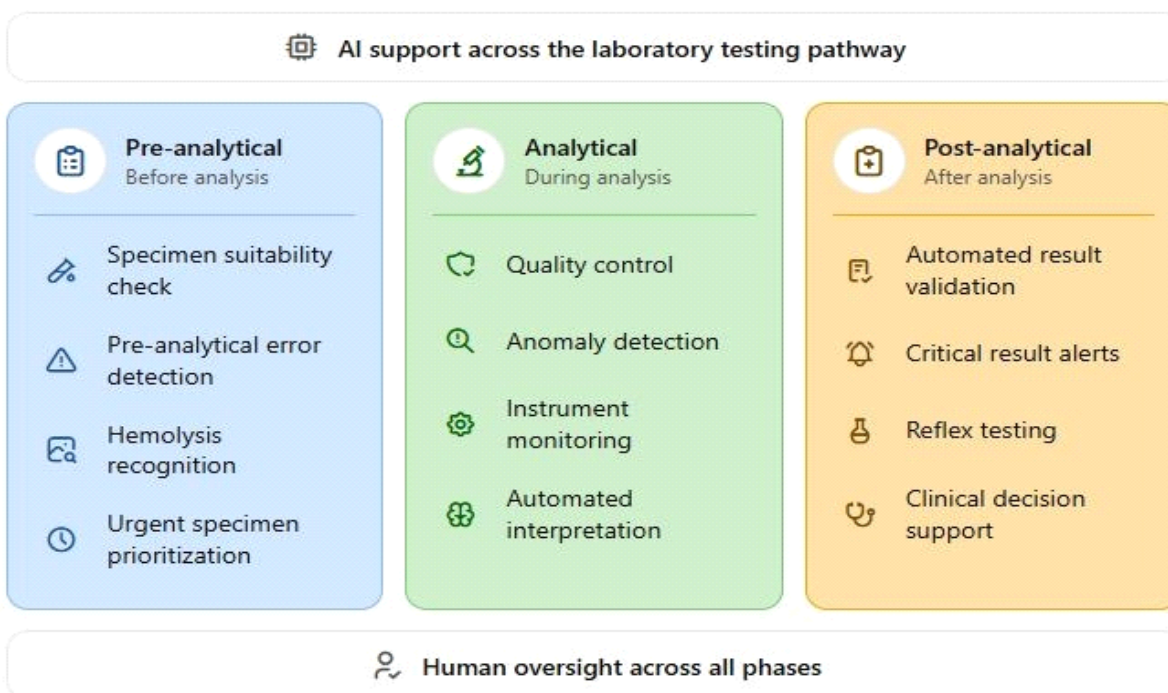
- **Post-Analytical Applications**

The post-analytical phase consists of the activities

of validation, interpretation, reporting and communication of the laboratory results. AI can be used for automated result validation, which could detect sets of results that are inconsistent or unusual within the clinical context. It can also help your priorities results if they are important and point to potentially urgent results for quick review.

Another potential application is AI-assisted reflex testing. Based on predefined laboratory and clinical patterns, an AI system could identify situations in which additional testing may provide clinically useful information. Similarly, integrated diagnostic models can combine laboratory results with patient characteristics and clinical information to provide decision support.

The broader integration of AI across the laboratory pathway therefore provides an opportunity to move from isolated automation toward intelligent laboratory systems. However, human oversight remains essential, particularly when AI-generated recommendations may directly influence diagnostic or therapeutic decisions.



- **Integration of AI across the pre-analytical, analytical, and post-analytical phases of the clinical laboratory.**
- **Data Quality, Model Interpretability, and Clinical Validation**

Though the applications of Artificial Intelligence (AI) in clinical laboratory medicine are increasingly gaining ground, its successful application is not just dependent on the performance of the algorithm but also on the decision-making process. The predictiveness of laboratory AI models is built on the quality, completeness, and representativeness of the data used in their development and testing. Moreover, models with good research accuracy may not have reliable prediction in other laboratories, patient populations or analysis platforms. Therefore, data quality, model interpretability, validation and clinical utility are key aspects that should be considered when deciding if an AI system is appropriate for routine

clinical use [29].

- **Importance of Laboratory Data Quality**

There are many sources of variability affecting laboratory data. Data may be unavailable due to the failure to order a test, failure to obtain an appropriate specimen, or failure to move data between systems. Inappropriate handling of the missingness may lead to the AI model learning a relationship that is more representative of how data was collected than of a real biological relationship.

Another factor that is important is measurement error. Experimental conditions such as different analytical platforms, reagents, calibration methods, and laboratories can result in systematic differences in values. Laser focusing on molecular and proteomic data, where samples analyses at

different times or with different platforms might have technical differences that are not related to the disease biology, batch effects are especially important.

Specimen collection, storage, transportation and processing can also affect laboratory measurements, which is why pre-analytical variation can further influence the measurement. This indicates that AI algorithms developed from highly controlled research cohorts can yield varying results with routine clinical samples. Laboratory procedures need to be standardized to build reliable models, and the appropriate preprocessing needs to be performed.

- **Dataset-Related Challenges**

The features of the training data sets have the potential to have a significant impact on AI models. A limitation of many studies is the small sample size, especially for those using special molecular biomarkers. If the number of candidate variables is large compared to the number of patients, the models can overfit the training data and not work well on independent data.

Another significant challenge is class imbalance. A relatively small number of positive cases may represent some clinical conditions, especially rare cancers and uncommon diseases. Overall, the accuracy of a model can thus be very high, but it can be very low when trying to recognize the clinically relevant minority class.

Selection bias may arise from the fact that study subjects do not reflect the population in which the model is intended to be applied. This is especially important for diagnostic research, as samples may include patients who are obviously healthy controls or patients who have a more intermediate or unclear clinical presentation.

Another important problem is called dataset shift. The relationship between input variables and outcomes may change as patient characteristics, disease prevalence, clinical practice, laboratory methods or instrument platforms change. Thus, the performance of the models created at one institution may turn out to be lower at another institution. Generalizability needs to be validated by using external and independent and representative data sets.

- **Model Interpretability and Explainable AI**

In clinical laboratory medicine, interpretability of the predictions by AI models is especially relevant because of the necessity of understanding the basis for the predictions before they can be used in patient care. In some cases, the relationships between the input variables and the resulting outcomes are relatively straightforward, such as logistic regression and decision trees. In contrast, complex neural networks could provide an extremely precise forecast but provide little direct insight into how individual features led to the outcome.

It is often referred to as the black-box problem. Transparency can diminish clinician confidence and be challenging to detect inappropriate predictions or systematic errors. Therefore, the need for Explainable AI (XAI) methods has grown in the field of understanding complex models increasingly [30].

- **Interpretable Models**

Some interpretable methods are logistic regression, decision trees, and rule-based models. Decision trees can be visually assessed, and logistic regression can give an estimate of the direction and magnitude of the association between individual variables and the outcome. These characteristics can aid clinical interpretation and can assist laboratory personnel in determining the components of

a prediction.

Interpretability, however, can have a cost in terms of the complexity of the prediction. Simple models are often very easy to interpret but do not necessarily capture the relationships in complex laboratory or molecular datasets that are not necessarily linear. The selection of a model should therefore not only be based on predictive performance but also consider the level of transparency that is required for the intended clinical application.

- **Explainability for Complex Models**

In complicated ML and DL systems, feature-attribution techniques can give information about which variables are most vital to the individual prediction. Global or local interpretations are possible with model visualization and other explanation techniques. Global explanations are broad and summaries the overarching behavior of a model, while local explanations are specific and deal with how a patient's prediction comes about.

Explainability should not be interpreted as evidence that a model is clinically correct, however. An explanation could explain the mechanism by which a model led to a prediction but not be a statement of whether a biological association is valid. Thus, explainability should be used in conjunction with, and not in place of, good clinical validation.

- **Model Validation**

Before being able to use an AI model for clinical applications, it must be adequately validated. Typically, datasets are split into three sets during development: training, validation, and test sets. The training data can be used to determine the model parameters, while the data from the validation set can help in the selection of the model and optimization of the model parameters. One set of test data is used to give an estimation of performance on data

not seen before.

Cross validation may be employed in small data sets but is not a substitute for evaluation with truly independent data sets. Internal validation is used to determine if a model performs in a consistent manner in the development data set, and external validation is used to determine if a model performs in an independent data set, preferably from another institution or healthcare setting.

Prospective validation is another step towards clinical rollout, as it evaluates the model behavior in a real-world context prior to a wider rollout. This is especially significant if the patient population, analytical platform or laboratory workflow are different than those used in the development of the model.

- **Clinical Utility Versus Statistical Performance**

But high statistical performance does not guarantee the improvement of clinical care with an AI model. A model can have a good AUROC but has poorly calibrated risk estimates, for instance. Calibration evaluates the accuracy of the predictions of probabilities in comparison to the actual probabilities of the outcomes and is especially relevant if models are applied to estimate the risks of individual patients.

It is important to assess the utility of using a model over current diagnostic methods using decision curve analysis and other related methods across relevant clinical decision thresholds. The utility of an AI system is also related to whether it can be incorporated into the current workflow in the lab, when it can deliver results, and if it can impact clinical management.

Finally, clinical validation should not only focus on technical accuracy but also on the potential

benefits of AI on the diagnostic process, such as increased efficiency, reduced unnecessary testing, early detection, and better patient outcomes. Ultimately, to successfully translate AI into the clinical laboratory medicine environment, it is essential to

use high-quality data sets, be transparent about the method, have solid external validation, ensure proper calibration and demonstrate clinical utility [31].

**5. Major methodological and clinical challenges affecting implementation of AI in clinical laboratory medicine**

| Challenge         | Potential effect                     | Example                                    | Possible mitigation                              |
|-------------------|--------------------------------------|--------------------------------------------|--------------------------------------------------|
| Missing data      | Prediction bias                      | Incomplete laboratory records              | Appropriate imputation and missing-data analysis |
| Measurement error | Reduced model reliability            | Variation between analytical platforms     | Standardization and quality control              |
| Batch effects     | Spurious associations                | Different molecular assay batches          | Batch correction and standardized protocols      |
| Class imbalance   | Poor minority-class detection        | Rare cancers                               | Resampling or weighted models                    |
| Selection bias    | Limited population generalizability  | Highly selected research cohort            | Representative datasets                          |
| Spectrum bias     | Overestimated diagnostic performance | Advanced cases versus screening population | Evaluation across disease stages                 |
| Dataset shift     | Reduced generalizability             | Different hospitals or laboratory systems  | External and multicenter validation              |

|                             |                                  |                                   |                                        |
|-----------------------------|----------------------------------|-----------------------------------|----------------------------------------|
| Black-box models            | Reduced clinical trust           | Deep neural networks              | Explainable AI and feature attribution |
| Poor calibration            | Incorrect risk estimates         | Diagnostic probability prediction | Calibration assessment                 |
| Limited external validation | Uncertain real-world performance | Single-center model               | Independent prospective validation     |

In conclusion, data quality and clinical validation should be seen as part and parcel of the development of AI, not as an add-on. The key features of a clinically useful laboratory artificial intelligence system are reliability across the relevant patient population and laboratory environment and outputs which are interpretable and can be integrated into the professional decision-making process. Understanding this difference between the algorithm performance and clinical utility is key to responsible use of AI in laboratory medicine.

- **Clinical Integration, Ethical Considerations, and Future Directions**

To successfully apply artificial intelligence (AI) in clinical laboratory medicine, one would not only need to create accurate predictive models but also make the systems user-friendly and intuitive. For AI systems to be implemented, they must be integrated into existing laboratory and clinical environments, addressing data quality, privacy,

transparency and clinical responsibility. Research to practice, thus, is a process that brings forth technical, clinical, ethical and regulatory issues.

- **Integration into Routine Laboratory Practice**

For the integration of AI to be a part of the everyday workflow of laboratory medicine, it must be compatible with laboratory information systems (LIS), electronic health records (EHR), analytical instruments, and clinical decision-support systems. The AI algorithms can be used to analyses results in the lab, to automatically process incoming test results, recognize abnormal patterns, priorities results of critical importance and generate risk estimates for certain diseases. Laboratory data can be combined with EHR-based clinical data to further enhance prediction by adding to the information the following: demographic data, medical history, medications, symptoms and prior laboratory measures.

Automated reporting is another possible use. AI-powered systems can not only provide individual test results but also identify clinically significant patterns of test results and provide standardized information on test interpretation. However, it is important that recommendations based on AI are professionally supervised appropriately. The collaboration between human and AI is particularly important when predictions can impact cancer screening, treatment, and/or diagnostic testing. The main goal of using AI should be to support, not supplant, the knowledge, expertise and experience

of laboratory and clinical professionals [32].

- **Ethical and Regulatory Considerations**

Patient privacy, data security, algorithmic bias, and accountability are ethical concerns related to the application of AI in laboratory medicine. Laboratory data may be extremely sensitive clinical and genomic information requiring appropriate protection during data collection and sharing of laboratory data for model development. While there are ways to anonymize and control access to reduce the privacy risks for genomic and longitudinal clinical data, there are limitations.

Another worry is algorithmic bias – algorithms developed from non-representative samples can have different performance on different groups of users, in different healthcare environments or in different geographic areas. This can be particularly important for screening applications because a false prediction (either positive or negative) may directly affect patient management. Accountability should also be clearly defined in the case of a recommendation by an AI that leads to an incorrect diagnosis or clinical decision. Therefore, it is vital for AI systems to be validated and compliant with regulations before use in clinical environments.

- **Requirements for Clinical Translation**

To enable clinical translation, standardized and enough representative datasets, solid pre-processing procedures, and specific performance criteria need to be in place. The studies conducted in multiple centers are especially significant, as there could be variations in laboratory, instrument, reference interval, patient population, and clinical practice across centers. Thus, it is crucial to test externally and not simply use an internal test set.

However, future clinical trials could provide additional information on the potential of AI systems to

improve diagnostic accuracy, laboratory efficiency, clinical decision-making, or patient outcomes. Post-implementation monitoring is also required to identify any shifts in the performance of the model that could result from changes in the patient population, laboratory platforms, prevalence of disease or clinical practice. If significant changes take place, model recalibration or redevelopment might be needed.

- **Future Directions**

This will be a recurring process in future uses of AI in the lab, incorporating clinical, imaging, molecular and pathological data. Individual data sources can be complemented by multimodal AI. Likewise, the integration of genomic, transcriptomic, proteomic and metabolomic measurements may contribute to the creation of more detailed biomarker signatures and personalized laboratory medicine.

Federated learning and privacy-preserving approaches have the promise of reducing the need for sharing sensitive patient data and facilitating collaborative model development. Real-time diagnostic prediction also would enable continuous monitoring of disease risk when new lab data is available. For cancer screening, a combination of AI and any analysis of circulating biomarkers, measurements from liquid biopsies, or other lab assessments may help in the population-based risk stratification and earlier identification of people who require further investigation.

The future of AI in lab medicine will depend increasingly on increasingly complex algorithms, but it also will rely on reliable data and the transparent validation and regulation of such systems, in addition to a successful partnership between AI systems and health care workers.

## • Conclusion

With the vast amounts of information and the complexity of today's clinical lab, the AI-based computational method is now playing an important role in the clinical laboratory. Multivariate, machine-learning, and deep-learning approaches can use several biochemical, hematological, molecular, proteomic, and image-based variables to uncover patterns that might not be apparent from the individual measurements of each lab parameter. All these capabilities offer avenues for enhancement of biomarker interpretation, diagnostic classification, prognostic prediction and clinical decision support.

The creation of Mult biomarker and multimodal applications is one of the most promising areas of application of artificial intelligence. The efficacy of AI models to provide a more comprehensive understanding of a disease and to assist in personalized risk assessment can be further enhanced by leveraging complementary information from laboratory assays, together with molecular and clinical and imaging data. The combination of circulating biomarkers, liquid-biopsy measurements and digital pathology can be used in cancer screening to facilitate earlier malignancy detection and better stratification of people who need further diagnostic evaluation. AI can also be used to help with pre-analytical, analytical, and post-analytical tasks in the lab, such as quality checks, identifying anomalies, automating interpretation, and optimizing workflow.

However, the benefits of AI in clinical practice go beyond merely predicting outcomes. The accuracy, comprehensiveness and representativeness of the data that underpins the lab-based AI models are critical. The reliability and generalizability of the models can be affected by a variety of issues, such as missing data, analytical variability, batch effects, class imbalance, selection bias, spectrum bias, and dataset shift. Moreover, complex models might have interpretability issues, and explainability and

transparent clinical validation are crucial to gain trust from professionals. It is therefore essential to first validate and then calibrate and assess the clinical usefulness of promising algorithms before translation to a reliable clinical tool.

Ethical and practical aspects are of the same importance. But privacy and security of patient information, algorithmic bias, accountability and regulation must be addressed before it can be widely adopted. Laboratory information systems and electronic health record integration, along with the current clinical workflows, need to be complemented with proper human supervision. AI should not replace humans' clinical or laboratory knowledge or experience; it is meant to complement it.

Overall, the potential applications of AI in clinical laboratory medicine are vast and promising, with the promise of enabling more accurate and timely diagnosis, better interpretation of complex laboratory data, and the potential for improved personalized care. Future advances will require adequate and representative databases to be created, a standard laboratory method to be found, multi-center validation, transparent algorithms and prospective proof of clinical value. Given these needs, AI-enabled lab medicine could be a significant element in data-driven diagnostic care without compromising patient safety, clinical accountability and professional oversight.

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