Review of Contemporary Philosophy
ISSN: 1841-5261, e-ISSN: 2471-089X
Vol 23 (2), 2024
Pp 1000 - 1012

Epigenetic Biomarkers in Chronic Disease Progression: Applications for Personalized Care Plans by General Physicians and Nurses in Saudi Arabia's Vision 2030 Healthcare Model

[1]Sanad Khemais Alshammari,[2]Hamoud Mukhlid Aldhafeeri,[3]Mersal Majed Mersal Aldfery,[4]Ahmed Sanad Aldafeeriy ,[5]Fatimah Fayez Alouslb,[6]Amal Fayez Alaslab,[7]Mohamed Mubark Aldafeeri,[8]Mohammad Fhaid Gaith Almutairi

[1] Internal Medicine
[2] General Physician
[3] Nursing
[4] Long-Term Care
[5] Nursing
[6] Nursing
[7] Nurse Assistant
[8] Nursing Specialist

Abstract

The Kingdom of Saudi Arabia's Vision 2030 healthcare model emphasizes the importance of personalized medicine in addressing the growing burden of chronic diseases. Epigenetic biomarkers have emerged as promising tools for disease risk prediction, early diagnosis, and targeted interventions in chronic conditions such as cardiovascular diseases, cancer, and diabetes. This review explores the potential applications of epigenetic biomarkers in personalized care plans delivered by general physicians and nurses in Saudi Arabia. We conducted a comprehensive literature search of relevant databases and selected studies based on predefined inclusion criteria. The quality of the included studies was assessed using standardized tools, and the data were extracted and synthesized using a narrative approach. The findings highlight the role of epigenetic biomarkers in identifying high-risk individuals, guiding treatment decisions, and monitoring disease progression and treatment response. We also discuss the challenges and opportunities for integrating epigenetic biomarkers into clinical practice, including the need for standardized protocols, training of healthcare professionals, and ethical considerations. The review provides recommendations for policy, practice, and research to support the implementation of epigenetic biomarkers in personalized care plans in Saudi Arabia's Vision 2030 healthcare model.

Keywords: epigenetics, biomarkers, chronic diseases, personalized medicine, general physicians, nurses, Saudi Arabia, Vision 2030

Received: 10 October 2024 **Revised**: 24 November 2024 **Accepted**: 08 December 2024

1. Introduction

Chronic diseases, such as cardiovascular diseases, cancer, diabetes, and respiratory diseases, are the leading causes of morbidity and mortality worldwide, accounting for over 70% of all deaths (World Health Organization, 2021). In Saudi Arabia, chronic diseases are a major public health challenge, with a rapidly increasing prevalence due to factors such as an aging population, unhealthy lifestyles, and environmental exposures (Al-Hanawi et al., 2019). The Kingdom's Vision 2030 strategic plan recognizes the importance of addressing the burden of chronic diseases through a comprehensive and personalized approach to healthcare (Vision 2030, n.d.).

Personalized medicine is an emerging paradigm that aims to tailor prevention, diagnosis, and treatment strategies to an individual's unique genetic, epigenetic, and environmental profile (Kronfol et al., 2017). Epigenetic biomarkers have gained increasing attention as promising tools for personalized medicine, as they can provide insights into the complex interplay between genes and the environment in the development and progression of chronic diseases (García-Giménez et al., 2017).

Epigenetics refers to the study of heritable changes in gene expression that occur without alterations in the DNA sequence (Rodríguez-Paredes & Esteller, 2011). Epigenetic mechanisms, such as DNA methylation, histone modifications, and non-coding RNAs, regulate gene expression in response to environmental factors, such as diet, stress, and toxins (Berdasco & Esteller, 2018). Epigenetic alterations have been implicated in the pathogenesis of various chronic diseases, and they can serve as biomarkers for disease risk, diagnosis, prognosis, and treatment response (Baccarelli & Ordovás, 2023).

General physicians and nurses play a crucial role in the prevention, early detection, and management of chronic diseases in primary care settings (Al-Homayan et al., 2013). The integration of epigenetic biomarkers into personalized care plans delivered by these healthcare professionals can potentially improve patient outcomes and reduce healthcare costs (Carlota, 2023). However, the implementation of epigenetic biomarkers in clinical practice faces several challenges, such as the lack of standardized protocols, the need for training and education of healthcare professionals, and ethical and social considerations (Jeremias et al., 2020).

This review aims to explore the potential applications of epigenetic biomarkers in personalized care plans delivered by general physicians and nurses in Saudi Arabia's Vision 2030 healthcare model. The specific objectives are:

1. To identify the role of epigenetic biomarkers in the prevention, diagnosis, prognosis, and treatment of chronic diseases.
2. To discuss the challenges and opportunities for integrating epigenetic biomarkers into clinical practice in Saudi Arabia.
3. To provide recommendations for policy, practice, and research to support the implementation of epigenetic biomarkers in personalized care plans in Saudi Arabia's Vision 2030 healthcare model.

The findings of this review will inform policymakers, healthcare professionals, and researchers on the current state of knowledge and future directions for the application of epigenetic biomarkers in personalized medicine in Saudi Arabia, and their potential to improve the prevention and management of chronic diseases in line with the Vision 2030 goals.

2. Literature Review

2.1 Epigenetics and Chronic Diseases

Epigenetic mechanisms play a crucial role in the regulation of gene expression and the maintenance of cellular identity and function (Rodríguez-Paredes & Esteller, 2011). Epigenetic alterations, such as changes in DNA methylation patterns, histone modifications, and non-coding RNA expression, can occur in response to environmental factors and contribute to the development and progression of chronic diseases (Berdasco & Esteller, 2018).

Several studies have identified epigenetic alterations associated with various chronic diseases, such as cardiovascular diseases (Baccarelli & Ordovás, 2023), cancer (Jung et al., 2020), diabetes (Liu et al., 2022), and neurodegenerative diseases (Martínez-Iglesias et al., 2021). For example, a systematic review by Soler-Botija et al. (2019) found that DNA methylation changes in specific genes, such as ALOX12, ABCA1, and SREBF1, were associated with an increased risk of atherosclerosis and coronary artery disease. Another study by Sapienza et al. (2011) identified DNA methylation differences between diabetes patients with and without end-stage renal disease, suggesting that epigenetic alterations may contribute to the development of diabetic nephropathy.

Epigenetic alterations can also serve as biomarkers for disease risk, diagnosis, prognosis, and treatment response (García-Giménez et al., 2017). For example, a systematic review by Barchitta et al. (2019) found that DNA methylation changes in specific genes, such as SEPT9, MLH1, and MGMT, were associated with the development and progression of colorectal cancer and could be used as biomarkers for early detection and treatment selection. Another study by Giacopelli et al. (2019) identified DNA methylation subtypes in chronic lymphocytic leukemia that were associated with different clinical outcomes and could guide personalized treatment decisions.

Table 1. Examples of Epigenetic Alterations Associated with Chronic Diseases

Disease	Epigenetic Alteration	Associated Genes	Reference
Cardiovascular diseases	DNA methylation	ALOX12, ABCA1, SREBF1	Soler-Botija et al. (2019)
Diabetes	DNA methylation	-	Sapienza et al. (2011)
Colorectal cancer	DNA methylation	SEPT9, MLH1, MGMT	Barchitta et al. (2019)
Chronic lymphocytic leukemia	DNA methylation subtypes	-	Giacopelli et al. (2019)

2.2 Epigenetic Biomarkers in Personalized Medicine

Personalized medicine aims to tailor prevention, diagnosis, and treatment strategies to an individual's unique genetic, epigenetic, and environmental profile (Kronfol et al., 2017). Epigenetic biomarkers have the potential to advance personalized medicine by providing insights into the complex interplay between genes and the environment in the development and progression of chronic diseases (García-Giménez et al., 2017).

Several studies have explored the applications of epigenetic biomarkers in personalized medicine for various chronic diseases. For example, a review by Schiano et al. (2020) discussed the potential of epigenetic biomarkers in guiding personalized therapy for major cardiovascular diseases, such as heart failure and atrial fibrillation. The authors highlighted the role of epigenetic biomarkers in identifying patients who may benefit from specific therapies, such as histone deacetylase inhibitors or DNA methylation inhibitors, based on their epigenetic profile.

Another study by Hussain et al. (2021) reviewed the recent advancements in epigenetic therapies and biomarkers for cancer treatment. The authors discussed the potential of epigenetic biomarkers, such as DNA methylation and histone modifications, in predicting response to epigenetic therapies, such as histone deacetylase inhibitors and DNA methyltransferase inhibitors, and guiding the selection of personalized treatment regimens.

Epigenetic biomarkers can also be used to monitor disease progression and treatment response in personalized care plans. For example, a study by Bedon et al. (2021) developed a novel epigenetic machine learning model to predict the risk of progression for hepatocellular carcinoma patients based on their DNA methylation profile. The model could potentially be used to guide personalized surveillance and treatment strategies for patients at different risk levels.

Table 2. Examples of Epigenetic Biomarkers in Personalized Medicine

Disease	Epigenetic Biomarker	Application	Reference
Cardiovascular diseases	DNA methylation, histone modifications	Guiding personalized therapy (e.g., histone deacetylase inhibitors, DNA methylation inhibitors)	Schiano et al. (2020)
Cancer	DNA methylation, histone modifications	Predicting response to epigenetic therapies (e.g., histone deacetylase inhibitors, DNA methyltransferase inhibitors)	Hussain et al. (2021)
Hepatocellular carcinoma	DNA methylation	Predicting risk of progression and guiding personalized surveillance and treatment strategies	Bedon et al. (2021)

2.3 Challenges and Opportunities for Integrating Epigenetic Biomarkers into Clinical Practice in Saudi Arabia

The integration of epigenetic biomarkers into clinical practice in Saudi Arabia faces several challenges and opportunities. One of the main challenges is the lack of standardized protocols and guidelines for the collection, processing, and analysis of epigenetic biomarkers (García-Giménez et al., 2017). This can lead to variability in the quality and reproducibility of epigenetic data and limit their clinical utility.

Another challenge is the need for training and education of healthcare professionals, including general physicians and nurses, on the principles and applications of epigenetics in personalized medicine (Jeremias et al., 2020). This requires the development of curricula and continuing education programs that cover the basic concepts of epigenetics, the interpretation of epigenetic data, and the ethical and social implications of epigenetic testing.

Ethical and social considerations, such as informed consent, data privacy and security, and access to epigenetic testing and interventions, also need to be addressed in the implementation of epigenetic biomarkers in clinical practice (Jeremias et al., 2020). This requires the development of regulatory frameworks and policies that ensure the responsible and equitable use of epigenetic information in healthcare.

Despite these challenges, there are also opportunities for integrating epigenetic biomarkers into clinical practice in Saudi Arabia. The Kingdom's Vision 2030 strategic plan emphasizes the importance of preventive care, early diagnosis, and personalized medicine in addressing the burden of chronic diseases (Vision 2030, n.d.). This provides a supportive policy environment for the development and implementation of epigenetic biomarkers in healthcare.

Moreover, Saudi Arabia has a high prevalence of consanguinity and genetic disorders, which can increase the risk of chronic diseases and the need for personalized approaches to prevention and treatment (Younis et al., 2022). Epigenetic biomarkers can potentially provide insights into the gene-environment interactions that contribute to the development of these conditions and guide targeted interventions.

Saudi Arabia also has a growing digital health infrastructure, including electronic health records and telemedicine services, which can facilitate the integration of epigenetic data into clinical decision-making and personalized care plans (Qaffas et al., 2020). This can improve the accessibility and efficiency of epigenetic testing and interventions, particularly in remote and underserved areas.

3. Methods

3.1 Search Strategy

A comprehensive literature search was conducted in September 2023 using the following electronic databases: PubMed, Scopus, Web of Science, and Google Scholar. The search strategy included a combination of keywords and MeSH terms related to epigenetics, biomarkers, chronic diseases, personalized medicine, general physicians, nurses, and Saudi Arabia, such as "epigenetics," "biomarkers," "chronic diseases," "personalized medicine," "general physicians," "nurses," "Saudi Arabia," and "Vision 2030." The search was limited to English-language articles published between 2010 and 2023. The reference lists of the included articles were also hand-searched for additional relevant studies.

3.2 Study Selection and Eligibility Criteria

The study selection process was conducted in two stages. First, the titles and abstracts of the retrieved articles were screened independently by two reviewers for relevance and eligibility based on the following inclusion criteria:

- Original research articles (quantitative, qualitative, or mixed-methods)
- Reviews or systematic reviews
- Studies focusing on epigenetic biomarkers in chronic diseases
- Studies discussing the applications of epigenetic biomarkers in personalized medicine
- Studies conducted in Saudi Arabia or relevant to the Saudi healthcare system

Articles were excluded if they were:

- Editorials, commentaries, or conference abstracts
- Studies focusing on non-epigenetic biomarkers or non-chronic diseases
- Studies conducted in other countries with limited relevance to the Saudi context
- Studies published before 2010 or in languages other than English

Second, the full texts of the potentially eligible articles were reviewed independently by the same reviewers for final inclusion. Any discrepancies between the reviewers were resolved through discussion and consensus.

3.3 Data Extraction and Synthesis

The following data were extracted from the included studies using a standardized form: author(s), year of publication, study design, sample size, setting, epigenetic biomarker(s) studied, chronic disease(s) studied, key findings, and implications for personalized medicine and clinical practice in Saudi Arabia.

The data were synthesized using a narrative approach, which involved a descriptive summary and interpretation of the findings, taking into account the quality and heterogeneity of the studies (Popay et al., 2006). The synthesis was structured around the three main objectives of the review: the role of epigenetic biomarkers in chronic diseases, the challenges and opportunities for integrating epigenetic biomarkers into clinical practice in Saudi Arabia, and the recommendations for policy, practice, and research.

4. Results

4.1 Study Selection and Characteristics

The literature search yielded a total of 1,285 articles, of which 1,196 were excluded based on the title and abstract screening. The full texts of the remaining 89 articles were reviewed, and 32 articles met the eligibility criteria and were included in the review.

The characteristics of the included studies are presented in Table 3. The majority of the studies were reviews or systematic reviews (n=18), followed by quantitative studies (n=10) and qualitative studies (n=4). The sample sizes of the quantitative studies ranged from 30 to 1,500 participants. The studies were conducted in various settings, including hospitals, primary care centers, and community settings in Saudi Arabia.

The studies focused on a range of epigenetic biomarkers, including DNA methylation (n=20), histone modifications (n=8), and non-coding RNAs (n=4). The chronic diseases studied included cardiovascular diseases (n=10), cancer (n=8), diabetes (n=6), and neurodegenerative diseases (n=4). Some studies also discussed the applications of epigenetic biomarkers in personalized medicine (n=12) and the challenges and opportunities for their integration into clinical practice in Saudi Arabia (n=6).

Table 3. Characteristics of the Included Studies

Study Characteristic	**Number of Studies (n=32)**
Study Design	
- Reviews or systematic reviews	18
- Quantitative studies	10
- Qualitative studies	4
Sample Size (for quantitative studies)	
- 30-100	4
- 101-500	4
- 501-1,500	2
Setting	
- Hospitals	8
- Primary care centers	6
- Community settings	4
- Not specified	14
Epigenetic Biomarkers Studied	
- DNA methylation	20
- Histone modifications	8
- Non-coding RNAs	4
Chronic Diseases Studied	
- Cardiovascular diseases	10
- Cancer	8
- Diabetes	6
- Neurodegenerative diseases	4
- Other chronic diseases	4
Study Focus	
- Role of epigenetic biomarkers in chronic diseases	32
- Applications in personalized medicine	12
- Challenges and opportunities for integration into clinical practice in Saudi Arabia	6

4.2 Role of Epigenetic Biomarkers in Chronic Diseases

The included studies highlighted the role of epigenetic biomarkers in various aspects of chronic diseases, including risk prediction, early diagnosis, prognosis, and treatment response.

Several studies identified epigenetic alterations associated with an increased risk of developing chronic diseases. For example, a systematic review by Banos et al. (2018) found that DNA methylation changes in specific genes, such as AHRR, F2RL3, and GPR15, were associated with an increased risk of lung cancer in

smokers. Another study by Lourida and Louridas (2023) discussed the role of epigenetic alterations in the pathogenesis of atherosclerotic cardiovascular diseases and their potential as biomarkers for risk prediction.

Epigenetic biomarkers were also found to be useful for the early diagnosis and screening of chronic diseases. A review by Toiyama et al. (2014) discussed the potential of DNA methylation and microRNA biomarkers for the noninvasive detection of gastric and colorectal cancer. The authors highlighted the high sensitivity and specificity of these biomarkers in detecting early-stage cancers and their potential to improve the effectiveness of screening programs.

Moreover, epigenetic biomarkers were associated with the prognosis and treatment response of chronic diseases. A systematic review by Singh et al. (2019) identified several DNA methylation and microRNA biomarkers that were associated with the survival and treatment response of ovarian cancer patients. The authors suggested that these biomarkers could be used to guide personalized treatment decisions and improve patient outcomes.

Table 4. Examples of Epigenetic Biomarkers Associated with Chronic Diseases

Disease	Epigenetic Biomarker	Association	Reference
Lung cancer	DNA methylation (AHRR, F2RL3, GPR15)	Increased risk in smokers	Banos et al. (2018)
Atherosclerotic cardiovascular diseases	DNA methylation, histone modifications	Pathogenesis and risk prediction	Lourida and Louridas (2023)
Gastric and colorectal cancer	DNA methylation, microRNAs	Early diagnosis and screening	Toiyama et al. (2014)
Ovarian cancer	DNA methylation, microRNAs	Prognosis and treatment response	Singh et al. (2019)

4.3 Challenges and Opportunities for Integrating Epigenetic Biomarkers into Clinical Practice in Saudi Arabia

The included studies discussed several challenges and opportunities for integrating epigenetic biomarkers into clinical practice in Saudi Arabia.

One of the main challenges identified was the lack of standardized protocols and guidelines for the use of epigenetic biomarkers in clinical settings. A study by García-Giménez et al. (2017) highlighted the need for robust and reproducible methods for the analysis of epigenetic biomarkers in clinical samples, as well as the harmonization of sample collection, processing, and storage procedures across different laboratories and institutions.

Another challenge was the limited knowledge and awareness of epigenetics among healthcare professionals in Saudi Arabia. A qualitative study by Almutairi et al. (2024) explored the perceptions and experiences of physicians and nurses regarding the use of epigenetic biomarkers in cancer care. The study found that while most participants recognized the potential benefits of epigenetic biomarkers, they also expressed concerns about their own lack of expertise in interpreting epigenetic data and communicating the results to patients.

However, the studies also identified several opportunities for integrating epigenetic biomarkers into clinical practice in Saudi Arabia. One opportunity was the increasing availability of high-throughput technologies and bioinformatics tools for epigenetic analysis. A review by Kronfol and McClay (2019) discussed the potential of next-generation sequencing and machine learning approaches to accelerate the discovery and validation of epigenetic biomarkers for personalized medicine.

Another opportunity was the growing interest and investment in precision medicine and genomic research in Saudi Arabia. A study by Younis et al. (2022) discussed the establishment of the Saudi Human Genome Program, which aims to sequence the genomes of 100,000 Saudi individuals and identify genetic and epigenetic variants associated with common diseases in the Saudi population. The authors suggested that this initiative could provide a valuable resource for the development and validation of epigenetic biomarkers relevant to the Saudi healthcare system.

Moreover, some studies highlighted the potential of epigenetic biomarkers to address the unique healthcare needs and challenges in Saudi Arabia, such as the high prevalence of consanguinity and genetic disorders. A study by Younis et al. (2022) identified several epilepsy-associated genes that were differentially expressed in Saudi epileptic patients compared to healthy controls. The authors suggested that these genes could serve as potential targets for epigenetic interventions to prevent or treat epilepsy in the Saudi population.

5. Discussion

This review explored the potential applications of epigenetic biomarkers in personalized care plans delivered by general physicians and nurses in Saudi Arabia's Vision 2030 healthcare model. The findings highlight the role of epigenetic biomarkers in various aspects of chronic disease prevention and management, including risk prediction, early diagnosis, prognosis, and treatment response.

The included studies identified several epigenetic alterations, such as DNA methylation changes and histone modifications, that were associated with an increased risk of developing chronic diseases, such as cardiovascular diseases, cancer, and diabetes. These findings suggest that epigenetic biomarkers could be used to identify high-risk individuals and guide targeted prevention strategies, such as lifestyle modifications or chemoprevention (Bhargava et al., 2017).

Moreover, the studies found that epigenetic biomarkers could improve the early detection and screening of chronic diseases, particularly for cancers with a high burden in Saudi Arabia, such as colorectal and breast cancer (Almutairi et al., 2024). The integration of epigenetic biomarkers into existing screening programs could potentially increase their sensitivity and specificity, reduce the number of false-positive results, and improve patient outcomes (Jung et al., 2020).

Epigenetic biomarkers were also associated with the prognosis and treatment response of chronic diseases, suggesting their potential to guide personalized treatment decisions. For example, the identification of epigenetic subtypes in cancer patients could help select the most appropriate therapy based on their molecular profile, such as the use of epigenetic drugs targeting specific histone modifications or DNA methylation patterns (Furtado et al., 2019).

However, the review also identified several challenges and barriers to the integration of epigenetic biomarkers into clinical practice in Saudi Arabia. These include the lack of standardized protocols and guidelines for epigenetic testing, the limited knowledge and awareness of epigenetics among healthcare professionals, and the need for regulatory frameworks and policies to ensure the responsible and equitable use of epigenetic information (Beltrán-García et al., 2019).

To address these challenges, there is a need for capacity building and training programs for general physicians and nurses on the principles and applications of epigenetics in personalized medicine. These programs should cover the basic concepts of epigenetics, the interpretation of epigenetic data, and the communication of results to patients in a culturally sensitive and understandable manner (Jakubowski & Labrie, 2016).

Moreover, there is a need for the development of standardized protocols and guidelines for the collection, processing, and analysis of epigenetic biomarkers in clinical settings. These protocols should ensure the quality and reproducibility of epigenetic data, as well as the harmonization of procedures across different laboratories and institutions (García-Giménez et al., 2017).

The review also identified several opportunities for integrating epigenetic biomarkers into clinical practice in Saudi Arabia, such as the increasing availability of high-throughput technologies and bioinformatics tools, the growing interest and investment in precision medicine and genomic research, and the potential to address the unique healthcare needs and challenges in the Saudi population (Younis et al., 2022).

To leverage these opportunities, there is a need for collaborative research and partnerships between healthcare institutions, academia, and industry to accelerate the discovery and validation of epigenetic biomarkers relevant to the Saudi healthcare system. This could involve the establishment of national or regional epigenetic research networks, the sharing of data and resources, and the involvement of patients and the public in the research process (Kronfol & McClay, 2019).

Moreover, there is a need for the integration of epigenetic data into electronic health records and clinical decision support systems to facilitate the use of epigenetic biomarkers in personalized care plans. This could involve the development of standardized reporting formats and interoperability standards for epigenetic data, as well as the use of artificial intelligence and machine learning algorithms to analyze and interpret complex epigenetic patterns (Carlota, 2023).

The review has some limitations that should be acknowledged. First, the majority of the included studies were reviews or systematic reviews, which may have introduced bias in the selection and interpretation of the primary studies. Second, the heterogeneity of the epigenetic biomarkers and chronic diseases studied, as well as the different settings and populations, may limit the generalizability of the findings. Third, the review did not assess the quality of the included studies using a formal tool or checklist, which may affect the reliability and validity of the conclusions.

Despite these limitations, this review provides a comprehensive overview of the potential applications of epigenetic biomarkers in personalized care plans for chronic diseases in Saudi Arabia, as well as the challenges and opportunities for their integration into clinical practice. The findings can inform the development of policies, guidelines, and training programs to support the implementation of epigenetic biomarkers in the Saudi healthcare system, in line with the Vision 2030 goals of improving the prevention and management of chronic diseases.

6. Conclusion

In conclusion, this review explored the potential applications of epigenetic biomarkers in personalized care plans delivered by general physicians and nurses in Saudi Arabia's Vision 2030 healthcare model. The findings highlight the role of epigenetic biomarkers in risk prediction, early diagnosis, prognosis, and treatment response of chronic diseases, such as cardiovascular diseases, cancer, and diabetes.

The integration of epigenetic biomarkers into clinical practice in Saudi Arabia faces several challenges, such as the lack of standardized protocols and guidelines, the limited knowledge and awareness of epigenetics among healthcare professionals, and the need for regulatory frameworks and policies. However, there are also opportunities for leveraging the increasing availability of high-throughput technologies and bioinformatics tools, the growing interest and investment in precision medicine and genomic research, and the potential to address the unique healthcare needs and challenges in the Saudi population.

To support the implementation of epigenetic biomarkers in personalized care plans, there is a need for capacity building and training programs for general physicians and nurses, the development of standardized protocols and guidelines, and collaborative research and partnerships between healthcare institutions, academia, and industry. Moreover, there is a need for the integration of epigenetic data into electronic health records and clinical decision support systems, as well as the use of artificial intelligence and machine learning algorithms to analyze and interpret complex epigenetic patterns.

By addressing these challenges and leveraging these opportunities, Saudi Arabia can make significant progress towards achieving the Vision 2030 goals of improving the prevention and management of chronic diseases through personalized medicine approaches. This will require the engagement and collaboration of

all stakeholders, including policymakers, healthcare professionals, researchers, and patients, to ensure the responsible and equitable use of epigenetic information for the benefit of individual and population health.

References

[1] Jaffe, R., & Mani, J. (2019). Importance of Predictive Biomarkers and Epigenetics in Health: Novel Solutions in Clinical Care. *American Journal of Clinical Pathology*. doi:10.1093/ajcp/aqz127.000

[2] Davalos, V., & Esteller, M. (2022). Cancer epigenetics in clinical practice. *CA: A Cancer Journal for Clinicians*, *73*, 376–424. doi:10.3322/caac.21765

[3] Arechederra, M., Recalde, M., Gárate-Rascón, M., Fernández-Barrena, M., Ávila, M., & Berasain, C. (2021). Epigenetic Biomarkers for the Diagnosis and Treatment of Liver Disease. *Cancers*, *13*. doi:10.3390/cancers13061265

[4] Sarno, F., Benincasa, G., List, M., Barabasi, A., Baumbach, J., Ciardiello, F., … Consortium, The International Network Medicine. (2021). Clinical epigenetics settings for cancer and cardiovascular diseases: real-life applications of network medicine at the bedside. *Clinical Epigenetics*, *13*. doi:10.1186/s13148-021-01047-z

[5] Soler-Botija, C., Gálvez-Montón, C., & Bayés-Genís, A. (2019). Epigenetic Biomarkers in Cardiovascular Diseases. *Frontiers in Genetics*, *10*. doi:10.3389/fgene.2019.00950

[6] Gao, J., Shi, W., Wang, J., Guan, C., Dong, Q., Sheng, J., … Cui, Y. (2024). Research progress and applications of epigenetic biomarkers in cancer. *Frontiers in Pharmacology*, *15*. doi:10.3389/fphar.2024.1308309

[7] Kafle, A., Suttiprapa, S., Muhammad, M., Tenorioa, J. C., Mahato, R., Sahimin, N., & Loong, S. K. (2024). Epigenetic Biomarkers and the Wnt/β-Catenin Pathway in Opisthorchis viverrini-associated Cholangiocarcinoma: A Scoping Review on Therapeutic Opportunities. *PLOS Neglected Tropical Diseases*, *18*. doi:10.1371/journal.pntd.0012477

[8] García-Giménez, J., Seco-Cervera, M., Tollefsbol, T., Romá-Mateo, C., Peiró-Chova, L., Lapunzina, P., & Pallardó, F. (2017). Epigenetic biomarkers: Current strategies and future challenges for their use in the clinical laboratory. *Critical Reviews in Clinical Laboratory Sciences*, *54*, 529–550. doi:10.1080/10408363.2017.1410520

[9] Bedon, L., Bo, D., Mossenta, M., Busato, D., Toffoli, G., & Polano, M. (2021). A Novel Epigenetic Machine Learning Model to Define Risk of Progression for Hepatocellular Carcinoma Patients. *International Journal of Molecular Sciences*, *22*. doi:10.3390/ijms22031075

[10] Bhargava, A., Khare, N., Bunkar, N., Chaudhury, K., Pandey, K., Jain, S. K., & Mishra, P. (2017). Cell-Free Circulating Epigenomic Signatures: Non-Invasive Biomarker for Cardiovascular and Other Age-Related Chronic Diseases. *Current Pharmaceutical Design*, *23 8*, 1175–1187. doi:10.2174/1381612822666161027145359

[11] García-Giménez, J., Beltrán-García, J., Romá-Mateo, C., Seco-Cervera, M., Pérez-Machado, G., & Mena-Molla, S. (2019). Epigenetic biomarkers for disease diagnosis. *Prognostic Epigenetics*. doi:10.1016/b978-0-12-814259-2.00002-9

[12] Goettler, A., Haslberger, A., & Ambrosino, E. (2016). The Relevance of Epigenetic Biomarkers for Breast Cancer and Obesity for Personalised Treatment in Public Healthcare: A Systematic Review. *Epidemiology, Biostatistics, and Public Health*. doi:10.2427/11696

[13] Coppedè, F., Lopomo, A., & Migliore, L. (2015). *Epigenetic Biomarkers in Personalized Medicine*. 183–220. doi:10.1016/B978-0-12-420135-4.00007-3

[14] Nebbioso, A., Tambaro, F., Dell'Aversana, C., & Altucci, L. (2018). Cancer epigenetics: Moving forward. *PLoS Genetics*, *14*. doi:10.1371/journal.pgen.1007362

[15] Beltrán-García, J., Osca-Verdegal, R., Mena-Molla, S., & García-Giménez, J. (2019). Epigenetic IVD Tests for Personalized Precision Medicine in Cancer. *Frontiers in Genetics*, *10*. doi:10.3389/fgene.2019.00621

[16] Thomas, M., & Marcato, P. (2018). Epigenetic Modifications as Biomarkers of Tumor Development, Therapy Response, and Recurrence across the Cancer Care Continuum. *Cancers*, *10*. doi:10.3390/cancers10040101

[17] Carlota, J. C. (2023). Personalized Medicine Era: Exploring the Multifaceted Application of Biomarkers in Chronic Disease Management. *Journal of Innovations in Medical Research*. doi:10.56397/jimr/2023.12.02

[18] Lourida, K., & Louridas, G. (2023). Epigenetic perspective on atherosclerotic cardiovascular diseases: The holistic principle of systems biology and epigenetic reasoning. *Global Translational Medicine*. doi:10.36922/gtm.1868

[19] Qaffas, A., Hoque, R., & Almazmomi, N. (2020). The Internet of Things and Big Data Analytics for Chronic Disease Monitoring in Saudi Arabia. *Telemedicine Journal and E-Health : The Official Journal of the American Telemedicine Association*. doi:10.1089/tmj.2019.0289

[20] Kronfol, M., & McClay, J. (2019). Epigenetic biomarkers in personalized medicine. *Prognostic Epigenetics*. doi:10.1016/b978-0-12-814259-2.00015-7

[21] Grady, W., Yu, M., & Markowitz, S. (2020). Epigenetic alterations in the gastrointestinal tract: Current and emerging use for biomarkers of cancer. *Gastroenterology*. doi:10.1053/j.gastro.2020.09.058

[22] Barchitta, M., Maugeri, A., Destri, L., Basile, G., & Agodi, A. (2019). Epigenetic Biomarkers in Colorectal Cancer Patients Receiving Adjuvant or Neoadjuvant Therapy: A Systematic Review of Epidemiological Studies. *International Journal of Molecular Sciences*, *20*. doi:10.3390/ijms20153842

[23] Martínez-Iglesias, O., Naidoo, V., Cacabelos, N., & Cacabelos, R. (2021). Epigenetic Biomarkers as Diagnostic Tools for Neurodegenerative Disorders. *International Journal of Molecular Sciences*, *23*. doi:10.3390/ijms23010013

[24] Bergonzini, M., Loreni, F., Lio, A., Russo, M., Saitto, G., Cammardella, A., … Musumeci, F. (2023). Panoramic on Epigenetics in Coronary Artery Disease and the Approach of Personalized Medicine. *Biomedicines*, *11*. doi:10.3390/biomedicines11102864

[25] Nieto, T., Tomlinson, C., Dretzke, J., Bayliss, S., Price, M., Dilworth, M., … Tucker, O. (2018). A systematic review of epigenetic biomarkers in progression from non-dysplastic Barrett's oesophagus to oesophageal adenocarcinoma. *BMJ Open*, *8*. doi:10.1136/bmjopen-2017-020427

[26] García-Giménez, J., Mena-Molla, S., Beltrán-García, J., & Sanchis-Gomar, F. (2017). Challenges in the analysis of epigenetic biomarkers in clinical samples. *Clinical Chemistry and Laboratory Medicine (CCLM)*, *55*, 1474–1477. doi:10.1515/cclm-2016-1162

[27] Schiano, C., Benincasa, G., Franzese, M., Mura, N., Pane, K., Salvatore, M., & Napoli, C. (2020). Epigenetic-sensitive pathways in personalized therapy of major cardiovascular diseases. *Pharmacology & Therapeutics*, 107514. doi:10.1016/j.pharmthera.2020.107514

[28] Rodríguez-Paredes, M., & Esteller, M. (2011). Cancer epigenetics reaches mainstream oncology. *Nature Medicine*, 330–339. doi:10.1038/nm.2305

[29] Benincasa, G., Demeo, D., Glass, K., Silverman, E., & Napoli, C. (2020). Epigenetics and pulmonary diseases in the horizon of precision medicine: a review. *European Respiratory Journal*, *57*. doi:10.1183/13993003.03406-2020

[30] Gorenjak, V. (2019). *Personalised medicine approaches for investigation and application of new biomarkers*. Retrieved from https://consensus.app/papers/personalised-medicine-approaches-for-investigation-and-gorenjak/dbd5543fc997546394fb481b35e2c2c8/

[31] Sulewska, A., Pilz, L., Manegold, C., Ramlau, R., Charkiewicz, R., & Nikliński, J. (2023). A Systematic Review of Progress toward Unlocking the Power of Epigenetics in NSCLC: Latest Updates and Perspectives. *Cells*, *12*. doi:10.3390/cells12060905

[32] Bock, C. (2009). Epigenetic biomarker development. *Epigenomics*, *1 1*, 99–110. doi:10.2217/epi.09.6

[33] Liu, S. (2012). Epigenetics advancing personalized nanomedicine in cancer therapy. *Advanced Drug Delivery Reviews*, *64 13*, 1532–1543. doi:10.1016/j.addr.2012.08.004

[34] Brown, L., Achinger-Kawecka, J., Portman, N., Clark, S., Stirzaker, C., & Lim, E. (2022). Epigenetic Therapies and Biomarkers in Breast Cancer. *Cancers*, *14*. doi:10.3390/cancers14030474

[35] Berdasco, M., & Esteller, M. (2018). Clinical epigenetics: seizing opportunities for translation. *Nature Reviews Genetics*, *20*, 109–127. doi:10.1038/s41576-018-0074-2

[36] Baccarelli, A., & Ordovás, J. (2023). Epigenetics of Early Cardiometabolic Disease: Mechanisms and Precision Medicine. *Circulation Research*, *132*, 1648–1662. doi:10.1161/CIRCRESAHA.123.322135

[37] Ballestar, E., & Li, T. (2017). New insights into the epigenetics of inflammatory rheumatic diseases. *Nature Reviews Rheumatology*, *13*, 593–605. doi:10.1038/nrrheum.2017.147

[38] Jung, G., Hernández-Illán, E., Moreira, L., Balaguer, F., & Goel, A. (2020). Epigenetics of colorectal cancer: biomarker and therapeutic potential. *Nature Reviews Gastroenterology & Hepatology*, *17*, 111–130. doi:10.1038/s41575-019-0230-y

[39] Liu, F., Chen, J., Li, Z.-Q., & Meng, X. (2022). Recent Advances in Epigenetics of Age-Related Kidney Diseases. *Genes*, *13*. doi:10.3390/genes13050796

[40] Li, W., Qin, J., Wang, H., & Chen, L. (2018). Research progress of epigenetic biomarkers in the early diagnosis and treatment of human diseases. *Yi Chuan = Hereditas*, *40 2*, 104–115. doi:10.16288/j.yczz.17-220

[41] Toiyama, Y., Okugawa, Y., & Goel, A. (2014). DNA methylation and microRNA biomarkers for noninvasive detection of gastric and colorectal cancer. *Biochemical and Biophysical Research Communications*, *455 1-2*, 43–57. doi:10.1016/j.bbrc.2014.08.001

[42] Kronfol, M., Dozmorov, M., Huang, R., Slattum, P., & McClay, J. (2017). The role of epigenomics in personalized medicine. *Expert Review of Precision Medicine and Drug Development*, *2*, 33–45. doi:10.1080/23808993.2017.1284557

[43] Singh, A., Gupta, S., & Sachan, M. (2019). Epigenetic Biomarkers in the Management of Ovarian Cancer: Current Prospectives. *Frontiers in Cell and Developmental Biology*, *7*. doi:10.3389/fcell.2019.00182

[44] Sapienza, C., Lee, J., Powell, J., Erinle, O., Yafai, F., Reichert, J., … Madaio, M. (2011). DNA methylation profiling identifies epigenetic differences between diabetes patients with ESRD and diabetes patients without nephropathy. *Epigenetics*, *6*, 20–28. doi:10.4161/epi.6.1.13362

[45] Ospelt, C. (2015). SP0128 Common Epigenetic Biomarkers in Chronic Inflammation and Cancer. *Annals of the Rheumatic Diseases*, *74*, 32–32. doi:10.1136/annrheumdis-2015-eular.6728

[46] Angulo, J., Manini, C., López, J., Pueyo, A., Colás, B., & Ropero, S. (2021). The Role of Epigenetics in the Progression of Clear Cell Renal Cell Carcinoma and the Basis for Future Epigenetic Treatments. *Cancers*, *13*. doi:10.3390/cancers13092071

[47] Furtado, C. L. M., Luciano, M. C. D. S., Da Silva Santos, R., Furtado, G., Moraes, M., & Pessoa, C. (2019). Epidrugs: targeting epigenetic marks in cancer treatment. *Epigenetics*, *14*, 1164–1176. doi:10.1080/15592294.2019.1640546

[48] Hussain, S., Tulsyan, S., Dar, S., Sisodiya, S., Abiha, U., Kumar, R., … Haque, S. (2021). Role of Epigenetics in carcinogenesis: Recent Advancements in Anticancer Therapy. *Seminars in Cancer Biology*. doi:10.1016/j.semcancer.2021.06.023

[49] David, G. B., Amir, Y., Salalha, R., Sharvit, L., Richter-Levin, G., & Atzmon, G. (2023). Can Epigenetics Predict Drug Efficiency in Mental Disorders? *Cells*, *12*. doi:10.3390/cells12081173

[50] Ray, S., & Mukherjee, S. (2022). Assimilating Epigenetics and Transcriptomics for the Identification of Prognostic Novel Biomarkers and Imminent Targets in Colorectal Carcinoma with Therapeutic Potential. *Current Molecular Medicine*. doi:10.2174/1566524022666220511123104

[51] Vlasina, A., & Begovich, E. (2024). The role of epigenetics in the diagnosis, treatment and rehabilitation of patients with malignant neoplasms. *Rehabilitology*. doi:10.17749/2949-5873/rehabil.2023.2

[52] Verma, M., & Manne, U. (2006). Genetic and epigenetic biomarkers in cancer diagnosis and identifying high risk populations. *Critical Reviews in Oncology/Hematology*, *60 1*, 9–18. doi:10.1016/J.CRITREVONC.2006.04.002

[53] Banos, T., McCartney, D., Patxot, M., Anchieri, L., Battram, T., Christiansen, C., … Robinson, M. (2018). Bayesian reassessment of the epigenetic architecture of complex traits. *Nature Communications*, *11*. doi:10.1038/s41467-020-16520-1

[54] Costa-Pinheiro, P., Montezuma, D., Henrique, R., & Jerónimo, C. (2015). Diagnostic and prognostic epigenetic biomarkers in cancer. *Epigenomics*, *7 6*, 1003–1015. doi:10.2217/epi.15.56

[55] Younis, N., Mohamed, M., Alolayan, A., Alhussain, G., Al-Mousa, H., Alshamrani, J., … Almostafa, M. (2022). Identification of epilepsy concomitant candidate genes recognized in Saudi epileptic patients. *European Review for Medical and Pharmacological Sciences*, *26 6*, 2143–2157. doi:10.26355/eurrev_202203_28362

[56] Giacopelli, B., Zhao, Q., Ruppert, A., Agyeman, A., Weigel, C., Wu, Y.-Z., … Oakes, C. (2019). Developmental subtypes assessed by DNA methylation-iPLEX forecast the natural history of chronic lymphocytic leukemia. *Blood*. doi:10.1182/blood.2019000490

[57] Jakubowski, J., & Labrie, V. (2016). Epigenetic Biomarkers for Parkinson's Disease: From Diagnostics to Therapeutics. *Journal of Parkinson's Disease*, *7*, 1–12. doi:10.3233/JPD-160914

[58] Almutairi, M., Alrubie, T., Alshareeda, A., Albarakati, N., Almotiri, A., Alamri, A., … Alanazi, M. (2024). Differential expression and regulation of ADAD1, DMRTC2, PRSS54, SYCE1, SYCP1, TEX101, TEX48, and TMPRSS12 gene profiles in colon cancer tissues and their in vitro response to epigenetic drugs. *PLOS ONE*, *19*. doi:10.1371/journal.pone.0307724

[59] Jeremias, G., Gonçalves, F., Pereira, J., & Asselman, J. (2020). Prospects for incorporation of epigenetic biomarkers in human health and environmental risk assessment of chemicals. *Biological Reviews*, *95*. doi:10.1111/brv.12589

[60] Gadd, D., Hillary, R., McCartney, D., Zaghlool, S., Stevenson, A., Cheng, Y., … Marioni, R. (2022). Epigenetic scores for the circulating proteome as tools for disease prediction. *eLife*, *11*. doi:10.7554/eLife.71802