PROOVE GENOMICS

Proove Pain Perception

Report Date August 24, 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: marfield
Account Name: jzzzzzz
Physician Name: xxxxxxxxxxx

Results Summary

Patient Self-Reported

Severe Pain

Perceived Stress Scale

Moderate Perceived Stress

Genetic Predisposition

Average Pain Sensitivity

Patient's Self-Reported Pain (Numeric Pain Rating Scale)	7	**Demographics:** Asian	
Psychological Influence on Pain (Perceved Stress Scale)	19	**Genetic Predisposition (COMT Haplotype):** Average Pain Sensitivity	

Clinical Analytics Interpretation & Report

Numerical Rating Scale	**7 of 10**	The Patient reports Severe Pain.
Perceived Stress Scale	**Moderate Perceived Stress**	The Patient answers suggest Moderate Perceived Stress.
COMT Haplotype	**Average Pain Sensitivity**	APS , The Patient has a genetic predisposition to average sensitivity to pain, what may appear an average threshold, and may be associated with expected self-reported scores.

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INFINITILABS

Laboratory Performing Test

Laboratory Director : Dr. Barroso-Vicens, MD

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Proove AI Powered-Clinical Summary

Patient's Self-Reported Pain (Numeric Pain Rating Scale)

- Your Numeric Pain Rating Scale (NPRS) score of 7 out of 10 indicates severe pain, which is an important factor for your care team to consider.
- A severe pain level often suggests the need for careful evaluation and monitoring of pain management strategies to ensure your comfort and safety.
- This score helps your clinician understand the intensity of your pain, guiding them in developing a safe and effective approach to manage your discomfort.

Psychological Influence on Pain (Perceived Stress Scale)

- Your Perceived Stress Scale (PSS) score of 19 indicates a moderate level of perceived stress, which measures how much you feel life events are unpredictable, uncontrollable, and overwhelming.
- This moderate level of perceived stress suggests that psychological factors may be influencing your overall well-being and potentially your experience of pain.
- Acknowledging this moderate stress level can be a helpful step in understanding its potential connection to your health and exploring supportive strategies.

Genetic Predisposition (COMT Haplotype) Analysis

- Your COMT haplotype indicates an average pain sensitivity, meaning this genetic factor alone is not typically associated with unusually high or low pain perception.
- The COMT gene plays a role in how your body processes certain neurotransmitters that are involved in pain signaling.
- This average sensitivity suggests that other factors, such as your reported severe pain and moderate stress, are likely more significant contributors to your current pain experience.

Questions to Ask Your Clinician

- Given my severe pain and moderate stress, could you help me understand how these factors might be connected and what comprehensive pain management approaches might be suitable for me?
- Would it be helpful to discuss how my average pain sensitivity, as indicated by my COMT haplotype, fits into my overall pain experience and potential management plan?
- What strategies can I explore to manage my perceived stress, and how might reducing stress potentially impact my pain levels?

Possible Additional Testing or Assessments

- A comprehensive pain assessment might be considered to identify specific pain generators and contributing factors beyond the self-reported score.
- A behavioral health assessment could be helpful to further explore the impact of stress and emotional well-being on your pain experience.
- Reviewing current lifestyle factors, such as sleep patterns, physical activity, and nutrition, might provide additional insights into your overall health and pain management.

Supporting Clinical Evidence

Accuracy of the Pain Perception Test

The Pain Perception Profile (PPP) is built on one of the most extensively studied genetic mechanisms in pain science —the catechol-O-methyltransferase (COMT) gene — and its clinical accuracy is supported by over a decade of independent, peer-reviewed research spanning more than 6,000 patients across multiple countries, specialties, and clinical settings. The core foundation rests on four COMT single nucleotide polymorphisms (rs6269, rs4633, rs4818, and rs4680) that combine into three functionally distinct haplotypes — Low Pain Sensitivity (LPS), Average Pain Sensitivity (APS), and High Pain Sensitivity (HPS) — which account for 95–97% of all COMT haplotypic diversity observed across both Caucasian and Asian populations. Critically, the LPS haplotype produces COMT enzyme activity 4.8 times higher than APS and 11.4 times higher than HPS ($p<0.01$ for both; Diatchenko et al., 2005), meaning genetic pain sensitivity is not a minor effect — it represents a biologically dramatic difference that directly predicts clinical outcomes. In the landmark foundational study (Diatchenko et al., 2005; N=202), COMT haplotypes explained approximately 11% of variability in pain sensitivity (overall ANOVA $p=0.0004$), and carriers of HPS or APS haplotypes developed temporomandibular disorder at 2.3 times the rate of LPS carriers (Incidence Density Ratio=2.3, 95% CI: 1.1–4.8; $p=0.02$), with a population attributable risk of 29% — meaning nearly one-third of all TMD cases in the population are genetically attributable to these haplotypes. Subsequent research confirmed and extended these findings: in a post-motor vehicle collision cohort (McLean et al., 2011; N=85), pain-vulnerable COMT genotype carriers had a 2.11-fold greater risk of moderate-to-severe acute neck pain ($p=0.021$) and 3.15-fold greater risk of moderate-to-severe headache than non-vulnerable carriers, and COMT genotype was a more powerful predictor of acute pain severity than crash characteristics including collision type and airbag deployment. In a prospective surgical cohort (George et al., 2008; N=58), a model combining COMT haplotype with pain catastrophizing explained 51% of variance in post-operative pain ($R^2=0.510$, $F=10.62$, $p<0.001$), with high-catastrophizing APS/HPS patients experiencing a 6.8-fold relative risk of severe post-surgical pain compared to all other groups. In the largest multi-ethnic cohort (Tan et al., 2016; N=973), COMT haplotypes significantly predicted post-operative morphine requirements ($p=0.010–0.029$) and pain scores ($p=0.022$), while a 429-patient hernia repair study (Belfer et al., 2015) demonstrated that combining COMT with GCH1 genetic markers improved a clinical prediction model's discriminatory power from "fair" (AUC=0.78) to "good" (AUC=0.82) for chronic post-surgical pain. In the direct clinical validity study of the PPP itself (Sharma et al., 2017; N=134 chronic pain patients across multiple U.S. research sites), 85% of physicians found the genetic result fully consistent with their clinical evaluation of the patient's pain — with an inconsistency rate of only 7.57% — across all three risk categories (81% consistency for low, 90% for moderate, and 84% for high pain perception scores). The laboratory methodology underlying the test has been validated to 100% repeatability, 100% intermediate precision, 99.62%–100% inter-laboratory reproducibility, and 100% concordance with bidirectional Sanger sequencing — the gold-standard reference method — confirming the PPP's results are analytically precise, reproducible, and laboratory-independent.

Key Advantages & Benefits of the Pain Perception Test

The Pain Perception Profile offers a set of clinically transformative advantages that no traditional pain assessment method can replicate, beginning with its fundamental distinction: it provides an objective, biologically-anchored measure of a patient's genetically determined pain sensitivity that is entirely independent of subjective self-report. Standard pain tools — the Numeric Rating Scale, Visual Analog Scale, and clinical observation — are all patient-reported instruments vulnerable to under-reporting (stoic patients, patients fearing stigma), over-reporting (patients seeking validation or medication), cognitive impairment, cultural bias, and implicit provider bias. The PPP cuts through these confounders by revealing whether a patient is genetically predisposed to high, moderate, or low pain sensitivity before interpreting their reported pain score — enabling physicians to distinguish between a patient whose reported pain of 8/10 is genetically plausible versus one whose pain report may warrant additional diagnostic investigation. This was demonstrated powerfully in a published case study (Gazzaniga et al., 2017) in which a patient labeled a "drug seeker" had a PPP low-sensitivity result, correctly prompting further imaging that discovered an untreated bone fragment causing calf pain — overturning the drug-seeking label and leading to definitive, appropriate treatment.

In the primary clinical utility study (Sharma et al., 2017; N=134), 40% of patients had their treatment plans directly changed as a result of PPP results, producing improvement rates of 72% when medications were adjusted, 82% when alternative therapies were initiated, 71% when additional diagnostic testing was ordered, and 69% when non-pharmacological interventions were implemented — outcomes that substantially exceed typical chronic pain management success rates under standard clinical assessment alone. The PPP further enables precision pharmacology: a randomized controlled crossover trial (Tchivileva et al., 2010; N=40) established that COMT haplotype predicts response to propranolol therapy for temporomandibular disorder, with 0-LPS-allele patients (approximately one-third of any population) showing the greatest benefit, while LPS-homozygous patients received no benefit — meaning without genotyping, 20% of patients received an ineffective treatment with no way to identify them in advance. Similarly,HPS-genotype surgical patients require up to 29% more opioid analgesia than LPS patients in the 48 hours post-surgery (Zhang et al., 2015; p=0.032), enabling evidence-based, individualized opioid dosing rather than one-size-fits-all prescribing. At the population level, the PPP also addresses a critically overlooked dimension of health equity: African-American patients are 4.3 times more likely to score high pain perception than Caucasian patients (p=0.001; 95% CI: 1.8–11.1; Sharma 2017) — providing a biological basis for understanding and correcting documented racial disparities in pain management, where minority patients are systematically undertreated. In the largest real-world outcomes study drawn from Medicare beneficiaries (N=6,161 patients, 158 clinics), PPP-guided pain management produced an average 45% reduction in pain scores (from NRS 7.2 to 4.0), with 39% of patients achieving at least 50% pain relief, only 7% reporting no improvement or worsening, and 12% of the cohort reducing their opioid medication burden — generating an estimated $12.4 million in healthcare cost savings in the first year and more than $62 million over five years from a single patient cohort, purely through moving patients from severe to moderate or mild pain categories. Taken together, the PPP's combination of genetic precision, physician decision support, personalized treatment guidance, demonstrated patient improvement rates, and measurable economic value positions it as a uniquely powerful tool for transforming chronic pain management from reactive and subjective to proactive, objective, and individualized.

Genotypes	RS Number	SNP
COMT	rs6269	G/A
COMT	rs4633	T/T
COMT	rs4818	C/C
COMT	rs4680	A/A

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

Genotypes

COMT (Catechol-O-methyltransferase) haplotypes, variations in the COMT gene, have been linked to differences in pain sensitivity and perception. Specifically, the three major haplotypes (LPS, APS, and HPS) are associated with low, average, and high pain sensitivity, respectively. These haplotypes influence COMT enzyme activity, which in turn affects neurotransmitter metabolism and pain signaling. COMT is an enzyme that breaks down catecholamines like dopamine, noradrenaline, and adrenaline. These neurotransmitters are involved in pain modulation and other physiological processes. COMT haplotypes, which are combinations of genetic variations in the COMT gene, affect the activity of this enzyme. Based on increasing evidence that the genetic component of pain has been shown to account for significant variability in human pain perception and modified by easily measurable phenotypic and clinical measures, the Proove Pain Perception® profile was created as a reference tool to guide the treatment of acute and/or chronic, nociceptive pain. The profile is a precision medicine tool that evaluates genetic and non-genetic factors shown to influence the variability in the processing of pain and response to opioids, and is intended to assist physicians in clinical decision making when presented with a patient with acute or chronic nociceptive pain. It has been used by clinics specializing in primary care/internal medicine, pain management and rehabilitation, and surgery for musculoskeletal indications. The profile provides information that allows physicians to tailor treatment according to a patient’s pain sensitivity, as predicted by an algorithm that evaluates both genetic and clinical factors. Included in the profile’s algorithm are phenotypic variables such as sex, ethnicity, degree of stress, and the presence of genetic polymorphisms in one of the most studied genes in pain genetics: Catechol-O-Methyltransferase (COMT). COMT is an enzyme that catabolizes catecholamines, such as dopamine, epinephrine, and norepinephrine, and is critically involved in pain transmission. Genetic variation in the COMT gene leads to a reduction in its enzymatic activity, and subsequent changes in the concentration and downstream signaling of catecholamines. These genetic variations have been examined in over 40 independent association studies of human pain. Reduced COMT enzymatic activity, which results in increased catecholamine levels, has been shown to be associated with higher sensitivity to painful stimuli and vice versa. As summarized in the table in Section III: Clinical Validity, the phenotypic effects of COMT genetic variations, i.e. single nucleotide polymorphisms (SNPs), are described in dozens of studies. The presence of COMT SNPs is associated with increased sensitivity to thermal, ischemic, and mechanical pain experimentally and is linked to clinical differences in pain intensity, functional outcomes and opioid consumption in postoperative settings, acute trauma, chronic pain, and fibromyalgia. COMT genetic changes have also been associated with pain catastrophizing and psychological distress. Psychological traits that influence the perception of pain may predispose some individuals to exhibit pain disorders more severely than others, despite having similar prognoses or other physical similarities. Furthermore, low COMT activity also increases availability of opioid receptors and may enhance opioid analgesia and adverse effects. [1-25]
Published clinical utility studies of Proove Pain Perception demonstrate that based on genetic testing results, physicians adjusted treatment plans for 40% of patients using the test. When medication changes were made based on genetic testing results, 72% of patients showed improvement in clinical status. When non-pharmacological actions were performed, 69% of physicians felt their patients' clinical status improved. Moreover, physicians believed the genetic test results were consistent with patient pain levels in 85% of cases. [26]

Phenotypes

The Perceived Stress Scale (PSS) is widely considered the gold standard instrument for measuring stress perception [27-29]. Informed by Lazarus and Folkman's transactional model of stress [30], this self-report questionnaire is used to assess the degree to which a respondent finds circumstances in their life to be unpredictable, uncontrollable, and/or overwhelming. In contrast to measures that assess environmental stress exposures (e.g., life events checklists [31, 32]), the PSS captures a respondent's subjective appraisal of whether life circumstances and experienced events exceed their adaptive capacity [27, 33]. Questions on the PSS ask the respondent to rate their feelings and thoughts for the past month [27], indicating that a relatively recent time frame is assessed. Since 1983, the PSS has been cited >30,000 times and used to demonstrate the wide-ranging effects of stress in both healthy and patient populations. Higher PSS scores are associated with higher levels of pain intensity and pain interference. [34] HPS haplotype, stress, and sex interact with each other and modify pain sensitivity. Stress and sex may impact the ability to detect COMT-dependent pain sensitivity due to their effects on the adrenergic system. Specifically, because low COMT activity (HPS haplotype) and exposure to stress can increase the epinephrine load in the system, an increase to pain sensitivity may also result. [8]

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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.