



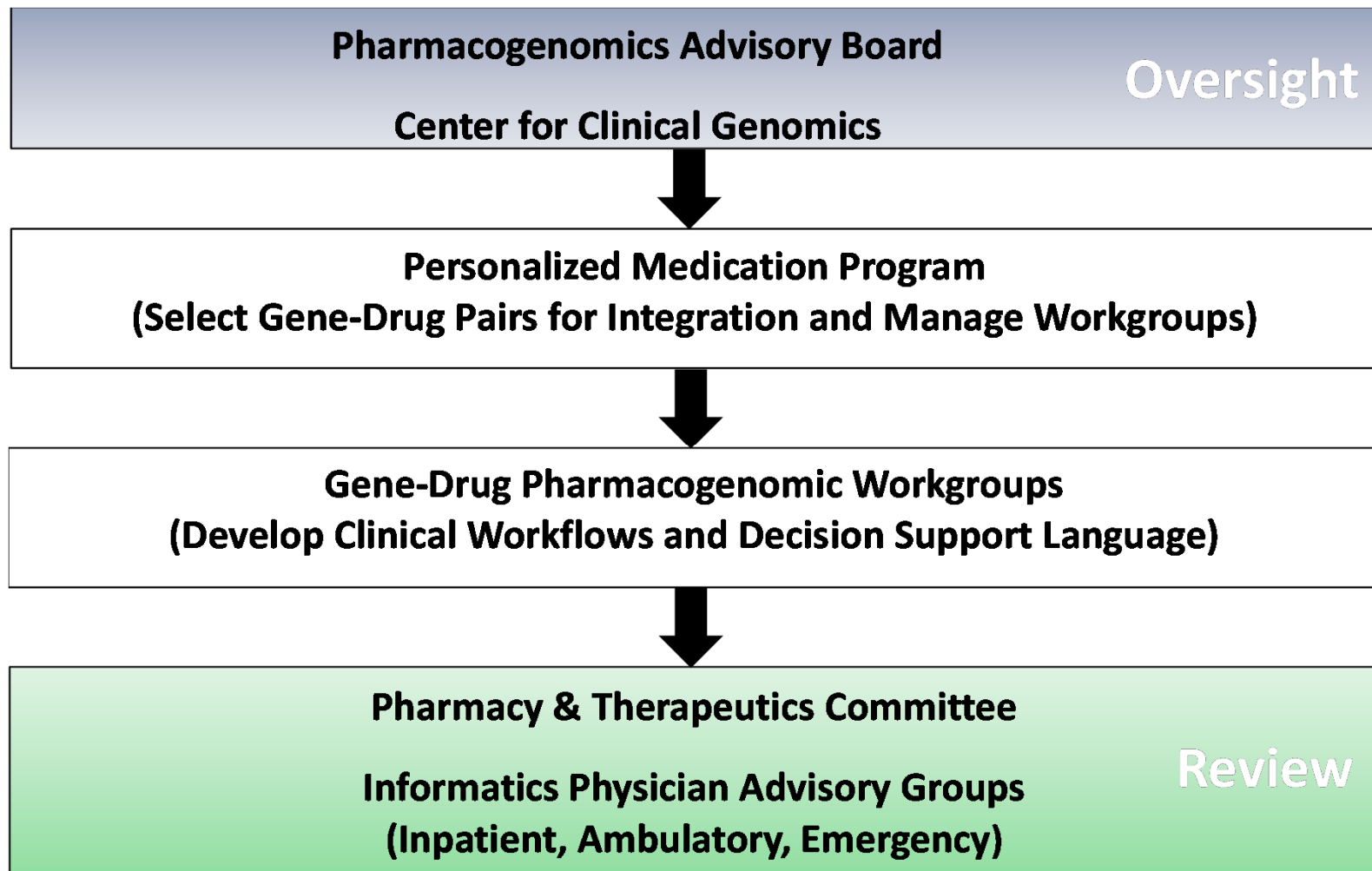
Implementation of CPIC Guidelines into Clinical Practice

Cleveland Clinic Experience



- **10 adult hospitals & a children's hospital in Ohio**
- **Hospital in Florida**
- **Over 90 ambulatory locations in Ohio and Florida**
- **5.5 million patient visits per year**

Schematic of Pharmacogenomic Implementation Oversight and Review



Implementation Science

Gene-Drug Pairs Integrated into EHR

TPMT – thiopurines

Predictive of severe life-threatening myelosuppression

HLA-B*57:01 – abacavir

FDA boxed warning. Predictive of serious and sometimes fatal hypersensitivity reaction

HLA-B*15:02 – anticonvulsants

FDA boxed warning. Predictive of Stevens-Johnson syndrome/epidermal necrolysis

G6PD – oral dapsone

Predictive of acute hemolytic anemia

Clinical Decision Support for Guiding PGX Testing

- **Cleveland Clinic does not have a preemptive genotyping protocol**
- **For gene-drug pairs selected for implementation, point-of-care reminders needed**
- **Interruptive pre-test alerts were deployed to the EHR that reminded (educate) clinicians to consider genetic testing**

Example of Pharmacogenomic CDS

HLA-B*57:01 – Abacavir

Place orders

Order Set Interactions Providers New Order Pending Orders Held Orders Pending Orders Sign & Hold Sign & Verify **Sign Orders** Settings Reports

New order: Search

Order mode: New order defaults: Not using defaults

During visit (1 Order)

abacavir 300 mg - lamivudine 150 mg - zidovudine 300 mg tablet (TRIZIVIR)
1 tablet, ORAL, 2 TIMES DAILY, First Dose Today at 2100, Until Discontinued

BestPractice Advisory - Zzdonotdischarge,Epic G

FDA BLACK BOX WARNING: RISK OF A SERIOUS/FATAL HYPERSENSITIVITY REACTION. A HLA-B*57:01 genotype test is recommended before prescribing abacavir or reinitiating abacavir therapy, including for those who previously tolerated abacavir therapy. Please click 'accept' below to order the HLA-B*57:01 genotype test or a reason for not ordering the test.

[Click here for additional information regarding HLA-B*57:01 - Abacavir](#)

Acknowledge reason:

Test drawn and pending in lab External result noted by clinician
External test result records requested a... Other Document in note Med Update
Patient declined test

☒ Open order: HLA B5701

Used to identify those with PGx tests from outside health systems

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Accept Cancel

Example of Pharmacogenomic CDS

*HLA-B*15:02 – Carbamazepine*

⚠ RISK OF A SERIOUS/FATAL DERMATOLOGIC REACTION: HLA-B*15:02 genotyping is recommended before prescribing this medication to patients of Asian ancestry. Please determine if the patient is of Asian ancestry, including but not limited to the following countries of origin:

- China
- Singapore
- Malaysia
- Thailand
- India
- Korea
- Japan
- Taiwan
- Philippines

If the patient is of Asian ancestry, select the HLA-B*15:02 genotype test or a reason for not ordering the test.

[Click here for additional information about HLA*B15:02 - Anticonvulsants](#)

Acknowledge reason:

☐ Open Order Set: HLAB*1502 TYPING [preview](#)

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Selection of these acknowledgements suppresses future pre-test alerts to prevent alert fatigue

Education Documents & EHR Stage 2 Meaningful Use

 **RISK OF A SERIOUS/FATAL DERMATOLOGIC REACTION:** The patient is positive for the HLA-B*15:02 allele and is at an increased risk of a serious/fatal dermatologic reaction to the following antiepileptic medications:

- carbamazepine
- oxcarbazepine
- eslicarbazepine
- phenytoin
- fosphenytoin
- lamotrigine

These medications should NOT be prescribed unless the benefit outweighs the risk, or if the patient has consistently been



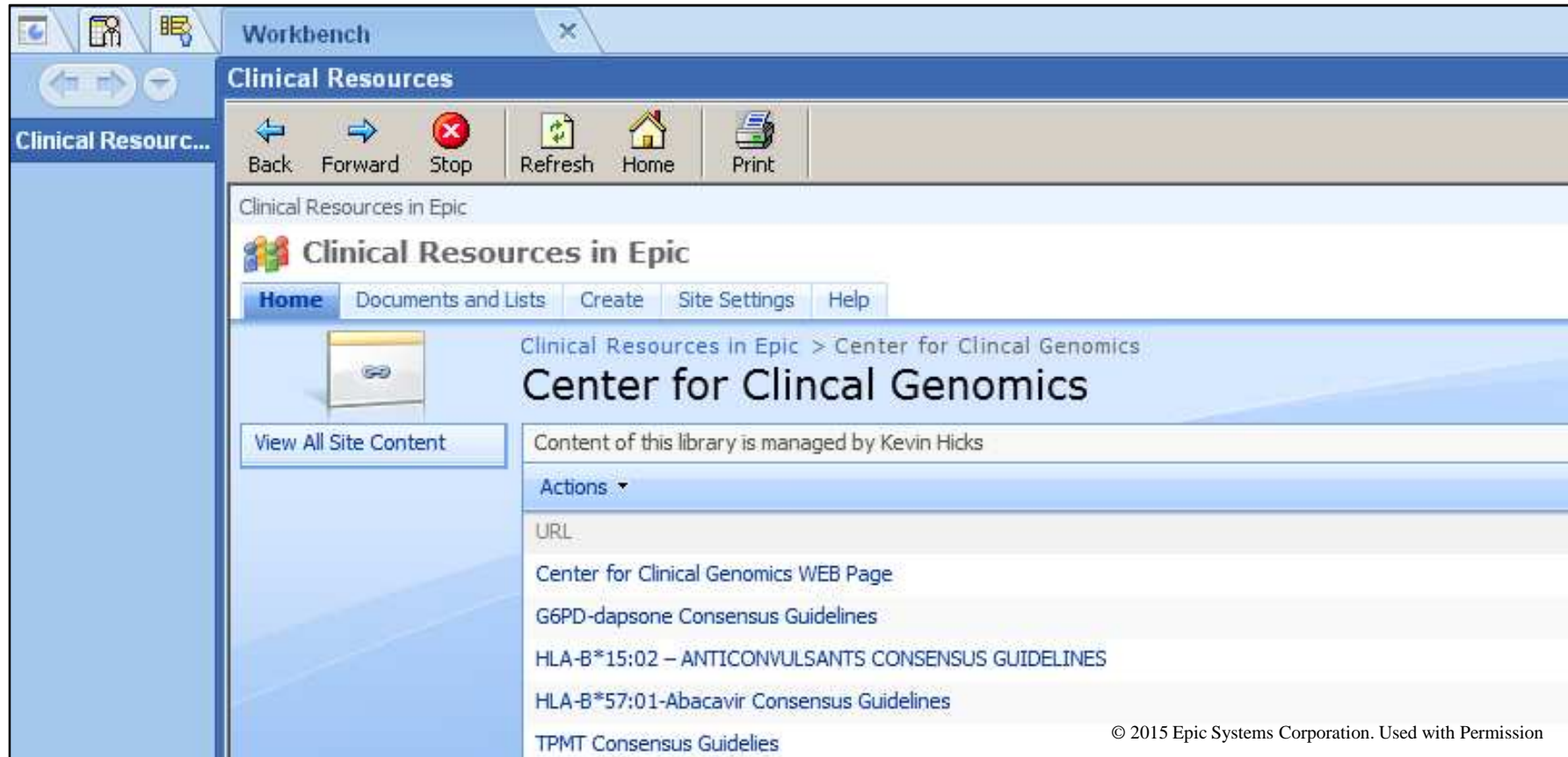
CLEVELAND CLINIC PERSONALIZED MEDICATION PROGRAM

*HLA-B*15:02* – ANTICONVULSANTS CONSENSUS GUIDELINES

PURPOSE OF DOCUMENT: Individuals who carry the *HLA-B*15:02* allele are approximately 100-fold more susceptible to carbamazepine-induced Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) than those who are non-carriers of the allele. Although this document focuses on carbamazepine, carriers of the *HLA-B*15:02* allele may also be more susceptible to oxcarbazepine, eslicarbazepine acetate, phenytoin, fosphenytoin, and lamotrigine-induced SJS/TEN than non-carriers. *HLA-B* genotyping is offered at Cleveland Clinic (test name **HLA B*1502**) to help identify those at an increased risk of drug-induced SJS/TEN. The purpose of this document is to provide guidance for when this test should be ordered, how to interpret the result, and how to modify pharmacotherapy based on the *HLA-B*15:02* test result.

Evidence-based referenced education documents linked to decision support for CMS Stage 2 meaningful use criteria

Pharmacogenomic Decision Support Clinical Resources



Stored in a Microsoft SharePoint© site that interfaces with the EHR

Integrating Pharmacogenomic Results into the EHR

The screenshot displays the 'Results Review' interface in an Epic EHR system. The top navigation bar includes buttons for 'Back', 'Forward', 'View', 'Hide Tree', 'Ref Range', 'Load All', 'Flowsheet', 'Graph', and 'Time Mark'. The left sidebar lists various result categories, with 'Results Review' currently selected. The main content area shows a search bar and a tree view of 'ALL TOPICS' under 'Results', with 'MOLECULAR GENETICS' highlighted. To the right, a table displays the results for 'MOLECULAR GENETICS' on 7/23/2015. The results show 'HLA B5701' as 'Negative' and 'HLA B5701 Interpre...' as '(NOTE) *'. The 'HLA B5701 Reviewed By' field is redacted. A copyright notice at the bottom right reads '© 2015 Epic Systems Corporation. Used with Permission'.

1 7/23/2015 1426	
MOLECULAR GENETICS	
HLA B5701	Negative
HLA B5701 Interpre...	(NOTE) *
HLA B5701 Reviewed By	[REDACTED]

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Entry of *HLA* results (negative/positive) is an automated process

Integrating Pharmacogenomic Results into the EHR

The screenshot displays an EHR interface with a sidebar on the left containing navigation options: SnapShot, Summary, Chart Review, Care Everywhere, Synopsis, Results Review (highlighted), Review Flowsh..., Problem List, History, and Inpatient Notes. The main content area is divided into a search and filter section at the top, a tree view of medical topics on the left, and a results table on the right.

Search: ☐ Hide data prior to: 5/15/2014

ALL TOPICS

- [-] Results
 - [-] LAB GENERAL
 - [+] CHEMISTRY
 - [+] HEMATOLOGY
 - [+] MOLECULAR GENETICS (highlighted)
 - [+] MISCELLANEOUS
 - [-] PATHOLOGY
 - [+] SURGICAL PATHOLOGY

1	
7/17/2015	
1725	
MOLECULAR GENETICS	
TPMT Genotype	TPMT*1/TPMT*1
TPMT Genetics	Alleles presen... *

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Entry of *TPMT* results into discrete data field requires manual annotation

HLA-B*15:02 – Carbamazepine

Patient Safety Alerts

⚠ RISK OF A SERIOUS/FATAL DERMATOLOGIC REACTION: The patient is positive for the HLA-B*15:02 allele and is at an increased risk of a serious/fatal dermatologic reaction to the following antiepileptic medications:

- carbamazepine
- oxcarbazepine
- eslicarbazepine
- phenytoin
- fosphenytoin
- lamotrigine

These medications should NOT be prescribed unless the benefit outweighs the risk, or if the patient has consistently been taking the medication for greater than 3 months without a cutaneous reaction. Please cancel this drug order and prescribe an alternate drug, or select a reason for ordering.

Please page the pharmacogenomics pharmacist at 22924 for more information.

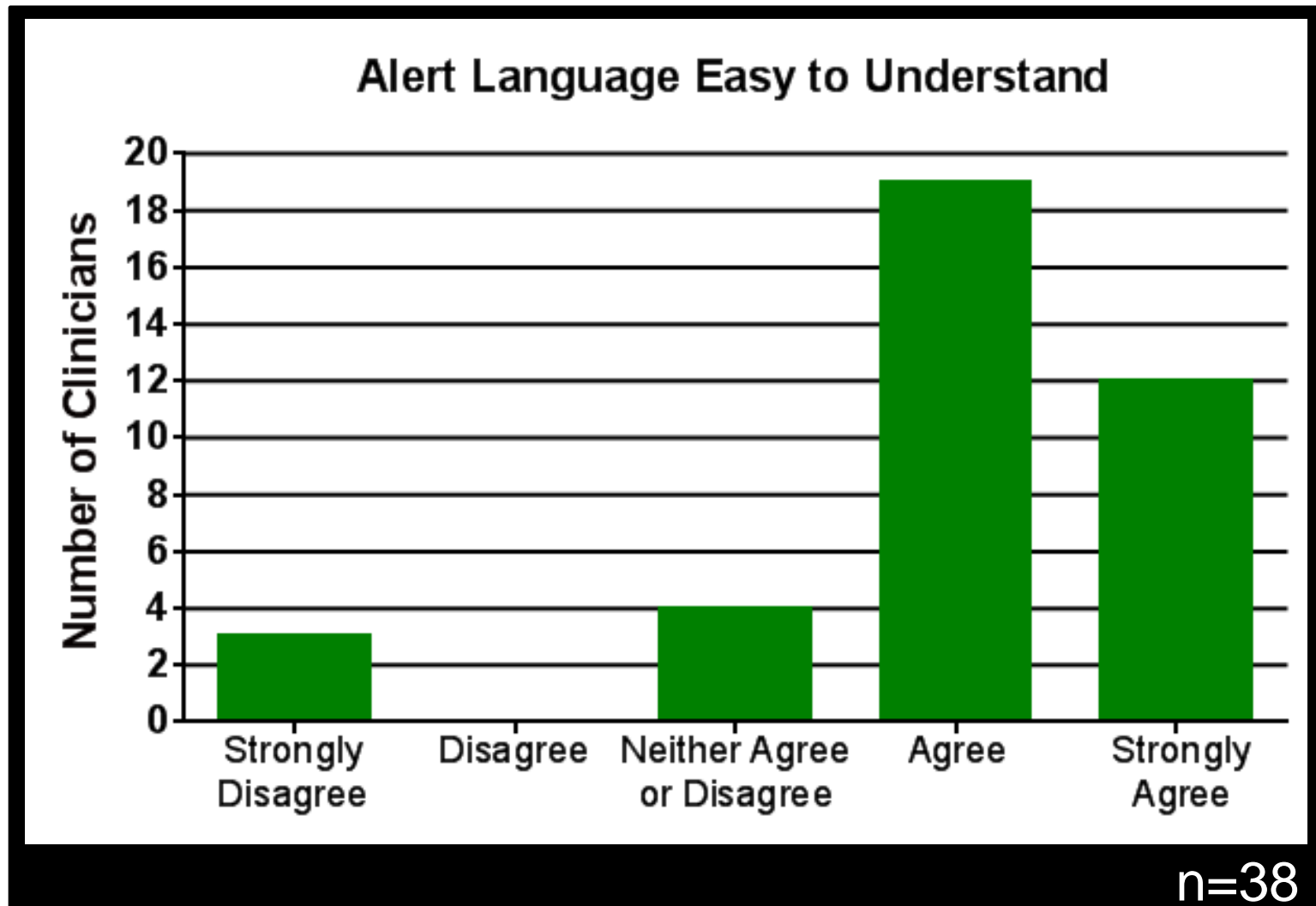
[Click here for additional information about HLA*B15:02 - Anticonvulsants](#)

Last HB1502=Positive on 8/12/2015

Acknowledge reason:

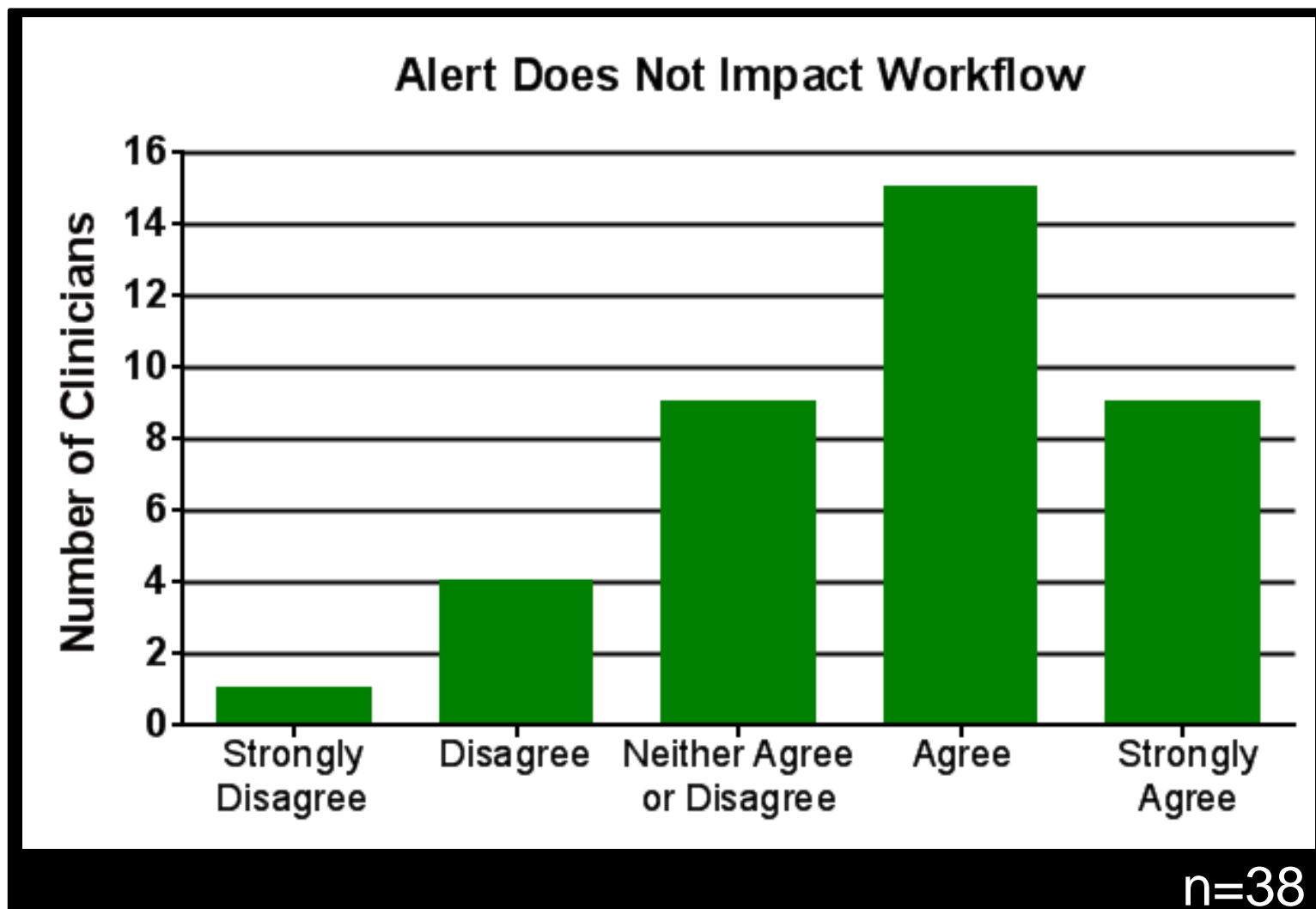
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CDS Formative Evaluation



Practice Recommendations: Involve clinicians early

CDS Formative Evaluation



Practice Recommendations: Involve clinicians early

Passive Clinical Decision Support for Guiding PGX

- Reserve interruptive PGx alerts for very high-risk gene-drug
- Passive decision support for other gene-drug interactions
 - Reduce alert fatigue
 - Faster integration of PGx data into EHR
- PGx data initially resulted in the EHR is textual
 - Not sustainable to manually annotate results

Pharmacogenomic Test Reporting in Drug Entry Screen

carBAMazepine 200 mg tab(s) (TEGretol) ✓ Accept ✗ Cancel
200 mg, ORAL, 2 TIMES DAILY, First Dose Today at 2100, Until Discontinued

Priority:

Report: Lab Test Results

Component	Time Elapsed	Value	Range	Status	Comments
HLA B*1502 Typing	506 days (03/05/14 0700)	POSITIVE (NOTE) The allele HLA-B*1502 is associated with increased risk of developing severe skin reactions to carbamazepine therapy (Stevens-Johnson Syndrome and toxic epidermal necrolysis).		Final result	

Reference Links: 1. HLA-B*15:02 Pharmacogenomic Summary Sheet 2. Drug Info - Adult 3. Drug Info - Peds

Dose: mg 200 mg 400 mg 600 mg

Administer Dose: **200 mg**

Administer Amount: **1 tablet**

Route: ORAL

Frequency: BID TID QID

For: ☒ Doses ☐ Hours ☐ Days

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Pharmacogenomic Test Reporting in Drug Entry Screen

Manage Orders

?

Actions

Resize

Close

azaTHIOprine tab(s) (IMURAN)

Accept

Cancel

ORAL, DAILY, First Dose Today at 1200, Until Discontinued

Priority:

Report:

Lab Test Results

Component	Time Elapsed	Value	Range	Status	Comments
TPMT Enzyme Value	202 days (01/06/15 1453)	<div>22.4</div> <div>Unit: U/mL RBC</div> <div>(NOTE)</div> <div>This result can be interpreted as normal for TPMT activity.</div> <div>-----REFERENCE VALUE-----</div> <div>>=15.0 (Normal)</div> <div>10.1-14.9 (Low normal)</div> <div>6.0-10.0 (Carrier)</div> <div><6.0 (Deficient)</div>		Final result	

Reference Links:

1. TPMT Summary-Prescribing Info

2. Drug Info - Adult

3. Drug Info - Peds

Dose:

50 mg

100 mg

150 mg

Route:

ORAL

ORAL

Frequency:

DAILY

For:

Doses

Hours

Days

Starting:

7/28/2015

Today

Tomorrow

First Dose:

Include Now

As Scheduled

First Dose:

Today 1200

Until Discontinued

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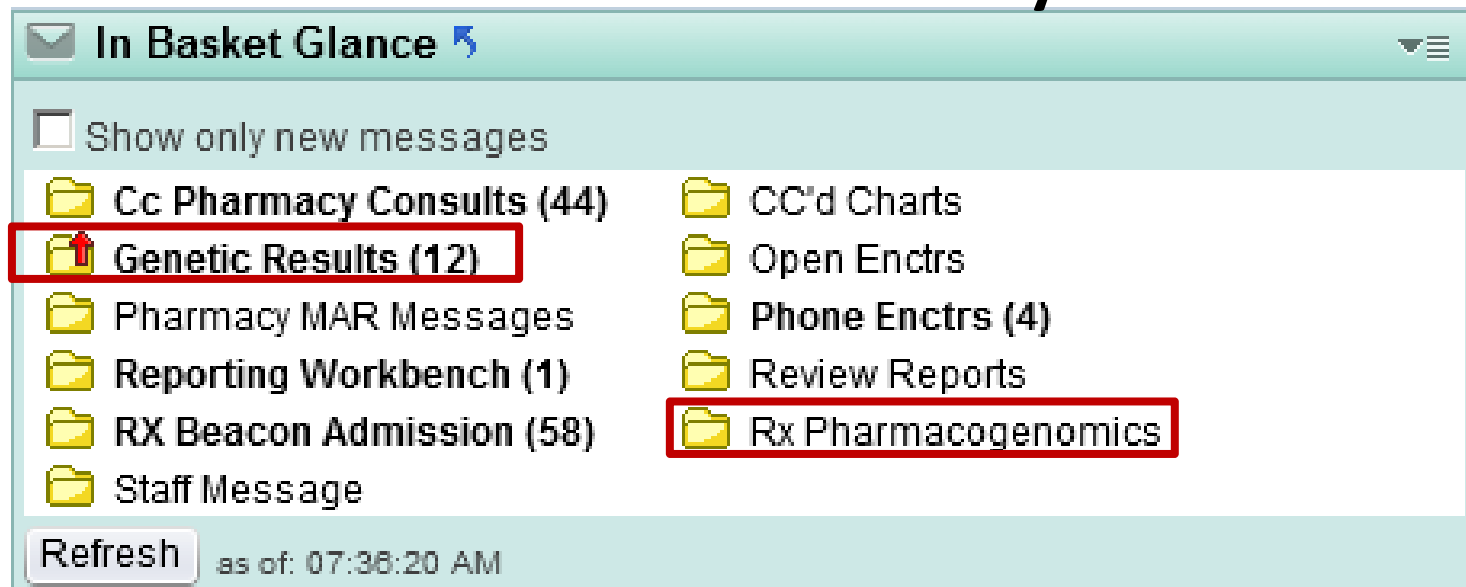
Pharmacogenomic Decision Support

Impact on Patient Care

- **Compliance with clinical recommendations**
 - **Contraindications – 100% compliant**
 - **Dose reductions – 90 to 95% compliant**

Pharmacy Managed Behind-The-Scenes Review of Pharmacogenomic Test Ordering & Results

EHR In Basket – Pharmacy View



- Provides a summary of PGx Enterprise wide
- Review for correct test selection – Cost Savings
- Follow up with clinicians when necessary

Personalized Medication Program

EHR Pharmacogenomic Consult Request

CONSULT CLINICAL PHARMACOGENOMICS											
Routine, ONCE First occurrence Today at 1545, For emergent questions, contact the pharmacogenomics clinical pharmacist at pager 22924.											
! Questions:	<table border="1"><thead><tr><th>Prompt</th><th>Answer</th></tr></thead><tbody><tr><td>1. Is the consult for clinical interpretation and drug dosing recommendations for a pharmacogenomic test result? !</td><td>Yes, indicate which test result and which drug No</td></tr><tr><td>2. Is the consult for an opinion on whether pharmacogenomics may help explain drug intolerances? !</td><td>Yes, indicate which drug(s) and the observed adverse drug effect No</td></tr><tr><td>3. Is the consult for an opinion on whether pharmacogenomics may help explain non-response to a drug? !</td><td>Yes, indicate which drug(s) No</td></tr><tr><td>4. What other information is being requested (if applicable)?</td><td></td></tr></tbody></table>	Prompt	Answer	1. Is the consult for clinical interpretation and drug dosing recommendations for a pharmacogenomic test result? !	Yes, indicate which test result and which drug No	2. Is the consult for an opinion on whether pharmacogenomics may help explain drug intolerances? !	Yes, indicate which drug(s) and the observed adverse drug effect No	3. Is the consult for an opinion on whether pharmacogenomics may help explain non-response to a drug? !	Yes, indicate which drug(s) No	4. What other information is being requested (if applicable)?	
	Prompt	Answer									
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	2. Is the consult for an opinion on whether pharmacogenomics may help explain drug intolerances? !	Yes, indicate which drug(s) and the observed adverse drug effect No									
	3. Is the consult for an opinion on whether pharmacogenomics may help explain non-response to a drug? !	Yes, indicate which drug(s) No									
4. What other information is being requested (if applicable)?											
	Single response										
Priority:	Routine										
Frequency:	ONCE										
	Once										

MyConsult Pharmacogenomic Service

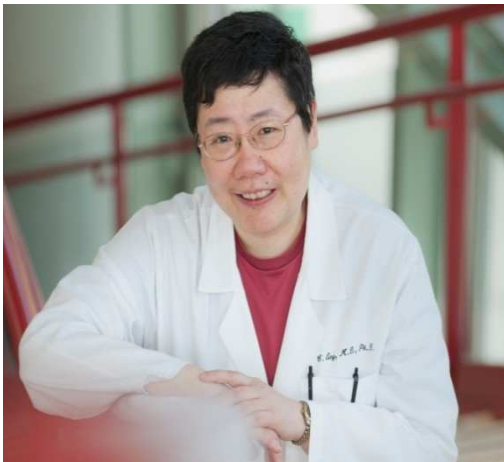


Pharmacogenomics
Consultations

Cleveland Clinic's MyConsult[®] Online Medical Second Opinion now offers a consultation service for individuals who are seeking an expert second opinion regarding pharmacogenomics

Implementation of Pharmacogenomic Services

- Outpatient Pharmacogenomics Clinic



Dr. Charis Eng
Chair, Genomic Medicine Institute



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Cole Eye Institute

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Cleveland Clinic

Every life deserves world class care.