Lab & Pharmacy: Turning Daily Interaction into a Partnership

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Objectives

Identify areas of healthcare where lab and pharmacy intersect

Learn how lab and pharmacy produce better outcomes together

Determine where lab and pharmacy collectively improve Population Health

Describe how Precision Medicine initiatives require both lab and pharmacy for success

Topic Outline

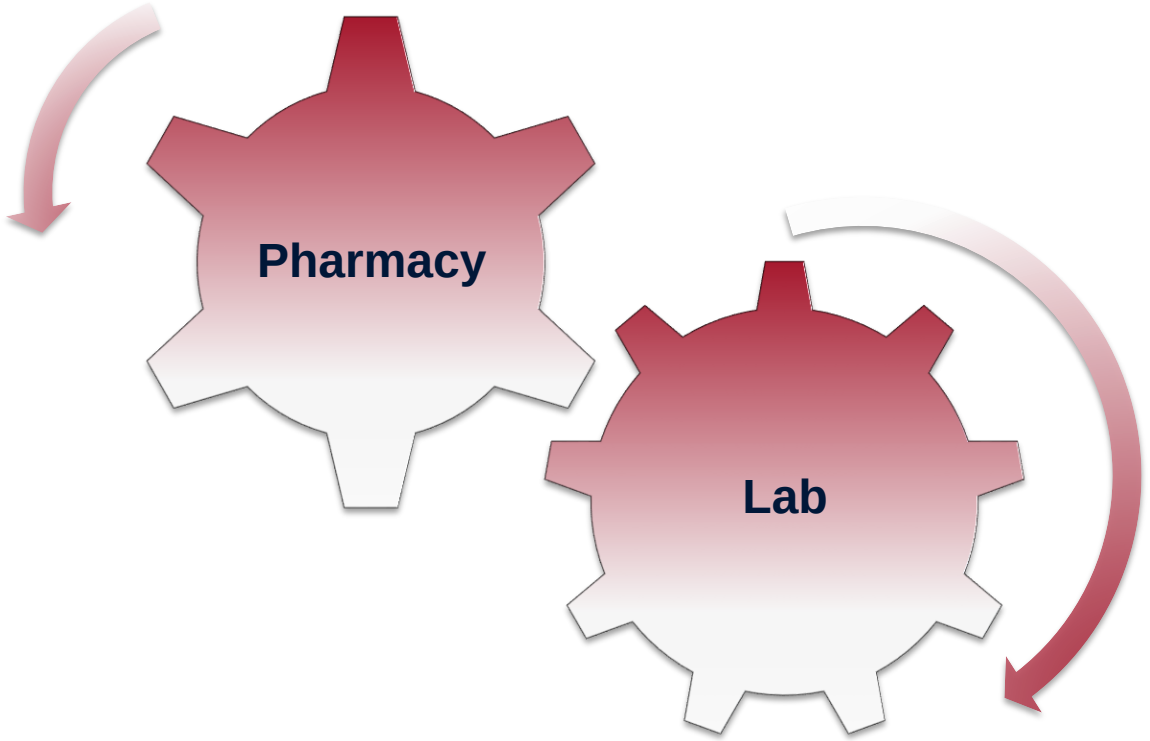
Make the **Link** Between Lab and Pharmacy

- Areas of Intersection
- Therapeutic Drug Monitoring & Sensitivity
- Lab/Pharmacy Budgets & Workflows

Next Level Initiatives

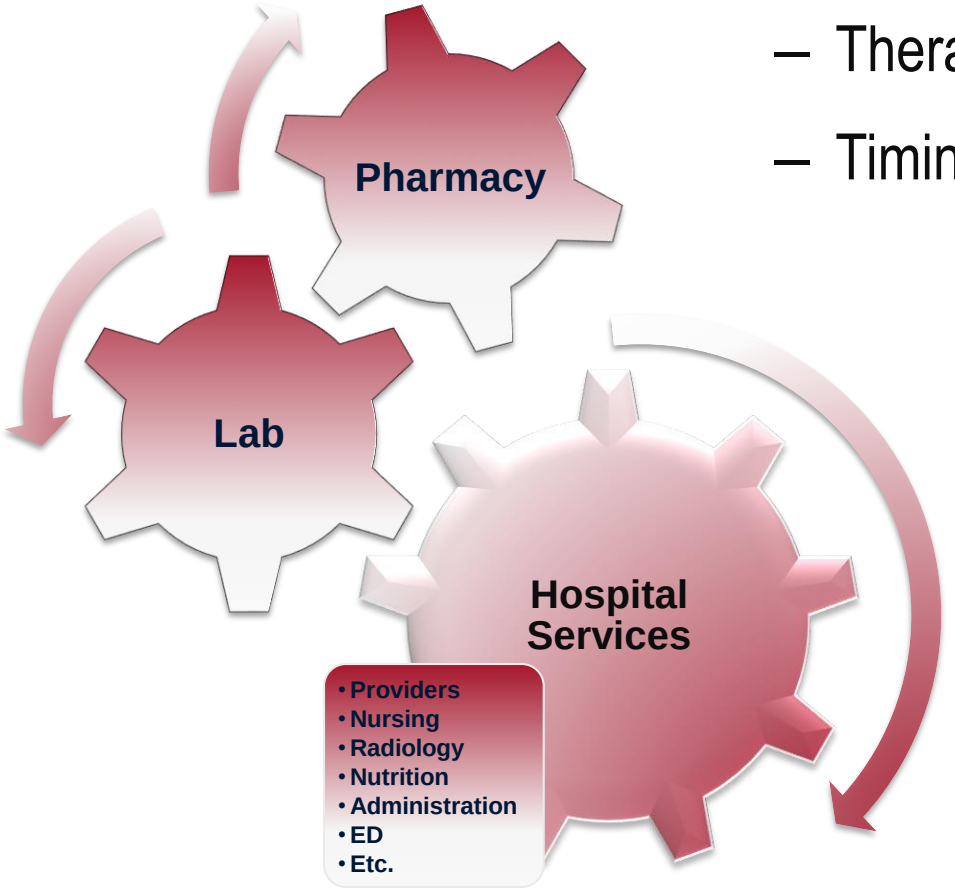
- Population Health
- Precision Medicine (Pharmacogenomics)

Main Focus



Link: Areas of Intersection

- **Pharmacy**
  - Drug choice
  - Therapeutic drug monitoring
  - Timing



- **Lab**
  - Culture and sensitivity results
  - Drug concentrations
  - Therapy response

Link: Therapeutic Drug Monitoring (TDM) & Sensitivity Tests

- Lab tests
  - Ensure therapeutic concentrations
  - Minimize toxicity and side effects
  - Determine adherence
  - Avoid drug interactions

- Better utilization and cost savings
  - Remicade (inFLIXimab): concentration and neutralizing antibodies
  - Gleevec (imatinib): drug concentration
  - NS5A inhibitor: sensitivity

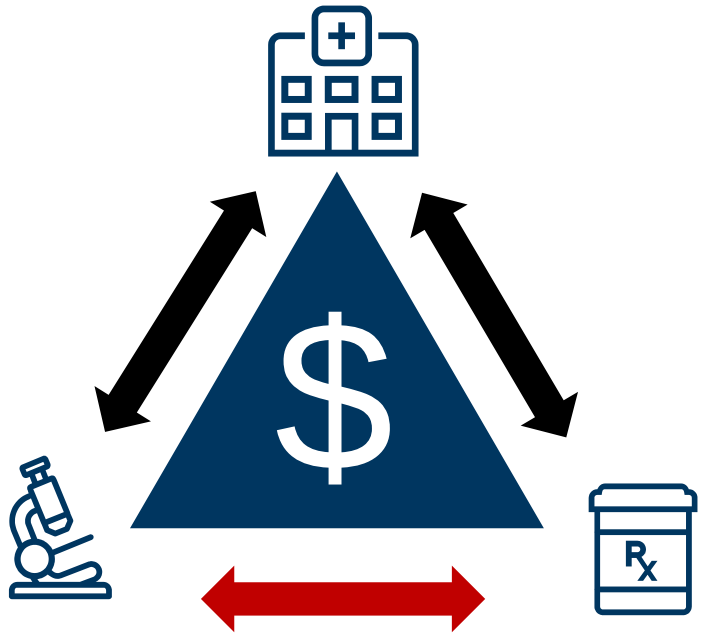
New addition: Precision Medicine
(*upcoming slides*)

Link: Budget Planning and Monitoring

Hospital

Composed of rolled up combined expenses

Hospital Combined Expense



Lab

Knows what tests are available internally or by reference labs

Lab Test Expense

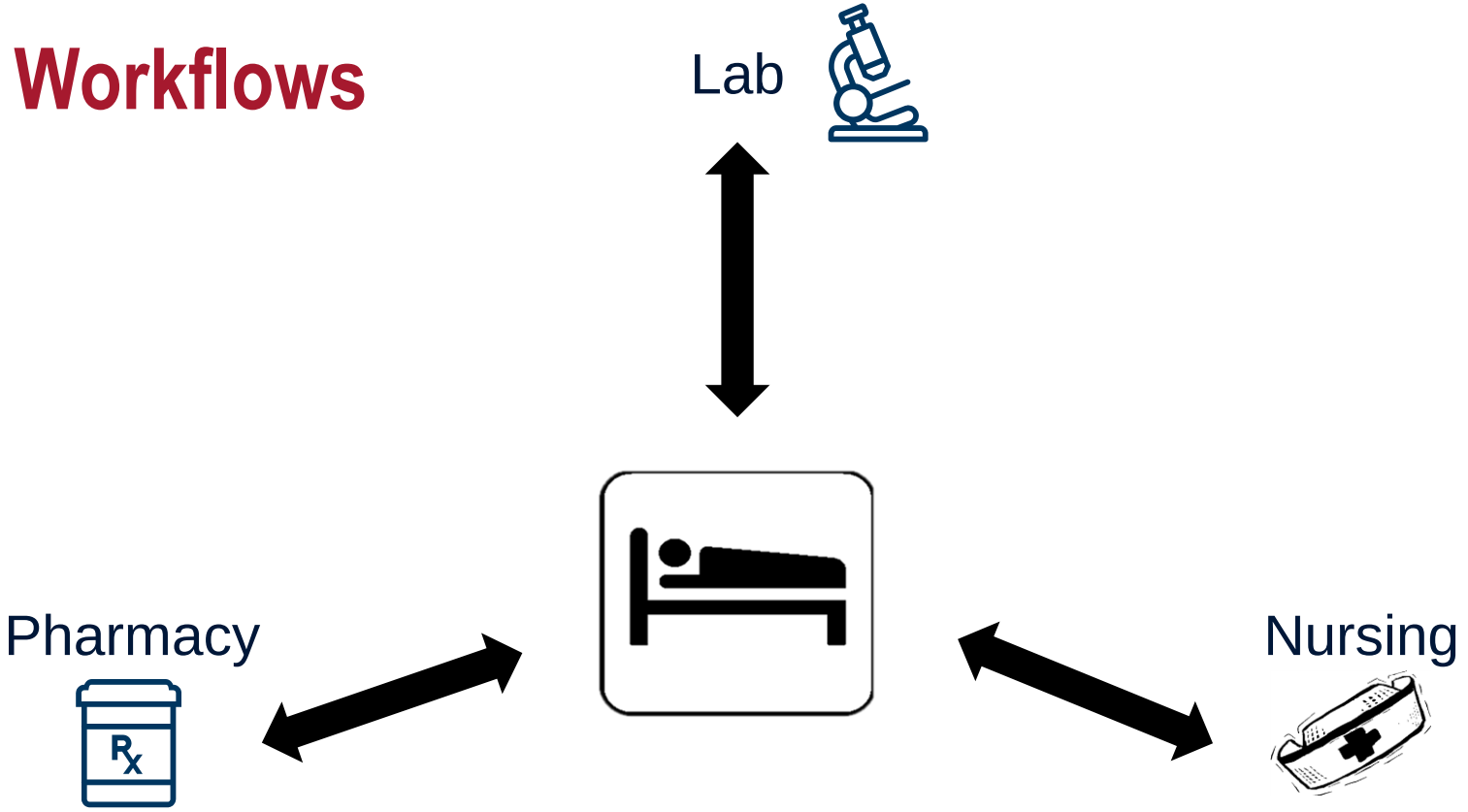
Pharmacy

Knows what drugs are being used throughout the hospital

Pharmacy Drug Expense

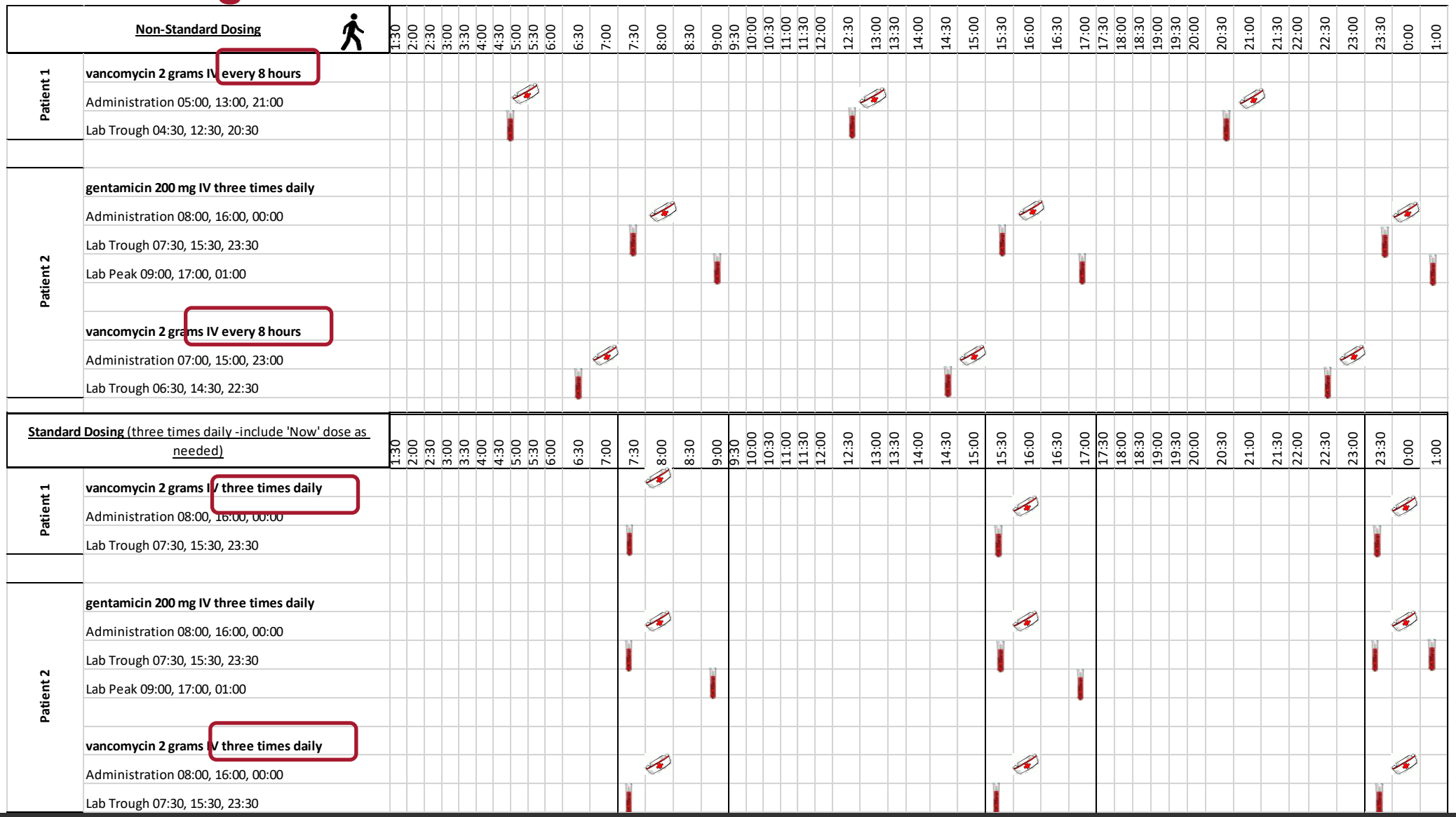
Both pharmacy and lab would benefit from the other's knowledge for better budget planning.

Link: Shared Workflows



- **Pharmacy**: ↓ Drug deliveries ↑ Time monitoring patients
- **Nursing**: ↓ Trips to the dispensing cabinet ↑ Time at the bedside
- **Lab**: ↓ Blood draws, collection, cultures ↑ Time in the lab running tests

Standard Drug Administration Times



Population Health & Precision Medicine

Next Level Initiatives

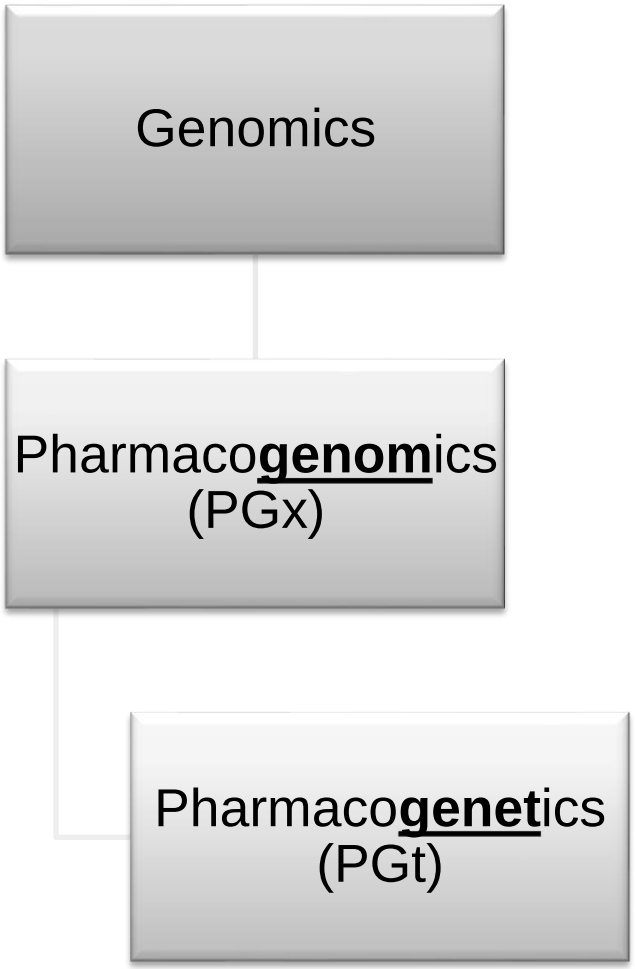
Population Health - Definition

- Landscape
  - Hospital Systems are becoming **increasingly responsible** for general health in their regions
- Definition
  - 'Population Health Management is … the actions through which care providers can improve both clinical and financial outcomes'. [1]
  - '…improve the health outcomes of a group by monitoring…individual patients within that group'. [1]
  - Involves: managing risk factors, monitoring drug side effects, increasing quality of life, providing preventative services

[1] https://www.usa.philips.com/healthcare/medical-specialties/population-health/what-is-population-health-management/

Precision Medicine - Definitions

- Precision Medicine
  - "treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person"[1]
  - Improve health outcomes of the community by customizing care for the individual
    - Target patient response to prescription drugs
    - Prevent adverse events and **readmissions** (i.e. *increase* care & *decrease* expense)



[1] https://ghr.nlm.nih.gov/primer/precisionmedicine/definition
[2] https://labsoftnews.typepad.com/lab_soft_news/2019/03/momentum-in-pharmacogenetics-including-direct-access-testing.html

Precision Medicine - Considerations

Personalized care

- One size (drug) does not fit all
- Patients want to be treated as individuals

Growing public awareness and focus

- Ancestry.com, 23andMe
- People are taking a greater role in their own healthcare

Improved care and budgets

- Cost savings for patients and healthcare entities
- Expand and enrich TDM and clinical monitoring

Enhanced stewardship initiatives

- Choose a therapeutic drug/dose combination more quickly
- Fewer therapy adjustments with reduced monitoring
- Minimizes toxicity and increases efficacy

Drug Metabolism

Traditional Dosing

- Based on average drug response in a population
- **Reality**: There is huge variability in metabolism and response
- **Risk**:
  - ~7 million **ED visits** per year due to adverse drug events (ADEs) at a cost of $3.5 billion

Sources of Variation

- Pharmacogenetics
  - *Poor metabolizers*
  - *Intermediate metabolizers*
  - *Normal metabolizers*
  - *Ultrarapid metabolizers*
- Concomitant drug therapy
- Environmental factors
- Disease states

https://www.cdc.gov/MedicationSafety/Adult_AdverseDrugEvents.html

Emperic Dosing vs. Precision Medicine

- Note: PGx testing should not replace TDM and clinical monitoring

Empiric (Standard) Dosing	Precision Medicine
• Takes longer to discover response • Starting with a low dose requires more time to become effective • A standard dose could be toxic	• Get the right drug & dose the first time • Less monitoring for subsequent doses • Precise dosing prevents ADEs

Patient Case

- Patient treated with Prilosec for heartburn has ongoing issues with headaches and nausea
- ***Lab Evaluation***: PGt test for CYP2C19 metabolism
  - Patient was found to be a poor metabolizer
- ***Pharmacy Assessment***: Drug assessment
  - Headache and nausea are side effects of Prilosec (proton pump inhibitor that treats heartburn)
  - Low drug inactivation caused higher-than-normal levels of drug in the system, producing adverse drug effects
- ***Solution***: Medication switched to an H2 Blocker (Pepcid) - not influenced by CYP2C19
- ***Result***: Headache and nausea issues were resolved and patient satisfaction increased

You'll never know some drugs are not working until they fail

Plavix (clopidogrel)

Antiplatelet medication

Prodrug activated by CYP2C19

- If it's not activated it's not working
- Approx. 30% poor metabolizers
- *Genetic testing: prevent adverse events and readmissions*

WARNING: DIMINISHED ANTIPLATELET EFFECT IN PATIENTS WITH TWO LOSS-OF-FUNCTION ALLELES OF THE *CYP2C19* GENE

- Effectiveness of Plavix depends on conversion to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19.
- Tests are available to identify patients who are CYP2C19 poor metabolizers.
- Consider use of another platelet P2Y12 inhibitor in patients identified as CYP2C19 poor metabolizers.

Plavix package insert, revised September 2016. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020839s072lbl.pdf
https://www.pharmgkb.org/chemical/PA450704/labelAnnotation/PA166104921

Plavix Package Insert

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PLAVIX safely and effectively. See full prescribing information for PLAVIX.

PLAVIX® (clopidogrel bisulfate) tablets, for oral use
Initial U.S. Approval: 1997

WARNING: DIMINISHED ANTIPLATELET EFFECT IN PATIENTS WITH TWO LOSS-OF-FUNCTION ALLELES OF THE CYP2C19 GENE

See full prescribing information for complete boxed warning.

- **Effectiveness of Plavix depends on conversion to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. (5.1, 12.3)**
- **Tests are available to identify patients who are CYP2C19 poor metabolizers. (12.5)**
- **Consider use of another platelet $P2Y_{12}$ inhibitor in patients identified as CYP2C19 poor metabolizers. (5.1)**

----------INDICATIONS AND USAGE----------

Plavix is a $P2Y_{12}$ platelet inhibitor indicated for:

- Acute coronary syndrome
  - For patients with non–ST-segment elevation ACS (unstable angina [UA]/non–ST-elevation myocardial infarction [NSTEMI]), Plavix has been shown to reduce the rate of myocardial infarction (MI) and stroke. (1.1)
  - For patients with ST-elevation myocardial infarction (STEMI), Plavix has been shown to reduce the rate of MI and stroke. (1.1)
- Recent MI, recent stroke, or established peripheral arterial disease. Plavix has been shown to reduce the rate of MI and stroke. (1.2)

----------DOSAGE AND ADMINISTRATION----------

- Acute coronary syndrome (2.1)
  - Initiate Plavix with a single 300 mg oral loading dose and then continue at 75 mg once daily.
  - Initiating Plavix without a loading dose will delay establishment of an antiplatelet effect by several days.
- Recent MI, recent stroke, or established peripheral arterial disease: 75 mg once daily orally without a loading dose. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

Tablets: 75 mg, 300 mg (3)

----------CONTRAINDICATIONS----------

- Active pathological bleeding, such as peptic ulcer or intracranial hemorrhage (4.1)
- Hypersensitivity to clopidogrel or any component of the product (4.2)

----------WARNINGS AND PRECAUTIONS----------

- CYP2C19 inhibitors: Avoid concomitant use of omeprazole or esomeprazole. (5.1)
- Bleeding: Plavix increases risk of bleeding. (5.2)
- Discontinuation: Premature discontinuation increases risk of cardiovascular events. Discontinue 5 days prior to elective surgery that has a major risk of bleeding. (5.3)
- Thrombotic thrombocytopenic purpura (TTP) has been reported. (5.4)
- Cross-reactivity among thienopyridines has been reported. (5.5)

----------ADVERSE REACTIONS----------

Bleeding, including life-threatening and fatal bleeding, is the most commonly reported adverse reaction. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership at 1-800-633-1610 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- Opioids: Decreased exposure to clopidogrel. Consider use of parenteral antiplatelet agent. (7.2)
- Nonsteroidal anti-inflammatory drugs (NSAIDs), warfarin, selective serotonin and serotonin norepinephrine reuptake inhibitors (SSRIs, SNRIs): Increases risk of bleeding. (7.3, 7.4, 7.5)
- Repaglinide (CYP2C8 substrates): Increases substrate plasma concentrations. (7.6)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Plavix package insert, revised September 2016.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020839s072lbl.pdf

Opioid Epidemic

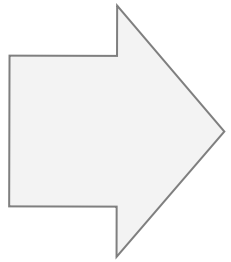
Problem:

Overdose deaths related to opioids *(data from the CDC[1])*:

1999 - 2017 > 700,000 people died from drug overdoses

68% of all overdose deaths in 2017 involved an opioid (6x greater than in 1999)

130 die each day from opioid overdoses



Collaboration is essential to combat this epidemic

- ***Lab***
  - test results tell what is being used in your population (umbilical cord, drug testing)
  - identifies PGx variants
- ***Pharmacy***
  - guides appropriate drug selection
  - evaluates PGx drug/dose adjustments

[1] https://www.cdc.gov/drugoverdose/epidemic/index.html. Accessed July 2019.

You may not know there is a problem until there is an overdose

Codeine sulfate

Opioid agonist – Schedule II Controlled Substance

CYP2D6 converts codeine to active morphine

- Too much activation leads to adverse events and overdose situations
- Approx. 5% ultra-rapid metabolizers
- *Genetic testing: prevent adverse events, emergency care, and admissions*

"WARNING: …DEATH RELATED TO ULTRA-RAPID METABOLISM OF CODEINE TO MORPHINE…

Life-threatening respiratory depression and death have occurred in children who received codeine;

…evidence of being an **ultra-rapid metabolizer** of codeine due to a CYP2D6 polymorphism…"

codeine package insert, revised September 2016
https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022402s010s011lbl.pdf

Patient Case

- Patient treated with codeine for mild pain tells their provider “My medication is not working. I still have pain.”
- ***Lab Evaluation***: PGt test for CYP2D6 metabolism
  - Patient was found to be a poor metabolizer
- ***Pharmacy Assessment***: Drug assessment
  - Low drug activation prevents adequate pain control
  - Tylenol (a non-opioid) is effective for mild pain and avoids using an unnecessary opioid
- ***Solution***: Medication switched to Tylenol
- ***Result***: Pain resolved and patient satisfaction increased

Antibiotic Stewardship Committee

Lab

- Identify PGx variants
- Perform culture and sensitivity tests
- Clarify viral vs. bacterial infection

Pharmacy

- Evaluate drug treatment
- Determine PGx drug choice

Antibiotics and PGt

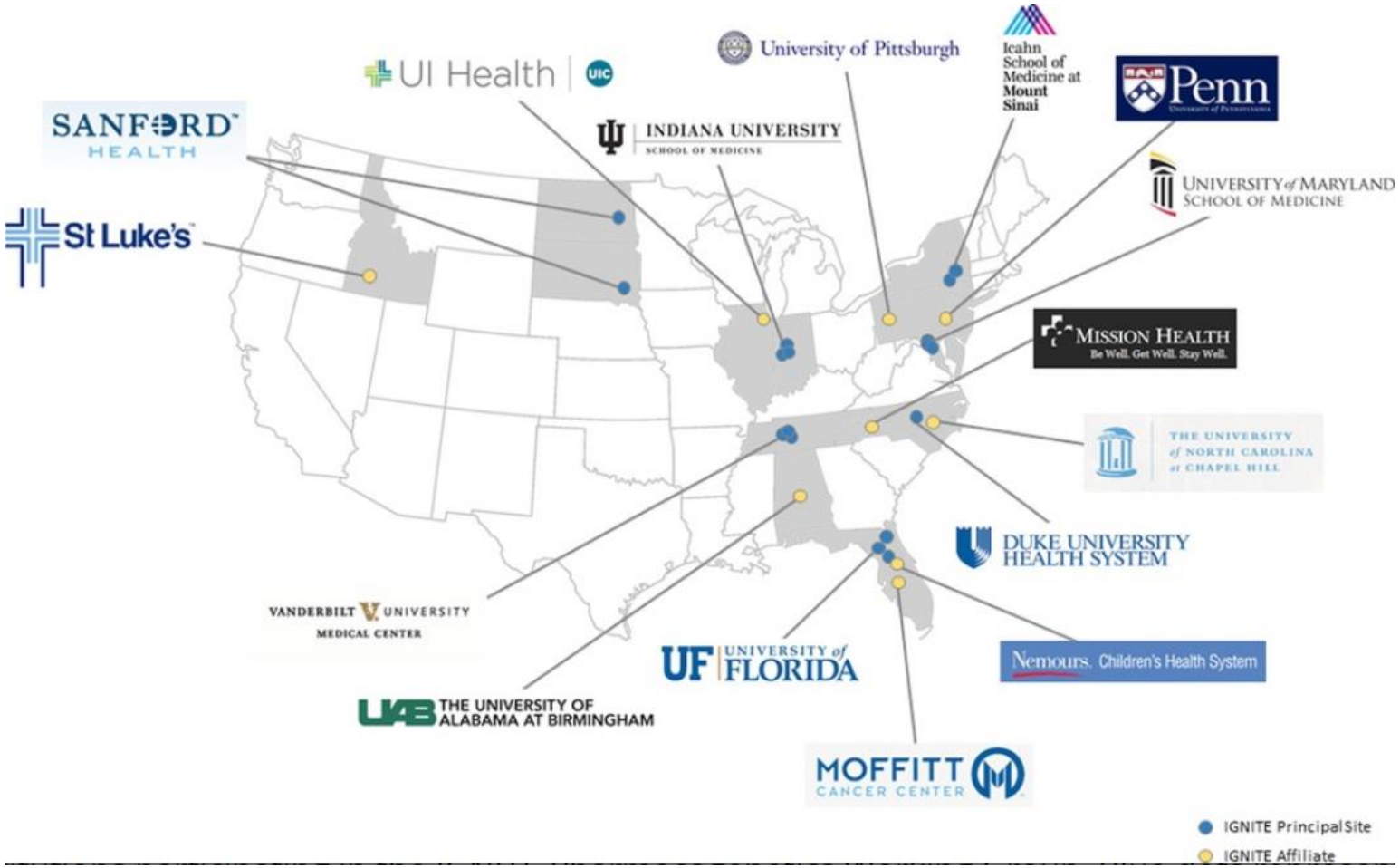
DRUGS TO AVOID IN G6PD DEFICIENCY

DEFINITE RISK OF HAEMOLYSIS		POSSIBLE RISK OF HAEMOLYSIS	
Pharmacological Class	**Drugs***	**Pharmacological Class**	**Drugs***
Anthelmintics	• ß-Naphthol • Niridazole • Stibophen	**Analgesics**	• Acetylsalicylic acid (Aspirin) • Acetanilide • Paracetamol (Acetaminophen) • Aminophenazone (Aminopyrine) • Dipyrone (Metamizole) • Phenacetin • Phenazone (Antipyrine) • Phenylbutazone • Tiaprofenic acid
Antibiotics	• Nitrofurans - Nitrofurantoin - Nitrofurazone • Quinolones - Ciprofloxacin - Moxifloxacin - Nalidixic acid - Norfloxacin - Ofloxacin • Chloramphenicol • Sulfonamides - Co-trimoxazole (Sulfamethoxazole + Trimethoprim) - Sulfacetamide - Sulfadiazine - Sulfadimidine - Sulfamethoxazole - Sulfanilamide - Sulfapyridine - Sulfasalazine (Salazosulfapyridine) - Sulfisoxazole (Sulfafurazole)	**Antibiotics**	• Furazolidone • Streptomycin • Sulfonamides - Sulfacytine - Sulfaguanidine - Sulfamerazine - Sulfamethoxypyridazole
		Anticonvulsants	• Phenytoin
		Antidiabetics	• Glibenclamide
		Antidotes	• Dimercaprol (BAL)
		Antihistamines	• Antazoline (Antistine)

MIMS Summary Table. Accessed October 2019. http://www.cych.org.tw/pharm/MIMS%20Summary%20Table-G6PD.pdf

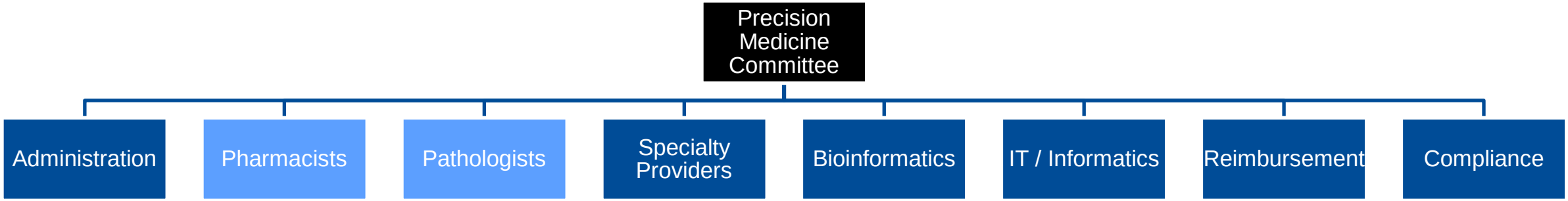
Highlight on Precision Medicine

- This is a **new** and quickly **growing** concept
  - Emerging consulting companies
  - Multiple genetic testing companies
  - Development of software and related functionality
  - Increased research and implementation efforts
- IGNITE collaboration



https://ascpt.onlinelibrary.wiley.com/doi/full/10.1111/cts.12456

Precision Medicine Multidisciplinary Committee



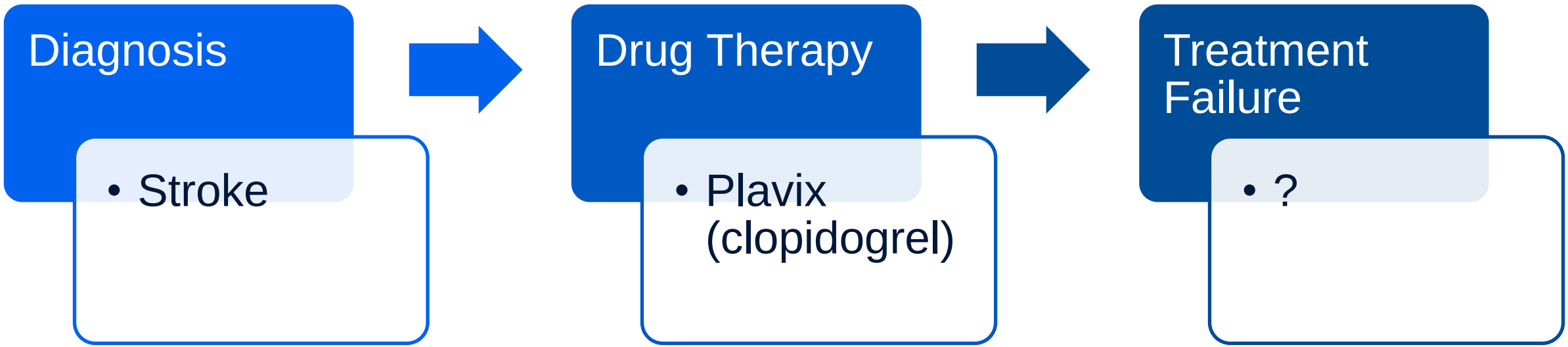
Evaluate Genetic Testing Products

- ⬆ genetic testing products
- ~14 new tests per day enter the market
- ⬆Demand = ⬆Test Availability

- Collaboration
  - Pharmacy helps determine what drugs to target
  - Lab helps choose and interpret the PGx test

Precision Medicine for Health Plans [online webinar]. Concert Genetics, Feb 13, 2019. https://www.concertgenetics.com/blog/webinar-precision-medicine-health-plans/. Accessed April 2019.

When to Test


Diagnosis
• Stroke
Drug Therapy
• Plavix (clopidogrel)
Treatment Failure
• ?

Lab and Pharmacy are Better Together

Benefiting the care environment	• Budgets • Workflow • Patient care
Improving Population Health	• Stewardship initiatives • Precision Medicine

Concluding Challenge