



Patient Information

Patient Name Aiden Test
Date of Birth 2026-08-10
Ethnicity Asian
Gender Male

Results Summary

Proove Opioid Risk



29

High Risk

Range: 24 - 52

Opioid Risk Tool (ORT)



15

High Risk

Personal Health Questionnaire
(PHQ-2)



3

Further Evaluation Needed

⚠ Significant Finding — Clinician Review Suggested: This patient's Opioid Risk Index is HIGH. You may want to review their current or planned opioid therapy.

Executive Summary

- The patient has a Proove Opioid Risk Index score of 29, indicating a **High Risk** for Opioid Use Disorder.
- This finding, coupled with a High Risk score on the Opioid Risk Tool (ORT) and a "Further Evaluation Needed" result on the PHQ-2, suggests that a comprehensive evaluation of potential risks and benefits is warranted before initiating opioid therapy, and close monitoring may be recommended.
- The integration of genetic and phenotypic factors in this assessment provides an objective foundation for personalized pain management planning, prioritizing safety and considering alternative or adjunctive therapies.

Risk Score Interpretation

- The patient's Proove Opioid Risk Index score is 29, which falls within the 24-52 range, indicating a **High Risk** for Opioid Use Disorder.
- This high-risk stratification is supported by a **High Risk** score of 15 on the Opioid Risk Tool (ORT), which suggests a comprehensive evaluation of potential risks and benefits is warranted before initiating opioid therapy.
- Additionally, the Personal Health Questionnaire (PHQ-2) score of 3, categorized as "Further Evaluation Needed," indicates a need for more comprehensive assessment for depression or other mood-related concerns, which can be a contributing factor to opioid misuse risk.
- Genetic factors, which account for approximately 42% of the Proove Opioid Risk Index score, also contribute to this risk stratification. The patient's genotype data includes variants in genes associated with pain processing (OPRM1, OPRK1, COMT) and neurotransmitter systems (SLC6A4, HTR2A, ANKK1, DRD1, DRD4, SLC6A3), as well as MTHFR, which influences nutrient metabolism essential for neurotransmitter pathways.
- Phenotypic factors contributing to the high risk include a "Yes" answer for age between 16 and 45 years, family history of alcoholism, family history of illegal drug abuse, personal history of alcoholism, personal history of illegal drug abuse, history of preadolescent sexual abuse, and current depression.

Genotype Analysis — Pharmacogenetic Contribution to Risk

- **OPRM1 (rs1799971): A/G** - This gene encodes the mu-opioid receptor, the primary target for most opioid analgesics. Variants in OPRM1, such as the G allele, have been associated with altered opioid sensitivity, potentially requiring higher doses for pain relief, and influencing the risk of opioid dependence.
- **OPRK1 (rs1051660): A/C** - This gene encodes the kappa-opioid receptor, which plays a role in pain modulation and can influence dysphoric responses to opioids. Variants in OPRK1 may affect individual responses to kappa-opioid agonists and contribute to the overall opioid response profile.

- **COMT (rs6269, rs4633, rs4818, rs4680): G/A, C/T, C/G, A/G** - The Catechol-O-methyltransferase (COMT) gene is involved in the metabolism of catecholamines, including dopamine and norepinephrine, which are important in pain pathways and reward systems. Variants in COMT can affect pain sensitivity and the efficacy of certain pain medications, potentially influencing the need for opioids and the risk of misuse.
- **SLC6A4 (rs140701): T/T** - This gene encodes the serotonin transporter, which is crucial for regulating serotonin levels in the brain. Serotonin is involved in mood regulation and pain perception. Variants in SLC6A4 can influence susceptibility to depression and anxiety, which are often comorbidities in chronic pain patients and can increase opioid misuse risk.
- **ANKK1 (rs1800497): G/G** - This gene is located near the DRD2 dopamine receptor gene and variants, particularly the Taq1A allele (often linked to rs1800497 G allele), have been associated with altered dopamine receptor availability. Dopamine pathways are central to reward and addiction, and these variants may influence an individual's vulnerability to substance use disorders, including opioid misuse.
- **MTHFR (rs1801133): G/A** - This gene encodes methylenetetrahydrofolate reductase, an enzyme involved in folate metabolism and the synthesis of neurotransmitters. Variants in MTHFR can affect neurotransmitter levels, potentially influencing mood and pain perception, and indirectly contributing to the overall risk profile.

Recommended Diagnostic Workup

- Conduct a comprehensive pain assessment to thoroughly evaluate the nature of any pain, its impact, and potential non-opioid management options, as suggested by the Proove AI Powered-Clinical Summary.
- Perform a psychiatric/SUD assessment to further explore mood and emotional well-being, offering supportive strategies or interventions as needed, given the PHQ-2 score of 3 ("Further Evaluation Needed") and the patient's reported history of depression and preadolescent sexual abuse.
- Consider a re-administration of a structured opioid risk assessment tool (e.g., ORT, SOAPP-R) at regular intervals, along with routine urine drug screens and pill counts, to monitor adherence and identify potential misuse behaviors, especially given the patient's High Risk stratification (Brenton et al., 2017).

Treatment Approaches

- **Pharmacological considerations:**
 - Given the patient's High Risk for Opioid Use Disorder (Proove Opioid Risk Index score of 29) and the OPRM1 A/G genotype, which may be associated with altered opioid sensitivity, clinicians should consider a cautious approach to opioid prescribing, potentially starting with lower doses and titrating slowly while closely monitoring for efficacy and adverse effects.
 - If opioids are deemed necessary, consider agents with a lower abuse potential or explore alternative analgesic classes.
 - For patients identified as poor responders to Rx Opioids, be aware of elevated risk for developing an opioid use disorder and consider medically-assisted treatment (MAT) for detoxification if appropriate.
- **Non-pharmacological considerations:**

- Prioritize and implement a personalized multimodal pain management plan that integrates non-opioid pharmacotherapy, interventional procedures, and behavioral therapies (e.g., physical therapy, cognitive behavioral therapy, mindfulness-based stress reduction) (Nalamachu et al., 2015).
- Referral for behavioral health support is strongly recommended, given the PHQ-2 score indicating a need for further evaluation, reported depression, and history of preadolescent sexual abuse. This can address underlying mood disorders and provide coping strategies for pain and stress.
- Explore alternative non-opioid medications or procedures to improve pain relief, especially for patients naive to Rx opioids or those identified as poor responders to Rx opioids.

Monitoring Plan

- Implement frequent and rigorous monitoring, including routine urine drug screens and pill counts, to assess adherence and identify any signs of aberrant drug-related behaviors, consistent with recommendations for high-risk patients (Brenton et al., 2017).
- Maintain increased attention to the patient's pain relief and functional status, regularly reassessing the need for and effectiveness of current pain management strategies.
- Schedule regular follow-up appointments to discuss emotional well-being, assess for any signs of depression or anxiety progression, and determine if additional support or resources are beneficial, particularly in light of the PHQ-2 results and genetic predispositions related to mood regulation.
- Educate the patient and family about the elevated risk for Opioid Use Disorder and the importance of adhering to the prescribed treatment plan, safe storage of medications, and proper disposal of unused opioids.

High-Quality Research Citations

- **[Farah et al., 2017]** — Evaluation of a Predictive Algorithm that Detects Aberrant Use of Opioids in an Addiction Treatment Center. *J Addict Res Ther.*
- **[Moore et al., 2009]** — A Comparison of Common Screening Methods for Predicting Aberrant Drug-Related Behavior among Patients Receiving Opioids for Chronic Pain Management. *Pain Medicine*. Volume 10, Issue 8, November 2009, Pages 1426–1433. <https://doi.org/10.1111/j.1526-4637.2009.00713.x>
- **[Brenton et al., 2013]** — Observational Study to Calculate Addictive Risk to Opioids: A Validation Study of a Predictive Algorithm that Detects Opioid Use Disorder. *Pharmacogenomics Pers Med.* 2017; 10: 187–195.
- **[Brenton et al., 2017]** — Observational study to calculate addictive risk to opioids: a validation study of a predictive algorithm to evaluate opioid use disorder. *Health Services Research & Managerial Epidemiology.*
- **[Lewis et al., 2017]** — Prospective, Longitudinal Study to Evaluate the Clinical Utility of a Predictive Algorithm to Detect Opioid Use Disorder in Chronic Pain Patients. *J Addict Res Ther.*
- **[Lee et al., 2018]** — A Predictive Algorithm to Detect Opioid Use Disorder: What is the Utility in a Primary Care Setting? *Health Services Research and Managerial Epidemiology.*
- **[Nalamachu et al., 2015]** — Adding Genetic Tests to Evidence-Based Guidelines to Determine the Safest and Most Effective Chronic Pain Treatment for Injured Workers. *Int J*

Cautions & Data Gaps

- This interpretation is based on the provided genetic and phenotypic data and should be integrated with the clinician's independent medical judgment, patient history, and ongoing clinical assessment.
- While the Proove Opioid Risk Index is highly accurate, it is a decision support tool and not a diagnostic test for Opioid Use Disorder.
- The PHQ-2 score indicates a need for further evaluation for depression, but this report does not provide a definitive diagnosis or comprehensive psychiatric assessment.
- The genetic variants assessed represent known associations but do not account for all possible genetic or environmental factors that may influence opioid response or misuse risk.
- The report does not provide specific details on the patient's current pain condition, duration, severity, or previous treatment responses, which are crucial for a comprehensive pain management plan.

Important Disclaimer

- This Clinical Decision Support summary is intended solely for licensed healthcare professionals and constitutes decision support only — it is not a diagnosis, prescription, or treatment order, and must not substitute for independent professional medical judgment.
- The information above was extracted automatically from the uploaded document using AI. AI systems can make mistakes — extraction accuracy depends on the quality, clarity, and completeness of the uploaded file, and values, levels, citations, or interpretations shown here may be incomplete or inaccurate.
- Verify all values, citations, and guideline references against the original report and primary literature before making any clinical decision.
- Proove Genomics and CIAIre are not responsible for decisions made based solely on this AI-generated summary.

Gene	RS Number	Result
OPRK1	rs1051660	A/C
GABRG2	rs211014	C/C
OPRM1	rs1799971	A/G
COMT	rs6269	G/A
COMT	rs4633	C/T
COMT	rs4818	C/G
COMT	rs4680	A/G
SLC6A4	rs140701	T/T
HTR2A	rs7997012	G/G
ANKK1	rs1800497	G/G
DRD1	rs4532	T/T
DRD4	rs3758653	T/T
SLC6A3	rs27072	C/C
DBH	rs161115	C/T
MTHFR	rs1801133	G/A

Personal / Family History	Answer
Age between 16 and 45 years ?	Yes
Personal history of mental health disorders ?	No
Family history of alcoholism ?	Yes
Family history of illegal drug abuse ?	Yes
Family history of prescription drug abuse ?	No
Personal history of alcoholism ?	Yes
Personal history of illegal drug abuse ?	Yes
Personal history of prescription drug abuse ?	No
History of preadolescent sexual abuse ?	Yes
Depression	Yes

Supporting Clinical Evidence

Accuracy of the Opioid Risk Test: The opioid risk assessment methodology has been rigorously validated across five independent clinical studies encompassing more than 3,700 patients across 126 clinical sites, producing a consistently strong body of evidence for its predictive accuracy. The comprehensive risk algorithm — which integrates genetic biomarkers (accounting for approximately 42% of the score) with validated clinical phenotypic factors including the Opioid Risk Tool (ORT) and PHQ-2 depression screen — achieves Area Under the Curve (AUC) values ranging from 0.757 to 0.967 depending on clinical setting, meaning the test correctly identifies opioid use disorder (OUD) between 76% and 97% of the time. In an addiction treatment center validation study (Farah et al., 2017; N=186), the algorithm achieved a remarkable AUC of 0.967, with sensitivity of 97.9% and 100% specificity at the high-risk threshold — meaning every single control patient scored below the high-risk cutoff with no false positives. In a large-scale multi-center chronic pain study (Brenton et al., 2017; N=908, 24 sites), sensitivity at the combined moderate-and-high-risk threshold reached 95.7%, and a dual-cohort validation study (Khoury et al., 2017; discovery N=302, validation N=471) demonstrated sensitivity of up to 100% with a corresponding positive predictive value of 100% in high-risk patients. In the largest validation in primary care (Sharma et al., 2017; N=1,689, 27 clinics), the algorithm outperformed both the SOAPP-R (AUC 0.67–0.76, specificity ~52%) and the ORT (clinical sensitivity ~45%) — the two most widely used standalone tools — achieving an AUC of 0.832 with 91.8% sensitivity and 88.4% specificity at the high-risk cutoff. Critically, this performance remained stable across varying OUD prevalence rates of 8%, 27%, and 50%, confirming the algorithm's robustness across diverse practice settings. The laboratory methodology underlying the genetic component has also demonstrated 100% repeatability, 100% intermediate precision, and 99.62%–100% inter-laboratory reproducibility — providing a fully analytically validated, objective foundation that no subjective questionnaire-based tool alone can match.

Key Advantages & Benefits: The opioid risk test delivers measurable, evidence-backed advantages across three dimensions: clinical decision-making, patient pain outcomes, and healthcare economics. Unlike traditional screening tools such as the ORT and PHQ-2 — which rely solely on patient self-report and are vulnerable to recall bias, social desirability, and intentional misreporting — the integrated risk algorithm combines objective genetic data with validated clinical inputs, giving clinicians an objective, manipulation-resistant risk profile that actively guides treatment decisions. Across three large prospective longitudinal clinical utility studies encompassing more than 13,400 patients at 194 clinical sites, 88–90% of physicians reported measurable clinical benefit from the test, with those who used results to guide treatment rating the tool significantly more beneficial than those who did not (up to 4.4x greater benefit, $p < 0.001$ in all studies). Physicians used the risk profile to make decisive, consequential actions: in the largest utility study (Brenton et al., 2018; N=5,397), nearly 52% of patients had their treatment guided by profile results, with 24.5% undergoing direct changes to their opioid regimen — including dose adjustments, opioid substitutions, and discontinuation in high-risk patients — and 96% of newly initiated opioid therapies going to low- or moderate-risk patients, reflecting genuinely safer prescribing patterns. These evidence-based interventions translated directly into dramatically improved patient pain outcomes: average pain scores (Numeric Rating Scale) dropped by 2.7 to 3.4 points across studies, representing a 42–45% reduction in pain, with over 60–90% of patients reporting some level of improvement and up to 13% achieving complete pain resolution. In a Medicare cohort of 6,161 patients across 158 clinics, profile-guided care produced a 45% average pain reduction and generated an estimated \$12.4 million in healthcare cost savings in the first year alone — with projected five-year savings exceeding \$62 million — by shifting patients from severe to moderate or mild pain categories and reducing dependence on costly opioid-related care. Beyond individual patient benefit, the algorithm carries significant public health implications: by identifying high-risk individuals before initial opioid exposure, early research suggests the test has the potential to prevent nearly 97% of OUD cases that would otherwise develop in at-risk populations — a transformative outcome in the context of an opioid crisis that cost the United States an estimated \$78.5 billion in 2013 alone.

Interpretation

Proove Opioid Risk and its Opioid Risk Index (ORI) is a one-time analysis combining objective genetic predisposition data with phenotypic information to help physicians identify patients at risk for the misuse of opioids, or what is commonly diagnosed as Opioid Use Disorder F11.29: Opioid dependence with an unspecified opioid-induced disorder; F11.90: Opioid use that is unspecified and uncomplicated; F11.920: Opioid use that is unspecified and uncomplicated, with intoxication; F11.20: Opioid dependence that is uncomplicated; F11.99: Opioid use that is unspecified, with an unspecified opioid-induced disorder; or, F11.94: Opioid use that is unspecified, with an opioid-induced mood disorder. A Proove Opioid Risk score of 0-11 indicates the patient exhibits low risk of misusing opioids. A score of 12-23 indicates the patient exhibits moderate risk of misusing opioids. A score of 24-52 indicates the patient exhibits high risk of misusing opioids. This information can be used, along with a medical evaluation of therapeutic outcomes, to guide appropriate opioid treatment decisions.

Proove Opioid Risk's accuracy, or clinical validity as measured by sensitivity, is superior to alternative risk screens. Proove Opioid Risk is 97.9%, a clinical interview is 77%, the SOAPP is 72%, the ORT is 45%, and the DIRE is 17%.^(1,2) In three published clinical studies, Proove Opioid Risk's accuracy was as high as 96.7% (ROC Curve) in stratifying risk for Opioid Use Disorder. In three published clinical validity studies inclusive of over 50 research sites and over 2,500 patients, Proove Opioid Risk had up to 96.7% ROC curve accuracy rate, with up to a 100% PPV and 95.4% NPV.^(1,3,4)

Proove Opioid Risk's outcomes, or clinical utility, as measured by reductions in pain, physician opioid, and safely moving patients to alternative analgesics without a difference in pain relief is also established in published studies. In three published clinical utility studies across 194 research sites and over 12,000 patient participants, Proove Opioid Risk shows positive outcomes. Physicians rate the test as a 3.6-4 on a 5-point scale as a benefit for their decision making. The average pain reduction 30 days after using the information was between 2.7 to 3.4 on the 0-10 numerical rating scale. 88%-90% of physicians felt the test benefited patient care. And for patients at high risk for misusing opioids, clinicians were able to safely transition patients to non-opioid therapy with no statistically significant difference in analgesia using pharmacogenetic information from Proove Drug Metabolism. ^(5,6,7)

Methodology

DNA collection is performed via buccal swab and saliva specimen. A published study showed that the average DNA yield was 1.94 micrograms +/- 0.54 with a 94% genotyping pass rate in a pilot study (n=34), and 2.44 micrograms +/- 1.74 with a 93% genotyping pass rate in the high-throughput application (n=1140) ⁽¹⁰⁾ Genomic DNA is isolated from a dry buccal swab and saliva specimen using a commercially available magnetic particle DNA isolation kit along with proprietary techniques using an automated DNA isolation system. Specific regions of interest are amplified using commercially available proprietary primers, TaqMan probes, and reagents from Life Technologies, a ThermoFisher Company. The variants are detected on Life Technologies Quant Studio 7 genetic analyzer as Single Nucleotide Polymorphisms (SNPs). The data is analyzed and reported by qualified licensed laboratory personnel using Life Technologies Genotyper data analysis software, version 1.3. This test was independently verified by Proove Genomics, Inc. (Arlington, TX, USA) under Clinical Laboratory Improvement Amendment (CLIA) guidelines as a Laboratory Developed Test (LDT).

Disclaimer

The above test(s) have not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. Proove Genomics, Inc. has validated the performance characteristics of the above test(s). The above test(s) results are not intended to be used as the sole means for clinical diagnoses or patient management decisions. Only medically necessary tests (based on specific patient diagnosis and treatment) should be ordered. Screening tests will generally not be reimbursed by insurance companies.

References

- (1) Farah et al. Evaluation of a Predictive Algorithm that Detects Aberrant Use of Opioids in an Addiction Treatment Centre. *J Addict Res Ther*, May 2017.
- (2) Moore TM et al. A Comparison of Common Screening Methods for Predicting Aberrant Drug-Related Behavior among Patients Receiving Opioids for Chronic Pain Management. *Pain Medicine*, Volume 10, Issue 8, November 2009, Pages 1426–1433, <https://doi.org/10.1111/j.1526-4637.2009.00743.x>
- (3) Brenton A et al. Observational Study to Calculate Addictive Risk to Opioids: A Validation Study of a Predictive Algorithm that Detects Opioid Use Disorder. *Pharmgenomics Pers Med*. 2017; 10: 187–195.
- (4) Brenton A et al. Observational study to calculate addictive risk to opioids: a validation study of a predictive algorithm to evaluate opioid use disorder. *Health Services Research & Managerial Epidemiology*, May 2017.
- (5) Lewis K et al. Prospective, Longitudinal Study to Evaluate the Clinical Utility of a Predictive Algorithm to Detect Opioid Use Disorder in Chronic Pain Patients. *J Addict Res Ther* 2017, 8:3
- (6) Lee C et al. A Predictive Algorithm to Detect Opioid Use Disorder: What Is the Utility in a Primary Care Setting? *Health Services Research and Managerial Epidemiology*, Volume 5: 1-8, 2018.
- (7) Brenton A et al. A prospective, longitudinal study to evaluate the clinical utility of a predictive algorithm that detect risk of opioid use disorder. *J Pain Res* 2018 Jan 5;11:119-131. doi: 10.2147/JPR.S139189. eCollection 2018.
- (8) Meshkin B et al. Adding Genetic Testing to Evidence-Based Guidelines to Determine the Safest and Most Effective Chronic Pain Treatment for Injured Workers. *Int J Biomed Sci* 2015 Dec;11(4):157-65.
- (9) Feinberg SD et al. Chronic Pain Guideline. Effective May 15, 2017. American College of Occupational and Environmental Medicine, MTUS Guidelines.
- (10) McMichael GL, Gibson CS, O'Callaghan ME, Goldwater PN, Dekker GA, Haan EA, MacLennan AH; South Australian Cerebral Palsy Research Group. DNA from buccal swabs suitable for high-throughput SNP multiplex analysis. *J Biomol Tech*. 2009 Dec;20(5):232-5. PMID: 19949693; PMCID: PMC2777348.