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Review Article

Biochemistry Section

A Narrative Review on Emergence of Digital Biomarkers as the Future Frontiers in Medical Practice

JYOTSNA NEEDAMANGALAM BALAJI[1], SREENIDHI PRAKASH[2], KRISHNA MOHAN SURAPANENI[3]

BY-NC-ND

ABSTRACT

The healthcare landscape has undergone a profound transformation due to digitalisation in recent decades, shifting from manual practices to automated processes. Digital biomarkers have become increasingly important in healthcare across multiple domains for regular monitoring of health parameters, aiding in early disease detection and prevention. The present narrative review aims to explore the utility and advantages of digital biomarkers in healthcare. Notably, the literature emphasises portable biomarkers capable of actively recording user data. These advanced biomarkers efficiently identify physiological, biochemical and psychological parameters, offering predictive capabilities for health conditions and treatment outcomes. In this dynamic healthcare landscape, digital science has brought transformative changes. Investments in digital health show promising outcomes for disease management and patient care. Overall, the integration of digital biomarkers into healthcare represents a significant leap forward in improving healthcare delivery, diagnosis and treatment. It leverages technology to enhance the precision and efficiency of healthcare, ultimately benefiting both healthcare professionals and patients. While the scope of digital biomarkers continues to expand and is expected to grow in the future, addressing potential challenges is essential for sustained innovation in this field.

Keywords: Digital health, Digital intervention, Early detection, Personalised medicine

INTRODUCTION

The global healthcare landscape is undergoing a transformation to provide efficient, accessible and affordable services through technological advancements and increased internet and smartphone usage [1,2]. The term "digital health," which encompasses eHealth, mobile health, telehealth and telemedicine, leverages technology to enhance medical care [3]. In line with the United Nations' Sustainable Development Goals, the World Health Organisation advocates for digital health technologies through the Global Strategy on Digital Health 2020-2025, aiming for universal health and welfare [4,5].

Concurrently, digital biomarkers have emerged as a secure means of health data collection [6]. Defined by the National Institute of Environmental Health Sciences, digital biomarkers digitally collect and monitor physiological and behavioural patterns to predict health outcomes [7]. These non invasive devices are wearable, portable and even ingestible, capturing various patterns of normal and abnormal functioning [8-10].

Digital biomarkers offer several advantages, replacing conventional vital sign measurements with rapid, user-friendly methods [11]. They are cost-effective for analysing blood samples, enhancing patient safety and facilitating timely diagnosis [12,13]. Categorised as passive and active, digital biomarkers revolutionise healthcare by aiding in early disease detection and assessing treatment effectiveness through digital phenotyping [14,15]. Notably, digital biomarkers, which facilitate remote patient monitoring, proved valuable during the Coronavirus Disease-2019 (COVID-19) pandemic and are expected to optimise clinical trials in the post-COVID era [16]. Future research aims to develop digital resilience biomarkers for tailored health feedback [17]. With broad applications, digital biomarkers shift healthcare from a reactive to a preventive approach, providing rich data for accurate clinical studies [18,19].

Thus, research on digital biomarkers and their utility in healthcare settings is expected to soar in the future, with higher investments in wearable technologies and technology-based medicine. The market size of digital biomarkers is projected to reach USD 27.17 billion by the year 2030 [20]. Digital biomarkers will reduce the number of clinical trials required and consequently decrease the overall cost of drug development [18]. However, challenges do exist in this nascent field that impede the market growth of digital biomarkers. Concerns include validation testing, privacy, misuse of data, data bias, credibility of the data, interoperability, integration and cost-benefit analysis [20]. Research on digital biomarkers lacks clear protocols for rural use and definitive evidence of their superiority over traditional health practices. Unexplored areas include the risks of self-medication, decreased clinical visits and ethical concerns about safety, privacy and data accuracy. Additionally, issues such as counterfeit products and subpar device quality require further investigation [19]. Thus, the present review was conducted to explore the utility and usability of digital biomarkers in healthcare, while also highlighting potential concerns regarding their full implementation in day-to-day practice.

Impact and Challenges of Digital Biomarkers

Digital biomarkers are rapidly transforming the landscape of medical practice, signifying a significant shift in health data collection, analysis and application [21]. This evolution is largely driven by technological advancements, such as wearables, mobile devices and a variety of sensor technologies. These tools facilitate continuous, real-time monitoring of various physiological and behavioural parameters, including heart rate, physical activity, sleep patterns and even more nuanced data like fecal matter, voice and typing behaviour [22]. This wealth of information offers unprecedented insights into individual health statuses, paving the way for more personalised and effective healthcare [23].

The impact of digital biomarkers in medicine is multifaceted. They enhance personalised healthcare by providing data specific to individuals, moving away from the reliance on broader, population-based norms. This personalisation is crucial in tailoring treatments and interventions to individual needs. Additionally, digital biomarkers play a pivotal role in preventive healthcare [22]. By constantly monitoring health indicators, they enable early detection of potential health issues, allowing for preventive measures and timely interventions. This approach is particularly beneficial in managing

chronic diseases like diabetes and heart disease, where continuous monitoring can lead to better disease management and improved outcomes [24].

However, the rise of digital biomarkers is not without challenges. Data privacy and security concerns are paramount, as managing sensitive health data demands stringent protection and ethical use [25]. Furthermore, integrating these biomarkers into the healthcare system involves overcoming regulatory and standardisation hurdles to ensure data accuracy, reliability and interoperability across various platforms. These challenges necessitate not only technological integration but also adaptations in healthcare practices and policies, as well as shifts in patient and provider mindsets. Despite these obstacles, the potential of digital biomarkers to revolutionise healthcare is immense, offering new avenues for personalised medicine, preventive care and enhanced patient outcomes [26].

Types of Digital Biomarkers

Digital biomarkers, which encompass various data types and technologies, are proving to be invaluable tools in modern healthcare [27]. These markers come in different forms, each with its own distinct applications, collectively reshaping the landscape of healthcare delivery [28]. The different types of digital biomarkers and their applications [Table/Fig-1] [29-33].

Type of biomarker	Primary function	Applications in healthcare and research
Physiological biomarkers [29]	Real-time insights into vital signs	Monitoring health conditions and chronic diseases
Behavioural/ psychological biomarkers [30,31]	Tracking daily activities Monitoring sleep patterns, social media usage, speech, etc.	Assessing lifestyle-related risks and mental health conditions Diagnosing and managing mental health conditions (e.g., depression, insomnia); remote monitoring and telehealth; reducing hospitalisations; improving patient outcomes; pivotal in drug development and clinical trials; offering real-time data on drug efficacy and safety
Genomic biomarkers [30]	Derived from Deoxyribonucleic Acid (DNA) sequencing	Personalised medicine; identifying genetic susceptibilities to diseases
Biometric biomarkers [32]	Enhancing patient identification and data security	Used in healthcare settings
Environmental biomarkers [33]	Assessing exposure to environmental factors	Shedding light on health risks

[Table/Fig-1]: Digital biomarkers and their application [29-33].

Latest Trends in Digital Biomarkers

The articles were studied in depth and the following relevant variables were identified: the disease under study, the system under study and the type of digital biomarker. There are three types of digital biomarkers: i) wearable devices, which are worn on the body, such as smartwatches and fitness bands that monitor parameters like heart rate and physical activity; ii) portable devices, which are easily carried and include mobile apps and handheld monitors that provide flexibility in measuring health data; and iii) implantable devices, which are placed inside the body, such as cardioverter-defibrillators and neurostimulators, that continuously monitor and regulate specific health aspects. Other relevant variables include the sensor, mode of data collection, domain of focus, type of data and data sensed.

In the context of mode of data collection, active data collection refers to situations where users actively provide data, such as responding to surveys, manually entering information, or engaging with applications to gather data. In contrast, passive data collection occurs when data is automatically gathered by devices without user interaction, tracking metrics like sleep activity or respiration. Data from previous studies is represented in [Table/Fig-2] [34-47].

Most research in the field of digital biomarkers has focused on their application in the early detection, treatment and prevention of neurodegenerative disorders such as Alzheimer's disease and Parkinsonism [34,35]. These biomarkers are collected using wearable, portable and implantable devices, with portable devices being preferred over smartwatches or bands due to their lower maintenance requirements [36-38]. Digital biomarkers are also used to assess motor functions in the management of Alzheimer's disease. Tasks such as drawing shapes, tapping screens and virtual object placement are employed to detect abnormal changes and provide personalised care, including gender-based care [39].

Digital biomarkers have also been explored for monitoring pulmonary health in diseases such as tuberculosis, cystic fibrosis and lung cancer [46]. Sweat samples are collected using sweat patches and analysed for predictive diagnosis, leveraging night sweats as a diagnostic marker for tuberculosis. Cystic fibrosis diagnosis relies on analysing sweat constituents, particularly chloride concentrations [46]. Additionally, studies have demonstrated the effectiveness of using smartphones and smartwatches to collect lung biomarkers, including breathing patterns, coughing, spirometry and breathlessness [47].

Author name	Place/year of study	Disease under study (system involved)	Type of digital biomarker/Mode	Name of digital biomarker	Sensor	Domain of focus	Type of data	Data sensed
Kourtis LC et al., [34]	USA, 2019	Alzheimer's disease/ Central nervous system	Touch screen, barometer/Active and passive	Not mentioned	Camera, microphone, barometer, geo positioned, light sensor, Ultraviolet (UV) sensor	Early detection and monitoring	Physiological	Heartbeat, voice, gait, reflexes, memory, eye movements
Dillenseger A et al., [35]	Germany, 2021	Multiple sclerosis/ Central nervous system	Smart phone applications/ Active	MSPT (Multiple sclerosis Performance Test), FitBit, Garmin	Software applications	Treatment and monitoring	Physiological	Eye movements, gait, coordination, balance
Dorsey ER et al., [36]	USA, 2017	Neurodegenerative disorders/Central nervous system	Smart phones, wearables and implantable devices/Passive	Q motor	Software applications	Detection, treatment and monitoring	Biochemical and physiological	Blood glucose, Blood Pressure (BP), Serum sodium and heart rate
Paolo F et al., [37]	UK, 2019	Schizophrenia and bipolar disorder/Central nervous system	GPS, Bluetooth, GSM cellular network, WIFI/ Active	Not mentioned	GPS and GSM mobile network	Early detection and monitoring	Psychological	Distance travelled, location visited, time spent outdoors
Youn BY et al., [38]	Korea, 2021	Neuromuscular disorder/Central nervous system and musculoskeletal system	Mobile application/Active	Open smile and Praat	Home monitoring sensor, magneto inertial sensors, Microsoft Kinect sensor	Early detection and monitoring	Physiological	Motor movements

Alfalahi H et al., [39]	United Arab Emirates, 2022	Neuropsychiatric disorder/Central nervous system	Smart phones, iPad, Smartwatches/ Active	Not mentioned	Camera, microphone	Early detection and monitoring	Physiological	Motor movements
Wesselius FJ et al., [40]	Netherlands, 2021	Atrial fibrillation/ Cardiovascular system	Electrocardiogram (ECG)/Active	Not mentioned	Electric leads	Early detection and monitoring	Physiological	Electric activity
Chen I M et al., [41]	Taiwan, 2022	Mental illness/Central nervous system	Mobile apps/ Active	Know addiction and Mental	Software applications	Early detection	Physiological	Computing circadian rhythm, sleep patterns, record working hours
Piau A et al., [42]	USA,2019	Mild cognitive impairment and mild Alzheimer's disease/ Central nervous system	Embedded environmental devices and wrist worn device/ Passive	Not mentioned	Cameras, software applications	Monitoring	Psychological	Cognitive functions, memory, gait, hand movements
Gold M et al., [43]	USA, 2018	Alzheimer's disease/ Central nervous system	Wearables and embedded devices/Active and Passive	Not mentioned	Cameras, software applications	Treatment and monitoring	Psychological	Sleep movements, gait pattern, eating pattern, time and location of sleep opening and closing of doors, use of gadgets
Frohlich H et al., [44]	Germany, 2022	Parkinson's disease/ Central nervous system	Wearables pressure sensors embedded cameras/Active	Not mentioned	Cameras, voice recorder, GPS sensors	Treatment and monitoring	Physiological and psychological	Speech and voice, facial expressions, gait parameters, muscular activity, handwriting
Ding Z et al., [45]	China, 2022	Mild cognitive impairment and dementia/Central nervous system	Computers and testing devices/ Active and Passive	Not mentioned	Cameras, speed detectors, smart phone applications, video games	Early detection and monitoring	Physiological and psychological	Voice pattern, handwriting, attention testing, psychomotor speed, emotion testing, finding a way home, gaming, memory testing
Brasier N and Eckstein J, [46]	Switzerland 2019	Tuberculosis, psoriasis, arthritis, Parkinson's disease, schizophrenia, diabetes mellitus, cystic fibrosis, kidney damage, lung cancer/pulmonary system, articular system, central nervous system, endocrine system, renal system, immune system	Sweat patches/ Active	Not mentioned	Biosensors	Early detection	Biochemical	Sweat droplets
Brasier N et al., [47]	Switzerland 2021	Tuberculosis/ Respiratory system	On -skin sweat biosensor, tooth mounted biosensor, e-nose for exhaled breath/Passive	Not mentioned	Biosensors	Early detection	Biochemical	Sweat droplets, saliva, exhaled breath, coughing, spirometry

[Table/Fig-2]: Characteristics of data extracted [34-47].
Passive digital biomarkers ($): refer to the data collected with the help of wearable devices. The sensors installed within these devices detect mild actions done by the user
Active devices (#): track prompt movements alone and monitor with the help of a transmitter device, like a smartphone, tablet, etc.

Digital devices have shown promise in managing mental health conditions such as schizophrenia, neuropsychological manifestations, impaired cognitive function, dementia, bipolar disorder and depression [29,37,41,43]. These devices analyse various parameters, including cognitive functions, memory, eye movements, voice changes, sleep patterns, location, activity and social participation to detect and prevent the progression of mental illnesses [38,42]. These digital biomarkers can be incorporated into wearables or implants equipped with built-in cameras or microphones, simplifying data collection and aiding in diagnosis and treatment decisions [41,42,45]. Therefore, digital biomarkers offer a cost-effective and convenient approach to complement traditional diagnostic techniques, leading to accurate diagnosis, personalised treatment strategies and improved healthcare outcomes [38,40].

Directions for Future Research

Digital biomarkers are a rapidly evolving field within healthcare and medical research, combining technology and medicine to revolutionise patient monitoring and disease diagnosis. Future research in this area should focus on the development of more sophisticated algorithms for data analysis, ensuring the accuracy and reliability of digital biomarkers [48]. There is a pressing need to standardise these markers across different platforms and devices for consistency in data interpretation. Ethical considerations, particularly regarding patient privacy and data security, should be a priority in future studies [49]. Additionally, research should explore the integration of digital biomarkers into existing healthcare systems for seamless patient management. It is also crucial to conduct extensive clinical trials to validate the effectiveness and applicability of these biomarkers in various medical conditions. Finally, there should be an emphasis on increasing patient engagement and education about digital biomarkers, as patient participation is critical for the successful implementation of these technologies in routine healthcare [50].

Limitation(s)

The present study is subject to certain limitations. The evidence for the use of digital biomarkers in healthcare was primarily obtained from review articles; therefore, experimental proof established through other research methods is not included in the present study. Additionally, only two databases-PubMed and Google Scholar-were used for the screening and selection of articles. Furthermore, only manuscripts published in English were selected.

CONCLUSION(S)

The field of digital biomarkers is poised to transform healthcare through its innovative integration of technology and medicine. The research conducted so far has shown promising applications in the early detection, treatment and prevention of a wide range of conditions. These biomarkers, collected via various digital devices, offer a more personalised, accurate and efficient approach to healthcare, allowing for early intervention and better management of diseases. However, the path forward requires careful navigation. Integrating these biomarkers into existing healthcare systems and conducting extensive clinical trials are also crucial steps toward their broader adoption. Ultimately, the success of digital biomarkers hinges not only on technological advancements but also on patient involvement. Educating and engaging patients in the use of these technologies is essential for realising their full potential. As we continue to advance in this field, digital biomarkers stand as a beacon of hope for a more personalised, effective and accessible healthcare system.

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PARTICULARS OF CONTRIBUTORS:
1. Undergraduate Student, Department of Biochemistry, Panimalar Medical College Hospital and Research Institute, Chennai, Tamil Nadu, India.
2. Undergraduate Student, Department of Biochemistry, Panimalar Medical College Hospital and Research Institute, Chennai, Tamil Nadu, India.
3. Professor, Department of Biochemistry, Panimalar Medical College Hospital and Research Institute, Chennai, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Krishna Mohan Surapaneni,
Professor, Department of Biochemistry, Panimalar Medical College Hospital and Research Institute, Varadharajapuram Poonamallee,
Chennai-600123, Tamil Nadu, India.
E-mail: krishnamohan.surapaneni@gmail.com

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