Bridging the Gap: Pharmacogenomic Challenges in Buprenorphine Therapy for Opioid Use Disorder

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Introduction

Opioid use disorder (OUD) is a condition characterized by the chronic use of opioids that causes significant distress or impairment. The ongoing OUD epidemic poses a major public health burden, with many overdoses involving illicit substances laced with fentanyl or xylazine. Therefore, making OUD treatment available saves lives.

Buprenorphine, a partial μ-opioid receptor agonist, is preferred for its safety ceiling and accessibility through office-based programs. Pharmacogenomics offers a promising approach to individualize buprenorphine dosing. The drug is mainly metabolized by CYP3A4, an enzyme with genetic variants that affect metabolism rate. Individuals with the CYP3A4*1B allele are ultrarapid metabolizers who may experience subtherapeutic levels, withdrawal, and increased relapse risk.

This case highlights the dosing challenges in a CYP3A4 ultrarapid metabolizer receiving buprenorphine and the critical need for pharmacogenomic considerations in OUD management. Pharmacists play a critical role in integrating genomic insights, advocating for appropriate dosing, and addressing system barriers to optimize outcomes.

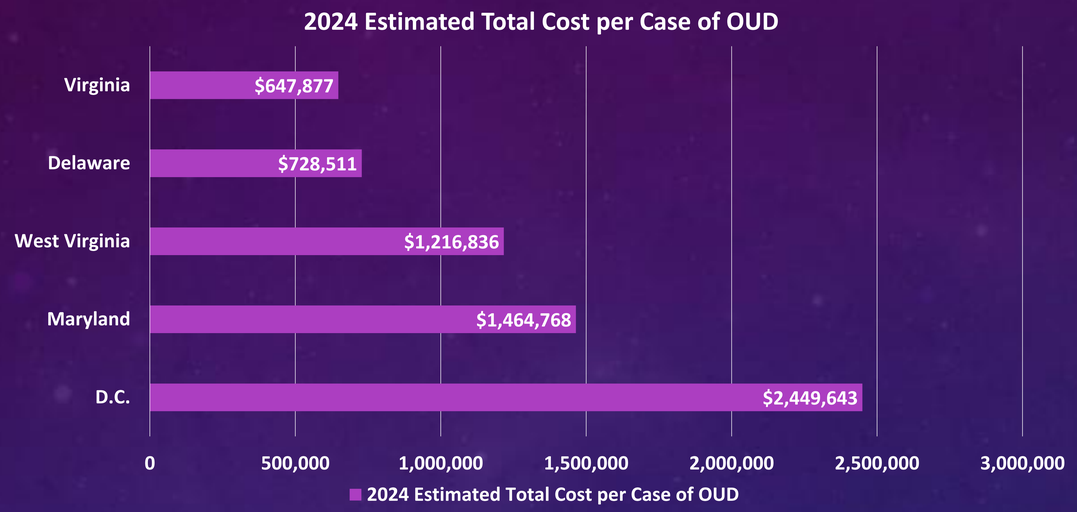
Objectives

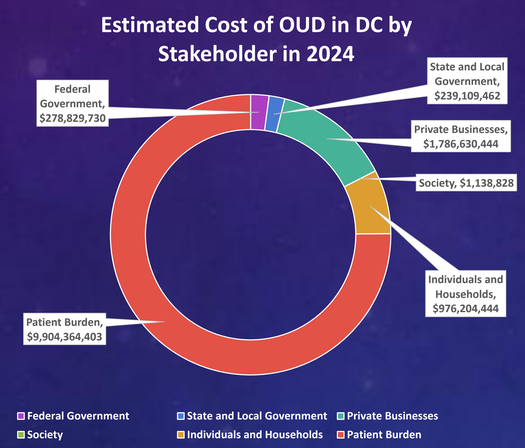
- **Describe** the clinical challenges of managing opioid use disorder (OUD) in a patient with a CYP3A4 ultrarapid metabolizer phenotype receiving buprenorphine therapy.
- **Evaluate** the impact of pharmacogenomics on buprenorphine metabolism, dosing requirements, and treatment outcomes.
- **Highlight** the pharmacist's role in optimizing OUD management through individualized dosing strategies, pharmacogenomic interpretation, and patient-centered approaches such as Appreciative Inquiry.

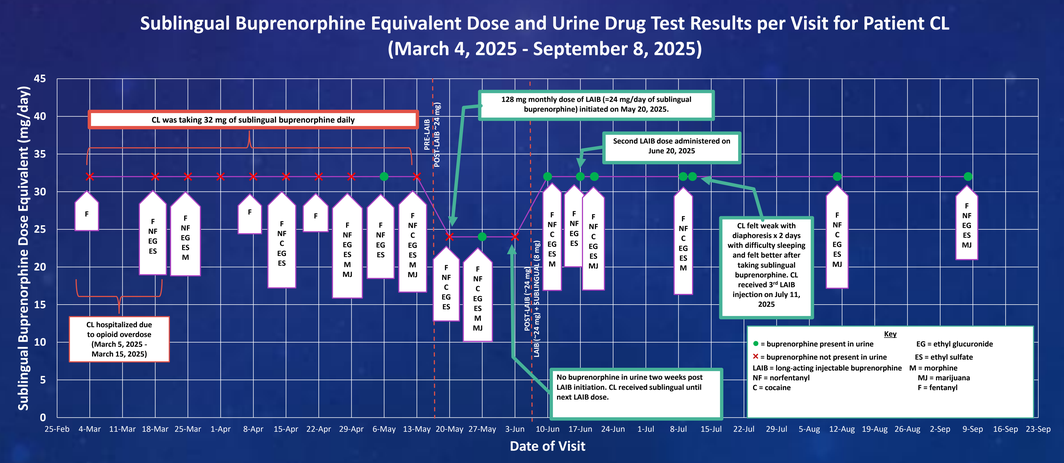
Methods

This case study describes the clinical course of a 67-year-old male with opioid use disorder (OUD) who is a confirmed CYP3A4 ultrarapid metabolizer. The patient's medical history, pharmacogenomic data, and treatment records were reviewed retrospectively to evaluate buprenorphine response and dosing challenges over a 4-month period (March 4 – July 11, 2025). Clinical data were obtained from weekly outpatient visits, which included comprehensive medical examinations, withdrawal assessments, and urine drug testing.

Treatment progression was analyzed from initiation of long-acting injectable buprenorphine (LAIB) therapy following hospitalization for opioid overdose. Documentation of sublingual buprenorphine adherence, LAIB dosing intervals, urine drug results, and patient-reported symptoms were reviewed to assess medication exposure, withdrawal onset, and response to altered dosing frequency.







Results

Over the seven-month observation period, the patient attended 20 clinic visits. Despite long-term use of 32 mg sublingual buprenorphine daily, he demonstrated variable adherence and frequent early depletion of medication, resulting in multiple negative urine drug tests. Following hospitalization for a fentanyl-related overdose in March 2025, long-acting injectable buprenorphine (LAIB) was initiated at the maximum dose on May 20, 2025.

Two weeks post-injection, urine testing revealed no detectable buprenorphine. Supplemental sublingual buprenorphine was provided until the next injection, and dosing frequency was shortened from every 28 days to every 21 days.

By July 2025, the patient continued to experience intermittent withdrawal symptoms and self-supplemented with leftover sublingual films. Adjusting the LAIB interval improved symptom control, though subtherapeutic trough levels persisted, underscoring the need for pharmacogenomic-guided dosing and pharmacist involvement in optimizing buprenorphine therapy based on individualized dosing.

Discussion

This case highlights the challenges of managing opioid use disorder (OUD) in patients receiving buprenorphine-based medication-assisted treatment (MAT). The patient experienced subtherapeutic drug levels, withdrawal, and cravings that increased relapse and overdose risk. Management was further complicated by limited dosing guidance, insurance restrictions, and misinterpretation of urine drug tests.

Integrating pharmacogenomic data into clinical decision-making can help individualize buprenorphine dosing for these patients. Pharmacists are uniquely positioned to lead these efforts through pharmacogenomic interpretation, adherence monitoring, and empathetic communication that reduces stigma and fosters trust.

Conclusion

This case underscores the importance of personalized, pharmacogenomics-informed approaches in opioid use disorder (OUD) management. CYP3A4 ultrarapid metabolizers may require higher or more frequent buprenorphine dosing to prevent withdrawal and relapse. Pharmacists play a key role in optimizing therapy, addressing access barriers, and fostering supportive, stigma-free communication.

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