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Exploring the Future of Diagnostic Industry, Emerging Breakthroughs in Diagnosis and their Impact on Patient Management

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Abstract

IVDs constitute one of the major mainstays in today's healthcare system. The utilization of advanced technologies for disease diagnosis can improve patient outcomes and aid in monitoring and treatment of the disease. The developments of AI tools can aid in maximizing patient care with multiple chronic conditions (MCC) by envisaging drug receptivity, adherence and interactions, while using data repositories to provide personalized medicine and care. The POCT can aid in rapid diagnosis which can be helpful for timely management of the disease. The use of non-invasive liquid biopsy helps in the detection of a broader range of cancers and other diseases at earlier stages. Moreover, it can support in detection of tumor recurrence and real-time monitoring of tumor dynamics and treatment response by recognizing specific markers in body fluids. Integration of digital technologies into healthcare platforms has several advantages. Electronic Health Records (EHRs), telemedicine, mobile health apps (mHealth), wearable devices, Laboratory Information Management System (LIMS) are some of the examples of cutting-edge digital technologies. Block chain technology can help in clinical trial management. Genomic medicine can be potentially useful in diagnosing rare disease genetic conditions, and many types of cancer. These futuristic prospects seem to have huge scope of technology based diagnosis thereby providing accurate results with small TATs aiding in timely and correct clinical decisions by HCPs for the patients.

Introduction

One of the primary cornerstones in today's healthcare system is the use of *in-vitro* diagnostics (IVDs) for better patient's clinical outcomes. Though the total expenditure accounts for only 2% of total healthcare budget the effect of IVDs use is huge as it impacts over 66% of clinical decision-making in the patient management.[1]

IVD's cover a broad spectrum of clinical ailments and are so crucial facet of modern medicine that 122 test categories are selected as "essential" by World Health Organization(WHO).[2] However, even with their remarkable utility, current diagnostic testing has a scope for upgrade and improvement. [2] One challenge is that test results are normally reported as a single static number without any account of uncertainty, which might lead to the erroneous postulation that laboratory results are accurate.[3] The biological variation, generally, is main contributor to variation in the laboratory results,[3] which might be ignored when measurements are taken at one specific

"snapshot" moment in time. Another restriction is that test data is often siloed and used in isolation for a single purpose.

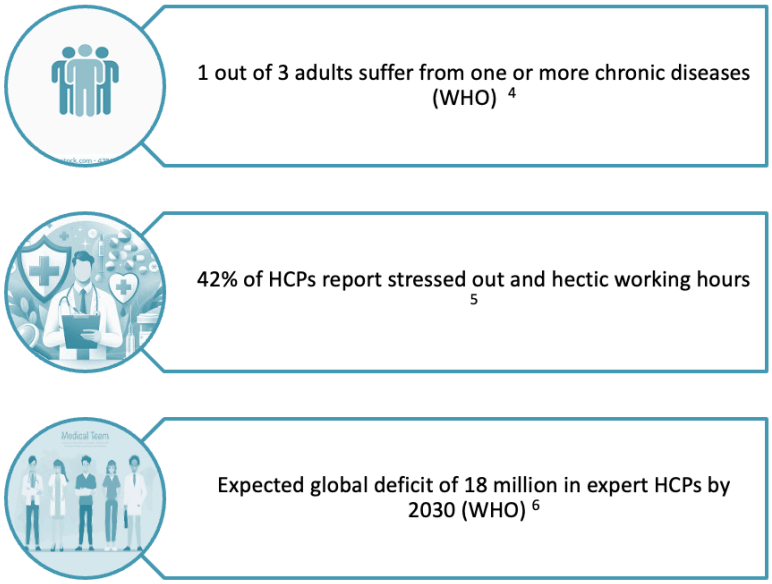
The convergence of digital technologies and diagnostic tests creates a paradigm shift in modern healthcare system. Clinicians can leverage the digital technologies for improving patient experience and outcomes. Further, the use of these advanced technologies might alleviate some of the resource pressures on the healthcare system and might help in augmenting the speed and efficiency of the testing process. [4]

In this new era, several emerging breakthroughs are set to reform the diagnostics industry, modifying the approaches to detect and manage diseases. Top emerging trends in the diagnostic industry are discussed as follows:

1. Integration of Artificial Intelligence (AI) in Diagnostics

1.1 AI in Healthcare: A Paradigm Shift in Patient Care

The necessity for AI in healthcare has been sensed strongly in past few years as the prevalence of chronic diseases is on rise and the existing healthcare systems are struggling to meet growing demand of patient care. The advancements in digital technology are facilitating the more data capture than ever before by building the solutions that can assist healthcare professionals(HCPs) and patients in making sense of all that data. AI aids in maximizing patient care with multiple chronic conditions (MCC) by envisaging drug receptivity, adherence and interactions, while using data repositories to provide personalized medicine and care.[4]



Healthcare systems exposed to unsustainable burden [4-6]

Even with numerous advancements in medicine today, efficient disease diagnosis is still considered a challenge worldwide. The development of early diagnostic tools is an continuing challenge owing to the complex disease mechanisms and the underlying symptoms.AI is a rapidly growing field based on the computer programming that can transform the clinical diagnosis; aiming to create machines to execute tasks that typically require human intelligence. AI includes various techniques such as machine learning

(ML), deep learning (DL), and natural language processing (NLP).[7]

AI and ML are most advanced statistical approaches that have provided new opportunities for better patient care by enhancing diagnostic accuracy, reliable prognosis prediction, precision treatment, and accurate operational efficiency for health systems. Novice AI/ML technologies such as image-based diagnostic applications have showed early clinical promise for personalized treatment.[8] The medical imaging plays a key role in medical diagnosis and treatment and support clinical decision making for physician. DL successfully carries out image processing tasks such as image classification, target recognition, and target segmentation by analyzing images. Some examples of DL applications include: detecting retinopathy, bone age, and skin cancer identification. DL achieves expert level in these tasks.[9]AI algorithms can analyze medical images (e.g., X-rays, magnetic resonance imaging(MRIs), ultrasounds, computed tomography(CT) scans, and dual energy x ray absorptiometry(DXAs)) and support HCPs in diagnosing diseases more precisely and quickly.[10]

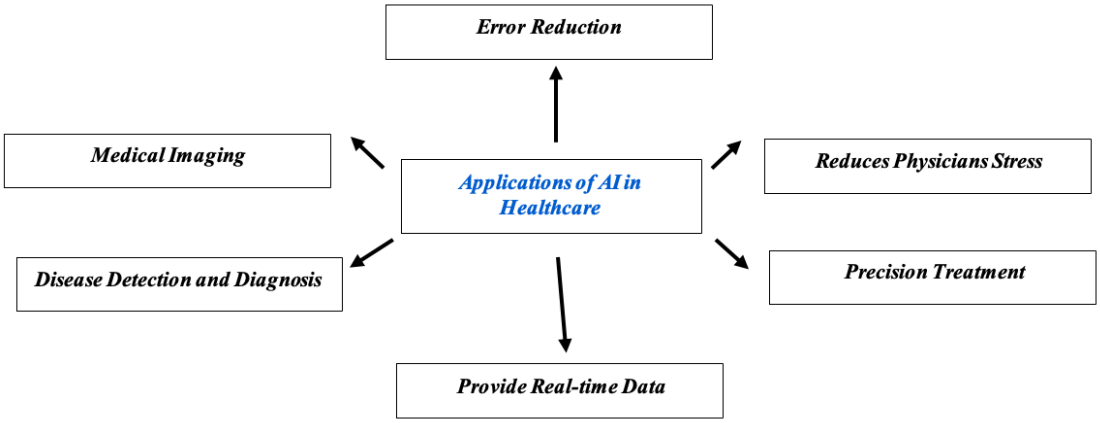


Figure 1: Main applications of AI in healthcare[11]

1.2 Glimpses from Clinical Evidences

1.2.1 Diagnostic Accuracy of AI in a Virtual Healthcare Setting

The evaluations obtained from tools such as digital symptom checkers and medical chatbots have one challenge of small sample size of patients. Small sample sizes limit general applicability and the ability to determine differences in diagnostic accuracy across different diagnoses and different patient groups.[12]

A retrospective study was conducted to overcome the small sample size gap which evaluated the diagnostic accuracy of AI-based suggestions by examining over 102,059 AI-augmented clinical encounters from a large virtual healthcare practice from 1st October, 2022, to 31st January, 2023. The patients were subjected to an AI- based medical interview, after which the interview was reviewed by virtual care providers. AI-provided differential diagnoses, communicated to the patients, and finalized diagnoses and treatment actions. The findings reported an agreement in accuracy measures between AI diagnoses, virtual care providers, and blind panel of judges.[12] The overall diagnostic agreement was reported in 84.2% (n= 85,976) of cases in whom providers selected an AI diagnosis. However, the agreement between AI differential diagnoses and the provider differed across various provider-selected diagnoses, with high agreement rates for bladder infection (98.9%)

conjunctivitis (98.7%), and upper respiratory infection (97.3%), and lower agreement rates for dermatitis (42.4%), acute bronchitis (41.7%), asthma (32.9%), and unspecified abdominal pain (20.8%).[12]

Furthermore, there was a variation in agreement rates by diagnosis, for 35 diagnoses (47% of cases, n= 47,679), ≥95% agreement and for 57 diagnoses (69% of cases, n=70,697), ≥90% agreement was observed between provider and AI diagnosis. For the most accurate 47% of cases covering 35 diagnoses, included diagnoses such as bladder infection, conjunctivitis, and upper respiratory infection. [12]

The judges' accordance diagnosis was obtained in 58.2% (n=128) of adjudicated cases was always included in the AI differential diagnosis. The ***AI model retraining*** (improvement in AI performance after retraining of the prediction model with new clinical data from the virtual primary care service) increased diagnostic accuracy for retrained conditions (vaginal yeast infection, pyelonephritis, bladder infection, bacterial vaginosis, genital herpes, and vulvovaginitis) from 96.6% to 98.0%.[12]

1.2.2 Application of AI in Digital Pathology: Diagnostic Accuracy on Whole Slide Images (WSIs)

A systematic review and meta-analysis was conducted on 148 diagnostic accuracy studies (100 included in systematic review and 48 in meta-analysis). More than 152,000 whole slide images (WSIs) from patients of multiple countries were included comprising largely cancers but also other clinical conditions. The findings reported a mean sensitivity of 96.3% (confidence interval (CI) 94.1-97.7) and mean specificity of 93.3% (CI 90.5-95.4) for AI in WSIs.[13]

The studies including gastrointestinal pathology, breast pathology and urological pathology accounted for major subgroups (over 60% of AI models included in the meta-analysis) of studies available for inclusion in the meta-analysis. AI-models showed a high mean sensitivity (93%) and specificity (94%) for the gastrointestinal subgroup and included AI models for colorectal cancer, gastric cancer, and gastritis. Similarly, studies of uropathology (including AI models for renal cancer and prostate cancer) had mean sensitivities and specificities of 95% and 96%, respectively. Studies of breast pathology (including AI models for breast cancer) had slightly lower performance at mean sensitivity of 83% and mean specificity of 88% (Table 1). [13]

Although a high diagnostic accuracy was seen in other subspecialties such as neuropathology (mean sensitivity and specificity of 100% & 95%, respectively) and soft tissue and bone pathology (mean sensitivity and specificity of 98% & 94% respectively), the number of studies were few to draw out a concrete conclusion. Besides, AI models in lymphoma(cancers of lymphatic system), liver cancer, melanoma (skin cancer), pancreatic cancer, brain cancer, lung cancer and rhabdomyosarcoma (soft tissue sarcoma) all showed a high sensitivity and specificity. This emphasises the extent of potential diagnostic tools for clinical applications with a high diagnostic accuracy in digital pathology (Table 1).[13]

Table 1: Diagnostic accuracy of AI models in various pathological subspecialties (including cancers in each type) in WSIs (Adapted from McGenity etal; 2023) [13]

Pathological subspecialty including cancers	Number of AI models	Mean sensitivity	Mean specificity
Gastrointestinal pathology	14	93 %	94%
Uropathology	8	95%	96%
Breast pathology	8	83%	88%
Hepatobiliary (liver) pathology	5	90%	87%
Dermatopathology (skin)	4	89 %	81%
Cardiothoracic pathology (heart & thorax)	3	98 %	76%
Haematopathology (blood)	3	**95 %**	86%
Gynaecological pathology	2	**87 %**	83%
Soft tissue & bone pathology	1	**98 %**	94%
Head & neck pathology	1	**98 %**	72%
Neuropathology (nervous system)	1	**100 %**	95%

2. Relevance of Point-of-care Testing (POCT) in Medical Diagnostics

Point-of-care testing (POCT) is defined as near to the patient testing which facilitates the rapid detection of analytes enabling better disease diagnosis and aid in better patient outcomes. It aids in rapid medical decision because of diagnosis of the diseases at a very early stage, thereby enabling the early initiation of the treatment. [14]

The miniaturization of testing instruments has led in the rapid growth of POCT as vital aides to patient management by HCPs. POCT has several advantages as compared to traditional, centralized laboratory testing such as: small specimen volume requirement, easy analysis, small instrument size, and most important a decrease of turnaround time (TAT) for rapid decision in patients' diagnosis, monitoring and treatment of disease.[15,16]

Main POCT tests for a big network might include, ketones, blood gases, occult blood, electrolytes, creatinine, urea, pH, glucose, hemoglobin A1c ,drugs of abuse, human chorionic gonadotropin (hCG), coagulation and infectious disease testing (influenza, streptococcus, HIV, and mononucleosis). POCT devices can provide bothy qualitative (drug screen urine) and quantitative (glucometer) results and are incorporated with microfluidics, biosensors, and lateral flow immunoassays. [16]

1. IFCC Committee on Point-of-Care Testing (IFCC C-POCT) Guideline Recommendations on POCT

For outside hospital setting POCT, IFCC C-POCT recommends following areas are crucial for implementation of an effective and successful POCT:

(1) Reasoning for using POCT, (2) Oversight and regulatory compliance, (3) Appropriate device selection and method verification, (4) Quality management system(QMS) and key performance indicators(KPIs), (5) Operator training and competency evaluation, and (6) Integration of result into patient medical records.[15,16]

2.1.1 Reason for using POCT

The primary reasons to implement POC tests is to improve the efficiency of the clinical pathways for disease management by leveraging its strengths (ease of use, ease of patient identification, smaller TAT, smaller sample volumes, portability) when compared to centralized laboratory testing.[15,16]

2.1.2 Regulatory compliance

Qualified laboratory personnel with adequate knowledge should be positioned to guarantee safe and effective POCT oversight and regulatory compliance. A compliance is recommended with national regulatory requirements wherever present and in their absence advice from local national societies and/or specialists in laboratory medicine should be pursued, to attain accreditation relative to international standards (e.g. International Organization for Standardization (ISO), College of American Pathologists (CAP), Joint Commission International etc.).[15,16]

2.1.3 Appropriate device selection and method verification

The POC director and other personnel should select most appropriate device and/or test for POC testing. Apposite verification studies should be performed with the device. Only those POC tests should be selected for evaluation which have been approved by the appropriate regulatory body. Verification studies should be conducted by POCT staff and device performance claims from package/kit inserts (including imprecision, sensitivity & specificity, linearity over the normal patient reference intervals (for quantitative results) and normal patient biological reference interval should correlate with those obtained from verification studies. The users should establish the analytical performance specifications (APS) and also identify lot-to-lot variation in results which could lead to erroneous interpretation. Device robustness, size and space required by the device, ease-of-use, and sample type requirements are other critical factors to be considered while selecting a POCT device.[15, 17]

2.1.4 Quality Management System(QMS)

A QMS is a customary of processes which assures proper analytical and clinical performance of POCT. The QMS evaluates three phases of testing: pre-analytical, analytical and post-analytical phases of the testing process to identify gaps for improvement in the QMS and quality testing standards. Key components of a QMS should include implementation of: (a) corrective actions in case of unsatisfactory quality control results (i.e. outside target limits or interferences); (b) audits to verify effective dates/new expiry dates are written on reagents and controls according to the manufacturer recommendations or according to good laboratory practices; (c) regular and suitable training of POC operators; (d) monitoring storage conditions (temperature and humidity for controls, reagents and instruments/kits); (e) Periodic review of procedures for each POCT including protocols for the appropriate management of abnormal test results.16,17

Association of Diagnostics and Laboratory Medicine (ADLM 2023) emphasizes on the implementation of critical components as proposed by Clinical Laboratory and Standards Institute (CLSI) known as the quality system essentials (QSE) of the QMS model (Figure 2). [18]

3. Enabling Broad Spectrum Disease Detection by Liquid Biopsy Technology

During the last few years, liquid biopsy, a non-invasive diagnostic technique which utilizes body fluids such as blood, cerebrospinal fluid, urine, saliva, semen, and many others is gaining recognition and significant advancements in liquid biopsy technology is predicted in the coming era transforming the detection of a broader range of cancers and other diseases at earlier stages. It is a novel approach for the detection of tumor recurrence and real-time monitoring of tumor dynamics and treatment response by recognizing specific markers in body fluids, contrary to traditional tissue biopsies that involve direct examination of tumor tissue. Though the tumor biopsies will be considered as mainstay for diagnosis, prognosis and treatment selection in cancer

genomics for many years; the addition of liquid biopsies as an alternate approach for patients at risk for an invasive tumor biopsy facilitates for many clinical applications such as screening, mutation detection for therapy selection, disease prognosis, drug response, and drug resistance. The liquid biopsy enables to perform serial blood sampling thereby providing efficient mechanism for monitoring the course of disease overcoming the challenge of procuring tissue samples at regular intervals. In the tissues where sample extraction limits the timely diagnosis, liquid biopsy has become a feasible alternative diagnose primary tumors or the assessment of the metastatic stage of cancer. Besides, it can reduce the associated complications of invasive tissue biopsy, including pain, bleeding, and infections. Liquid biopsy uses various types of analytes uc as circulating tumor cells (CTCs), circulating tumor DNA (ctDNA), and cell-free DNA (cfDNA) in blood or other body fluid samples. [19]

3.1 Liquid biopsy applications

3.1.1 Identification of Minimal Residual Disease (MRD):

Minimal residual disease (MRD) is defined as the submicroscopic disease, characterized by the presence of residual tumor cells or sparse malignant cells which remains during or after the treatment eventually leading to relapse and cannot be detected through standard radiological examinations or traditional techniques. Liquid biopsy is a potentially sensitive technique to detect MRD.[20]

3.1.2 High-Risk Population Screening

Liquid biopsy is potentially useful for screening high-risk populations for early cancer detection. High-risk populations are more prone to cancer development owing to the reasons such as family history, earlier cancer therapies, gene mutations, and exposure to carcinogens, which requires analysis of the circulatory metabolites of malignant neoplasm or other body fluids. [21]

3.1.3 Disease Recurrence Monitoring

Liquid biopsy can aid in monitoring of signs of disease recurrence. It can identify the emergence of treatment-resistant clones. It provides a non-invasive and dynamic tool for monitoring disease development by examining ctDNA, CTCs, or other biomarkers in the circulating body fluids.[22]

3.1.4 Treatment Response Monitoring

The use of ctDNA monitoring has shown utility in assessing treatment response for MRD and its recurrence after chemotherapy. Somatic mutation detection (BRAF and RAS oncogenes) in ctDNA act as prognostic marker and improve treatment response and patient survival outcomes. The prediction of immunotherapy response and evaluation of microsatellite instability (MSI) and tumor mutational burden (TMB) by determining ctDNA levels are other applications in treatment response monitoring by the use of liquid biopsy.[21]

3.1.5 Identifying Resistance Mechanisms

Liquid biopsy can be utilized for identifying resistance mechanisms but it depends on individual's health and type of cancer. For example, in non-small cell lung cancer (NSCLC), specific gene modifications and mutations of epidermal growth factor receptor (EGFR), rearrangements of the anaplastic lymphoma kinase (ALK)gene , and ROS proto-oncogene 1 (ROS1) can help in guiding treatment decisions.[23] Moreover, liquid biopsy can evaluate patients who show more probability to respond to immune checkpoint inhibitors (ICIs) based on their biomarkers, such as TMB and programmed death 1 (PD-L1) expression. [24]

3.2 Sensitivity and specificity of liquid biopsy-based methods

The clinical data document overall sensitivity of liquid biopsies ranging from 60%-85%. Its sensitivity & specificity vary according to tumor type, patient health, or other clinical factors.[25] According to The Circulating Cell-free Genome Atlas study (CCGA; NCT02889978), a blood-based liquid biopsy multi-cancer early detection (MCED) test using cfDNA sequencing and machine learning showed a sensitivity & specificity of 51.5% and 99.5%, respectively across cancer types. The sensitivity increased with stage [stage I: 16.8% (14.5% to 19.5%), stage II: 40.4% (36.8% to 44.1%), stage III: 77.0% (73.4% to 80.3%), stage IV: 90.1% (87.5% to 92.2%)]. However, the low concentration ctDNA in stage I, limits the success rate of the test for detecting early-stage cancers (16.8% for stage I in this study).[26] Due to this limitation physicians mostly suggest tissue biopsies for more reliable diagnosis for cancer detection if liquid biopsy findings show positive results. [27]

4. Empowering Medical Diagnostic Laboratories with Digital Health Technologies (DHTs)

One of the major breakthroughs in the improvement of healthcare delivery is digital health aimed to provide more valuable, efficient, and accessible health by leveraging the power of digital tools to gather, analyze, store and share health data. Some of the examples of cutting-edge digital health technologies include: Electronic Health Records (EHRs), telemedicine, mobile health apps (mHealth), wearable devices, Laboratory Information Management System (LIMS), and the internet of medical things (Figure 3). Numerous factors contribute to the growth of digital health market including the growing acceptance of smartphones and other digital devices, the increasing requirement for telemedicine services and remote monitoring, and the increasing interest to tackle the challenges posed by the COVID-19 pandemic.[28,29]

The drug development process is also benefitted by DHTs such as (i) drug design by virtual screening techniques, (ii) minimizing pre-clinical trials (animal usage) by predictive toxicology, and (iii) use of digital data management for streamlining clinical trials.[28]

Another digital technology which will help in huge improvement of clinical trial management is the block-chain technology, also called as Distributed Ledger Technology. Block-chain technology provides peer-to-peer platform and creates the prospects for secured storage of the information on thousands of servers that can be shared and used concurrently within a decentralized and open network. This approach restricts the user to control or change it. Besides, block-chain technology can support in regulatory compliance, and a decentralized structure for sharing EHRs. [30]

5. Genomic Medicine

According to National Human Genome Research Institute (NHGRI), genomic medicine is defined as “an emerging branch of medicine utilizing the genomic information about a person as an element of their clinical care such as diagnostic or therapeutic decision-making and the health outcomes and policy propositions of that clinical use.” [31]

Genomic medicine can be potentially useful in diagnosing rare disease genetic conditions, and many types of cancer. The diagnosis of diseases by practicing genomic medicine has four stages of care (1) phenotypic estimation and evaluation of a prior risk for a genetic disorder, (2) assessing the clinical utility of genomic testing, (3) analysing and interpreting of genomic variation, and (4) patient management based on obtained genomic information. [32]

As there is continuing decrease in the cost of DNA sequencing ,[2] clinical exome and genome sequencing are being increasingly used across various clinical settings aiming to increase

diagnostic rates and improving clinical management. Exome sequencing, includes the decoding of the protein-coding regions (exons) of the genome whereas in genome sequencing both exons and introns (non-protein-coding) regions of the genome. [33] Figure 4 illustrates proposed model for implementing genomic medicine for patients with undiagnosed diseases

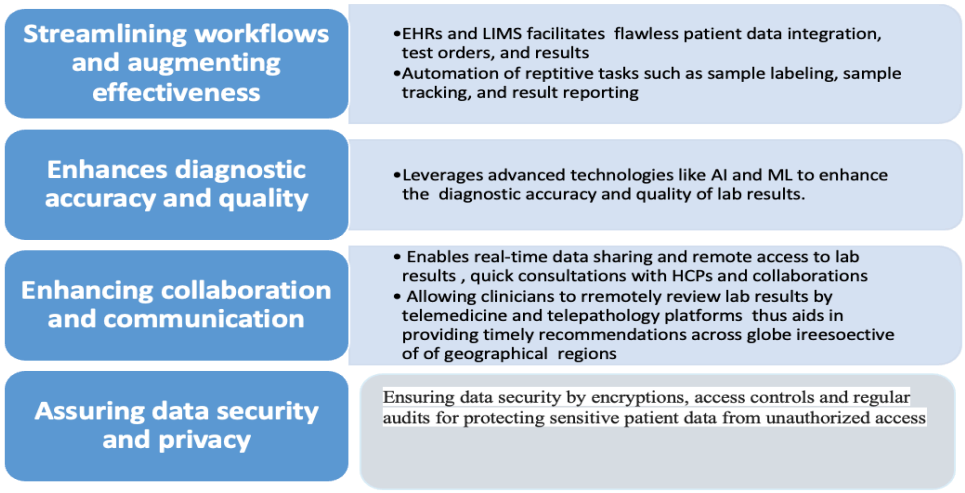


Figure 3 Advantages of Digital Technologies in Transforming Diagnostics Landscape [30]

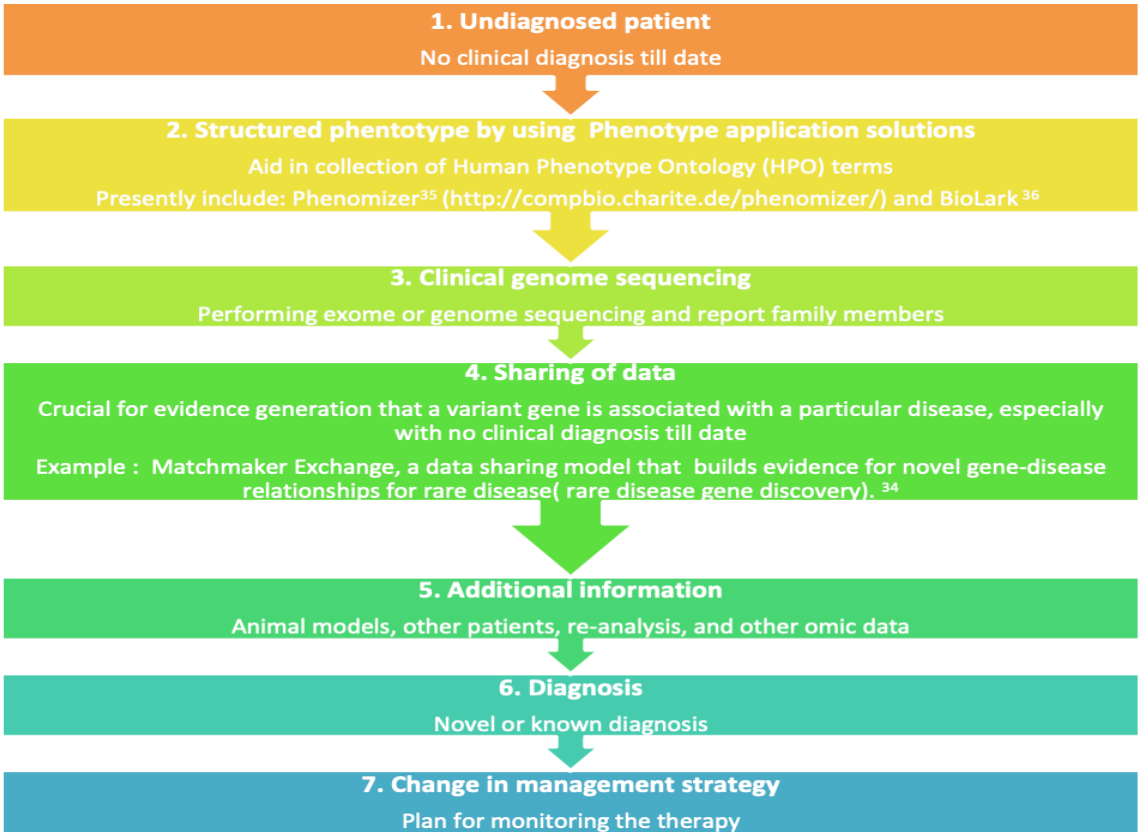


Figure 4: Visualization model for implementing genomic medicine for patients with undiagnosed diseases [34]

ORGANIZATION AND LEADERSHIP

- Identication of skilled & qualified personnel to assign responsilbilities for all phases of POC testinf: patient preparation, test performance, and reporting of test results.[18]
- Assessment of effectiveness of key performance indicators (KPIs) by the POCT committee : patient misidentification, instrument lockouts/ breakage, errors in sample collection, failure in quality control, transcription errors, result alterations, TAT, and training and competency[16-18]

CUSTOMER CENTRICITY

- A potent POCT program should seek customer feedback, assesses the suuficiency of customer education, and evaluates timeliness of communications [18]

FACILITIES AND SAFETY GOVERNANCE

- The POC QMS should ensure the safe appilcation of POCT devices, minimizing risks of contamination and exposure, and review the reported and potential injuries to customers [18]

PERSONNEL MANAGEMENT

- Establishing collaborative communication between managers and users.[18]
- Ensure that test personnel are properly trained to operate equipment, assess the ampleness and quality of samples, conduct patient and quality control testing, and determine if obtained results can be released and reported [18]

SUPPLY AND INVENTORY MANAGEMENT

- Delegate responsibilities for communicating with manufacturers and suppliers, and maintain purchase management, management of supply chain disruptions, and identifying provisions for alternate testing [18]

EQUIPMENT MANAGEMENT

- Equipment vendors should be selected based on desired operating specifications in requests for proposals (RFP) and evaluating the suitability of equipment [18]
- Other aspects include: determining maintenance calendar, calibration and frequency of calibration verification , and determining operating procedures related to instrumentation [18]

PROCESS ADMINISTRATION

- Meticulous workflow diagrams should be established to include processes of preexamination, examination, and postexamination phases of testing.
- These workflow diagrams shouls identify potential risks and implement processes to overcome them for facilitating timely decisions decisions for patient care.[18]

DOCUMENTATION AND RECORDS —INFORMATION MANAGEMENT

- Establishing systems to ensure secure and confidential records and the flow of information. Aversatile system should include: the integration of results from different measurement procedures, test connectivity, provide backup processes for disturbances to connectivity, and incorporate billing practices to capture all aspects of POCT [17,18]

NONCONFORMITIES HANDLING

- Nonconformities may arise from quality control reviews, proficiency testing or external quality assessment (EQA)failures, and patient chart reviews. Define precisely your mechanism for performing a thorough root cause analysis (RCA) process [18]

AUDITS AND ASSESSMENTS

- Periodic audits are critical to identify nonconformities [17,18]
- Complete records of training and competency evaluation, pass/fail rates in EQAs, compliance in conducting IQC as per manufacturer's recommendations, repeating of critical results, and mislabeling of samples [17,18]
- Patient related adverse incidents should be reported investigated and audited for continuous quality mprovement [17,18]

Figure 2: Main pillars of QMS for POCT testing (adapted from ADLM (2023) and CLSI 2016) [18]

Conclusion

The diagnostics industry is on the verge of huge transformation in the coming era and holds promising futuristic aspects driven by avant-garde technologies and assurance to better patient outcomes. The integration of AI, an ascend in POC testing, developments in liquid biopsy technology, assimilation of digital health platforms, and the expanding functions of genomic medicine are emerging breakthroughs which are facilitating more accurate, more accessible, timely, and patient-centric approach to the management of diseases. With the unfurling of these developments in the coming years, there is a reassurance of reformation in the disease diagnosis and treatment approaches, surfacing the way for a healthier and better connected human world.

References

1. Rohr U-P, Binder C, Dieterle T, Giusti F, Messina CGM, Toerien E*etal* The Value of In Vitro Diagnostic Testing in Medical Practice: A Status Report. *PLoS ONE*. 2016; 11(3): e0149856. doi:10.1371/journal.pone.0149856
2. Second WHO model list of essential in vitro diagnostics. Geneva: World Health Organization; 2019 (WHO/MVP/EMP/2019.05).
3. Your results may vary: the imprecision of medical measurements.*BMJ.*2020;368:m149.
4. Hajat C, Stein, E. The global burden of multiple chronic conditions: A narrative review. *Preventive medicine reports*.2018;12:284–293.
5. Kane L. Medscape National Physician Burnout & Suicide Report 2021 https://www.medscape.com/slideshow/2021-lifestyleburnout-6013456 (Accessed on January 25, 2024).
6. World Health Organization. 2019. https://www.who.int/news/item/28-05-2019-addressing-the-18-million-health-worker-shortfall-35-concrete-actions-and-6-key-messages (Accessed on January 25, 2024).
7. Alowais SA, Alghamdi SS, Alsuhebany N, Alqahtani T, Alshaya AI, Almohareb SN *etal.*Revolutionizing healthcare: the role of artificial intelligence in clinical practice. *BMC Med Educ*. 2023; 23, 689.
8. Habehh H, Gohel S. Machine Learning in Healthcare. Curr Genomics. 2021;22(4):291-300.
9. Yang S, Zhu F, Ling X, Liu Q, Zhao P. Intelligent Health Care: Applications of Deep Learning in Computational Medicine. *Front. Genet.* 2021; 12:607471.
10. Al-Antari MA. Artificial Intelligence for Medical Diagnostics-Existing and Future AI Technology! *Diagnostics (Basel)*. 2023.12; 13(4):688.
11. Srivastava R. Applications of Artificial Intelligence in Medicine. *Explor Res Hypothesis Med*. Published online: 2023.
12. Zeltzer D, Herzog L, Pickman Y, Steuerman Y, Ilan Ber R, Kugler Z. Diagnostic Accuracy of Artificial Intelligence in Virtual Primary Care. *Mayo Clin Proc Digital Health*. 2023;1(4):480-489.
13. McGenity C, Clarke EL,Jennings C,Matthews G, Cartlidge C, Freduah-Agyemang H *etal*. Artificial intelligence in digital pathology: a diagnostic test accuracy systematic review and meta-analysis. 2023; https://arxiv.org/ftp/arxiv/papers/2306/2306.07999.pdf (Accessed on February 10, 2024).
14. Vashist SK. Point-of-Care Diagnostics: Recent Advances and Trends. *Biosensors (Basel)*. 2017;18;7(4):62.
15. Point of Care Testing Resources https://ifcc.web.insd.dk/ifcc-education-division/emd-committees/c-poct/poctresources/ (Accessed on March 10, 2024)
16. Chokkalla AK, Recio BD, Devaraj S. Best Practices for Effective Management of

Point of Care Testing. *EJIFCC*. 2023; 34(3):245-249.
17. Venner AA, Beach LA, Shea JL, Knauer MJ, Huang Y, Fung AWS *etal*. Quality assurance practices for point of care testing programs: Recommendations by the Canadian society of clinical chemists point of care testing interest group. *Clin Biochem*. 2021; 88:11-17.
18. Maggiore JA.Designing a Dynamic Quality Management System for Point-of-Care Testing.
19. Association for Diagnostics & Laboratory Medicine // Clinical Laboratory News 2023. Available from URL: https://www.myadlm.org/cln/articles/2023/janfeb/designing-a-dynamic-quality-management-system-for-point-of-care-testing#:~:text=QSE13AOrganizationandLeadership,determiningappropriatenessforeachoffering. (Accessed on March 10, 2024).
20. Noor J, Chaudhry A, Noor R, Batool S. Advancements and Applications of Liquid Biopsies in Oncology: A Narrative Review. Cureus. 2023;15(7):e42731.
21. Honoré N, Galot R, van Marcke C, Limaye N, Machiels J-P. Liquid Biopsy to Detect Minimal Residual Disease: Methodology and Impact. *Cancers*. 2021; 13(21):5364.
22. Ding J and Zhao W.The Application of Liquid Biopsy Techniques in High-Risk Population for Hepatocellular Carcinoma. Cancer Management and Research.2022; 2735-2748.
23. de Miranda FS, Barauna VG, dos Santos L, Costa G, Vassallo PF, Campos LCG. Properties and Application of Cell-Free DNA as a Clinical Biomarker. *International Journal of Molecular Sciences*. 2021; 22(17):9110.
24. Freitas AJAd, Causin RL, Varuzza MB, Calfa S, Hidalgo Filho CMT, Komoto TT, Souza CdP, Marques MMC. Liquid Biopsy as a Tool for the Diagnosis, Treatment, and Monitoring of Breast Cancer. *International Journal of Molecular Sciences*. 2022; 23(17):9952.
25. Liu J, Chen Z, Li Y, Zhao W, Wu J and Zhang Z. PD-1/PD-L1 Checkpoint Inhibitors in Tumor Immunotherapy. *Front. Pharmacol.* 2021;12:731798.
26. Kim M. A Simpler Way to Sample: Liquid Biopsies in Lung Cancer. 2020;
27. https://www.curetoday.com/view/a-simpler-way-to-sample-liquid-biopsies-in-lung-cancer (Accessed on April 27, 2024).
28. Klein EA, Richards D, Cohn A, Tummala M, Lapham R, Cosgrove D etal. Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set. Ann Oncol. 2021; 32(9):1167-1177.
29. Connal S, Cameron, JM, Sala A, Brennan PM, Palmer DS, Palmer JD etal. Liquid biopsies: the future of cancer early detection. J Transl Med. 2023;21, 118.
30. Kasoju N, Remya NS, Sasi R, Sujesh S, Soman B, Kesavadas C, etal. Digital health: trends, opportunities and challenges in medical devices, pharma and bio-technology. CSIT. 2023;11(1):11–30.
31. What is Digital Health? 2020; What is Digital Health? | FDA(Accessed on May 4, 2023).
32. Senbekov M, Saliev T, Bukeyeva Z, Almabayeva A, Zhanaliyeva M, Aitenova N, etal. The Recent Progress and Applications of Digital Technologies in Healthcare: A Review. Int J Telemed Appl. 2020; 2020:8830200
33. Genomic Medicine. https://www.genome.gov/health/Genomics-and-Medicine (Accessed on July 8th , 2024).
34. Handra J, Elbert A, Gazzaz N, Moller-Hansen A, Hyunh S, Lee HK etal. The practice of genomic medicine: A delineation of the process and its governing principles. Front Med (Lausanne). 2023;9:1071348.

35. The cost of sequencing a human genome. https://www.genome.gov/about-genomics/fact-sheets/Sequencing-Human-Genome-cost (Accessed on July 8th , 2024).
36. Marwaha S, Knowles JW, Ashley EA. A guide for the diagnosis of rare and undiagnosed disease: beyond the exome. Genome Med. 2022; 14, 23. https://doi.org/10.1186/s13073-022-01026-w
37. Köhler S, Schulz MH, Krawitz P, Bauer S, Dölken S, Ott CE etal. Clinical diagnostics in human genetics with semantic similarity searches in ontologies. Am J Hum Genet. 2009;85(4):457-64.
38. Groza T, Köhler S, Doelken S, Collier N, Oellrich A, Smedley D etal. Automatic concept recognition using the human phenotype ontology reference and test suite corpora. Database (Oxford). 20157;2015:bav005