Using Pharmacogenetic Testing in a Pain Practice

The results of this pilot study suggest that pharmacogenetic testing is used to influence patient care, specifically treatment planning, patient education, and as a rationale for making adjustments in medication regimens and dosages.

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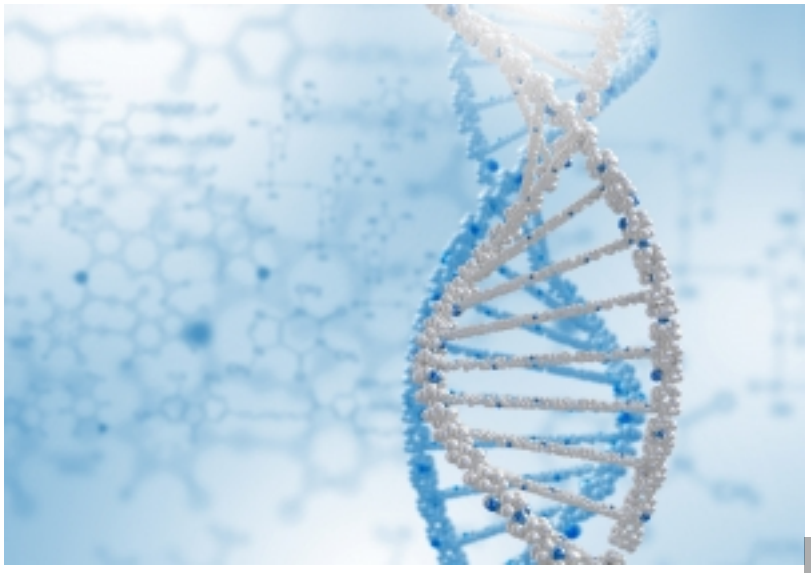
Pharmacogenetic testing (PGT) is an objective clinical tool that has the potential to help clinicians improve treatment in many areas of medicine, including pain management. PGT can be a vital component of personalized medicine, assisting clinicians in choosing medications based on patient genetics to increase benefit and decreased risks.

PGT also can be a valuable tool for troubleshooting when patients are having idiosyncratic reactions, require higher than normal doses, or simply exhibit poor response to a specific medication or a class of medications. Finally, PGT can play an important role in facilitating doctor–patient communication about expectations, outcomes, and adherence as well as patient education about the role of genetics in determining, in part, outcomes related to opioid therapy.



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In pain management specifically, PGT gives clinicians insight and guidance on the management of complicated patients with chronic pain who may have struggled with problematic side effects or suboptimal benefits from medications such as opioids.[1,2] Abnormal PGT results in complicated chronic pain patients are relatively common.[3] PGT provides information that can help clinicians guide personalized treatment plans, identify medication meta-
bolism abnormalities, clarify urine drug testing (UDT) results, improve patient functional outcomes, avoid potential medication interactions, and guide therapeutic decisions such as changing medication dose, or rotating opioids.[4-10] This information, combined with general risk assessment strategies, a thorough history and physical examination, knowledge of potential concomitant medication interactions, and UDT can improve clinicians' understanding of the unique and highly individualized responses to pain treatment so often seen in specialty care settings.[11,12]

The out-of-pocket costs associated with obtaining PGT are not negligible and must be considered. However, substantial costs savings eventually might be realized throughout the healthcare system if PGT realizes its full potential in the avoidance of unnecessary trial and error in drug selection. Thus, as with all tests, there is a need to document the medical necessity and purpose for ordering PGT and to demonstrate the subsequent use of the results in patient care.

Pilot Study

One of the authors (Eric Ehlenberger) has a large medical practice in Louisiana, where he has been ordering PGT on all new patients treated for chronic pain at his facility. He had been struggling with a large number of patients with difficult and idiosyncratic reactions to commonly used medications and also was trying to manage the polypharmacy that typifies the management of refractory pain by the time patients end up in specialty pain care. His regular use of PGT presented an excellent setting for the piloting of a study on the documentation of the uses of PGT in the areas of treatment planning, troubleshooting, and support of doctor–patient communication and patient education.

This study reports on the results of a structured chart review of patients with chronic pain receiving opioid therapy for whom PGT had been ordered (samples submitted to a laboratory for PGT on 3 subtypes of the cytochrome P 450 [CYP450] enzyme system [CYP2B6, CYP2C19, and CYP2D6] and 1 test on the UGT [UGT2B15] enzyme) using a chart review tool to examine instances of documentation of the uses of PGT in clinical care.

How the Study Was Designed

For the purposes of this research study, which was approved by Aspire IRB in San Diego, California, the researchers developed a novel checklist to assess the effects of PGT results on patient care (Figure 1). Two trained research assistants used this checklist on de-identified medical records of 85 patients from a single physician’s office. The PGT was conducted on the patients to assess safety prior to prescribing medications and/or as a clinical test for a differential assessment due to negative outcomes (excessive side effects, intolerance of medications, lack of efficacy, etc.)

Figure 1. Chart review tool.

PGT Chart Review

Patient ID # _____ Data Collector:_____

Date of Data Collection: _ _ / _ _ / _ _

Inclusion Criteria: 1 to 3 visits, up to 90 days after the results are delivered

DEMOGRAPHIC INFORMATION

Patient Age: _____ Gender: ❑ Male ❑ Female

Ethnicity:

____ Caucasian
____ African-American
____ Hispanic
____ Asian
____ Other (specify):
_____

Current Employment Information:

____ Full time
____ Part time
____ Homemaker
____ Disabled
____ Unemployed
____ Retired
____ Student

Patient on worker's compensation? ❑ Yes ❑ No

Medical History/Information:

Primary Chronic Pain Diagnosis: _____

ICD9 Code: _____ Secondary Chronic Pain Diagnosis: _____

_____ [do you need an ICD for secondary diagnosis?] ❑ Yes ❑ No

Lifestyle:

Documentation that patient smokes? ❑ Yes ❑ No
If yes: How many packs per day? _____ How many years? _____
Documentation that patient drinks alcohol? ❑ Yes ❑ No
History of illicit drug use? ❑ Yes ❑ No
History of non-prescribed medication use? ❑ Yes ❑ No

Risk Assessment:

Outcome? Low / Moderate / High
Which tool(s)? _____

Provider Type:

____Physician ____NP ____PA ____Other: _____

Specialty:

❑ Pain ❑ Addiction ❑ Psychiatry ❑ Primary Care ❑ PM&R ❑ Neurology ❑ Anesthesiology
❑ Internal Medicine ❑ Family Practice ❑ Other: _____

PGT:

What tests were ordered? Result?

❑ CYP 2D6 date:
❑ EM/Normal
❑ IM
❑ PM
❑ UM
❑ Undetermined / Unknown / Other

❑ CYP 2C19 Date:
❑ EM/Normal
❑ IM
❑ PM
❑ UM
❑ Undetermined / Unknown / Other

❑ CYP 2B6 Date:
❑ EM/Normal
❑ IM
❑ PM
❑ Undetermined / Unknown / Other

❑ UGT 2B15 Date:
❑ EM/Normal
❑ IM
❑ PM
❑ Undetermined / Unknown / Other

Reasons for PGT:

❑ Safety assessment prior to prescribing meds
❑ Clinical test for differential assessment (ie, due to side effects, intolerance, lack of medication efficacy)
❑ Unexpected UDT results
❑ Patient complaint of lack of efficacy
❑ Patient complaint of intolerable side effects

Patient History of:

❑ Lack of efficacy
❑ Side effects
❑ Multiple opioid trials
❑ Multiple medication trials
❑ Requiring higher than typical dose
❑ Genetic or inheritable disease that causes their pain
❑ Adverse effects of alcohol or need larger amounts of alcohol for any effect

[8]

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Family History of:

- ❑ Lack of efficacy
- ❑ Side effects
- ❑ Multiple opioid trials
- ❑ Multiple medication trials
- ❑ Requiring higher than typical dose
- ❑ Genetic or inheritable disease that causes their pain
- ❑ Adverse effects of alcohol or need larger amounts of alcohol for any effect

Visits following PGT:

Check all that apply:
Treatment Planning / Current Treatment:

- ❑ No change in patient care
- ❑ Reconsider diagnosis
- ❑ Decrease visit frequency
- ❑ Increase visit frequency
- ❑ Decrease frequency of monitoring
- ❑ Increase frequency of monitoring
- ❑ Prompt reevaluation of eligibility for opioid treatment

Communication:

- ❑ Review PGT results with patient [present tense for consistency]
- ❑ Prompts conversation with patient about medication needs
- ❑ Collaborate with treatment team to plan future treatment
- ❑ Use findings to communicate with insurance company
- ❑ Use findings to assess or corroborate adherence
- ❑ Educate patient about PGT
- ❑ Encourage patient to share PGT result with other healthcare providers and/or pharmacy
- ❑ Share PGT result with other providers

Medication:

- ❑ Increase dosage
- ❑ Decrease dosage
- ❑ Add another controlled substance for symptom control (short-acting added, stimulant for sedation, etc.)
- ❑ Remove controlled substance (other than opioid)
- ❑ Discontinue medication
- ❑ Stop opioid
- ❑ Change to long-acting opioid only
- ❑ Change to short-acting opioid only
- ❑ Use findings to investigate possible drug-drug interactions
- ❑ Switch to a different class of medication
- ❑ Switch to another in-class medication

Miscellaneous:

- ❑ Order additional PGT

CYP, cytochrome; **EM**, extensive metabolizer; **IM**, intermediate metabolizer; **PGT**, pharmacogenetic testing; **PM**, poor metabolizer; **UDT**, urine drug test; **UM**, ultra-rapid metabolizer

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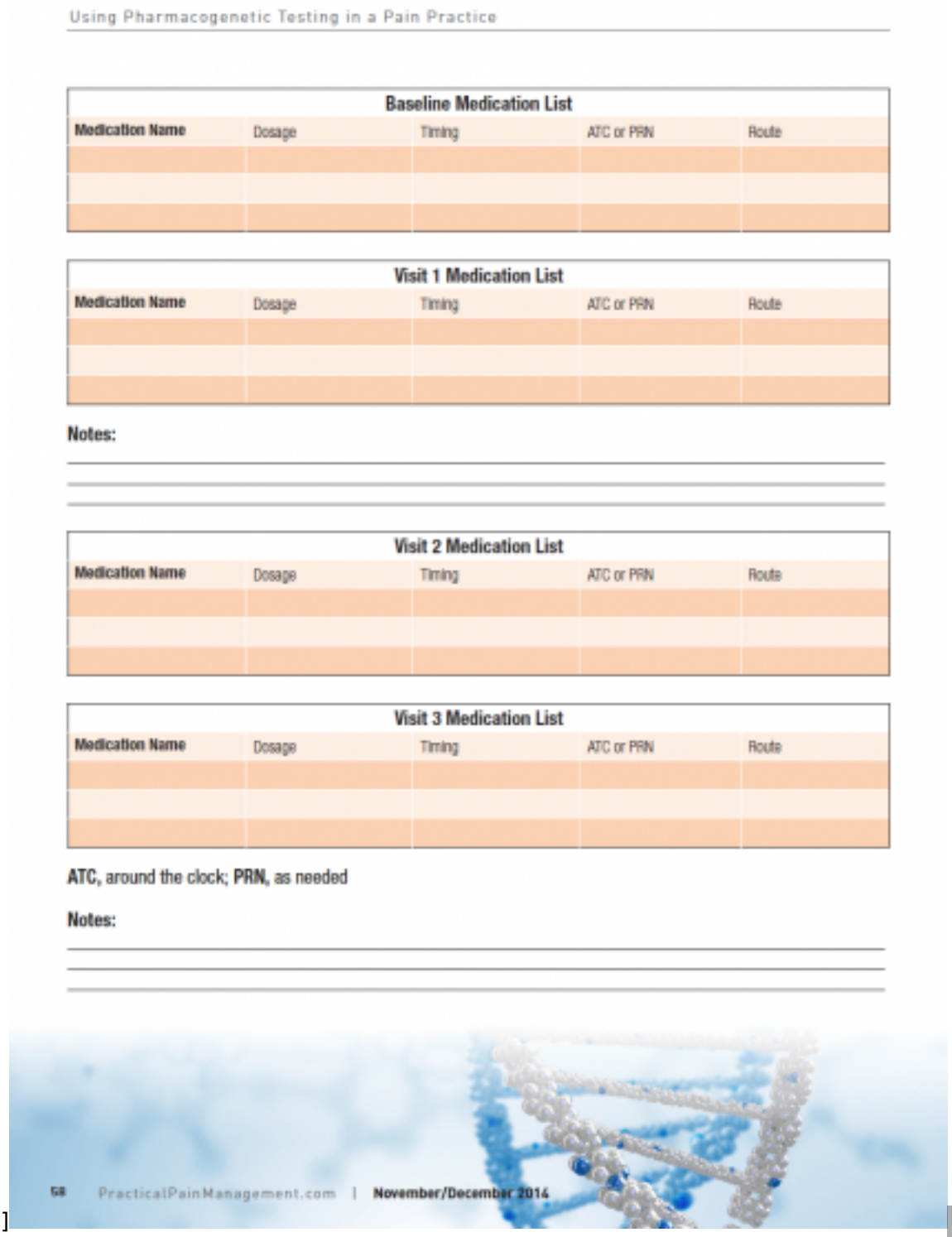

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Baseline Medication List

Medication Name	Dosage	Timing	ATC or PRN	Route

Visit 1 Medication List

Medication Name	Dosage	Timing	ATC or PRN	Route

Notes:

Visit 2 Medication List

Medication Name	Dosage	Timing	ATC or PRN	Route

Visit 3 Medication List

Medication Name	Dosage	Timing	ATC or PRN	Route

ATC, around the clock; **PRN**, as needed

Notes:

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[11]

The researchers used the checklist to record data from 2 visits: the “baseline” visit, when the patient PGT was originally ordered, and the first visit after the report was received (the first opportunity for the results to be presented to the patient). They used patient history, PGT results, medications, and office visit notes to complete the checklist, and categorized the changes made and their effects on the subsequent patient visit using a binary coding system (checkbox marked or left blank).

Results of the Study

The researchers randomly selected 85 charts of patients who had PGT from Millennium Laboratories between the dates of November 28, 2012 and December 16, 2013. The population was 67% male, with an average age of 45 (±10) years.

The most common pain diagnosis among study patients was low back pain (n=57; 67%), followed by neck pain (n=14; 16%). A full description of the population's diagnoses can be found in Table 1.

Table 1. Listing of Most Frequent Pain Diagnoses

Primary Pain Diagnosis	N	Percent of Population
Low Back	57	67%
Neck	14	16%
Shoulder	3	4%
Other	11	13%

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The majority of instances of documentation about the use of PGT results were for patient education (n=72; 85%), cooperative treatment decision making (n=58; 68%), and support for increases (n=16; 19%) or decreases (n=10; 12%) in medication dosages.

PGT Phenotype Results

Table 2 displays the genetic results for each of the 4 genes tested on each saliva sample. The rates for extensive (or normal) metabolizers was 84.7% for CYP2D6, 42.4% for CYP2C19, 56.5% for CYP2B6, and only 18.8% for UGT2B15.

Table 2. Genetic Results for Four Genes Tested

Results	CYP2D6	CYP2C19	CYP2B6	UGT2B15
Poor Metabolizers	5	4	6	20
Intermediate Metabolizers	4	20	29	49
Extensive Metabolizers	72	36	48	16
Ultra-rapid Metabolizers	1	25	0	0
Unable to Determine	1	0	2	0
Indeterminate	2	0	0	0

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Using the study checklist to evaluate each patient's chart, the research team identified the most commonly noted impact of the PGT. Due to the retrospective nature of this study, these data only are able to evaluate the effects noted as a part of standard patient notes. The most commonly noted impact of the PGT was related to educating patients about how their PGT status would be used to make changes or maintain their present medication regimen. This was specifically noted in 85% (n=72) of the charts analyzed. The other most commonly noted result was the physician reviewing results and using

them to contextualize the patient's prior pain experiences, side effects, and pain relief (68%; n=58).

In addition to visit notes, the checklist also was used to track changes in medication dose and type. Of the 85 patients, 47% (n=40) had some change in their medication regimen during the visit immediately following the release of their PGT results. A full summary of the most common noted actions can be found in Table 3.

Table 3. Actions Most Commonly Documented in Chart

Action	N	Percentage
Education of patient	72	85%
Reviewing and explaining individual results with patient	58	68%
Medication dosage increase	16	19%
Medication dosage decrease	10	12%
Discontinue medication	14	16%

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Discussion

We set out to pilot the use of a chart review tool to examine whether instances of documentation could be found in the medical record that exemplify the uses of the results of PGT in patient care. In brief, the results of this chart review suggest that it is possible to detect the use of PGT results in treatment planning, patient education, and potentially in the making of adjustments in medication regimens and dosages.

On a cautionary note, the senior clinician, whose charts were surveyed in this pilot, may be particularly adept at the documentation of treatment, education, and communication issues, and these results might not be reflective of the use of PGT by the broader pain community; this is an issue for future research. That said, the learning of a vocabulary and adaptation of it in charting in the manner described above might be a goal for the pain community as it seeks to continue to use PGT and have it supported by our reimbursement system.

Practical Implications

With a growth in the ordering and use of PGT, it has become necessary to ensure that the tests are medically needed and applied in a meaningful way. Simply put, there is a great need to both identify and chart why PGT, or any test, is ordered and what effect the results had on patient care. This should be done, even if it is simply to note, for example, that a medication regimen will be maintained because the patient is an extensive metabolizer of a particular gene and continued use of the drug is acceptable from this one vantage point. Samples of educational conversations with patients about their PGT results, as well as sample ideas for charting, are included in Table 4. These are intended as teaching examples of how the results of PGT can be practically communicated to patients and noted in patient charts.

Even when used in the hands of an expert clinician, the old adage "it isn't written, it didn't happen" applies. As can be seen from the study, there was a good degree of documentation about the application of PGT findings to clinical care. However, there also is a need to explicitly document medical necessity for ordering the test. As stated above, the clinic chosen for this chart review is in the practice of proactively testing chronic pain patients with PGT as a safety measure and to gain insight before prescribing because it is a referral center for patients with complicated medical problems and histories. However, charting of medical necessity for ordering PGT is needed and can be as simple as some of the

reasons noted in the chart review tool (See Appendix), such as a lack of success with current medication regimen, safety concerns over side effects experienced by the patient, a history of higher than expected dose needed, unexpected UDT results, etc. As PGT use continues to grow, this will become a crucial step to ensure payers will cover the services and that patients will receive a better standard of care that works towards truly personalized medicine.

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