

## **PRECISION MEDICINE AND MOLECULAR ENDOCRINOLOGY: ADVANCES IN THE DIAGNOSIS AND TREATMENT OF HORMONAL DISORDERS**

### **Precision Medicine And Molecular Endocrinology: Advances In The Diagnosis And Treatment Of Hormonal Disorders**

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#### **ABSTRACT**

Precision medicine has made significant advances in endocrinology by enabling individualized diagnostic and therapeutic approaches based on the genetic, molecular, and clinical characteristics of patients. The objective of this integrative review was to critically analyze recent scientific evidence on the application of precision medicine and molecular endocrinology in the diagnosis and personalized treatment of hormonal disorders. The methodology consisted of an integrative literature review, with systematic searches in the PubMed/MEDLINE, PubMed Central, Scopus, and Web of Science databases, including original articles and scientific reviews published between 2015 and 2025. Twenty studies were selected that addressed molecular, genomic, and “omic” tools applied to different endocrine conditions. The results demonstrate that the incorporation of molecular endocrinology increases diagnostic accuracy, allows for the etiological redefinition of complex hormonal diseases, and enables therapeutic personalization, with a positive impact on clinical outcomes, especially in monogenic disorders, endocrine tumors, and diabetes mellitus. It is concluded that precision medicine represents a central axis in the evolution of contemporary endocrinology, although its consolidation depends on overcoming challenges related to infrastructure, professional training, and equity in access to molecular technologies.

**Keywords:** precision medicine; molecular endocrinology; hormonal disorders; molecular diagnosis.

## INTRODUCTION

Precision medicine has established itself as a new paradigm in contemporary medical practice by proposing the individualization of diagnosis, prognosis, and therapeutic strategies based on the genetic, molecular, environmental, and clinical characteristics of each patient [1]. In endocrinology, this approach acquires special relevance, as hormonal disorders present high heterogeneity biological and pathophysiological, often not contemplated by uniform diagnostic and therapeutic models [2,3].

The advancement of molecular endocrinology, driven by the development of genomic technologies and the increased use of hormonal and molecular biomarkers, has allowed for a more refined understanding of the underlying mechanisms of endocrine diseases [3]. Studies show that the incorporation of targeted genetic tests and next-generation sequencing (NGS) methodologies significantly increases diagnostic accuracy in complex and rare endocrine conditions, reducing the time to etiological diagnosis and enabling more assertive therapeutic decisions [2,4,11].

Recent evidence indicates that several endocrine conditions, previously treated as homogeneous clinical entities, comprise distinct molecular subgroups with relevant clinical implications. In the context of thyroid diseases, the use of molecular tests has proven fundamental for stratifying the risk of malignancy in thyroid nodules, contributing to the reduction of unnecessary surgical procedures and the adoption of more conservative and individualized approaches [5]. These findings consolidate the thyroid as one of the main models for the clinical application of precision medicine in endocrinology.

In the field of metabolic disorders, particularly in diabetes mellitus, precision medicine has enabled the phenotypic and molecular subclassification of both type 1 and type 2 diabetes. Studies demonstrate that genetic and immunological subgroups present distinct clinical trajectories, with significant differences in therapeutic response and risk of complications, reinforcing the inadequacy of standardized therapeutic approaches [6–10]. The identification of these subphenotypes has

direct implications in pharmacological choice, clinical monitoring, and long-term outcome prediction [8,9,15,16].

The application of molecular endocrinology is particularly impactful in monogenic diseases and rare endocrine syndromes, where genetic diagnosis can completely redefine clinical management. Robust evidence demonstrates that the identification of specific mutations associated with hormonal secretion or action allows for the replacement of conventional therapies with targeted and more effective treatments, as exemplified in neonatal diabetes and monogenic diabetes [17,18]. These models represent paradigmatic examples of precision medicine applied to endocrinological practice.

Furthermore, advances in molecular profiling of tumors endocrine, especially in acromegaly, have enabled therapeutic individualization based on the expression of hormonal receptors and tumor molecular characteristics. Clinical and observational studies demonstrate that personalized

strategies result in better biochemical control rates, lower incidence of adverse effects, and optimization of the use of pharmacological therapies [12–14].

Despite the observed advances, the incorporation of precision medicine in endocrinology still faces significant challenges, including limitations in access to molecular tests, high costs, the need for professional training, and methodological heterogeneity among the available studies [1,2,11]. In light of this scenario, it becomes essential to conduct integrative reviews that critically synthesize recent scientific evidence, assessing the real impact of precision medicine and molecular endocrinology on the diagnosis and personalized treatment of hormonal disorders.

In this context, the present study aims to conduct an integrative review of the literature on the advances of precision medicine and molecular endocrinology in the personalized diagnosis and treatment of hormonal disorders, gathering and critically analyzing the scientific evidence published in the last ten years.

## METHODOLOGY

This study consists of an integrative literature review, a method that allows for a broad and systematic synthesis of scientific evidence from different methodological designs, enabling critical analysis and integration of the knowledge produced about a particular phenomenon of interest [1,20]. This approach is particularly suitable for investigating the application of precision medicine and molecular endocrinology in the diagnosis and personalized treatment of hormonal disorders, given the diversity of clinical, genetic, and translational studies available in the recent literature.

### Search Strategy

The bibliographic search was conducted systematically and structured in the main international scientific databases recognized by the academic community, namely: PubMed/MEDLINE, PubMed Central (PMC), Scopus, and Web of Science. The selection of these databases aimed to ensure broad coverage of peer-reviewed journals and to guarantee the traceability and quality of the included evidence [2,3].

Controlled descriptors from the MeSH (Medical Subject Headings) and DeCS

(Descriptors in Health Sciences) vocabularies were used, combined through Boolean operators. The search strategy adopted included the following terms:

“Precision Medicine” AND  
 “Endocrinology” AND  
 (“Molecular Diagnosis” OR  
 “Genomics” OR “Pharmacogenomics”) AND (“Endocrine Disorders” OR  
 “Hormonal Disorders”).

The search was conducted considering publications from January 2015 to December 2025, with no restriction on the country of origin of the studies, limited to the English language, due to the predominance of indexed publications in that language in the selected databases.

### Inclusion and Exclusion Criteria

Studies that simultaneously met the following criteria were included in the review:

- (i) original articles or peer-reviewed scientific reviews;
- (ii) publications indexed in recognized databases;
- (iii) studies that explicitly addressed the application of precision medicine and/or molecular endocrinology in diagnosis, stratification

of risk or personalized treatment of hormonal disorders;

(iv) availability of full text;

(v) publication within the established time frame.

Excluded were: editorials, letters to the editor, comments, clinical guidelines, consensus statements, isolated case reports, experimental studies without direct endocrine clinical application, as well as non-indexed publications or those without adequate traceability [1,2, 11].

### Study Selection Process

The selection of studies was carried out in sequential stages. Initially, the titles and abstracts were read to identify potentially relevant publications. Subsequently, the full texts of eligible articles were carefully evaluated for adherence to the review's objective and the predefined inclusion criteria. Any discrepancies in selection were resolved by consensus, based on methodological analysis and the scientific relevance of the study [1].

At the end of the process, 20 scientific articles were included, deemed suitable to form the basis of the integrative review, encompassing

narrative reviews, systematic reviews, observational clinical studies, and translational studies.

### Data Extraction and Analysis

The data extraction was carried out in a standardized manner, encompassing the following information: author(s), year of publication, country, journal, type of study, objective, methodological basis, endocrine disorder addressed, molecular endocrinology tools used, main results, contributions to precision medicine, and limitations pointed out by the authors.

This step allowed for the cross-sectional comparison of studies and the identification of convergences and divergences among the available evidence [3,6, 10].

The extracted data were analyzed descriptively and critically, followed by thematic organization, enabling the integrated synthesis of findings and the construction of a consistent interpretative analysis on the impact of precision medicine and molecular endocrinology in contemporary endocrine clinical practice [1,20].

## RESULTS

After applying the eligibility criteria and the comprehensive analysis of the selected studies, **20 scientific articles** published between 2015 and 2025 were included, all indexed in recognized international databases. The final sample comprised **narrative reviews, systematic reviews, observational clinical studies, and translational studies**, reflecting the methodological diversity characteristic of scientific production in precision medicine and molecular endocrinology.

In an integrated manner, the findings evidenced that the application of precision medicine in endocrinology focuses on four **main axes**:

- (i) enhancement of molecular diagnosis;
- (ii) risk stratification and phenotypic subclassification;
- (iii) therapeutic personalization;
- (iv) clinical impact on outcomes and prognosis.

## Molecular Diagnosis and Etiological Redefinition

The majority of studies highlighted that the incorporation of targeted genetic tests, multigene panels, and next-generation sequencing (NGS) promoted a substantial increase in diagnostic accuracy in complex and rare endocrine disorders [1,2,3, 11]. These methods allowed the identification of previously unrecognized pathogenic variants, reducing diagnostic uncertainty and the time to etiological definition, especially in monogenic diseases, hereditary hormonal syndromes, and endocrine tumors [11, 17, 18].

In thyroid disorders, tests molecular demonstrated high predictive

value in stratifying the risk of malignancy in indeterminate nodules, contributing to more conservative clinical decisions and reducing unnecessary surgical procedures [5]. These findings consolidate the thyroid as one of the most advanced fields of precision endocrinology.

## Risk Stratification and Phenotypic Subclassification

Another recurring finding was the ability of molecular endocrinology to reveal the biological heterogeneity of diseases traditionally treated as homogeneous. Studies on type 1 and type 2 diabetes mellitus demonstrated that the integration of genetic, immunological, and metabolic data enables the identification of distinct subphenotypes, with significantly different clinical trajectories and complication risks [6–10, 15, 16].

The molecular subclassification of type 2 diabetes, in particular, highlighted significant differences in disease progression, cardiovascular risk, and response to hypoglycemic agents, reinforcing the inadequacy of uniform therapeutic approaches [9, 10]. Furthermore, population studies emphasized that genetic diversity directly influences the applicability of precision medicine models, pointing to the need for strategies sensitive to ethnic and population differences [19].

## Therapeutic Personalization and Treatment Response

The personalization of treatment has emerged as one of the main benefits of applying precision medicine in endocrinology.

Robust evidence has demonstrated that identifying the underlying molecular mechanism of the disease allows for the selection of more effective and safer therapies. In monogenic and neonatal diabetes, genetic diagnosis enabled the replacement of conventional therapeutic regimens with targeted treatments, having a significant and sustained clinical impact [17,18].

In acromegaly, clinical and observational studies have shown that tumor molecular profiling, including the assessment of hormonal receptor expression, is associated with response to somatostatin analogs and better biochemical control rates [12–14]. These findings position acromegaly as

a consolidated model of practical application of molecular endocrinology.

## Clinical Impact and Identified Limitations

Overall, studies indicated that the application of precision medicine in endocrinology is associated with improved clinical outcomes, reduced adverse effects, and optimized use of therapeutic resources [1,6,8,12]. However, significant limitations were noted, including high costs of molecular testing, the need for specialized infrastructure, methodological heterogeneity among studies, and inequality in access to precision technologies [1,2,11].

**Table 1 – Integrated Summary of the Included Studies**

Author/Year	Type of study	Disorder of endocrine	molecular tool	Main findings	Contribution to precision medicine
Bidlingmaier et al., 2022 [1]	Review narrative	Disorders various endocrine	Tests genetic, NGS	Higher diagnostic accuracy	Conceptual and clinical basis
Izatt et al., 2022 [2]	Review practice	Diseases hereditary	Genetic tests Targeted	Reduction of errors diagnostic	Use rational of genetics
Tumino et al., 2020 [5]	Review narrative	Thyroid nodules	Tests molecular	Reduction of unnecessary surgery	Risk stratification
Prasad & Groop, 2019 [6]	Narrative review	Type 2 diabetes	Genetics, biomarkers	Identification of sub-phenotypes	Personalized therapy
Misra et al., 2023 [10]	Systematic review	Type 2 diabetes	“Omics” data	Molecular sub-classification	Outcome prediction of



Marques-Pamies et al., 2024 [12]	Clinical study	Acromegaly	Molecular profile	Better hormonal control	Therapeutic selection
Puig-Domingo et al., 2020 [13]	Study observational	Acromegaly	Hormonal receptors	Prediction of response	Personalized medicine
Gloyn et al., 2015 [17]	Study translational	Diabetes neonatal	Monogenic genetics	Directed therapeutic change	Model paradigmatic
Bonnefond et al., 2023 [18]	Review narrative	Diabetes monogenic	Genetics molecular	Redefinition therapeutic	Diagnosis of precision
Misra et al., 2025 [19]	Review narrative	Diabetes	Population genetics	Ethnic influence	Population personalization

Complementary to the synthesis presented in Table 1, it is observed that the included studies converge to demonstrate that precision medicine and molecular endocrinology are not limited to isolated technological advances, but represent a structural change in the diagnostic and therapeutic logic of contemporary endocrinology. The integration of genetic, molecular, and clinical data has allowed for the redefinition of diagnostic flows, reducing empirical approaches and promoting greater alignment between the pathophysiological mechanism of the disease and the adopted therapeutic strategy [1,3,11].

In the diagnostic realm, studies indicate that the use of advanced molecular tools, such as targeted genetic panels and next-generation sequencing, has significantly expanded

the capacity for etiological identification

in rare and atypical hormonal disorders, reducing the so-called "diagnostic odyssey" observed in traditional models [2,11,18]. This advancement has proven particularly relevant in monogenic diseases, hereditary endocrine syndromes, and conditions with overlapping clinical presentations, where the diagnosis based solely on clinical-laboratory criteria if shows

insufficient [17,18].

Regarding risk stratification, the findings demonstrate that the molecular subclassification of metabolic diseases, such as diabetes mellitus, allowed for the identification of subgroups with



different clinical trajectories, risks of complications, and therapeutic responses [6,9,10]. This approach contributes to a more preventive and individualized clinical practice by enabling early interventions targeted at higher risk profiles, in addition to avoiding excessive treatments in subgroups with a more benign evolution [15,16].

In the therapeutic field, studies demonstrate that the personalization of treatment, based on molecular and genetic markers, is associated with better clinical outcomes, higher biochemical control rates, and a reduction in adverse events [12–14,17]. Acromegaly and monogenic diabetes emerge as consolidated models of clinical application in molecular endocrinology, where the identification of specific molecular characteristics directly guides pharmacological choice and therapeutic strategy [13,17,18].

Additionally, studies emphasize that the effectiveness of precision medicine is intrinsically related to the consideration of population genetic diversity. Evidence indicates that ethnic and genetic differences influence both the risk of developing endocrine diseases

and the response to available therapies, reinforcing the need for precision models that are sensitive to population and contextual characteristics [19].

Despite the widely described benefits, the included studies also point out important limitations for the broad implementation of precision medicine in endocrinology, such as high costs, the need for specialized infrastructure, inequality in access to molecular technologies, and methodological variability among the analyzed studies [1,2,11]. These aspects reinforce the importance of integrative analyses that not only describe advancements but also critically contextualize their applicability in real clinical practice.

Together, the results highlight that precision medicine and molecular endocrinology represent central tools for the evolution of endocrine care, with a direct impact on diagnostic accuracy, therapeutic individualization, and improvement of clinical outcomes, while also signaling structural challenges that need to be overcome for their consolidation in different health systems.

## DISCUSSION

This integrative review highlights that precision medicine and molecular endocrinology have promoted a structural change in the understanding and management of hormonal disorders, surpassing the traditional paradigm of uniform diagnostic and therapeutic approaches. The comparative analysis of the studies included demonstrates

convergence regarding the central role of molecular tools in the etiological redefinition, risk stratification, and treatment personalization in different areas of endocrinology [1,3,6].

One of the main advances identified relates to the enhancement of diagnostic accuracy. Studies that incorporated targeted genetic testing and next-generation sequencing demonstrated a significant increase in the rate of conclusive diagnoses, especially in rare and monogenic endocrine diseases [2,11,17,18]. Compared to classical diagnostic models, predominantly based on clinical-laboratory criteria, molecular endocrinology allows for the identification of the causal mechanism of the disease, reducing diagnostic uncertainty and the time to etiological definition [1,2]. However, there is

methodological heterogeneity among the studies regarding the genetic panels used and the criteria for test indication, which limits the standardization of these approaches in clinical practice [11].

In the context of metabolic disorders, particularly in diabetes mellitus, comparative analysis shows that molecular subclassification represents one of the most promising pillars of precision medicine. Studies on type 1 and type 2 diabetes demonstrate that genetic, immunological, and metabolic subphenotypes exhibit distinct clinical trajectories, with direct implications for the risk of complications and response to pharmacological treatments [6–10,15,16]. This biological heterogeneity challenges the traditional therapeutic model and supports the need for individualized strategies. However, most studies still rely on retrospective analyses or reviews, reinforcing the need for prospective trials that validate the clinical applicability of these subclassifications on a large scale [9,10].

Therapeutic personalization emerges as one of the most established aspects of the application of precision medicine in endocrinology. Examples paradigmatic include diabetes

Monogenic and neonatal, in which molecular diagnosis allowed the replacement of conventional therapies with targeted treatments, having a significant and sustained clinical impact [17,18]. Similarly, in acromegaly, clinical and observational studies have demonstrated that tumor molecular profiling, especially the assessment of hormone receptor expression, is associated with the response to somatostatin analogs and the optimization of biochemical control [12–14]. These findings contrast with areas of endocrinology where therapeutic personalization is still in its infancy, highlighting different levels of maturity of precision medicine among hormonal disorders.

Another relevant aspect discussed in the studies refers to population genetic diversity. Evidence indicates that ethnic and genetic differences influence both susceptibility to endocrine diseases and response to therapeutic interventions, which may limit the generalization of precision medicine models developed from specific populations [19]. This finding reinforces the need for more inclusive and representative studies, as well as the adaptation of precision models to local epidemiological and genetic realities.

Precision to local epidemiological and genetic realities.

Despite the evident advances, the critical analysis of the studies reveals significant structural challenges for the broad implementation of precision medicine in endocrinology. Among the main obstacles are the high costs of molecular testing, the need for specialized laboratory infrastructure, the insufficient training of professionals for interpreting genetic results, and the inequality in access to precision technologies among different health systems [1,2,11]. Furthermore, the heterogeneity of methodological designs and the predominance of narrative reviews in some areas limit the robustness of the available evidence, highlighting gaps to be explored by prospective studies and controlled clinical trials.

In summary, the comparative discussion of the findings indicates that precision medicine and molecular endocrinology already have a concrete impact on the diagnosis and treatment of various hormonal disorders, especially in monogenic diseases, endocrine tumors, and selected metabolic disorders.

However, the consolidation of this

The approach as a routine practice depends on overcoming methodological, structural, and ethical challenges, as well as producing more robust clinical evidence to support its broad and equitable incorporation into contemporary endocrinology.

## CONCLUSION

This integrative review highlights that precision medicine and molecular endocrinology represent structural advances in the diagnosis and personalized treatment of hormonal disorders, marking a progressive transition from the standardized therapeutic model to approaches individualized and based on specific biological mechanisms. The synthesis of evidence demonstrates that the incorporation of genetic, molecular, and “omic” tools has significantly increased diagnostic accuracy, especially in rare endocrine diseases, monogenic conditions, and those with heterogeneous clinical presentation [1,2,11].

The findings indicate that the application of molecular endocrinology enables the etiological redefinition of various hormonal conditions, reducing diagnostic uncertainties and allowing

More targeted therapeutic interventions.

This impact is particularly evident in disorders such as monogenic and neonatal diabetes, where genetic diagnosis decisively alters clinical conduct and patient outcomes [17,18]. Similarly, in acromegaly and other endocrine diseases associated with hormonal tumors, molecular profiling has proven fundamental for therapeutic selection and optimization of biochemical control [12–14].

In the context of metabolic disorders, the review reinforces that the biological heterogeneity of diabetes mellitus challenges traditional clinical management models. Molecular and phenotypic subclassification emerges as a promising strategy for risk stratification, treatment personalization, and complication prediction, although it still depends on greater clinical validation for broad implementation [6–10,15,16]. Furthermore, the influence of population genetic diversity highlights the need for precision medicine approaches that are sensitive to ethnic and contextual differences, avoiding biases and expanding the applicability of personalized models [19].

Despite the evidenced benefits, the review also points out relevant limitations, including high costs, the need for specialized

infrastructure, insufficient professional training, and methodological heterogeneity among the analyzed studies [1,2,11]. These factors reinforce that the consolidation of precision medicine in endocrinology requires not only technological advances but also investments in training, health policies, and the production of more robust clinical evidence.

In conclusion, precision medicine and molecular endocrinology constitute central tools for the evolution of contemporary endocrine care, with a direct impact on diagnostic accuracy, therapeutic individualization, and improvement of clinical outcomes. However, its broad and equitable incorporation into clinical practice will depend on overcoming the identified challenges and strengthening translational and clinical research, consolidating this approach as an integral part of the future of endocrinology.

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