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MODERN PSYCHIATRY AND PRECISION MEDICINE: ADVANCES IN DIAGNOSIS AND PERSONALIZED TREATMENT OF MENTAL DISORDERS

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ABSTRACT

Modern psychiatry has undergone a profound conceptual and methodological transformation driven by advances in precision medicine, especially in light of the limitations of categorical diagnostic models and the high clinical heterogeneity of mental disorders. This integrative review aimed to analyze scientific evidence on advances in diagnosis, clinical stratification, and personalized treatment of mental disorders, with an emphasis on dimensional models, pharmacogenomics, biomarkers, neuroimaging, artificial intelligence, psychiatric genomics, and predictive tools. Thirty traceable scientific studies were selected, published in international databases and relevant journals, including conceptual articles, reviews, clinical guidelines, consensus statements, randomized clinical trials, longitudinal studies, genomic investigations, and computational models.The results were organized into five thematic axes: dimensional and transdiagnostic diagnostic models; pharmacogenomics and personalized prescribing; multimodal biomarkers in depression and therapeutic response; psychiatric genomics and polygenic risk scores; and artificial intelligence, neuroimaging, and individualized clinical prediction models. The evidence shows that precision medicine can help reduce the trial-and-error logic in psychiatric treatment, guide therapeutic decisions, improve the prediction of clinical response, and promote more individualized interventions. However, the broad clinical application of these tools still depends on external validation, methodological standardization, sample diversity, cost-effectiveness assessment, and ethical discussion regarding the use of genetic, neurobiological, and digital data in mental health. It is concluded that precision psychiatry represents one of the main frontiers of contemporary mental health and should be understood as an integrative approach that combines technological innovation, clinical judgment, and attention to the biopsychosocial complexity of the patient.

Keywords: Psychiatry; Precision Medicine; Mental Disorders; Biomarkers.

INTRODUCTION

Contemporary psychiatry is going through a period of profound conceptual, methodological, and translational reconfiguration. Historically, the diagnosis of mental disorders was structured around classificatory predominantly categorical systems, based on syndromic groupings defined by signs, symptoms, and clinical criteria operationalized. Although these models have played an essential role in standardizing diagnosis, in communication among professionals and in the organization of clinical research, their limitations have become progressively evident in the face of to elevated heterogeneity of mental disorders, of the symptomatic overlap between diagnostic categories, of individual variability in therapeutic response, and of the absence of biomarkers fully integrated into psychiatric clinical practice (1-4) .

In this scenario, precision medicine emerges as a strategic approach to overcome the traditional paradigm of treatment based on trial and error, seeking to integrate clinical, genetic, neurobiological, cognitive, behavioral, and environmental data to guide diagnostic decisions, prognostic and therapeutic individualized. Applied to psychiatry, this perspective proposes that patients with the same formal diagnosis may present distinct pathophysiological mechanisms, heterogeneous clinical trajectories, and variable therapeutic responses, requiring assessment models more sensitive to the biological and psychosocial individuality of each individual (2,5,6) .

One of the main theoretical foundations of this transformation is represented by the Research Domain Criteria (RDoC) project, proposed by the National Institute of Mental Health, which seeks to reorganize psychiatric research based on functional dimensions related to neural circuits, behavior, cognition, and biological systems, rather than limiting it exclusively to traditional diagnostic categories (1-3). In a complementary way, the Hierarchical Taxonomy of Psychopathology (HiTOP) proposes a dimensional and hierarchical organization of psychopathology, offering an alternative to classical nosological models and promoting an understanding of mental disorders as interrelated spectra of clinical manifestations (4). These approaches do not eliminate the importance of clinical assessment, but expand its interpretive capacity by bringing it closer to quantitative measures and underlying mechanisms.

In the therapeutic field, pharmacogenomics represents one of the most advanced areas of precision psychiatry. The genetic variability involved in the metabolism, transport, and response to psychotropic drugs can influence efficacy, tolerability, the risk of adverse effects, and the need for dosage adjustments. International guidelines, such as those prepared by the Clinical Pharmacogenetics Implementation Consortium have consolidated recommendations related to genes such as CYP2D6, CYP2C19, and CYP2B6, especially in the use of selective serotonin reuptake inhibitor antidepressants and tricyclic antidepressants (11-13). In addition, reviews, consensus statements, and randomized clinical trials have investigated the usefulness of pharmacogenomic testing in guiding antidepressant prescribing, particularly in patients with major depression, a history of multiple therapeutic failures, or relevant adverse effects (10,14-18).

Despite advances, the incorporation of pharmacogenomics into clinical practice still requires careful interpretation. Trials such as GUIDED and PRIME Care have shown that using pharmacogenomic tests can reduce prescriptions with predicted gene–drug interactions and contribute to higher response or remission rates in certain clinical contexts, although the observed effects on symptomatic outcomes are not always robust or sustained at every follow-up point (15,16). These findings indicate that pharmacogenomics should not be understood as an isolated solution, but as a component of a multimodal clinical decision-making strategy, integrated with the patient’s history, illness severity, comorbidities, concomitant medication use, and therapeutic preferences.

At the same time, molecular, neurophysiological, and neuroimaging biomarkers have been investigated as potential tools for diagnostic stratification and prediction of therapeutic response. Studies such as GENDEP and CAN-BIND exemplify efforts to understand the antidepressant response through the integration of genetic data, peripheral gene expression, electroencephalography, functional neuroimaging, cognition and clinical characteristics (19-24). This perspective is particularly relevant in major depression, a highly prevalent, heterogeneous disorder associated with a high individual and social burden, in which the early identification of predictors of response could reduce the time of suffering, exposure to ineffective treatments, and the risk of chronicity.

The use of electroencephalography, functional magnetic resonance imaging, and advanced computational models has expanded the possibility of identifying neurobiological signatures associated

with therapeutic response. Recent studies indicate that patterns of functional connectivity, electrophysiological measures, and multimodal brain networks may contribute to the development of individualized predictive models in major depression (22-25). However, translating these findings into clinical practice depends on external validation, reproducibility, cost-effectiveness, standardization of protocols, and the development of tools

that can be interpreted for use in real-world care settings (7,8).

Another key axis of precision psychiatry is psychiatric genomics. Large-scale genome-wide association studies have revealed the complex polygenic architecture of disorders such as schizophrenia and bipolar disorder, identifying multiple loci associated with risk and implicating biological pathways related to synaptic function, neurodevelopment, and neural regulation (26,27). Although polygenic risk scores do not yet have stand-alone diagnostic application in clinical practice, they represent a promising tool for understanding vulnerability, stratification

population-level, risk trajectories, and possible biological subgroups within highly heterogeneous psychiatric disorders (28) .

In addition to biological markers, predictive models based on artificial intelligence and machine learning have been playing an increasingly important role in modern psychiatry. Integrated analysis of large volumes of clinical, genetic, neuropsychological, digital, and neuroimaging data can help estimate individual risk, predict clinical course, support therapeutic decision-making, and identify profiles with greater vulnerability (5-7) . In the psychosis field, for example, individualized risk calculators developed in high clinical-risk cohorts, such as the

NAPLS-2, have demonstrated the ability to estimate the probability of conversion to psychosis based on clinical, cognitive, and psychosocial variables, and were subsequently subjected to external validation (29,30) .

Meanwhile, advances in precision psychiatry also bring scientific, clinical, ethical, and operational challenges. Among them are the need for validation in diverse populations, the reduction of algorithmic bias, the protection of sensitive data, the clinical interpretation of genetic and neurobiological findings, equitable access to technologies, and the prevention of reductive uses of biomarkers. The complexity of mental disorders requires that precision medicine be understood as an integrative approach, not merely a technological one, preserving the centrality of clinical listening, subjectivity, the psychosocial context, and the therapeutic relationship.

Given this context, it becomes relevant to critically synthesize the evidence available on the advances of modern psychiatry and precision medicine in the diagnosis and personalized treatment of mental disorders. Thus, this integrative review aims to analyze recent and relevant scientific studies on dimensional models, pharmacogenomics, biomarkers, neuroimaging, artificial intelligence, psychiatric genomics, and predictive tools applied to personalizing mental healthcare, discussing their contributions, limitations, and perspectives for clinical practice and for international psychiatric research.

METHODOLOGY

This study is characterized as an integrative literature review, a method that makes it possible to gather, analyze, and synthesize available scientific evidence on a given phenomenon of interest, considering different methodological designs and enabling a broad and critical understanding of the topic under investigation. The choice of this type of review is justified by the complexity and multidimensionality of precision psychiatry, a field that involves contributions from conceptual studies, systematic reviews, clinical guidelines, randomized clinical trials, genomic studies, investigations using biomarkers, neuroimaging, electroencephalography, artificial intelligence and predictive models applied to mental disorders.

The guiding question for this review was defined as follows: what are the main scientific advances related to precision medicine in the diagnosis, clinical stratification, and personalized treatment of mental disorders? From this question, the aim was to identify evidence addressing the transition from categorical diagnostic models to dimensional approaches, the use of molecular, genetic, neurophysiological, and neuroimaging biomarkers, the application of pharmacogenomics in prescribing psychotropic medications, the development of individualized predictive models, and the use of artificial intelligence in clinical decision-making in psychiatry.

The bibliographic search was conducted in internationally recognized scientific databases, with priority given to PubMed/MEDLINE, the National Center for Biotechnology Information, and high-impact journals in psychiatry, neurosciences, genetics, clinical pharmacology, and translational medicine, as well as published guidelines and consensus statements in specialized journals. Studies indexed in journals such as the American Journal of Psychiatry, JAMA, JAMA Psychiatry, Nature, Nature Genetics, Molecular Psychiatry, Translational Psychiatry, Schizophrenia Bulletin, Clinical Pharmacology & Therapeutics, Frontiers in Psychiatry, BMC Psychiatry, NeuroImage: Clinical, Neuroscience & Biobehavioral Reviews, and other journals compatible with the scope of the investigation were considered.

The search strategy was guided by controlled vocabulary descriptors and free-text terms related to the study's central theme, combining expressions in English due to the predominance of international literature on the subject. Terms such as "precision psychiatry", "precision medicine", "mental disorders", "pharmacogenomics", "pharmacogenetics", "biomarkers", "machine learning", "artificial intelligence", "neuroimaging", "electroencephalography", "genome-wide association study", "polygenic risk score", "major depressive disorder", "schizophrenia", "bipolar disorder","psychosis risk", "RDoC", and "HiTOP". The combinations were carried out to encompass both studies based on conceptual foundations and associated clinical and translational research related to the diagnosis and personalized treatment of mental disorders.

The following were adopted as inclusion criteria: studies published in traceable scientific journals; articles in English or Portuguese; studies directly related to precision psychiatry, biomarkers, pharmacogenomics, psychiatric genomics, neuroimaging, electroencephalography,

artificial intelligence, predictive models, dimensional diagnosis, or personalized treatment in mental disorders; systematic reviews, meta-analyses, randomized clinical trials, observational studies, clinical guidelines, international consensus statements, broad genomic association studies, and conceptual articles of high relevance for the theoretical foundation of the topic. Classic and foundational studies were also included, even if published earlier, when considered essential for understanding the conceptual evolution of modern psychiatry, such as work related to the Research Domain Criteria and the Hierarchical Taxonomy of Psychopathology.

Studies with no direct relationship to precision medicine in psychiatry were excluded, as were opinion articles without relevant conceptual contribution, non-trackable publications, duplicate studies, texts without clear identification of authorship or journal, works focusing exclusively on psychotherapy without an approach to diagnostic or therapeutic personalization, as well as studies whose content did not provide objective contribution to the analysis of advances in diagnosis and personalized treatment of mental disorders.

After the search stage, the studies were submitted to an initial screening based on title, abstract, publication journal, study design type, and adherence to the proposed theme. Then, potentially eligible articles were assessed for scientific relevance, traceability, contribution

methodological contribution and pertinence to the analytical axes of the review. At the end of the process, 30 studies were selected to form the article's main scientific foundation. The selection aimed to ensure methodological diversity and balance between conceptual foundations, evidence clinical guidelines pharmacogenomic studies, genomic studies, research with biomarkers, and artificial intelligence applications.

For the extraction of the data, a standardized matrix was developed containing the following information: author and year of publication, country or predominant institutional origin, study design, sample or population analyzed, mental disorder investigated, autonomic marker or precision marker assessed, main findings, and contribution to the article's discussion. Considering that not all of the included studies assessed markers

autonomic parameters as such, such as heart rate variability, the galvanic skin response, or cardiovascular parameters; when applicable, the primary accuracy marker addressed was recorded, including genetic markers, pharmacogenomic,

neurophysiological, molecular, neuroimaging, polygenic scores, computational models, or dimensional frameworks.

The analysis of the studies was conducted in a qualitative and interpretive manner, aiming to identify convergences, limitations, gaps, and clinical implications related to precision psychiatry. The findings were organized into five main thematic axes: diagnostic models dimensional, and transdiagnostic; pharmacogenomics and personalized prescribing; multimodal biomarkers applied to depression and therapeutic response; psychiatric genomics and polygenic risk scores; and predictive models based on artificial intelligence, neuroimaging, and individualized clinical risk calculators. This categorization made it possible to synthesize the studies coherently with the article's proposal and facilitated the development of a critical discussion about the clinical applicability of the evidence.

Because this is an integrative review based exclusively on secondary data from studies already published, there was no direct involvement of human beings, collection of primary data, clinical intervention, or access to identifiable patient information. Thus, submission to an Research Ethics Committee was not necessary, in accordance with the applicable rules for literature review studies. Even so, the principles of scientific integrity, source traceability, fidelity to the original evidence, and proper citation of the included works were upheld.

The presentation of the results was planned in a concise manner, with the organization of the studies by thematic axes, in order to avoid an excessively long table in the body of the article. The complete extraction matrix served as a methodological support tool for critical analysis, while the results table was structured to highlight the groups of evidence, the types of studies included, and their main contributions to the understanding of the advances of modern psychiatry and precision medicine in diagnosis and personalized treatment of mental disorders.

RESULTS

This integrative review included 30 studies selected for their scientific relevance to understanding advances in modern psychiatry and precision medicine in the diagnosis, clinical stratification, and personalized treatment of mental disorders. The studies covered different methodological designs, including conceptual articles, narrative reviews, systematic review, meta-analyses, and guidelines clinical, consensus international, randomized clinical trials, longitudinal studies, genome-wide association studies, investigations using electroencephalography, functional neuroimaging, gene expression, artificial intelligence, and individualized models for clinical prediction.

The qualitative analysis of the studies made it possible to organize the findings into five main thematic axes: dimensional diagnostic models dimensional and transdiagnostic; pharmacogenomics and personalized prescribing; multimodal biomarkers applied to depression and therapeutic response; genomics psychiatric and polygenic risk scores; and predictive models based on artificial intelligence, neuroimaging, and individualized clinical risk calculators. This categorization made it possible to synthesize the contributions of the included studies and highlight how different approaches are being integrated into the development of precision psychiatry.

Conceptual and taxonomic studies showed that modern psychiatry has been progressively shifting from models exclusively categorical diagnoses toward dimensional and biologically oriented proposals. The Research Domain Criteria and the Hierarchical Taxonomy of Psychopathology were identified as relevant milestones in this process, because they offer alternatives to the traditional classification of mental disorders and support a more integrated understanding of symptoms, neurobiological circuits, behavioral domains and psychopathological spectra (1-4) .

In the field of pharmacogenomics, evidence has been identified from clinical guidelines, consensus statements, meta-analyses, and randomized clinical trials. These studies indicated that genetic variants related to the metabolism of psychotropic drugs, especially in genes such as CYP2D6, CYP2C19, and CYP2B6, may guide decisions regarding drug selection and dose adjustment, particularly in the treatment of depressive disorders. Clinical trials such as GUIDED and PRIME Care demonstrated potential clinical benefits of pharmacogenomic testing, although they also showed that their effects on remission and symptomatic response may vary according to the clinical and methodological context (10- 18).

Studies on multimodal biomarkers focused predominantly on major depressive disorder, reflecting the clinical and epidemiological relevance of depression and its well-recognized biological heterogeneity. Investigations were identified that assessed peripheral gene expression, electroencephalography, functional connectivity via functional magnetic resonance imaging, and multimodal integration of clinical and neurobiological data. These studies suggested that combining molecular, neurophysiological, and neuroimaging markers may help predict response to antidepressant treatment and stratify patient subgroups (19-25) .

Psychiatric genomics was represented by large-scale genome-wide association studies and investigations using polygenic risk scores. The findings showed that disorders such as schizophrenia and bipolar disorder have complex, polygenic genetic architectures distributed across multiple loci. Although these markers do not yet constitute stand-alone diagnostic tools in clinical practice, the analyzed studies indicated their relevance for understanding vulnerability, risk trajectories, possible biological subtypes, and pathophysiological mechanisms associated with severe mental disorders (26-28) .

Finally, studies related to artificial intelligence, machine learning, and individualized predictive models showed the growth of approaches computational approaches focused on the integrated analysis of clinical, genetic, neuropsychological, and neurobiological data. Models based on machine learning, deep learning, neuroimaging, and individualized risk calculators have demonstrated potential to support clinical decision-making, estimate the risk of conversion to psychosis, and predict therapeutic response. However, the studies also highlighted challenges related to external validation, reproducibility, interpretability of the models, and implementation in real clinical environments (5-8,24,25,29,30) .

Table 1 - Synthesis of the studies included in the integrative review according to the contribution axis for precision psychiatry

Thematic axis	Included studies	Type of evidence	Main contributions
Dimensional and transdiagnostic diagnostic models	Insel et al. (1); Insel (2); Cuthbert (3); Kotov et al. (4)	Conceptual, taxonomic, and theoretical foundation articles	They underpin the transition from psychiatry based exclusively on diagnostic categories to dimensional, transdiagnostic, and biologically oriented models. RDoC proposes investigating mental disorders from functional domains, neural circuits, and levels of analysis, while HiTOP organizes psychopathology into hierarchical spectra.
Pharmacogenomics and personalized prescribing	Bousman et al. (10); Bousman et al. (11); Hicks et al. (12); Hicks et al. (13); Bousman et al. (14); Greden et al. (15); Oslin et al. (16); Tiwari et al. (17); Arnone et al. (18); Uher et al. (19)	Clinical guidelines, consensus statements, meta-analyses, randomized clinical trials, and pharmacogenomic studies	They show that genetic variants, especially in CYP2D6, CYP2C19, and CYP2B6, may contribute to personalizing antidepressant prescribing and reducing gene–drug interactions. Clinical trials indicate potential benefits of pharmacogenomic testing, although with variable magnitude across clinical outcomes.
Multimodal biomarkers in depression and therapeutic response	Lam et al. (20); Fiori et al. (21); Schwartzmann et al. (22); Jaworska et al. (23); Harris et al. (24); Jiao et al. (25)	Longitudinal studies, multicenter protocols, gene expression, EEG, fMRI, machine learning, and deep learning	They highlight the potential of integrating molecular, electrophysiological, and neuroimaging biomarkers to predict response to antidepressant treatment. The findings reinforce that multimodal approaches may be more promising than isolated biomarkers in stratifying patients with major depression.
Psychiatric genomics and polygenic risk scores	Trubetskoy et al. (26); Mullins et al. (27); Jiang et al. (28)	Wide-genome association studies and investigations with a polygenic risk score	They demonstrate the complex, polygenic genetic architecture of disorders such as schizophrenia and bipolar disorder. The studies identify risk-associated loci, genes related to synaptic biology, and possible future applications of polygenic scores in stratifying vulnerability.
Artificial intelligence, neuroimaging, and individualized clinical prediction models	Bzdok and Meyer-Lindenberg (5); Chen et al. (6); Salazar de Pablo et al. (7); Etkin and Mathalon (8); Harris et al. (24); Jiao et al. (25); Cannon et al. (29); Carrión et al. (30)	Reviews, computational models, functional neuroimaging, deep learning, risk calculators, and external validation	They reinforce the role of artificial intelligence and predictive models in the integrated analysis of clinical and neurobiological data. Psychosis risk calculators and neuroimaging-based models indicate potential for individualized prediction, although they still depend on external validation, standardization, and clinical applicability.

Overall, the results indicate that precision psychiatry is not limited to a single technology or biomarker, but is an integrative field that combines dimensional diagnosis, pharmacogenomics, multimodal biomarkers, psychiatric genomics, and artificial intelligence. The main trend observed in the analyzed studies is the search for models capable of reducing the clinical heterogeneity of mental disorders, improving the prediction of therapeutic response, and guiding more individualized interventions. However, it was also observed that much of the evidence is still at a translational stage, requiring further validation in diverse populations and cautious incorporation into clinical practice.

DISCUSSION

The findings of this integrative review show that modern psychiatry is moving toward a paradigm shift, marked by the gradual incorporation of dimensional models, biomarkers, pharmacogenomics, psychiatric genomics, neuroimaging, electroencephalography and artificial intelligence in understanding mental disorders. The analysis of the 30 included studies shows that precision medicine in psychiatry should not be understood as a replacement for traditional clinical assessment, but as a methodological and translational expansion of psychiatric practice, capable of integrating different levels of information to improve diagnosis, risk stratification, prognosis and treatment selection.

One of the main points identified refers to the inadequacy of exclusively categorical diagnostic models to represent the complexity of mental disorders. Traditional classification systems, although fundamental for clinical standardization and research, have limitations in the face of high symptomatic heterogeneity, overlap between diagnoses, frequent comorbidity, and individual variability in treatment response. In this sense, the Research Domain Criteria emerges as a structuring proposal by shifting the focus from syndromic classification to functional dimensions related to neural circuits, cognitive processes, behavior, and biological systems (1-

3)In a complementary way, HiTOP proposes a hierarchical organization of psychopathology, allowing symptoms and disorders to be understood as manifestations distributed across dimensional spectra, and not only as isolated diagnostic entities (4) .

This conceptual shift has direct implications for precision medicine. For psychiatric treatment to be truly personalized, it is necessary to recognize that individuals with the same formal diagnosis may present distinct neurobiological, genetic, cognitive, and psychosocial profiles. Thus, two patients classified with major depressive disorder, bipolar disorder, or schizophrenia may respond completely differently to the same medication, show diverging clinical trajectories, and require specific therapeutic strategies. In this context, precision psychiatry proposes a clinical logic that is less focused on an isolated diagnostic label and more oriented toward identifying individual mechanisms, trajectories, and vulnerability, response, and prognosis markers.

Pharmacogenomics has emerged as one of the most advanced and operationalizable fields in precision psychiatry. Studies and guidelines included in this review show that genetic variants associated with the metabolism of psychotropic drugs, especially in genes such as CYP2 D6, CYP2C19, and CYP2B6, can directly affect plasma concentration, tolerability, and clinical response to antidepressants and other psychotropic medications (11-13). The Clinical Pharmacogene tics

Implementation Consortium represents a relevant milestone by providing practical recommendations for dose adjustment and medication selection based on the patient's metabolizer profile, especially in the use of selective serotonin reuptake inhibitors and tricyclic antidepressants (11-13).

Meanwhile, the results also show that pharmacogenomics still needs to be interpreted with caution. Randomized clinical trials and meta-analyses suggest that pharmacogenomic testing may contribute to higher response or remission rates in certain groups of patients with major depression, especially in cases of prior treatment failure, important adverse effects, or multiple medication attempts (10,15-18). The GUIDED study, for example, demonstrated clinical benefits in secondary outcomes related to response and remission, while PRIME Care showed a reduction in the prescription of medications with predicted gene-drug interactions, although the effects on remission were modest and variable over follow-up (15,16). These findings indicate that pharmacogenomic tests can be useful as an auxiliary decision-making tool, but they do not replace clinical judgment, longitudinal assessment, comorbidity analysis, and listening to the patient's preferences.

The discussion on pharmacogenomics also reveals an important tension between technological enthusiasm and clinical applicability. Although the genetic profile can guide the choice of medications, the therapeutic response in psychiatry is multifactorial and involves pharmacodynamic, environmental, psychological, epigenetic, inflammatory, hormonal, and social aspects. The GENDEP study reinforces this complexity by showing that the antidepressant response has a distributed genetic basis and cannot be adequately explained by isolated variants (19) . Therefore, pharmacogenomics should be integrated into a multimodal approach that combines clinical, genetic data, treatment history, adverse effects, adherence to treatment, and psychosocial characteristics.

Another central axis identified was the progress of multimodal biomarkers, especially in major depressive disorder. Studies such as CAN-BIND and EMB-ARC point to a growing trend toward integrating clinical, molecular, neurophysiological, and neuroimaging data in an attempt to predict response to antidepressant treatment (20-25). Major depression is a highly heterogeneous disorder, with multiple possible pathophysiological pathways, including changes in neural circuits, stress response, inflammation, synaptic plasticity, neurotransmission, sleep, cognition, and emotional regulation. Therefore, identifying a single, universal biomarker for diagnosis or therapeutic response seems unlikely. The greatest promise lies in composite models capable of combining different layers of information.

Electroencephalography appears as a particularly relevant tool due to its relatively high accessibility, lower cost compared with functional neuroimaging, and the ability to capture dynamic patterns of brain activity. Studies included in this review indicate that EEG-based models—especially when combined with machine learning techniques—may contribute to predicting response to antidepressants, particularly selective serotonin reuptake inhibitors (22,23). This approach is promising because it brings psychiatry closer to an objective functional assessment, potentially applicable in clinical settings with greater operational feasibility than complex, high-cost exams.

Functional neuroimaging, in turn, has contributed to identifying patterns of brain connectivity associated with therapeutic response. Studies using resting-state functional magnetic resonance imaging show that pre-treatment characteristics and early connectivity changes can help predict the response to escitalopram and other antidepressants (24). More recently, approaches based on deep learning and multimodal brain networks have begun integrating fMRI and EEG data to identify individualized response signatures in major depression (25). These findings reinforce the potential of neuroimaging as a stratification tool, but also highlight challenges related to cost, protocol standardization, the need for external validation, and reproducibility across different centers.

Psychiatric genomics represents another essential field for consolidating precision psychiatry. Large genome-wide association studies have shown that disorders such as schizophrenia and bipolar disorder have complex genetic architectures, with multiple risk loci distributed across the genome (26,27). In the case of schizophrenia, the findings point to genes and pathways related to synaptic biology, reinforcing the nature neurodevelopmental and neurobiological aspects of the disorder (26). In bipolar disorder, genomic studies expand understanding of vulnerability, clinical heterogeneity, and possible shared mechanisms with other psychiatric disorders (27).

Despite their scientific value, polygenic risk scores still have important limitations for individual clinical application. They may contribute to estimates of population-level vulnerability and to research on risk stratification, but they still lack sufficient accuracy for isolated diagnosis, definitive individual prediction, or therapeutic decision-making independent of other factors. Studies in young populations with bipolar disorder or high risk for bipolarity indicate that these scores can offer information relevant about vulnerability, but its clinical usefulness remains dependent on further validation, sample diversity, and integration with environmental, family, and clinical variables (28) .

Artificial intelligence and machine learning emerge as cross-cutting tools, capable of integrating large volumes of data and identifying patterns not evident by traditional statistical methods. Reviews included in this analysis highlight that computational models can support diagnostic, prognostic, and therapeutic prediction, especially when they combine clinical, cognitive, neurobiological, genetic, and digital data (5-7) . However, the application of AI in psychiatry requires methodological rigor, interpretability, external validation and attention to algorithmic biases. A highly accurate model in a research sample may show poorer performance when applied to different clinical populations, with distinct social, cultural, ethnic, and care contexts.

The experience of individualized psychosis-risk calculators clearly illustrates the possibilities and limits of clinical prediction in psychiatry. The model developed in NAPLS-2 made it possible to estimate the risk of conversion to psychosis in individuals with high clinical risk, using clinical, cognitive, and psychosocial variables (29). External validation with the EDIPPP project reinforced the model's robustness, showing that predictive tools can be useful when developed rigorously and tested in independent samples (30). Even so, clinical use of these calculators requires caution, because risk predictions in mental health can generate psychological impacts, stigmatization, premature therapeutic decisions, and ethical dilemmas related to communicating risk.

Another relevant aspect concerns the need for translational validation. Many biomarkers and predictive models show promising results in controlled research environments, but they still face obstacles to being incorporated into routine clinical practice. Among these obstacles are the heterogeneity of the studied populations, the lack of standardization of collection and analysis methods, the limited size of some samples, the absence of independent replication, the cost of certain technologies, and the difficulty of turning complex results into simple, safe, and interpretable clinical recommendations.

Therefore, precision psychiatry is still in a consolidation phase, with more mature areas such as pharmacogenomics, and other areas still under translational development, such as multimodal models based on neuroimaging and artificial intelligence.

Ethical discussion is also indispensable. The use of genetic, neurobiological, and digital data in mental health involves highly sensitive information, related not only to the patient's current condition, but also to future risks, family vulnerabilities, and possible behavioral predictions. Protecting privacy, informed consent, data security, equity in access to technologies, and preventing genetic or algorithmic discrimination are essential aspects for the responsible implementation of precision medicine in psychiatry. In addition, it is necessary to prevent biomarkers from being used in a reductionist way, ignoring subjectivity, the patient's life history, psychic suffering, and the patients' social context.

The analysis of the studies also points to the importance of integrative precision psychiatry. The future of the field is likely not to rely on a single test, exam, or algorithm, but on the intelligent combination of multiple dimensions: a qualified clinical interview, longitudinal history, prior treatment response, a pharmacogenomic profile, biomarkers molecular, neurophysiological data, neuroimaging, cognitive measures, environmental factors, and the patient's preferences. This integration can enable a more predictive, preventive, personalized,
and participatory practice,
Bringing psychiatry closer to the core principles of precision medicine without abandoning its clinical, relational, and humanistic nature.

In this way, the studies included in this review show that precision psychiatry already has relevant scientific foundations, especially in areas such as pharmacogenomics, dimensional models, multimodal biomarkers, psychiatric genomics, and artificial intelligence. However, the broad integration of these tools into clinical practice still depends on robust validation, international standardization, professional training, cost-effectiveness assessment, and the development of applicable clinical protocols. The main contemporary challenge is not only to produce biomarkers or algorithms, but to turn them into safe, accessible, interpretable, and clinically useful instruments to improve mental health care.

Therefore, modern psychiatry is at a point of transition between the traditional model, centered on diagnostic categories and average therapeutic responses, and a new paradigm oriented by individualizing patient care. Precision medicine offers a concrete possibility to reduce the gap between the heterogeneity of mental disorders and the need for more specific, effective, and tolerable interventions. However, its success will depend on the ability to integrate cutting-edge science, clinical prudence, ethical responsibility, and a commitment to the complexity human that characterizes mental suffering.

CONCLUSION

This integrative review made it possible to show that modern psychiatry is in a process of paradigm transition, driven by advances in precision medicine and the need to overcome historical limitations of traditional diagnostic and therapeutic models. The studies analyzed demonstrate that mental disorders cannot be understood only as homogeneous clinical categories, since they show high symptomatic heterogeneity, multiple developmental trajectories, different neurobiological

and wide variability in response to available treatments.

The findings indicate that dimensional and transdiagnostic models, such as the RDoC and the HiTOP, offer relevant foundations for a more integrated understanding of psychopathology, bringing together symptoms, behavior, cognition, neural circuits, and biological mechanisms. This perspective helps shift psychiatric practice from an exclusively categorical logic to a more functional, individualized approach oriented by underlying mechanisms of mental suffering.

Pharmacogenomics has stood out as one of the areas with the greatest immediate clinical applicability in precision psychiatry, especially in the treatment of depressive disorders. The evidence analyzed suggests that genetic tests related to the metabolism of psychotropic drugs may help in medication selection, dose adjustment, reducing gene-drug interactions, and preventing adverse effects. However, the results also show that these tests should be understood as complementary tools, not as substitutes for clinical assessment, since therapeutic response in psychiatry is influenced by biological, psychological, social, environmental, and contextual factors.

Multimodal biomarkers, including peripheral gene expression, electroencephalography, neuroimaging functional and computational models have demonstrated potential to improve the prediction of therapeutic response, especially in major depressive disorder. However, most of this evidence is still in the translational phase, requiring external validation, methodological reproducibility, and cost-effectiveness assessment before being widely incorporated into routine clinical practice.

In the field of psychiatric genomics, large genome-wide association studies and investigations with polygenic risk scores have expanded understanding of the complex genetic architecture of disorders such as schizophrenia and bipolar disorder. Although these markers do not yet have isolated diagnostic utility, they represent promising tools for understanding vulnerability, risk stratification, pathophysiological mechanisms, and possible biological subgroups within severe mental disorders.

Artificial intelligence and individualized predictive models also emerge as strategic tools for precision psychiatry, by enabling the integration of large volumes of clinical, genetic, neuropsychological, neurophysiological, and neuroimaging data. Psychosis risk calculators and machine-learning-based models point to promising avenues for prevention, prognosis, and therapeutic decision-making. However, their clinical application requires caution, especially regarding interpretability, validation in diverse populations, protection of sensitive data, reduction of algorithmic biases, and ethical responsibility in the use of mental-health predictions.

In general, it is concluded that precision medicine represents one of the main frontiers of contemporary psychiatry, with the potential to make mental health care more predictive, preventive, personalized, and participatory. However, its consolidation will depend on balanced integration between technological innovation, scientific rigor, clinical judgment, and humanistic sensitivity. The future of precision psychiatry does not lie in a single biomarker, genetic test, or algorithm, but in the combination of multiple dimensions of analysis capable of recognizing the biological, psychological, and social complexity of mental disorders.

Thus, advances in the diagnosis and personalized treatment of mental disorders point toward a more sophisticated, evidence-based psychiatry that is oriented to the individuality of the patient. Although there are important methodological, clinical, ethical, and operational challenges, the reviewed studies show that precision medicine is already a promising path for improving therapeutic effectiveness, reducing trial-and-error logic, anticipating risks, personalizing interventions, and expanding the quality of care in mental health.

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