MedStar Health

It's how we treat people.

Pharmacogenomics-guided optimization of antiplatelet therapy and impact on patient management: a health-system's perspective

October 7, 2025

D. Max Smith, PharmD, BCPS
Clinical Pharmacogenomics Specialist, MedStar Health
Associate Professor, Georgetown University Medical Center

Conflicts of Interest

- This continuing education activity is supported by **Genomadix**.
- Dr. Smith will discuss the **Genomadix Cube™ CYP2C19 test** during this presentation.
- Dr. Smith has no other relevant financial relationships with commercial interests related to this content.

Objectives

- Recognize the current evidence on *CYP2C19*-guided antiplatelet therapy
- Describe the use of rapid *CYP2C19* genotyping at MedStar Health

The Evidence

The Problem:
Clopidogrel is Less Effective in Select Patients

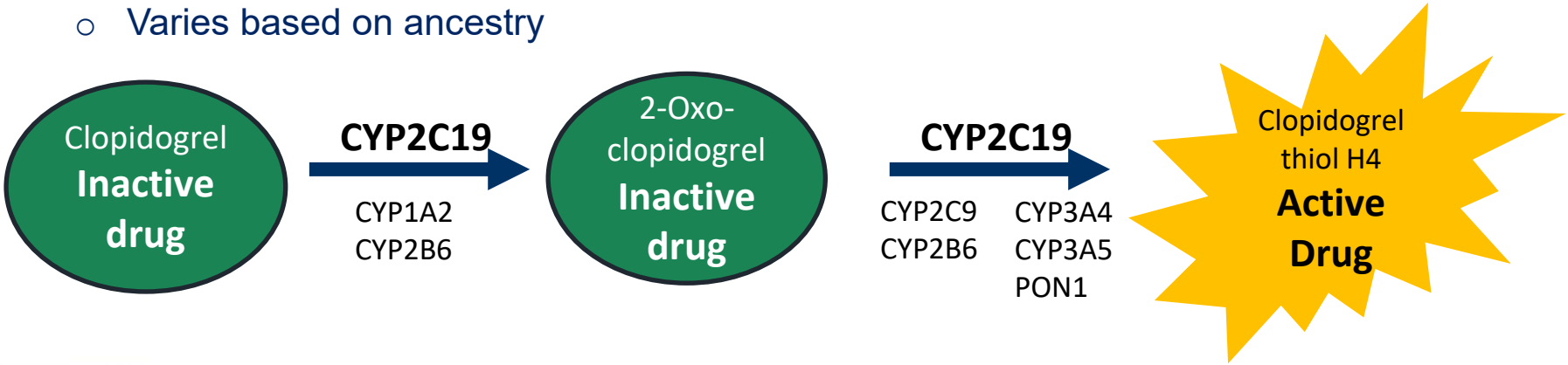
- Clopidogrel works by inhibiting platelet activation and aggregation
- However, 30-40% of patients experience high platelet reactivity (i.e., clopidogrel resistance)
- High platelet reactivity increases risk of clopidogrel failure
  - Example - Relative risk: 2.7 (95% CI: 2.03-3.89)

MedStar Health

Aradi D, *et al. Eur Heart J. 2015 Jul 14;36(27):1762-71*

CYP2C19 Genotype is Associated with Clopidogrel Response

- Clopidogrel is a prodrug
- *CYP2C19* genotype is associated with bioactivation of clopidogrel
- ~30% of patients have poor or intermediate CYP2C19 metabolism
  - Varies based on ancestry



MedStar Health

Sangkuhl K, *et. al.* 2010. PMID: 20440227.

Genotyping Terminology & Implications

CYP2C19 phenotype	Implications	Other Terminology in Literature	Therapeutic recommendation
Ultrarapid metabolizer **Rapid metabolizer**	• Normal or increased clopidogrel active metabolite formation • Normal or lower on-treatment platelet reactivity • No association with higher bleeding risk	CYP2C19 wild type or LOF non-carrier	Standard dose clopidogrel
Normal metabolizer	• Normal clopidogrel active metabolite formation • Normal on-treatment platelet reactivity		
Intermediate metabolizer **Poor metabolizer**	• Reduced clopidogrel active metabolite formation • Increased on-treatment platelet reactivity • Increased risk for ischemic events	Loss-of-function (LOF)carrier	**Avoid clopidogrel** if possible. Use prasugrel or ticagrelor at standard dose if no contraindication.

MedStar Health

Lee CR, *et al. Clin Pharmacol Ther.* 2022 Nov;112(5):959-967. PMID: 35034351.

Ancestry & *CYP2C19*

Phenotype	African-American/ Afro-Caribbean	American*	Central/ South Asian	East Asian	European	Latino	Near Eastern	Oceanian	Sub-Saharan African
Ultrarapid Metabolizer	4%	1%	3%	0%	5%	3%	4%	0%	3%
Rapid Metabolizer	24%	14%	19%	3%	27%	24%	26%	2%	21%
Normal Metabolizer	33%	63%	30%	38%	40%	52%	45%	4%	37%
Intermediate Metabolizer (IM)	**34%**	**21%**	**41%**	**46%**	**26%**	**19%**	**24%**	**37%**	**34%**
Poor Metabolizer (PM)	**5%**	**1%**	**8%**	**13%**	**2%**	**1%**	**2%**	**57%**	**5%**

Frequencies and biogeographical groups per PharmGKB

*Populations from both North and South America with ancestors predating European colonization, including American Indian, Alaska Native, First Nations, Inuit, and Métis in Canada, and Indigenous peoples of Central and South America.

High variant frequency across populations

MedStar Health

Lee CR, *et al. Clin Pharmacol Ther.* 2022 Nov;112(5):959-967. PMID: 35034351.

Summary: They recognize the role of CYP2C19 genotype but do not recommend routine testing

Guidelines and the FDA

FDA & Medical Society Perspectives

FDA

- Boxed warning to avoid clopidogrel in CYP2C19 poor metabolizers
- FDA Table of PGx: Consider alternative therapy in poor & intermediate metabolizers
- Does not comment on whether or not to test

AHA/ACC

- June, 2024: Published an updated scientific statement
- "Evidence to date supports *CYP2C19* genetic testing before oral P2Y12 inhibitors are prescribed"

CPIC

- Provides therapy recommendations based on CYP2C19
  - Consider alternative therapy in poor & intermediate metabolizers
- Does not comment on whether or not to test

FDA: Food and Drug Administration
AHA/ACC American Heart Association and American Colleges of Cardiology
CPIC: Clinical Pharmacogenetics Implementation Consortium

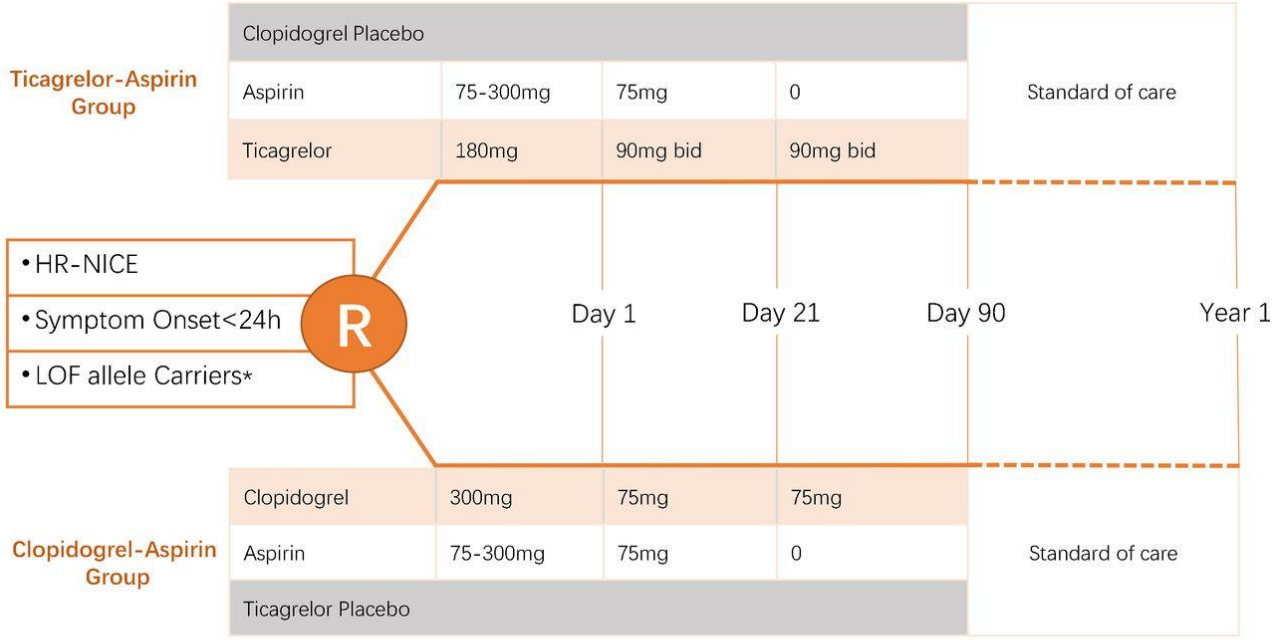
Pereira, *et al. Circulation.* 2024. PMID: 38899464
Lee, *et al. Clin Pharm Ther.* 2022. PMID: 35034351

MedStar Health

Recent evidence - Stroke and Transient Ischemic Attack (TIA):
The CHANCE-2 Trial

Landmark Trial: CHANCE-2

- **Population**:
  - Patient with minor stroke or transient ischemic attack (TIA)
  - All had CYP2C19 intermediate or poor metabolism
- **Design**:
  - Randomized, double-blind, placebo-controlled trial at 202 centers in China
  - Randomized 6412 patients



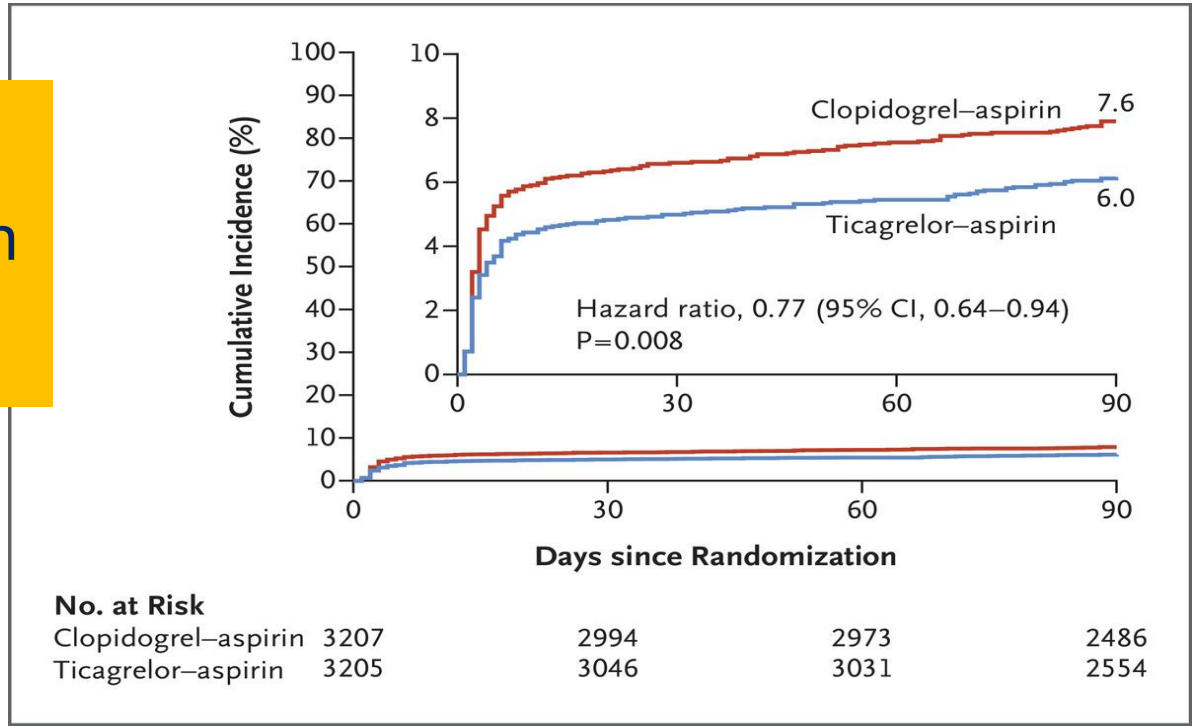
* Screen three common *CYP2C19* genotype variants (*2, *3, *17)
LOF allele Carriers indicate those with intermediate metabolizers (*1/*2 or *1/*3) and poor metabolizers (*2/*2, *3/*3 or *2/*3)

MedStar Health

Y Wang *et al. N Engl J Med* 2021. PMID: 34708996

CHANCE-2 Primary Endpoint: Secondary Stroke within 90 Days

Among CYP2C19 LOF-carriers, stroke was more common in patients treated with clopidogrel



MedStar Health

Y Wang *et al. N Engl J Med* 2021. PMID: 34708996

CHANCE-2 Secondary Endpoints

- Turnaround time is critical
  - Trial returned results in 80 minutes for >95% of patients
  - Used point-of-care testing (machine not available in US)
  - Results then informed antiplatelet therapy decision
- Bleeding
  - Similar risk of severe or moderate bleeding (0.3% vs 0.3%)
  - Ticagrelor has a higher risk of minor bleeding (5.3% vs 2.5%)

MedStar Health

IM/PMs: intermediate or poor metabolizers

Y Wang *et al. N Engl J Med* 2021. PMID: 34708996

Why not use ticagrelor for all?

Safety

- Higher risk of minor bleeding

Adherence

- Twice daily dosing → patients more likely to miss doses

Cost

- More expensive for the patient

MedStar Health

Can We Implement Like The CHANCE-2 Trial?

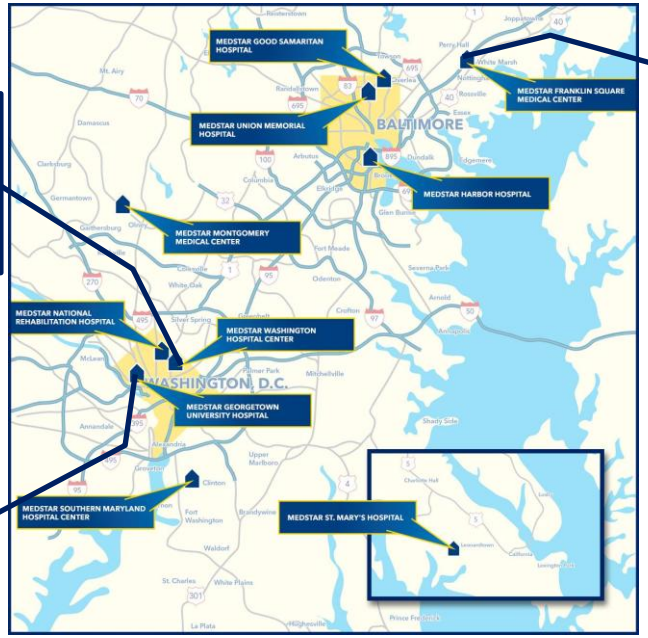
MSH Stroke Initiative: System Level Program

MWHC

- Expected Volume: 250/year
- Dir. Stroke Program: Amie Hsia, MD
- Lab Dir: Marie Wanys
- Dir. Of Pathology: Patricia Tsang, MD
- Stroke Coord.: Karen (Moriarty) Poole

MGUH

- Expected Volume: 225/year
- Dir. Stroke Prog.: Andrew Stemer, MD
- Lab Dir: Devin Lockard
- Dir. Of Pathology: Jay Zeck, MD
- Stroke Coord.: Kelsey Dawson, RN



MFSMC

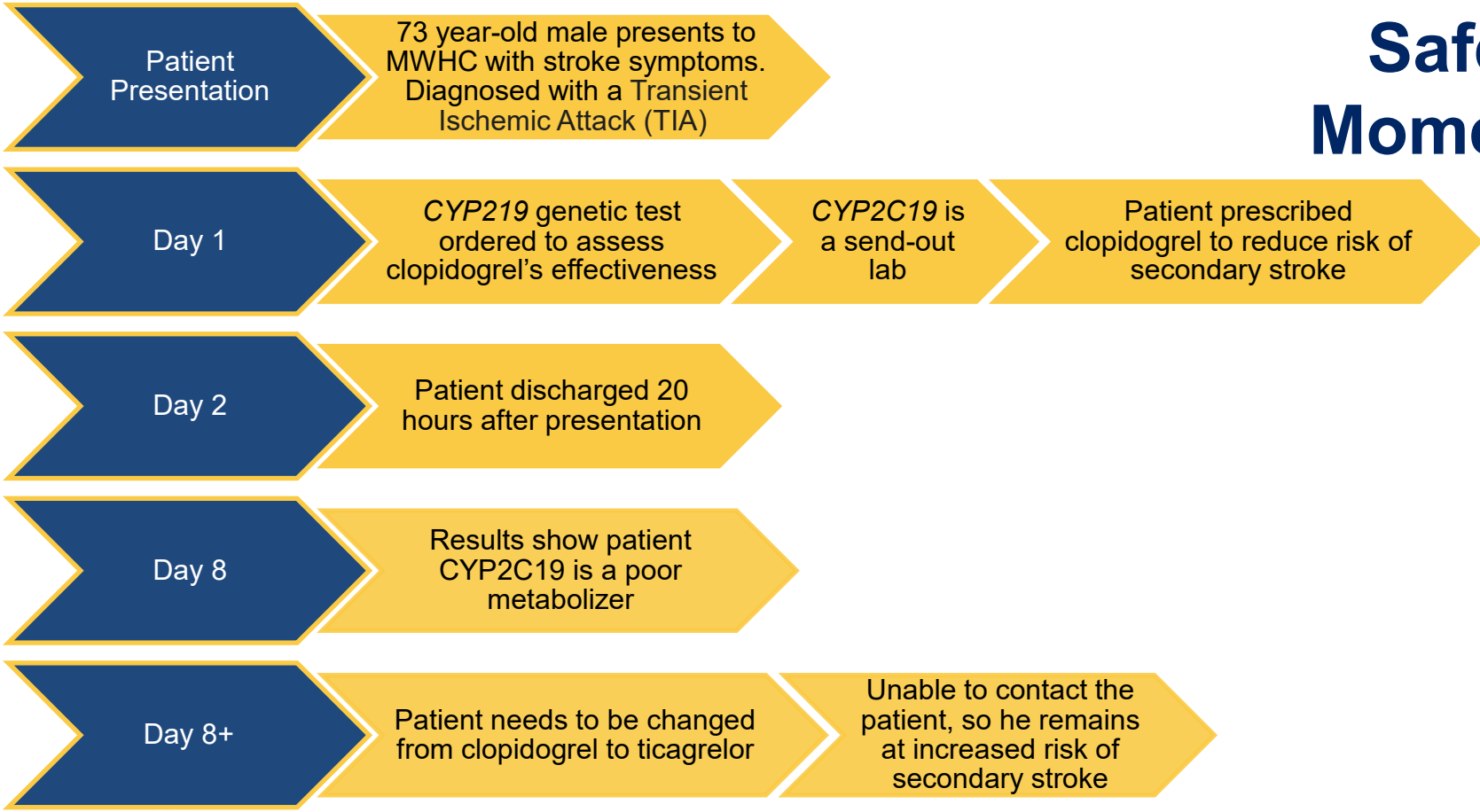
- Expected Volume: 250/year
- Dir. Stroke Program: Paul Singh, MD
- Lab Dir: Adi Nkwonta
- Dir. Of Pathology: Jennifer Brousard, MD
- Stroke Coord.: Ariel Woodward BSN, RN

Steering Team & Roles

- **PGx Program Dir.** Max Smith, PharmD & Sandra Swain, MD
- **Lab Coord.:** Justin Reuter
- **Pathology Coord.:** Moira Larsen, MD
- **Neurology Council:** Carlo Tornatore, MD
- **Project Manager:** Rhajni Gooden

MedStar Health

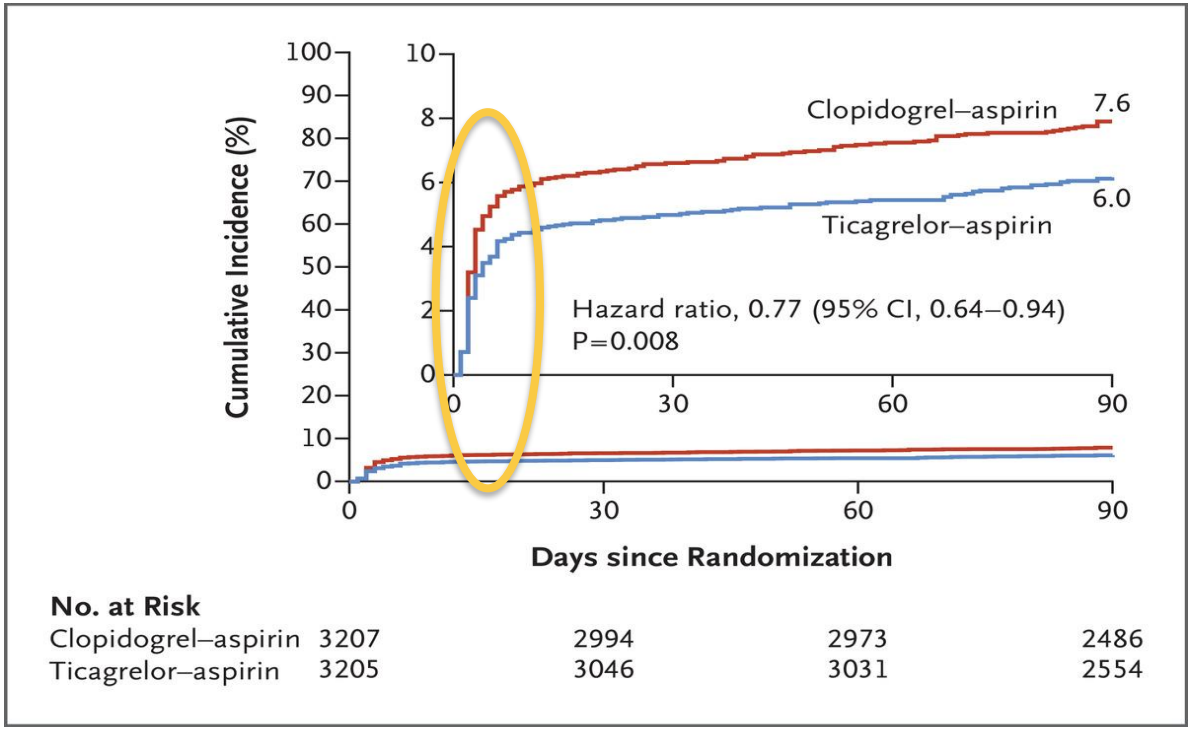
Safety Moment



MedStar Health

Can We Implement like the CHANCE-2 Trial?

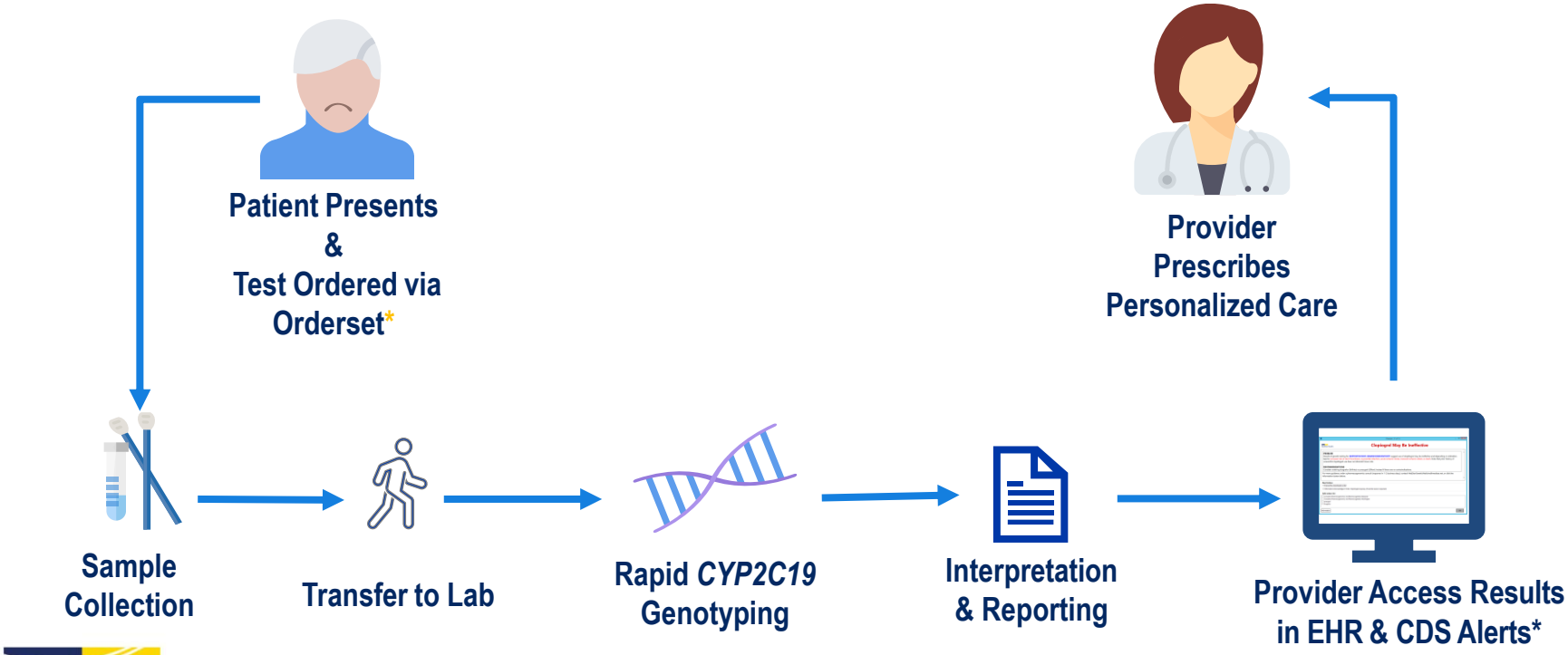
- Window for benefit may be early
- Implementation efforts stalled in 2022
- Rapid assay became available in 2023



MedStar Health

Y Wang *et al. N Engl J Med* 2021. PMID: 34708996

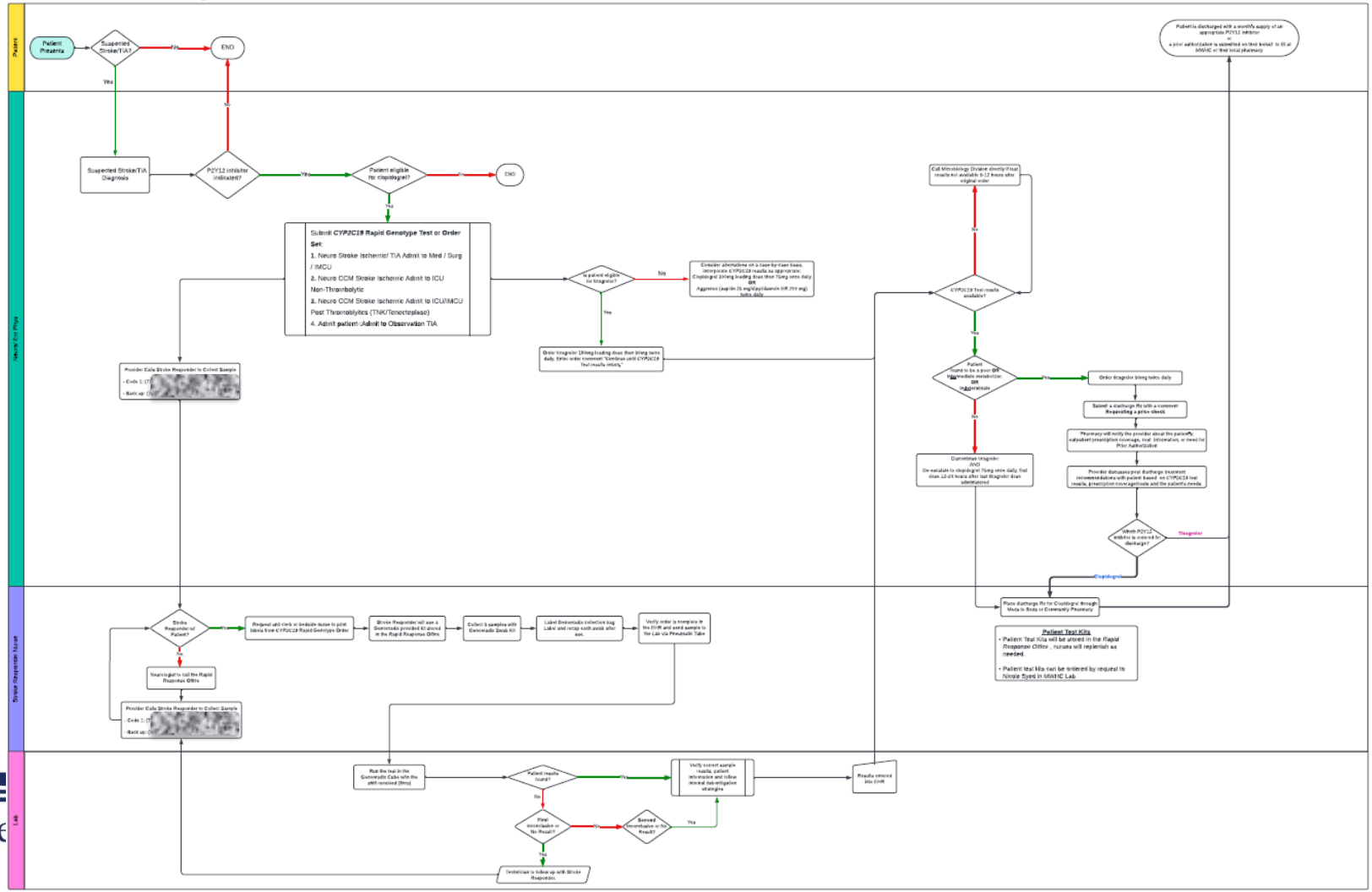
General Workflow (~ 8-12 hours)



MedStar Health

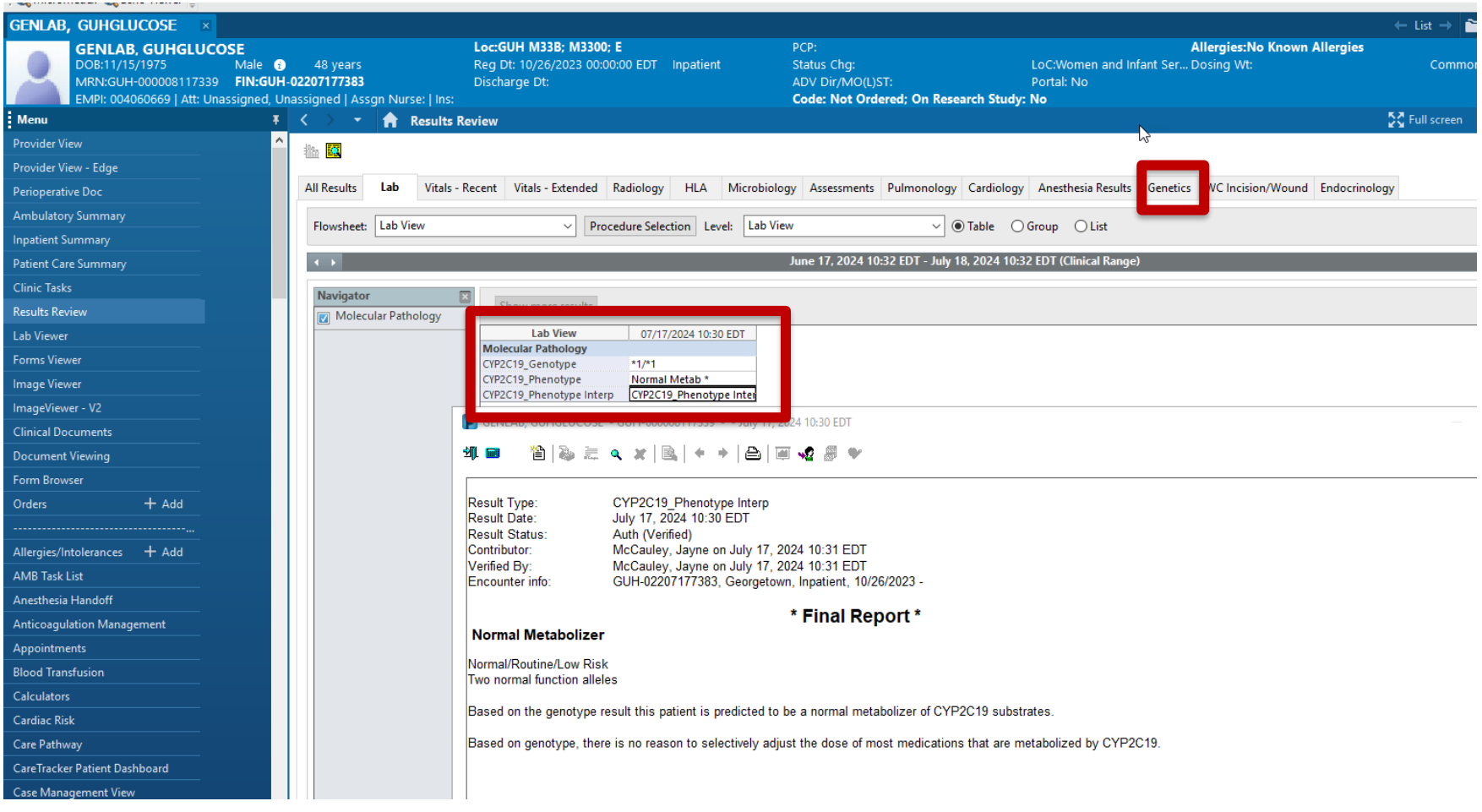
*First dose ticagrelor for all patients while the test is pending

MWHC *CYP2C19* Testing: Basic Workflow

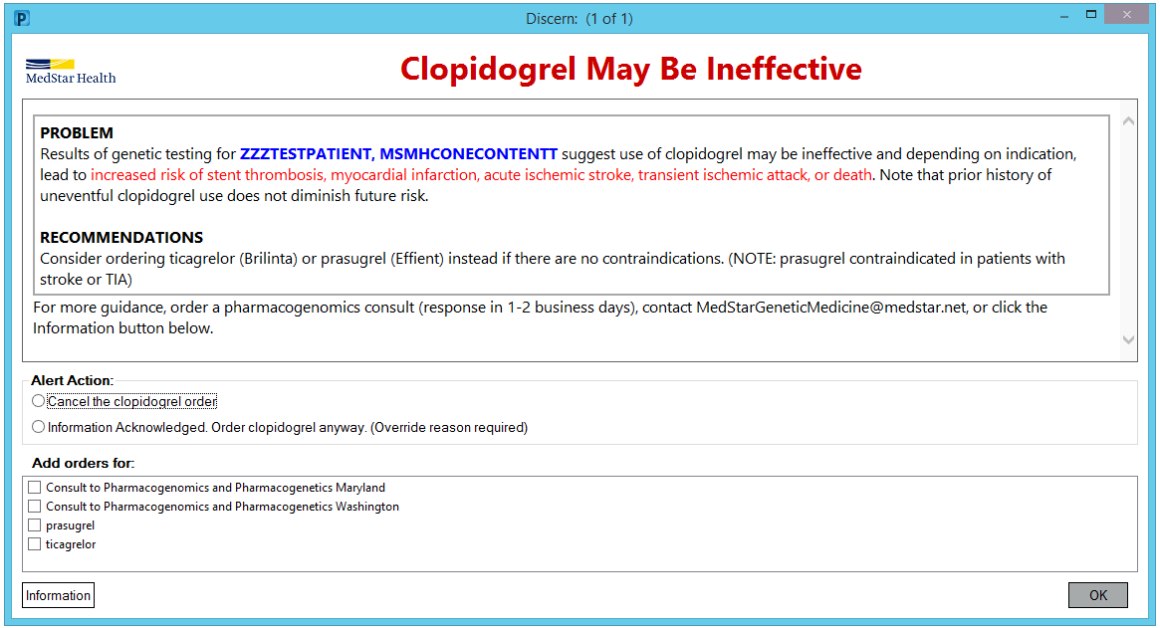


Interdisciplinary Team

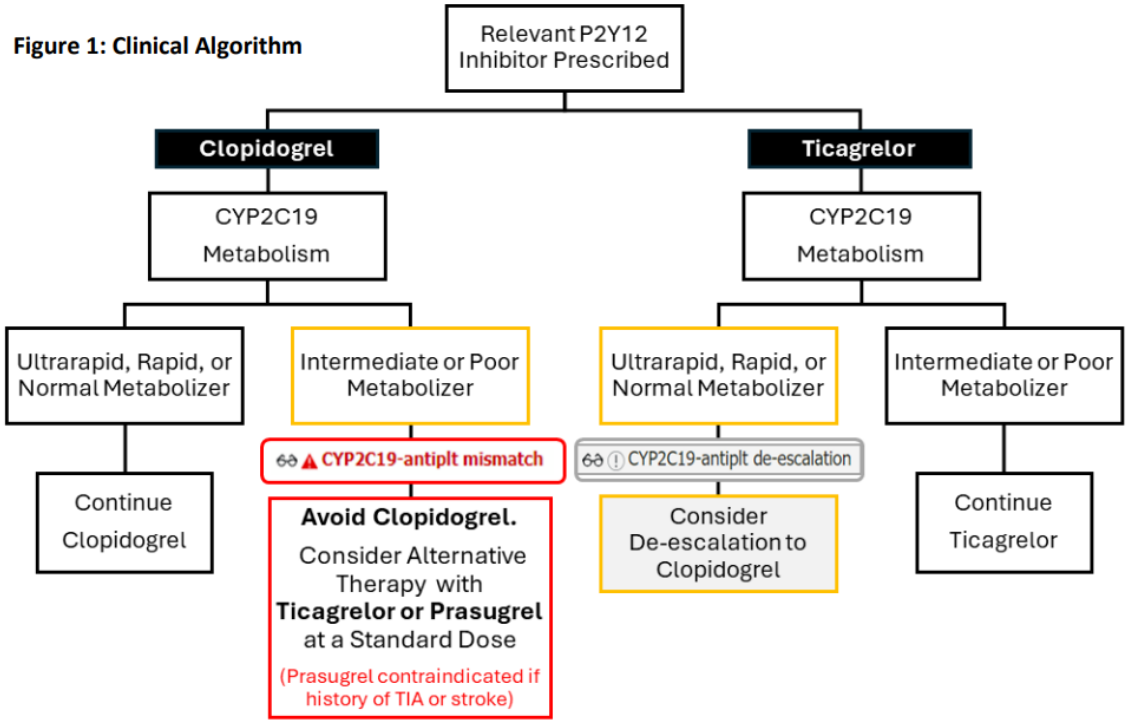
Physicians	Stroke Responders (nurses)	Lab personnel	Pharmacists
• Order test • React to results	• Collect the sample	• Run the test	• Second layer of support


GENLAB, GUHGLUCOSE
GENLAB, GUHGLUCOSE
DOB:11/15/1975 Male 48 years
MRN:GUH-000008117339 FIN:GUH-02207177383
EMPI: 004060669 | Att: Unassigned, Unassigned | Assgn Nurse: | Ins:
Loc:GUH M33B; M3300; E
Reg Dt: 10/26/2023 00:00:00 EDT Inpatient
Discharge Dt:
PCP:
Status Chg:
ADV Dir/MO(L)ST:
Allergies:No Known Allergies
LoC:Women and Infant Ser... Dosing Wt:
Portal: No
Code: Not Ordered; On Research Study: No
Menu
Provider View
Provider View - Edge
Perioperative Doc
Ambulatory Summary
Inpatient Summary
Patient Care Summary
Clinic Tasks
Results Review
Lab Viewer
Forms Viewer
Image Viewer
ImageViewer - V2
Clinical Documents
Document Viewing
Form Browser
Orders Add
Allergies/Intolerances Add
AMB Task List
Anesthesia Handoff
Anticoagulation Management
Appointments
Blood Transfusion
Calculators
Cardiac Risk
Care Pathway
CareTracker Patient Dashboard
Case Management View
Results Review
Full screen
All Results
Lab
Vitals - Recent
Vitals - Extended
Radiology
HLA
Microbiology
Assessments
Pulmonology
Cardiology
Anesthesia Results
Genetics
VC Incision/Wound
Endocrinology
Flowsheet: Lab View
Procedure Selection
Level: Lab View
Table
Group
List
June 17, 2024 10:32 EDT - July 18, 2024 10:32 EDT (Clinical Range)
Navigator
Molecular Pathology
Lab View 07/17/2024 10:30 EDT
Molecular Pathology
CYP2C19_Genotype *1/*1
CYP2C19_Phenotype Normal Metab *
CYP2C19_Phenotype Interp CYP2C19_Phenotype Inter
Result Type: CYP2C19_Phenotype Interp
Result Date: July 17, 2024 10:30 EDT
Result Status: Auth (Verified)
Contributor: McCauley, Jayne on July 17, 2024 10:31 EDT
Verified By: McCauley, Jayne on July 17, 2024 10:31 EDT
Encounter info: GUH-02207177383, Georgetown, Inpatient, 10/26/2023 -
* Final Report *
Normal Metabolizer
Normal/Routine/Low Risk
Two normal function alleles
Based on the genotype result this patient is predicted to be a normal metabolizer of CYP2C19 substrates.
Based on genotype, there is no reason to selectively adjust the dose of most medications that are metabolized by CYP2C19.

If an Order is Placed for Clopidogrel in a CYP2C19 Poor or Intermediate Metabolizer:



Pharmacist Clinical Surveillance Alerts



MedStar Health

Initial Experiences with Stroke & TIA

Through 6/30/2025

Sites [Start Date]	Tests Ordered per Week	Tests Completed	Turnaround Time Order to Results (Median, 25th, 75th percentile)	CYP2C19 IM/PMs	Prescribing aligned with PGx Results[1]
MGUH [Aug '24]	4.9	203	6.6 (4.1, 12) hrs	63 (31%)	93%
MFSMC [Dec '24]	4.9	123	6.1 (3.3, 17) hrs	46 (37%)	89%
MWHC [Mar '25]	3.0	42	4.4 (2.9, 7.6) hrs	18 (43%)	94%
Overall	**4.6**	**368**	**6.1 (3.6, 12) hrs**	**131 (35%)**	**92%**

N/A: Data not yet available.

[1]Analysis ongoing. Current data include those with CYP2C19 results prescribed a P2Y12i at discharge (MFSMC: 66; MGUH: 74; MWHC: 16). CYP2C19 IM/PMs prescribed ticagrelor and other CYP2C19 results are prescribed clopidogrel.

Summary

- Clopidogrel use in CYP2C19 poor and intermediate metabolism is associated with increased ischemic events
- MedStar Health launched rapid *CYP2C19* genotyping at its comprehensive stroke centers
- An engaged interdisciplinary team was critical to successful implementation

MedStar Health

MedStar Health: Rapid CYP2C19 Genotype

Why do I need a Rapid CYP2C19 Genotype test?

- Clopidogrel (Plavix) is widely used in the treatment of stroke, acute coronary syndrome, and other conditions characterized by a high risk of ischemic events. However, CYP2C19 is necessary to bioactivate clopidogrel and clopidogrel's effectiveness can vary significantly among individuals due to genetic differences in the CYP2C19 metabolism of clopidogrel.
- The in-house Genomadix Cube CYP2C19 System detects three alleles (*2, *3, and *17) using three buccal swabs, which is used to determine the phenotype of a patient.

Who is the target population for testing?

- Patients who may start clopidogrel
  - For example, patients presenting with ischemic stroke, transient ischemic attack (TIA), acu coronary syndrome (ACS), or undergoing a percutaneous coronary intervention (PCI)
- Patients with a complex history of medication response or current clopidogrel therapy is ineffective

When do I order a test?

- Before initiating clopidogrel therapy: to improve treatment outcomes by preventing unnecessary drug exposure to ineffective therapy and reducing the risk of complications
- In patients already on clopidogrel therapy: to reassess the need for alternative therapy to prevent treatment failure and identify risk of complications

How do I order a test?

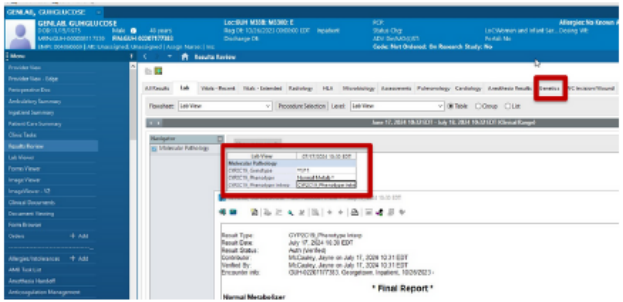
1. Search for the "CYP2C19 Rapid Genotype" order or select it from a relevant order set
2. Typical turnaround time: within 12 hours

How is the sample collected?

- The test requires 3 test-specific buccal swabs. At MFSMC, ED nurses have been trained to collect these samples. To obtain the unique buccal swabs needed for this test, call lab: [redacted]
- An example of the collection method can be found in the first minute of the following video:
  - https://www.youtube.com/watch?v=_n5t9TmksLw

Where can I find the test results?

Results are located in the Genetics tab, within Results Review.



What do I do with the test results?

CYP2C19 Result	Preferred P2Y12 Inhibitor
Ultrarapid Metabolism	Clopidogrel (Plavix)
Rapid Metabolism	Clopidogrel (Plavix)
Normal Metabolism	Clopidogrel (Plavix)
Intermediate Metabolism	Ticagrelor (Brilinta)
Poor Metabolism	Ticagrelor (Brilinta)
Unknown or indeterminate	Ticagrelor (Brilinta)

For additional support call pharmacy, place an order for a PGx Consult, or refer to CPIC guidelines.

References

1. Lee CR, et. al. Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2C19 Genotype and Clopidogrel Therapy: 2022 Update. *Clin Pharmacol Ther*. 2022;112(5):959-967. PMID: 35034351.
2. Wang Y, et. al. Ticagrelor versus Clopidogrel in CYP2C19 Loss-of-Function Carriers with Stroke or TIA. *N Engl J Med*. 2021;385(27):2520-2530. PMID: 34708996.

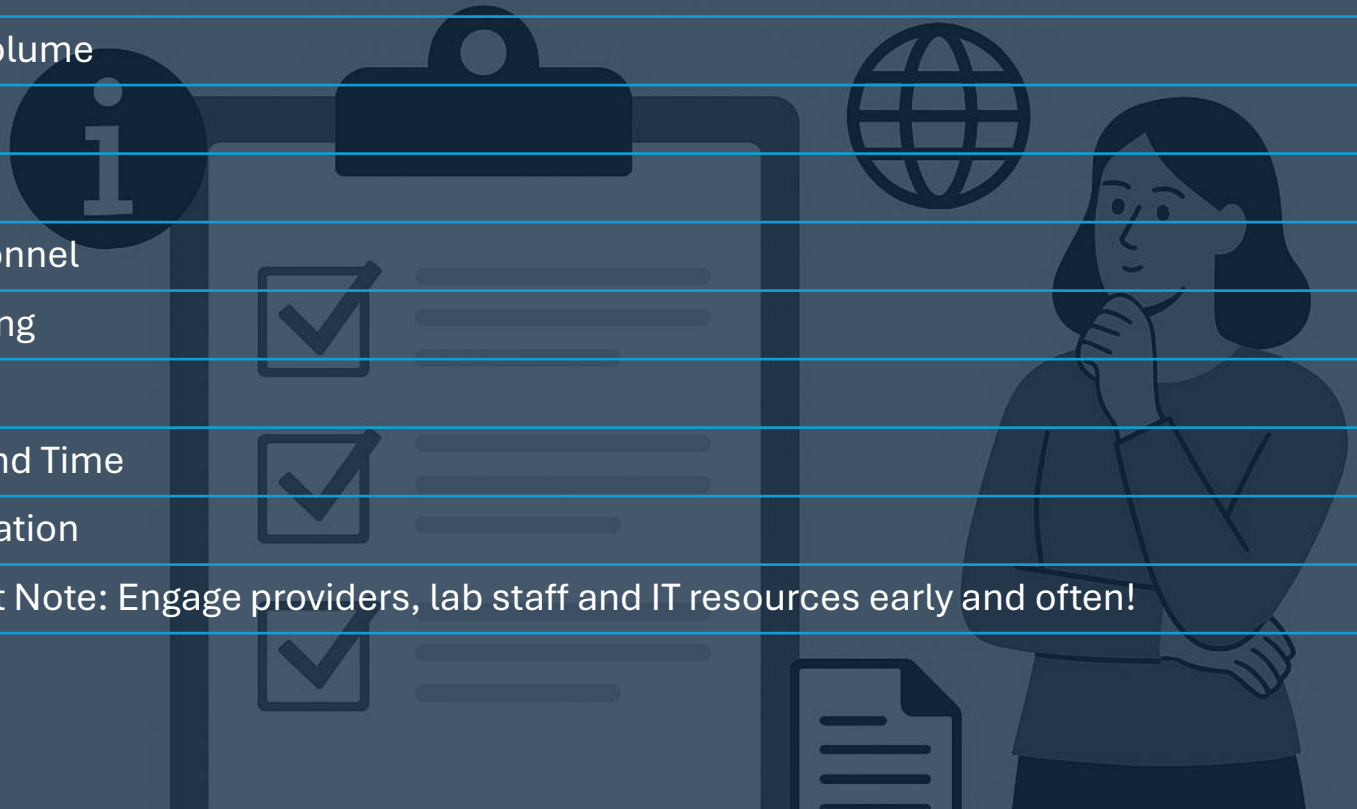
Precision Medicine Integration

Pharmacogenomic testing integration enhances personalized treatment decisions and improves overall survival rates

Laboratory Implementation

Strategic Considerations

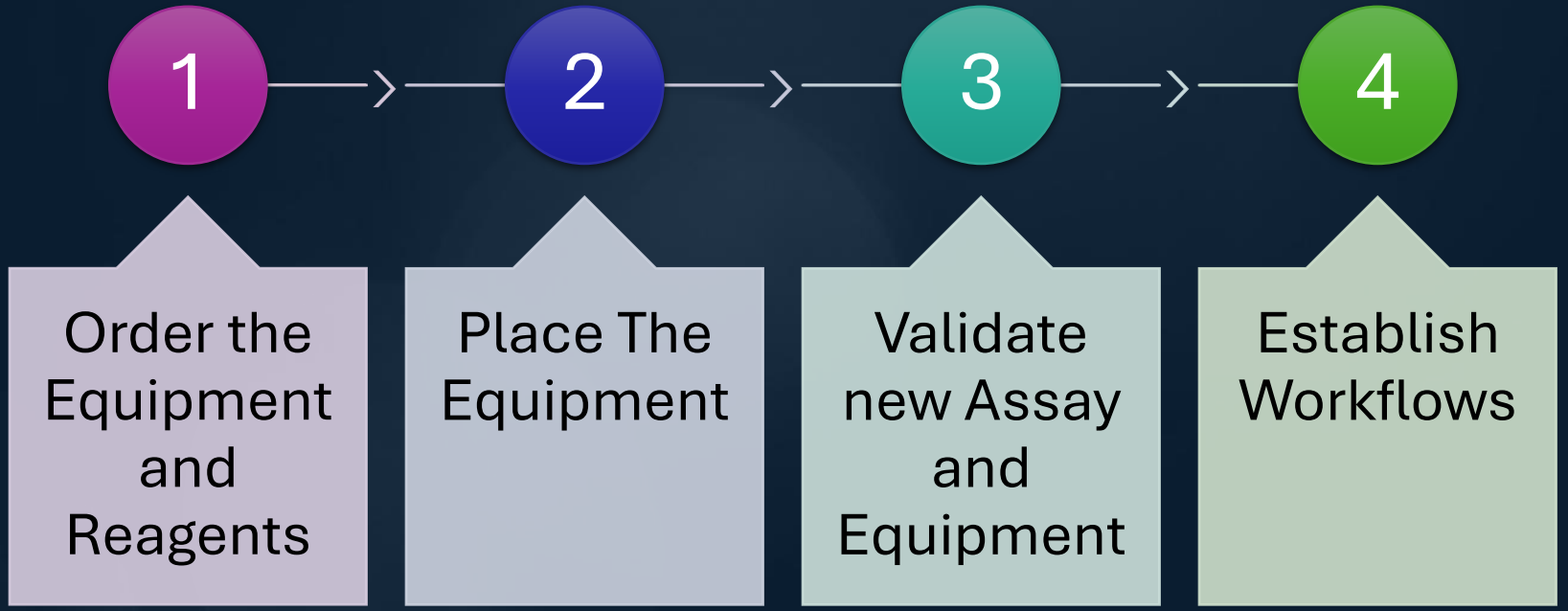
Do your due diligence



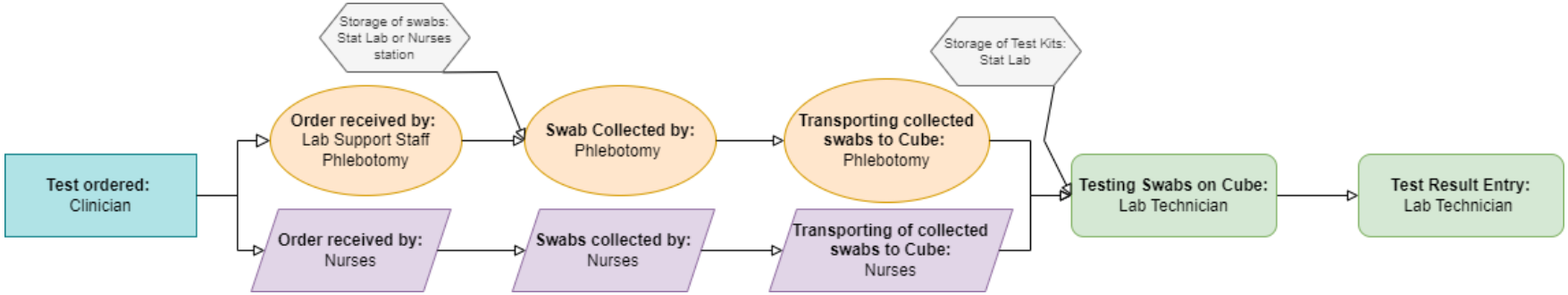
- Testing Volume
- Space
- FDA/LDT
- Lab Personnel
- Cost/Billing
- Workflow
- Turnaround Time
- LIS integration

Important Note: Engage providers, lab staff and IT resources early and often!

Decision to Deployment



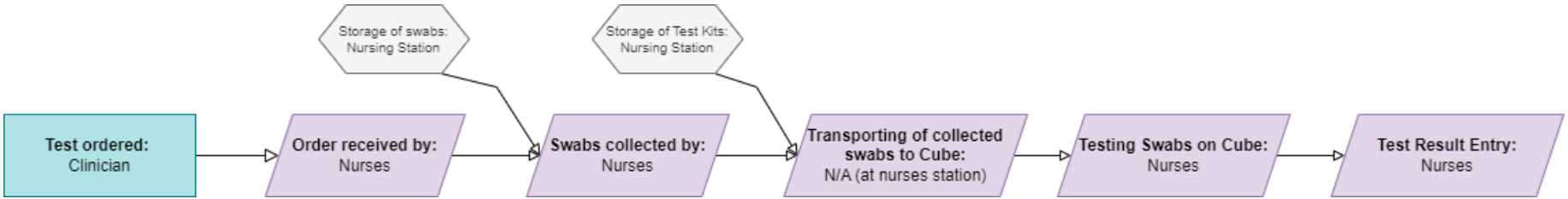
Implementation: Case Study 1



	Run By	Overseen By
CAP Accreditation	Lab Technician	Lab Management
Quality Controls	Lab Technician	Lab Management
Proficiency Testing	Lab Technician	Lab Management
Training Management	Lab Management	Lab Management
	Nurses/Phlebotomy	

Minimum Personnel Requirements	Test Offered (hrs/days)		
	24/7	12/5	12/7
Nurses/Phlebotomy	3	2	3
Lab Management	3	2	3

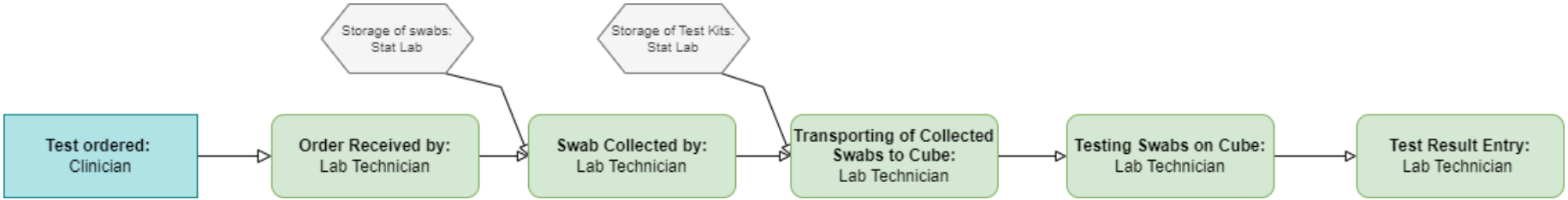
Implementation: Case Study 2



	Run By	Overseen By
CAP Accreditation	Lab Management	Lab Management
Quality Controls	Nurses	Lab Management
Proficiency Testing	Lab Management	Lab Management
Training Management	Nurse Management	Lab Management

Minimum Personnel Requirements	Test Offered (hrs/days)		
	24/7	12/5	12/7
Nurses	3	2	3

Implementation: Case Study 3



	Run By	Overseen By
CAP Accreditation	Lab Technician	Lab Management
Quality Controls	Lab Technician	Lab Management
Proficiency Testing	Lab Technician	Lab Management
Training	Lab	Lab

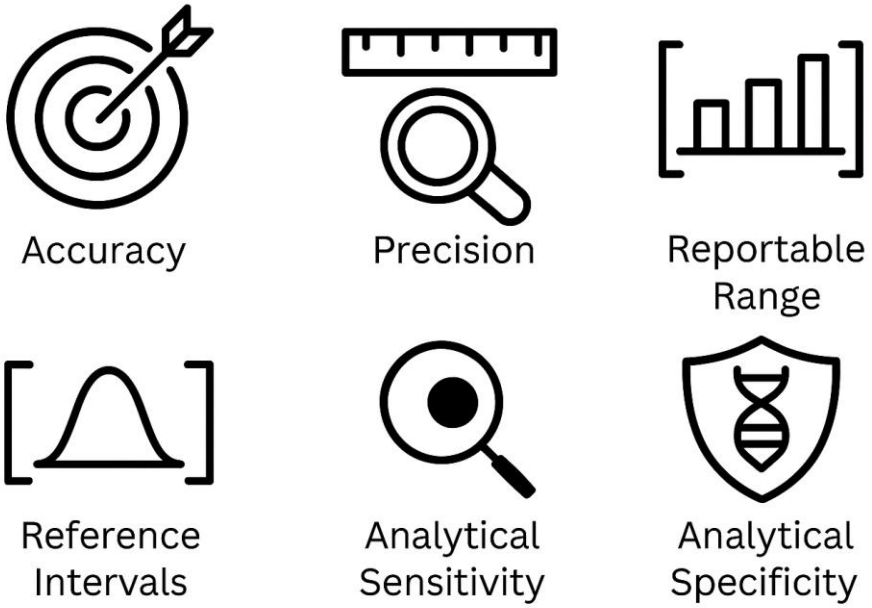
Minimum Personnel Requirements	Test Offered (hrs/days)		
	24/7	12/5	12/7
Lab Staff	3	2	3

Perform CAP-Compliant Test Validation

COLLEGE of AMERICAN PATHOLOGISTS

Laboratories are required to perform analytical validation of each assay, method, or instrument system before use in patient testing

6 Required Components:



Creating the SOP:
Turning Strategy into Standard Practice

Sample Handling

List all required reagents, equipment and software

Step-by-step instructions for performing the tasks

Quality Control and Assurance

Safety and Precautions

Documentation and Records

Troubleshooting Steps

The Lab Is Ready-Now Let's Operationalize

Define Workflows and Drive Education

How to Order?

- 📋 Paper Requisition
- 💻 Electronic Order
- 🔁 Routing
- 📍 Tracking
- Insurance Coverage

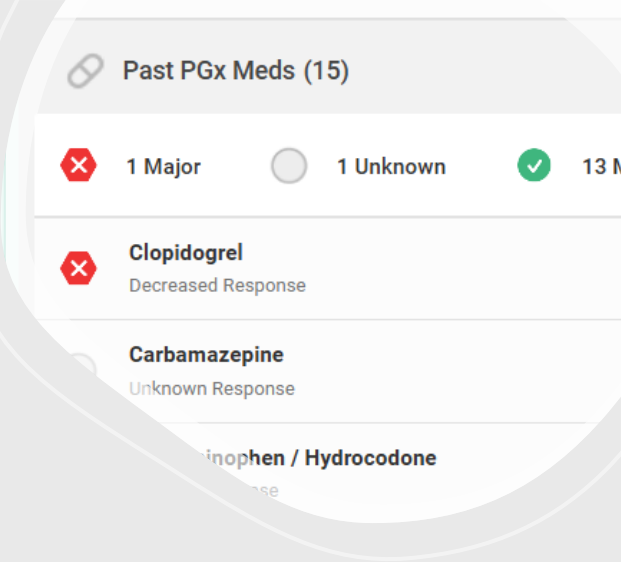
How to Collect?

- Swab
- 💉 Blood Draw
- 🫁 Sputum
- Tissue

Delivering PGx Insights Effectively

- Training and Education
- Access to Guidelines
- Clear Result Summaries
- Educational Materials
- Follow up and Care Coordination
- Audit Trails
- Regulatory alignment
- Consent and Communication
- HIPAA-Compliant Data Handling

POLYPHARMACY PGX RIS



More Than Just a Lab Value

- 🧬 Genomic Data Integration
- 💻 Decision Support Tools
- 📊 Outcome Tracking and Collaboration

Quality and Lab Stewardship

Regular quality audits and staff training ensure ongoing stewardship and alignment with patient care needs.

- Negative Controls
- Patient population frequency changes
- QNS rates
- Result acknowledgement
- Treatment changes

Key Takeaways

- Pharmacogenomic Testing Benefits
- Laboratory Implementation Considerations
- Clinical Workflow Alignment
- Personalized Medicine Impact

References

- *All images and icons used in this presentation were generated using Microsoft Copilot in PowerPoint. These visuals are license-free and safe for commercial use under Microsoft's Copilot Copyright Commitment.*
- *Source: Microsoft 365 Commercial License – AI-generated content via Copilot and Designer tools. No external or third-party copyrighted images were used.*

Thank you

- Amanda Hanson
  ahanson@srhs.com