pagepress

Mental Wellness

Mental Wellness 2026; 4:39
doi: 10.4081/mw.2026.39

Culturally informed pharmacogenomics in opioid prescribing

Mohsen Khosravi[1-3]

[1]Department of Psychiatry, School of Medicine, Zahedan University of Medical Sciences; [2]Health Promotion Research Center, Zahedan University of Medical Sciences; [3]Community Nursing Research Center, Zahedan University of Medical Sciences, Iran

Abstract

This minireview examines how integrating cultural factors with pharmacogenomics can enhance opioid prescribing practices. Cultural context, including traditional beliefs, family dynamics, and collective identity, significantly impacts patient engagement and treatment outcomes, particularly among minoritized populations. Concurrently, genetic differences in opioid metabolism and response, notably involving genes such as *CYP2D6*, *CYP2B6*, *OPRM1*, *COMT*, and *ABCB1*, underscore the need for personalized pharmacogenomic approaches. Actionable genetic variants are not evenly distributed across populations, further highlighting the importance of culturally informed care. Combining culturally sensitive frameworks with pharmacogenomic testing can improve equity and effectiveness in pain management and opioid use disorder treatment. Key recommendations include integrating cultural competence into clinical pathways, expanding access to pharmacogenomic screening, improving provider education, and promoting inclusive research. Ongoing challenges include limited representation in genomic studies and practical barriers to implementation. Future efforts should prioritize developing scalable, inclusive models and evaluating long-term outcomes to optimize culturally informed pharmacogenomics in opioid prescribing.

Key words: pharmacogenomics, opioid analgesics, cultural competency.

Correspondence to: Mohsen Khosravi, Department of Psychiatry, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran.
E-mail: dr_khosravi2016@yahoo.com

Introduction

The intersection of culture and pharmacogenomics is rapidly emerging as a critical frontier in equitable and effective opioid prescribing. As opioid use disorder and pain management continue to challenge diverse global populations, there is growing recognition that both cultural context and genetic variation fundamentally shape opioid treatment outcomes. Failing to integrate these dimensions risks perpetuating a universalist, trial-and-error paradigm that inadequately serves patients from minoritized and marginalized backgrounds.[1-3]

The imperative for culturally-informed opioid prescribing

A growing body of evidence demonstrates that the effectiveness and acceptability of substance use disorder interventions, including medications for opioid use disorder, are closely linked to the cultural context in which care is provided.[1,2] Standard evidence-based treatments often fail to achieve optimal outcomes, or may even cause unintended harm, when cultural factors are overlooked. For populations such as Latinx and American Indian/Alaska Native (AI/AN) communities, elements like collective identity, family engagement, traditional healing practices, and culturally grounded definitions of wellness are central to the recovery process.

Recent reviews and implementation science research highlight that culturally tailored adaptations of evidence-based treatments, ranging from superficial modifications (*e.g.*, translation of materials, incorporation of culturally relevant examples) to deeper changes (*e.g.*, integration of traditional values, acknowledgement of historical trauma), significantly enhance engagement, retention, and clinical outcomes, especially among individuals with strong cultural identities and those facing systemic barriers.[1,2,4-8] In AI/AN contexts, integrating traditional ceremonies, involving extended family systems, and addressing intergenerational trauma are essential for building trust and facilitating healing.[2]

Culturally informed opioid prescribing is therefore foundational to achieving health equity and optimizing clinical efficacy. The literature suggests that uniform, "one-size-fits-all" approaches are insufficient and may exacerbate disparities. Consequently, clinicians and healthcare systems must systematically incorporate linguistic appropriateness, community knowledge, traditional practices, and social determinants such as discrimination and access to care (Table 1).[1,2]

Table 1. Cultural dimensions and practical adaptations for opioid prescribing and opioid use disorder care.

Cultural dimension	Practical adaptations in practice	Impact on treatment and recovery
Language	Bilingual/translated materials; bicultural/bilingual staff; sessions in preferred language	Increased engagement, comprehension, and trust
Family/inclusion	Family-based interventions; inclusion of extended family, clan, and community elders; family nights	Enhanced support, retention, and collective healing
Traditional healing	Integration of ceremonies, herbal medicines, sweat lodges, talking circles, drumming, storytelling	Increased acceptability; holistic and spiritual wellness
Context (history/trauma)	Addressing historical/intergenerational trauma; explicit discussion of colonialism, racism, discrimination; service location in trusted community venues	Builds trust, mitigates barriers, fosters empowerment
Values/worldview	Emphasis on collectivism, spirituality, indigenous or community values (*e.g.*, familismo, respeto); recognition of traditional concepts of pain and endurance	Aligns care with patient priorities and increases cultural congruence
Persons	Inclusion of traditional healers, community health workers/promotores, elders, and staff representative of the community	Culturally resonant care, improved rapport
Metaphors and storytelling	Use of culturally relevant metaphors, analogies, stories, and media (*e.g.*, telenovelas, indigenous stories)	Facilitates understanding, cultural resonance, and engagement
Goals	Co-creation of treatment goals that reflect cultural values (*e.g.*, community responsibility, spiritual milestones)	Improved motivation, relevance, and sustainability
Methods	Use of CBPR, community advisory boards, culturally adapted assessments and measures	Increased relevance, ownership, and implementation success
Setting/environment	Delivering services in culturally safe, welcoming, and non-stigmatizing spaces (*e.g.*, community centers, tribal clinics)	Reduces stigma, increases accessibility and safety
Structural factors	Addressing social determinants (insurance, transportation, legal status, language proficiency)	Reduces barriers, supports equity and continuity

CBPR, *community-based participatory research.*

The promise and challenge of pharmacogenomics in opioid therapy

Recent advancements in pharmacogenomics have underscored the pivotal influence of genetic variability on opioid metabolism, efficacy, and the risk of adverse effects. Critical genes such as *CYP2D6*, *CYP2B6*, *OPRM1*, *COMT*, and *ABCB1* have been identified as key determinants of individual responses to opioids. These genetic factors can significantly affect clinical outcomes, thereby highlighting both the promise and complexity of integrating pharmacogenomic data into opioid prescribing practices.[3-14]

CYP2D6 is particularly notable for its role in the metabolism of several opioids, including codeine, tramadol, oxycodone, and hydrocodone. Its extensive polymorphism gives rise to a range of metabolizer phenotypes (poor, intermediate, normal, and ultrarapid), each with distinct clinical implications. For instance, ultrarapid metabolizers are at increased risk of opioid toxicity even at standard doses, whereas poor metabolizers experience reduced analgesic efficacy (Table 2).[3,4] The prevalence of these actionable *CYP2D6* variants varies considerably among different ethnic groups, which has important implications for opioid selection and dosing. For example, the frequency of poor metabolizers is highest among individuals of British descent (up to 12%), while ultrarapid metabolizers are more common in North African populations (up to 40%).[5,6] While the most robust pharmacogenomic evidence and clinical guidelines currently pertain to codeine and tramadol, ongoing research is evaluating the utility of pharmacogenomic testing for other opioids, such as oxycodone, hydrocodone, and methadone (affected by *CYP2D6* and *CYP2B6*, respectively).[4] Other genes, including *OPRM1* and *COMT*, have also been implicated in variability in opioid response and pain sensitivity, although the evidence for routine clinical implementation remains limited.[3]

Despite the potential benefits, several barriers hinder the widespread adoption of pharmacogenomics in opioid prescribing. These include limited clinician awareness, logistical and economic challenges related to genetic testing, and a lack of validated gene-drug pairs beyond codeine and tramadol. Nevertheless, as pharmacogenomic knowledge bases (*e.g.*, PharmGKB, CPIC) expand and testing becomes more accessible, individualized opioid therapy is likely to become more feasible and effective (Table 3).[3]

Synergy at the intersection: opportunities for person-centered care

The integration of cultural and pharmacogenomic considerations in opioid prescribing represents a synergistic, rather than merely additive, opportunity for advancing person-centered care. Culturally tailored approaches enhance trust and engagement, foundational elements for the effective application of pharmacogenomic data in clinical practice. In turn, pharmacogenomics can address historical pharmacologic disparities by enabling more precise, individualized, and equitable treatment for pain and opioid use disorder, especially among underrepresented populations.[1,15]

To harness the full potential of culturally-informed pharmacoge-

Table 2. Key pharmacogenomic variants impacting opioid metabolism.

Gene	Variant(s)	Impact on opioid metabolism	High-risk populations/ancestry	Clinical implications	CPIC/PharmGKB evidence
CYP2D6	*3, *4, *5, *6, *10, *17, gene duplications	Alters metabolism of codeine, tramadol, Europeans; oxycodone, hydrocodone	PM: 12% British, high in UM: up to 40% North African	PM: reduced analgesia, risk of therapeutic failure; UM: increased risk of toxicity	Codeine/Tramadol: Level A/1A; Oxycodone/Hydrocodone: Level B/1A or 2A
CYP2B6	*4, *6, *18	Alters methadone clearance	*6 allele more common in Africans, *4 in Europeans	Variation in methadone plasma levels, potential for toxicity or lack of efficacy	Methadone: Level B/2A
OPRM1	rs1799971 (A118G)	Alters mu-opioid receptor binding and function	Highest frequency in East Asians (49%), lower in Europeans (15%), African Americans (5%)	May require higher opioid doses for optimal analgesia; effect size is modest	All opioids: Level C/3
COMT	rs4680 (Val158Met)	Alters catecholamine breakdown, affects pain sensitivity	G allele (Val) more common in Europeans	May influence opioid sensitivity and pain perception; not currently actionable	All opioids: Level C/3
ABCB1	rs1045642, others	Affects P-glycoprotein-mediated opioid transport across blood-brain barrier	Varies by ancestry; high in Europeans	May modulate central opioid effects and side effect risk	Morphine/Fentanyl: Level C/3

PM, poor metabolizer; UM, ultrarapid metabolizer. CPIC Level A/B: prescribing action recommended; Level C: No current prescribing action. PharmGKB Level 1A: Strong evidence/guideline; 2A: Moderate evidence; 3: Low/conflicting evidence.

Table 3. Clinical recommendations based on genotype-phenotype.

Opioid	Genotype/phenotype	Clinical recommendation
Codeine	Ultrarapid metabolizer	Avoid use due to increased risk of toxicity; select alternative opioid
	Poor metabolizer	Avoid use due to lack of efficacy; select alternative opioid
	Normal/intermediate	Use recommended dosing; monitor for efficacy and side effects
Tramadol	Ultrarapid metabolizer	Avoid use due to increased risk of toxicity; select alternative opioid
	Poor metabolizer	Avoid use due to lack of efficacy; select alternative opioid
	Normal/intermediate	Use recommended dosing; monitor for efficacy and side effects
Oxycodone	Ultrarapid/poor metabolizer	No specific recommendation due to insufficient evidence; monitor closely
Hydrocodone	Poor metabolizer	Consider alternative opioid if analgesia inadequate
Methadone	*CYP2B6* *6 or *18	Potential for higher plasma levels; monitor for toxicity

nomics, several practical recommendations are proposed. First, cultural frameworks, including community-defined wellness, family involvement, and traditional healing practices, should be systematically embedded into all pain and opioid use disorder care pathways. Second, pharmacogenomic screening for critical genetic variants (such as *CYP2D6*, *CYP2B6*, *OPRM1*, *COMT*, and *ABCB1*) should be incorporated into opioid prescribing algorithms, particularly for groups with a high prevalence of actionable variants.[15] Third, clinicians require comprehensive training in both cultural humility and genomic literacy to effectively interpret genetic results in the context of patients' cultural identities and beliefs. Lastly, research should prioritize evaluating the efficacy and implementation of culturally and genomically tailored interventions, with a focus on ensuring robust representation of minoritized populations in clinical trials.[1]

Limitations and future research directions

Despite these advances, several limitations persist. The current evidence base for culturally-informed pharmacogenomics is limited by the underrepresentation of diverse populations in genomic research and clinical trials, potentially restricting the generalizability of findings. Additionally, there are challenges related to the standardization of culturally tailored care frameworks and the integration of pharmacogenomic data into routine clinical workflows. Future research should address these gaps by promoting inclusive genomic studies, developing scalable models for the integration of culture and genomics in clinical practice, and investigating the long-term outcomes of such interventions across diverse populations. Interdisciplinary collaboration and policy support will be essential in overcoming these barriers and realizing the full promise of culturally-informed pharmacogenomics in opioid prescribing.

Conclusions

In summary, integrating cultural competence with pharmacogenomics in opioid prescribing offers a transformative pathway toward more equitable, effective, and individualized pain management and opioid use disorder treatment. Cultural factors, such as traditional practices, family involvement, and collective identity, significantly influence patient engagement and outcomes, particularly among minoritized groups. Concurrently, genetic variability in key pharmacogenes (*e.g.*, *CYP2D6*, *CYP2B6*, *OPRM1*, *COMT*, *ABCB1*) affects

opioid metabolism and response, with actionable variants distributed unevenly across populations. By embedding both cultural frameworks and pharmacogenomic screening into clinical practice, healthcare providers can address both social and biological determinants of opioid therapy, reducing disparities and enhancing person-centered care. However, challenges such as underrepresentation in genomic research, standardization of culturally tailored interventions, and integration into clinical workflows remain. Future efforts should focus on inclusive research, clinician education, and scalable implementation strategies to fully realize the benefits of culturally-informed pharmacogenomics in opioid prescribing.

References

1. Venner KL, Hernandez-Vallant A, Hirchak KA, Herron JL. A scoping review of cultural adaptations of substance use disorder treatments across Latinx communities: guidance for future research and practice. J Subst Abuse Treat 2022;137:108716.
2. Hirchak KA, Nadeau M, Vasquez A, et al. Centering culture in the treatment of opioid use disorder with American Indian and Alaska Native Communities: contributions from a National Collaborative Board. Am J Community Psychol 2023;71:174-83.
3. Wong AK, Somogyi AA, Rubio J, Philip J. The role of pharmacogenomics in opioid prescribing. Curr Treat Options Oncol 2022;23:1353-69.
4. Ghassemzadeh H, Mojtabai R, Karamghadiri N, Ebrahimkhani N. Psychometric properties of a Persian-language version of the Beck Depression Inventory—Second edition: BDI-II-PERSIAN. Depress Anxiety 2005;21:185-92.
5. Hai AH, Lee CS, Abbas BT, et al. Culturally adapted evidence-based treatments for adults with substance use problems: a systematic review and meta-analysis. Drug Alcohol Depend 2021;226:108856.
6. Marsiglia FF, Ayers SL, Han S, Weide A. The role of culture of origin on the effectiveness of a parents-involved intervention to prevent substance use among Latino middle school youth: results of a cluster randomized controlled trial. Prev Sci 2019; 20:643-54.
7. Torres VN, Williams EC, Ceballos RM, et al. Participant satisfaction and acceptability of a culturally adapted brief intervention to reduce unhealthy alcohol use among Latino immigrant men. Am J Mens Health 2020;14:1557988320925652.
8. Vega-López S, Marsiglia FF, Ayers S, et al. Methods and rationale to assess the efficacy of a parenting intervention targeting diet improvement and substance use prevention among Latinx adolescents. Contemp Clin Trials 2020;89:105914.
9. Crews KR, Monte AA, Huddart R, et al. Clinical pharmacogenetics implementation consortium guideline for CYP2D6, OPRM1, and COMT genotypes and select opioid therapy. Clin Pharmacol Ther 2021;110:888-96.
10. Gaedigk A, Sangkuhl K, Whirl-Carrillo M, et al. Prediction of CYP2D6 phenotype from genotype across world populations. Genet Med 2017;19:69-76.
11. Koopmans AB, Braakman MH, Vinkers DJ, et al. Meta-analysis of probability estimates of worldwide variation of CYP2D6 and CYP2C19. Transl Psychiatry 2021;11:141.
12. Kane M. CYP2D6 overview: allele and phenotype frequencies. In: Pratt V, Scott S, Pirmohamed M, et al., eds. Medical genetics summaries. Bethesda, MD, USA: National Center for Biotechnology Information (US); 2021.
13. Cox B. Recent developments in the study of opioid receptors. Mol Pharmacol 2013;83:723-8.
14. Lennard L. Implementation of TPMT testing. Br J Clin Pharmacol 2014;77:704-14.
15. Whirl-Carrillo M, Huddart R, Gong L, et al. An evidence-based framework for evaluating pharmacogenomics knowledge for personalized medicine. Clin Pharmacol Ther 2021;110:563-72.

Received: 14 March 2026; Accepted: 18 March 2026.

Conflict of interest: the author declares no conflict of interest regarding the publication of this article.

Ethics approval and consent to participate: not applicable.

Informed consent: not applicable.

Patient consent for publication: not applicable.

Availability of data and materials: data and materials are available from the corresponding author upon request.