Considerations for Implementing a Personalized Medicine Program at a Community Health System: The Mission Health Experience

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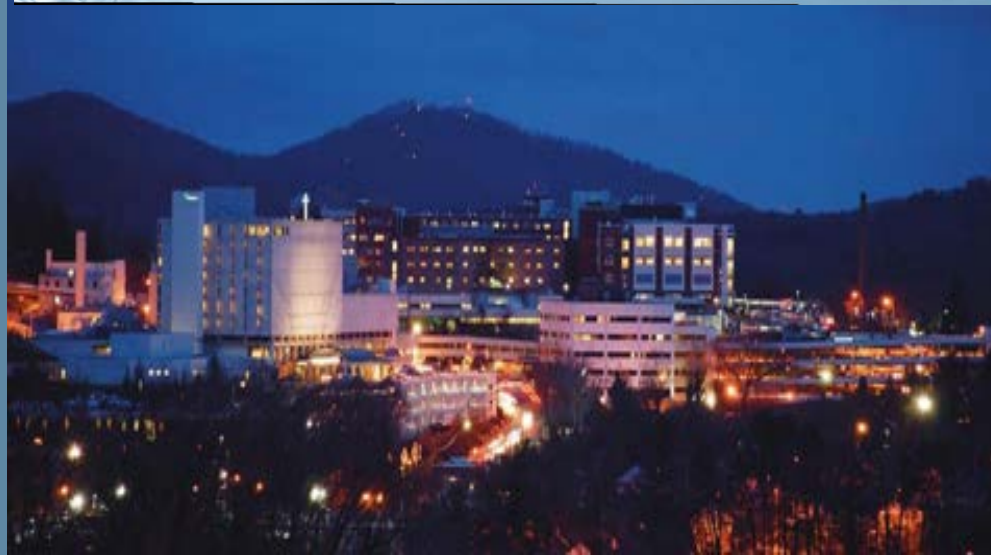


Disclosures

- Neither Lynn G. Dressler nor Gillian Bell has disclosures or conflicts of interest

Who is Mission Health?

- **Federally designated rural health care system, WNC**
  - Only regional tertiary care referral center (750 bed)
  - 6 affiliate hospitals (+400 beds)
- **Highly rated:**
  - Truven/Reuters: top 15 health systems
- **Underserved community**
  - All 18 counties MUA
  - 75% CMS/self pay
  - Stable population

- **Excellent infrastructure**
  - Fullerton Genetics Center
  - HIT/CDS/Cerner
  - Primary care network/ACO
  - Integrated cancer center
- **Innovative leadership**
  - CEO, Dr Ron Paulus
  - Cutting edge care locally
  - Prepare region for genomic medicine

MISSION HEALTH

Mission's Personalized Medicine Program Vision and Focus 2013-present

- Utilize genetic and genomic information to minimize adverse response and maximize drug effectiveness.
  - **Cancer:** focus on predicting response to anti-cancer drugs, where testing is already standard of care.
  - **Non-Cancer:** focus on addressing drug – gene associations with highest level of evidence, where testing is emerging as a best practice.

Focus: 2013-present
Drug safety and effectiveness in cancer and non cancer patients

SERVICES:

Clinical consultation:

- Personalized Medicine Consultative Clinic (non-cancer)
- Comprehensive cancer genomic profiling (oncology)

Clinical decision support in EMR

- Alerts, alternative drugs

Quality Improvement/Operations:

- Meet/exceed national guidelines
- QI studies for compliance

Clinical Research:

- PCP pilot demonstration project
- Supportive care study in oncology

Awareness/Education/Training:

- Providers and Community

Current PM Team

- **VP Mission Health, Jonathan Bailey, MHA**
- **Director, Lynn Dressler, Dr.P.H.**
- **Clinical Pharmacist, Gillian Bell, PharmD.**
- **Coordinator: Paige Krug, B.S.**
- **Part time:**
  - Research Nurse (Pearl Abernathy, RN); (0.5FTE)
  - Peds Pharmacist (Karl Ruch, PharmD); (0.2FTE)
- **Trainees:** Pharmacy Students, Residents, Fellows
- **Consultants:** Howard McLeod (Moffit Cancer Center, Tampa);Mark Dunnenberger (North Shore, Chicago)
- **Partners:** UNC, Duke, Vanderbilt, St Jude, UFlorida, Innova Health, IGNITE, DIGITIZE

Conceiving a Personalized Medicine Program at Mission Health

OVERALL THEME: SAFETY AND QUALITY

1. **Assessment and strategic planning:**
    - Focus on low hanging fruit: **Oncology**
    - Focus on testing with high impact and where reimbursement is likely: **FDA black boxed warnings**
2. **Implementation:**
    - Demonstrate how a personalized medicine approach is good value and solves existing clinical problems
    - Conduct pilot feasibility studies for clinicians to “try out” PGx in IRB approved study
3. **Evaluation and Continuous Quality Improvement (CQI):**
    - Quality improvement studies: CDS-black box, oncology
    - Strategic planning with leaders of multiple service lines

Conceiving Mission's personalized medicine program Non-Cancer Initial Strategy-(2013)

- **Focus: Testing where impact/reimbursement is likely**
  - 1st Tier: (2nd Tier=CPIC drug-gene pairs)
    - PGx testing associated with FDA black box drugs
  - Assess use of drugs at Mission Hospital (in-patient)
    - Abacavir: HLAB*-5701 (20 pts/yr)
    - Carbamazepine: HLAB*-1502 (6 Asian/yr)
    - **Clopidogrel: CYP2C19 (1432 PCI pts/yr)**
    - Codeine: CYP2D6 (400 peds/yr)
- **Implementation plan:**
  - Start with highest area of impact –Cardiology
  - Education, pilot studies, CDS in EMR

However, cardiology pilot study was not implemented

- **Challenges:**
  - **Locally**:
    - Variable and uncertain value/benefit among local physicians
    - **Plavix failures were “not a problem”**
    - **No physician champion**
  - **Nationally:**
    - Conflicting results regarding association of PGx and outcomes in clinical trials
    - **AHA does not endorse routine testing**
    - Variation in adoption across academic settings
  - **Cost-effectiveness:** estimation for testing all patients, with 15% assumed IM/PM; based on Medicare LOS, re-admission: +$50K.
  - **Research Project**: Danielle Schlafer P4 Pharmacy student identifies patients who might benefit from testing.
    - **Over 18 mos: 75/1753 (4%) with MACE events**
    - In-patient complications or hospital readmissions due to:
      - Stroke, MI, thrombosis/stenosis or death
    - **Funding needed to conduct case control study to evaluate contribution of CYP2C19 variation to cardiac events**

2013- present: National effort to prevent lethal response to codeine in children (and infants)

- FDA black box warning on codeine for post op pain in tonsillectomy for sleep apnea in children.
- WHO takes codeine off pain ladder
- Childrens Hospitals' remove codeine from formulary
- **Mission CEO, VP Pediatrics want to respond to concern, decrease opioid use**

First tangible success of program: Remove codeine from pediatric formulary (2014/15)

- ✓ **Education programs:**
  - For clinicians (and new moms) about codeine risks
  - In person meetings w practices, MDs, service lines
- ✓ **Practice policy change**:
  - Remove codeine from pediatric formulary: approved by Mission Pharmacy and Therapeutics committee
  - No Codeine to new moms, alternate pain medications
- ✓ **Integration into EMR, system wide approach:**
  - Decision support, warnings, drug/dose alternatives
- **X Pre-emptive Testing:**
  - Not an option for Mission, most pediatric patients are Medicaid

Tx Equiv Med

Codeine containing products are non-formulary for pediatric patients.
*Codeine-containing medications are contraindicated for tonsillectomy and adenoidectomy (T & A) for any child under 18 years of age. [3]

- For pain management for >/= 2 yo to < 18 yo, please use alternative medications as indicated below[1]:
  - **Non-opioid (preferred if appropriate):**
    - acetaminophen 15 mg/kg PO Q4H prn pain (not to exceed 5 doses/day)
    - ibuprofen 10 mg/kg PO Q6H prn pain
    - ketorolac 0.5 mg/kg IV Q6H prn pain (* not in T&A patients)
  - **Opioid:**
    - morphine 0.2 mg/kg PO Q4H prn pain
    - oxycodone 0.1 mg/kg PO Q4H prn pain
    - acetaminophen-hydrocodone (Hycet) 7.5mg-325mg/15mL 0.2 mL/kg PO Q4H prn pain (0.2 mL/kg of this product delivers 0.1 mg/kg hydrocodone component)
- If indication is for cough suppression, no codeine-containing cough suppressants are available at Mission.[2]

If you wish to continue ordering the Nonformulary item, choose Do Not Substitute option, and click on NFRequest to complete the justification form. Once the request form is signed, you can click OK to order. If the NFRequest is not completed, this order will be rejected and therapy will be delayed.

References

[1] http://www.ncbi.nlm.nih.gov/pubmed/24210703 Jerome J et al. A single institution's effort to translate codeine knowledge into specific clinical practice. J Pain Symptom Manage. 2014 Jul;48(1):119-26.

[2] http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm051137.htm Public Health Advisory: FDA Recommends that Over-the-Counter (OTC) Cough and Cold Products not be used for Infants and Children under 2 Years of Age

[3] http://www.fda.gov/Drugs/DrugSafety/ucm339112.htm FDA Drug Safety Communication: Safety review update of codeine use in children; new Boxed Warning and Contraindication on use after tonsillectomy and/or adenoidectomy

Alert Action

- (•) Stop ordering codeine-promethazine
- ( ) Do not substitute

Add Order for:

- [ ] acetaminophen -> 15 mg/kg, Liquid, PO (by Mouth), Q4HR, PRN, pain
- [ ] ibuprofen -> 10 mg/kg, Susp, PO (by Mouth), Q6HR, PRN, pain
- [ ] ketorolac -> 0.5 mg/kg, Inj, IV, Q6HR, PRN, pain
- [ ] morphine -> 0.2 mg/kg, Oral Soln, PO (by Mouth), Q4HR, PRN, pain
- [ ] oxyCODONE solution 1 mg/mL -> 0.1 mg/kg, Liquid, PO (by Mouth), Q4HR, PRN, pain

Codeine CDS alert ≥2yo to <18yo

Thanks to St Jude's And Mission IT teams!

The codeine story continues

- NC Medicaid considering following Mission's lead to removed codeine from pediatric formulary

However:

- **2017: QI Study of CDS alerts finds that alert is firing inpatient but not ambulatory (both inpatient and ambulatory on same EMR)**
- 2017: Codeine still being given to kids in URGENT care and some outpatient clinics
- 2017: In-patient alerts for codeine and tramadol now being tied to pediatric Powerplans
- Currently being addressed and updated by IT

Integrating Personalized Medicine into Primary Care

- **Educational conferences:**
  - PCPs: Fall 2015
  - Pharmacists: Spring, 2016
- **Pilot demonstration project PCP:** March 2016, NC Biotech Center
  - *"When cost is not the issue, and education/training provided by PM team, what are the barriers to PGx testing in a busy primary care practice?"*
    - Eligibility: 65yo, Medicare, polypharmacy, 1 drug CPIC
    - ~30% of patients had recommendations for medication change
- **Development of Personalized Medicine Clinic**
  - April, 2016. Director, Gillian Bell, PharmD.
  - Outpatient, requiring MD referral , 2 visit process
    - 100% of patients have genetic variations
    - ~27% of patients: immediate actionability based on PGx results
      - PM Pharmacist suggested changes to current meds
- **PMP as resource: "we've got your back"**
  - Training/education/clinical consultation for clinicians

Primary care pilot study (IRB approved): Preliminary findings: 12 4 17

- **Testing as a clinical care test :**
  - Testing provided by a commercial lab (ONEOME)
- **Number of practices recruited:**
  - 3 Practices: 4 physicians, 2 pharmacists, 2 nurses
- **Eligible patients:**
  - At least 65yo, on Medicare, polypharmacy (4), where 1 Rx is CPIC drug-gene interaction
- **Number of patients recruited:**
  - 51 patients with PGx testing completed, surveys pre/post testing
- **PM Pharmacist suggests changes to consider for current drug use:** 15/51 (29%)
    - Change current drug to alternative (Drug-gene)
    - Change dose of current drug (drug-gene)
    - Consider effects of other drugs (Drug-drug-gene):

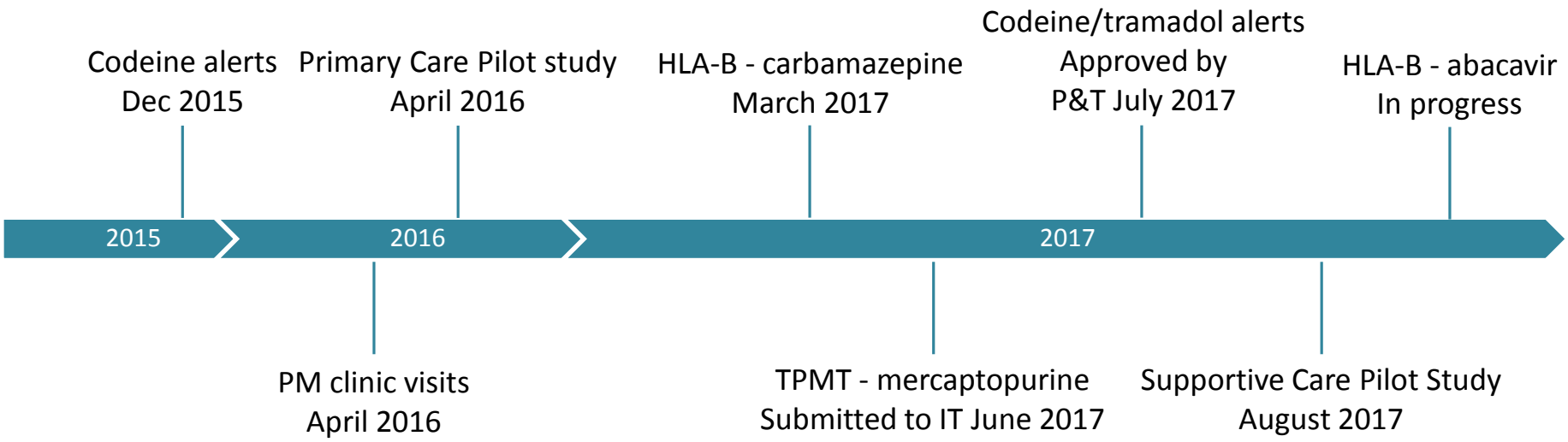
Preliminary Data: PCP Pilot

- **Clinician pre test surveys**
  - **Top 4 barriers to implementing testing in their practice:**
    - Out of pocket expense for my patient (80%)
    - Lack of comfort with interpreting and applying results (80%)
    - Lack of expertise to address complex cases (80%)
    - Lack of time to spend with patient to explain results (50%)
  - 100% SA/A: I would be more inclined to use PGx testing if I had access to an expert consult service to help interpret and evaluate difficult cases.
- **Clinician post test survey**
  - **MD: Top 4 barriers to implementation:**
    - Lack of orderable in EMR
    - Lack of ability to integrate discrete results into EMR
    - Lack of ability to utilize results over time
    - Concern for out of pocket expense for patients
  - **Altered care based on PGx results:** ex) Changed Plavix to alternate; Lowered statin dose, increased PPI dose, better able to explain past treatment failure on SSRI

-Examples of Recommendations-

- **Change current drug to alternative (Drug-gene)**
  - Patient currently taking Plavix (clopidogrel-antiplatelet)
  - Testing shows variation in CYP2C19 (IM)
  - Recommend to consider alternate drug (prasugrel or ticagelor), if no contraindication and indication is ACS/PCI
- **Change dose of current drug (drug-gene):**
  - Patient currently taking lower dose esomeprazole (PPI; GERD)
  - Based on PGx results (CYP2C19 RM), the patient may benefit from a higher dose if the usual dose is not working
- **Consider effects of other drugs (Drug-drug-gene)**:
  - Patient on Simvastatin 40mg and amlodipine
  - SLCO1B1 intermediate function (*1/*5)
  - Monitor for s/s of myopathy, consider alternative

PGx Clinical implementation at Mission Health



Challenges to implementing pharmacogenetic testing in clinical practice at Mission Health

- Who and when to test?
- Clinician awareness and engagement
- Choice of lab to perform testing/cost of testing
- Electronic health record integration

Who and when to test?

- Start with low hanging fruit
  - Medications with boxed warnings
  - Guidance from disease specific guidelines
  - Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines
  - Utilize existing infrastructure
- Meet with stakeholders to determine clinical questions
  - Evaluate prescribing practices so you know who to target
  - Could genetic testing help make decisions among equal choices
- Identify engaged clinicians who will be champions

Personalized Medicine Clinic Visits at Fullerton Genetics Center

Goal: provide mechanism for clinicians to refer patients needing specialized visits to discuss the implications pharmacogenomics tests and to counsel on results if tests are indicated

Structure:

- Appointments to discuss testing and review results
- Uses existing genetics infrastructure
- PharmD takes detailed medication history, discusses risk, limitations, cost
- PharmD/MD answer questions
- If testing appropriate, send to reference lab
- PharmD goes over report and creates summary for patient/provider

Challenges:

- Scheduling within an existing clinic
- Creating new documentation in the EHR
- Process for receiving and denying referrals
- Advertising new service
- Patients with unrealistic expectations
- Reimbursement
- Sustaining momentum

Getting the Message Out at Mission Health!
50 Community and Provider Education Initiatives in FY2017

- Provider awareness initiatives
  - Grand Rounds
  - Personalized Medicine Conference for Pharmacists
  - Monthly staff meetings/leadership meetings
  - Family Practice Office visits
  - Digital media (screensaver and website)
  - Podcasts
  - Mailings
  - Institutional newsletters
- Community education initiatives
  - Health fairs
  - Local radio/newspapers
  - Blogs/social media
  - Speaking at community organizations

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Four domains for evaluating pharmacogenomic laboratories

Gene selection	1. What gene(s) is/are applicable to my clinical setting? 2. How are the genes aggregated for testing? (disease specific panel, broad panel testing) 3. Can the laboratory provide a customized panel of genes? 4. What variants are interrogated and are they representative of my patient population?
Logistics	1. What type of sample is required? 2. What is the turnaround time? 3. Are samples stored for future testing? 4. Are samples used for research purposes?
Reporting of results	1. How are the results returned to a provider/patient? 2. Are the results easy to interpret for a provider/patient? 3. Is the evidence for each recommendation available? 4. Does the evidence support the recommendations? 5. What education materials are available to aid in discussion of the results?
Test cost and reimbursement	1. Does the laboratory bill patient insurance directly? 2. What patient financial assistance programs does the laboratory provide? 3. Does the laboratory provide a maximum cost for the patient?

Vo TT. Pharmacotherapy. 2017 Jul 12.

Challenges to implementing pharmacogenetic testing in clinical practice at Mission Health

- Who and when to test?
- Clinician awareness and engagement
- Choice of lab to perform testing/cost of testing
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Define a location in EHR for pharmacogenetic results

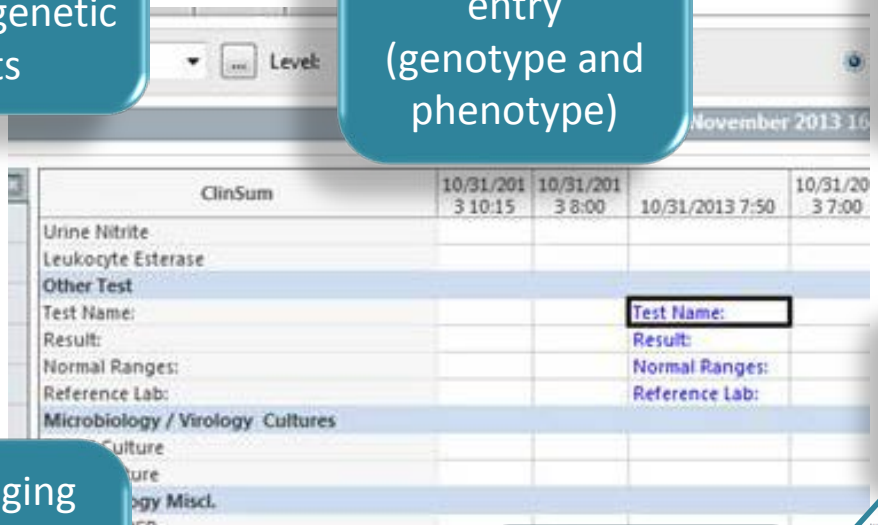
Create a discrete result entry (genotype and phenotype)

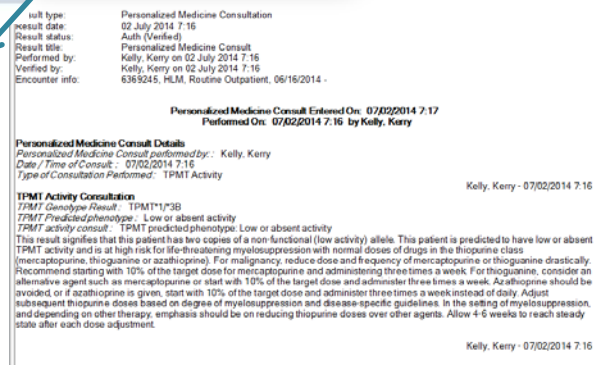
Determine mechanism for knowing when results are back

Design a consult to accompany result

Create pre- and post-test clinical decision support alerts

Event logging of each alert occurrence for prescribing attempts





MISSION HEALTH

Lessons Learned

- **Physician champions and support critical at all levels**
- **Solve existing clinical problems**
- **Respond to national/regional concerns**
- **Provide opportunity for clinicians to "test out" through pilot studies**
- **Know your clinicians and organization:**
  - Policy change vs testing implementation
  - Build on successes: codeine, then CBZ and Abacavir
  - Multi-prong approaches: (ex. PGx in PCP)
    - Targeted education conference for PCP
    - Individualized in-services for PCP practices
    - Pilot demonstration and feasibility study for PCP
    - Personalized Medicine consultation clinic for PCP

MISSION HEALTH AIM:

"Getting every person to their desired outcome,
Without harm, without waste,
With an exceptional experience for each person, family and team member.."

Thank You!

Questions and Comments?

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Mission Personalized Medicine Program