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Nanotechnology and nanosensors in personalized healthcare: A comprehensive review

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ABSTRACT

Healthcare is one of the most essential fields in providing accurate and fast medical care. With the advancement of technology, nanosensors have become a new tool that has enabled early diagnosis and continuous monitoring of diseases with high accuracy. With the ability to identify molecular and cellular changes, nanosensors can accurately detect biomarkers of diseases even in the initial stages and provide detailed information about the state of the body, especially in complex and costly diseases such as cancer. However, in this process, there are challenges such as biocompatibility and long-term stability of nanosensors in biological environments, immune reactions, and the possibility of their destruction. The present article has identified the challenges and evaluated the new methods of this technology by systematically reviewing the application of nanosensors in healthcare. This article aims to provide a comprehensive view of how to use nanotechnology as nanosensors in healthcare. The findings show that using nanosensors in the healthcare field can increase the accuracy of disease diagnosis (ADD) by 35 % and improve the quality of personal health monitoring (PHM) by 23 %. Also, this technology has reduced diagnostic response time (DRT) by 21 %. Finally, this research has taken a practical step towards further developing the application of nanosensors in the healthcare field by providing valuable recommendations and examining open issues.

1. Introduction

Nanosensors, as one of the advanced technologies in nanoscience, play a vital role in the transformation of the health field and provide unique possibilities for early diagnosis and continuous monitoring of diseases by providing high sensitivity and accuracy [1]. With the ability to detect and measure molecular and cellular changes, these sensors can identify disease-specific biomarkers in very small amounts, even in the early stages of the disease [2]. This feature is especially important in complex and costly diseases such as cancer because nanosensors can provide accurate information about the cellular and molecular status of the body and help doctors quickly diagnose the disease, assess it, and choose the best treatment strategies [3]. Nanoscale materials such as carbon nanotubes, metal nanoparticles, and quantum dots are widely used in the manufacture of these sensors due to their unique physical and chemical properties, which help increase sensitivity and reduce interference with other biological compounds [4]. In addition to detection, nanosensors have wide applications in drug delivery, so they

can deliver drugs to diseased tissues in a targeted manner and avoid side effects on healthy tissues [5]. This feature is especially essential in sensitive treatments such as chemotherapy and can minimize side effects and increase the efficacy of treatment. However, challenges such as biocompatibility and long-term stability of nanosensors in biological environments remain important issues in clinical applications [6]. Immune reactions to these nanoparticles and their potential degradation over time can reduce the efficiency and durability of these sensors. In addition, nanosensors play a significant role in monitoring vital parameters and biomarkers in real time and can provide accurate and continuous information about the physiological status of the patient [7]. By continuously measuring biomarkers such as glucose, lactate, and oxygen in blood or other biological fluids, these sensors enable accurate monitoring of disease progression and the effectiveness of treatment. This technology helps doctors quickly respond to unexpected changes in a patient's condition and adjust treatment strategies based on updated data [8].

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1.1. Motivation and challenges

The significant challenges in the health field, especially in the processes of diagnosis and treatment of diseases, are mostly related to the need for more accuracy and sensitivity in identifying and analyzing diseases. One of the most critical problems is the accurate and timely diagnosis of the symptoms of diseases that can easily be confused with other similar conditions. It is tough to identify cellular and molecular changes in the early stages of diseases, especially in complex diseases such as cancer, due to the limitations of diagnostic tools and complex biological processes. Also, accurate data interpretation is still challenging in many medical imaging methods and biological experiments. In addition, choosing the correct treatment method, such as surgery, chemotherapy, or targeted therapies, requires complex analyses due to the dependence on tumor characteristics and disease stage. In the treatment field, drug resistance and tumor cell diversity caused by traditional treatments are some of the biggest obstacles in disease control. On the contrary, nanosensors can significantly overcome these challenges [9,10]. Hence, the nanosensors, with the ability to accurately and timely identify molecular and cellular changes at the nano level, can very effectively help in the early diagnosis of diseases, especially in the early stages of diseases such as cancer. These sensors can provide more detailed information about the molecular and chemical structure of diseases, which causes more accuracy in diagnosing and differentiating diseases from similar conditions. Also, nanosensors can make disease detection faster and more accurate using multi-faceted analysis, including imaging data, genetic markers, and biomarkers. In the therapy field, nanosensors can help target drugs and targeted therapies more precisely and improve their effectiveness by reducing the side effects of treatments. Therefore, by providing more accurate monitoring and analysis capabilities, nanosensors can help predict and minimize drug resistance to treatments and facilitate the treatment process effectively [11,12]. Many published reviews on the applications of nanotechnology and nanosensors in health monitoring have addressed the potential of these technologies to revolutionize disease diagnosis and treatment. However, most of these reviews either focus on specific diseases such as cancer or are limited to particular nanosensor technologies and do not provide a comprehensive and systematic analysis of the applications of these technologies in personalized health. This review aims to fill this gap and provide a comprehensive perspective on recent advances in nanosensors for customized diagnosis, therapeutic monitoring, and realtime health management. Unlike previous studies, this work emphasizes the synergistic impact of nanosensors across different health domains, identifies emerging trends, and provides practical recommendations for optimizing their applications. By linking technological advances with pragmatic needs in the health field, this review provides new insights and directions for future research and development.

1.2. Our contribution

This review article systematically examines the application of nanosensor technology in health care. This research aims to evaluate and analyze different nanosensor approaches to improve efficiency in diagnosing and treating diseases. This study includes several main achievements:

- Providing a comprehensive review of existing studies on the use of nanosensor technology in the diagnosis and treatment of diseases
- Analysis and evaluation of the latest methods and techniques of nanosensors to improve care and treatment processes
- Investigate and categorize different approaches researchers have used to diagnose and treat diseases using nanosensor technology.
- Assessing the current challenges and issues, along with introducing recommendations to optimize the applications of nanosensors in the diagnosis and treatment of diseases.

1.3. Organization of the article

This paper is organized as follows: Section 2 reviews the background and various aspects of applying nanosensor technology in health care. Section 3 reviews research studies and comparative evaluations on the use of nanosensors in health. Section 4 describes the research strategy for selecting appropriate articles for review and analysis. Also, this section provides a classification for nanosensor approaches in diagnosing and treating common diseases and briefly reviews each disease-related approach. Section 5 presents a detailed evaluation of the comparative effective parameters in the form of a discussion. Section 6 presents suggestions for applying nanosensor technology in health care and open issues related to this field. Finally, Section 7 ends with a conclusion. Table 1 lists the acronyms and their full descriptions in the field of nanosensors and advanced healthcare technologies.

2. Background

This section examines nanosensor applications in healthcare for diagnosing and monitoring diseases and discusses their critical aspects.

2.1. Overview of nanosensors

Nanosensors are microscopic devices designed to detect and measure physical, chemical, or biological changes at the nanoscale. These sensors use nanotechnology to increase sensitivity and accuracy in measurements. Due to their small dimensions, nanosensors can detect minor changes and are used in various fields, such as disease diagnosis, environmental monitoring, food safety, and biomedical technologies [13,14]. The performance of these sensors is based on molecular interactions, and they often use nanostructured materials such as carbon nanotubes, metal nanoparticles, and nanoscale polymers. Due to the high accuracy of these sensors, they can detect changes in the concentration of molecules, the presence of viruses or bacteria, and even thermal changes with unparalleled accuracy [15,16]. These characteristics have made nanosensors important in developing portable and noninvasive devices that can receive and analyze data in real time. Nanosensors have unique properties that make them powerful tools in technology and science. Below are the full features of the nanosensors:

- Very high sensitivity: Due to their nanometer dimensions, nanosensors can detect minimal chemical or physical substance concentration changes. This feature makes them suitable for applications such as early detection of diseases or environmental pollutants.
- Small dimensions: These sensors' nanometer size allows them to be embedded in limited spaces and complex systems. This feature is crucial in making small, portable devices and biomedical applications that work in restricted environments [17].
- Fast response: Due to their low material volume, nanosensors react faster to environmental changes. This speed of response makes them

Table 1Acronyms and Their Full Forms Related to Nanosensors and Advanced Healthcare Technologies.

Acronym	Full Form
EDD	Early Disease Detection
RTCM	Real-Time and Continuous Monitoring
IDTA	Improving Diagnostic and Therapeutic Accuracy
RMM	Remote Monitoring and Management
EPSQ	Enhancing Product Safety and Quality
IHA	Improving Healthcare Accessibility
HSA	High Sensitivity and Accuracy
CRM	Continuous and Rapid Monitoring
NIC	Non-invasive and Convenient
ETD	Enhanced Therapeutic Decision-making
IACE	Improved Accessibility and Cost-effectiveness
REC	Reduced Equipment Complexity

suitable for applications that require real-time monitoring (such as monitoring environmental or health conditions).

- **High accuracy:** Nanosensors are highly accurate in identifying molecular targets due to molecular solid interactions and nanostructured materials such as carbon nanotubes and metal nanoparticles. They can identify specific molecules in complex and highly interfering environments [18].
- Multifunctionality: Nanosensors can measure several parameters simultaneously in a sample. For example, nanosensors can simultaneously detect a chemical's temperature and concentration.
- Ability to integrate with electronic and digital systems: Nanosensors can be easily integrated with electronic and digital systems to quickly process and analyze the collected information in intelligent systems [19].
- High stability: Many nanosensors have long-term stability due to their unique structure and can maintain their performance in harsh and diverse environmental conditions.
- High selectivity: Nanosensors can accurately distinguish target molecules from similar molecules, increasing their high selectivity due to the unique design and use of nanostructured materials.
- Application in various fields: Nanosensors are used in multiple fields, including medicine (to diagnose diseases), agriculture (to monitor soil and products), the environment (to detect pollution), and security (to detect dangerous substances).
- Ability to work on a small scale and noninvasively: Due to their small size and biocompatibility, nanosensors can be used non-invasively in the human body, for example, to monitor medical conditions or precisely release drugs [20].

These features make nanosensors critical in emerging technologies and provide great potential for developing new sensor systems.

2.2. Application of nanosensors

Nanosensors have become critical tools in various fields. They use nanotechnology and can accurately detect changes on tiny scales. Due to features such as high sensitivity, fast response speed, and small dimensions, these sensors have found wide applications in various fields, including medicine, the environment, the food industry, agriculture, security, and intelligent technologies. The unique capabilities of nanosensors in these areas have helped to improve the performance and increase the efficiency of systems and have provided the possibility of

accessing more accurate data and optimizing various processes [21,22]. Table 2 provides a comprehensive overview of the applications of nanosensors in different fields. Due to the significant advances in nanotechnology and the increase in the use of nanosensors in various fields, this table aims to clarify the role and effects of these advanced sensors in the fields of medicine and health, environmental monitoring, food industry, agriculture, security and defense, intelligent technologies and industry and energy. Also, by mentioning the examples, advantages, disadvantages, and goals related to each field, this table aims to help decision-makers and researchers better understand the optimal use of nanosensors and lay the groundwork for developing and improving this technology to solve the challenges in each field.

2.2.1. Comparative evaluation of nanosensors and strategies

By exploiting nanostructured features, nanosensors enable the detection of molecules and biological signals with high accuracy and sensitivity. However, the functional differences between types of nanosensors make their correct selection for specific applications a complex challenge. For example, metallic nanoparticles such as gold and silver are suitable for applications such as the detection of disease biomarkers in complex solutions due to their outstanding plasmonic properties. In contrast, carbon nanotubes, with their excellent electrical conductivity and high mechanical strength, are often used in the measurement of physical and chemical parameters such as gases or ions [23]. On the other hand, quantum dots, with their ability to emit light at various wavelengths, are ideal for bioimaging and optical applications. Hence, to select the right nanosensor, it is necessary to consider a set of parameters. For example, high sensitivity and accuracy in detection are crucial for medical applications and early disease diagnosis. At the same time, robustness to environmental factors and the ability to perform under harsh conditions are more important for environmental sensing. Also, fast response in applications such as real-time monitoring and the ability to maintain long-term performance in bioimplants are other key factors. Manufacturing cost, mass production capability, and ease of integration with other electronic systems should also be evaluated according to the needs of the project or target application. Ultimately, determining the right nanosensor requires a comprehensive and combined approach that leverages the advantages of a variety of available technologies. For example, in advanced applications such as continuous monitoring of biomarkers in the body, combining metallic and polymeric nanomaterials can lead to increased system efficiency and stability. In addition, advances in fabrication methods, such as 3D printing

Table 2Applications of Nanosensors Across Various Fields: Examples, Advantages, Disadvantages, and Goals.

Field of Application	Examples	Advantages	Disadvantages	Goals
Medical & Health	■ Disease diagnosis ■ Drug delivery ■ Health monitoring	■ Early disease detection ■ Non-invasive monitoring ■ Precision in drug delivery	■ Complexity in integration ■ High cost ■ Potential toxicity	 Improve diagnostic accuracy Enhance treatment outcomes Facilitate personalized medicine
Environmental Monitoring	Pollutant detectionWater quality monitoring	Accurate monitoring of air and water qualityEarly detection of pollution	Sensitivity to environmental conditionsMaintenance costs	■ Protect the environment ■ Improve air and water resource quality
Food Industry	■ Food safety monitoring ■ Packaging quality control	■ Ensure food safety ■ Reduce health risks	■ Limited detection for certain materials ■ Need for complex systems	■ Enhance food safety ■ Increase the shelf life of products
Agriculture	■ Soil and plant condition monitoring ■ Pest and disease detection	■ Increase crop yield ■ Optimize resource usage	 Sensitivity to environmental conditions Installation and maintenance costs 	■ Optimize resource use ■ Reduce crop damage
Security & Defense	Detection of hazardous chemicals and biological agentsBattlefield monitoring	Quick detection of dangerous substancesEnhance environmental safety	Technical complexityPotential interference with other materials	 Improve security Reduce risks from chemical and biological threats
Intelligent Technologies	Wearable devicesSmart homes	 Real-time data collection Improve smart device performance 	High costNeed for processing large data sets	■ Enhance daily life ■ Increase efficiency and productivity
Industry & Energy	Production process monitoringGas leak detection	Increase energy efficiencyOptimize energy consumption	■ Continuous maintenance required ■ High initial costs	 Improve energy efficiency Reduce environmental and industrial hazards

and precision layering technologies, have enabled the development of customized nanosensors for specific applications. In this way, the integration of materials knowledge and applied engineering can lead to the development of nanosensors with optimal performance in various fields [24].

2.3. Effect of mechanical stresses on Nanosensor performance

Due to their small size and complex structures, nanosensors are highly sensitive to mechanical changes. Stresses such as bending, twisting, and stretching can directly affect the performance of these devices, affecting parameters such as their sensitivity, selectivity, and stability. These effects can be much more pronounced in areas such as wearable nanosensors and bioimplants that are subjected to repeated mechanical changes. One key aspect of the impact of mechanical stress is the change in the sensitivity of nanosensors [25]. For example, in nanosensors made of carbon nanotubes or metal nanoparticles, stretching or compressing the structure can cause changes in their electronic properties and conductivity. These changes directly affect the ability of nanosensors to recognize target molecules and provide an accurate response. For example, when nanosensors are used to monitor biological fluids, mechanical stress can cause changes in the signal flow and reduce the accuracy of the measurement. Mechanical stresses can also affect the stability of nanosensors. Continuous stretching or bending may reduce the useful life of these devices, as the materials used in their construction may fatigue or deform under repeated stresses. Hence, this is especially important for nanosensors used in dynamic environments, such as wearable medical devices. Therefore, the selectivity of nanosensors may also be affected by mechanical stresses. For example, in nanosensors made of flexible electrodes, mechanical changes can cause noise or interference in the detection of target molecules. Thus, this can be particularly problematic in applications that require high accuracy, such as cancer detection or continuous monitoring of vital signs. Therefore, investigating the effect of mechanical stresses on the performance of nanosensors is a crucial aspect of the development and design of these devices [26].

2.4. Overview of healthcare

In today's world, healthcare faces various challenges that make technological innovations even more necessary. One of the critical areas that can be affected by new technologies is improving the diagnosis of diseases and facilitating the treatment process. With the use of advanced tools, it is possible to collect and accurately analyze medical data, which can help in the early detection of diseases. In addition, healthcare innovation is leading to the provision of personalized treatments. Using the collected data, doctors can design treatments based on the specific characteristics of each patient and increase their effectiveness. This approach not only improves the quality of treatment but also can prevent the occurrence of unwanted side effects. In care management, new technologies can help create advanced systems for public health monitoring and faster identification of epidemics and diseases. By collecting and analyzing health data in real-time, disease outbreaks can be quickly identified, and necessary measures can be taken to control and manage them. These developments can reduce costs and increase access to health services for different communities. In addition, expanding communication technologies in healthcare allows patients to communicate with doctors and health professionals easily and be informed about their treatment options. This can improve patients' awareness and increase their participation in the treatment process. Finally, all these developments show the urgent need to accept and implement new technologies in health care to improve patient's quality of life and increase the efficiency of health systems [27]. Healthcare includes a wide range of fields, each of which plays a vital role in maintaining and improving the health of individuals and society. These areas include public health and prevention, diagnosis and assessment, treatment and

medical interventions, rehabilitation and aftercare, mental health, chronic disease management, maternal and child health, personalized medicine, health information technology, emergency and critical care, education, and Informing patients and managing health systems [28]. Each area increases the quality of health services and promotes public health. Fig. 1 shows these areas.

2.5. Overview of nanosensors in healthcare

Nanosensors, as one of the new technologies in the field of health, have a high potential to change the methods of diagnosis, treatment, and monitoring of the health status of patients. These sensors, made using nanotechnology, can obtain accurate and sensitive information at the nanoscale, which is especially effective in diagnosing diseases. One of the main applications of nanosensors is in diagnosing infectious diseases and cancer [29,30]. By designing particular nanosensors, it is possible to identify biological molecules such as proteins and specific DNAs that act as biomarkers of diseases. These sensors can detect changes at the molecular level in real time, allowing doctors to make early and more accurate diagnoses. In addition to diagnosis, nanosensors are also used in targeted drug delivery. Hence, drugs can be delivered directly to specific body areas using innovative nanosensors, reducing side effects and increasing treatment effectiveness [31-33]. This technology can be especially effective in treating cancer and chronic diseases. Also, nanosensors can play an essential role in monitoring the health status of patients. These sensors can continuously measure biological parameters such as blood sugar level, blood pressure, and other vital signs and instantly send the information to doctors and patients. Hence, this enables continuous monitoring of the patient's health status and helps in the early diagnosis of health problems. In general, the application of nanosensors in the health field not only increases the accuracy and speed of diagnosis and treatment but can also improve patients' quality of life and reduce treatment costs [34,35]. With further advances in this field, nanosensors are expected to play a more fundamental role in the future of healthcare systems. Nanosensors are advanced tools that provide continuous and non-invasive monitoring of vital body activities. These sensors can provide accurate information about the health status of different body parts and play an influential role in the early diagnosis of diseases. For example, in the brain, nanosensors can detect neural activity and brain disorders such as Alzheimer's. In the heart, these sensors can monitor heart rate and detect heart problems such as arrhythmia. Also, they have similar uses in the lungs, liver, kidneys, stomach, and intestines that can help improve health and manage diseases [36-38]. Fig. 2 shows the possible applications of nanosensors in different body

Table 3 provides a detailed overview of the applications of nanosensors in the health sector. Due to the rapid advances in nanotechnology and the increase in the use of nanosensors in medical diagnosis and monitoring, this table seeks to explain the role and vital effects of these innovative sensors in identifying and managing various chronic and difficult-to-diagnose diseases. By highlighting the specific applications, advantages, disadvantages, impact, measurable parameters, and essential factors associated with each application, this table helps health professionals, researchers, and decision-makers more comprehensively understand the potential of nanosensors. Additionally, this table is a foundation for future developments and improvements in this technology, paving the way for improved disease diagnosis, treatment, and patient care.

2.6. Evolution metrics

This section examines five key parameters that can be used to evaluate the performance of nanosensors. These parameters include sensitivity, specificity, accuracy, response time, and stability. It further clarifies their role in improving disease diagnosis and treatment, especially in medical and clinical fields. These properties help nanosensors

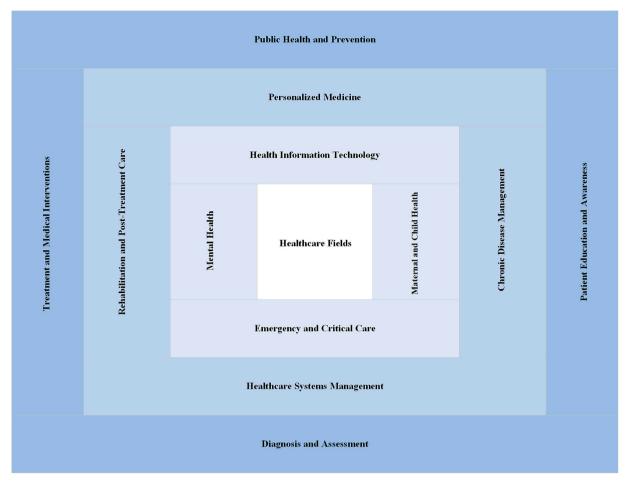


Fig. 1. Structure of Different Fields in Healthcare.

detect diseases effectively, reduce false positives, and provide accurate results in variable environmental conditions. Overall, this text aims to introduce readers to the unique capabilities of nanosensors and their impact on improving healthcare.

• Sensitivity: The sensitivity of nanosensors, their ability to detect and measure tiny changes in the concentration of analytes, is a gamechanger in the health field. High-sensitivity nanosensors can be particularly useful in diagnosing chronic diseases such as diabetes and cancer. They can detect low concentrations of biomarkers in biological fluids such as blood and urine, aiding in the early detection of diseases and preventing their progress. In cancer diagnosis, sensitive nanosensors can identify specific tumor markers at the molecular level, leading to a more accurate and timely diagnosis. This reassuring accuracy instills confidence in the potential of nanosensors in healthcare. Moreover, the optimization of sensor materials and the structure of nanosensors can further increase their sensitivity, ensuring even more precise diagnoses. To quantify the sensitivity of nanosensors in detecting changes in the concentration of analytes in health applications, we can use a more complex equation where various factors affect sensitivity, such as detection limit, signal-to-noise ratio (SNR), and calibration [55]. Eq. (1) is used to determine this quantity.

$$S_{en} = \left(rac{\delta_{ au}}{P_b} imes rac{\Delta P}{\Delta \delta} imes rac{SNR}{arphi}
ight) imes e^{-rac{\delta_{ au}}{\delta_0}}$$
 (1)

In this equation, the S_{en} of a nanosensor measures its ability to detect small changes in analyte concentration, influenced by the detection limit δ_{τ} and baseline resistance P_b . When an analyte is introduced, the change

in resistance ΔP is proportional to the change in concentration $\Delta \delta$. The signal-to-noise ratio SNR enhances detection accuracy during a calibration constant φ accounts for sensor characteristics. The sensitivity also decreases exponentially with increasing analyte concentration, with δ_0 representing the initial concentration.

• Specificity: Specificity refers to the ability of nanosensors to identify specific analytes without being affected by other substances in the sample. In healthcare, interfering substances such as proteins and ions in biological samples may affect the measurement results. Nanosensors with high specificity can only respond to the target analyte, which helps reduce false positives. For example, nanosensors should be able to identify specific bacteria without being affected by other microorganisms in diagnosing bacterial infections [56]. One way to improve this parameter is to use antibodies or other particular molecules to increase the specificity of nanosensors. Eq. (2) is used to determine this metric.

$$S_{pe} = \frac{T_p}{T_p + F_p + \sum_{i=1}^{N} \left(F_{p_i} \times \left(\frac{K_d^i}{K_d^{larger}} \right)^n \right)} \times \left(1 - \frac{\sigma_{noise}}{\sigma_{signal}} \right)$$
(2)

In this equation, the S_{pe} of several vital factors determine a nanosensor. T_p represents the number of true positives, indicating correct detection of the target analyte, while F_p and F_{p_i} account for false positives caused by interfering substances. The dissociation constants, K_d^i and K_d^{target} , represent the binding strength of the sensor to interfering substances and the target analyte, respectively, with their ratio raised to the exponent n reflecting the binding affinity difference. The total

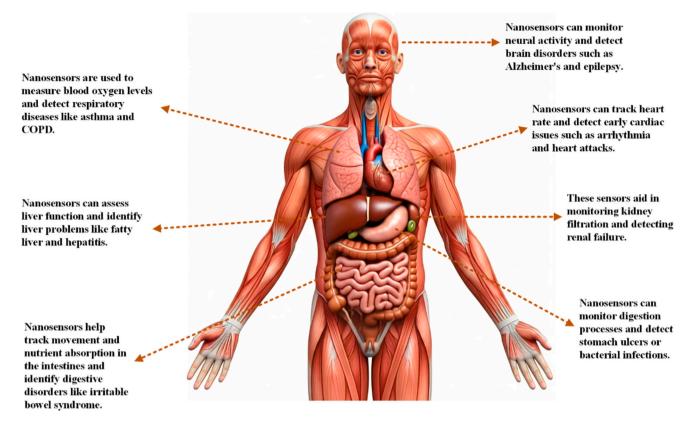


Fig. 2. Potential Locations for Nanosensor Placement in Body Organs for Monitoring Functions and Early Disease Detection.

number of interferents in the sample is N, and the effect of background noise is captured by comparing the standard deviation of noise σ_{noise} to the signal σ_{signal} from the target analyte. These parameters together define the sensor's ability to accurately identify the target analyte amidst potential interference.

• Accuracy: Accuracy refers to the closeness of the measurement results to the actual amount of analyte. In health, the accuracy of nanosensors is of particular importance because incorrect diagnosis can lead to inappropriate treatments and severe consequences for patients. Nanosensors with high accuracy, especially in the early stages of diagnosing diseases such as cancer or cardiovascular diseases, can significantly improve treatment outcomes. Also, regular calibration and using reference methods to assess accuracy can help increase confidence in results. Designing nanosensors in such a way that they work accurately in different concentration ranges is one of the other ways to improve this parameter [57]. Eq. (3) is used to determine this metric.

$$A_{cc} = \left(1 - rac{|\lambda - arrho|}{arrho} imes \left(rac{1}{1 + \left(rac{\sigma_{\lambda}}{\sigma_{arrho}}
ight)^{2}}
ight)
ight) imes \left(1 - rac{\eta_{cal}}{\lambda}
ight) imes \left(1 - rac{ au_{dirt}}{ au_{total}}
ight)$$
 (3)

In this equation, the A_{cc} Of a nanosensor depends on several key factors. λ represents the measured value of the analyte, while ϱ Is the actual concentration, and the difference between the two determines measurement error. The standard deviations σ_{λ} and σ_{ϱ} represent the variability in the sensor's readings and the actual value, respectively, influencing precision. Calibration error η_{cal} measures the discrepancy between the sensor's calibration and the true value, impacting accuracy. Time-dependent drift τ_{dirt} decreases accuracy over time, and this is compared against the total operational time τ_{total} .

• Response Time: The response time refers to the time that the nanosensors need to reach a stable response to changes in analyte concentration. In healthcare, short response times can be very important in cases where rapid diagnosis is required, such as infections or medical emergencies. Nanosensors that can quickly respond to changes in the concentration of analytes can help doctors make faster decisions and improve treatment outcomes. Hence, this is especially important in clinical trials and continuous monitoring of patients' health. Optimization of sensor design, selection of suitable materials and application of new technologies can reduce the response time of nanosensors [58]. Eq. (4) is used to determine this metric

$$R_{est} = au_{\omega} + au_{arphi} imes \left(1 - e^{-rac{arepsilon_{oniple}}{arepsilon_{off}}}
ight) + rac{\Delta\Phi}{S_{singnal}} + rac{\psi_{noise}}{\psi_{signal}} imes T_{arrho}$$
 (4)

In this equation, the R_{est} of nanosensors is influenced by several factors. The time constant for diffusion τ_{ω} depends on how quickly the analyte reaches the sensor surface, while the binding kinetics τ_{φ} describe the time needed for the analyte to bind to the sensor's recognition element, with ξ_{on} and ξ_{off} representing the rates of association and dissociation. The sensor's response change $\Delta\Phi$ is related to its sensitivity $S_{singnal}$, and the overall response time is also affected by noise ψ_{noise} compared to the actual signal ψ_{signal} , with T_{ϱ} accounting for the time needed to process and filter the signal for accuracy. Together, these factors determine the speed and reliability of the nanosensor's response.

Stability: Stability refers to the ability of the nanosensors to maintain their performance over time and under different environmental conditions. In the health field, stable nanosensors can provide accurate results over time, essential for clinical applications requiring continuous monitoring. Instability can lead to unpredictable changes in measurement results and thus lead to misdiagnosis. Therefore, it is

Table 3Applications of Nanosensors in Healthcare: Overview of Advantages, Disadvantages, Impact Measurable Parameters, and Important Factors.

Application of Nanosensors	Advantages	Disadvantages	Impact	Measurable Parameters	Important Factors
Cancer Detection (e.g., Breast Cancer)	■ Early and accurate detection	High costNeed for specialized equipment	■ Increased patient survival ■ Early treatment	■ Tumor Markers: CA 15–3, HER2; ■ Genetic Alterations: BRCA1/2 mutations	■ Sensitivity and Specificity: True positive and negative rates; ■ Linear Range: Range where measurement accuracy is maintained [39,40]
Lung Cancer Detection	 Rapid and accurate identification at early stages 	■ Requires further research	■ Improved treatment success rates	■ Tumor Markers: CEA, CYFRA 21–1; ■ Specific Proteins: KL-6	■ Response Time: Time taken to obtain results; ■ Sensor Stability: Durability and performance consistency under varying conditions [41,42]
Prostate Cancer Detection	■ Early detection	■ Requires clinical confirmation	■ Reduced complications and disease progression	■ PSA Levels (Prostate-Specific Antigen); ■ Biomarker Changes	 Validation Methods: Use of standard techniques to confirm results; Specificity: Ability to correctly identify cancer without false positives [43,44]
Colon Cancer Detection	■ Early detection and reduced mortality	Requires advanced equipment	■ Prevention of complications and rapid diagnosis	■ Tumor Markers: CEA, CA 19–9; ■ Presence of Circulating DNA	 Accuracy in Staging: Ability to identify various cancer stages; Reduced Time to Diagnosis: Speed of early detection [45,46]
Autoimmune Disease Detection	■ Early identification, improved treatment management	■ Complexity in interpreting results	■ Enhanced quality of life for patients	■ Specific Antibodies: ANA, anti-dsDNA; ■ Cytokine Levels	 Diagnostic Accuracy: Ability to differentiate between various autoimmune diseases; Immune Responses: Monitoring immune responses in patients [47,48]
Chronic Infection Detection	 Rapid and accurate identification of infections 	■ Requires clinical confirmation	■ Reduced infections ■ improved management	Bacterial Markers:Leptin,Chiral proteins; CRP and ESR Levels	Early and Accurate Detection: Ability to identify chronic infections in early stages; Timeliness of Analysis: Capability to monitor infections over time [49,50]
Kidney Disease Detection	■ Early identification of kidney failure	■ Requires further research	■ Improved management of kidney diseases	 Creatinine and Urea Levels Protein-to- creatinine ratio in urine 	■ Accuracy and Sensitivity: Ability to detect early changes in kidney function; ■ Long-term Analysis: Monitoring changes in kidney function over time [51]
Alzheimer's Disease Detection	■ Early identification of brain changes	Requires further research	Improved quality of life and disease management	■ β-Amyloid and Tau Protein Levels ■ EEG Changes	Predictive Ability: Identifying patients in early stages; Data Availability: Utilizing biomarker data for analysis [52]
Detection of Hard-to- Diagnose Infections (e. g., Tuberculosis)	 Accurate and rapid identification of infections 	■ Time and high cost of testing	■ Reduced health risks and infections	MycobacteriumPresence in samplesCytokine andAntibody Levels	 Early Detection: Identifying infections before symptom onset Genetic Diversity Analysis: Investigating genetic diversity of pathogens [53]
Endocrine Disorders Detection (e.g., Hypothyroidism)	 Accurate identification of hormonal changes 	■ High costs	■ Improved treatment of hormonal disorders	■ Thyroid Hormone Levels (T3, T4) ■ TSH Levels	 Treatment Response: Evaluating patient response to treatment Monitoring Hormonal Changes: Continuous monitoring of hormone levels [54]

necessary to evaluate and improve the stability of nanosensors through the selection of appropriate materials, appropriate design and periodic tests. Stable nanosensors can maintain their performance in different environments, including variable temperature and humidity conditions, thus providing more reliability for doctors and researchers [59,60]. Eq. (5) is used to determine this metric.

$$S_{ta} = \left(\frac{\chi_0}{\chi(t)}\right) \times e^{-\left(\frac{T_u}{T_o}\right)^a} \times \frac{\theta_r}{\theta_e} \times \left(1 - \frac{\Delta D(t)}{D_{init}}\right) + \frac{v_n(t)}{v_s(t)}$$
(5)

In this equation, the S_{ta} of nanosensors reflects its ability to maintain consistent performance over time. Initially, the sensor's performance χ_0 serves as a baseline, with performance at later times $\chi(t)$ affected by environmental factors and material degradation. Temperature fluctuations T_η and the critical temperature T_ϱ impact stability, with greater fluctuations leading to performance degradation, modeled by the exponent α . Humidity variations also play a role, as the actual humidity. θ_e deviates from ideal conditions θ_r . Over time, the sensor's structural integrity $\Delta D(t)$ deteriorates, influencing stability and changes in the signal-to-noise ratio $\frac{v_n(t)}{v_s(t)}$ further affect performance, particularly in sensitive healthcare applications.

3. Related works

This section examines articles related to the application of nanosensor technology in the healthcare field to provide a comprehensive view of the advances and applications of this technology. These review articles will be compared based on various parameters such as advantages, disadvantages, applications, objectives, year, and publisher. This comparison will help readers understand the differences and compatibility between approaches and make more informed decisions about research and development in this area. Ghasemi et al. [61] researched to investigate and introduce paper-based nanostructured sensors for onsite detection and analysis. In this study, paper-based analytical devices (PADs) using nanostructures and their optical properties are developed to improve detection accuracy and efficiency. These sensors have been used to receive and interpret the results using optical measurement mechanisms and data analysis. The results have shown that these devices can be used as an efficient and cost-effective solution in remote areas for quick and easy diagnosis. Also, due to the high advantages of PADs, their commercialization opportunities will increase. Sargazi et al. [62] conducted this research to investigate and evaluate fluorescence-based nano biosensors for detecting biological and chemical agents with high accuracy and sensitivity. In this research, sensors using nanomaterials such as quantum dots and metal-organic frameworks have been used to detect a wide range of biological macromolecules, including proteins, enzymes, and cancer biomarkers. Different methods for identifying these molecules have been compared in this research, and their selective and sensitive characteristics have been discussed. The results have shown that these nanoprobes have performed well as fast and accurate sensors in vitro and in vivo detection. Yang and Duncan [63] conducted this research to investigate the technical, legal, economic, political, and ethical challenges facing the development and use of nanosensors in food safety quality and agriculture. In this research, the existing obstacles to the development of this technology have been examined in detail and solutions to solve them have been presented. The results have shown that focusing on financing, creating suitable research environments, and designing nanosensors that can be analyzed quickly in non-laboratory environments can effectively remove these obstacles. Khazaei et al. [64] conducted this research to investigate the use of nanosensors for early cancer detection and new methods for identifying the level of biomarkers in cancer patients. This study used nanomaterials to identify tumor-specific biomarkers and tumor cells. Different techniques were compared according to their sensitivity and accuracy in detecting cancer biomarkers. The results have shown that nanosensors can make early cancer diagnosis possible and increase patients' chances of survival and long-term recovery. Sabzehmeidani and Kazemzad [65] conducted this research to develop accurate and rapid methods for detecting antibiotic residues in food products using quantum dots (QDs) based on carbon and metals. This study investigated the efficiency of sensors based on QDs in different diagnostic systems, including optical luminescence, electrochemical, chemiluminescence, and electrochemiluminescence. The results have shown that the detection mechanism of these sensors was dependent on specific properties and interactions with antibiotics. Also, environmental applications and future perspectives of this technology for antibiotic detection are analyzed. Javaid et al. [66] conducted this research to review and introduce nanosensors and their measurement techniques to detect physical properties at the nanoscale. In this study, the classification of nanosensors from an industrial point of view and their diagnostic components have been graphically analyzed. The results have shown that nanosensors have a high potential to identify and accurately monitor physical characteristics such as pressure, temperature, and magnetic forces. This research can be a basis for future research to find comprehensive reports about the different potentials of nanosensors.

Table 4 compares different research on using nanosensors in healthcare. The comparison is based on four main parameters: objectives, advantages, disadvantages, applications, years, and publisher. This comparison provides a comprehensive view of the different methods used in this field and examines their strengths and weaknesses.

4. Overview of the proposed taxonomy and research methodology

This section is prepared to classify and analyze the applications of nanosensors in health and treatment for selected research articles based on the proposed classification. Several applications of nanosensors in health technology have been investigated in the scientific literature [67,68]. This research paper focuses on the applications of nanosensors to detect health-related issues [69]. The thematic identification approach has identified four main categories and related studies. According to Fig. 3, this paper introduces four main applications of nanosensors in healthcare. In the health field, nanosensors' applications

are divided into the following categories: disease diagnosis, therapeutic applications, wearables and implants, and infection monitoring and biosafety. Therefore, we will briefly review the various applications of Nanosensors in health technology based on digested categories and briefly describe the studies related to each application. Also, this study uses a systematic method to identify, filter, select, discover, and evaluate research articles. Therefore, in searching for appropriate keywords and critical combinations of sensitive search terms for Nanosensores applications in healthcare, consider factors such as (("Disease Diagnosis" OR "Medical Diagnosis" OR "Health Monitoring" OR "Biomarker Detection" OR "Nanodiagnostics" OR "Cancer Detection" OR "Infectious Disease Detection")) AND (("Therapeutic Applications" OR "Drug Delivery" OR "Targeted Therapy" OR "Gene Therapy" OR "Nanoscale Therapeutics" OR "Nano-medicine" OR "Cell Therapy")) AND (("Wearables and Implants" OR "Wearable Sensors" OR "Implantable Sensors" OR "Bodyworn Devices" OR "Smart Health Devices" OR "Healthcare Monitoring Devices" OR "Health Implants")) AND (("Infection Monitoring" OR "Biosafety" OR "Pathogen Detection" OR "Contamination Monitoring" OR "Environmental Biosafety" OR "Real-time Infection Monitoring" OR "Health Security")). In addition, this study examines the main aspects and techniques used in the published articles at the given time and the main issues and challenges related to Nanosensores' applications in the health field.

4.1. Disease diagnosis approach

Disease diagnosis is one of the critical applications of nanosensors in the health field, and due to the high sensitivity of these sensors, it provides the possibility of quick and accurate identification of pathogenic agents. Nanosensors can play a vital role in the early detection of diseases by detecting specific biomolecules, proteins, DNA, and RNA in biological samples. Among the standard techniques in this field is using metal nanostructures, semiconductors, and quantum dots to amplify diagnostic signals, dramatically increasing the accuracy and sensitivity of tests. These sensors can also detect biological compounds at deficient concentrations, which is critical in diagnosing diseases such as cancer, viral and bacterial infections, and even genetic diseases. Therefore, nanosensors are a revolutionary tool in the early and accurate diagnosis of diseases that can provide significant results in prevention and timely treatment. Hence, we will analyze and describe the various implementation approaches for disease diagnosis using nanosensors.

Gupta and Basu [70] conducted this research to develop nanosensors with advanced detection capabilities for the early detection of diseases without the need for outward symptoms. In this study, nanotechnology was used, and nanosensors were designed to mimic immune responses and transmit diagnostic data to monitor the patient's condition. The results showed that nanosensors can be effectively used for drug delivery, detecting contamination in organ implants, and diagnosing tumor masses. This model also addresses the creation of a network of nanosensors to overcome the challenges related to the small size and low power of individual nanosensors.

Table 4Comparison of Nanosensor Research in Healthcare: Objectives, Advantages, Disadvantages, and Applications.

Ref	Objectives	Advantages	Disadvantages	Applications	Years	Publisher
[61]	• Evaluate paper-based analytical devices	Affordable and portable	• Limited sensitivity	Quick detection in remote areas	•	• Elsevier
	for rapid detection			and healthcare	2023	
[62]	 Review fluorescent nano biosensors for 	 High sensitivity and 	 Challenges in development 	 Early detection of drug-induced 	•	 Elsevier
	detecting biological and chemical agents	environmentally friendly	and commercialization	damage and biological diseases	2022	
[63]	 Examine nanosensor technologies in 	 Improved food quality and 	 Technical and regulatory 	 Monitoring food health, 	•	 Nature
	food safety	safety	challenges	combating fraud and bioterrorism	2021	
[64]	 Review the application of nanosensors 	 Improved diagnosis and 	 Need for better sensitivity 	 Detection of cancer biomarkers 	•	 Elsevier
	for early cancer detection	survival		and tumor cells	2023	
[65]	 Review quantum dots for detecting 	 High accuracy in antibiotic 	 Interference with other 	 Detection of antibiotics in food 	•	 Elsevier
	residual antibiotics	detection	substances	and improving safety	2022	
[66]	 Review nanosensors for monitoring 	 Precise detection at 	 Requires complex 	 Medical monitoring, pathogen 	•	 Elsevier
	physical and chemical characteristics	nanoscale	infrastructure	detection, and pollution control	2021	

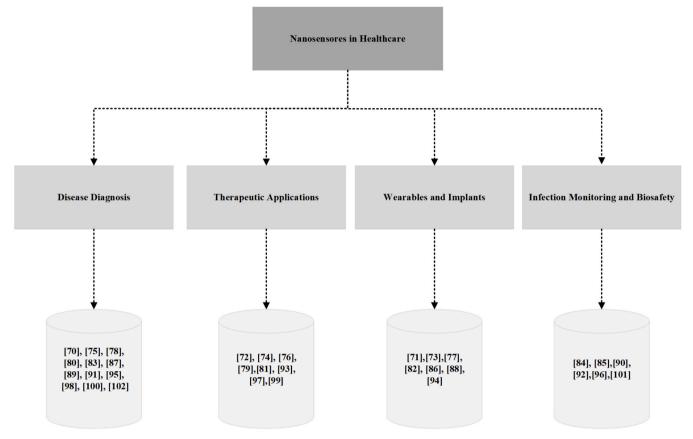


Fig. 3. A detailed taxonomy of nanosensors applications in healthcare.

Saylan et al. [75] This research was conducted to investigate and evaluate nanosensors for medical applications. This study uses nanosensors to identify biomolecules such as tears, saliva, and sweat in biological fluids. The results showed that nanosensors can non-invasively check a person's health status by accurately identifying clinical markers. Also, these nanosensors have attracted much attention due to their features, such as sensitivity, portability, and low cost. Finally, this research addressed the challenges and future trends in nanosensors development and emphasized the need for further developments.

Sahi and Kaushik [78] conducted this research to investigate the application of the combination of Artificial Intelligence (AI) and the Internet of Things (IoT) in health and medical systems. In this study, machine learning and computer vision techniques have been used to improve human-machine interactions and increase the efficiency of IoT operations in various medical fields. The results showed that this new combination, artificial intelligence of objects (AIoT), can help improve data management, analytics, and surgical operations with the help of medical robotics and nanotechnology.

Kim et al. [80] conducted this research to improve the accuracy of breath analysis as a non-invasive and low-cost diagnostic tool. This study uses chemical-resistant respiratory sensors with high sensitivity and selectivity to identify disease biomarkers. The results showed that combining protein nanocatalysts with metal oxide nanostructures can significantly improve the efficiency of the sensors by increasing the contact surface and facilitating gas penetration into the sensor layers. This research has addressed the challenges related to identifying biomarkers at the ppb level and the importance of selectivity in the presence of disturbing gases.

Yang et al. [83] conducted this research to develop functional transistor sensors for detecting various viruses, toxins, cancers, and disease or injury markers. This study uses functional transistors with features such as fast response (less than 5 min) and high specificity for accurate

identification. The results showed that these sensors can simulate and analyze disease-related information with high accuracy and speed. Also, the possibility of integrating these sensors with wireless data transmission has helped speed up the clinical diagnosis process.

Palaniyandi et al. [83] conducted this research to investigate the use of nanosensors in the diagnosis and treatment of neurodegenerative and inflammatory diseases such as Alzheimer's disease (AD) and inflammatory bowel disease (IBD). In this study, nanosensors have been used to identify and treat diseases that have become increasingly common. The results showed that nanosensors can be effective in quickly and accurately identifying these diseases and contribute to new developments in the field of diagnosis and treatment. Also, this research investigated the capability of nanosensors in diagnosing inflammatory and neurodegenerative diseases and explained their role in improving treatment methods.

Rabbani et al. [89] conducted this research to investigate the application of nanotechnology in the design of biosensors and improve their performance in medical diagnostics. This study uses nanomaterials such as nanoparticles, carbon nanotubes, and graphene to develop miniature, flexible sensors. The results showed that these nano-designed sensors have reliable and multidimensional features that can improve the quality of life in various applications, including medical diagnostics and environmental monitoring. Also, using these sensors in biomedical applications such as medicine and nanotechnology has helped to identify diseases more accurately and quickly.

Mujawar et al. [91] conducted this research to investigate new technologies in the design of biosensors and their application in early disease detection and personal health management. This study investigated nanotechnology advances in constructing sensors and diagnostic devices to identify disease biomarkers at low levels (pM) accurately. The results showed that these advanced sensors can effectively help evaluate the disease's progress under treatment, optimize treatment methods,

and relate the level of biomarkers to the pathology of diseases. Also, this article points out the importance of intelligent and cost-effective diagnostic tools for disease management, especially in crises like the COVID-19 pandemic.

Preetam et al. [95] conducted this research to investigate the applications of nanotechnology and nanosensors in diagnosing different types of cancers. In this study, nanoscale biosensors were used to identify and detect biomarkers of diseases such as prostate cancer, lung cancer, brain cancer, breast cancer, and pancreatic cancer. The results showed that nanosensors can effectively help quickly and sensitively identify disease biomarkers and act as a promising tool in diagnosing diseases in the early stages. This article also deals with using different nanomaterials in making sensors and their role in diagnosing various diseases.

Noah and Ndangili [98] conducted this research to investigate using nanosensors to diagnose and rapidly manage diseases in the initial stage. This study used nanosensors to detect disease analytes and monitor their progress near the patient to make medical decisions faster. The results showed that using nanotechnology can improve the sensitivity and accuracy of diagnostic methods and thereby help in the early diagnosis of diseases and more effective treatment. This research also deals with developing and fabricating nanosensors for on-site (POC) disease diagnosis.

Yaari et al. [100] conducted this research to develop a perceptual-based platform for multiple detection of protein markers in biological fluids through an optical nanosensor array and machine learning algorithms. In this study, new methods, such as antibodies, were used

instead of conventional detection molecules, which made the detection process faster and more cost-effective. The results showed that this platform can detect several disease markers simultaneously with high accuracy (F1 distance of about 0.95) in uterine washing samples of cancer patients. This system was effective in detecting women's cancers that are usually diagnosed at advanced stages and can help improve patient survival rates.

Peng et al. [102] conducted this research to investigate the ability of a nanosensor array to distinguish between breath VOCs that characterize healthy conditions and different types of lung, breast, colorectal, and prostate cancers. In this study, the technique of gas chromatography coupled with mass spectrometry (GC–MS) and an array of gold nanosensors with organic functionality were used to identify specific VOC patterns. The results showed that the nanosensor array can distinguish between the breath of healthy and sick people and determine the differences in the breath of patients with different types of cancer. This method was able to identify unique VOC patterns for each type of cancer, independent of factors such as age, gender, and lifestyle.

Table 5 comprehensively examines the goals, advantages, disadvantages, approach, application, impact on results, and Evaluation Metrics by focusing on techniques for disease diagnosis using nanosensors. The primary objective is to provide a comparative perspective on methods and results.

4.1.1. Summary and discussion

Table 5 compares technical studies on nanosensor-based methods for disease diagnosis and examines parameters such as objectives,

Table 5

A comprehensive examination of nanosensor-based techniques for disease diagnosis: goals, advantages, disadvantages, approaches, applications, impact on results, and evaluation metrics.

Ref	Goals	Advantages	Disadvantages	Approach	Application	Impact on Results	Evolution metrics
[70]	Development of nanosensors for early disease detection	High sensitivity allows detection without visible symptoms	High production costs require controlled environments for manufacturing	Use of nanosensors and nanonetworks	Drug delivery, tumor detection	More accurate and faster diagnosis	Accuracy
[75]	Continuous monitoring and real- time detection	Portable, low-cost, non-invasive	Limited long-term stability and accuracy, calibration challenges	Detection of biomarkers through nanosensors	Disease diagnosis from body fluids	Facilitates personalized care	Accuracy, Specificity, Sensitivity
[78]	Combining AI and IoT to enhance diagnostics	Increased efficiency, better data analysis	Data privacy and security concerns, implementation complexity	AI in IoT for diagnostics	Health monitoring, nano-implants	High accuracy in health tracking	Stability, Accuracy, Sensitivity
[80]	Diagnosis through breath analysis	Non-invasive, low-cost	Interference from other gases affects accuracy and requires specific equipment.	Breath sensors	Detecting respiratory biomarkers	High accuracy in breath-based disease detection	Stability, Specificity, Sensitivity
[83]	Rapid and precise detection of viruses and cancers	Quick response, portable	Limited selectivity for some biomarkers	Functionalized transistors	Quick virus and cancer marker detection	Enables immediate, on-site diagnosis	Response Time, Accuracy,
[87]	Enhancing sensor performance for disease detection	Precise, versatile detection	Sensitivity to environmental factors and storage conditions affects performance.	Use of nanomaterials	Diagnosing neurological and inflammatory diseases	Advances in complex disease diagnostics	Specificity, Sensitivity
[89]	Improved biomarker detection	High selectivity, cost-effective	Limited capability for simultaneous multi- biomarker detection	Nano-based biosensors	Personal health monitoring, disease management	Early detection with high sensitivity	Accuracy, Specificity, Sensitivity
[91]	Precise, cost-effective biomarker monitoring	Non-invasive, easy to use	Reduced sensitivity in contact with complex body fluids requires specific adjustments.	Biosensors for personalized health	Biomarker detection for disease management	Enhances health and quality of life	Stability, Response Time, Specificity, Sensitivity
[95]	Improved detection and monitoring of various cancers	Ability to detect multiple biomarkers	Adaptability issues with different cancer types	Nano-biosensors for cancer diagnosis	Prostate, lung, brain, and breast cancer detection	Increases cancer diagnostic accuracy	Specificity, Sensitivity
[98]	Facilitating rapid diagnosis near the patient	Quick diagnosis, better decision- making	Accuracy challenges in the presence of interfering substances, uncontrolled conditions	Nanosensors in disease diagnosis	Diagnosis and management of diseases	Improves therapeutic outcomes	Stability, Response Time,
[100]	Multiplex biomarker detection without molecular recognition	High accuracy and speed	High complexity in manufacturing, costly for commercialization	Optical nanosensors with ML	Gynecologic cancer diagnosis	High accuracy in multiplexed detection	Accuracy, Specificity, Sensitivity
[102]	Non-invasive cancer detection	Low-cost, simple	Lower sensitivity to specific markers of each cancer	Breath nanosensors	Detecting cancer via VOCs	Improves non- invasive diagnosis	Stability, Accuracy,

advantages, disadvantages, approach, applications, effects on results, and evaluation metrics. In these studies, nanosensors have been used as key technologies to increase the accuracy and speed of diagnosis and improve the monitoring of patient's health status. The advantages of these approaches include high sensitivity, the possibility of continuous monitoring, and accurate real-time analysis, which improve diagnostic results and accelerate treatment processes. On the other hand, the disadvantages of these methods include high production costs, the need for controlled environments for production, and long-term sustainability challenges in some devices, which necessitate the need to improve these technologies for wider applications. Studies show that various approaches, such as the use of biomarkers, the combination of artificial intelligence and the Internet of Things (IoT), and diagnosis based on breath analysis, have been used, which demonstrates the versatility of these technologies in various healthcare environments. Among the technologies used are nanomaterials, functional transistors, and advanced nano biosensors that enable the detection of multiple biomarkers. Performance evaluation criteria include accuracy, detection speed, non-invasive monitoring, and production cost, which indicate the importance of improving these criteria to improve the quality of healthcare services and reduce costs. Ultimately, the goals of these methods include early detection, improved personal health monitoring, and reduced disease prevalence. The correct selection of these methods based on the needs of specific operating environments can help maximize the productivity and efficiency of healthcare systems.

4.2. Therapeutic applications approach

The therapeutic applications of nanosensors in the health field have attracted much attention due to their unique capabilities in precise drug delivery, treatment monitoring, and influencing at the cellular and molecular level. Nanosensors can deliver drugs to diseased cells in a targeted manner and prevent damage to healthy tissues, which is crucial in treating cancer and chronic diseases. These sensors can also monitor the body's vital parameters, evaluate the treatment's effectiveness in real time, and help change the dosage of the drugs or modify the treatment protocols. In addition, nanosensors can facilitate the process of tissue repair and regeneration by quickly identifying inflammatory agents and other damaging factors. Therefore, nanosensors are recognized as an advanced tool in targeted and intelligent therapies that can significantly improve the efficiency and accuracy of medical treatments. Hence, we will analyze and describe the various implementation approaches for therapeutic applications using nanosensors.

Khan et al. [72] conducted this research to investigate nanoscale sensors' applications in competent healthcare in smart cities. This study described the communication between nanosensors for healthcare applications, including intelligent drug delivery, body network, implantable devices for treating injuries and disorders, and the Internet of Nano-Things. Also, the challenges of implementing nanosensor networks for biomedical applications were discussed. The results showed that due to the limitations of nanosensors processing power and storage, there is a need to create a network of nanosensors for any health application.

Ahirwar and Khan [74] conducted this research to investigate and develop innovative wireless nanosensors for remote health care. This study uses small sensors with high biocompatibility, wireless connectivity, and cloud storage to monitor health, send medical data, and provide therapeutic interventions outside medical centers. The results showed that these sensors can increase access to treatment by improving the quality of care and reducing the need for expensive and invasive diagnostic methods. This research has also addressed the challenges of accuracy, reproducibility, patient security, and privacy.

Agoulmine et al. [76] conducted this research to develop nanoscale biosensors and communication technology to create new solutions in electronic health. This research uses miniaturized biosensors capable of detecting and exchanging information about the concentration of molecules and chemical compounds. In this study, two methods of

electromagnetic communication in the terahertz band and molecular communication were investigated, and the characteristics of both methods and the general architecture of nano biosensors were presented. The results of the experiments showed that these sensors can identify biomolecules with high accuracy.

Sonia et al. [79] conducted this research to investigate the development of non-invasive and implantable nanosystems for monitoring and drug delivery for accurate disease prevention. In this research, various implantable and wearable nanosensors have been used for continuous and non-invasive monitoring of electrolytes and metabolites in saliva, sweat, and tears. The results showed that these systems can monitor people's health without disrupting their daily activities. This study also examined the physiological parameters and diseases that can be controlled using these systems.

Alba-Patiño et al. [81] conducted this research to review recent advances in developing diagnostic tools for managing sepsis, relying on micro- and nanostructured materials. This study introduces common sepsis biomarkers, including lactate, procalcitonin, cytokines, C-reactive protein, and bacteremia detection methods. The role of nano and microstructured materials in the design of biosensors for fast and accurate detection of these markers at different points of sepsis care was investigated. The results showed that these materials can quickly and sensitively detect blood markers and pathogens for personalized and appropriate treatment.

Pathak et al. [93] conducted this research to investigate using nanomaterials such as nanosensors in diagnosing and treating diabetes. In this study, nanotrast has been used as a novel tool to combine therapy and imaging to improve diabetes management and facilitate targeted delivery of drugs and insulin to the pancreas. The results showed that nanotrastics can revolutionize the diagnosis and treatment of diabetes and improve the quality of life of diabetic people. Also, nanocarriers and nanomaterials with special functions were introduced as therapeutic tools for diabetes.

Dinesh Kumar [97] conducted this research to monitor people's health status through nanosensors placed in mobile phones. This study uses a TI MSP430 microcontroller and ZigBee wireless communication to transmit health data to the hospital. Nanosensors detect minor changes in people's bodies without needing different sensors and measure indicators such as asthma, cancer, blood pressure, and body temperature. This device showed the health status and suggested ways to improve it without needing a doctor.

Mosayebi et al. [99] conducted this research to use mobile nanosensors (MNS) for early detection of cell abnormalities such as cancer cells. This study used MNSs to detect cancer biomarkers that blood tests cannot detect in the early stages. These nanosensors were injected into the blood vessels app, roached cancer cells' location, and activated by surrounding biomarkers. The results of simulations showed that MNSs provided higher efficiency than fixed sensors by collecting and sending data to the combination center.

Table 6 comprehensively examines the goals, advantages, disadvantages, approach, application, impact on results, and Evaluation Metrics by focusing on techniques for therapeutic applications using nanosensors. The primary objective is to provide a comparative perspective on methods and results.

4.2.1. Summary and discussion

Table 6 compares technical studies related to the application of nanosensors in improving therapeutic applications and examines parameters such as objectives, advantages, disadvantages, approach, applications, effects on results, and evaluation metrics. In these studies, nanosensor networks and mobile systems have been used as key technologies to improve diagnostic accuracy, continuous monitoring, and telecare delivery. The advantages of these approaches include easy access, noninvasive real-time tracking, and accurate monitoring of biomarker levels, which accelerates the treatment process and improves personalized care. The disadvantages of these methods include

Table 6
A comprehensive examination of nanosensor-based techniques for therapeutic applications: goals, advantages, disadvantages, approaches, applications, impact on results, and Evaluation Metrics.

Ref	Goals	Advantages	Disadvantages	Approach	Application	Impact on Results	Evaluation Metrics
[72]	Improve therapeutic care within intelligent cities	Enables precise drug delivery, enhanced health monitoring	Limited processing power and energy; network complexity for managing nanosensors	Nanosensor networks	Targeted drug delivery, implantable therapeutic devices	Streamlines drug delivery and intervention efficiency	Stability
[74]	Enable remote therapeutic monitoring	Portability, biocompatibility, remote access	Data security, patient privacy issues; device sensitivity and accuracy concerns in long-term use	Wireless, cloud- enabled nanosensors	Remote monitoring, implantable therapeutics	Supports patient mobility and continuous, comfortable care	Sensitivity, Accuracy
[76]	Develop cost- effective, scalable therapeutic eHealth systems	Direct, in-body communication, adaptable to patient needs	Complex protocols; in-body transmission interference; challenges in molecular communication	Bio-nanosensors using terahertz/ molecular communication	Real-time response to biomolecule levels for treatment	Enhances therapeutic accuracy and timely interventions	Accuracy, Specificity
[79]	Continuous non- invasive health monitoring for personalized therapy	Non-intrusive, precise tracking in real time	Limited long-term reliability in non-invasive sensors, high sensitivity to environmental factors	Wearable and implantable nanosystems	Monitoring therapeutic markers in saliva, sweat, tears	Provides reliable, real-time health indicators for proactive treatment	Specificity, Stability
[81]	Rapid sepsis detection for effective therapeutic response	Fast and sensitive biomarker detection; point-of-care utility	Device durability and calibration for accuracy; limited pathogen specificity	Nano-structured biosensors	Sepsis management in emergency and ICU settings	Enables fast, targeted therapeutic action, reducing mortality risk	Accuracy
[93]	Diagnose and treat diabetes through nano-theranostics	Enhanced glucose control, pancreas- specific drug delivery	Risk of bioaccumulation and potential toxicity; regulatory and cost challenges	Nano-theragnostic	Diabetes monitoring, targeted insulin/ drug delivery	Improves patient outcomes and quality of life with precise management	Stability
[97]	Therapeutic monitoring via accessible mobile nanosensors	Broad accessibility detects early health issues	Accuracy variations due to sensor limitations; high initial cost for widespread use	Mobile-integrated nanosensors	Monitoring of asthma, cancer, ECG, blood pressure	Supports remote management and real-time alerts for faster care	Response Time
[99]	Early detection and intervention for cancer	Highly sensitive to cancer biomarkers at low concentrations	Requires targeted sensor positioning; potential interference in complex biological systems	Mobile nanosensors in the bloodstream	Detecting cancer biomarkers for early therapy	Increases chances of early intervention, improving therapeutic success rates	Specificity, Response Time

limitations in processing power, data security issues, network complexity challenges in managing nanosensors, and high sensitivity to complex biological environments, which require the improvement of these technologies for greater efficiency in broader applications. Studies show that various methods, such as wearable nanosensors, nanothranost systems, and mobile nanosensors, have been applied, which enable a wider use of these technologies in medical care. Among the technologies used are special nanostructures and nanosensors based on molecular communication, which will allow rapid and accurate identification of pathogen markers. Performance evaluation criteria include accuracy, detection speed, portability, and cost-effectiveness of production, which indicate the importance of improving these criteria to improve the quality of medical services. Ultimately, the goals of these methods include continuous monitoring, early diagnosis, and improvement of patients' quality of life. The correct selection of these methods based on the needs of specific medical environments can help increase the efficiency and effectiveness of medical systems.

4.3. Wearables and implants approach

The application of nanosensors in wearable devices and implants is considered one of the critical developments in the field of intelligent medicine, which enables constant and real-time monitoring of the health status of patients. Nanosensors in these devices can accurately measure physiological parameters, such as glucose level, blood pressure, heart rate, and blood oxygen, and send them wirelessly to monitoring and analysis systems. These features are precious for patients with chronic diseases, such as diabetes and heart disease, as they allow real-time monitoring and rapid response to body changes. Also, implants equipped with nanosensors can monitor inflammatory reactions or the

effectiveness of drugs inside the body and provide doctors with valuable information to optimize treatments. In this way, wearable nanosensors and implants are new tools in preventive and therapeutic medicine that improve the quality of life and treatment results. Hence, we will analyze and describe the various implementation approaches for wearables and implants using nanosensors.

Kumar et al. [71] conducted this research to comprehensively investigate the types of metal oxide nanostructures and electrochemical sensors for biomedical and environmental applications. This study investigated the physicochemical properties and synthesis methods of nanomaterials such as Bi2O3, Al2O3, Cr2O3, CuO, Fe2O3, and ZnO. Due to their low cost and high cross-sectional area, these nanomaterials have been used to detect biomolecules, gases, and chemicals. The results showed that these nanomaterials have made significant achievements in the fields of health and environment.

Adam and Gopinath [73] conducted this research to investigate the status of nanosensors and their capabilities in detecting physical, chemical, and biological substances using dimensions less than 100 nm. This study analyzed and reviewed various structures of nanosensors and surface engineering methods for general and specific applications. The findings showed that these sensors have had significant success in medicine, security, agriculture, and COVID-19 diagnosis due to their ability to measure chemical and physical characteristics efficiently and cost-effectively.

Rani [77] conducted this research to investigate the role of nano biosensors in improving healthcare applications and connecting electronic devices with biological phenomena at the nano level. This study reviewed the applications of nanosensors in the health field, including diagnostic tools, implants, and wearable devices. The results showed that this technology can help diagnose and treat diseases by identifying

and measuring biological substances. Also, the Internet of Medical Things (IoMT) was introduced as an influential factor in connecting micro and nanosensors by wireless technologies and the Internet to develop intelligent medical systems.

Yang et al. [82] conducted this research to develop a wearable nanobased microfluidic sensor capable of continuously analyzing heavy metals from body sweat using a mobile phone as a wireless reading device. This study uses printed design techniques to make the sensor and apply active methods to stimulate sweating. The results showed that the proposed system can normalize the concentration of heavy metals according to the sample volume and transpiration rate. With a sensitivity of 2.3 nA/ppb and a linear range of up to 2500 ppb, this system provided a detection capability with a detection limit of 396 ppb.

Dorj et al. [86] conducted this research to design an intelligent healthcare data management system (IHDMS) using nanosensors and develop an application for mobile devices. In this study, the IHDMS system is designed to coordinate patient health data from nanosensors and convert it to the HL7 standard for health data exchange. The converted data was sent to the system server, reducing the delay time in data transfer. The results showed that the system's battery life can be increased, its memory consumption is less than 100 KB, and it performs data operations with limited resources. Finally, the proposed system provided security and high efficiency in health data management by using a secure channel to transfer data in HL7 format.

Sarkar and Misra [88] conducted this research to investigate the evolution of embedded and microelectromechanical systems (MEMS) and their impact on improving healthcare. In this study, the history and advances of physiological sensors that were developed in the 1980s to measure physiological parameters of the human body have been reviewed. This research has also investigated wireless body sensor networks (WBANs), where sensed data from body sensors is transmitted to an analysis center. The results showed that by using wireless networks, data is collected and analyzed more effectively, and this has led to significant improvements in healthcare delivery.

Vivekananthan et al. [94] conducted this research to develop a flexible electronic skin (e-skin) device inspired by human skin for medical, sports, and health applications. In this study, new technologies in advanced materials and device design for making wearable sensors have been investigated. Also, nanosensor techniques have been used to

include sensors inside these devices and use flexible energy sources such as nanotriboelectric generators to provide energy for sensors instead of batteries. The results showed that these e-skin devices can automatically collect the energy necessary for their operation from the surrounding environment and thus reduce the need for batteries.

Table 7 comprehensively examines the goals, advantages, disadvantages, approach, application, impact on results, and evaluation metrics by focusing on techniques for wearables and implants using nanosensors. The primary objective is to provide a comparative perspective on methods and results.

4.3.1. Summary and discussion

Table 7 provides a comparison of technical studies conducted on wearable and implantable nanosensors in medical diagnostics and health monitoring, examining criteria such as objectives, advantages, disadvantages, methods, applications, and impacts on outcomes. In these studies, nano-biosensors and wireless networks have been used as key technologies to improve the accuracy and accessibility of real-time health data and provide telehealth services. The advantages of these methods include high sensitivity, low manufacturing cost, and easy integration with smart devices, which allow continuous and noninvasive monitoring of health indicators. The disadvantages of these methods include power limitations, the need for external energy sources, data security challenges, and memory and storage limitations, indicating the need to improve these technologies for wider use in health systems. Studies show that various technologies, such as flexible electronic skin, wearable microfluidics, and surface-engineered nanosensors, have been used to create new applications for accurate diagnosis and optimal management of health data. Among the technologies used, nano-biosensors integrated with the Internet of Things (IoMT), wireless body area networks (WBANs), and self-healing electronic skins can be mentioned, which enable continuous and remote monitoring of physiological parameters. The evaluation criteria include diagnostic accuracy, improved energy efficiency, and reduced waiting time in health data transmission, which shows the importance of these criteria in improving the quality of care and rapid access to health data. Ultimately, the goals of these methods include enhancing continuity of care, early detection of diseases, and optimization of health data flow, and the appropriate selection of these methods based on the specific

Table 7

A comprehensive examination of nanosensor-based techniques for wearables and implants: goals, advantages, disadvantages, approaches, applications, impact on results, and evaluation metrics.

Ref	Goals	Advantages	Disadvantages	Approach	Application	Impact on Results	Evaluation Metrics
[71]	Enhance biomedical diagnostics	Cost-effective, high surface area, easy modification	Limited selectivity; potential interference in complex fluids	Metal oxide-based nano-biosensors	Detecting biomolecules, gases	Improved diagnostic accuracy in wearables	Stability, Accuracy
[73]	Miniaturized sensing in healthcare	High sensitivity, low- cost fabrication	Surface engineering limitations for complex applications	Nano-sensors with surface engineering	COVID-19 detection, medical diagnostics	Broadened medical application potential	Sensitivity, Response Time
[77]	Real-time health monitoring via nanosensors	Precise and minimally invasive	Power limitations in nanosensors, integration with IoMT required	Nano-biosensors in IoMT	Wearables, implants for real-time monitoring	Enhanced data accessibility and treatment response	Stability, Specificity
[82]	Non-invasive heavy metal detection in sweat	Easily accessible biomarkers, smartphone integration	Variability in sweat rate and sampling issues	Printed wearable microfluidic nanosensor	Sweat-based detection of metal ions	Increased accessibility for continuous health tracking	Sensitivity, Accuracy
[86]	Intelligent data management for health wearables	Optimized data handling, battery efficiency	Limited memory and data storage	Mobile-integrated nanosensors with HL7 standard	Patient data management in mobile devices	Streamlined healthcare data flow and reduced wait times	Response Time, Specificity
[88]	Wireless health monitoring in body area networks	Continuous monitoring, remote access	Privacy concerns, data security	Wireless Body Area Networks (WBAN)	Monitoring physiological parameters	Enhanced quality of care via real-time monitoring	Sensitivity, Stability
[94]	Development of electronic skin for health tracking	Flexible, self-healing, and energy-efficient	Complex fabrication, reliance on external power sources	Flexible electronic skins with energy harvesting	Biomedical and prosthetic devices	Expands wearable functionality and energy autonomy	Accuracy, Specificity

needs of healthcare centers can help improve the efficiency and quality of health services.

4.4. Infection monitoring and biosafety approach

Using nanosensors to monitor infections and increase biological immunity is vital in preventing and controlling infectious diseases. These sensors can quickly and with high sensitivity detect the presence of pathogenic agents such as viruses, bacteria, and biological toxins in the environment or body and provide the possibility of quick intervention. In hospital conditions, nanosensors can prevent the spread of hospital infections by momentarily monitoring the environment and surfaces and help maintain the safety of patients and medical staff. Also, as early warning systems, these in-body sensors can detect early signs of infection and optimize immune responses. By using advanced nanosensors, it is possible to continuously monitor parameters related to biological safety, which is of great importance in preventing epidemics and improving infection control in high-risk environments. Hence, we will analyze and describe the various implementation approaches for infection monitoring and biosafety using nanosensors.

Saylan and Denizli [84] conducted this research to investigate the use of nanosensors in detecting viruses in intelligent cities. This study discussed the importance of using nanosensors in the early detection of viruses, especially considering the speed of their changes and transmission from one person to another. The results showed that nanosensors make it possible to closely monitor various resources and services in smart cities and reduce the costs and time related to maintenance and inspections.

Younis et al. [85] conducted this research to investigate the application of nano biosensors in livestock management and improve livestock production. In this study, new biosensor techniques have been used to closely monitor animals' environmental and physiological factors, including health status, detection of pathogenic agents, and reproductive cycles. The results showed that nano biosensors could provide continuous and accurate monitoring of animals' feeding and grazing behavior, the side effects of antibiotics, and their environmental status

Postica et al. [90] conducted this research to investigate gas sensing characteristics at room temperature using gold nanoparticles (AuNPs) coating zinc oxide nanotubes (ZnO/NW). In this study, gold nanoparticles/zinc oxide nanotubes were deposited using the electrochemical method in a three-electrode electrochemical cell. Also, focused ion beam combined electron microscopy (FIB/SEM) has been used to integrate individual nanostructures into gas sensing devices. The results are promising and show that these devices can be helpful in future applications such as hydrogen gas (H2) monitoring for patients' breath analysis in the healthcare field.

Srivastava et al. [92] conducted this research to investigate the application of nanosensors and nano biosensors as an alternative to traditional measurement methods in the health and food sectors. In this study, metal nanoparticles, metal nanoclusters, metal oxide nanoparticles, metal and carbon quantum dots, graphene, carbon nanotubes, and nanocomposites are used to enhance sensitivity and incorporate innovative signal conversion principles such as electrochemical, optical, Raman amplification, catalytic activity, and superparamagnetic properties. The results showed that electrochemical, optical, electronic nose, electronic tongue, nano barcode technology, and wireless sensors have revolutionized monitoring in the health and food sectors with multiple capabilities and real-time measurements.

He et al. [96] conducted this research to investigate the application of nanosensor networks to detect human body injuries. In this study, nanosensors have been used to collect bioparameters of the damaged area of the body. A proposed architecture was designed for biomedical data processing through three structural layers: the sensing, networking, and application layers. These layers perform various data processing tasks to facilitate sensing, collecting, and analyzing vital signs.

Martins et al. [101] conducted this research to investigate the application of nanosensors in detecting viruses. In this study, recent advances in developing nanosensors for detecting viruses have been investigated. Nanosensors operate using biological components and can accurately and quickly detect viruses. The results showed that these technologies can replace the traditional and time-consuming virus detection methods in body fluids and cells. As a result, nanosensors have great potential for rapid and timely detection of viruses and reduce the challenges of late detection.

Table 8 comprehensively examines the goals, advantages, disadvantages, approach, application, impact on results, and evaluation metrics by focusing on techniques for infection monitoring and biosafety using nanosensors. The primary objective is to provide a comparative perspective on methods and results.

4.4.1. Summary and discussion

Table 8 provides a comparison of technical studies conducted on the use of nanosensors in infection monitoring and biosafety in healthcare settings, examining criteria such as objectives, advantages, disadvantages, methods, applications, and impacts on outcomes. These studies have used nanosensors and nano-biosensors as key technologies to increase the accuracy of diagnosis and real-time monitoring and improve the safety and quality of healthcare products. The advantages of these methods include cost and time savings through real-time monitoring, high sensitivity and accuracy, and the possibility of rapid analysis, which help improve patient care and prevent the spread of infection. The disadvantages of these methods include the need for continuous sensor upgrades, technical complexity in manufacturing, high initial costs, and resource constraints of the nanosensor network. The advancement of these technologies is essential for their wider applications and commercialization. Studies show that various methods, such as nanobiosensors for pathogen detection, gas sensors for respiratory analysis, and nanosensor networks for biological data collection, have been used, which indicates the diversity of applications of these technologies for various health purposes. Among the technologies used, gold nanoparticles, zinc oxide nanowires, nano-biosensors, and multilayer sensors can be mentioned, which enable rapid, accurate, and non-invasive diagnosis. Performance evaluation criteria include detection accuracy, response speed, reduction of the risk of infection spread, and improved safety of health products, which shows the importance of these criteria in improving the quality of health services and better control of health resources. Ultimately, the goals of these methods include continuous monitoring, rapid detection of infections, and improved safety in health products and environments, and the correct selection of these technologies based on the specific needs of health centers can help increase the efficiency and quality of care.

5. Discussion

This section investigates the goals, advantages, disadvantages, applications, and applications of nanosensors in health and analyzes their applications. This study aims to answer basic questions about the efficiency and limitations of these technologies in improving the diagnosis and treatment of diseases and to identify the related challenges accurately. Structured research questions are proposed to achieve these goals and provide a better understanding of this complex technology and its role in the health field. These questions are:

- TQ1: What are the main goals of using nanosensors in health care?
- TQ2: What are the key advantages of using nanosensors compared to traditional methods in healthcare?
- TQ3: What are the main disadvantages (challenges and limitations) of using nanosensors in healthcare?
- TQ4: What are the main ways to integrate manufacturing processes, structural optimization, and property-performance alignment to

 Table 8

 A comprehensive examination of nanosensor-based techniques for infection monitoring and biosafety: goals, advantages, disadvantages, approaches, applications, impact on results, and evaluation metrics.

Ref	Goals	Advantages	Disadvantages	Approach	Application	Impact on Results	Evaluation Metrics
[84]	Integration and monitoring of resources in intelligent cities	Cost and time reduction through real-time tracking, improved resource efficiency	Requires continuous sensor updates for accurate virus detection	Use of nanosensors for virus detection	Healthcare, transportation, infrastructure	Helps in faster detection and reducing disease spread through real-time monitoring	Stability
[85]	Monitoring patient health conditions	High sensitivity and accuracy, quick analysis, cost- effective	Commercialization challenges and initial costs	Nano biosensors for detecting pathogens and monitoring patient health status	Patient health monitoring and infection prevention	Enhances patient health monitoring and helps prevent infection spread in healthcare facilities	Sensitivity, Specificity
[90]	Gas sensors for respiratory analysis in healthcare	Room temperature operation, suitable for clinical breath analysis	Requires complex technology for production and installation	Gold nanoparticles and zinc oxide nanowires for gas sensors	Healthcare	It provides accurate respiratory monitoring and aids in quickly detecting respiratory issues.	Accuracy
[92]	Quality control and safety in healthcare products	High sensitivity, real- time monitoring, and cost reduction through nanoscale size	Challenges in translating methods from healthcare to hygiene products	Nanosensors and nano biosensors for detecting hygiene-related contaminants	Healthcare and hygiene products	Enhances hygiene product safety and reduces the risk of infection spread by detecting contaminants quickly	Sensitivity, Specificity
[96]	Injury detection in healthcare	Suitable for early and subtle injury detection, three-layer structure for data processing	Limited resources in nanosensor networks	Nanosensor networks for collecting and processing biophysical data	Healthcare	Improves accuracy and speed of injury detection, reducing unnecessary medical interventions	Response Time, Sensitivity
[101]	Virus detection in the body	High speed, accurate detection, usable with biological samples	Expensive and complex production processes	Nanobiosensors for detecting various viruses	Healthcare and viral diseases	Timely virus detection and reduced spread through effective and rapid diagnosis at early stages	Sensitivity, Specificity

enhance the design and application of nanosensors in medical technologies?

• TQ5: What recommendations can be made to improve the efficiency and effectiveness of nanosensors in healthcare?

The following section will provide detailed answers to the questions raised, and selected articles on using nanosensors in health care will be reviewed and analyzed. These articles are systematically evaluated to identify this technology's main goals, advantages, challenges, and limitations and provide recommendations to improve the efficiency and

effectiveness of nanosensors in diagnosing and treating diseases. The results of this analysis can contribute to a deeper understanding of the role of nanosensors in increasing the accuracy of diagnosis, speed, and quality of health services, as well as clarify the strengths and weaknesses of this new technology.

• TQ1: What are the main goals of using nanosensors in health care?

Fig. 4 shows a comparative analysis of the goals set for the use of nanosensors in the field of health care based on the proposed

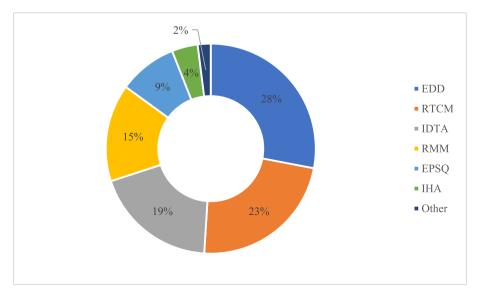


Fig. 4. The Comprehensive Goals of Using Nanosensor Technologies for Healthcare

classification. The proposed classification includes seven main categories: early disease detection (EDD), real-time and continuous monitoring (RTCM), improving diagnostic and therapeutic accuracy (IDTA), remote monitoring and management (RMM), enhancing product safety and quality (EPSQ), improving healthcare accessibility (IHA), and other purposes. Based on the analysis of this classification, the percentages of targets related to EDD, RTCM, IDTA, RMM, EPSQ, IHA, and Other are 28 %, 23 %, 19 %, 15 %, 9 %, 4 %, and 2 %, respectively. This figure shows that most identified targets are related to EDD, which includes 28 % of the identified targets.

• TQ2: What are the key advantages of using nanosensors compared to traditional methods in healthcare?

Fig. 5 shows a comparative analysis of the advantages of nanosensors in healthcare based on the proposed classification. The proposed classification includes seven main categories: High Sensitivity and Accuracy (HSA), Continuous and Rapid Monitoring (CRM), Non-invasive and Convenient (NIC), Enhanced Therapeutic Decision-making (ETD), Improved Accessibility and Cost-effectiveness (IACE), Reduced Equipment Complexity (REC), and other advantages. Based on this classification, the percentage of advantages attributable to HSA, CRM, NIC, ETD, IACE, REC, and O are 30 %, 25 %, 18 %, 14 %, 8 %, 3 %, and 2 %, respectively. This figure shows that most advantages are related to HSA, accounting for 30 % of the identified advantages.

• TQ3: What are the main disadvantages (challenges and limitations) of using nanosensors in healthcare?

Fig. 6 shows a comparative analysis of the objectives for using nanosensor techniques in healthcare. The proposed classification includes seven main categories: High Cost and Commercialization Challenges (HCCC), Complexity and Controlled Environments (CCE), Accuracy and Stability Limitations (ASL), Security and Privacy Concerns (SPC), Technical and Engineering Limitations (TEL), Interference and Environmental Sensitivity (IES), and Other. Based on the analysis of this classification, the percentage of targets related to CCE, ASL, HCCC, SPC, TEL, IES, and Other are 32 %, 20 %, 15 %, 12 %, 9 %, 7 %, and 5 %, respectively. This analysis shows that the most significant challenges are technical complexities and the need for controlled environments. Hence, this highlights the need to optimize nanosensor technology for practical applications in different conditions.

Based on Fig. 7, the review and analysis of the reviewed research

shows that using nanosensors has increased the accuracy of disease diagnosis (ADD) by 35 % and improved the quality of personal health monitoring (PHM) by 23 %. Also, this technology has reduced diagnostic response time (DRT) by 21 % and optimized real-time data processing (RTDP) by 11 %. In addition, these methods have increased the success rate of early disease interventions (EDI) by 10 %.

 TQ4: What are the main ways to integrate manufacturing processes, structural optimization, and property-performance alignment to enhance the design and application of nanosensors in medical technologies?

Nanosensors, as one of the advanced technologies in nanoscience, offer unique capabilities in the diagnosis, monitoring, and management of diseases. The performance of these devices is highly dependent on their manufacturing methods, nanoscale structure, and physical and chemical properties. A deep understanding of the relationships between the manufacturing processes, structure, properties, and performance of nanosensors can lead to optimized design and development of new generations of this technology. These relationships are not only effective in improving the sensitivity and accuracy of devices but also offer new avenues for the use of nanosensors in medical and biological applications. In the following, these relationships are examined in detail to define principles for future designs.

- Nanosensor Fabrication and Production Methods: The development and production of nanosensors are highly dependent on technological advances in the fabrication and processing methods of nanostructured materials. Methods such as nanoscale lithography, chemical vapor deposition (CVD), and the use of nanostructured materials such as carbon nanotubes, quantum dots, and metal nanoparticles have provided new capabilities for the fabrication of sensitive and accurate nanosensors. For example, the use of metal nanoparticles with precise surface engineering capabilities has led to improved sensing performance and increased sensitivity of nanosensors. These advanced fabrication methods not only enable the production of high-precision nanostructured devices but also lead to the design of sensors with unique performance and stability characteristics that are of great importance in medical and health applications [103].
- Effect of nanosensor structure on properties: The structure of nanosensors is known to be one of the key factors in determining their functional properties. For example, the use of multilayer

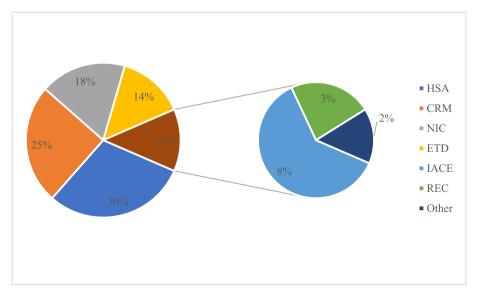


Fig. 5. The Comprehensive Advantages of Using of Using Nanosensor Technologies for Healthcare

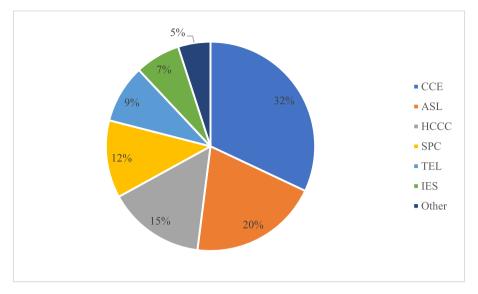


Fig. 6. The Comprehensive Disadvantages of Using of Using Nanosensor Technologies for Healthcare.

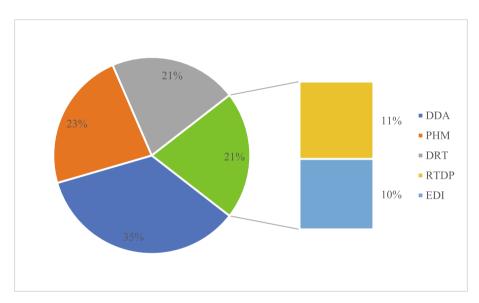


Fig. 7. Impact of Nanosensor Implementation on Key Healthcare Metrics.

nanostructures in the design of nanosensors can lead to improved sensitivity and selectivity, as these structures can amplify biological signals and minimize unwanted interferences. In addition, surface properties such as surface energy and electric potential distribution play an important role in improving molecular interactions at the sensor surface. By carefully engineering nanoscale structures, unique properties such as increased response speed, thermal and chemical stability, and high selectivity can be achieved, and these have wide applications in sensitive fields such as early diagnosis of diseases [104].

• Structure-function relationships for future designs: Understanding the relationship between structure, properties, and performance of nanosensors is crucial for the design and development of new generations of this technology. Advanced simulations and experimental tests can help analyze these relationships and deeply establish principles for performance-based design. For example, changing the nanoscale structure and optimizing properties such as surface-to-volume ratio or particle distribution can lead to improved sensing performance in complex biological environments. Furthermore, developing theoretical frameworks to predict and tune these

relationships paves the way for the design of novel nanosensors with specific applications. This approach not only improves the performance of current devices but also allows for innovation in future designs and helps to improve overall diagnostic and therapeutic systems [105].

Table 9 provides a comprehensive comparison based on parameters such as Production Processes, Structural Features, Key Properties, and Final Performance. The purpose of this table is to evaluate the techniques, Biocompatibility, Functional Optimization, Stability and Durability, Environmental Adaptability, Innovative Methods, Evaluation and Optimization, and Economic Feasibility of nanosensors in personal health applications. This comparison examines the impact of each of these parameters on the overall performance of nanosensors, including sensitivity, reliability, clinical usability, and economic feasibility.

5.1. Quantitative comparison of nanosensor performance

Nanosensors, as one of the most advanced technologies in the field of nanotechnology, play a fundamental role in improving diagnostic

Table 9Comparison of Key Parameters in Nanosensor Development for Personal Health Applications.

		- 11		
Comparison Axis	Production Processes	Structural Features	Key Properties	Final Performance
Techniques	Photolithography, Chemical Vapor Deposition (CVD), 3D Nano Printing	Porous structures, Carbon nanotubes, Quantum dots	High reactivity, Large effective surface area, High electrical conductivity	Fast and sensitive detection, Long-term stability
Biocompatibility	Surface modification, Coating with biocompatible polymers	Surfaces coated with biocompatible polymers, Biologically compatible compositions	Reduced immune responses, Enhanced biological stability	Increased clinical applicability
Functional Optimization	Molecular self-assembly, Layer deposition techniques	Increased structural homogeneity, Reduced defects	High sensitivity, Reduced diagnostic errors	Improved diagnostic accuracy
Stability and Durability	Use of robust nanostructured materials	Resistance to degradation in biological environments	Extended operational lifespan, Stable performance	Reduced replacement and maintenance costs
Environmental Adaptability	Tailoring surface properties for environmental tolerance	Nanostructures resistant to temperature and humidity variations	Sustained sensitivity under variable environmental conditions	Enhanced reliability in clinical settings
Innovative Methods	Inkjet printing, Nanofabrication	Flexible nanostructures, Adaptable to complex conditions	Reactivity in challenging environments, Rapid recovery capabilities	Real-time detection
Evaluation and Optimization	Advanced techniques like FTIR and XPS	Surface morphology and internal structure analysis	High sensitivity and selectivity indices	Improved operational applicability in clinical environments
Economic Feasibility	Cost reduction through optimized manufacturing processes	Simpler and more cost-effective structures	Reduced total production and application costs	Increased accessibility in personalized medicine

processes and health monitoring. A close examination of the performance of these sensors shows that the materials used, structural features, and sensing mechanisms have a direct impact on their efficiency and application. As can be seen in the table, gold nanoparticles are ideal for real-time applications such as glucose monitoring and breath analvsis due to their rapid response to chemical changes and high sensitivity. In contrast, carbon nanotubes are considered a suitable option for smart wearable devices due to their easy connectivity to digital systems and the Internet of Things (IoT). These differences indicate the importance of selecting materials based on the specific needs of each application, especially in areas where speed, accuracy, and integration are crucial. On the other hand, properties such as biostability and environmental compatibility play a key role in expanding the use of nanosensors in biological environments. For example, biocompatible coatings have enabled sensors with intrabody applications, which are well suited for medical implants, by reducing immune responses and increasing durability in biological environments. However, these types of sensors may require further structural modifications in more complex environments. From an economic perspective, simpler nanocoatings are a suitable option for the development of cost-effective medical devices due to their reduced production cost and easier fabrication processes. These data not only demonstrate the unique advantages of each technology but also highlight existing limitations and the need for further optimization in the design and fabrication of nanosensors for clinical and medical applications [106].

Table 10 is designed to provide a comprehensive and quantitative comparison of nanosensor performance in various medical and diagnostic applications. The table reviews key characteristics of nanosensors based on material type, key features, applications, advantages, and

limitations. The main goal of this comparison is to identify the strengths and weaknesses of different nanosensor technologies and provide comprehensive insight into the selection of the most appropriate materials and manufacturing methods for specific applications. The results of this analysis help make informed decisions about material selection and the design of nanosensor systems and suggest strategies to improve performance, reduce costs, and increase the applicability of this technology in clinical and medical settings.

5.2. New manufacturing methods in nanosensors for healthcare

In the healthcare field, the use of porous laser-induced graphene foam nanocomposites is one of the important advances in the development of low-cost nanosensors. These materials, which have properties such as high electrical conductivity, porous structure, and ability to adsorb biomolecules, have been widely used in the design of medical nanosensors. The porous structure of these materials has increased the sensitivity of the sensors and enhanced the ability to detect target molecules at very low concentrations, which is essential for applications such as early detection of diseases or continuous monitoring of vital signs. In addition, the low cost of production of these materials has enabled their use in wearable systems and portable medical devices, which can improve access to advanced medical devices. On the other hand, advances in manufacturing methods such as 3D printing and precision layering have enabled the production of flexible biosensors that are compatible with complex body surfaces. For example, 3D printing plays a key role in the development of wearable nanosensors due to its ability to design custom structures and produce devices at minimal cost. These sensors can be embedded directly on the skin or in

Table 10Key Criteria, Materials, and Applications of Nanosensors in Healthcare.

Criterion	Material Type	Key Features	Applications	Advantages	Limitations
High Sensitivity	Quantum Dots	Large surface area, optical sensitivity	Early cancer detection, enzyme monitoring	Detects extremely low concentrations of biomolecules	High sensitivity to light and unstable environments
Fast Response Time	Gold Nanoparticles	Rapid reaction to chemical changes	Real-time glucose monitoring, breath analysis	Quick response, suitable for real- time sensors	Complex manufacturing process, high cost
Biological Stability	Biocompatible Nanocoatings	Resistance to biological degradation	In vivo applications	Long-lasting stability in biological environments	Limited adaptability to all biological settings
Integration Ability	Carbon Nanotubes	Easy integration with digital systems	Wearable devices, IoT systems	Seamless connectivity with electronic devices	Sensitivity to environmental and temperature changes
Low Cost	Simple Nanocoatings	Simpler fabrication process	Cost-effective medical devices	Reduces production cost and broadens accessibility	Lower performance in advanced applications
High Biocompatibility	Biocompatible Polymers	Non-immunogenic properties	Medical implants, biosensors	Reduces side effects, suitable for long-term use	Complexity in coating processes

bioimplants to accurately monitor parameters such as blood sugar, blood pressure, or cancer-related biomarkers. In addition, precise layering has enabled the production of small, environmentally friendly sensors that are used in applications such as long-term monitoring of vital signs and optimizing personalized treatments for patients. These advances not only promise to improve the quality of medical care but can also reduce the costs of health systems and help improve access to advanced services [107,108].

6. Recommendation of the application of nanosensors in healthcare

The use of nanosensors in health care as one of the new and advanced technologies has a significant potential to improve the processes of diagnosis, monitoring, and treatment of diseases. Due to the ability to identify biological changes at the molecular and chemical level, these tiny and accurate sensors allow early diagnosis of diseases and allow doctors to assess the health status of patients more accurately and quickly. In addition, nanosensors are influential in improving healthcare quality in continuous and real-time monitoring of vital signs. Due to its high sensitivity and the ability to accurately separate biological data, this technology can help reduce diagnostic errors and optimize the treatment process. Considering the growing need for more accurate and less expensive systems in the health field, the use of nanosensor-based approaches as an advanced and specialized solution to improve the performance of health systems has been considered. However, there are many challenges in implementing this process in the health field. Therefore, in the following, we will provide suggestions in the form of answers to TQ5, which can significantly help researchers in this field. Also, in this section's continuation, we will examine the existing open

- TQ5: What recommendations can be made to improve the efficiency and effectiveness of nanosensors in healthcare?
 - > Enhancing Sensitivity and Selectivity of Nanosensors: Increasing the sensitivity and selectivity of nanosensors is one of the most critical factors in improving their applications in the health field. These sensors should accurately identify disease-related biomarkers among different body factors. Hence, using advanced nanomaterials such as carbon nanotubes, quantum dots, and engineered metal nanoparticles, nanosensors can amplify the weak signals of target molecules and reduce the interfering effects of other materials. These improvements allow for more accurate diagnosis of diseases even in the early stages, thereby helping to improve treatments and increase the chances of success in disease control.
 - > Improving Biocompatibility of Nanosensors: nanosensors are very important for clinical use because their direct interaction with cells and body tissues may cause adverse immune reactions. Biocompatible coating materials and nanostructured methods minimize inflammation and unwanted reactions and improve biocompatibility. These materials can be placed on implantable and wearable sensors to ensure they remain stable in the body and perform their function without triggering the immune system. These solutions are precious for long-term use and patients with chronic diseases requiring continuous monitoring.
 - > Reducing Response Time of Nanosensors: Reducing the response time of nanosensors is very important for times when fast diagnosis is needed, especially in emergencies or for vital patient monitoring. Optimization of nanosensor structures can accelerate their response to changes in the concentration of surrounding substances. The use of materials that have a higher speed of penetration and interaction with the target molecules, as well as new designs to reduce the size and dimensions of the sensor, can help reduce the response time. These improvements

- are helpful for rapid identification of infections, emergency changes in patient status, and other critical conditions.
- > Developing Cost-effective Fabrication Techniques: The high cost of manufacturing nanosensors is one of the main obstacles to their widespread use in medical and monitoring centers. To solve this problem, new production methods such as nanostructured creation, mass production with automated techniques, and using cheaper materials as substitutes for complex nanomaterials can be effective. These solutions reduce the cost of production and improve access to nanosensors for hospitals and health centers. As a result, nanosensor technology can be applied on a larger scale and even in areas with limited financial resources, which helps to develop clinical applications of this technology worldwide.
- ➤ Enhancing Stability and Durability in Variable Environments: One of the main challenges in working with nanosensors is their stability and durability in different environmental conditions. Nanosensors are usually exposed to temperature, humidity, and other ecological changes that can affect their accuracy and performance. Using materials that have high resistance to environmental changes, such as temperature-resistant nanoparticles or reinforced polymers, can guarantee the performance of sensors in harsh conditions. In addition, designing the sensors to be self-adjusting allows them to provide accurate results without the need for frequent calibration. These improvements can make using nanosensors in various environments, from hospitals to research centers, more feasible and reliable.
- > Integrating Nanosensors with Digital Health Systems: Nanosensors with digital health systems can increase efficiency and speed in diagnosing and managing medical conditions. These sensors can be connected to data analysis and health monitoring systems and record and send vital patient body information in real-time. With the help of Internet of Things (IoT) systems and cloud infrastructure, sensor data can be quickly transferred to medical centers, making the monitoring process more accessible for doctors and patients. These strategies benefit chronic patients who require continuous monitoring and enable improved clinical decision-making and treatment management.
- > Addressing Data Security and Privacy Concerns: Due to the high sensitivity of health and medical data, the security and privacy of the data produced by nanosensors are essential. Nanosensors record patients' vital biological and medical information, which requires protection against unauthorized access and misuse. Advanced encryption protocols, data storage in secure servers, and authentication methods can ensure the security of this data. With the implementation of these measures, the trust of patients and medical centers in the technology of nanosensors will increase, and the use of this technology in health systems will expand.
- > Advancing Regulatory and Standardization Efforts: Establishing strict standards and regulations for nanosensors can smooth the path of development and commercialization of this technology in the health field. Due to their technical complexity and high accuracy, nanosensors require special rules and standards to ensure their efficiency and security. Developing standards for testing, validating, and monitoring nanosensors can help users and healthcare organizations use these sensors more confidently. These measures can also help reduce operational costs, improve the quality of health services, and strengthen public trust in nanosensor technology.

6.1. Open issues

With the development of nanoscale technologies, nanosensors have become one of the critical tools in healthcare, and they have great potential to improve diagnostic and therapeutic processes with accurate detection and real-time monitoring capabilities. This emerging technology enables the detection and monitoring of biological molecules at the cellular level and helps doctors to be more efficient in the early diagnosis and management of diseases. However, the implementation of nanosensors in clinical applications and medical monitoring faces complex challenges that require detailed research and innovative solutions. In the following, we will examine the most critical issues and open challenges in this field that must be overcome to realize the full potential of this technology. The following discusses some of this field's most critical open issues.

- >> Sensitivity and Interference in Complex Biological Environments: One of the critical challenges for nanosensors in complex biological environments is achieving high sensitivity in accurately detecting target molecules without causing interference with other molecules and compounds. The body environment contains various combinations of proteins, ions, and other biomolecules that can affect the measurement results and lead to detection errors. Hence, to solve this problem, it is necessary to equip nanosensors with more selective materials and coatings to react only to specific target molecules. Therefore, this requires research and development in designing nanosensor coatings and using new nanomaterials with high selectivity properties.
- ➤ Long-term Stability and Biocompatibility: Biocompatibility and long-term stability of nanosensors are critical issues in clinical applications. Nanosensors should be able to remain in the body for a long time without degradation or loss of performance. Still, using nanomaterials in living environments may cause adverse immune reactions or the formation of biofilms, which can lead to sensor degradation and decrease efficiency. These challenges indicate the need to design biocompatible and stable protective coatings that can survive physiological conditions and prevent inflammatory reactions.
- > Data Security and Privacy in Healthcare Applications: Protecting the security and privacy of data in nanosensors in medical applications is a significant challenge due to the high sensitivity of medical information. Data generated by nanosensors are often transferred to cloud systems or other devices, which are vulnerable to unauthorized access and intrusion. To ensure this data's security, robust cryptographic protocols and advanced authentication methods are needed. Hence, this is especially necessary to increase patient trust in health monitoring systems and increase information security using the Internet of Things (IoT) in medicine.
- ➤ Integration Challenges with Existing Healthcare Infrastructure:

 Coordination and integration of nanosensors with existing healthcare infrastructure, such as electronic patient record systems (EHR), is a severe challenge. Due to their high accuracy and sensitivity, nanosensors generate significant continuous and timed data, which requires large-scale processing and storage. Reconciling these data with current systems requires a more robust infrastructure, data processing software, and rigorous integration protocols. The development of these infrastructures and their integration with existing health networks requires extensive investment and research in medical engineering and data science.
- ➤ Cost and Scalability of Nanosensor Production: The high cost of nanosensor production and scalability problems are severe obstacles to widespread use in healthcare systems. Nanoscale manufacturing processes are usually complex and expensive, and the limitations of mass production can limit the application of this technology to specialized environments. Hence, more cost-effective techniques, such as nanostructured printing and automated fabrication, are needed to solve this challenge, enabling mass-scale nanosensor production at reduced costs.
- Ethical and Regulatory Frameworks for Clinical Use: Nanosensors in clinical applications require legal and ethical frameworks that provide standards and detailed guidelines to ensure their safety

and efficiency. Since nanosensors interact directly with the patient's body, necessary tests and approvals must be performed to avoid side effects and unknown risks. Developing these regulatory frameworks and international standards in cooperation with health and government institutions can contribute to the general acceptance of this technology and reduce patient concerns.

6.2. Future direction

One of the new approaches in the development of nanosensors is the design and fabrication of multi-mode sensors with decoupled sensing mechanisms. These sensors' ability to simultaneously detect different parameters in complex environments allows for improved accuracy and reduced signal interference. Recent research has shown that combining advanced nanomaterials such as carbon nanotubes and quantum dots with optimized electronic circuit designs can help improve the performance of these sensors. For example, in biological monitoring systems, the use of signal separation mechanisms can minimize interference between parameters such as temperature, pressure, and chemical compounds and increase measurement accuracy under real-world conditions. The future horizons of multi-mode nanosensors lie not only in improving the performance of current devices but also in creating new systems with broader applications. For example, these sensors can play a key role in wearable medical devices, smart environmental monitoring, and advanced security systems. Recent studies have shown that multimode sensors are capable of detecting gaseous compounds in the presence of other environmental factors, which is very effective in controlling air quality and detecting hazardous pollutants. Also, advances in deposition techniques and nanostructure design have enabled the fabrication of sensors with high sensitivity and integration capabilities in multifunctional systems. To further develop this technology, it is suggested that future research should focus on combining advanced materials and artificial intelligence-based data processing methods. The use of machine learning algorithms for simultaneous analysis of multimode data can significantly increase the accuracy and speed of detection. Also, the development of new methods to reduce energy consumption and improve the stability of sensors in complex environments are among the issues that should be considered. Finally, strengthening interdisciplinary collaborations between experts in materials science, electronic engineering, and life sciences can lead to the creation of a new generation of multi-mode nanosensors with unique capabilities.

7. Conclusion

In healthcare, nanosensors are an advanced and vital tool in improving the accuracy and speed of disease diagnosis and health status monitoring. Due to the ability to detect molecular and cellular changes at the nanoscale, these sensors can accurately identify disease biomarkers even in the early stages and provide detailed information about the body's physiological state, especially in complex and costly diseases such as cancer. However, using nanosensors has several challenges, including biocompatibility issues, long-term stability in biological environments, and immune reactions, which can limit their productivity and effectiveness. The present article takes a comprehensive and systematic look at the application of nanosensors in health. While identifying the existing challenges, it has evaluated this technology's innovations and new methods. The main goal of this study is to provide a deep understanding of the effects of nanotechnology on improving diagnostic accuracy, reducing response time, and reducing costs associated with diagnostic and therapeutic processes. Based on the analysis, using nanosensors has increased the accuracy of disease diagnosis (ADD) by 35 % and improved the quality of personal health monitoring (PHM) by 23 %. Also, this technology has reduced diagnostic response time (DRT) by 21 % and optimized real-time data processing (RTDP) by 11 %. In addition, these methods have increased the success rate of early disease interventions (EDI) by 10 %. Finally, by providing practical recommendations and identifying open issues, this research provides the basis for further and more effective development of the application of nanosensors in the field of health care. Focusing on improving biocompatibility and sustainability and reducing production costs can facilitate the broader use of this technology in healthcare systems and help improve the quality of health services.

Ethical statement

According to Finnish legislation, register studies do not require approval by a hospital ethics committee.

CRediT authorship contribution statement

Mohsen Ghorbian: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. Mostafa Ghobaei-Arani: Writing – review & editing, Visualization, Validation, Supervision, Software, Project administration, Conceptualization. Mohamad Reza Babaei: Writing – original draft, Visualization, Data curation, Conceptualization. Saeid Ghorbian: Writing – review & editing, Visualization, Validation, Supervision, Software, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

This article did not analyze any specific data sets.

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