GTMRx Institute™

Get the medications right

www.gtmr.org

Pharmacogenomics: What you need to know during COVID-19 and lessons learned from implementation in team-based care

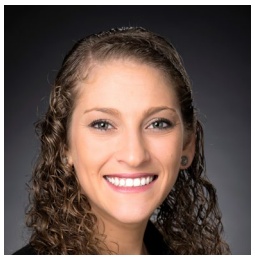
June 9, 2020 | 1 p.m. Eastern

GTMRx Learning Network Webinar

Agenda

- Welcome and Introductions
- Learning Objectives
- Presenters

Colleen Keenan, Consultant,
Advisory Board's Clinical Innovators Council



Emily J. Cicali, PharmD, BPCS, Clinical Assistant Professor, University of Florida, School of Pharmacy

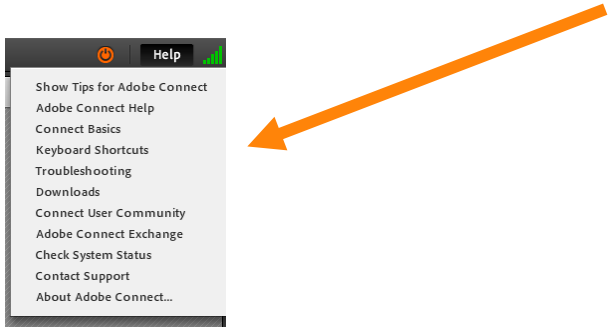
- Question and Answer Session

Audience Notes

There is no call-in number for today's event.

If you would like to switch to full screen, click this icon:

The troubleshooting guide to the right of your screen.



Submit questions at any time

How to submit a question

To submit a question, please use the "Q&A" pod below the slides to ask questions throughout the presentation.

Just type in your question at any time and then click the button to submit.

Please feel free to submit questions as they come to mind during the presentation—there is no need to wait until the end.

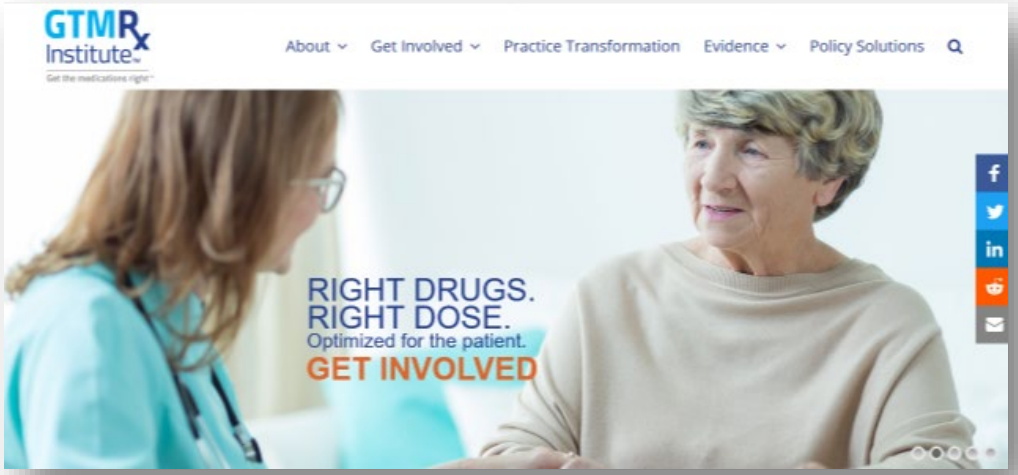
The questions will be asked by the moderator, at the conclusion of the presentation.

We will answer as many questions as time permits.

Audience Notes

The slides from today will be available after the webinar.

A recording of today's session will be posted within one week to our website, www.gtmr.org



Quick view of GTMRx Institute

A national platform creating a forum for more rapid practice and policy change to save lives and revolutionize the way care is delivered in order to optimize medication use.

Goal: To educate, inform and change the market so research and innovation moves to the practice level, payment models and policy align, and buyers receive value.

Vision: Enhance life by ensuring appropriate and personalized use of medication and gene therapies.

Mission: Bring critical stakeholders together, bound by the urgent need to optimize outcomes and reduce costs by *getting the medications right*.

Focus Areas

- **Practice Transformation**
- **Evidence & Innovation**
- **Payment & Policy Solutions**

The $528 billion opportunity

275,000+ lives are lost every year to medication errors **$528.4B** therapy (2016) is the cost of non-optimized medication[1]:

- $174 billion **hospitalization** costs
- $271.6 billion **long-term care** admissions
- $37.2 billion **emergency department** visits
- $37.8 billion additional **provider visits**
- $7.8 billion **additional prescriptions**

Medications are involved in **80%** of all treatments & impact every aspect of a patient's life.

Nearly **30%** of adults in the U.S. take **5+** medications.

10,000 prescription medications available on the market today.

Only **13%** of PCPs consult with a pharmacist before new prescriptions.

49 seconds spent between physicians and patients talking about new medication during a **15-minute** office visit.

1. Watanabe J, et al. Cost of Prescription Drug–Related Morbidity and Mortality. Annals of Pharmacotherapy, March 26, 2018. Accessed 3 April 2018. http://journals.sagepub.com/eprint/ic2iH2maTdI5zfN5iUay/full

A dynamic team of health care leaders!

(inclusion does not constitute an endorsement of any program, product or organization)

A sample of our 910+ members from 625+ companies

Getting the Job Done: GTMRx Workgroups

GTMRx Institute™
Get the medications right

VISION: To enhance life by ensuring appropriate and personalized use of medication and gene therapies.

MISSION: We bring critical stakeholders together, bound by the urgent need to optimize outcomes and reduce costs by ***getting the medications right.***

Focus of Workgroups

Practice & Care Delivery Transformation (Skills, Tools & Knowledge)	Evidence & Innovation (Experience-Based Best Practices)	Payment & Policy Solutions (Evidence-Based, Effective Solutions)
HIT and AI to Support Optimized Medication Use		Precision Medicine Enablement via Advanced Diagnostics

Operational Activities & Outputs from Working Groups

▪ Accessing clinical data to support CMM ▪ Collaborative practice agreements ▪ Developing value-based business agreements ▪ CMM team-based care R&F ▪ Physician engagement and activation ▪ Patient engagement tools ▪ Barriers and enablers ▪ Expanding access to health IT solutions that liberate clinical data exchange for CMM practice	▪ Quality metrics (process, satisfaction, outcomes) ▪ Value metrics (cost and quality) ▪ Effective integration into delivery models and across settings ▪ Program and process guidance ▪ Building consumer demand ▪ Building physician demand ▪ Identification of expert practices ▪ Evidence for advocacy ▪ Building purchaser demand	▪ Enabling policy for CMM program reimbursement ▪ Overcoming policy & payment barriers to appropriate medication use ▪ Enabling benefit design / guide for employers ▪ Enabling policy for risk-based contracting (product & appropriate use)/ guide for practices & plans ▪ Recognition of emerging outcomes-based and population-based research (CBO scoring) ▪ Enabling policy & payment for gene therapies

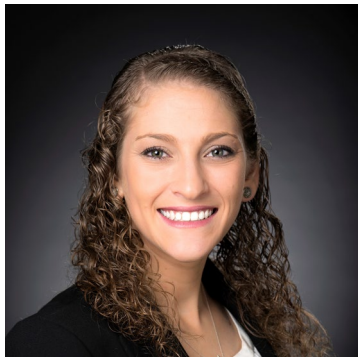
Learning Objectives

Some of the questions we'll address include:

- How are PGx practice activities implemented and impacted during COVID-19?
- In the post-pandemic environment, what will likely be the realities of team-based, person-centered care using PGx as a tool to support CMM?
- What are the barriers to implementation of PGx in team-based care in an ambulatory care setting?
- What are important process-of-care lessons learned during COVID-19?
- How will lessons learned from implementing team-based PGx in ambulatory care settings help shape future PGx clinical trials and clinical implementations?
- And more...

Our Presenters

Colleen Keenan
Consultant
Advisory Board's Clinical Innovators Council



Emily Cicali
PharmD, BCPS
Clinical Assistant Professor
University of Florida

Pharmacogenomics in the Covid-19 Era

Presented by

Colleen Keenan
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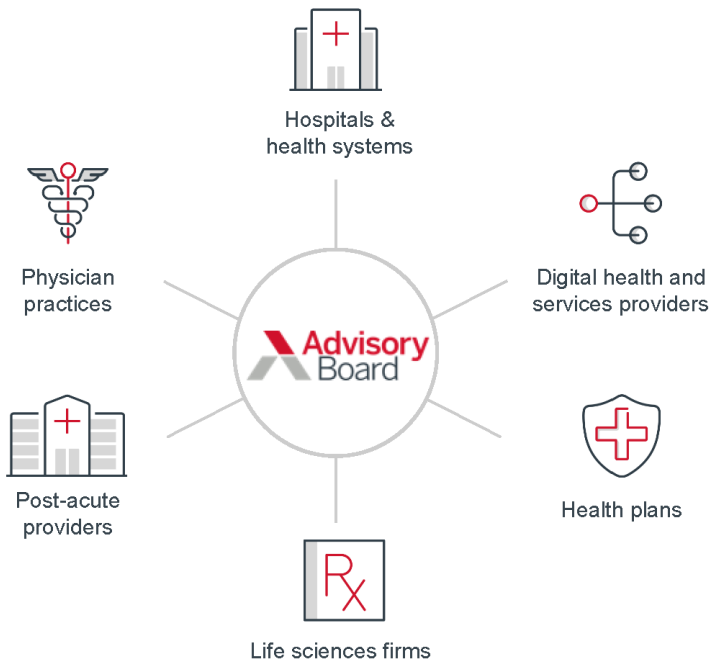
Advisory Board sits at the center of health care delivery



How we help

Access to unparalleled member network

4,900+ Member health care organizations

Consistent delivery of provocative insights and actionable strategies

200+ New research publications released each year

Extensive expert support for health care's top leaders

300+ Industry experts on call for consultative support

Rigorous research process identifies best practices, insights

1 Annual topic selection

Our research agenda is developed each year through meetings and surveys across the membership—resulting in fresh research focused on the most critical issues facing hospital leadership.

2 Literature review and interviews

A massive literature review and interviews with senior executives, key staff, and experts in the field helps develop deeper understanding of topic under study and provides a preliminary list of potential proven practices.

3 Original analysis

The lion's share of work involves a search for "right answer." Through rigorous root cause analysis and synthesis of all the information at hand, analysts isolate the most valuable, actionable, and original insights and ideas.

4 Screening proven practices

Interviews are conducted with all potential best practice organizations to assess whether practices truly merit further study.

- Is a practice truly innovative?
- Can it demonstrate results?
- Is it replicable?

5 In-depth case study research

In-depth interviews are conducted at select organizations to explore practices on a deeper level. The research focuses on how the ideas work in detail and what each practice's resource requirements, implementation requirements, benefits, and potential drawbacks are.

6 Comprehensive and actionable solutions

Insights gleaned from the research are shared with members through concise publications and presentations, as well as ready-to-use implementation resources. The goal is to help members rapidly apply the insights at their organizations.

1 Defining pharmacogenomics (PGx)

2 Covid-19 PGx applications

3 Ongoing PGx-Covid-19 initiatives

4 Outstanding implementation barriers

Ongoing pharmacogenomics (PGx) research

What is PGx?

- Pharmacogenomics is the study of how a person's unique genetic makeup (genome) influences his/her response to medications

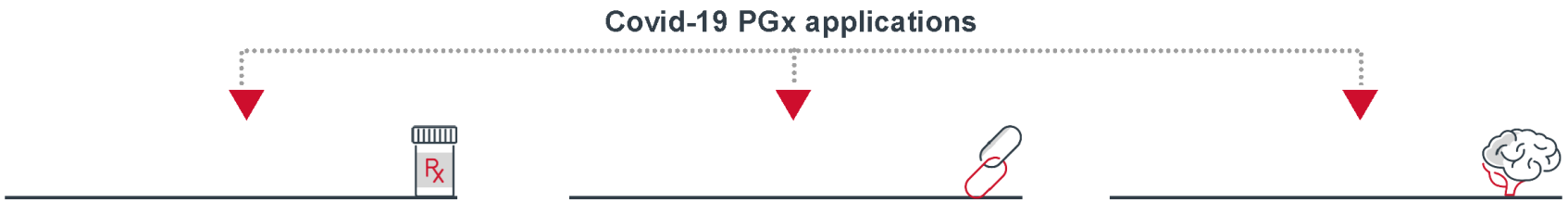
What are our goals?

- Demystify PGx for stakeholders across the health care ecosystem
- Understand the business case for a health system PGx program
- Clarify the PGx workflow and each stakeholder's role in the process
- Detail the barriers to widespread adoption and implementation

What are our guiding research questions?

- What are common PGx patient populations?
- What are the distinct steps in the PGx workflow? How do different stakeholders fit into this process?
- How do PGx stakeholders measure success and ROI?

PGx insights guide targeted Covid-19 treatment decisions



Drug-gene interactions

- Flag patients who may be at heightened risk of adverse drug events from experimental Covid-19 treatments

Susceptibility of infection

- Identify potential correlation between a patient's genetic makeup and his/her likelihood of contracting the disease as well as the severity of their symptoms

Mental health treatment

- Target treatments for resultant mental health diagnoses (e.g., depression, anxiety)

Source: Ray T, "Drug-gene testing could give experts insight into COVID-19 treatment," Genomeweb.

Experimental treatments have associated risks

PGx testing can help prevent adverse events

Hypothetical patient scenario

Patient takes citalopram to treat depression

Patient is a CYP2C19 poor metabolizer and at increased risk for QT prolongation when taking citalopram

Patient contracts Covid-19 and is admitted to the hospital

Doctors treat patient with hydroxychloroquine

Patient dies from a sudden cardiac event

Drug-drug-gene interactions with citalopram, hydroxychloroquine, and CYP2C19 poor metabolizer; opportunity for PGx testing

Source: Ray T, "Drug-gene testing could give experts insight into COVID-19 treatment," Genomeweb.

Genes may also impact susceptibility of infection…

…as well as symptom severity

Protein/Gene	*Function*	*PGx application*
HLA[1]	Proteins that the immune system uses to identify and kill germs in the body	• Identify people who are at a higher risk of contracting the virus based on mutations in these genes • Inform Covid-19 treatment strategy based on likely severity of symptoms • Identify people who would most benefit from vaccination or further social distancing—especially those who are asymptomatic
TMPRSS2[2]	Helps create a protein that coronaviruses use to enter cells in the body	
ACE2[3]	Helps produce receptors on the surface of human cells where the coronavirus latches onto	

1) Human leukocyte antigen.
2) Transmembrane protease, serine 2.
3) Angiotensin converting enzyme-2.

Source: Ray T, "Drug-gene testing could give experts insight into COVID-19 treatment," Genomeweb; Nguyen A, et al., "Human leukocyte antigen susceptibility map for SARS-CoV-2," medRxiv.

Likely to see biggest PGx impact in mental health

Expecting a mental health epidemic as a result of social isolation

DATA SPOTLIGHT

Covid-19 mental health statistics

1/3	of Americans showing signs of clinical anxiety or depression
24%	of respondents showed symptoms of major depressive disorder
30%	of respondents showed symptoms of generalized anxiety disorder

UnitedHealthcare[1] PGx coverage: Anxiety and depression

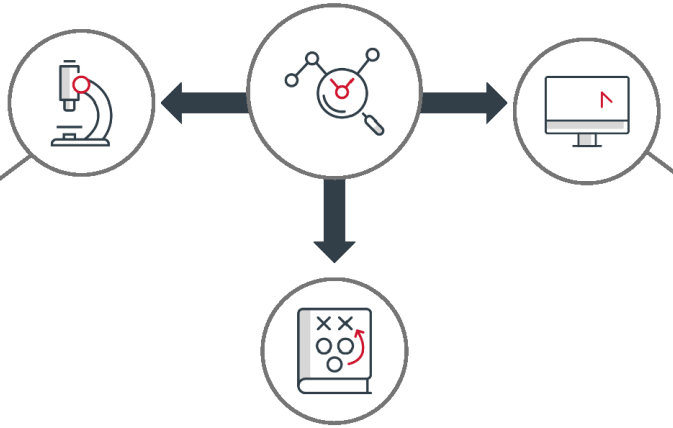
- Approved multi-gene panel for prescribing antidepressants and antipsychotics if:
  - Patient has major depressive disorder or anxiety disorder diagnosis
  - Patient failed at least one prior medication
  - Multi-gene panel has 15 or fewer genes
- Coverage policy includes 18 antidepressant or antipsychotic drugs with related genes (drug-gene pairs with moderate evidence of an association or higher)

1) Advisory Board is a subsidiary of Optum, which is a subsidiary of United Health Group. All Advisory Board research, expert perspectives, and recommendations remain independent.

Source: Fowers A, Wan W, "A third of Americans now show signs of clinical anxiety or depression, Census Bureau finds amid coronavirus pandemic," The Washington Post; "Pharmacogenetic testing," UnitedHealthcare, February 1, 2020.

A number of players are already involved

Leveraging PGx information across the spectrum



Research

- *University of Washington:* Collecting whole-genome sequencing data from 1,000+ Covid-19 patients
- *COVID-19 Host Genetics Initiative*: Centralizing and analyzing data from international PGx-Covid-19 studies and sharing results

Direct-to-consumer strategies

- *Negen Covid-19 PGx panel:* Analyzing existing genomic data—free of charge—for Covid-19-related drug-gene interactions

Information sharing

- *PharmGKB Therapeutic Resource for Covid-19*: Online resource of PGx considerations that could impact Covid-19 treatment

Source: "University of Washington to study COVID-19 pharmacogenetics," Modern Healthcare; "The COVID-19 Host Genetics Initiative," COVID-19 hg; "Therapeutic Resource for COVID-19," PharmGKB; "Negen opens a free COVID-19 pharmacogenomics panel," Negen.

Despite promise, still a number of implementation barriers

Industry grappling with unanswered questions

Provider adoption

- Will there be enough PGx evidence to justify integration into standard workflows?
- Will provider organizations have the necessary time and resources to invest in PGx processes?

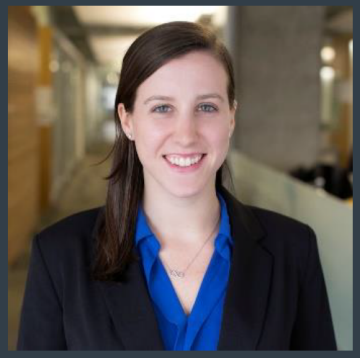
Payer adoption

- Will there be enough PGx evidence for the FDA to recommend PGx testing for certain medications and, as a result, for payers to cover more PGx testing?

Patient adoption

- Will there be enough PGx evidence for patients to buy in to the process/technology?
- Will patients be able to afford PGx testing?

Contact me if you have any questions



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Challenges and Lessons Learned from Clinical Pharmacogenetic Implementations

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Learning Outcomes

1. Discuss pharmacogenetic (PGx) implementations at University of Florida

2. Describe challenges and lessons learned from PGx implementations at University of Florida

Implementation Challenges

- **Challenge** - a task or situation that tests someone's abilities

Implementation Challenges

- **Challenge** - a task or situation that tests someone's abilities but does not prevent progress
  - Institutional support
  - Clinician acceptance
  - Education
  - Laboratory
  - Informatics
  - Logistical hurdles

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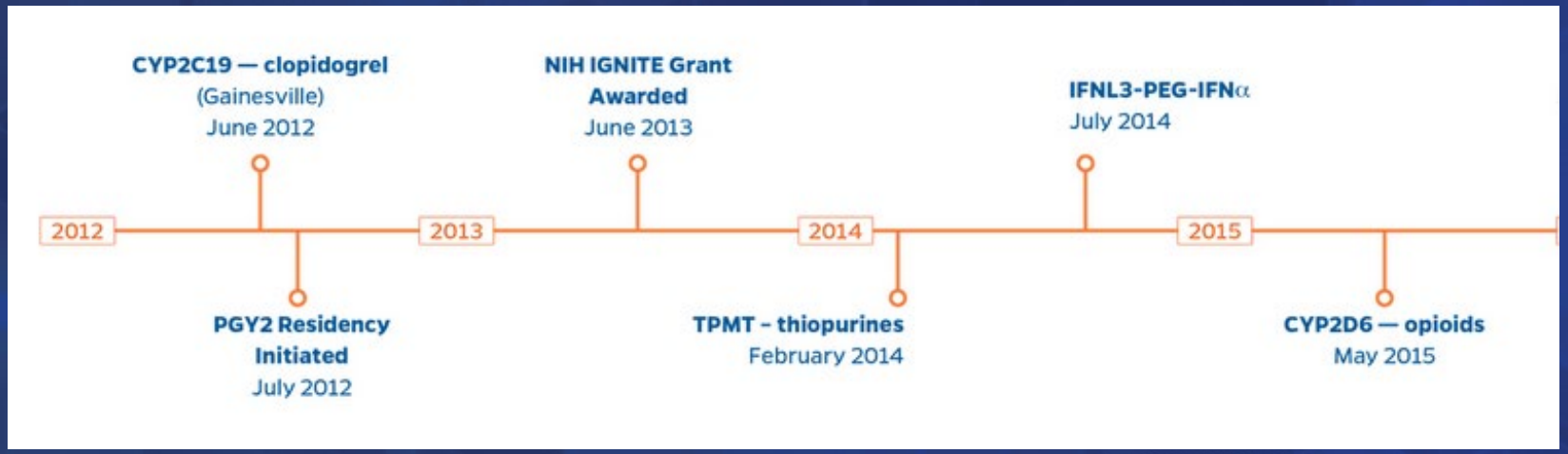

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Implementing GeNomics In pracTicE

Cavallari LH, et al. *Pharmacogenomics* 2017; 18 (5):421-426.
Johnson JA, et al. *Pharmacogenomics* 2013;14 (7): 723-726

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Implementation Success

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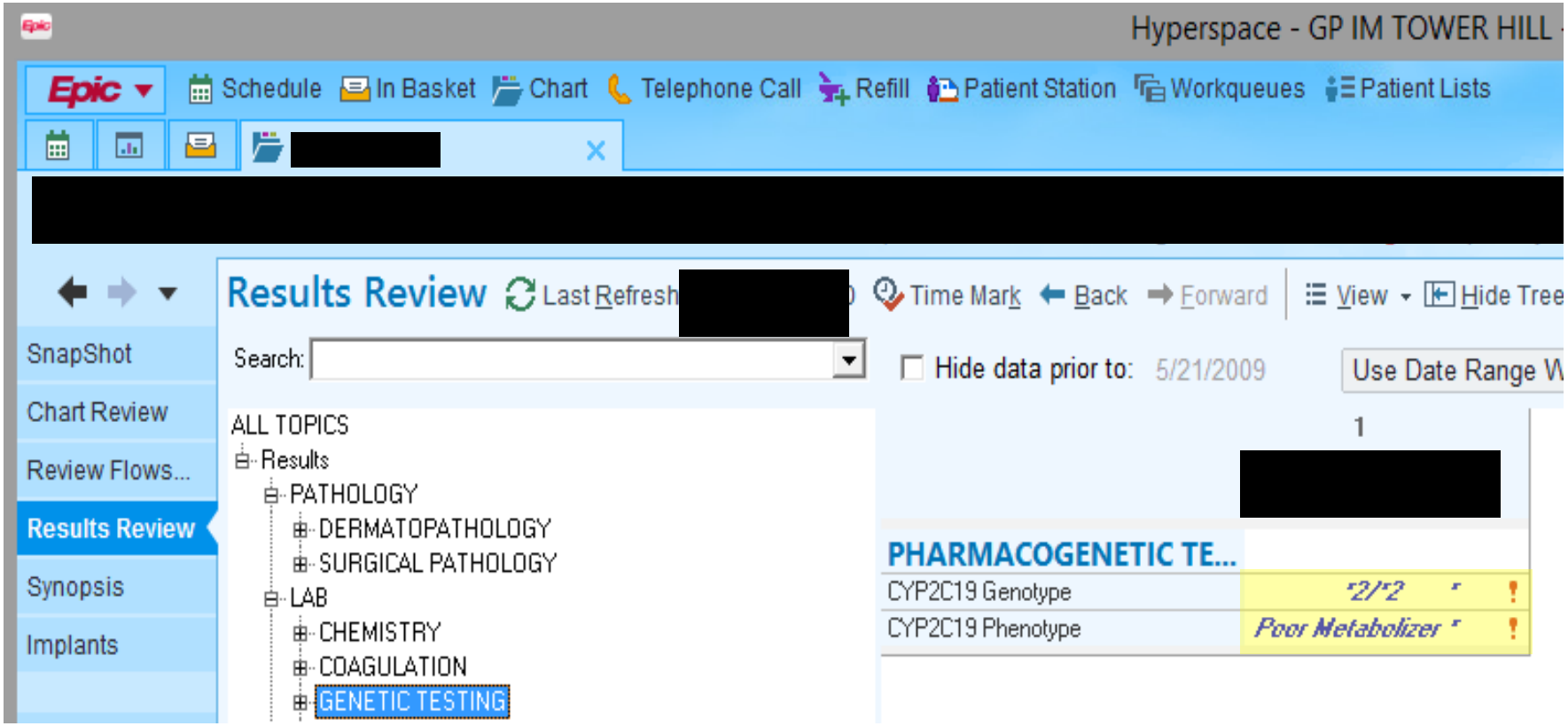
Pharmacogenetic Results in the Medical Record

Discrete fields



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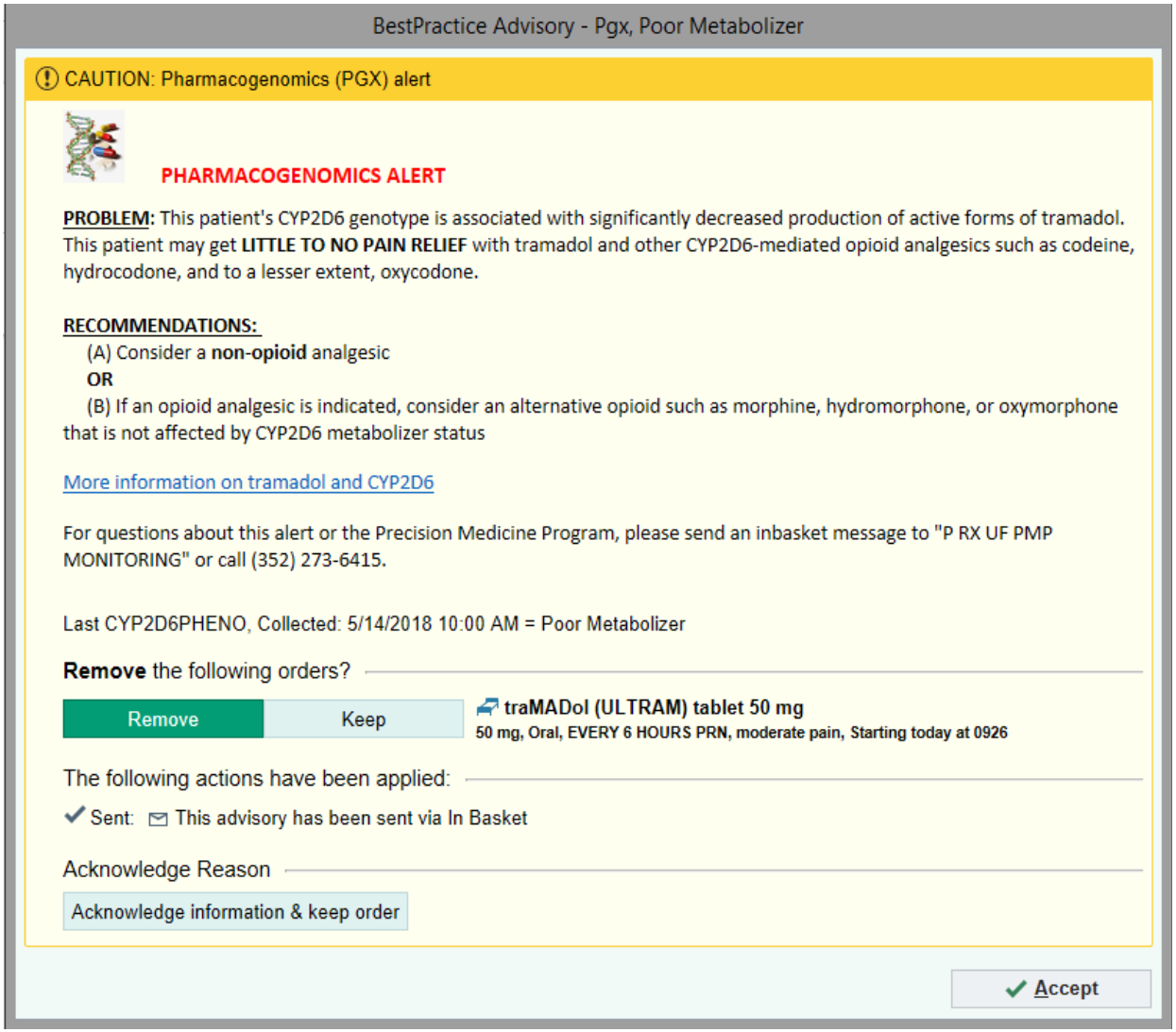
Best Practice Advisory (BPA)



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Pragmatic Clinical Research Trials

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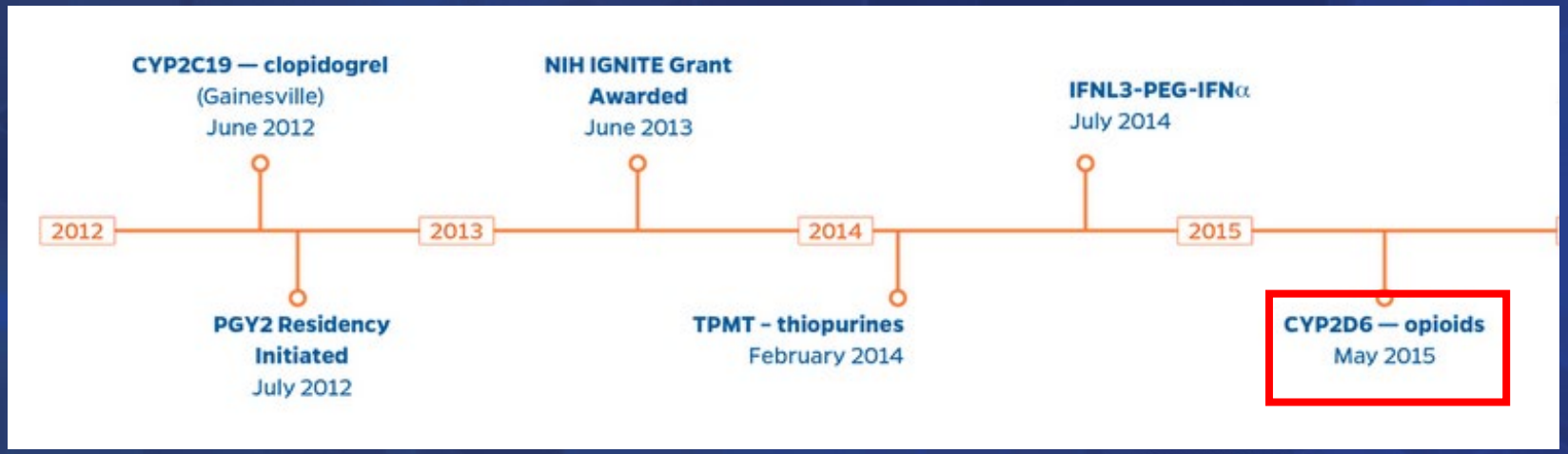

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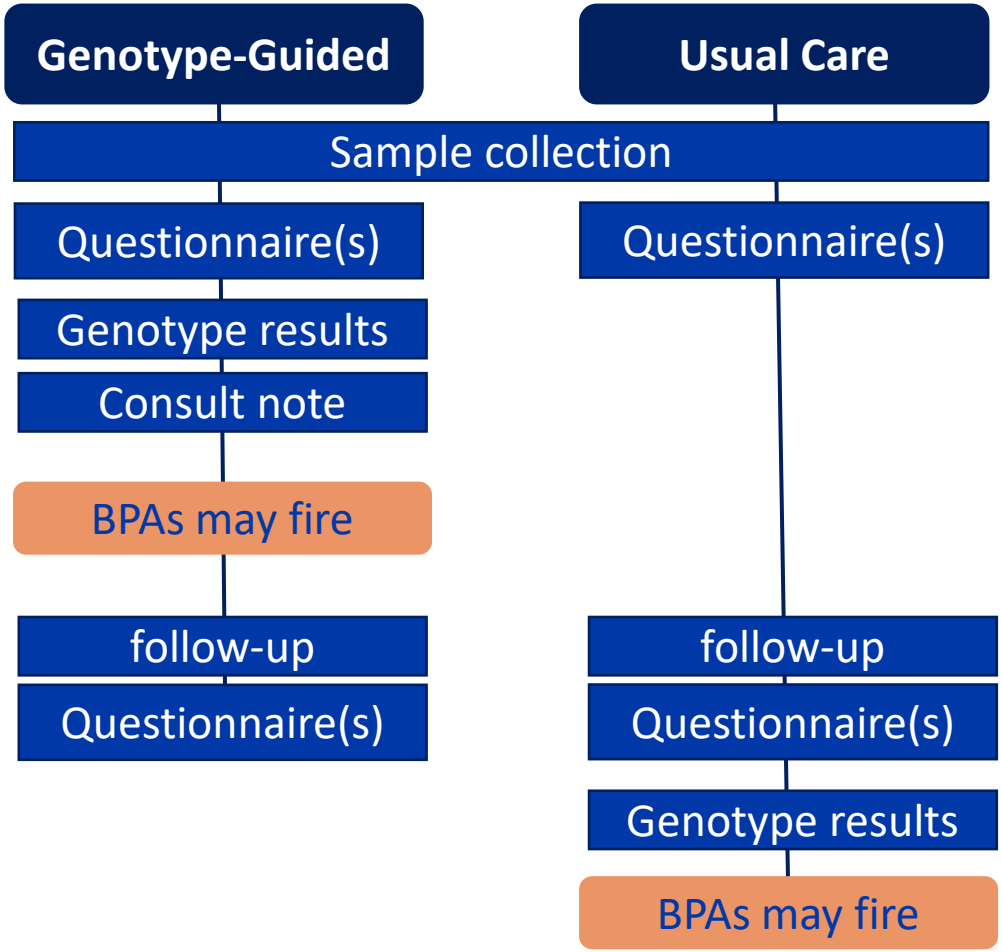
Genotype-guided vs Usual Care



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Pragmatic Clinical Trials

CYP2D6-Opioids

- Primary care clinics
- Specialty clinics
- Adults
- Chronic pain
- Cancer-associated pain

CYP2C19/CYP2D6-SSRIs

- Specialty clinic
- Children
- Depression, anxiety, or obsessive compulsive disorder

CYP2C19-PPIs

- Specialty clinics
- Children
- Adults
- Gastro-esophageal reflux disease

SSRI: Selective serotonin reuptake inhibitors
PPI: Proton pump inhibitors

Smith DM, et al. *Genet Med*. 2019;21(8):1842-1850.
Mosley SA, et al. *Contemp Clin Trials*. 2018;68:7-13.
Cicali EJ, et al. *Clin Transl Sci*. 2019;12(2):172-179.

Post-Implementation

- Compared infrastructure, challenges, and lessons learned among these coordinated implementations

Trial Design Challenges and Solutions

- Identifying who to test
  - Enrolled uncontrolled patients
  - Ideal solution: patients identified via electronic decision support tools

- Completion rate of participation questionnaires
  - Two time points: 97% completion
  - 5+ time points: 57% completion
  - Solution: limit frequency of questionnaires

Cicali EJ, et al. Genet Med. 2019 Oct;21(10):2264-2274.

Implementation Challenges and Solutions

Sample collection and testing

- Children do not like blood draws
  - When offered buccal: 100% consented
  - When offered blood: 73% consented
  - Solution: offer non-invasive sample collection
- Adults are generally comfortable with blood draw
  - Phlebotomist required
- Patients enthusiastic to have PGx data in their medical record
  - > 90% of control arm participants wanted PGx reported after trial completed

Cicali EJ, et al. Genet Med. 2019 Oct;21(10):2264-2274.

Prescriber education strategies

- Prescriber knowledge gaps
  - Pretrial prescriber education methods:
    - Grand rounds, web-based, in-office lunch meetings, clinical in-services, provided CME, case conferences, personal genotyping
  - Offering online CME is not enough incentive
  - 100% of individuals who underwent personal genotyping reported it was beneficial
  - Solution: patient-centered, case-based education is effective for prescriber education
    - Up front and throughout

Cicali EJ, et al. Genet Med. 2019 Oct;21(10):2264-2274.

Pharmacogenetic results

- Clinical phenotype is not reported on lab report
  - 22% participants had a clinical phenotype that was different from genotype-based phenotype because of an interacting drug (i.e., CYP2D6 inhibitors)
  - Considering CYP2D6 inhibitors increased the number of participants with an actionable phenotype 17% to 44%
  - Solution: interpret the phenotype by accounting for phenoconversion via consult note or integrate into clinical decision support

Cicali EJ, et al. Genet Med. 2019 Oct;21(10):2264-2274.

Return of results, prescriber communication, and clinical action

- Availability / recall of PGx results in the medical record
  - Scanned PDF document is not helpful and gets lost
  - Solution: integrate results as discrete variables, which allows alerts to fire to remind prescriber results are available
  - Ideal solution: section of EHR with lifetime (e.g. genetic) results likely optimal

Cicali EJ, et al. Genet Med. 2019 Oct;21(10):2264-2274.

Return of results, prescriber communication, and clinical action

- Interpreting PGx results
  - Prescribers highly valued pharmacist consult notes and BPAs
  - Solution: clear concise guidance should be provided through active alerts or through pharmacist consult note

Cicali EJ, et al. Genet Med. 2019 Oct;21(10):2264-2274.

Return of results, prescriber communication, and clinical action

- Waiting for genotype results
  - Acting on results at next visit results in low adherence to recommendations
  - Waiting to initiate drug of change therapy results in high adherence
    - Occurred in children, suggesting willingness to wait
  - Solution: genotype should be available during patient encounter

Cicali EJ, et al. Genet Med. 2019 Oct;21(10):2264-2274.

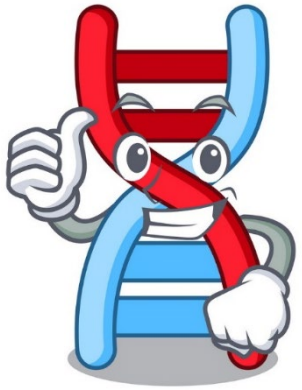
Lessons Learned Summary

- Utilizing PGx results in practice generally won't interrupt workflow
- PGx results need to be available at time of prescriber-patient encounter
- Guidance needs to be provided through active clinical decision support or clinical pharmacist consult
  - lab result quickly gets buried in EHR

Cicali EJ, et al. Genet Med. 2019 Oct;21(10):2264-2274.

Key Points for Success

- Create a strong relationship with laboratory
  - Validate non-invasive testing methods
  - Ensure results are available in medical record as discrete variables
- Conduct frequent case-based prescriber education
- Provide timely interpretation of results
  - Clinical decision support, consult notes
- Provide patient friendly education
  - Manage expectations



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- Amanda Elchynski, PharmD
- Amanda Elsey, MHA
- Erica Elwood, BA
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Thank you!

Questions?

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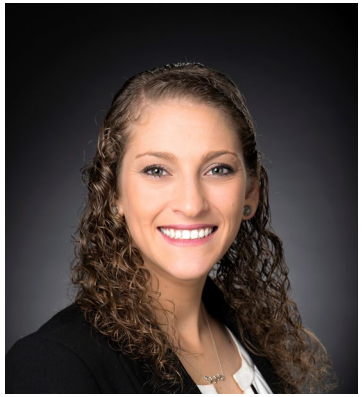
Question and Answer Session

Colleen Keenan

Consultant

Advisory Board's Clinical Innovators Council



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Thank you!

- Please fill out the survey after today's session
- Slides will be available today and the recording of today's webinar will be available in one week at www.gtmr.org
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