REVIEW

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Genetic Testing in Primary Care – Myth or Reality?

ABSTRACT

The Swiss scientist Friedrich Miescher first identified deoxyribonucleic acid (DNA) in 1869, marking the beginning of genetic research. Subsequent studies led to the discovery of DNA's composition and structure, culminating in Watson and Crick's 1953 model of its three-dimensional, double-helical structure. DNA's functional units, genes, encode proteins essential for biological processes, and variations in DNA sequences are classified as polymorphisms or mutations based on their population frequency. Advances in genetic research have facilitated the development of cytogenetic, biochemical, and molecular tests, enabling the precise analysis of genetic material. These tests provide valuable information for personalized medicine, particularly in pharmacogenomics and predictive medicine.

Once considered an exclusive domain of specialized medicine, genetic testing is now becoming an integral component of clinical practice. Technological advancements, declining costs, and increased understanding of DNA's role in disease susceptibility have contributed to its growing accessibility. Genetic testing holds significant potential in primary care, offering insights into disease predisposition, optimizing drug therapy, and enabling early interventions. However, despite its promise, the integration of genetic testing into routine medical practice remains a challenge due to concerns related to clinical utility, ethical considerations, and the need for physician education in genetics.

A key question persists: does genetic testing offer practical benefits for routine patient care, or does it remain largely theoretical? This review aims to explore the role of genetic testing in primary care, assessing its potential advantages while addressing challenges that may hinder its widespread adoption. By evaluating the current state of genetic testing, this analysis seeks to determine whether it represents a transformative tool in modern medicine or an evolving field with yet-to-be-fulfilled promises.

Keywords: DNA, Genetic Testing, Primary Care, General Practitioner.

Birinci Basamak Sağlık Hizmetlerinde Genetik Testler – Mit mi Gerçek mi?

ÖZET

İsviçreli bilim insanı Friedrich Miescher, 1869 yılında deoksiribonükleik asidi (DNA) keşfederek genetik araştırmaların temelini atmıştır. Sonraki çalışmalar DNA'nın bileşimi ve yapısını ortaya çıkarmış, bu süreç 1953 yılında Watson ve Crick'in DNA'nın üç boyutlu çift sarmallı yapısını tanımlamasıyla sonuçlanmıştır. DNA'nın işlevsel birimleri olan genler, biyolojik süreçler için gerekli proteinleri kodlamakta olup, DNA dizilimlerindeki değişiklikler popülasyon içindeki sıklıklarına bağlı olarak polimorfizm veya mutasyon olarak sınıflandırılmaktadır. Genetik araştırmalardaki ilerlemeler, sitogenetik, biyokimyasal ve moleküler testlerin gelişmesini sağlamış ve genetik materyalin hassas analizini mümkün kılmıştır. Bu testler, özellikle farmakogenomik ve prediktif tıp alanlarında kişiye özel tıbbi yaklaşımlar geliştirilmesine katkı sunmaktadır.

Bir zamanlar yalnızca uzmanlık gerektiren bir alan olarak görülen genetik testler, günümüzde klinik pratiğin ayrılmaz bir parçası haline gelmektedir. Teknolojik ilerlemeler, test maliyetlerinin azalması ve DNA'nın hastalık duyarlılığı üzerindeki rolünün daha iyi anlaşılması, genetik testlerin erişilebilirliğini ve klinik önemini artırmıştır. Genetik testler, hastalık yatkınlığı hakkında bilgi sağlama, ilaç tedavisinin bireyselleştirilmesi ve erken müdahale fırsatları açısından birincil sağlık hizmetlerinde büyük bir potansiyele sahiptir. Ancak, klinik fayda, etik kaygılar, veri gizliliği, sağlık politikaları ve hekimlerin genetik konularındaki eğitimi gibi zorluklar, bu testlerin rutin tıbbi uygulamalara entegrasyonunu sınırlayan önemli faktörlerdir.

Bu bağlamda, önemli bir soru ortaya çıkmaktadır: Genetik testler gerçekten hasta bakımında pratik faydalar sunmakta mıdır, yoksa büyük ölçüde teorik bir alan olarak mı kalmaktadır? Bu derleme, birincil sağlık hizmetlerinde genetik testlerin rolünü incelemeyi, potansiyel avantajlarını değerlendirmeyi ve yaygın kullanımını engelleyebilecek bilimsel, etik ve pratik zorlukları ele almayı amaçlamaktadır. Mevcut durumu analiz ederek, genetik testlerin modern tıpta dönüştürücü bir araç olup olmadığını veya hala tam anlamıyla gerçekleştirilememiş bir alan mı olduğunu belirlemeye çalışmaktadır.

Anahtar Kelimeler: DNA, Genetik Test, Birinci Basamak Sağlık Hizmetleri, Pratisyen Hekim.

INTRODUCTION

In 1869, the Swiss scientist Friedrich Miescher was the first to bring to the global scientific community's attention the existence of deoxyribonucleic acid (DNA). His research involved white blood cells, through which he successfully isolated a substance previously unknown to science. This substance, located in the cell nucleus, was named "nuclein," a term later replaced by "nucleic acid" and subsequently "deoxyribonucleic acid." Miescher conducted a chemical analysis and discovered that nuclein contained a high amount of phosphorus, leading him to recognize it as a novel molecule. Initially, he hypothesized that nuclein might play a role in hereditary transmission, although he later abandoned this idea (1).

Although Miescher's name faded into obscurity, Russian biochemist Phoebus Levene continued investigating the composition of nuclein (2). Through hydrolysis and the decomposition of nucleic acids from yeast, Levene proposed in 1919 that nucleic acids are composed of a series of nucleotides, each containing one of four nitrogenous bases, a sugar molecule, and a phosphate group. He was also the first scientist to identify the carbohydrate components of DNA-deoxyribose and RNA-ribose. He is credited with identifying the presence of the bases adenine, guanine, cytosine, and thymine in DNA, as well as uracil replacing thymine in RNA. Additionally, he proposed a tetranucleotide structure consisting of repeating units of four nucleotides arranged in a specific order (adenine, guanine, cytosine, thymine, and so forth), a hypothesis that was later refuted by other scientists. Nevertheless, his polynucleotide model remains valid today, as does his discovery that nucleotides are linked through bonds between the phosphate group of one nucleotide and the sugar of the next. This sequence forms the sugar-phosphate backbone, which constitutes the foundation of the DNA molecule. An interesting historical fact is that Levene believed the structure he proposed was too simple to serve as the carrier of genetic information. This notion somewhat delayed the acceptance of DNA as the molecule responsible for genetic material (3).

In 1944, Oswald Avery became the first scientist to make the groundbreaking discovery that DNA, and not proteins, is the carrier of genetic information and a fundamental component of genes and chromosomes (4). The next significant contribution to uncovering the structure of DNA came from American biochemist Erwin Chargaff, who was influenced by Avery's work. In 1950, Chargaff reported that the ratio and quantities of the four bases in the DNA double helix are constant but vary between different species of organisms (5). However, he was unable to explain the specific relationships between the bases, namely, that adenine pairs with thymine and cytosine pairs with guanine within the molecular structure of DNA (2).Chargaff's base-pairing rule, combined with the contributions of English researchers Rosalind Franklin and Maurice Wilkins through X-ray crystallography-a technique for determining the three-dimensional atomic structure of molecules-formed the foundation for the discovery of the **three-dimensional, double-helical model of DNA**, presented by Watson and Crick in 1953. Their model revealed that the bases are connected by hydrogen bonds, the strands are antiparallel and complementary, and the helix is predominantly right-handed (2).

The functional units of DNA are genes, which encode the synthesis of specific proteins essential for the structure and function of the cell and determine hereditary traits (6).

The continuous human endeavor to decode the genetic information embedded in DNA culminated in 1990 with the initiation of one of the most ambitious scientific projects of our time-the **Human Genome Project**, which aimed to sequence the entire human genome (i.e., determine the exact sequence of DNA bases). In 2000, the first reference genome was announced, leaving 8% of heterochromatic regions unanalyzed. However, in April 2022, the **Telomere-to-Telomere (T2T) Consortium** declared the completion of the sequencing process, providing information on the sequence of 3.055 billion base pairs, excluding the Y chromosome (7).

It is estimated that the human genome contains between 20,000 and 25,000 genes (8). Each individual has a unique genome, except for monozygotic twins. This uniqueness is attributed to the presence of **single nucleotide polymorphisms (SNPs)**-variations in which a single nucleotide, such as thymine, is replaced by another, or **short tandem repeats (STRs)** (9). It is estimated that there is one SNP for every 2.0 kilobase pairs, with over 1.4 million identified (10).

DNA variants with a frequency greater than 1% in the population are classified as SNPs, while those with a frequency below 1% are considered mutations (11). These genomic changes may have no impact on the synthesis of normal proteins, but in some cases, they can lead to pathological alterations in function and, consequently, be associated with disease development (12).

Advances in science and technological achievements now enable the use of genetic information for the diagnosis and treatment of diseases, forming the foundation of what is known as **genomic medicine**. This has the potential to entirely transform the way medicine is practiced (13).

Genetic testing, once considered a niche of specialized medicine, is rapidly entering clinical practice due to increased accessibility from decreasing test costs and a growing understanding

of the relationship between DNA changes and disease development. However, an important question arises: does genetic testing have practical applications in routine medical practice, or does it still reside in the realm of promises and theoretical possibilities?

The aim of this review is to analyze the role of genetic testing in primary care, exploring both its potential benefits and the challenges associated with its implementation.

Foundations of Genetic Testing: The primary goal of genetic testing is to identify changes in an individual's genetic material. The information obtained can indicate a disease or a predisposition to one and can be used to develop therapeutic or preventive strategies. It may also assist in family planning, career choices, or future professional development. The material analyzed for genetic testing can include blood, buccal mucosa, hair, skin, or other tissues.

Types of Tests: Depending on the genetic material or its product being analyzed, genetic testing can be categorized into the following types (14) (Table 1):

Table 1. Type of Genetic Testing

Type Genetic Testing	Description	Common Techniques	Clinical Applications
1. Cytogenetic	Examines entire chromosomes to detect structural and numerical abnormalities.	**-Karyotyping:** Microscopic observation of stained chromosomes. **-Fluorescent in situ hybridization (FISH):** Uses fluorescent molecules to detect genetic anomalies (insertions, deletions, translocations, and amplifications). .	DiGeorge syndrome, Chronic myelogenous leukemia (CML), B-cell lymphoma**.**
2. Biochemical	Measures protein levels, enzyme activity, and metabolic products encoded by specific genes.	**-Enzyme activity assays. -Metabolic product measurement. -Protein structural analysis.**	Detection of enzyme deficiencies, metabolic disorders, and structural protein abnormalities.
3. Molecular	Investigate DNA sequence variations, genetic variants, and mutations.	**-Whole-genome sequencing (WGS):** Analyzes the entire DNA sequence. **-Next-generation sequencing (NGS):** High-throughput DNA sequencing. **- Exome sequencing:** Focuses on protein-coding regions. **-Targeted gene analysis:** Uses polymerase chain reaction (PCR) and hybridization methods to detect specific mutations.	Identification of disease-causing mutations, SNPs, and genetic predispositions.

In addition to diagnosing diseases or risk assessment, genetic tests have found applications in **pharmacogenomics**, driven by the accumulation of data on the human genome and technological advancements. Numerous studies explore the impact of genetic variants on the distribution of drugs within the body (**pharmacokinetics**) and the sensitivity or response to treatment (**pharmacodynamics**). These findings are critical for **personalized medicine** (15).

The goal of pharmacogenomic testing is to optimize and maximize therapeutic efficacy while minimizing side effects and toxicity, based on the patient's individual genotype. Examples of medications with established genotype-related effects or risks include **warfarin**, **clopidogrel**, **abacavir**, **statins**, and others. This knowledge facilitates an individualized, lifelong treatment approach (16).

Another potential application of genetic testing in primary care lies in the field of **predictive medicine**. It can serve as a valuable tool for the early identification of patients at high risk for common diseases. Examples include testing for **BReast CAncer gene 1 (BRCA1)** and **BRCA2** mutations in women, which are associated with an increased risk of breast and ovarian cancers. Approximately 60% of women carrying such mutations will develop breast cancer during their lifetime. For BRCA1, the risk of developing ovarian cancer is estimated to be 39%–58%, while for BRCA2, the risk ranges between 13% and 29% (17). Information from these tests can guide decisions regarding targeted preventive measures,

such as regular screening or prophylactic surgery (18).

Additionally, **Apolipoprotein E (APOE)** genotypes have been associated with risks of dementia, Alzheimer's disease, and cardiovascular diseases (19). Such knowledge can inform early preventive interventions, including the implementation of dietary and cognitive strategies (20).

An important area where genetic screening tests can be conducted in primary care settings is **reproductive medicine**. Prenatal and carrier tests are particularly valuable for couples planning to start a family. These tests can identify the risk of severe hereditary diseases such as **cystic fibrosis** (21) or **thalassemia** (22).

Despite the great potential genomics holds, the expectations and opportunities for its implementation remain a process that is advancing at a slower pace (23). It is therefore crucial to identify the main barriers hindering its integration and to seek optimal solutions, particularly in primary care, where conditions are most favorable for the application of genetic testing in these areas. This is due to the close and long-term relationship with patients, familiarity with their medical and family histories, and broader opportunities for risk management and disease prevention.

As such, general practitioners can play a central role not only in identifying suitable patients but also in coordinating efforts with other healthcare professionals across the different levels of the healthcare system, including geneticists.

Challenges Faced by Primary Care Providers: The main barriers to the integration of genetic medicine into routine patient care can be categorized into the following areas, as identified in a systematic analysis of 38 publications (24):

1. **Knowledge:** The most frequently reported issue by participants in the studies was a **lack of general knowledge** in the field of genetics and the resulting lack of confidence (25,26), as well as insufficient training in clinical genetics (27). Other commonly noted deficits included inadequate preparation for obtaining a family history (28) and the necessary information required to collect (29).
2. **Skills:** The lack of **confidence** in possessing the necessary qualifications for genetic counseling was the most frequently cited issue in 16 of the 38 studies. A U.S.-based survey of 1,763 primary care physicians found that only 28.8% felt qualified to provide genetic counseling (30). Additionally, the inability to apply recommendations from guidelines regarding the interpretation of family history (31) and uncertainty in determining familial relationships between patients were also commonly identified problems (32).

Other studies reported that physicians lacked the skills to **interpret genetic test results** (33). For instance, a Canadian study of 341 primary care physicians revealed that only 15% felt capable of interpreting genetic results, and fewer than 10% were adequately informed about genetic testing (30). In 14 of the 38 studies, physicians admitted to lacking confidence in ordering genetic tests and struggled to explain the limitations of such tests to their patients, particularly concerning false-positive or false-negative results.

Moreover, 10 of the 38 studies reported difficulties in **assessing genetic risk**, including for specific conditions such as cancer (30). In a study conducted among 860 primary care physicians in the U.S., 38.3% felt uncomfortable conducting screening tests, providing preventive recommendations, or determining which patients should be referred for further consultation (34).

Another commonly identified barrier was the lack of awareness of available **educational resources** related to genetics and how to access them (26,35,36). Many physicians also expressed uncertainty about when and how to refer patients to a genetic specialist, a challenge cited in multiple studies (33,34).

These challenges highlight the need for targeted education and training programs to equip primary care providers with the knowledge and skills required for the effective application of genetic medicine in routine practice.

3. Ethical, Legal, and Social: The potential for patient **distress** and **anxiety** associated with genetic risk was frequently highlighted by physicians in 16 of the reviewed publications (25,35). Physicians also reported challenges related to the emotional reactions of patients upon receiving genetic test results (37). Identifying carrier status for a pathogenic gene could lead individuals to perceive themselves as unhealthy, even if no symptoms are present (38).

Another deterrent cited was the possibility of discovering **incidental findings** during testing, which could cause stress about the potential development of diseases in the future (39).

A significant concern raised in 15 of the 38 publications was the fear of social or insurance **discrimination**. For example, in a study of 1,251 primary care physicians, 80% expressed concern that patients with positive test results might face discrimination from insurers (30). Similar findings were reported in a study of 1,222 California physicians, where 75% shared the same concerns, noting that fear of discrimination could lead patients to decline genetic testing (40).

These challenges underscore the need for robust ethical guidelines, legal protections, and patient education to address concerns surrounding genetic testing and promote its adoption in clinical practice.

A significant barrier is the loss of **confidentiality** and the potential disclosure of genetic risk information to family members related

to the patient. In a study conducted among U.S. physicians**,** 53% reported that they would not be able to guarantee confidentiality to their patients after receiving genetic test results (30). Similarly, 61% of Swiss primary care physicians identified this issue as a major reason limiting their use of genetic testing for breast cancer due to its implications for other family members (41).

The use of **prenatal tests** has also presented challenges. Physicians expressed concerns that the results might negatively impact the emotional course of the pregnancy, lead to unnecessary medical interventions, or drive parents toward a desire for a "perfect" child. This could, in turn, result in social inequality and stigma against individuals with genetic disorders (41,42).

These findings highlight the ethical complexities and societal implications associated with genetic testing, emphasizing the need for careful consideration and policy development to address these barriers.

4. Organizational: The lack of access to **genetic services**, including consultations with genetic specialists, is the most frequently cited barrier by physicians (28,37,43,44). The reasons for this vary across studies and include inconvenient locations of genetic centers, lack of transportation in remote areas, absence of regulations for referrals to other levels of the healthcare system, and limited availability of genetic tests (30,32,34,44,45).

Time constraints are another significant factor reported by physicians. The need to take a detailed family history is often mentioned as a restrictive reason (32), as is the time required to explain genetic test results (31). In some studies, results indicated that the long turnaround time for prenatal test results impacted subsequent decisions regarding treatment (28).

These organizational challenges highlight the need for improved infrastructure, streamlined processes, and time-efficient solutions to facilitate the integration of genetic services into primary care.

A challenge highlighted by primary care physicians is their **perception of their role in providing genetic-related services** (41,46), with some reporting uncertainty about what their role entails (27,33,35,43). In several studies, it is noted that genetics is not perceived as an integral part of primary care and is considered to have less relevance at this level of the healthcare system (25,35,36,37,44,57,48). Many physicians believe that genetics falls under the domain of specialists and requires specific expertise (38,44,48).

The **cost** of genetic tests is frequently cited as a significant barrier to their integration into primary care, compounded by the lack of reimbursement for ordering such tests and the subsequent need for patient counseling (35).

The perception of genetics as a peripheral aspect of primary care responsibilities has also been identified as a reason for difficulties in integrating it into routine activities (26,45,49,50). In some studies, physicians reported challenges with incorporating family history into electronic health records (EHRs) (33).

These findings suggest that addressing misconceptions about the role of primary care physicians in genetics and providing clearer guidelines and resources may facilitate the integration of genetic services into primary care practice.

5. Scientific Evidence on Genetic Tests and Testing: Although genetic tests provide opportunities to identify diseases or assess the risk of their development, physicians perceive the **lack of therapeutic options** for certain conditions as a barrier to the broader application of these tests in practice (34,39,41,48). Additionally, some physicians believe that treatment approaches would not differ regardless of the availability of genetic test results (25,36,45,47,48).

In some studies, the insufficient **accuracy of genetic tests** is highlighted as a barrier to their use, particularly regarding false-positive results in cancer testing. Furthermore, 45% of physicians in one study believed that the risk of cancer development remains unclear even after genetic testing (30).

Similar findings were reported in another systematic review published in 2003, illustrating the lack of significant progress in integrating genetic testing into the routine activities of primary care physicians. Nonetheless, many physicians expressed a willingness to receive training in genetics, even though they did not consider it a priority (50).

These findings underscore the need for improved accuracy of genetic tests, development of actionable therapeutic strategies, and educational efforts to enhance the integration of genetics into primary care.

CONCLUSION

Despite significant progress in genetic research, both scientific and technological, the implementation of genetic testing as part of the routine activities of primary care physicians is advancing at a slow pace and currently holds limited significance. This lack of focus is attributed to various factors, with the most prominent being insufficient knowledge in this specialized field, a lack of confidence and experience in taking family histories, and challenges in ordering and interpreting test results, which often require subsequent genetic counseling. The high cost of genetic testing and the lack of reimbursement further restricts the broader adoption and use of these modern methods in routine patient care at this level of the healthcare system.

The outlined challenges can serve as a foundation for developing strategies to train general practitioners, equipping them with the necessary knowledge and skills in this promising field.

Additionally, national policies aimed at improving access to innovative testing methods could help unlock the potential of genetics to transform healthcare.

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