PROOVE GENOMICS

Proove Opioid Risk Profile Report

Report Date August 27, 2026

Patient Information

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

Date of Service: 2026-08-03
Customer ID: nimptsch
Account Name: jzzzzzz
Physician Name: xxxxxxxxxxx

Results Summary

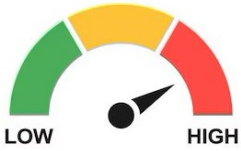
Proove Opioid Risk

High Risk

Opioid Risk Tool (ORT)

High Risk

Personal Health Questionnaire (PHQ-2)



Further Evaluation Needed

Clinical Analytics Interpretation & Report

Proove Opioid Risk	**High Risk**	**Score: 29** **Range: 24 - 52** **Published studies show that Proove Opioid Risk is up to 96.7% accurate in stratifying risk for Opioid Use Disorder.**	• **PATIENT NAIVE TO RX OPIOIDS -** Consider alternative analgesic medications or procedures to improve outcomes. • **PATIENT GOOD RESPONDER TO RX OPIOIDS -** Consider more routine urine drug testing; limit duration of Rx Opioids; main increased attention to patient's outcomes. • **PATIENT POOR RESPONDER TO RX OPIOIDS -** Consider titration down to end Rx Opioid therapy; be aware of elevated risk for withdrawal symptoms and treat accordingly; consider alternative analgesic medications or procedures; consider medically-assisted treatment (MAT) for detoxification.
Opioid Risk Tool (ORT)	**High Risk**	**Score: 15**	
Personal Health Questionnaire (PHQ-2)	**Further Evaluation Needed**	**Score: 3**	

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Labarium Diagnostic Systems, Inc.

InfinitiLabs, Inc.("InfinitiLabs") is an agent of Labarium Diagnostic Systems, Inc.("Labarium"). InfinitiLabs is one of Labarium's network of labs advancing health through intelligent tools to improve medical decisions.

425 Grand Boulevard, Suite 206, Miramar Beach, Florida, USA 32550 For more information, please visit www.Labarium.com

INFINITILABS

Laboratory Performing Test

Laboratory Director : Dr. Barroso-Vicens, MD

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Proove AI Powered-Clinical Summary

Opioid Risk Tool (ORT) Section

- The Opioid Risk Tool (ORT) is a screening questionnaire designed to assess an individual's risk for developing problematic opioid use.
- An ORT score of 15, categorized as "High Risk," suggests a significantly increased potential for developing issues related to opioid use, warranting careful consideration.
- This score can help a clinician evaluate appropriate pain management strategies, potentially emphasizing non-opioid options or requiring enhanced monitoring if opioids are considered.

Patient Health Questionnaire (PHQ-2) Section

- The PHQ-2 (Patient Health Questionnaire-2) is a brief screening tool used to assess for the presence of depressive symptoms over the past two weeks.
- A PHQ-2 score of 3, indicating "Further Evaluation Needed," suggests that you may be experiencing some symptoms that warrant a more in-depth discussion with your clinician about your emotional well-being.
- This level indicates that while not a diagnosis, further assessment could help determine if additional support or resources might be beneficial for your mood.

Genotype Analysis Section

- Your genetic profile includes variations in genes associated with neurotransmitter systems, such as those involved in dopamine, serotonin, and opioid signaling, which play roles in mood, pain perception, and stress response.
- Specifically, variations were noted in genes like COMT, OPRM1, and SLC6A4, which are sometimes studied in the context of individual differences in pain sensitivity and emotional well-being.
- The presence of a variant in the MTHFR gene suggests a potential influence on your body's folate metabolism, which is a process important for various bodily functions, including neurotransmitter production.

Questions to Ask Your Clinician Section

- Given my ORT score, could you help me understand how this information might influence our discussion about safe and effective pain management options?
- My PHQ-2 screening suggests further evaluation is needed; would it be helpful to discuss my emotional well-being in more detail or consider additional assessments?
- With the genetic variations identified in genes related to pain and mood, what might this mean for my health context, and are there any specific considerations we should discuss?

Possible Additional Testing or Assessments Section

- A comprehensive behavioral health assessment could provide a deeper understanding of the PHQ-2 results and explore any potential needs for emotional support.
- Further discussion with a pain specialist might be beneficial to explore a wide range of pain management strategies, considering the ORT score.
- A review of your genetic profile by a clinical geneticist or pharmacogenomic specialist could offer more personalized insights into how these variations might influence certain physiological processes or potential medication responses.

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 of the Opioid Risk Test

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.

Genotypes	RS Number	SNP
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	rs1611115	C/T
MTHFR	rs1801133	G/A

Phenotypes	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

The Proove Promise

We promise to respect the dignity and recognize the merit of individuality. Many define individual health from the perspective of the “average” treatment, doctor, or patient, assuming that the statistical average predicts the individual outcome. The average is a myth. There is “average” treatment, doctor, patient or person for that matter. We believe in the power of one - one person, one company, one clinician, and one patient - to make a difference.

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 unspecifi ed opioid-induced disorder; F11.90: Opioid use that is unspecifi ed and uncomplicated; F11.920: Opioid use that is unspecifi ed and uncomplicated, with intoxication; F11.20: Opioid dependence that is uncomplicated; F11.99: Opioid use that is unspecifi ed, with an unspecifi ed opioid-induced disorder; or, F11.94: Opioid use that is unspecifi ed, with an opioid-induced mood disorder. A Proove Opioid Risk score of 0-11 indicates the patient exhibits the patient exhibits low risk of misuing 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 benefi t 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 benefi ted 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 signifi cant difference in analgesia using pharmacogenetic information from Proove Drug Metabolism. (5,6,7)

A genetic predisposition to opioid use disorder can play an important role in chronic pain treatment guidelines,(8) and are including in leading chronic pain guidelines. (9)
(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.

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 Techologies Quant Studio 7 genetic analyzer as Single Nucleotide Polymorphisms (SNPs). The data is analyzed and reported by qualifi ed licensed laboratory personnel using Life Techologies Genotyper data analysis software, version 1.3. This test was independently verifi ed 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.