Personalized Genomic Medicine: What is it? Why should I care? How can I use it?

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Olli Lifelong Learning
Health Education Series
Lunch and Learn
UNC-Asheville Campus
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Case study (Canada): Nursing Mom taking Codeine

- **A post partum mom is breastfeeding her infant**
- **For her post-partum pain her physician gives her Tylenol 3 (codeine with Tylenol)**
- **On day 8, the nursing infant suffers respiratory depression and dies**
- **Autopsy of infant shows high levels of morphine: cause of death morphine toxicity**
- *Note: codeine is broken down to morphine for pain relief*

Case Study (Canada)

- Genetic testing of mother finds that she inherited multiple copies of the gene that breaks codeine down to morphine, resulting in higher than normal levels of morphine in her system (causing her to be lethargic, but she is already tired so doesn't really notice)
- The high levels of morphine, however, are also passed to her infant through breast milk causing morphine toxicity in the nursing infant and ultimately death

What could have been done to prevent this death?

- Although rare, 1-3% Caucasian population in the United States have this genetic variation; other ethnicities higher (ex. North Africa/Ethiopian up to 28% w variation)
- This response could have been predicted through genetic testing of mom and/or hospital policy to not give nursing moms codeine for pain management due to known genetic variations
- How can Personalized Medicine help?
  - **Practice policy**: No Codeine to new moms, alternate pain medications
  - **Education:** for new moms and providers about codeine risks
  - **Testing:** before drug is given to identify risk of adverse response

What is Personalized or Precision Medicine (PM)?

- **Individualizing prevention, diagnosis and treatment of disease/conditions**

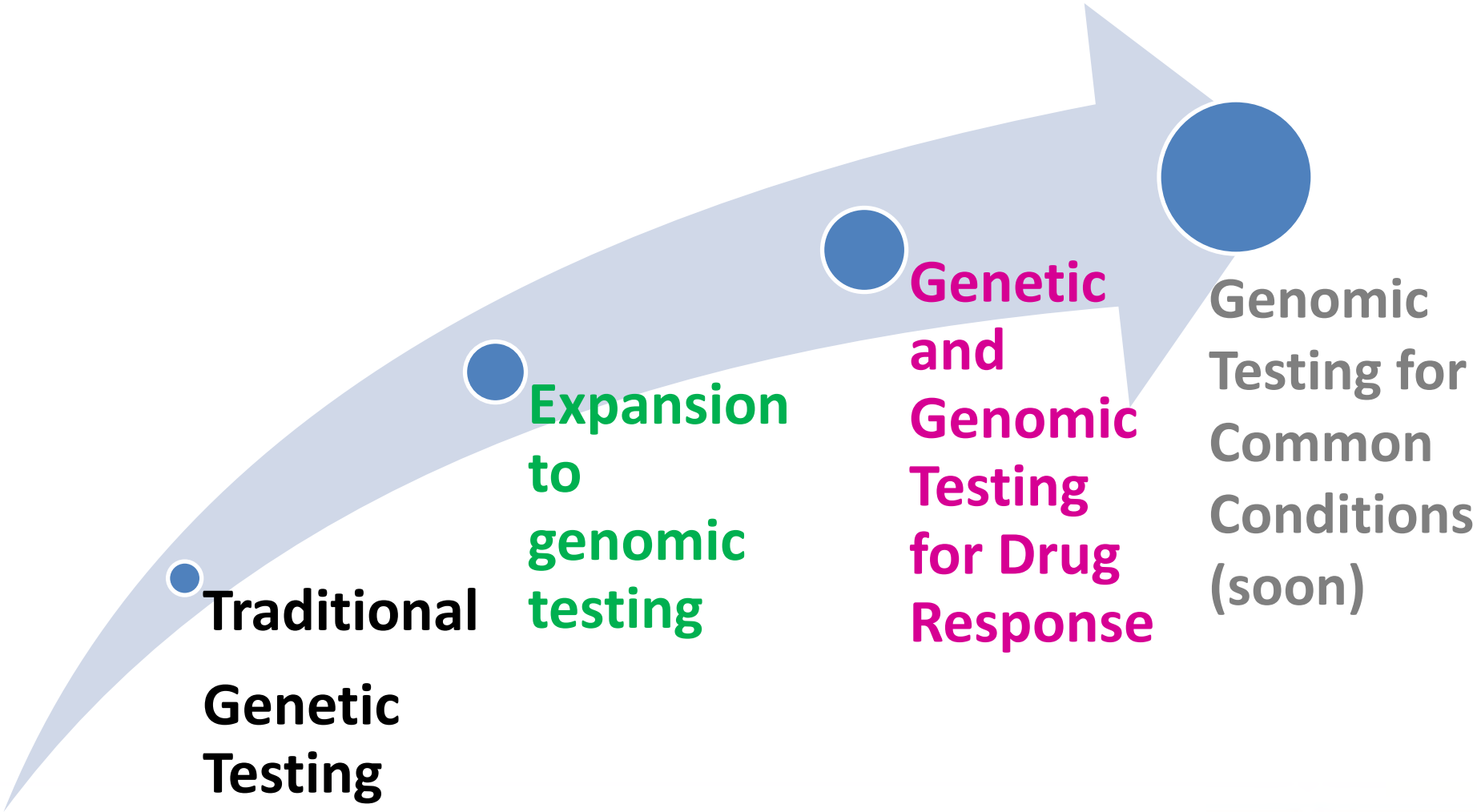
- **Coordinating and integrating care for each patient**
  - Health risk assessment, lifestyle/behavior modifications
  - Keeping people healthy as well as treating sick people

- **Don’t we already do this in medicine?**

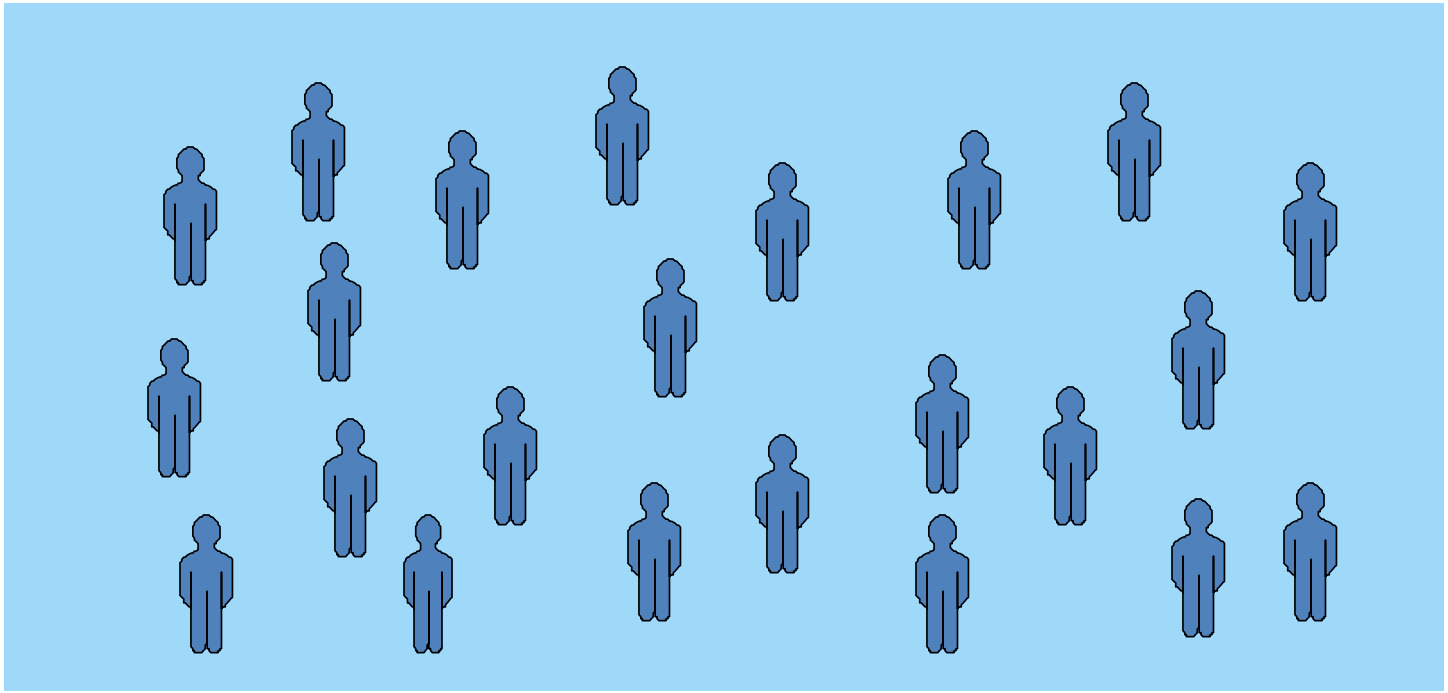
Personalized Medicine: Focus on genetics

- **Utilizing an individual's genetic make up to:**
  - **Predict likelihood of developing future disease**
  - **Enhance our ability to prevent, diagnose and treat conditions**
  - **Predict response to drugs**

Arc of Personalized Genetic and Genomic Medicine
Dressler, 2014

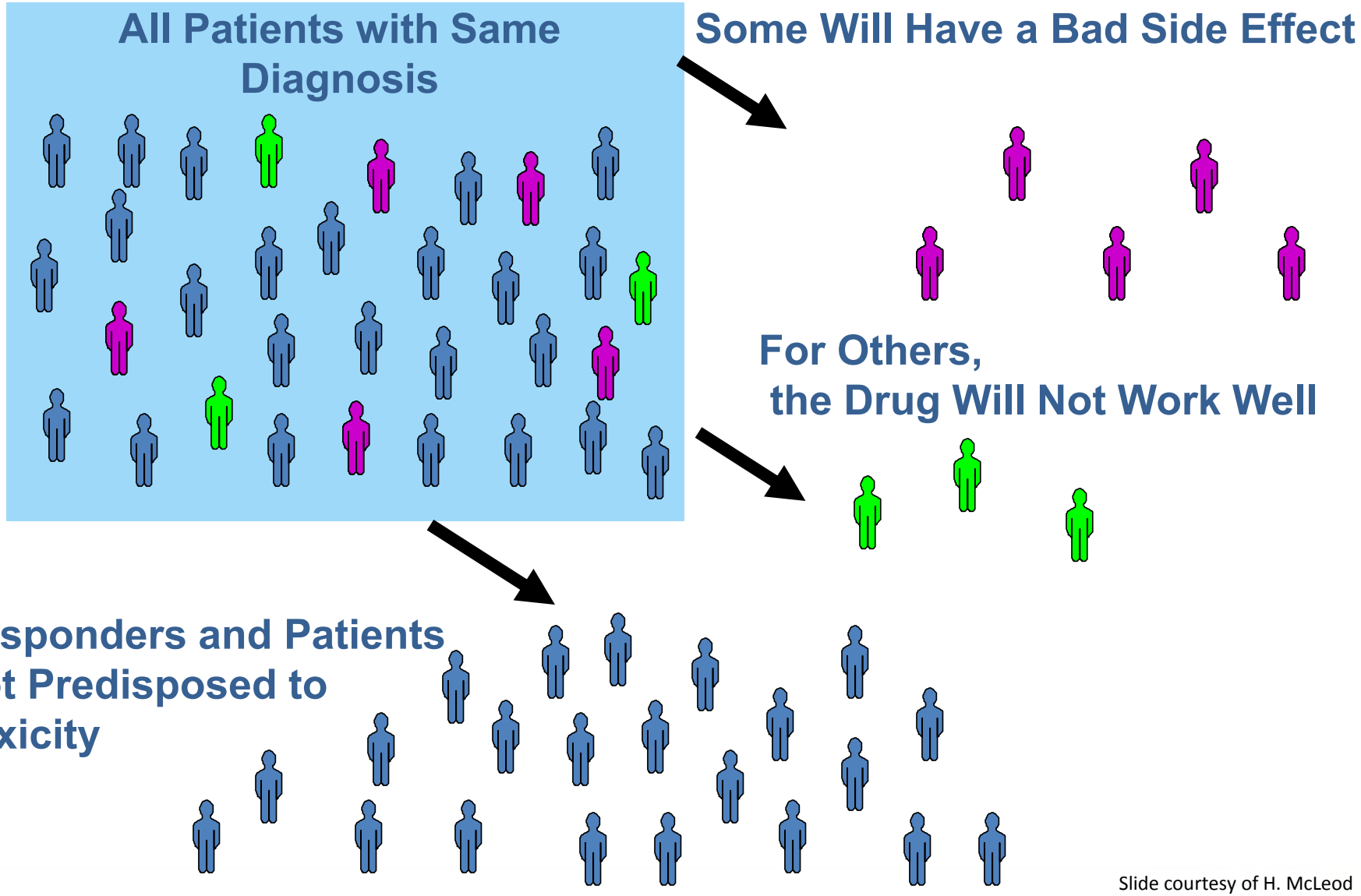


Predicting Response to Drugs



All Patients With The Same Diagnosis

Slide courtesy of H. McLeod



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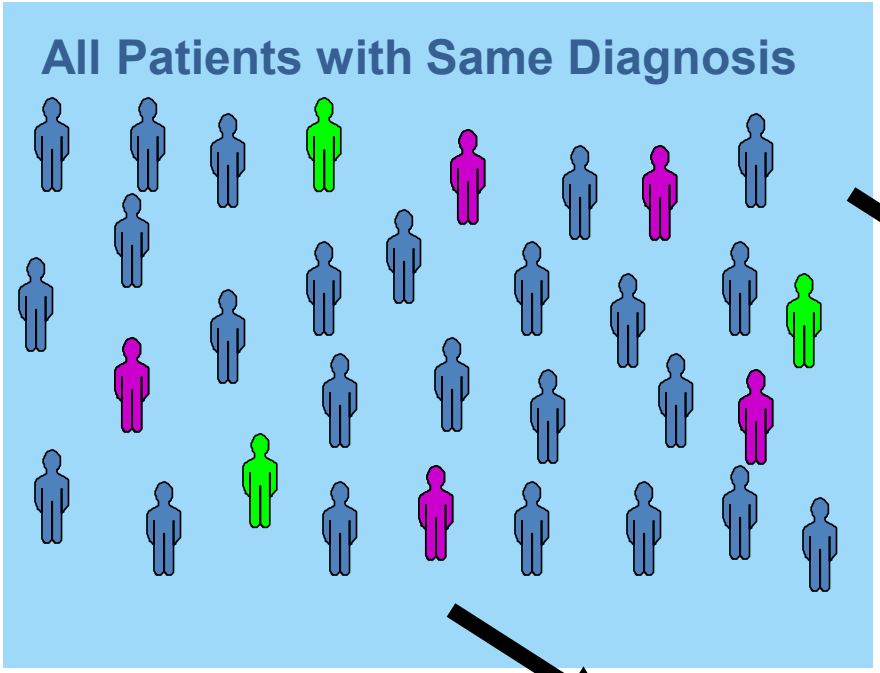
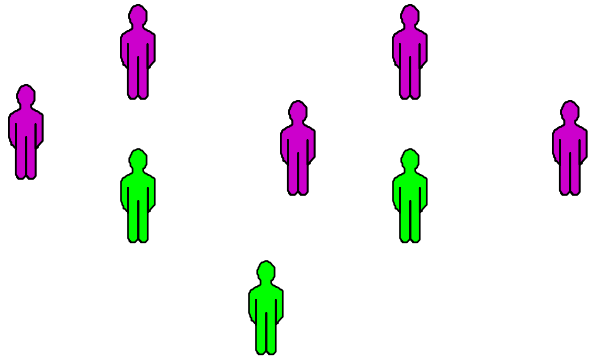
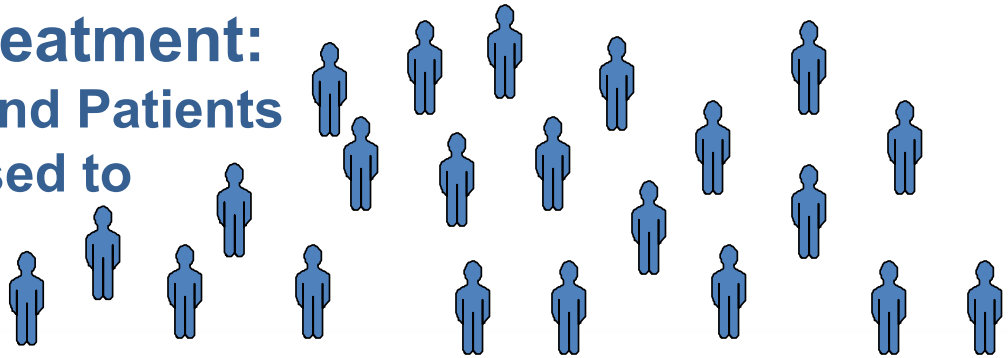
Genetic Testing Distinguishes These Patients



Alternate Therapy:
Non-responders
And Toxic Responders



Standard Treatment:
Responders and Patients Not Predisposed to Toxicity



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Predicting Response to Drugs (Pharmaco-genetics, PGx):

- Prevent/minimize toxic drug reactions
- Select most effective drug/dose at diagnosis
- BEFORE patient gets the drug
  - >100 FDA drug labels contain PGx info
  - Several have an FDA black box warning to test before use
    - Medicare reimbursement for testing (outpatient setting)

FDA Black Box Non-cancer Drugs
Implications for Genetic Testing to Prevent ADRs*

Drug	Corresponding genetic test	Intended use for gene-drug test	Implication of genetic variation (Frequency in population) *
Clopidogrel (Plavix)	CYP2C19 variation	Anti-platelet therapy in ACS/ PCI patients	Ineffective drug response; Risk for stent thrombosis, other cardiac events **25% whites; 35% AA; 60% Asian**
Abacavir	HLA-B*5701 variation/	1st, 2nd line treatment For HIV/AIDS	Potentially lethal hypersensitivity reaction **5-8% whites, AA; <4% Asians**
Carbamazepine (Tegretol)	HLA-B*1502 variation	Epilepsy, bipolar, neuropathy Especially in Asian ancestry	Potentially lethal hypersensitivity reaction, especially Han Chinese ancestry **Han: 36%; Asian Indians 20% Japanese/Korean .5-.1%**
Codeine	CYP2D6 variation	Pain management in children	Potentially lethal response in children **(1-3% white; 28% NAfrica)**

*: PharmGKB and FDA websites

Genetic vs Genomic testing

- **Genetic tests**: targets one or a small group of genes or gene variations in your DNA

- **Genomic tests:** looks at all your DNA, not just certain genes.

- We are 99.9% alike, but that .1% difference can be very important, especially in drug response and diseases:
  - 3 billion base pairs in our DNA x .1% =lots of differences!

Personalized DNA Testing: Inherited versus Acquired Variations

- **Inherited:** Variations in DNA that are inherited from parents and passed on from generation to generation (sample: blood/saliva)

- **Acquired:** Variations in DNA that develop after conception and are not passed down to your children (sample: tumor tissue)

Testing for inherited variations

Example: Gene test to predict response to PLAVIX, used to prevent clotting after stent procedure (CYP2C19)

Example: Gene test to predict effectiveness or toxicity to CODEINE for pain; potentially fatal response for some children and infants (CYP2D6)

Testing for Acquired Variations

Example: Gene test on breast tumor tissue to predict a patient's response to HERCEPTIN, used to prevent recurrence of cancer (multiple copies of HER2 gene)

Example: Gene test in lung cancer to predict a patient's response to ERLOTINIB used to prevent progression of disease (EGFR gene status)

Promise of Pharmacogenetics/Pharmacogenomics

- Safer and more effective drug treatment
- Increased adherence to drug therapy
- Decreased hospitalizations
- Improved health and health care
- Decreased overall costs of health care

Personalized Medicine Program
Why is this important?

– ***Get each patient to their desired outcome:***

– ***An effective drug to treat disease***

Without harm

- ***Prevent/decrease risk of bad drug side effects,***

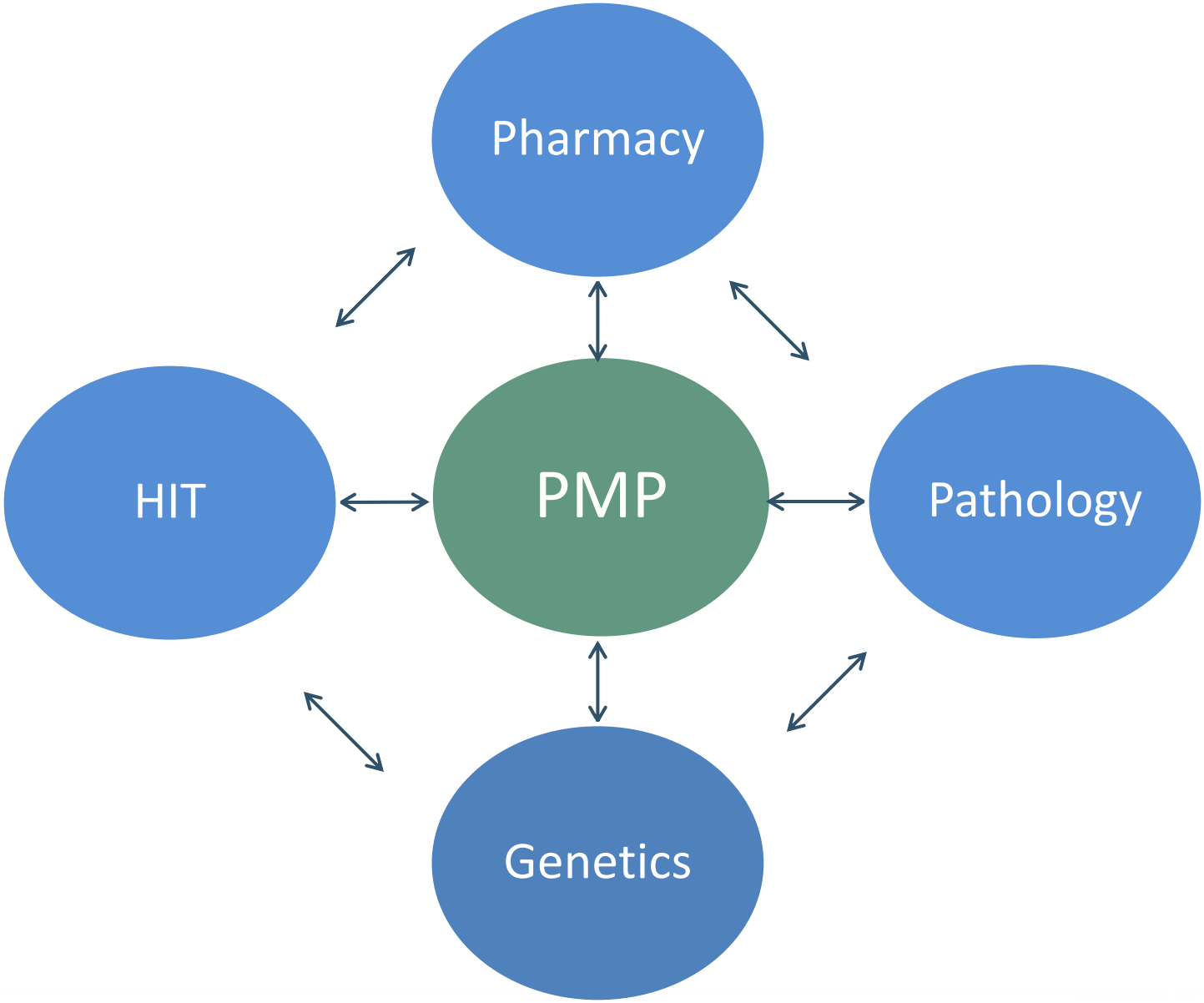
Without waste,

-At the time of diagnosis, not 3 months or years later after much time and money has been spent

And with an exceptional experience:

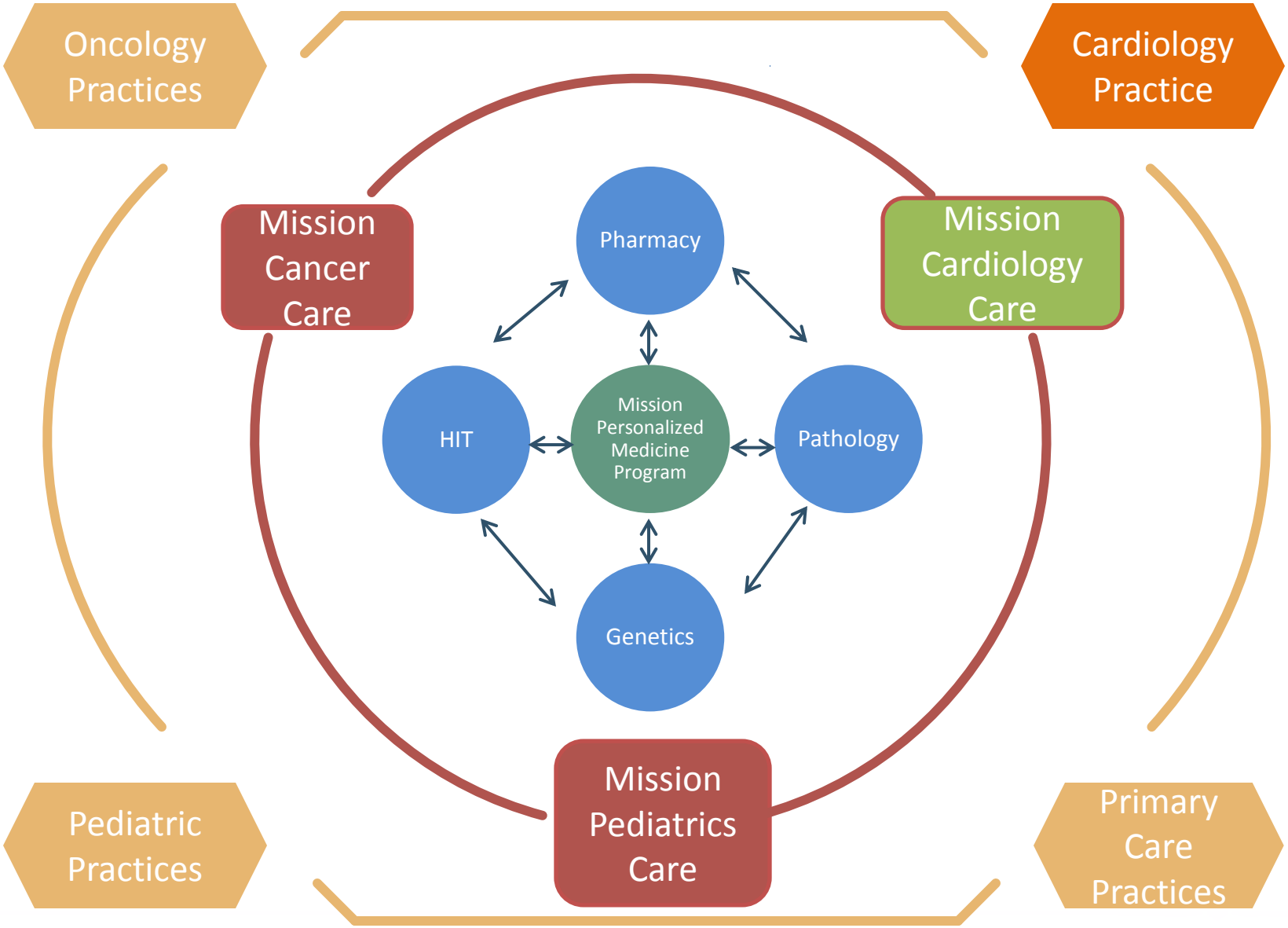
-Coordinated, efficient, high quality care locally

- **Prepare region for genomic medicine in chronic diseases**
- **Provide quality, cutting edge care, locally**



Integrated team approach: opportunities and challenges

MISSION HEALTH



Stakeholders/Challenges/Opportunities

MISSION HEALTH

Scenario 1: Mr M

- *Mr. M, an obese 67 year old Caucasian male with high blood pressure, presents to his primary care physician with shortness of breath for the past 2 months, and is referred to a cardiologist. He is seen in the cardiology clinic the following day and a cardiac cath procedure is recommended.*
- *The cardiologist indicates that, during the procedure, they may need to place a drug eluting stent in his artery. Mr. M would receive the anti-platelet drug clopidogrel (Plavix™). He is scheduled for a pre-op visit in three days.*

Scenario 1: Mr M
How can PGx testing help?

- **Ideally:** primary care physician already ordered the CYP2C19 test due to high risk nature of Mr. M
  - Testing results in EMR (primary care doc) are sent to cardiologist prior to visit.
  - **CYP2C19*2 variation (PM)**: cardiologist orders Prasugrel
- **Current reality**: neither primary care or cardiologist are aware of test/consider it useful, but some patients will have:
  - In house complication or re-admission within 30 days of discharge associated w ineffective drug response
  - MI, stroke and/or re-stented in same vessel
  - Harm to patient, increased cost of care, missed opportunity to prevent adverse event

Mission Health Personalized Medicine Program
-Services Planned-

- Education and Awareness
- Training and communication
- Clinical decision support tools
- Coverage and reimbursement assistance
- Resource and consult service
- Encourage pre-emptive testing in primary care

Promise of Personalized Medicine

- Safer and more effective drug treatment
- Increased adherence to drug therapy
- Decreased hospitalizations
- Improved health and health care
- Decreased overall costs of health care

Our Mission:

"Getting each patient to their desired outcome,
Without harm, without waste,
And with an exceptional experience."

Questions? Comments?

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