Putting Pharmacogenetics into Practice:
Health-system perspectives

James M. Hoffman, PharmD MS BCPS FASHP
Chief Patient Safety Officer
Associate Member, Pharmaceutical Sciences
St. Jude Children's Research Hospital

August 1, 2017

Outline

- Experiences from implementation at St. Jude Children's Research Hospital
- Broader trends across health-systems actively implementing pharmacogenetics
- Importance of informatics and implementation resources

2

One Model of Pharmacogenetic Services

PG4KDS: Clinical Implementation of Pharmacogenetics at St. Jude

Implementation Resources:
www.stjude.org/pg4kds/implement

PG4KDS: Protocol

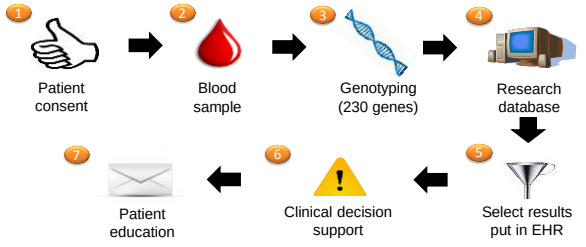
- Goal:
  - Migrate pharmacogenetic tests from the laboratory (array-based) into routine patient care, to be available preemptively
    - Implement all CPIC™ level A/B gene/drug pairs
- Exclusion criteria:
  - Patients who have received a prior allogeneic stem cell transplant
  - Patient who have received a prior liver transplant

www.stjude.org/pg4kds

Reactive vs. Preemptive Genotyping

Reactive Genotyping	Pre-emptive Genotyping
Ordered as drug therapy is being initiated or contemplated	• Test result in EHR as a pre-prescription characteristic • Independent of medication use
• Delay in start of therapy • Possible inadequate dosing if test ordered but medication initiated prior to receiving result	• Test result already available in the EHR • Results "reused" as other drugs are prescribed
Requires prescriber knowledge about drug/gene interaction to determine which test to order	Relies on clinical decision support tools to alert prescriber about drug/gene interaction
Turn-around time: ~5 business days	Turn-around time: already in EHR
Expensive relative to potential benefit of one therapeutic decision	Cost: roughly equivalent to 2 single gene tests
One pharmacogenetic test result	• Array or platform based • Multiple pharmacogenetic results

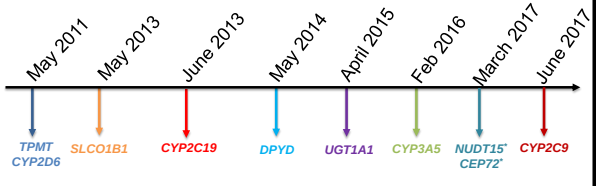
PG4KDS: The Process



Hoffman JM, et al. Am J Med Genet C Semin Med Genet. 2014;166C:45-55.

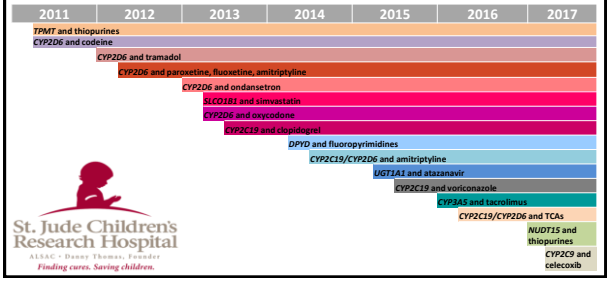
PG4KDS: Nearly 4000 Patients Enrolled

Gene implementation timeline



Implementation Timeline: Genes and Drugs

www.stjude.org/pg4kds/implement



PG4KDS:8 Genes and 22 Drugs Implemented

In 2,949 patients, 86% of patients had at least one actionable result in the EHR

- ***CYP2D6*** *(17%)*
  - Codeine
  - Oxycodone
  - Tramadol
  - Amitriptyline, Clomipramine, Imipramine, Trimipramine
  - Doxepin
  - Fluoxetine
  - Paroxetine
  - Ondansetron
- ***CYP2C19*** *(62%)*
  - Clopidogrel
  - Amitriptyline, Clomipramine, Imipramine, Trimipramine
  - Doxepin
  - Voriconazole
- ***CYP3A5*** *(41%)*
  - Tacrolimus
- ***SLCO1B1*** *(13%)*
  - Simvastatin
- ***TPMT*** *(11%)*
  - Mercaptopurine
  - Thioguanine
  - Azathioprine
- ***DPYD*** *(0.4%)*
  - Fluorouracil
  - Capecitabine
- ***UGT1A1*** *(28%)*
  - Atazanavir
- ***CYP2C9*** *(32%)*
  - Celecoxib

Percent represents patients on PG4KDS with actionable result for the gene

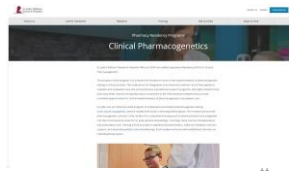
Implementing Pharmacogenetics: Health-System Trends

- Motivations for implementing pharmacogenetics
  - Improve patient safety and medication use
  - Alignment with health-system priorities
  - Innovation and marketing
- Models, resources, and structure
  - Inpatient focused or blended with outpatient
  - Pharmacists with entire position dedicated to implementing pharmacogenetics

10

Examples of Health-Systems with one or more FTEs devoted to Pharmacogenetics

Health System	Location	Comments
University of Florida	Gainesville, FL	ASHP Accredited Residency
St. Jude Children's Research Hospital	Memphis, TN	ASHP Accredited Residency

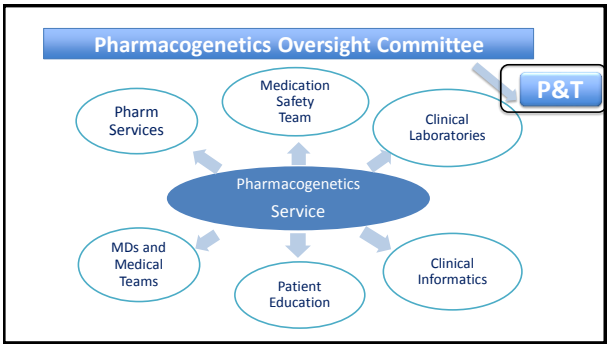


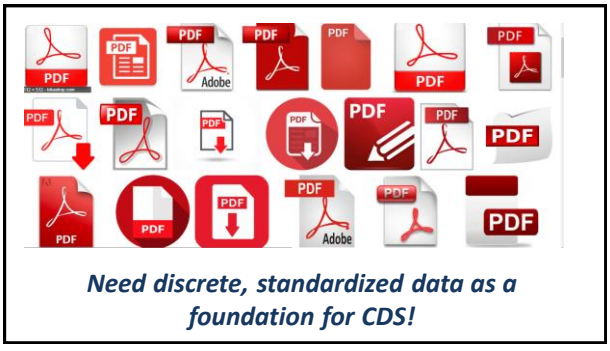
Examples of Health-Systems with one or more FTEs devoted to Pharmacogenetics

Health System	Location	Comments
Mission Health	Asheville, NC	Community health system
NorthShore University HealthSystem	Evanston, IL	Successful clinic model
Moffitt Cancer Center	Tampa, FL	Somatic first; expanded to germline
Avera	Sioux Falls, SD	Huge region across Midwest
Cleveland Clinic	Cleveland, OH	Seized opportunity to align
Children's Minnesota	Minneapolis, MN	New within last 2 years
Mount Sinai	New York, NY	Aligned with research institute
Mayo Clinic	Rochester, MN	High priority for organization

Several open positions (e.g. USC, U of Minn/Fairview, and UNC)
About 30 US implementers listed on https://cpicpgx.org/implementation/

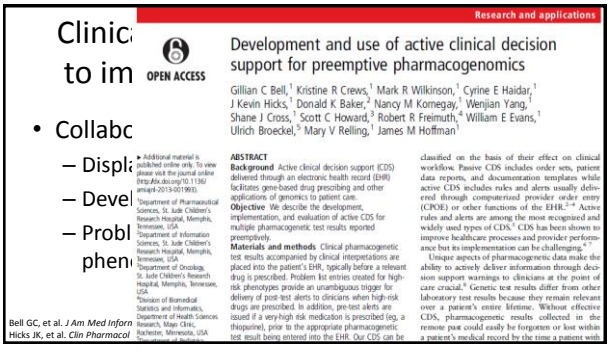
12



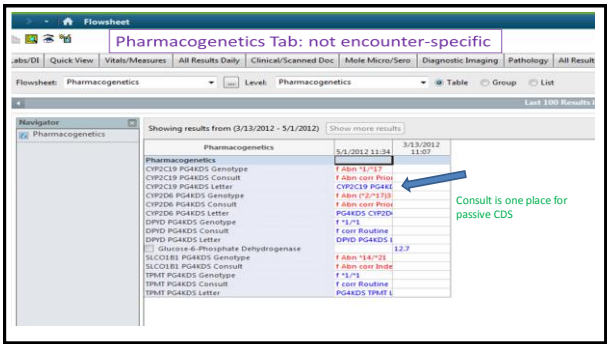


Clinic
to im

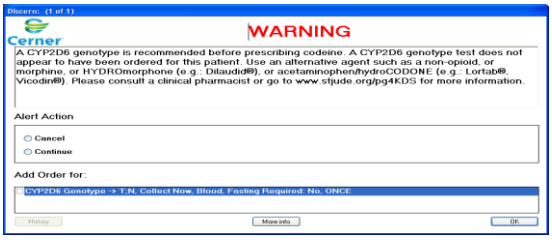
- Collabc
  - Displ
  - Devel
  - Probl
    phen



Bell GC, et al. *J Am Med Inform*
Hicks JK, et al. *Clin Pharmacol*

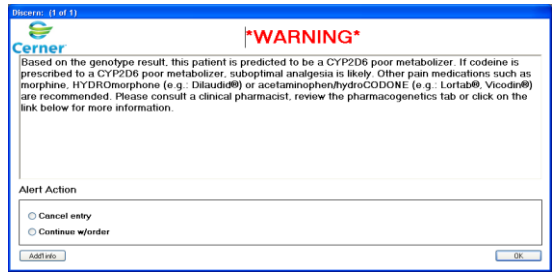


Pre-test (No-Genotype) Alerts



Relling, CC, et al. J Am Med Inform Assoc. 2014;21:e93-9

Post-test (High-Risk Genotype) Alerts



The Clinical Pharmacogenetics Implementation Consortium (CPIC)

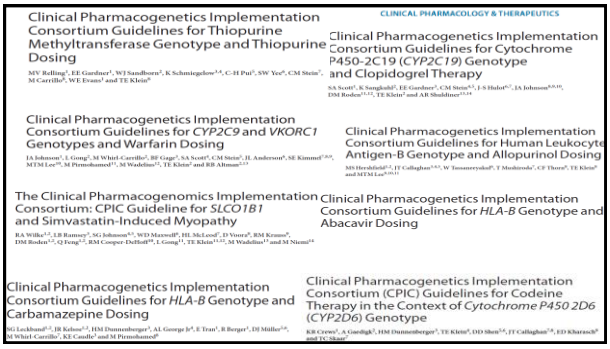
CPIC™
Clinical Pharmacogenetics Implementation Consortium

CPIC™
Clinical Pharmacogenetics Implementation Consortium

- CPIC guidelines are designed to help clinicians understand HOW available genetic test results should be used to optimize drug therapy.
  - Not WHETHER tests should be ordered.
- Key Assumption:
  - Clinical high-throughput and pre-emptive genotyping will become more widespread.
  - Clinicians will be faced with having patients' genotypes available even if they did not order test with drug in mind.

CPIC™
Clinical Pharmacogenetics Implementation Consortium

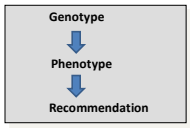
- Posted on PharmGKB and capitalize on PharmGKB resources
- Freely available, no limits on use
- Peer reviewed, *CPT* first right of refusal to publish, standardized format, minimum set of elements
- Grading of evidence and of recommendations
- Can be updated on CPIC website ahead of publications
- Authorship, COI policy
- Closely follow IOM practices
  - Curr Drug Metab. 2014 Feb;15(2):209-17



CPIC Informatics Working Group: Initial Focus

- Create comprehensive translation tables from genotype to phenotype to clinical recommendation for CPIC guidelines
  - Define structure and process to efficiently develop and maintain in the most useful format(s)
  - Publish as part of CPIC guidelines

CPIC™
Clinical Pharmacogenetics Implementation Consortium



Other Key Resources:

DIGITizE

http://www.nationalacademies.org/hmd/Activities/Research/GenomicBasedResearch/InnovationCollaboratives/EHR.aspx

Implementation Guide for *HLA-B* and *TPMT* provides extensive practical guidance

CDSKB provides many examples of pharmacogenetic CDS

https://cdskb.org/

Healthcare Professional Education

- PG4KDS website (www.stjude.org/PG4KDS)
- ASHP's Emerging Sciences Resource Center
  - Written pharmacist competencies
- CPIC (www.cpicpgx.org)
- PharmGKB (https://www.pharmgkb.org)
- NIH-NHGRI G2C2 http://genomicseducation.net/
- Training/Education:
  - Clinical staff
  - Clinical Pharmacists
    - ASHP accredited PGY2 pharmacy residency
  - Pharmacy students:
    - Clinical pharmacogenetics rotation

PG4KDS Team

SJ Pharmaceutical
Mary Relling
Cyrine Haidar
James Hoffman
Kristine Crews
Nancy Kornegay
Jennifer Hockings
Shane Cross
Emily Melton
Alejandro Molinelli
Colton Smith
William Evans
Wenjian Yang
Paula Condy
Terri Kuehner
Sheri Ring
Margaret Edwards
Shannon Gibbs
Kelly Caudle
Melinda Wood
Cathy Suggs

SJ Biostatistics
Cheng Cheng
Deqing Pei

St. Jude
Ching-Hon Pui
Amar Gajjar
Aditya Gaur
Alberto Pappo
Sima Jeha
Ulrike Reiss
Melissa Hudson

SJ Informatics
Donald Baker
David Zhao
Rajesh Parashuram
Yuri Yanishevski

MCW
Uli Broeckel
Rachel Lorier
Amy Turner

St. Jude Children's Research Hospital
CPIC Clinical Pharmacogenetics Implementation Consortium

Acknowledgements - CPIC

- CPIC Leaders
  - Mary Relling
  - Teri Klein
- CPIC Coordinator
  - Kelly Caudle
- PGRN
- PharmGKB
  - Russ Altman
  - Teri Klein
  - Michelle Whirl-Carrillo
  - PharmGKB curators
- CPIC members/observers
- CPIC Informatics working group
  - James Hoffman
  - Michelle Whirl-Carrillo
  - Bob Freimuth
- CPIC Steering Committee
  - Mary Relling
  - Julie Johnson
  - Teri Klein
  - Rochelle Long
  - Dan Roden
  - Rachel Tyndale

PharmGKB
CPIC Clinical Pharmacogenetics Implementation Consortium