Genetics and the Electronic Medical Records: Where are we now? and Where are we going?

Kathi C Huddleston, PhD, RN
Director, Clinical Projects
November 8, 2018

Genetics and the Electronic Health Record: where are we today? …. where are we going?

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Genomic and Family data
…….. A New Era in Medicine …

nature

insight commentary

VOL 429 | 27 MAY 2004

The case for a US prospective cohort study of genes and environment

Francis S. Collins

National Human Genome Research Institute, National Institutes of Health, Building 31, Room 4B09, MSC 2152, 31 Center Drive, Bethesda, Maryland 20892-2152, USA (e-mail: fc23a@nih.gov)

Information from the Human Genome Project will be vital for defining the genetic and environmental factors that contribute to health and disease. Well-designed case–control studies of people with and without a particular disease are essential for this, but rigorous and unbiased conclusions about the causes of diseases and their population-wide impact will require a representative population to be monitored over time (a prospective cohort study). The time is right for the United States to consider such a project.

1990–2003

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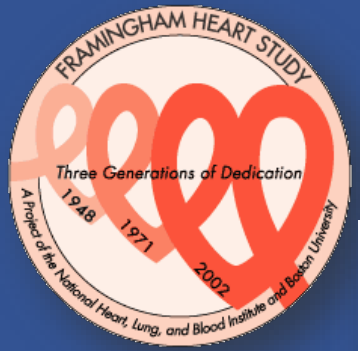
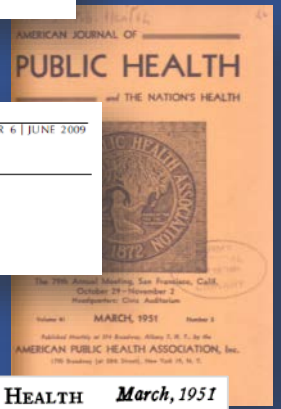
Longitudinal data and cohort studies



APRIL 1957 AMERICAN JOURNAL OF PUBLIC HEALTH

II. Coronary Heart Disease in the Framingham Study

THOMAS R. DAWBER, M.D.; FELIX E. MOORE, F.A.P.H.A.; and GEORGE V. MANN, M.D.



nature genetics VOLUME 41 | NUMBER 6 | JUNE 2009

Genome-wide association study of blood pressure and hypertension

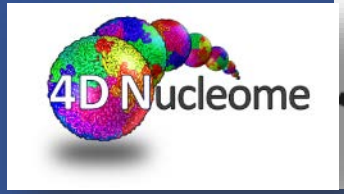
AMERICAN JOURNAL OF PUBLIC HEALTH *March, 1951*

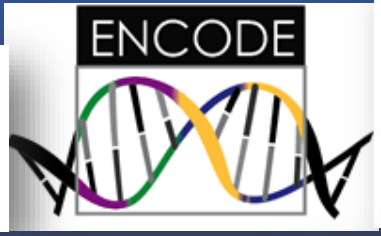
Epidemiological Approaches to Heart Disease: The Framingham Study*

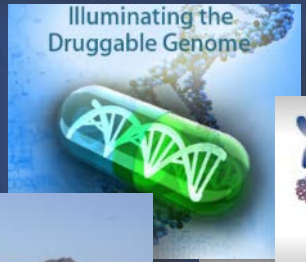
THOMAS R. DAWBER, M.D., GILCIN F. MEADORS, M.D., M.P.H., AND FELIX E. MOORE, JR.

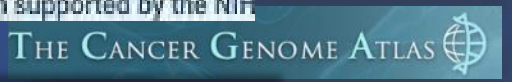
National Heart Institute, National Institutes of Health, Public Health Service, Federal Security Agency, Washington, D. C.

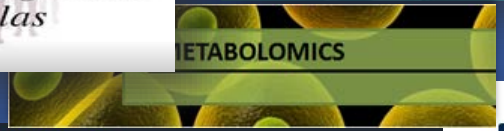
Bigger data sources and more integration for personalized health

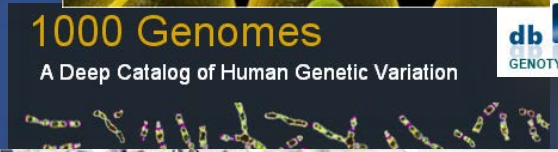


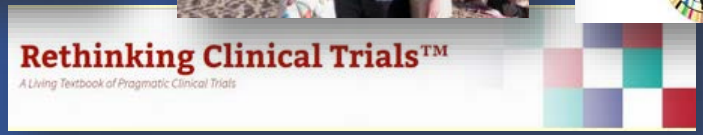












Genomics

Data Science

Patient Partnerships

Technologies

EHRs

There are really only three important things to remember in life: To care, to share, and to be fair. This is not a new idea at all, and yet, observing how most people live their lives, you might think it was.

Frederick Lenz


WHERE?
WHO?
WHAT?
WHY?
HOW?
WHEN?

What to Share?

Health Care Provider

- Genetic Data
- Existing DTC Data
- Medical Data
- Family History
- Demographics

With Whom to Share?

Clinical Care- The Hospital

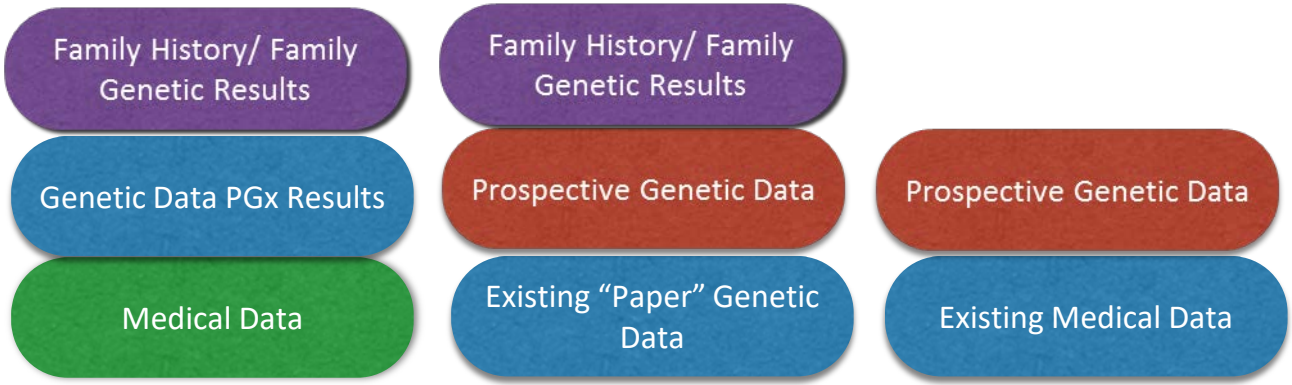
EPIC System

Health Care Provider

- Genetic Data PGx Results
- Medical Data
- Existing DTC Data
- Family History/ Family Genetic Results
- Demographics

Scientific Community- Researchers

How to Share? Now this is where the fun begins …..



When to Share?

Today

2021

Existing Full Data

Prospective Full Data

Prospective Genetic Data

Family History

Negative Genetic Results

Genetic Data PGx Results

Medical Data

Prospective Meta Data

Existing “Paper” Genetic Data

Existing “Paper” Family Genetic Data

EHR / MHR

Patient Portal

Paper Chart (no, really!)

Whilst Carefully Considering & Balancing

Research Participant(s)

Scientific Community- Researchers

Health Care Professional

Clinical Care- The Hospital

New Discoveries,

New Concerns,

Ethical Dilemmas.

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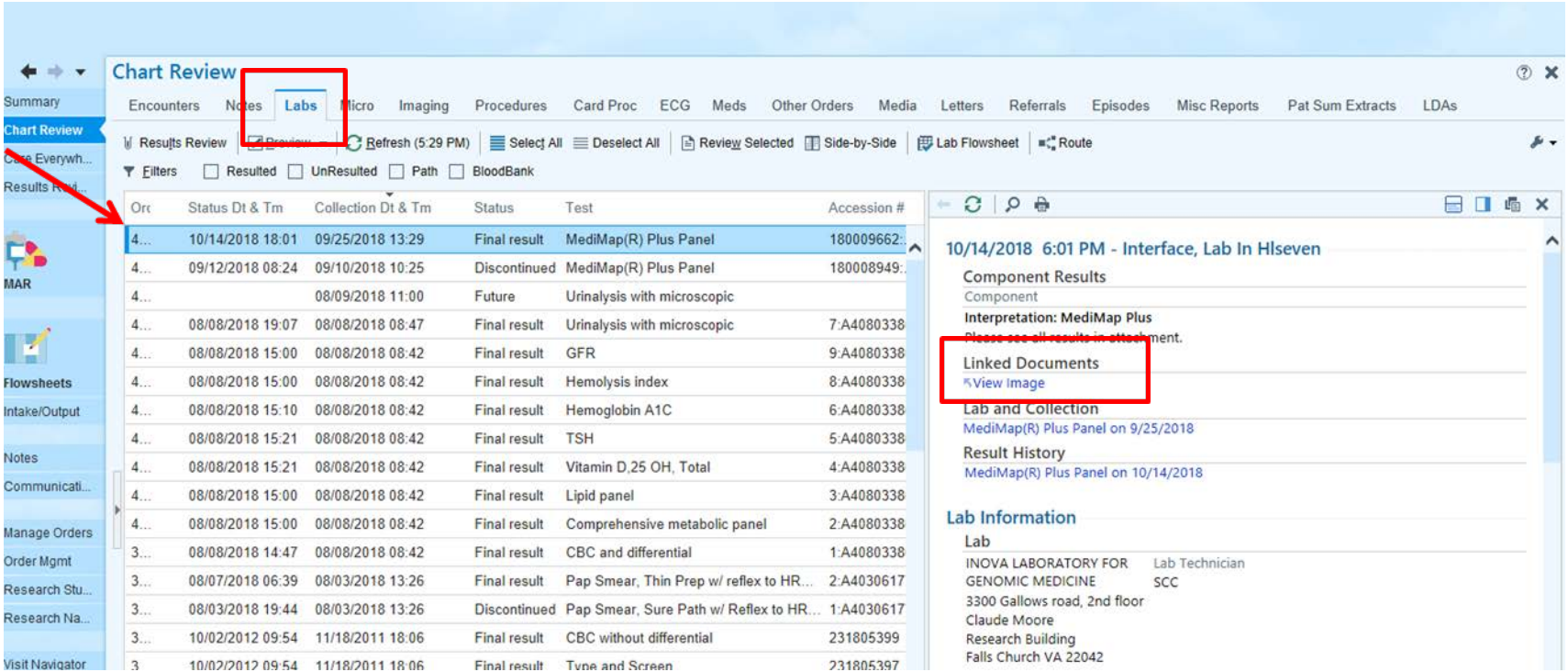
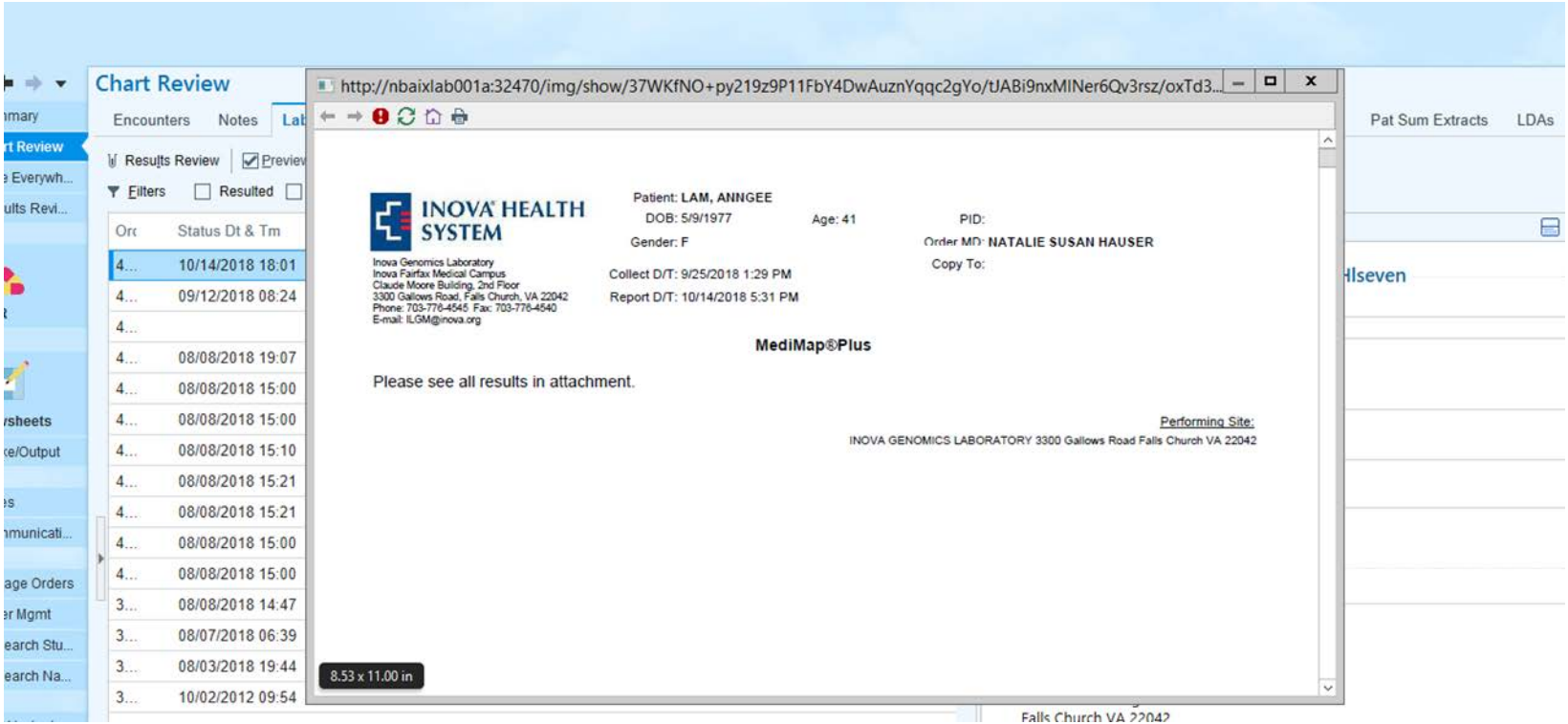
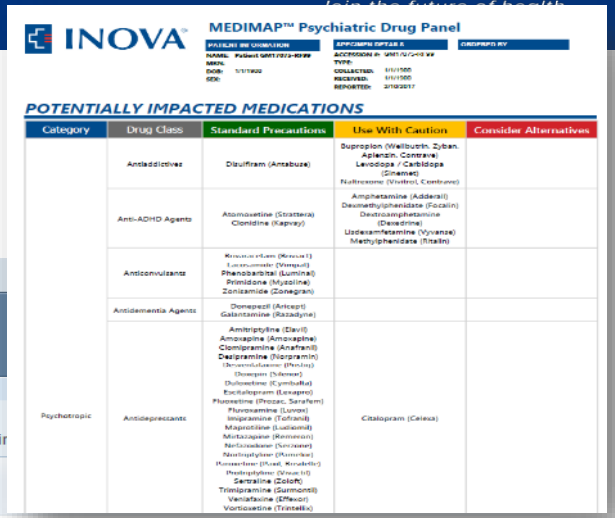
How to find results in EPIC



How to find results in EPIC



Universal Epic BPA Pop-Up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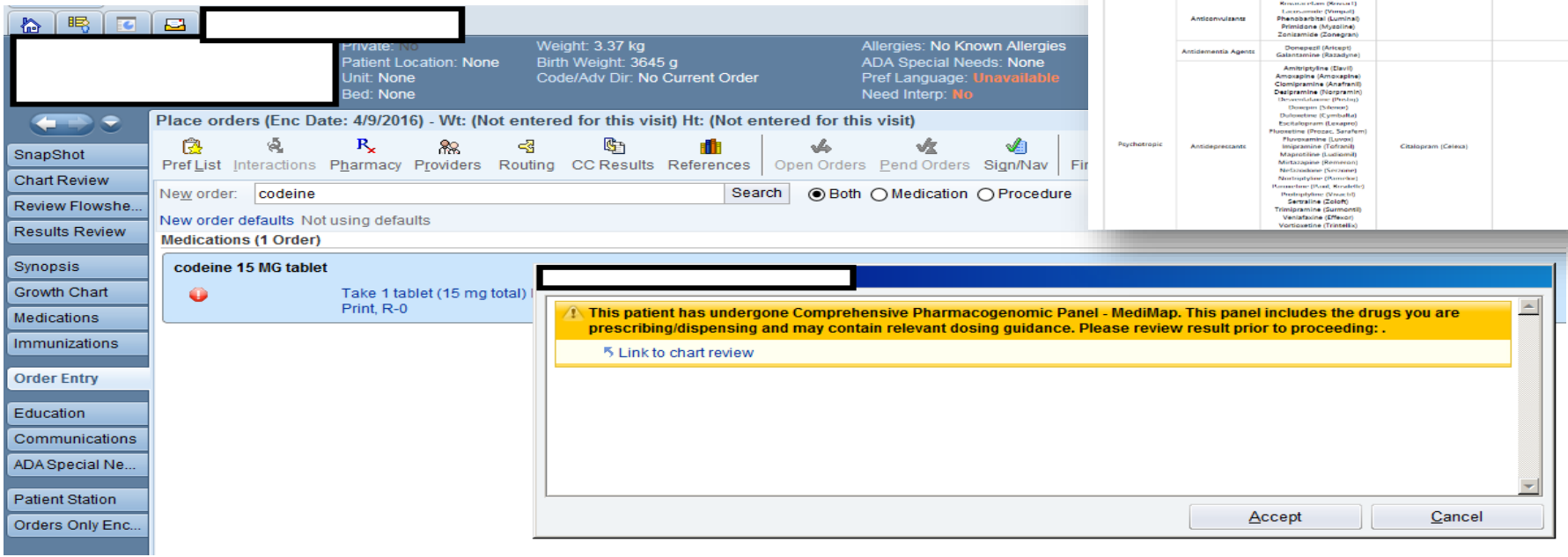
MEDIMAP™ Psychiatric Drug Panel

POTENTIALLY IMPACTED MEDICATIONS

Category	Drug Class	Standard Precautions	Use With Caution	Consider Alternatives
	Antiaddictives	Disulfiram (Antabuse)	Bupropion (Wellbutrin, Zyban, Aplenzin, Contrave) Levodopa / Carbidopa (Sinemet) Naltrexone (Vivitrol, Contrave)	
	Anti-ADHD Agents	Atomoxetine (Strattera) Clonidine (Kapvay)	Amphetamine (Adderall) Dexmethylphenidate (Focalin) Dextroamphetamine (Dexedrine) Lisdexamfetamine (Vyvanse) Methylphenidate (Ritalin)	
	Anticonvulsants	Lamotrigine (Lamictal) Phenobarbital (Luminal) Primidone (Mysoline) Zonisamide (Zonegran)		
	Antidementia Agents	Donepezil (Aricept) Galantamine (Razadyne)		
Psychotropic	Antidepressants	Amitriptyline (Elavil) Amoxapine (Amoxapine) Clomipramine (Anafranil) Desipramine (Norpramin) Doxepin (Sinequan) Duloxetine (Cymbalta) Escitalopram (Lexapro) Fluoxetine (Prozac, Sarafem) Fluvoxamine (Luvox) Imipramine (Tofranil) Maprotiline (Ludiomil) Mirtazapine (Remeron) Nefazodone (Serzone) Nortriptyline (Pamelor) Paroxetine (Paxil, Sraxetin) Protriptyline (Vivactil) Sertraline (Zoloft) Trimipramine (Surmontil) Venlafaxine (Effexor) Vortioxetine (Trintellix)	Citalopram (Celexa)	



Result Interpretation & Reporting

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Category	Drug Class	Standard Precautions	Use With Caution	Consider Alternatives
Psychotropic	Antiaddictives	Bupropion (Wellbutrin, Zyban, Aplenzin, Contrave) Disulfiram (Antabuse)	Naltrexone (Vivitrol)	
	Anti-ADHD Agents	Amphetamine (Adderall) Dextroamphetamine (Dexedrine) Lisdexamfetamine (Vyvanse)	Clonidine (Kapvay) Dexmethylphenidate (Focalin) Methylphenidate (Ritalin)	Atomoxetine (Strattera)
	Anticonvulsants	Fosphenytoin (Cerebyx) Lacosamide (Vimpat) Phenobarbital (Luminal) Phenytoin (Dilantin) Primidone (Mysoline) Zonisamide (Zonegran)		
	Antidementia Agents	Galantamine (Razadyne)	Donepezil (Aricept)	
		Desvenlafaxine (Pristiq) Duloxetine (Cymbalta) Escitalopram (Lexapro) Fluoxetine (Prozac, Sarafem)	Amoxapine (Amoxapine) Citalopram (Celexa)	Amitriptyline (Elavil) Clomipramine (Anafranil) Desipramine (Norpramin) Doxepin (Silenor) Imipramine (Tofranil)

Result Interpretation & Reporting

Drug	Findings	What to Do - Dosing Regimens Suitable for Adult Patients
Amitriptyline (Elavil)	• Increased Sensitivity to Amitriptyline • Genotype: CYP2D6 *4/*4 • Evidence Level: Actionable	Select an alternative drug, or consider prescribing amitriptyline at a reduced dose (50% reduction) with monitoring of plasma concentrations of amitriptyline and nortriptyline.
Clomipramine (Anafranil)	• Increased Sensitivity to Clomipramine • Genotype: CYP2D6 *4/*4 • Evidence Level: Actionable	Consider an alternative drug, or prescribe clomipramine at 50% of the recommended standard starting dose. Monitor plasma concentrations of clomipramine and desmethylclomipramine, and titrate accordingly until a favorable response is achieved.
Desipramine (Norpramin)	• Increased Sensitivity to Desipramine • Genotype: CYP2D6 *4/*4 • Evidence Level: Actionable	Consider an alternative drug, or prescribe desipramine at 50% of recommended standard starting dose. Monitor plasma concentrations of desipramine and metabolites and titrate accordingly until a favorable response is achieved.

Drug	Findings	What to Do - Dosing Regimens Suitable for Adult Patients
Amoxapine (Amoxapine)	• Possible Sensitivity to Amoxapine • Genotype: CYP2D6 *4/*4 • Evidence Level: Informative	Like other tricyclic and tetracyclic antidepressants, amoxapine is metabolized by CYP2D6. However, the overall contribution of this enzyme in the metabolism of this drug is not well documented. Decreased CYP2D6 activity may result in higher amoxapine concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased CYP2D6 function therefore, therapy must be initiated cautiously and adjusted according to the patient's response.

Result Interpretation & Reporting

SUMMARY OF RESULTS

RED CATEGORY

Based upon the patient's results, the medication has potentially reduced efficacy or increased toxicity. Medication change or dose adjustment with increased monitoring is highly recommended with this drug.

YELLOW CATEGORY

Based upon the patient's results, the medication has potentially reduced efficacy or increased toxicity. Dose adjustment with increased monitoring may be needed with this drug.

GREEN CATEGORY

Based upon the patient's results, the medication can be prescribed according to standard regimens.

Result Interpretation & Reporting

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PHARMACOGENOMIC TEST RESULTS

Gene	Genotype	Phenotype	Clinical Consequences
CYP2C19	*17/*17	Ultra-Rapid Metabolizer	Consistent with a significant increase in CYP2C19 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP2C9	*1/*2	Intermediate Metabolizer	Consistent with a moderate deficiency in CYP2C9 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP2D6	*1/*1	Normal Metabolizer	Consistent with a typical CYP2D6 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP3A5	*1/*3	Intermediate Metabolizer	Consistent with an intermediate CYP3A5 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
SLCO1B1	521T>C T/C	Decreased Function	Consistent with a decreased SLCO1B1 transporter function. The patient's risk for statin-induced myopathy is intermediate.
TPMT	*1/*1	Normal Metabolizer	Consistent with a typical TPMT activity and a typical risk of side effects with conventional doses of thiopurines.
VKORC1	-1639G>A A/A	High Warfarin Sensitivity	VKORC1 is the site of action of warfarin. The patient may require a substantial decrease in warfarin dose.

AllelesTested: CYP2C19 *2, *3, *4, *4B, *5, *6, *7, *8, *9, *10, *17; **CYP2C9** *2, *3, *4, *5, *6, *7, *8, *9, *10, *11, *13, *15, *16, *27; **CYP2D6** *2, *3, *4, *4M, *6, *7, *8, *9, *10, *11, *12, *14A, *14B, *15, *17, *20, *29, *35, *41, *5 (gene deletion), XN (gene duplication); **CYP3A5** *1D, *2, *3, *3B, *3C, *3K, *6, *7, *8, *9; **SLCO1B1** 388A>G, 521T>C; **TPMT** *2, *3A, *3B, *3C, *4; **VKORC1** -1639G>A, 1542G>C, 2255C>T, 3730G>A, 5808T>G, 1173C>T

Methodology: *Next generation sequencing based assay that detects the listed variants (please see 'Variants Tested' for list of variants) with known clinical significance at analytical sensitivity and specificity >95%.*

Limitations: *This test will only detect a subset of all known variants that result in altered activity for the genes tested. Only a subset of gene variants that have strong evidence for clinical relevance and utility are reported here. 21 medications are evaluated in the MediMap test; fewer medications may appear on the report if the drug*