Pharmacogenomics: Practice Driving Education and Education Supporting Practice

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Disclosures

- Mock laboratory reports for classroom use were provided by Genemarkers, LLC.

- The authors of this presentation report no other known or perceived financial conflicts of interest related to this presentation.

Outline

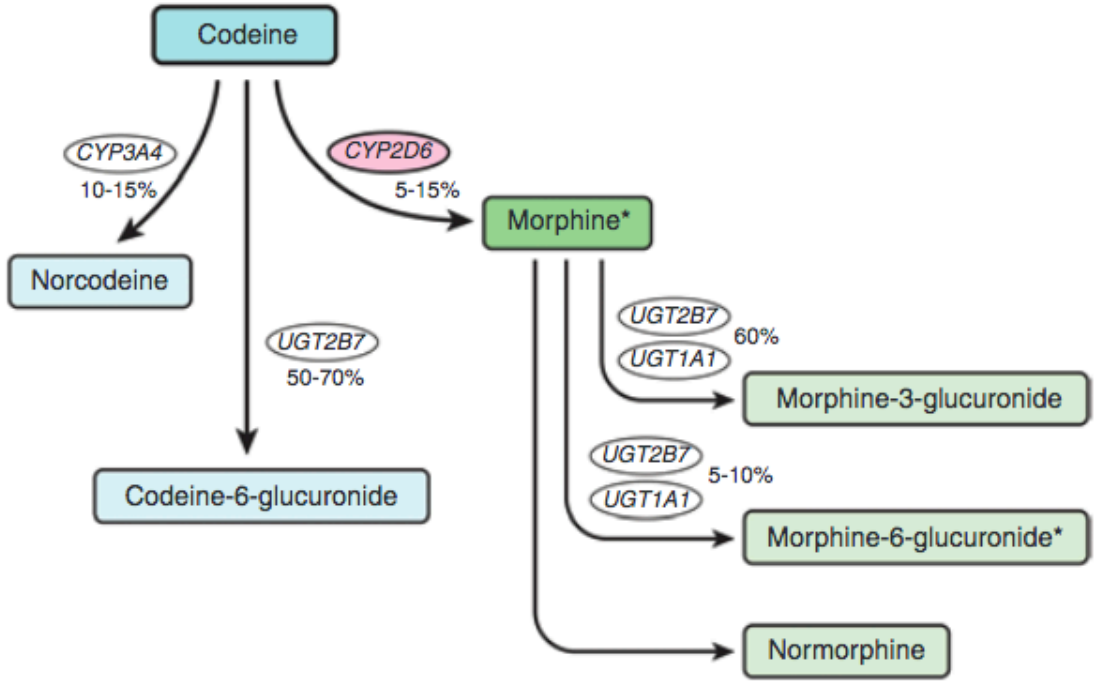
- What is pharmacogenomics?
- What does pharmacogenomics look like in practice?
- How has classroom-based pharmacogenomics education been built to mirror current practice?

Pharmacogenomics (PGx)

- **Precision medicine:** Determining which approaches would be effective for which patients based on genetic, environmental, and lifestyle factors
- **Personalized medicine:** Somewhat interchangeable with precision medicine, older term
- **Pharmacogenomics (PGx):** The study of how a patient's genetics may influence their response to medications
  - Component of precision medicine
  - Synonymous with pharmacogenetics?

https://ghr.nlm.nih.gov/primer/genomicresearch/pharmacogenomics
https://ghr.nlm.nih.gov/primer/precisionmedicine/precisionvspersonalized

PGx Example: CYP2D6 & Opioid Metabolism



CYP2D6

-Metabolizes codeine into morphine and M6G

-Polymorphisms in CYP2D6 are common and can result in10-fold difference in drug clearance

"Ultrarapid metabolizer" = SNPs ↑CYP2D6 activity

Est. 1-2% of patients*

Increased analgesia

Potentially increased toxicity

"Poor metabolizer" = SNPs ↓CYP2D6 activity

Est. 5-10% of patients*

Reduced analgesia

**likely varies by race*

KR Crews *et al.* Clinical Pharmacogenetics Implementation Consortium Guidelines for Cytochrome P450 2D6 Genotype and Codeine Therapy: 2014 Update. CPIC Update. Clin Pharm Ther. 2014

Where is PGx in practice?

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Codeine sulfate tablets safely and effectively. See full prescribing information for Codeine sulfate tablets.

Initial U.S. Approval: 1950

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

Respiratory depression and death have occurred in children who received codeine following tonsillectomy and/or adenoidectomy and had evidence of being ultra-rapid metabolizers of codeine due to a CYP2D6 polymorphism.

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

Codeine sulfate is an opioid analgesic indicated for the relief of mild to moderately severe pain where the use of an opioid analgesic is appropriate.

- FDA is beginning to include PGx data in drug labeling
- Direct-to-consumer testing outside US
- Testing within a health system
- Testing in community pharmacies

- **An increasing role for pharmacists**

PGx Laboratory Example

- Genemarkers, LLC is a PGx laboratory based in Kalamazoo, MI
- Offer pharmacist consult reports with laboratory testing to facilitate simpler interpretation by ordering health care professionals
- Physicians may benefit from familiarity with the laboratory report itself

- **Physicians may benefit from understanding what a pharmacist consult report can provide**
- **Pharmacists need to be able to interpret the laboratory report and generate clinical recommendations**

Education Inspired by Practice Needs

- **Barriers to PGx Implementation:**
  - *Physicians must understand laboratory reports and pharmacist consult reports*
  - *Pharmacists must be able to interpret laboratory reports and make clinical recommendations*

- **Educational Design:**
  - Collaboration between WMed and Ferris
  - Interprofessional Education (IPE): *learning about, from, and with other professionals*
    - ACPE Standards 2016: Standard 11, Standard 24.3, Standard 25.6
    - LCME Standards 2018: Standard 7.9
  - Telehealth model of virtual education to overcome logistical IPE hurdles and mirror practice

Quesnelle KM, Bright DR, Salvati LA. Curr Pharm Teach Learn 2018;10(8):1062-9.

Sickle Cell Anemia

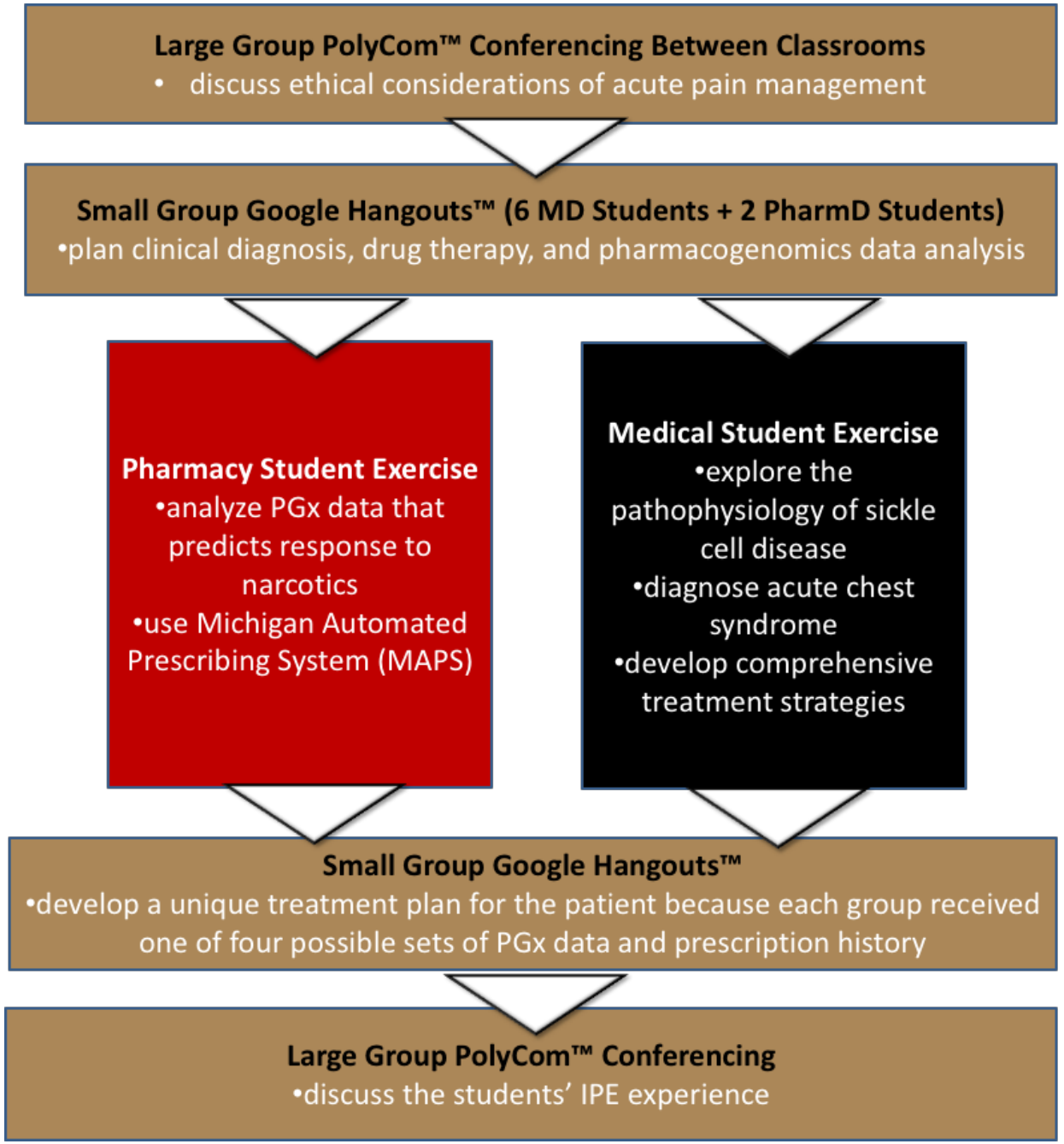
Telehealth Team-Based Learning

The Case:

A 21-year-old female presents in the emergency room with a pain crisis

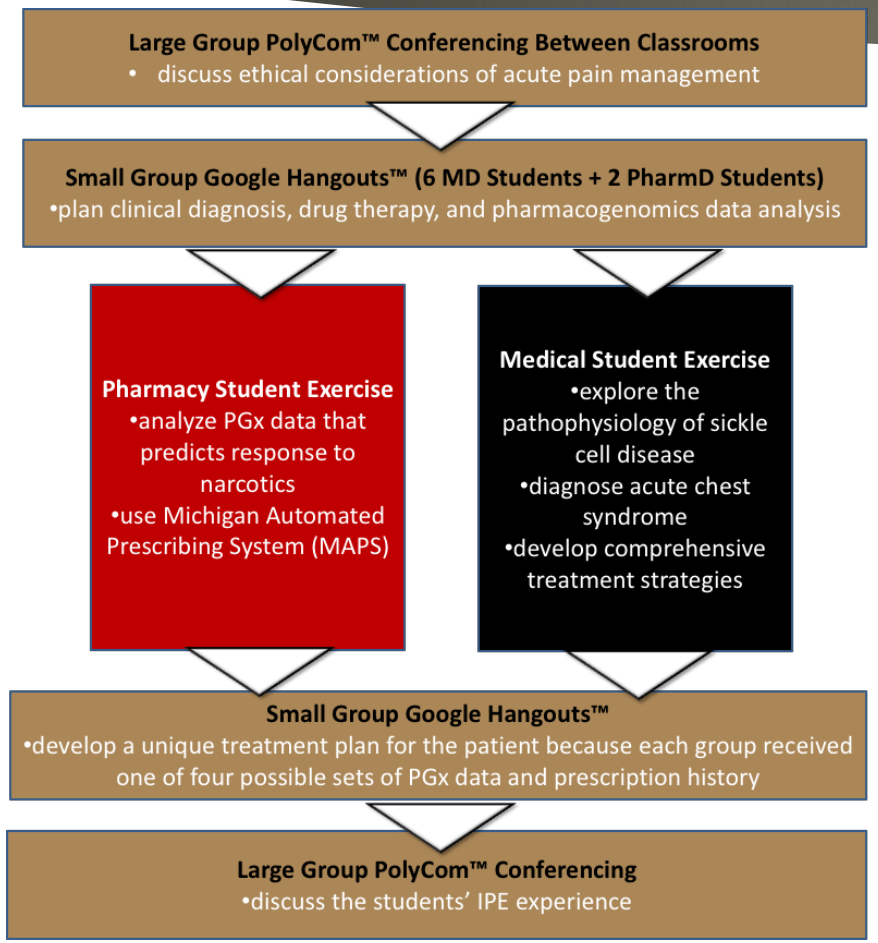
The PGx:

One part of a multi-faceted case presentation



Quesnelle KM, Bright DR, Salvati LA.
Curr Pharm Teach Learn 2018;10(8):1062-9.

Teaching Future Pharmacists & Physicians Effective Communication About PGx



- Survey data showed shifts in perceptions of the roles of different health care professionals
- Pharmacy students effectively taught medical students about PGx results and teams evaluated implications for clinical treatment of patient

	Medical Students	Pharmacy Students
Responsibility and Accountability	0.21±.06	0.11±.10
Shared Authority	0.08±.06	0.28±.09
Interprofessional Education	0.14±.05	0.30±.09
Pharmacogenomics Confidence	0.56±.09	0.14±.12

Quesnelle KM, Bright DR, Salvati LA. Curr Pharm Teach Learn 2018;10(8):1062-9.

Key Findings

- **Barriers to PGx Implementation:**
  - Physicians must understand laboratory reports and pharmacist consult reports.
  - Pharmacists must be able to interpret laboratory reports and make clinical recommendations.
- **Key Findings from Educational Initiative:**
  - Pharmacy students effectively taught medical students about PGx results and teams evaluated implications for clinical treatment of patient.
- ***Practice drove education, and education supported practice***

Questions

Pharmacogenomic Testing

Andrew Reeves, R.Ph.

Chief Executive Officer

Overview

- Who is **OptiMed Health Partners**?
- Our **mindset in delivering** patient care.
- Why **pharmacy/pharmacist** for PGx?
- How we **leverage PGx** at OHP.
- The **future of PGx** for OHP.

Who We Are

OptiMed HEALTH PARTNERS

ASCENDPBM

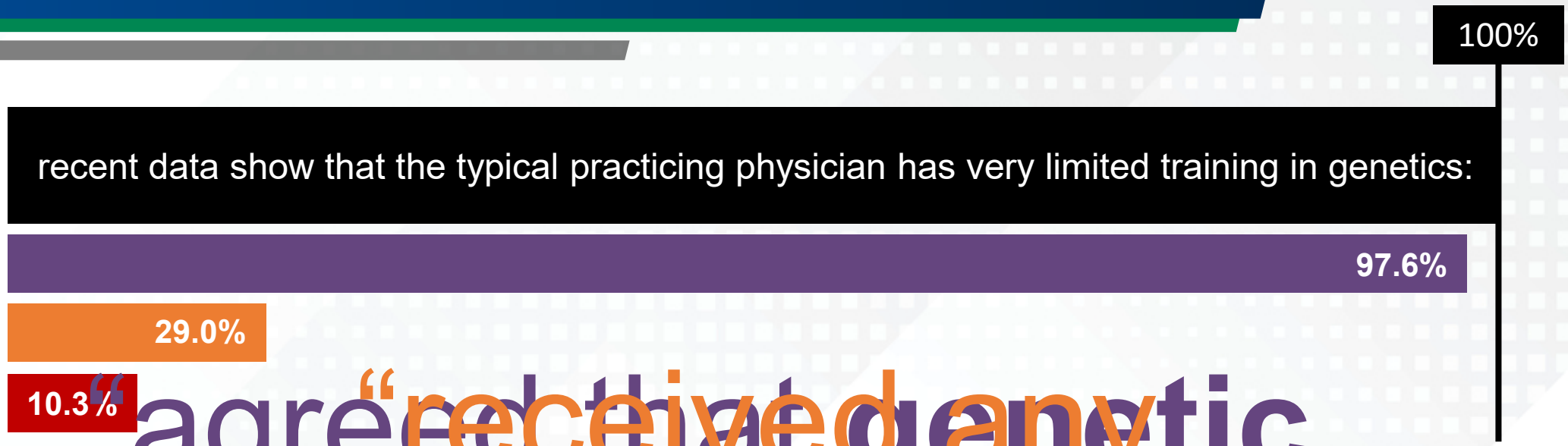
TRANSCEND ONSITE CARE

Creating excellence and value in everything we do

OptiMize360™

Why Pharmacist

10,303
Physicians



"agree that genetic variation influence pharmacogenomics"

"received any education about PGx testing"

"felt adequately informed"

OptiMed's Pharmacist Process

Team	Testing	Treatment	Therapy
Collaborative Agreement	**Advanced Findings**	**Personalized Plan**	**360º Care**
At OHP, we enter into a collaborative agreement with PCPs to order a consultation with the test	The pharmacist reviews the test results and runs a drug interaction report on the patient's current medication list	Pharmacist interprets the report findings and recommends treatment options or adjustments to patient's current medications	Results and reports are shared amongst the patient's clinical care team from prescriber to pharmacy to ensure consistent and streamlined care

Pharmacy Consult Information Request

GENEMARKERS

PGX Pharmacy Consultation Form

Genemarkers offers a pharmacy consultation service for PGX tests, performed upon request. There is no additional charge for this service. Trained pharmacists will provide clinical pharmacy consultations. This service will enhance the PGX report by providing additional drug-drug and drug-drug-gene interactions, identified with respect to the patient's disease states, medications, and supplements.

To include this service, please complete this form and return with the PGX Test Kit.

Patient Nar [redacted]	Date o [redacted]
Allergies:	

PGx Markers FULL Panel Report

GENEMARKERS

844 220 6231 | info@genemarkersllc.com

126 E. South Street | Kalamazoo | Michigan | 49007

Potentially Impacted Medications

Category	Class	Standard Precautions	Use With Caution	Consider Alternatives
Anticancer Agents	Antifolates	Methotrexate (Trexall)		
Cardiovascular	Angiotensin II Receptor Antagonists	Azilsartan (Edarbi, Edarbyclor) Candesartan (Atacand) Eprosartan (Teveten) Irbesartan (Avapro) Losartan (Cozaar, Hyzaar) Olmesartan (Benicar) Telmisartan (Micardis) Valsartan (Diovan, Entresto)		
	Antianginal Agents	Ranolazine (Ranexa)		
	Antiarrhythmics	Flecainide (Tambocor) Mexiletine (Mexitil) Propafenone (Rythmol)		
	Anticoagulants	Apixaban (Eliquis) Betrixaban (Bevyxxa) Dabigatran Etexilate (Pradaxa) Edoxaban (Savaysa) Fondaparinux (Arixtra) Rivaroxaban (Xarelto) Warfarin (Coumadin)		
	Antiplatelets	Clopidogrel (Plavix) Prasugrel (Effient)		

ng we do

Pharmacist Report

Genemarkers Sample ID#
DE-IDENTIFIED

Pharmacogenetic Testing Results

Pharmacy Consult Report

Patient Name: DE-IDENTIFIED	**Date of Birth:** DE-IDENTIFIED
Pharmacogenetic Test Panel Performed:	**Date of Sample Collection:** 6/7/2018

Recommendations:

Based on the patient's current medication list, current diagnoses, and pharmacogenetics testing results, the following recommendations should be considered:

Recommendation	Rationale
Substitute Fluoxetine for another anti-depressant such as sertraline, duloxetine, venlafaxine.	Use of other QTc prolonging medications with ziprasidone is contraindicated **[Highest risk of QTc prolongation].** Fluoxetine has shown to increase QTc interval and the patient is taking other QTc prolonging medications as needed (ondansetron). Fluoxetine also interacts with the patient's propranolol,

Pharmacist Report

Genemarkers Sample ID#
DE-IDENTIFIED

Potential Interactions Identified:

Drug(s)	Type*	Level of Severity	Discussion
Ziprasidone & Ondansetron & Fluoxetine	DD	Contraindicated	Ziprasidone is a high-risk drug for QTc prolongation and is contraindicated with the use of other QTc prolonging medications (ondansetron, cyclobenzaprine, fluoxetine).
Propranolol & Fluoxetine	DD	Major	Fluoxetine is a strong CYP2D6 inhibitor and propranolol is metabolized by CYP2D6. This may lead to increased serum levels of propranolol. Consider using an alternate SSRI or beta blocker, and monitor patient for bradycardia, hypotension, and other beta blocker related adverse effects.
Oxycodone/acetaminophen & topiramate & cyclobenzaprine & gabapentin & fioricet & geodon	DD	Major	CNS depressants may enhance the CNS depressant effect of oxycodone. These agents should only be combined if alternative treatment options are inadequate. If combined, limit dosages and duration of each drug to the minimum possible while achieving desired clinical

Limitations of Current Practice

- Current situation with current provider
- Most patients of chronic disease see **more than one provider** often with different EHR systems
- Patients do not often remember to **share key information with providers**
- There is **no good way to proactively address PGx** in EHR systems as well as provider education when **PGx is still limited**

Where we see our future with PGX

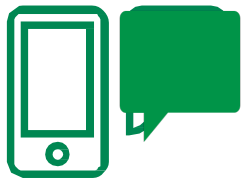
DPC and PBM Role

- Population Health & Risk Stratification
- Limit Initial Dispensing Quantities
- Coordinate Testing
- Integrate Point-of-Sale DUR Messaging
- Maximize Patient Outcomes and Value

Therapy

360º Care

Results and reports are shared amongst the patient's clinical care team from prescriber to pharmacy to ensure consistent and streamlined care



OptiMed
HEALTH PARTNERS

Thank you!

Andrew Reeves, R.Ph.

Chief Executive Officer

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Advancing Pharmacogenomics Practice and Research- Lessons Learned

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- Amy Pasternak: None
- Kristen Ward: None

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Objectives

1: Identify facilitators and barriers to pharmacogenomics (PGx) implementation and discuss potential strategies to overcome them.

2: Describe roles for pharmacists in implementing PGx into clinical practice.

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Outline

1. Overview of PGx benefits and challenges
2. Resources to guide implementation efforts
3. Initial implementation efforts at Michigan Medicine
    a. HLA-B*57:01 and abacavir
    b. PGx panels in psychiatry
4. Pharmacists' role in PGx implementation

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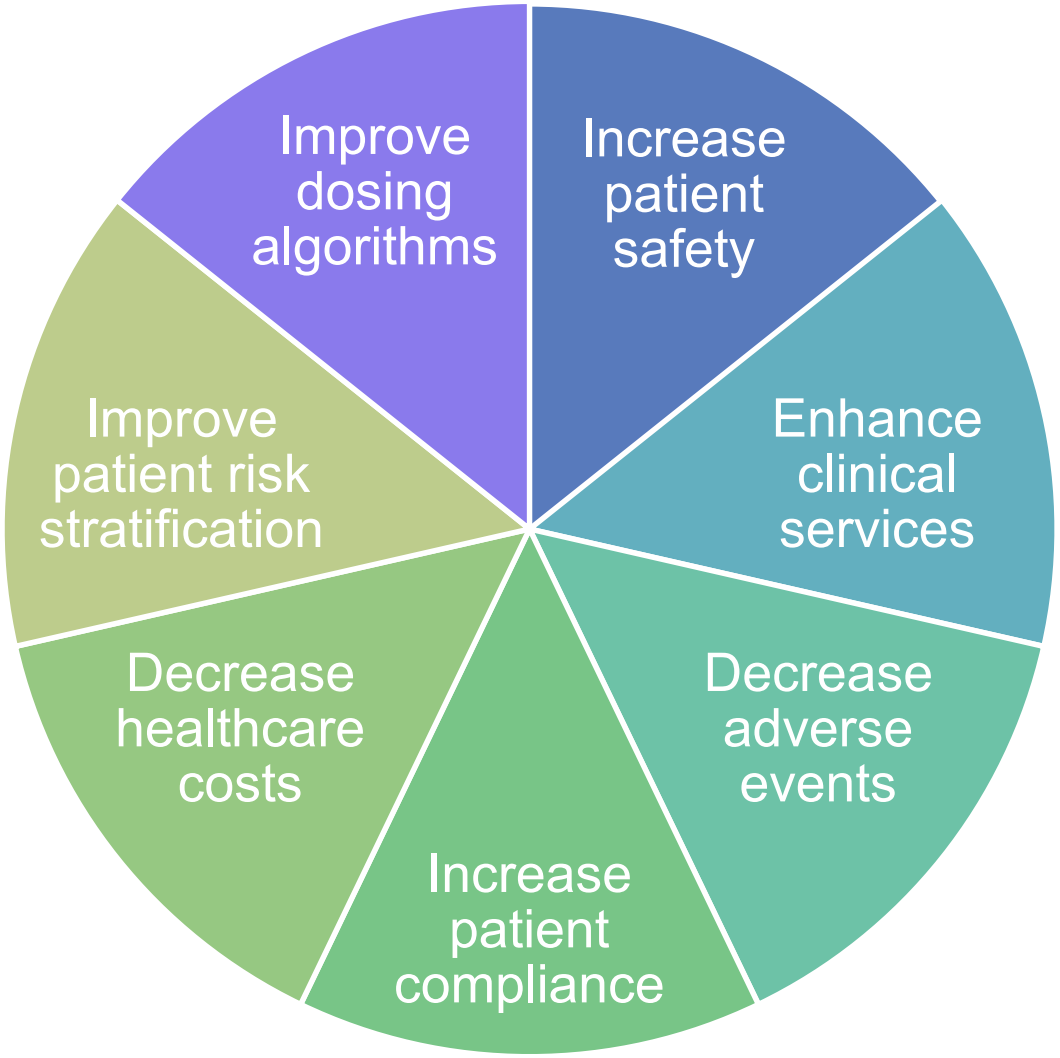
PGx implementation has the potential to:



Alessandrini et al. OMICS. 2016

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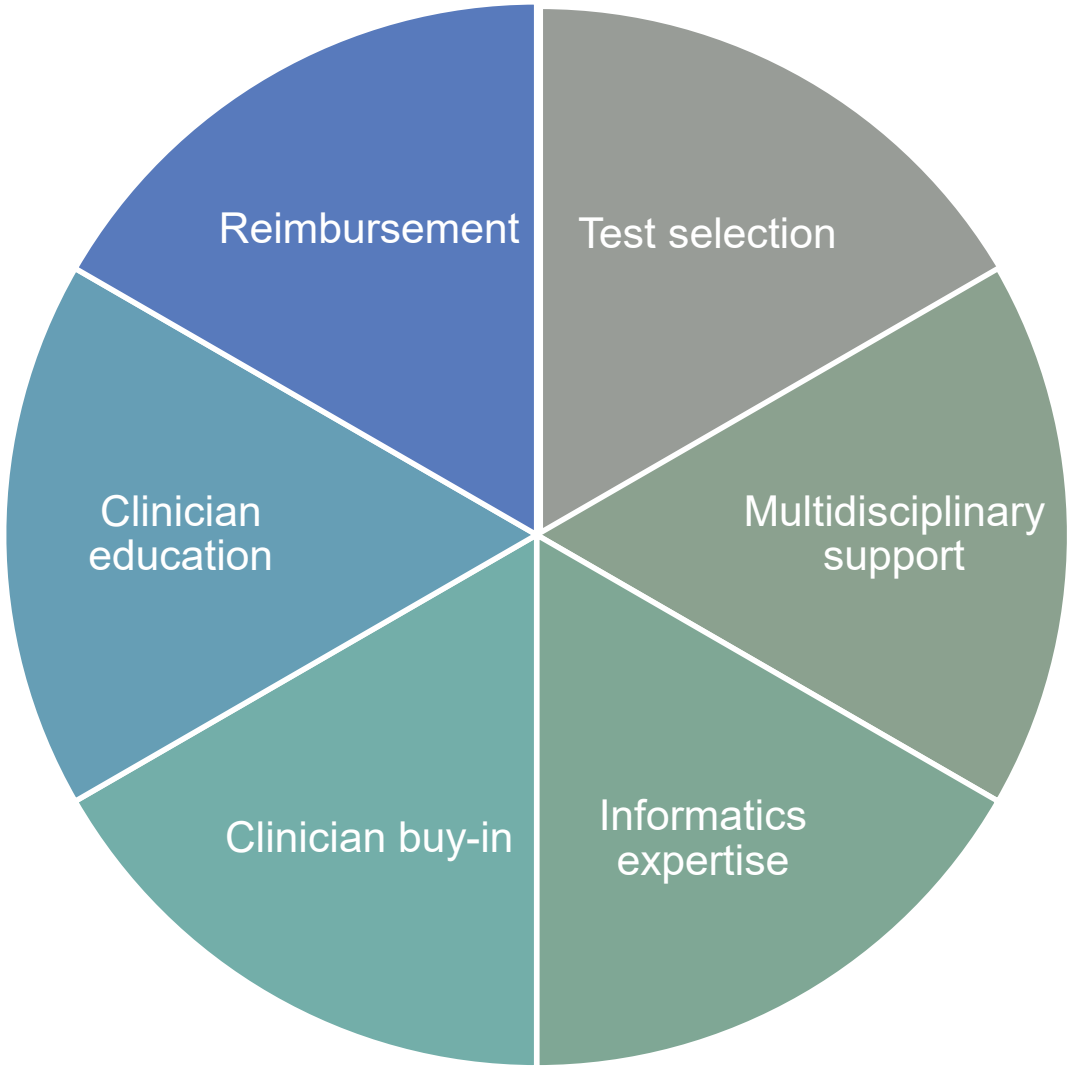
General challenges facing PGx implementation



Alessandrini et al. OMICS. 2016

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Overview of PGx implementation

- Not a question of if, but when, PGx will become routine clinical care
  - Pharmacists may not be aware of areas where this is already common practice
- Current workflows, electronic medical record features, and education strategies for clinicians create challenges for consistent implementation

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Overview of PGx implementation

- Multiple resources are available to determine the level of evidence of gene-drug pairs

CPIC®
Clinical Pharmacogenetics Implementation Consortium

cpicpgx.org

- International group that completes systematic reviews and publishes gene-drug dosing guidelines for high level of evidence gene-drug pairs
- Regularly updates guidelines
- Assumes preemptive testing will become standard practice
  - DO NOT recommend when to obtain testing

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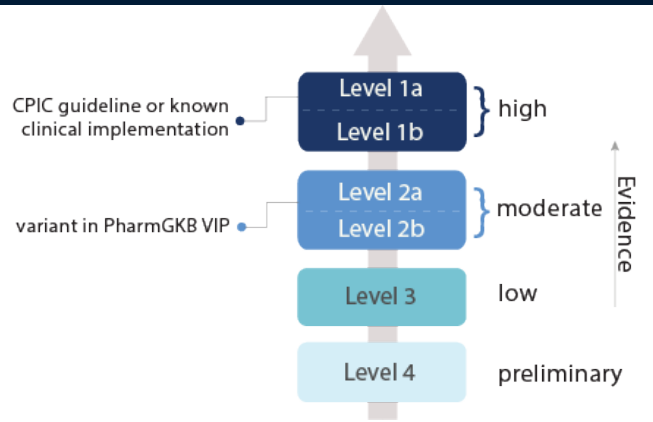
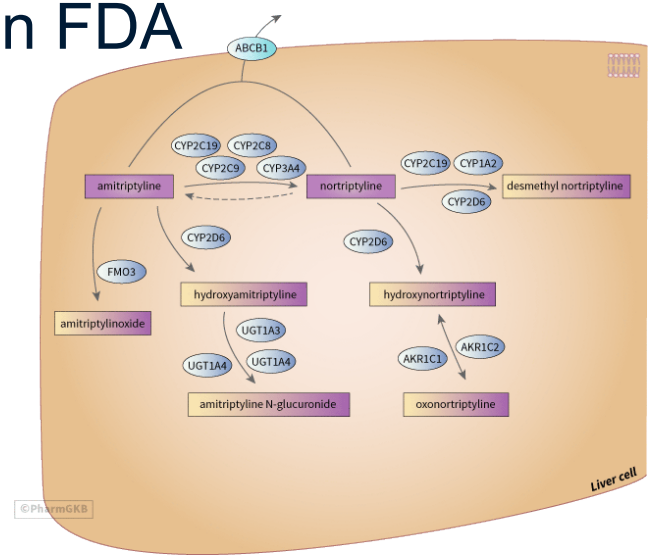
PGx Resources

PHARMGKB

pharmgkb.org



- NIH-funded resource on PGx
- Curates and categorizes information on all published drug-gene pairs into level of evidence
- Links to guidelines and PGx prescribing information based on FDA label
- Pharmacokinetic and pharmacokinetic drug pathways



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PGx Resources

FDA Biomarkers table
(https://www.fda.gov/Drugs/ScienceResearch/ucm572698.htm)

- Lists all medication with genetics included in package insert
  - Does not differentiate germline from somatic genetics
  - Not all are “actionable”

Drug	Therapeutic Area*	Biomarker†	Referenced Subgroup‡	Labeling Sections
Abacavir	Infectious Diseases	HLA-B	HLA-B*5701 allele carriers	Boxed Warning, Contraindications, Warnings and Precautions
Ado-Trastuzumab Emtansine	Oncology	ERBB2	HER2 protein overexpression or gene amplification positive	Indications and Usage, Warnings and Precautions, Adverse Reactions, Clinical Pharmacology, Clinical Studies
Afatinib	Oncology	EGFR	EGFR exon 19 deletion or exon 21 substitution (L858R) positive	Indications and Usage, Dosage and Administration, Adverse Reactions, Clinical Pharmacology, Clinical Studies
Alectinib	Oncology	ALK	ALK gene rearrangement positive	Indications and Usage, Adverse Reactions, Clinical Pharmacology, Clinical Studies
Alirocumab	Endocrinology	LDLR	LDL receptor mutation heterozygotes	Indications and Usage, Adverse Reactions, Clinical Studies

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PGx Implementation at Michigan Medicine

- A component of Precision Medicine efforts at Michigan Medicine
- Led by pharmacists with a variety of clinical and research backgrounds
- Initial steps
  - Evaluate current use of PGx testing to identify pilot services for initial projects
  - Identify physician champions
  - Collaborate with internal informatics group to understand options for results display and clinical decision support within the electronic medical record

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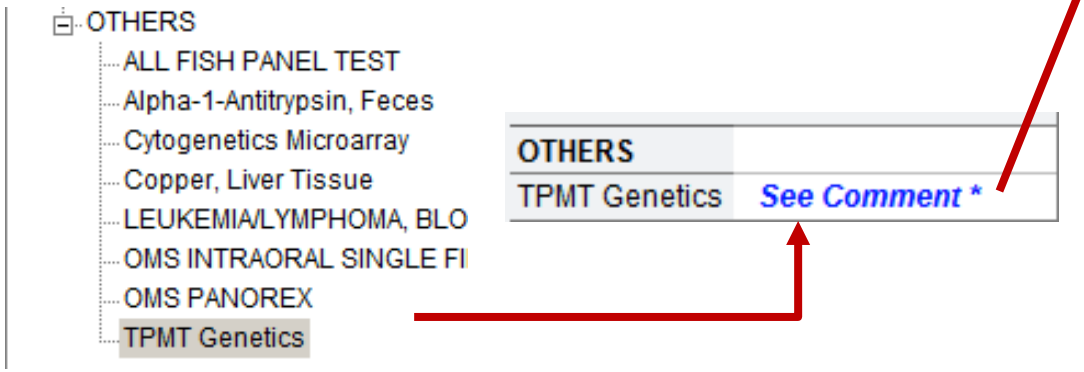
Identification of PGx testing at Michigan Medicine

PGx tests reported in medical record

Gene	Medication(s) with CPIC or FDA PGx
TPMT	Azathioprine, mercaptopurine, thioguanine
UGT1A1	Irinotecan, belinostat, atazanavir
HLA-B*57:01	Abacavir
HLA-B*1502	Carbamazepine, oxcarbazepine
IL28B/IFNL3	Peg-interferon



Resulting lab: PROMETHEUS LABS
Value: See Comment
Comment:

```
PROMETHEUS TPMT GENETICS
RESULTS:
ASSAY NAME                          RESULT      REFERENCE RANGE
Prometheus TPMT Genetics      TPMT*1/TPMT*1   TPMT*1/TPMT*1
           ALLELES PRESENT ARE ASSOCIATED WITH
                NORMAL ENZYME ACTIVITY
Prometheus TPMT Genetics is an analysis to determine an ability to
produce thiopurine methyltransferase(TPMT) activity. It is a method
to identify patients at risk for acute toxicity from 6-MP or
azathioprine. This profile provides a breakdown of a patient's
genetics. The distribution of TPMT activity is trimodal homozygous
normal (89%), heterozygous (11%) and homozygous recessive (0.3%) (1).
Approximately 1 in 1213 individuals may have a low TPMT enzyme
activity (homozygous low) resulting from known and theoretical
mutations that are not included in this panel.
NOTES: Genetic testing results are reported above as the individual
allele present on each chromosome for three different polymorphisms,
G238C, G460A, and A719G within the TPMT gene on chromosome 6. The
alleles are numbered based on order of discovery.
A combination of Cepheid Smart Mix Reagents with ABI (Applied
Biosystems Sequence Detection System) Prism 7500Fast allelic
discrimination was used in determining the presence or absence of 3
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Initial PGx implementation at Michigan Medicine: HLA-B*57:01

- Retrospective review of PGx tests identified:
  - Case of an HLA-B*57:01 positive patient being prescribed abacavir
  - 10% of patients had duplicate HLA-B*57:01 testing

- Implementation of abacavir and HLA-B*57:01 clinical decision support can improve patient safety and reduce healthcare expenditures

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Initial PGx implementation at MM: HLA-B*57:01

- Collaborated with pharmacy informatics to identify best practice advisory (BPA) strategies with current test reporting structure
  - Anticipate alerts will be active this Winter 2018
    - Recommend Pgx testing when missing
    - Warn against abacavir prescription when PGx test is positive
    - Recommend against duplicate PGx test

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Identification of PGx testing at Michigan Medicine

PGx tests external to medical record: panel testing in psychiatry and internal medicine

- Depression/ADHD
  - Often mentioned in clinical note
  - PDF report may be scanned into medical record
    - *Clinical decision support alerts aren't compatible with PDF results*

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Initial PGx implementation at Michigan Medicine: PGx panels in Psychiatry

- An initial implementation site due to interest and support from ambulatory psychiatry leadership
- All testing is currently done with commercial labs ordered outside Epic
- Current work includes developing a consult service, provider education, and standardized test ordering
  - Goals:
    - Ensure all results are entered into Epic
    - Provide an interpretation for clinicians and education for patients

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Initial PGx implementation at Michigan Medicine: PGx panels in Psychiatry

ANTIDEPRESSANTS

USE AS DIRECTED	MODERATE GENE-DRUG INTERACTION		SIGNIFICANT GENE-DRUG INTERACTION	
desvenlafaxine (Pristiq®)	**trazodone** (Desyrel®)	1	**bupropion** (Wellbutrin®)	1,6
levomilnacipran (Fetzima®)	**venlafaxine** (Effexor®)	1	**mirtazapine** (Remeron®)	1,6
vilazodone (Viibryd®)	**selegiline** (Emsam®)	2	**amitriptyline** (Elavil®)	3,8
	fluoxetine (Prozac®)	1,4	**clomipramine** (Anafranil®)	1,6,8
	citalopram (Celexa®)	3,4	**desipramine** (Norpramin®)	1,6,8
	escitalopram (Lexapro®)	3,4	**doxepin** (Sinequan®)	1,6,8
	sertraline (Zoloft®)	3,4	**duloxetine** (Cymbalta®)	1,6,8
			imipramine (Tofranil®)	1,6,8
			nortriptyline (Pamelor®)	1,6,8
			vortioxetine (Trintellix®)	1,6,8
			fluvoxamine (Luvox®)	1,4,6,8
			paroxetine (Paxil®)	1,4,6,8

https://genesight.com/wp-content/uploads/GeneSight_Psychotropic_Sample.pdf

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Initial PGx implementation at Michigan Medicine: PGx panels in Psychiatry

PATIENT GENOTYPES AND PHENOTYPES

PHARMACOKINETIC GENES (PK)

CYP1A2 — **Extensive (Normal) Metabolizer**
*1/*1

This genotype is most consistent with the extensive (normal) metabolizer phenotype.

CYP2B6 — **Intermediate Metabolizer**
*1/*6

CYP2B6*1 allele enzyme activity: Normal
CYP2B6*6 allele enzyme activity: Reduced

This genotype is most consistent with the intermediate metabolizer phenotype. This patient may have reduced enzyme activity as compared to individuals with the normal phenotype.

CYP2D6 — **Poor Metabolizer**
*4/*4 (Duplication)

CYP2D6*4 allele enzyme activity: None
CYP2D6*4 allele enzyme activity: None

This genotype is most consistent with the poor metabolizer phenotype. This patient may have reduced enzyme activity as compared to individuals with the normal phenotype.

A duplication of the gene CYP2D6 has been detected in this patient. While current genotyping techniques allow for the detection of this duplication, in the case of heterozygosity, such techniques do not allow for the identification of the allele that has been duplicated. This duplication, depending on the allele duplicated, can result in increased expression of CYP2D6.

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https://genesight.com/wp-content/uploads/GeneSight_Psychotropic_Sample.pdf

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Pharmacist's roles in PGx implementation

- Unique understanding of pharmacokinetics, pharmacodynamics and PGx puts pharmacy at an advantage for leading PGx implementation efforts

- Key roles:
  - Provider and patient education
  - Patient care recommendations
  - Evaluate outcomes of implementation strategies
    - Clinical or economic

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PGx Research and Future Goals

- Tracking outcomes of PGx-guided prescribing
- Implementation science evaluations to identify barriers and facilitators to PGx implementation across the health system
- Identifying educational needs for patients and health care providers

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Thank you for your time!

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Pharmacists, Pharmacogenomics (PGx) and the Public

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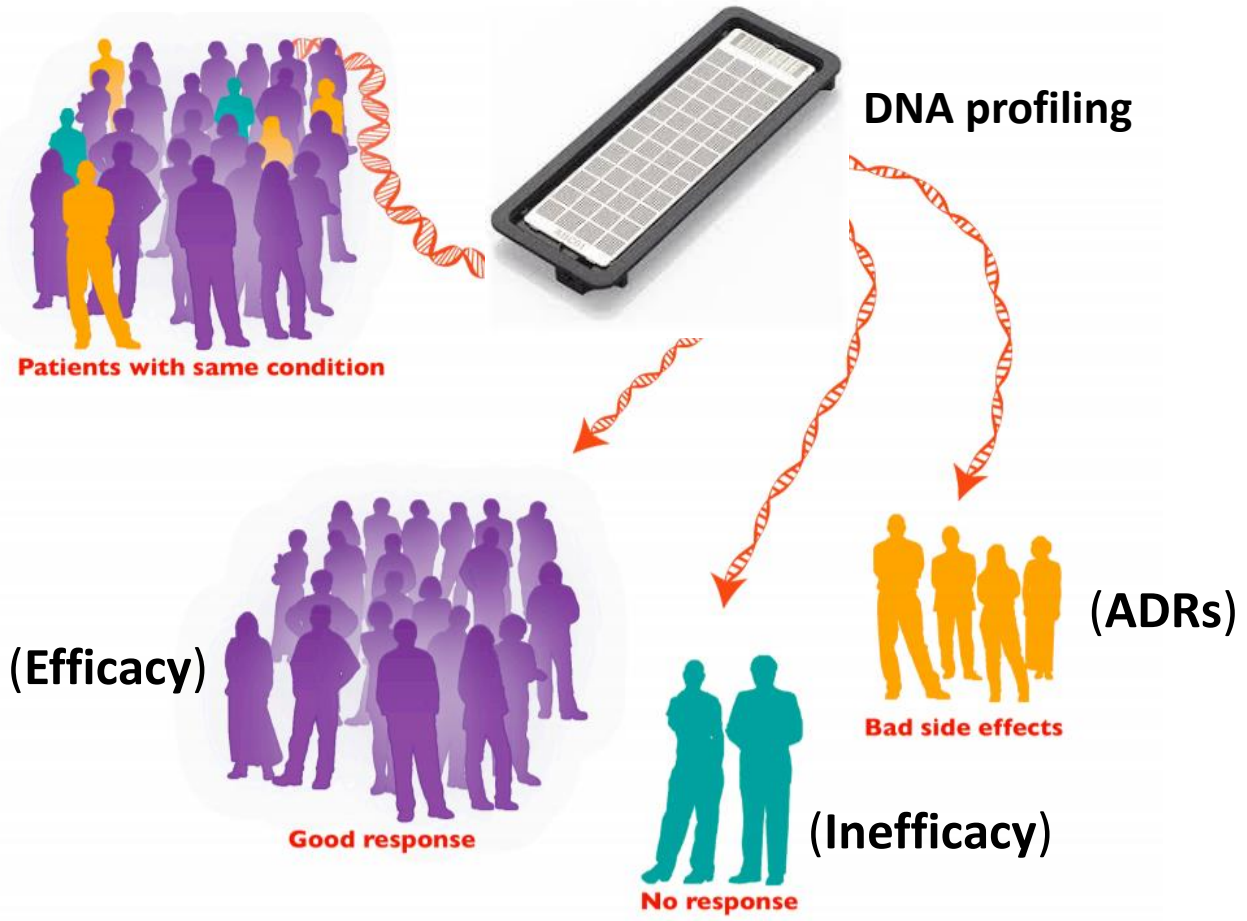
PGx: Drug Inefficacy • Adverse Drug Reactions

- The relationship between an individual's genetic make-up (DNA; genes) and their response to medications.



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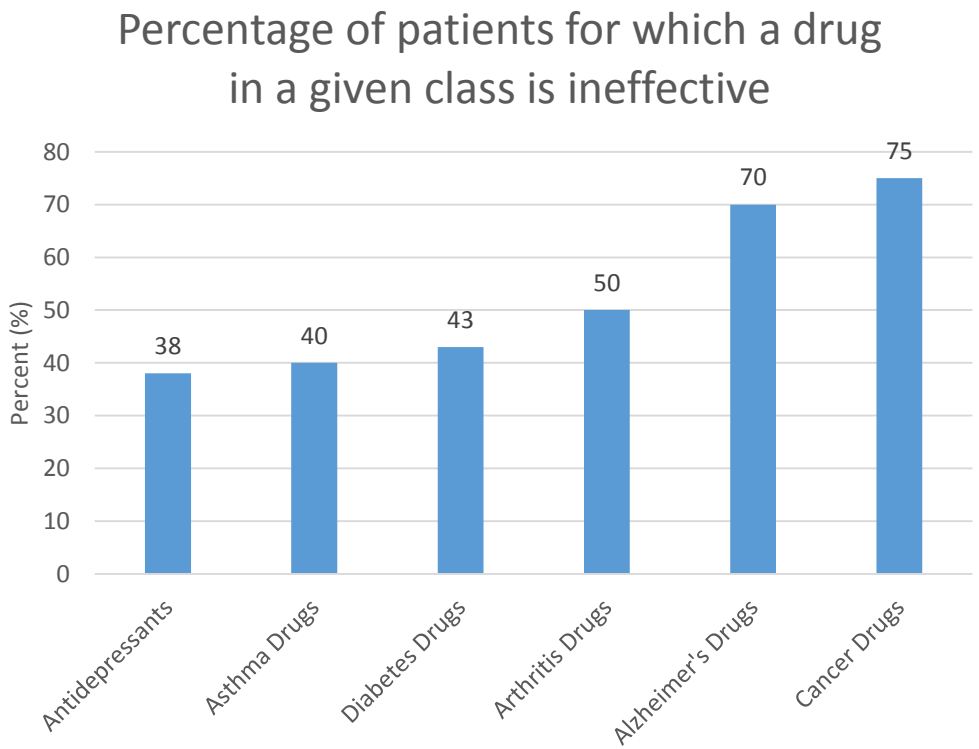
PGx: Drug Inefficacy • Adverse Drug Reactions

Inefficacy

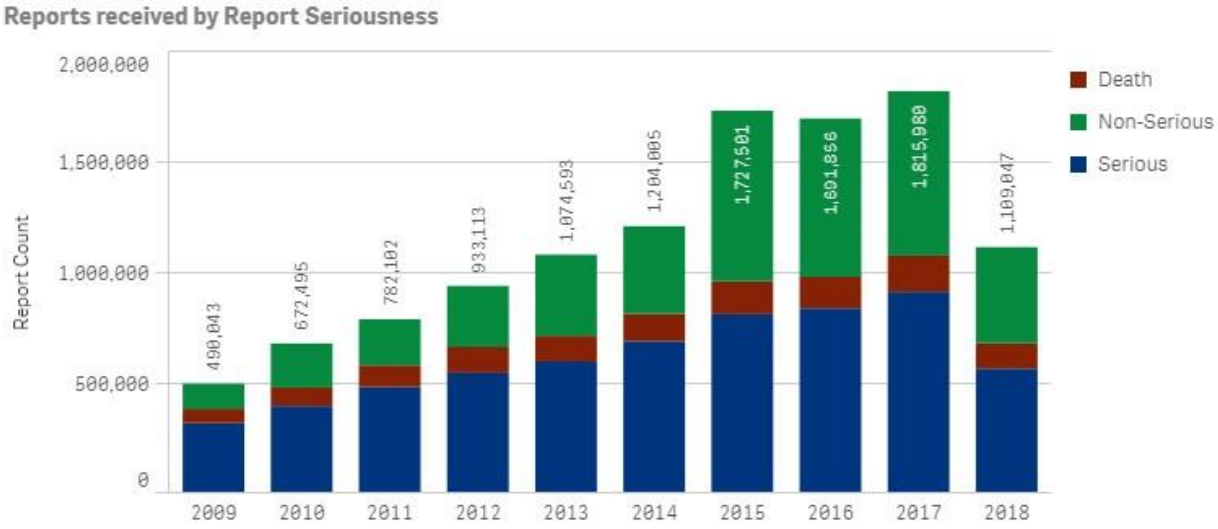


Adverse Drug Reactions/Events

2008 – 2017

Serious: 5,804,622

Deaths: 1,109,868



Adapted from: Spear BB, Heath-Chiozzi M, Huff J. Clinical application of pharmacogenetics. Trends in Molecular Medicine. 7(5):201-204, 2001.

FDA Adverse Event Reporting System (FAERS) is a database. https://fis.fda.gov/sense/app/777e9f4d-0cf8-448e-8068-f564c31baa25/sheet/7a47a261-d58b-4203-a8aa-6d3021737452/state/analysis. Accessed Sep 26, 2018.

PGx: Drug Inefficacy • Adverse Drug Reactions • Safety

Gene	Metabolism Phenotype	Drug (Standard Dose)	Potential Response	Outcome
CYP2C19	Normal (NM)	Clopidogrel # of prescriptions 2015: 21,312,667[+]	Desired antiplatelet effect	Efficacy
	Intermediate (IM)	Clopidogrel	Stent thrombosis - death	Inefficacy
CYP2C9	NM	Warfarin # of prescriptions 2015: 20,760,075[+]	Desired anticoagulation	Efficacy
	Poor (PM)	Warfarin	Bleeding - death	Adverse Drug Reaction
CYP2D6	NM	Codeine # of prescriptions 2013: 11,225,000[++]	Desired analgesic effect	Efficacy
	PM	Codeine	Pain	Inefficacy
	Ultrarapid (UM)	Codeine	Morphine overdose - death	Adverse Drug Reaction

[+]ClinCalc DrugStats Database. http://clincalc.com/DrugStats/. Accessed May 17, 2018.
[++]MD Magazine. http://www.mdmag.com/medical-news/top-10-painkillers-in-us. Accessed May 17, 2018.

Increased Sensitivity to Amitriptyline (CYP2C19 *1/*17 Rapid Metabolizer)

		Standard Precautions	Use with Caution	Consider Alternatives
Informative	Antidepressants	Amoxapine (Amoxapine®) Desipramine (Norpramin®) Desvenlafaxine (Pristiq®) Duloxetine (Cymbalta®) Fluoxetine (Prozac®, Sarafem®) Fluvoxamine (Luvox®) Levomilnacipran (Fetzima®) Maprotiline (Ludiomil®) Mirtazapine (Remeron®) Nefazodone (Serzone®) Nortriptyline (Pamelor®) Paroxetine (Paxil®, Brisdelle®) Protriptyline (Vivactil®) Trazodone (Oleptro®) Venlafaxine (Effexor®) Vilazodone (Viibryd®) Vortioxetine (Trintellix®)	Sertraline (Zoloft®)	Amitriptyline (Elavil®) Citalopram (Celexa®) Clomipramine (Anafranil®) Doxepin (Silenor®) Escitalopram (Lexapro®) Imipramine (Tofranil®) Trimipramine (Surmontil®)

Insufficient Response to Citalopram (CYP2C19 *1/*17 Rapid Metabolizer)

Actionable

	Standard Precautions	Use with Caution	Consider Alternatives
Antidepressants	Amoxapine (Amoxapine®) Desipramine (Norpramin®) Desvenlafaxine (Pristiq®) Duloxetine (Cymbalta®) Fluoxetine (Prozac®, Sarafem®) Fluvoxamine (Luvox®) Levomilnacipran (Fetzima®) Maprotiline (Ludiomil®) Mirtazapine (Remeron®) Nefazodone (Serzone®) Nortriptyline (Pamelor®) Paroxetine (Paxil®, Brisdelle®) Protriptyline (Vivactil®) Trazodone (Oleptro®) Venlafaxine (Effexor®) Vilazodone (Viibryd®) Vortioxetine (Trintellix®)	Sertraline (Zoloft®)	Amitriptyline (Elavil®) Citalopram (Celexa®) Clomipramine (Anafranil®) Doxepin (Silenor®) Escitalopram (Lexapro®) Imipramine (Tofranil®) Trimipramine (Surmontil®)

Insufficient response to omeprazole, pantoprazole

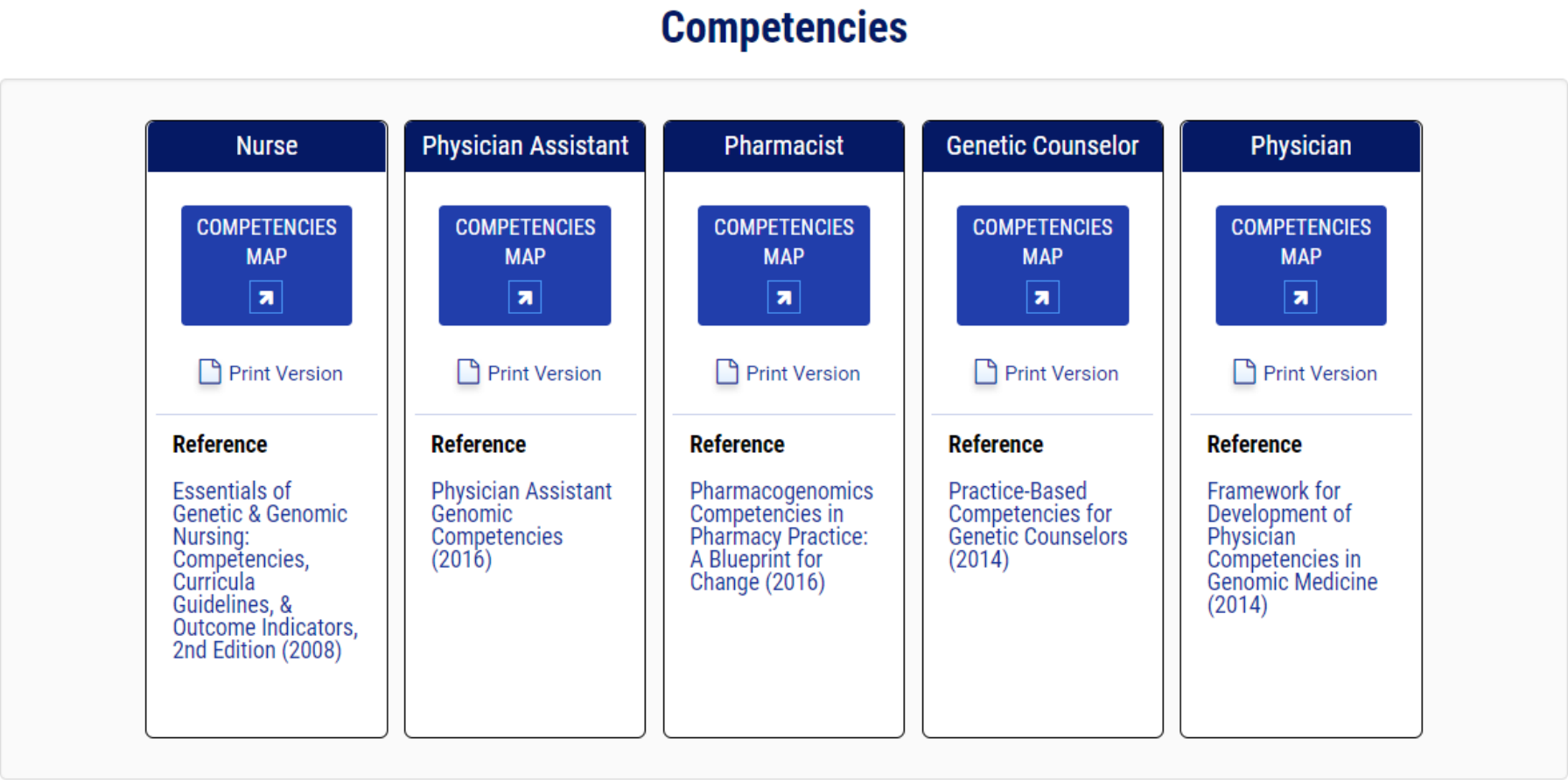
PGx: Drug Inefficacy • Adverse Drug Reactions

Pharmacist Competencies in Genetics/Genomics[+] Nurse•Physician Assistant•**Pharmacist**•Genetic Counselor•Physician	**ASHP: Pharmacists Role in Pharmacogenomics[++]**
Basic Genetic Concepts (B; four statements) • *Shared*	All pharmacists: • 4 items Pharmacists with **Specialized Education/Experience in PGx** • 13 additional items
Genetics and Disease (G; three statements) • *Shared*	
Pharmacogenetics/Pharmacogenomics (P; three statements) • ***Pharmacists Specifically***	
Ethical, Legal and Social Implications (E; five statements) • *Shared*	

[+]Roederer MW, Kuo GM, Kisor DF, et al. Pharmacogenomics competencies in pharmacy practice: A blueprint for change. J Am Pharm Assoc. 2017 ;57(1):120-125.

[++] ASHP Statement on the Pharmacist's Role in Clinical Pharmacogenomics. https://www.ashp.org/-/media/assets/policy-guidelines/docs/statements/pharmacists-role-clinical-pharmacogenomics.ashx?la=en&hash=AB636D7DAAEFFCAE8CAC1D575BAA82D0A2F138FF. Accessed May 17, 2018.

G2C2-Genetics Genomics Competency Center



Roederer MW, Kuo GM, Kisor DF, et al. Pharmacogenomics competencies in pharmacy practice: A blueprint for change. J Am Pharm Assoc. 2017 ;57(1):120-125.
G2C2 competency maps. https://genomicseducation.net/competency accessed September 26, 2018

Pharmacist Competencies in PGt/PGx

P: PHARMACOGENETICS/PHARMACOGENOMICS

P1: To demonstrate an understanding of how genetic variation in a large number of proteins, including drug transporters, drug metabolizing enzymes, direct protein targets of drugs, and other proteins (e.g. signal transduction proteins) influence pharmacokinetics and pharmacodynamics related to pharmacologic effect and drug response

P2: To understand the influence (or lack thereof) of ethnicity in genetic polymorphisms and associations of polymorphisms with drug response

P3: Recognize the availability of evidence based guidelines that synthesize information relevant to genomic/pharmacogenomic tests and selection of drug therapy (e.g. Clinical Pharmacogenomics Implementation Consortium)

Roederer MW, Kuo GM, Kisor DF, et al. Pharmacogenomics competencies in pharmacy practice: A blueprint for change. J Am Pharm Assoc. 2017 ;57(1):120-125.
G2C2 competency maps. https://genomicseducation.net/competency accessed September 26, 2018

Pharmacy Education In Pharmacogenomics

Student Pharmacists

- First required by ACPE – July 2016
  - **Genetic basis for** disease and individual **differences in metabolizing enzymes, transporters, and other biochemicals** impacting drug disposition and action that underpin the practice of **personalized medicine**.
  - Emphasis on patient safety, clinical efficacy, **pharmacogenomic** and pharmacoeconomic considerations, and treatment of patients across the lifespan.

- PGY2 Residencies
  - Limited number of slots nationwide. UF and St. Jude Children's Research Hospital

- Dual Degree Program (Manchester 2018)

Pharmacy Education In Pharmacogenomics: Manchester University

Pharmacists

- First Certification Program[+]
  - April/May 2015 Manchester University @Fort Wayne, IN
  - Repeated August/September 2016 @Indianapolis, IN
  - Planned October 2018 @Fort Wayne, IN

- University of Pittsburgh, University of Colorado, University of Florida, others

- First Online
  - Manchester University/RxGenomix/APhA

[+] Kisor DF, Bright DR, Chen J, Smith TR. Academic and professional pharmacy education: a pharmacogenomics certificate training program. Per Med. 2015;12(6),563–573.

Pharmacy Education In Pharmacogenomics: Manchester University

Dual Degree Program

- Summer 2018 P1 → P2 – 7 students;
- Summer P2 → P3;
- At least one PGx APPE rotation;
- Graduate in the same time period as their pharmacy colleagues.

Intervening in the Opioid Epidemic in the US:
Educating Health Professionals –
Challenges, Successes and Unintended Consequences

2018

Norman Kahn MD CPE

Convener, Conjoint Committee on Continuing Education (CCCE)

nkahn@cmss.org

Disclosure

- Convener, Conjoint Committee on Continuing Education (CCCE)
- 2008-2017: EVP/CEO Council of Medical Specialty Societies (CMSS) –
  - Hosting organization of CCCE

Conjoint Committee on Continuing Education (CCCE) Member Organizations (n=25)

Accreditation Council for Continuing Medical Education

Accreditation Council for Graduate Medical Education

Accreditation Council for Pharmacy Education

Alliance for Continuing Education in the Health Professions

American Academy of Family Physicians

American Association of Colleges of Nursing

American Association of Colleges of Osteopathic Medicine

American Academy of Physician Assistants

American Board of Medical Specialties

American College of Physicians

American Dental Association Commission for Continuing Education Provider Recognition

American Dental Education Association

American Hospital Association

American Medical Association

American Nurses Credentialing Center

American Osteopathic Association

Association for Hospital Medical Education

Association of American Medical Colleges

Council of Medical Specialty Societies

Federation of State Medical Boards

Hospice and Palliative Nurses Association (HPNA)

Medbiquitous Consortium

National Association of Boards of Pharmacy

National Board of Medical Examiners

Society for Academic Continuing Medical Education

Conjoint Committee on Continuing Education: Objectives

The CCCE's goal is to use accredited continuing education to improve the performance of the U.S. health care system.

The CCCE's strategic focus is to facilitate the education of prescribers of opioid analgesics, and their practice teams, in Risk Evaluation and Mitigation Strategies (REMS).

The CCCE member health professional organizations are using educational tools to impact the public health crisis of unintended deaths from prescription opioid analgesics.

Conjoint Committee on Continuing Education (CCCE), FDA and RPC

- FDA
  - Opioid Analgesic REMS Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain
- REMS Program Companies (RPC)
  - Collaboration to address Opioid Risk Evaluation and Mitigation Strategies (REMS) through clinician education

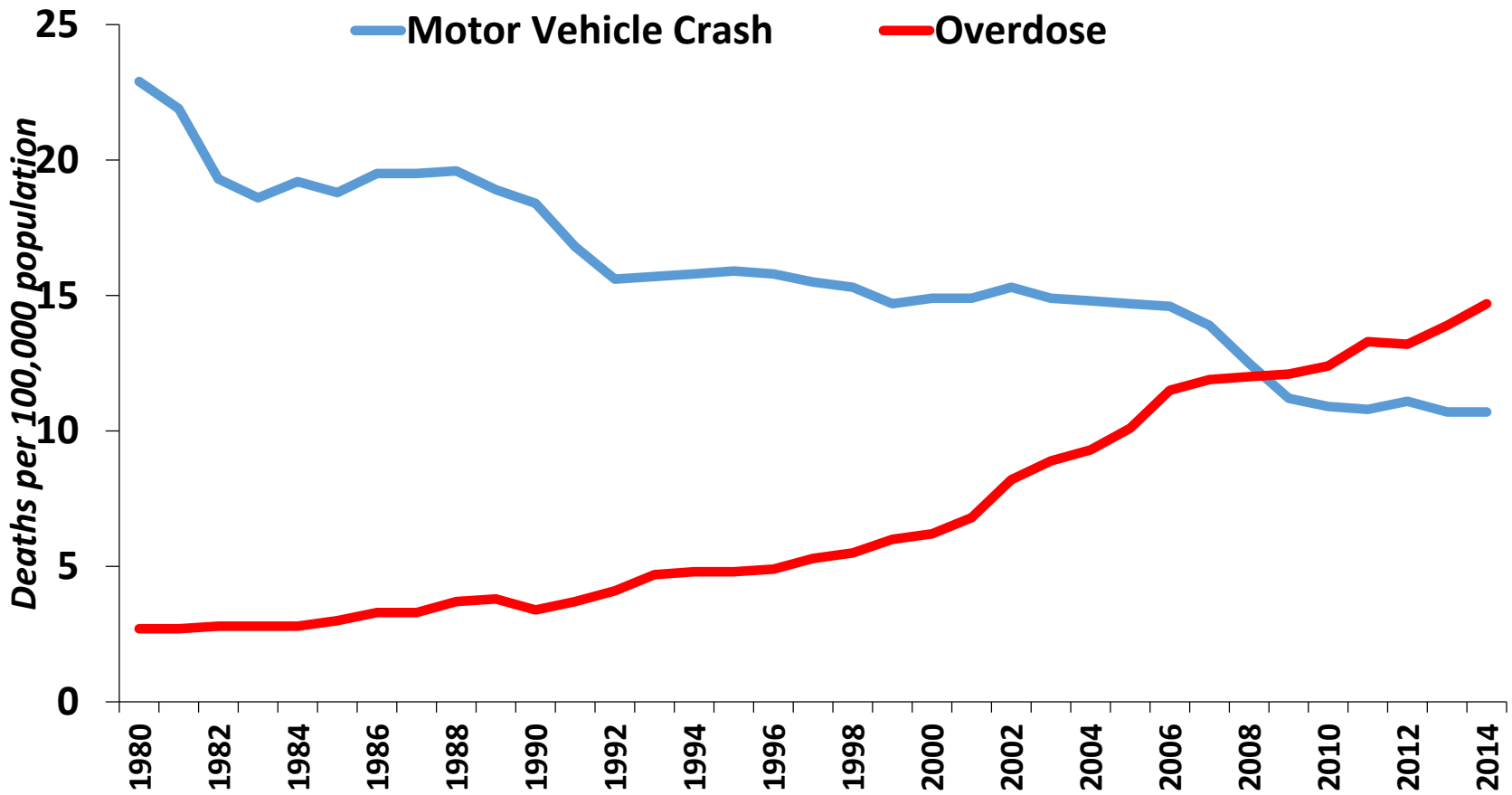
REMS Program Companies (RPC): 2017 (n=35/42)

- 3M Company
- Allergan Sales, LLC
- Apotex Inc.
- Aurolife Pharma, LLC
- BioDelivery Sciences International, Inc.
- Collegium Pharmaceutical, Inc.
- Daiichi Sankyo, Inc.
- Depomed, Inc.
- Egalet Corporation
- Elite Laboratories,Inc.
- Endo Pharmaceuticals Inc.
- Epic Pharma, LLC
- Hikma Pharmaceuticals USA, Inc.
- Impax Laboratories, Inc.
- Janssen Pharmaceuticals, Inc.
- Lupin Pharmaceuticals, Inc.
- Mallinckrodt, Inc.
- Mayne Pharma Inc.
- Mylan Inc.
- Nesher Pharmaceuticals (USA)
- Novel Laboratories, Inc.
- Osmotica Pharmaceutical Corp.
- Paddock Laboratories, LLC
- Par Pharmaceutical, Inc.
- Pernix Therapeutics Holdings, Inc.
- Pfizer, Inc.
- Purdue Pharma L.P.
- Ranbaxy Pharmaceuticals, Inc.
- Rhodes Pharmaceuticals L.P.
- Sandoz Inc.
- SpecGx LLC
- Sun Pharmaceutical Industries, Inc.
- Teva Pharmaceuticals USA LLC
- The PharmaNetwork LLC
- Upsher-Smith Laboratories, LLC
- VistaPharm, Inc.

National Landscape

- FDA
- CDC
- NIDA
- SAMHSA
- HRSA
- HHS
- AHRQ
- ONDCP
- DEA
- Surgeon General
- President’s Commission
- “Public Health Emergency”
- NGA
- *NAM*

Overdose Deaths in US- all types



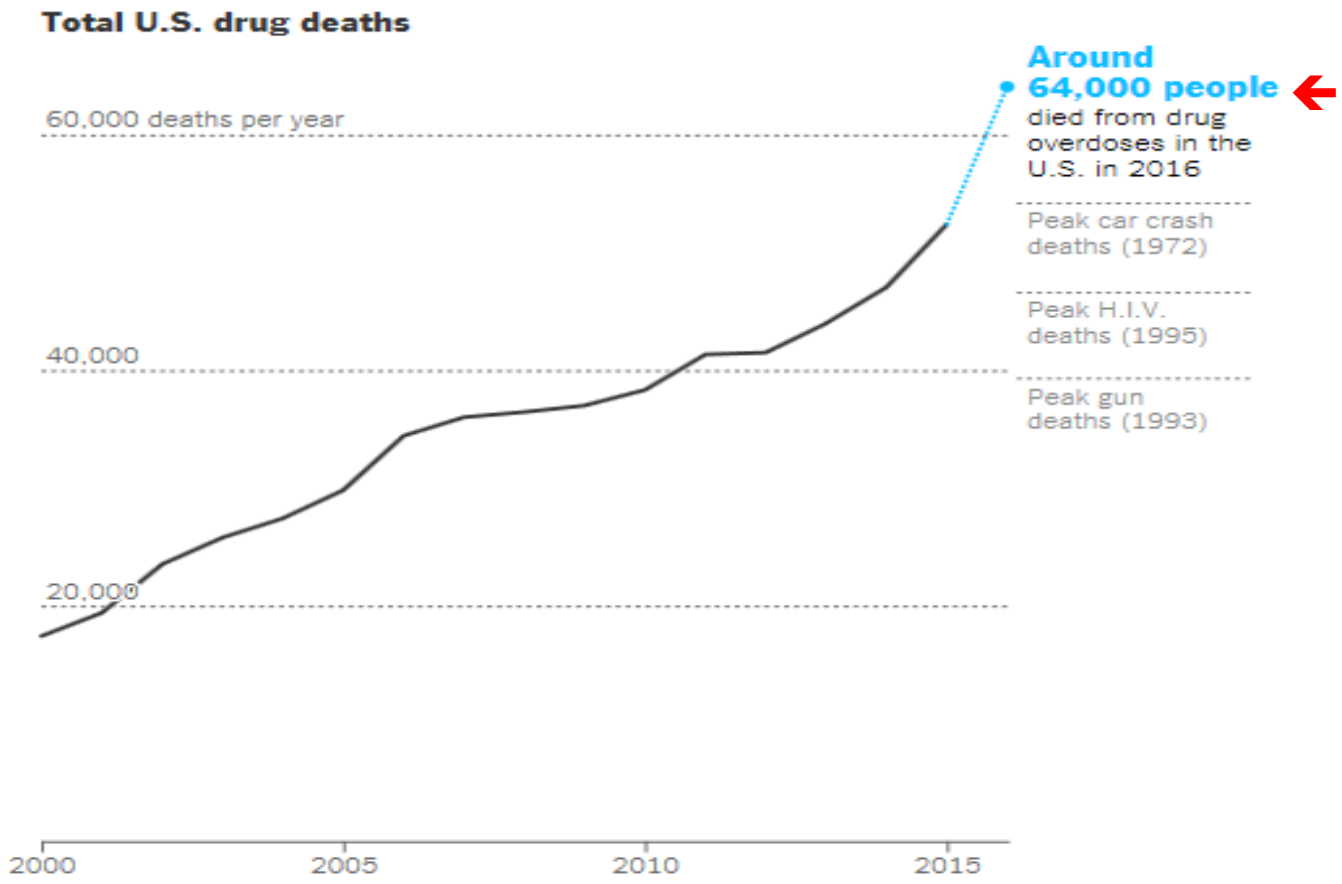
Source: National Center for Health Statistics

Opioid Epidemic – 19th Century US

- An estimated two million people used opiates to stem pain during and after the Civil War
- Between the1870's and 1880's, America's per capita consumption of opiates tripled
- Aggressive marketing and over-prescribing of painkillers resulted in opiate addiction
- Congress introduced a new law to reform painkiller prescribing: the first law to criminalize drug use, the Harrison Narcotic Act of 1915
  - Taxed narcotics, prohibited using narcotics in the treatment of addiction
- *The Guardian, US Edition, December 2017*

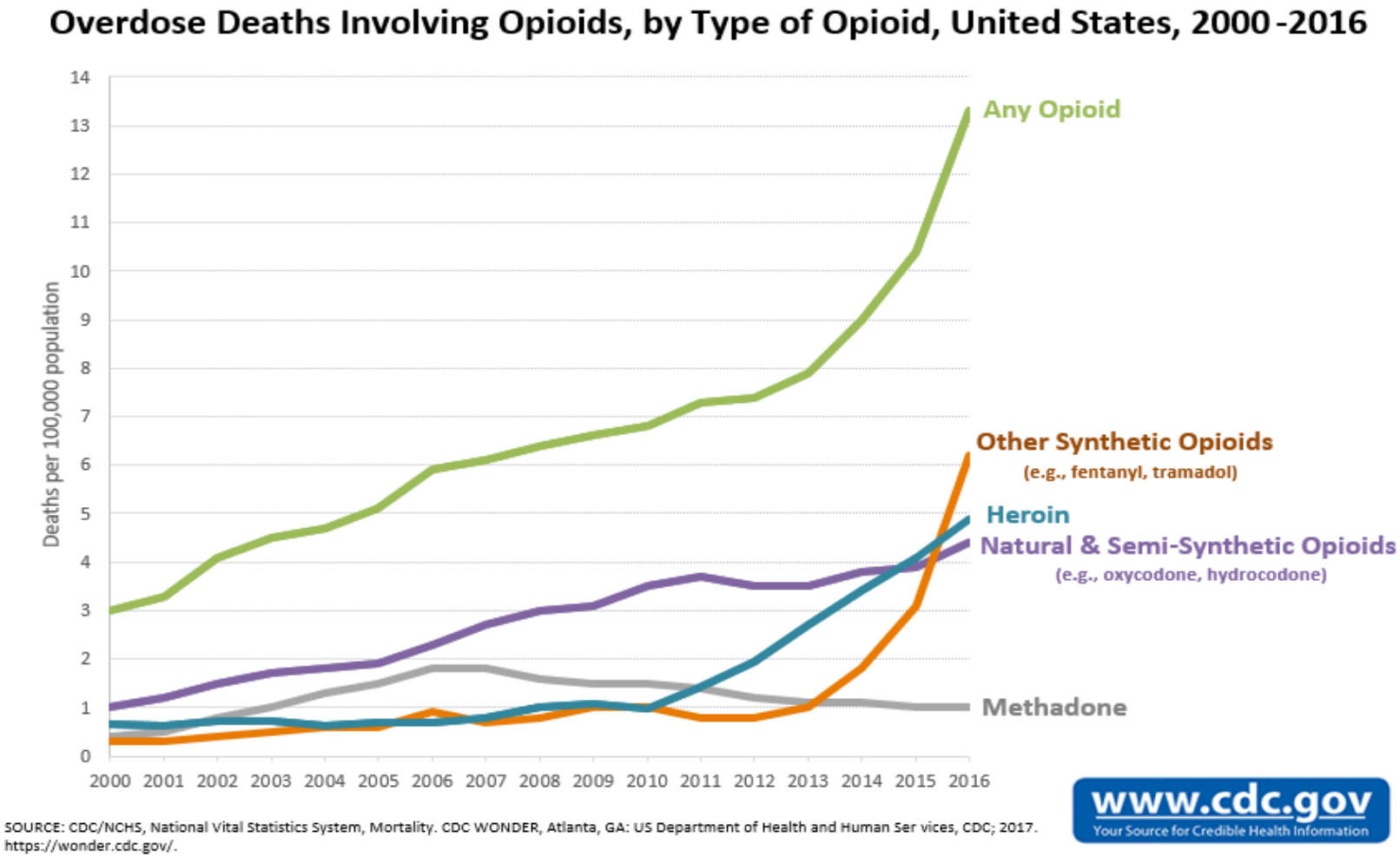
Drug overdose deaths in the United States: Continued to increase in 2016

New York Times, September 2, 2017



Source: National Center for Health Statistics, Centers for Disease Control and Prevention

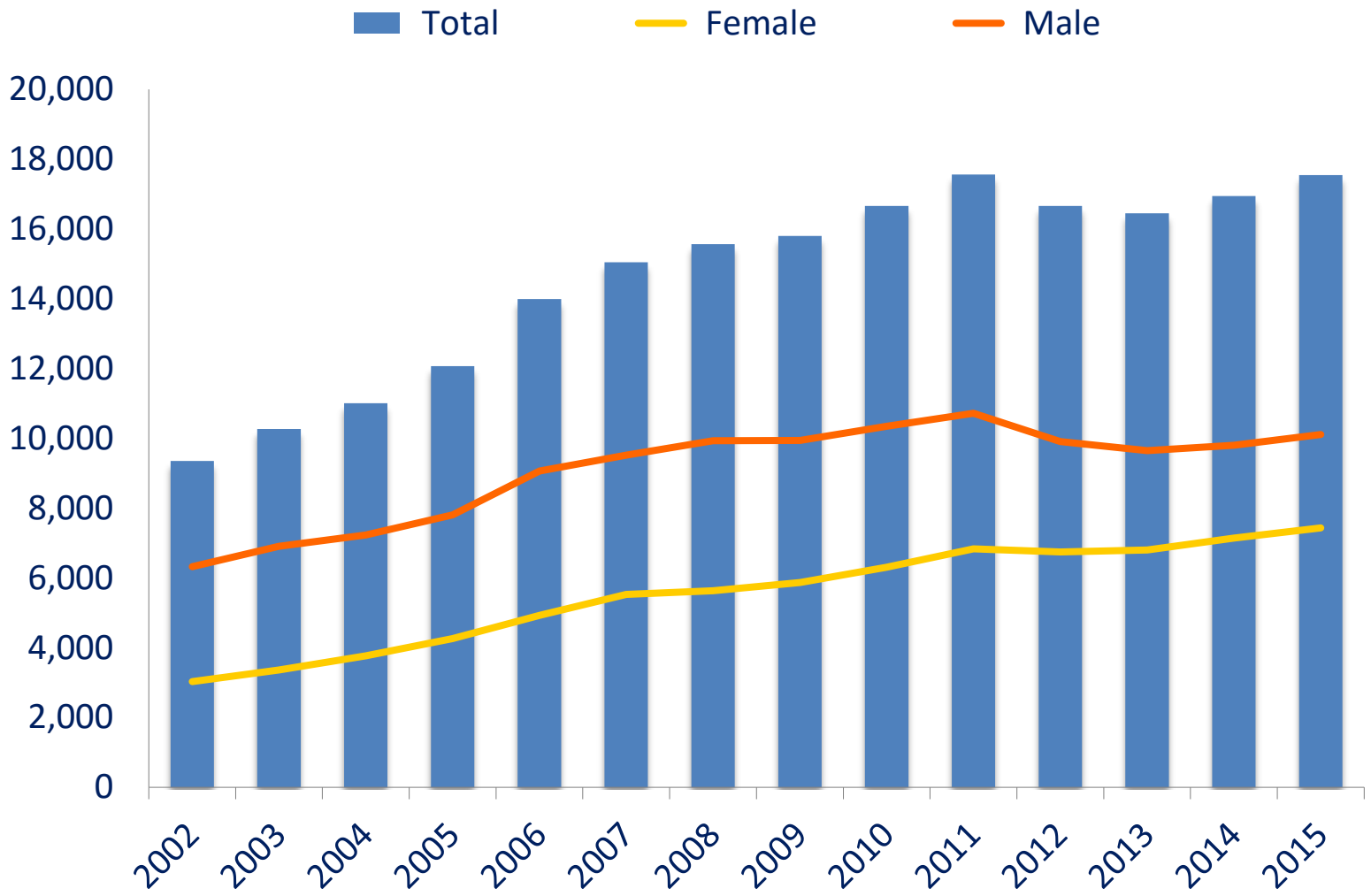
Opioid Deaths



National Institute on Drug Abuse

National Overdose Deaths

Number of Deaths Involving Prescription Opioid Pain Relievers (excluding non-methadone synthetics)



Source: National Center for Health Statistics, CDC Wonder

National Overdose Deaths

Number of Deaths from Heroin

Source: National Center for Health Statistics, CDC Wonder

The epidemic is national.

78 people

die every day from heroin and opioid overdoses in the U.S.

Source: National Vital Statistics System, Mortality file

5% of World's Population

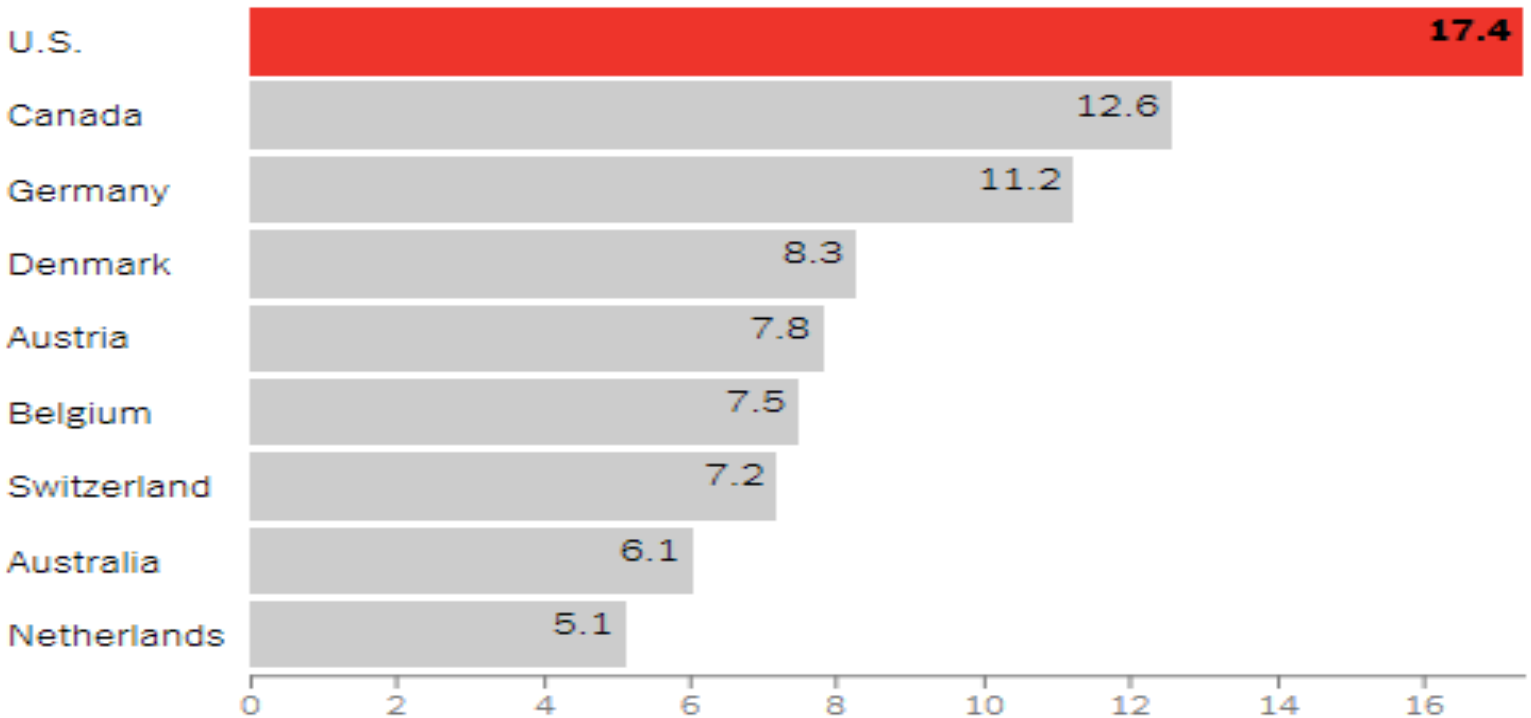
80% of World's Opioid Painkillers

99% of World's Vicodin

The influence of prescription monitoring programs on chronic pain management, Pain Physician, 2009

International Narcotics Control Board Report, 2008

Average days of opioid use per resident per year

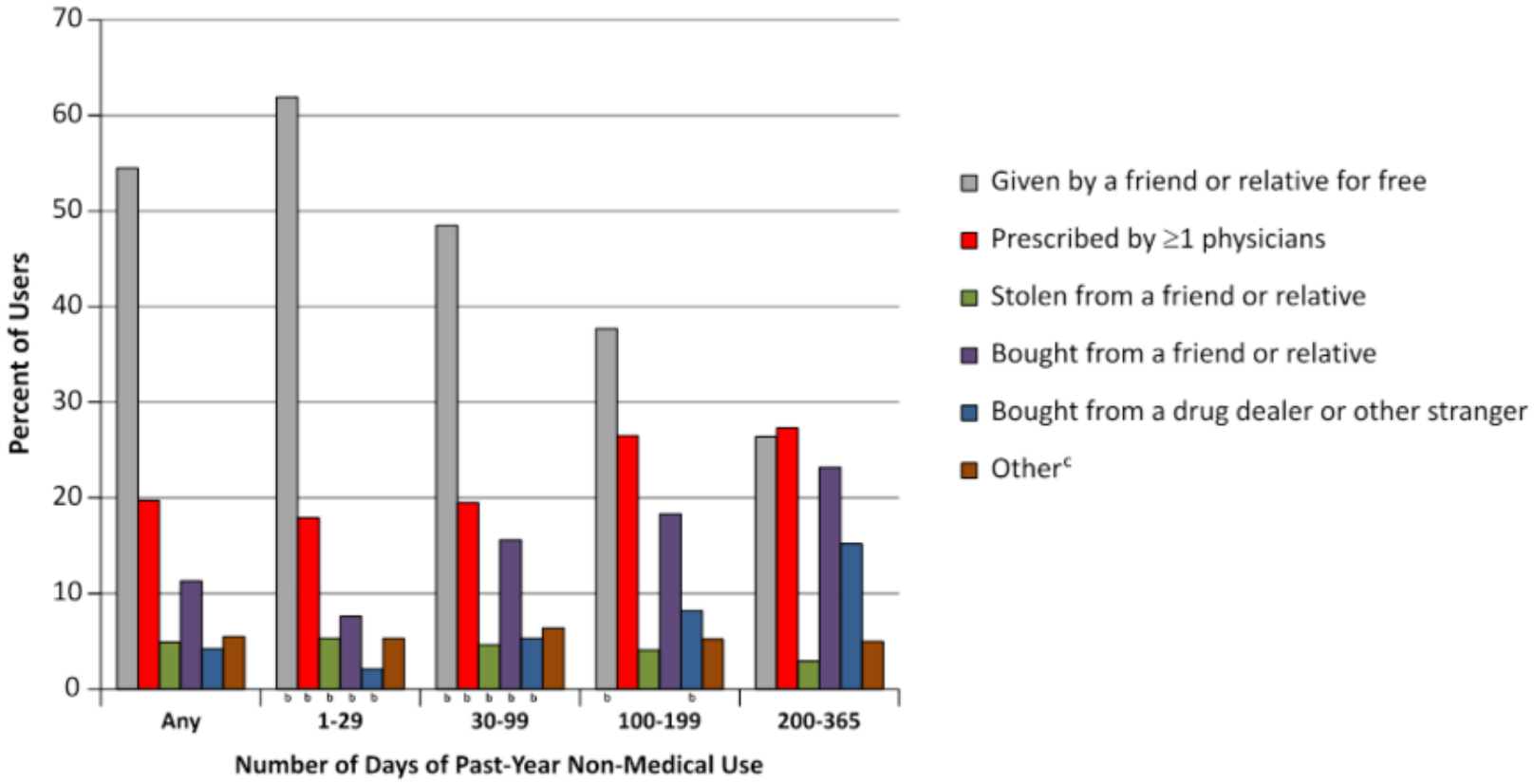


Values are three-year rolling averages for 2013 to 2015.

Source: International Narcotics Control Board

NYT: August 10, 2017

Sources of Rx Opioids Among Past-year Non-Medical Users



[a] Obtained from the US National Survey on Drug Use and Health, 2008 through 2011.[5]
[b] Estimate is statistically significantly different from that for highest-frequency users (200-365 days) ($P < .05$).
[c] Includes written fake prescriptions and those opioids stolen from a physician's office, clinic, hospital, or pharmacy; purchases on the Internet; and obtained some other way.

Jones, Paulozzi, et al. JAMA Int Med 2014

N Engl J Med. 1980 Jan 10;302(2):123.

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

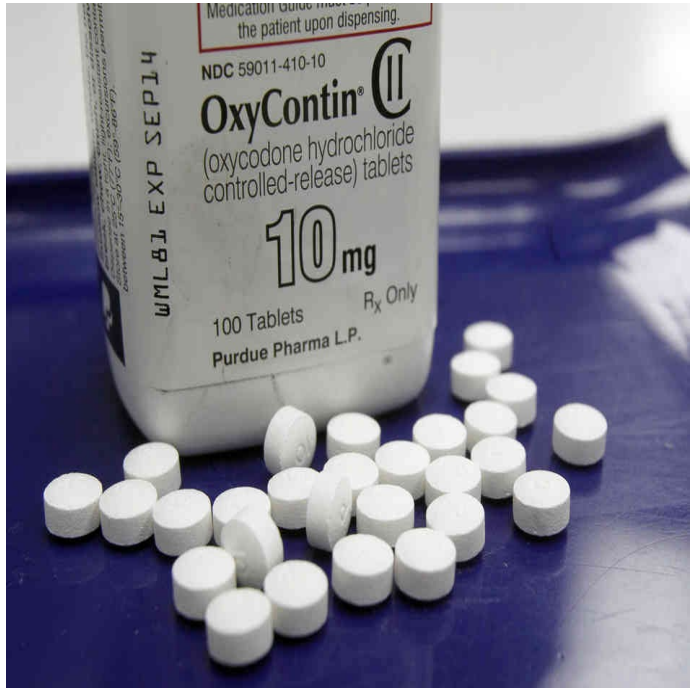
JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug Surveillance Program
Waltham, MA 02154 Boston University Medical Center

1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

Pain: The 5th Vital Sign

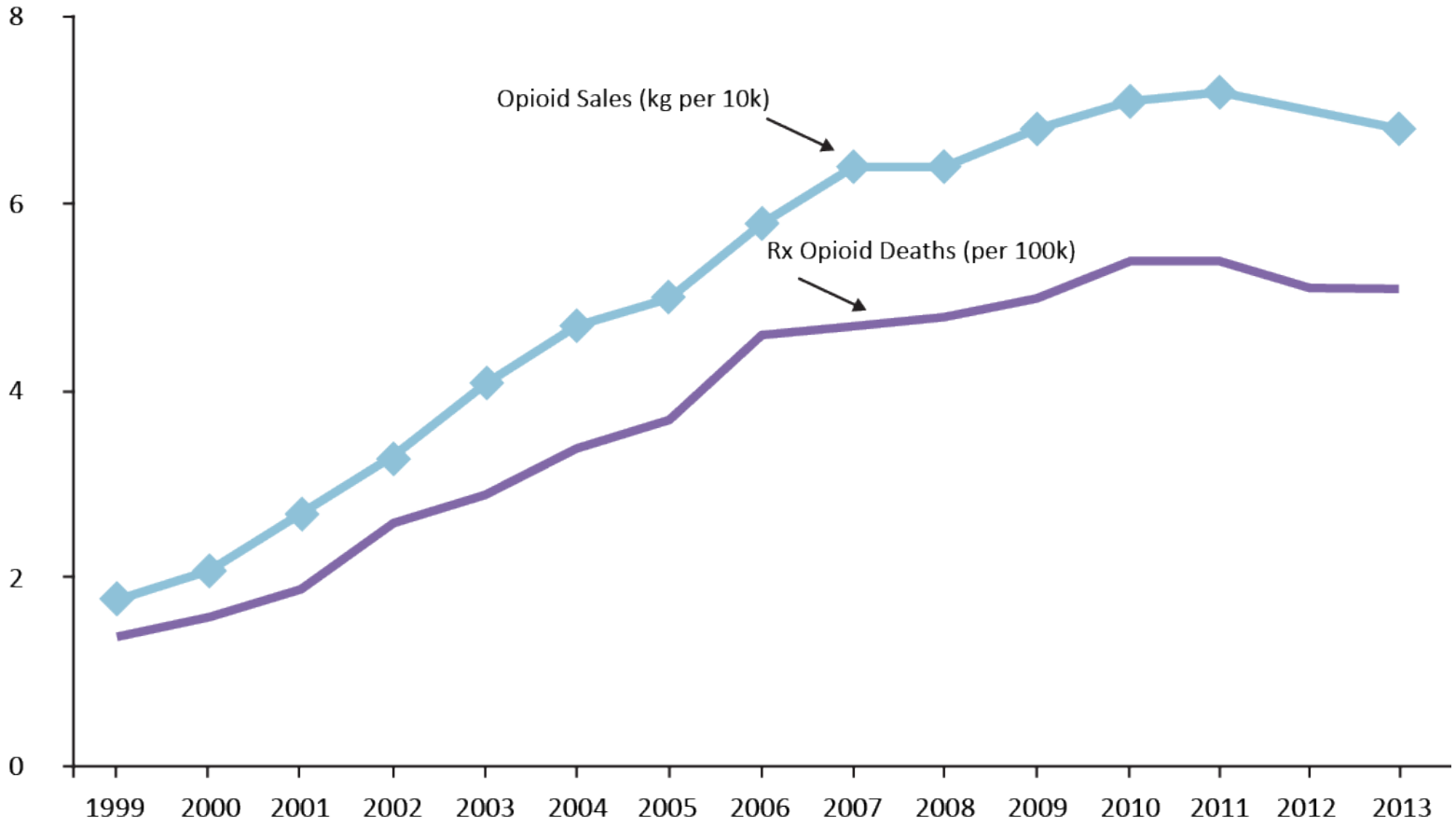
- History
  - Introduced by president of American Pain Society 1995
  - Embraced by VA system late 1990s
  - Became Joint Commission standard 2001 - 2017
- Because
  - Recognition pain undertreated
  - Untreated pain leads to chronic pain
  - Chronic pain interferes with quality of life, is costly, and common

Promotion: Oxycodone (OxyContin)



- Approved 1995
- Sales:
  - 1996 $45 million
  - 2000 $1.1 billion
  - 2010 $3.1 billion (30% of painkiller market)
- 1996-2002 funded >20,000 pain-related educational programs
- Provided financial support to: American Pain Society, the American Academy of Pain Medicine, the Joint Commission, members of Congress

Increase in Opioid Prescribing Associated with Increase in Death



National Vital Statistics System, DEA's Automation of Reports and Consolidated Orders System

Slide from and used with permission of CDC Division of Unintentional Injury Prevention

Two-thirds of heroin users

67%

misuse prescription painkillers first

Rx Opioids and Transition to Heroin

- Nonmedical use of Rx opioids is the strongest risk factor for heroin use[1]

- Majority of current heroin users initiated opioid use with Rx opioids for non-medical purposes (approx 75%)[2]

1- Compton W, et al. NEJM. 2016; 374; 154-63. 2- Cicero et al. JAMA Psychiatry; 2014; 71(7):821-826

Substance Use, Misuse, and Addiction are Highly Prevalent…

- **2015 National Survey on Drug Use and Health**:

  ≥12 years old, past 30 days

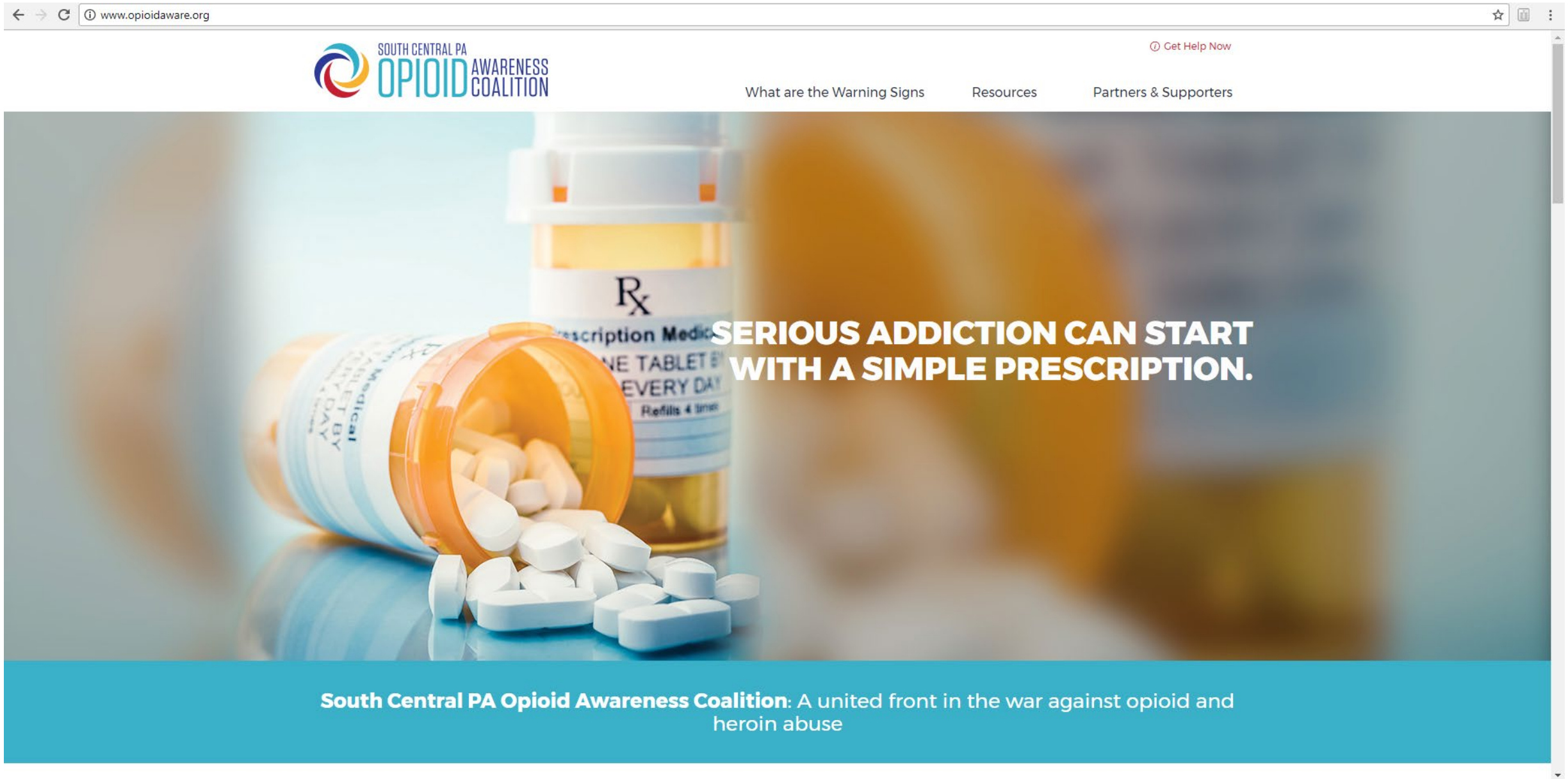
  - **10.1%** use illicit drugs
  - **1.4%** misuse prescription pain relievers

- **Despite this, there continues to be a large 'treatment gap' in the United States.**

  In 2015…

  - 21.7 million Americans (**8.1%**) needed specialized treatment for addiction
  - Only **10%** of those in need received treatment for addiction."

  [2015 NSDUH, *2016 Surgeon General's Report on Addiction*]


www.opioidaware.org
SOUTH CENTRAL PA OPIOID AWARENESS COALITION
Get Help Now
What are the Warning Signs
Resources
Partners & Supporters
SERIOUS ADDICTION CAN START WITH A SIMPLE PRESCRIPTION.
South Central PA Opioid Awareness Coalition: A united front in the war against opioid and heroin abuse

Interventions

- Enforcement
  - Closing “pill mills”
  - Disciplining prescribers
- Public Health
  - Availability of naloxone
  - Medication assisted treatment (good evidence for Methadone, Buprenorphine)
- Education
  - Prescribers
  - Health professional team members
  - Public?

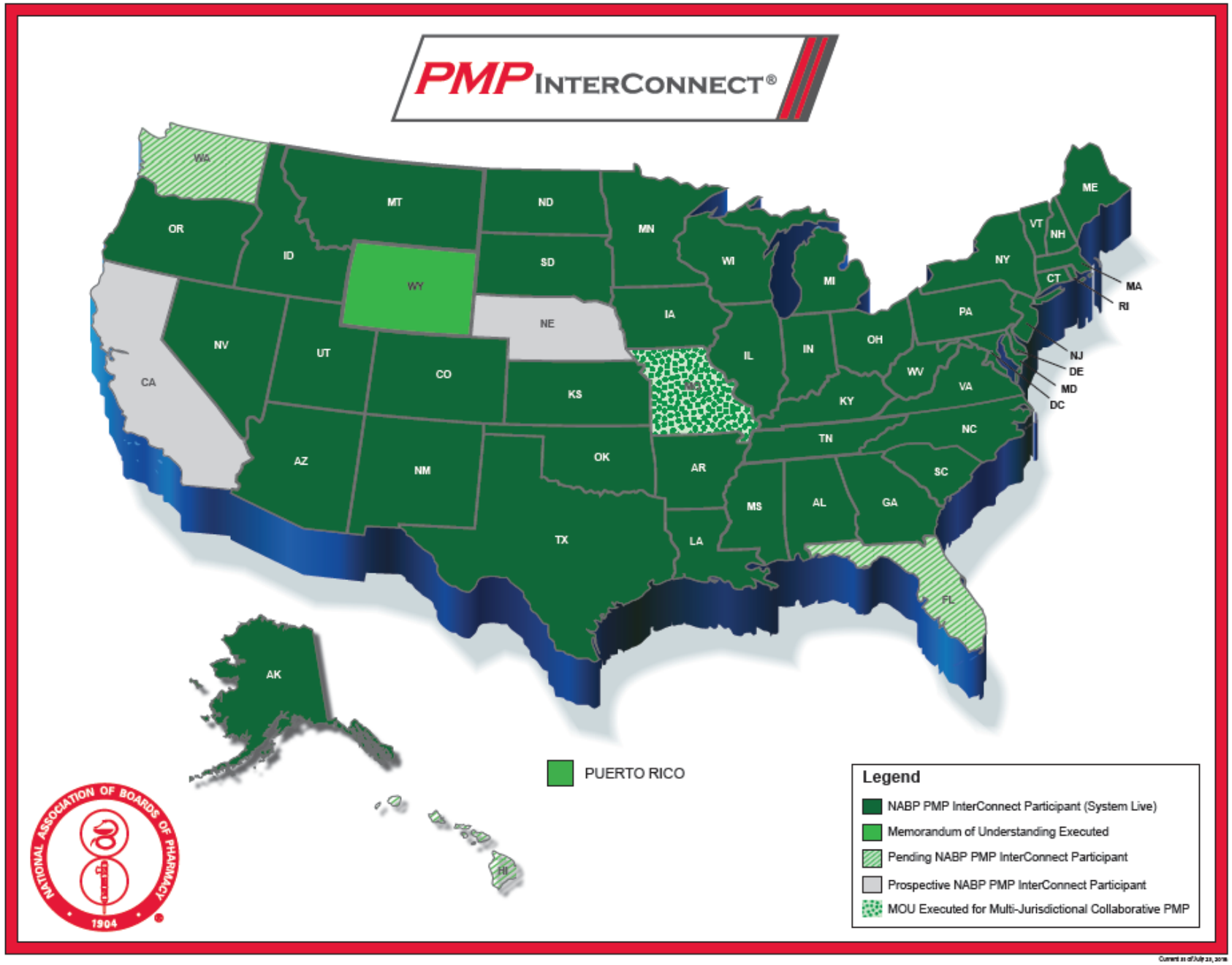
Enforcement – a few examples

- *2017 -*
- **Alabama** – John Couch MD - 20 years in prison for prescribing large quantities of opioids as part of his pain clinic practice, with no legitimate purpose
- **Rhode Island** - Jerrold Rosenberg MD - convicted of healthcare fraud for receiving kickbacks from the manufacturer to prescribe sublingual fentanyl spray for cancer pain patients did not have
- **Michigan** – Abdul Haq MD – conspiracy conviction for prescribing medically unnecessary opioids

4D Model (DEA)

- Dated
- Duped
- Disabled
- Dishonest

Prescription Monitoring Programs that Share Patient Data via PMP InterConnect- as of August 20, 2018



Annals of Internal Medicine

REVIEW

The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to Prevention Workshop

Roger Chou, MD; Judith A. Turner, PhD; Emily B. Devine, PharmD, PhD, MBA; Ryan N. Hansen, PharmD, PhD; Sean D. Sullivan, PhD; Ian Blazina, MPH; Tracy Dana, MLS; Christina Bougatsos, MPH; and Richard A. Deyo, MD, MPH

Background: Increases in prescriptions of opioid medications for chronic pain have been accompanied by increases in opioid overdoses, abuse, and other harms and uncertainty about long-term effectiveness.

Purpose: To evaluate evidence on the effectiveness and harms of long-term (>3 months) opioid therapy for chronic pain in adults.

Data Sources: MEDLINE, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, PsycINFO, and CINAHL (January 2008 through August 2014); relevant studies from a prior review; reference lists; and ClinicalTrials.gov.

Study Selection: Randomized trials and observational studies that involved adults with chronic pain who were prescribed long-term opioid therapy and that evaluated opioid therapy versus placebo, no opioid, or nonopioid therapy; different opioid dosing strategies; or risk mitigation strategies.

Data Extraction: Dual extraction and quality assessment.

Data Synthesis: No study of opioid therapy versus no opioid therapy evaluated long-term (>1 year) outcomes related to pain, function, quality of life, opioid abuse, or addiction. Good- and fair-quality observational studies suggest that opioid therapy for chronic oid abus dysfunct outcom creased ent opio

Limitati meta-analysis could not be done, and publication bias could not be assessed. No placebo-controlled trials met inclusion criteria, evidence was lacking for many comparisons and outcomes, and observational studies were limited in their ability to address potential confounding.

Conclusion: Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function. Evidence supports a dose-dependent risk for serious harms.

Primary Funding Source: Agency for Healthcare Research and Quality.

Ann Intern Med. doi:10.7326/M14-2559 www.annals.org

For author affiliations, see end of text.

This article was published online first at www.annals.org on 13 January 2015.

Conclusion: Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function. Evidence supports a dose-dependent risk for serious harms.

Indications for opioids

- End of life care
- Palliative care
- Chronic cancer pain
- Acute injury (i.e. battlefield)

- Chronic non-cancer pain in stable, reliable patients on high doses long-term?
  - (see *CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016)*

Determining When to Initiate or Continue Opioids for Chronic Pain (CDC)

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain.

2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh the risks.

3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation (CDC)

5. When opioids are started, clinicians should prescribe the lowest effective dosage.

6. Long-term opioid use often begins with treatment of acute pain. Three days or less will often be sufficient; more than seven days will rarely be needed.

7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation.

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms.

9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose.

Assessing Risk and Addressing Harms of Opioid Use (CDC)

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

- All recommendations are category A (apply to all patients outside of active cancer treatment, palliative care, and end-of-life care) …
  - except recommendation 10 (designated category B, with individual decision making required)

Chronic Pain Management:
Medical Management

- Nonopioid analgesics
  - Acetaminophen
  - NSAIDs

- Adjuvant medications
  - Antidepressants, such as SNRI's, TCAs (JAMA article on effectiveness of amitriptyline – October 1 2018)
  - Anticonvulsants, such as gabapentin, pregabalin, topiramate, carbamazepine, etc.

SOUTH CENTRAL PA OPIOID AWARENESS COALITION

Chronic Pain Management

- Medical management
- Interventional pain management procedures
- Cognitive-behavioral therapy
- Self directed home exercise program
- Complimentary medicine
  - Acupuncture
- Nutritional consult
- Life style changes

SOUTH CENTRAL PA OPIOID AWARENESS COALITION

FDA Opioid Policy Steering Committee

1. Decreasing Exposure & Preventing New Addiction

2. Supporting the Treatment of Those With Opioid Use Disorder

3. Fostering the Development of Novel Pain Treatment Therapies

4. Improving Enforcement & Assessing Benefit-Risk

Public Health Approaches to Opioid Crisis

- Primary prevention school education programs
- Safe opioid prescribing & disposal
  - Prescription Drug Monitoring Programs
  - Drug take-back initiatives
  - Provider education
  - Regulation and legal action around “pill mills”
  - Opioid prescribing limits
- Screening, Brief Intervention and Referral to Treatment (SBIRT)
- Abuse-deterrent opioid formulations
- Opioid Use Disorder (OUD) treatment with agonist therapy
- Overdose response education and naloxone distribution
  - Good Samaritan Laws
  - Laws to allow access without a prescription
- Safe Injection/Consumption Facilities

Would you consider an intervention that could be shown to…

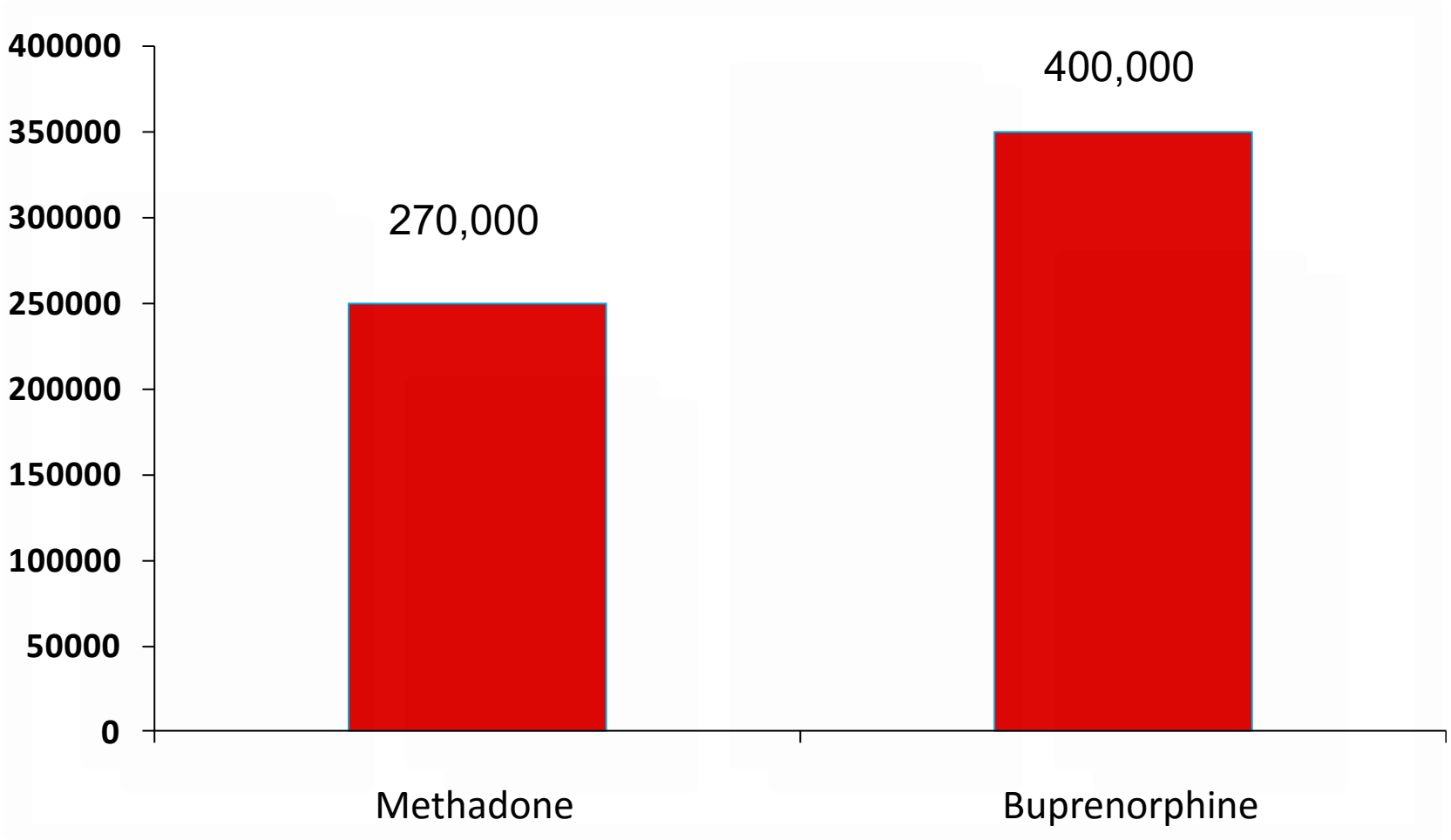
- Increase retention in treatment
- Reduce illicit opioid use
- Reduce risk of overdose
- Reduce risk of HIV, HBC, HCV infections
- Increase rates of employment
- Decrease crime
- Increase length of life

- Benefits Of Agonist (Methadone and Buprenorphine) Treatment

Opioid Use Disorder Treatment

- Medication assisted treatment (MAT):
  - Methadone
    - Only available in Opioid Treatment Programs ("methadone clinics")
  - Buprenorphine
    - Prescriber must have "waiver" to be able to prescribe and there are limits on size of patient population
  - Injectable extended release naltrexone

Public Health - Research to Policy:
Impact of Office-based Treatment - 2012



Medication Assisted Treatment (MAT)

Methadone

Dolophine, Methadose

Methadone (Full Agonist); Activates opioid receptors in the brain, fully replacing the effect of whichever opioid the person is addicted to

Buprenorphine

Suboxone, Subutex, Probuphine

Buprenorphine (Partial Agonist): Activates opioid receptors in the brain, partially replacing the effect of whichever opioid the person is addicted to

Naltrexone

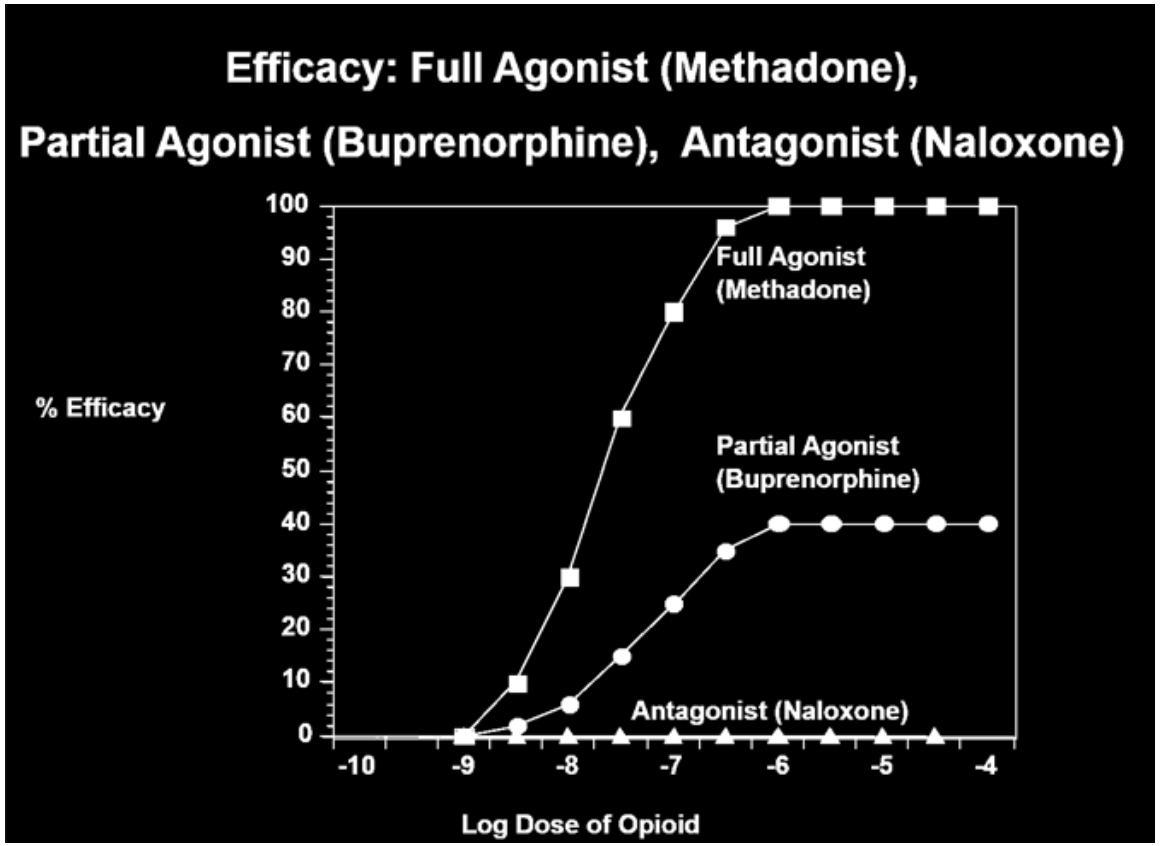
Vivitrol

Naltrexone (Antagonist): Binds to the opioid receptors in the brain, blocking the effects of opioids.

Source: National Institute on Drug Abuse, Pew Charitable Trusts Credit: Rebecca Hersher and Alyson Hurt/NPR

Medication Assisted Treatment

- Methadone
- Buprenorphine (tablet, film, implant)
- Naltrexone (oral and long-acting injectable)



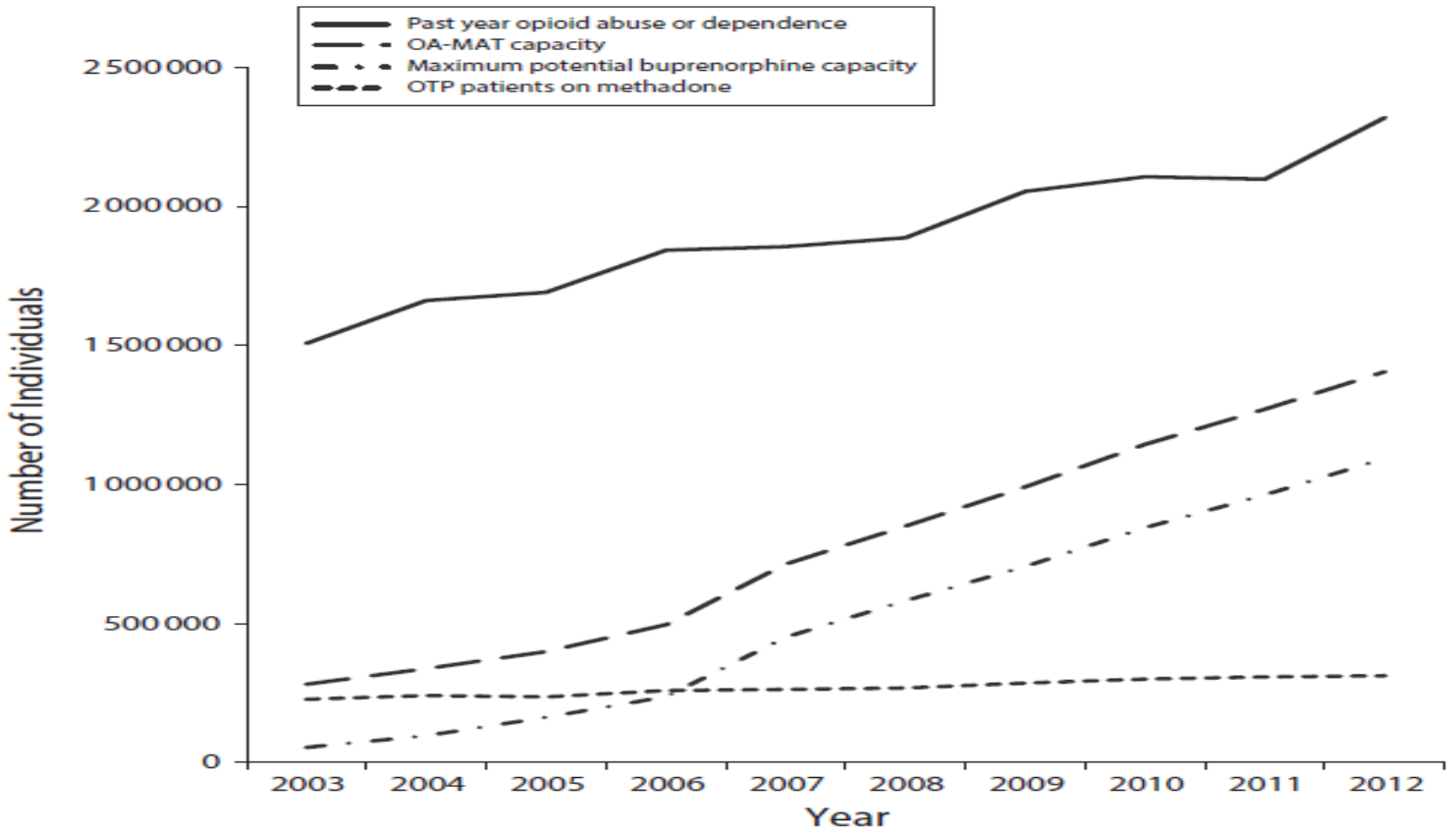
SOUTH CENTRAL PA OPIOID AWARENESS COALITION

Hospitals:
Withdrawal vs Treatment

- Medication Assisted Treatment
  - No special waver to start MAT in hospital
    - Methadone (full agonist)
    - Buprenorphine (partial agonist)
    - Naltrexone (antagonist)
  - Must be done with proper link to outpatient MAT program and counseling

SOUTH CENTRAL PA OPIOID AWARENESS COALITION

Access to opioid use disorder medication assisted treatment in US



Note. OA-MAT = opioid agonist medication-assisted treatment; OTP = opioid treatment program.

FIGURE 1—Trends in past-year opioid abuse or dependence and opioid agonist medication-assisted treatment capacity: United States, 2003–2012.

Jones CM, Campopiano M, et al. Am Journal of Public Health. 2015; 105(8):e55-e63

While waiting for EMS to arrive…

- At least try to get breathing restarted by giving the antidote via nasal spray
- Administer rescue breathing
  - (if pulse)
- Administer chest compressions
  - (if no pulse)

Important notes about naloxone (Narcan)

- If the first dose does not work, you can administer a 2nd dose
- It takes approximately 2-5 minutes to take effect
- Narcan stays in the system ~ one hour
    - Narcan has a shorter half-life than heroin
    - Someone can go back into overdose after Narcan wears off
- 40% of overdoses are witnessed, but rarely is Narcan available (MMWR)
- Someone who overdosed should NOT use any type of depressant following the overdose

Would you consider an intervention that could be shown to result in…

- Overdose death reduction
  - *Milloy et al, PLOS One, 2008*
  - *Marshall et al, Lancet 2011*
  - *Kerr et al., International Journal of Drug Policy, 2006*
- Reductions in syringe sharing
  - *Kerr et al., The Lancet, 2005*
  - *Wood et al. American Journal of Infectious Diseases, 2005*
- Increases in safer injection behaviors
  - *Stoltz et al, Journal of Public Health, 2007*
  - *Small et al., Drug and Alcohol Dependence, 2008*
- Increased use of addiction treatment
  - *Wood et al., New England Journal of Medicine, 2006*
  - *Wood et al., Addiction, 2007*
  - *DeBeck et al., Drug and Alcohol Dependence, 2010*
- Reductions in violence against women
  - *Fairbairn et al, Social Science and Medicine, 2008*

Slide credit: Sharon Stancliff, MD

Would you consider an intervention that could be shown to result in…

- Reductions in public disorder
  - *Wood et al., Canadian Medical Association Journal, 2004*
  - *Petrar et al., Addictive Behaviors,*
  - *Stoltz et al., Journal of Public Health, 2007*
- No negative changes in community drug use patterns
  - *Kerr et al., British Medical Journal, 2006*
- No increases in initiation into injection drug use
  - *Kerr et al., American Journal of Public Health, 2007*
- No increases in drug-related crime
  - *Wood et al., Substance Abuse Treatment. Prevention, and Policy, 2006*
- Promotes effective police-public health partnerships
  - *DeBeck et al, Substance Abuse Treatment. Prevention, and Policy, 2008*
- Cost-effective
  - *Bayoumi & Zaric, CMAJ, 2009*
  - *Andersen & Boyd, IJDP, 2010*
  - *Pinkerton, et al, Addiction, 2010*

Findings from Insite Vancouver BC

Slide credit: Sharon Stancliff, MD

Supervised Injection Facilities

- Facilities where people may go to consume drugs obtained elsewhere in a hygienic environment with appropriate equipment without fear of arrest under trained supervision

Hedrich, D., T. Kerr & F. Dubois-Arber (2010) 'Chapter 11; Drug consumption facilities in Europe and beyond. European Monitoring Centre for Drugs and Drug Addiction

The Conjoint Committee on Continuing Education (CCCE) does not have a position on supervised injection facilities.

Slide credit: Sharon Stancliff, MD

Insite, Vancouver
British Columbia

Photo Credit: Sharon Stancliff, MD

Internationally:
97 facilities
66 cities
11 countries
1 in the US[1]

1- http://www.abell.org/sites/default/files/files/Safe%20Drug%20Consumption%20Spaces%20final.pdf

American Journal of Preventive Medicine
Aug. 8, 2017

American Journal of
Preventive Medicine

CURRENT ISSUES

Addressing the Nation's Opioid Epidemic: Lessons from an Unsanctioned Supervised Injection Site in the U.S.

Alex H. Kral, PhD,[1] Peter J. Davidson, PhD[2]

Over half a million people have died of overdose in the U.S. since 2000.[1] As of 2014, an estimated 774,434 people inject drugs in the U.S., the majority of whom inject opioids including prescription opioids and heroin.[2] The prevalence of HIV and hepatitis C virus among people who inject drugs in the U.S. is 2% and 43%, respectively.[2] With the U.S. in the midst of an opioid epidemic causing morbidity and mortality at unprecedented levels, policymakers and public health practitioners are in need of innovative solutions.

Illicit drug use has been treated in the U.S. primarily as a criminal activity and only secondarily as a public health concern. When HIV/AIDS emerged in the early 1980s, activists and public health practitioners adopted and advocated for a more pragmatic approach to drug use—harm reduction—which consists of "a set of practical strategies and ideas aimed at reducing negative consequences associated with drug use."[3] Prominent examples of harm reduction programs include access to sterile syringes for injection of illicit drugs through syringe access programs and expanding provision of naloxone, a lifesaving opioid overdose-reversal medication, to lay persons, law enforcement, and other first responders.

countries currently allow legal operation of such sites (Australia, Canada, Denmark, France, Germany, Luxembourg, the Netherlands, Norway, Spain, and Switzerland), with approximately 98 facilities operating in 66 cities worldwide. Implementation of supervised injection sites has been shown to improve individual health, such as overdose mortality rates,[6] drug use and enrollment in drug treatment,[7,8] HIV and viral hepatitis risk,[9] and access to health and social services.[10,11] Improvements in community health and safety are also noted in neighborhoods with supervised injection sites, including reductions in public injection and improperly disposed of syringes,[12,13] drug related crime,[14] violence in the neighborhoods surrounding the site, and in the demand for ambulance services for opioid-related overdoses.[15] Once implemented, these sites have been found to have high community support, which increases over time.[16,17] A recent study estimated that placing a supervised injection site in a U.S. city would net cost savings of $3.5 million (U.S.) per year.[18]

The legal status of supervised injection sites in the U.S. is unclear, but laws such as the federal Controlled Substances Act could potentially be used to shut them

Figure 1. Photo of part of injection room at the unsanctioned supervised injection site in the U.S. (Photo by Greg Scott, PhD.)

Successful Strategies – Clinician Education

- Quality educational activities
  - On-line (more participants)
  - Live (more completers)
  - Incorporate the FDA Blueprint

    FDA's Opioid Analgesic REMS Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain (January 2018)
  - Tailored to audience (rural NP vs oncologist vs dentist)
  - Increases knowledge, changes practice behaviors in ways linked to improved patient outcomes

- Quantity educated
  - (ACCME PARS) 892 activities, 395,663 participants successfully completing
    - 194,328 registered to prescribe schedule 2/3 (n = 1.2 million in 2012)
    - 93,192 registered to prescribe and prescribed in the past year (n = 320,000 in 2012)
    - In addition to the majority of family physicians who are included in ACCME PARS data, an additional 3098 were educated through providers accredited by AAFP but not by ACCME
    - In addition to DO's who are included in the PARS system, 19,681 were educated through providers accredited by AOA but not by ACCME
  - Nursing CE (ANCC) 13,330 (6160 prescribers)
  - Pharmacy CE (ACPE) - CE activities: 293 live, 67 enduring; 105,030 pharmacists, 58,708 pharmacy technicians
  - Total > 595,510 completers

Mandatory or Voluntary Education?

- Twenty-six states mandate content-specific Continuing Education (CE)
  - End of life care
  - Domestic violence
  - Infection control
  - HIV/AIDS
  - Bioterrorism
  - *Pain management (24 states)*
- Mandatory CE
  - *No evidence in the literature of learning or practice behavior change*
  - *Diverts education from prioritized clinician needs*
- Voluntary CE
  - *Self-identified need or practice gap*
  - *Accreditation Council for Continuing Medical Education (ACCME) Program and Activity Review System (PARS) measures learning and practice behavior change*

And those choosing not to educate themselves? Challenges…

- Rarely prescribing - therefore not recognizing such education as a priority
- The prescriber is the expert - therefore not sensing a need to take advantage of the education
- Lack of awareness
- Trusting enforcement to manage the problem
- Requiring 2-3 hours of education discourages some from participating
- Mandated state CE other than pain management or opioid prescribing - results in clinicians forgoing opioid education to fulfill other requirements
- Overwhelmed by the many demands on practice

Future Considerations: 2019

- Adaptive learning
  - Tests knowledge first
  - Results in immediate needs assessment/gap analysis
  - Followed by learning specifically targeted to identified gaps
  - Personalized learning design

What else can we do?

TEAM BASED CARE

Objectives

- Team based care from a practitioner perspective
- Team-based care from the regulatory perspective
- Definitions: Team-based Care, Collaborative Practice
- Challenges, Barriers and Opportunities: Using an interdisciplinary team approach of educators, researchers, practitioners, policy makers, regulators and other stakeholders to address key issues of:
  - Legal and Regulatory Definitions
  - ROI: Financial, Time
  - Coordination of Care: Technology
  - Desired characteristics: Accountability, Professionalism
  - Outcome measures → outcome based reimbursement

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DEFINITION

"Team-based health care is the provision of health services to individuals, families, and/or their communities by at least two health providers who work collaboratively with patients and their caregivers—to the extent preferred by each patient– to accomplish shared goals within and across settings to achieve coordinated high-quality care."

Institute of Medicine 2012

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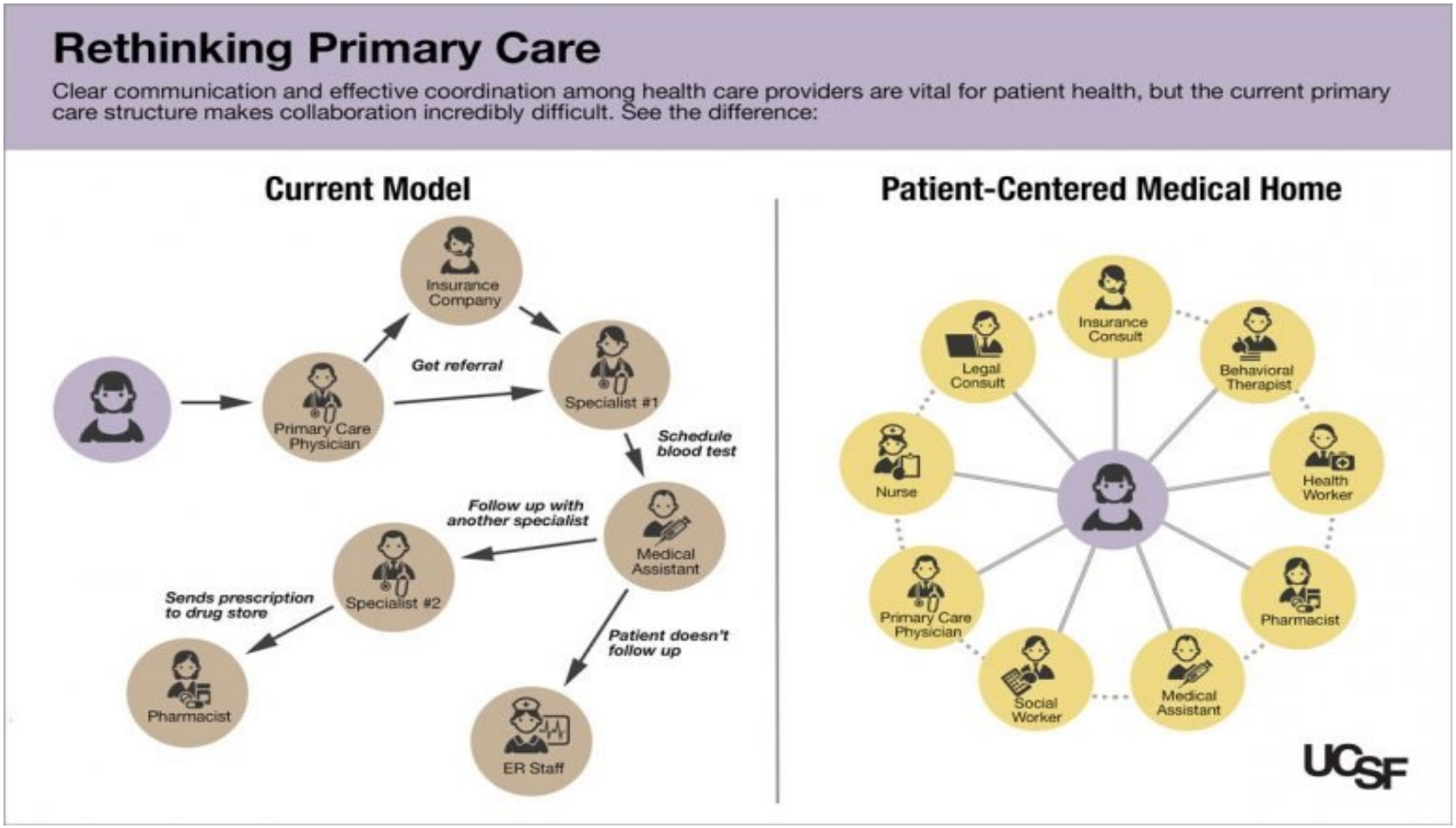
COMMON MODEL OF TEAM BASED CARE



THE IOM DEFINITION OF TEAM BASED CARE INCLUDES

"across settings"

HOW DO WE INCORPORATE THE PHYSICIAN SPECIALISTS AND COMMUNITY PHARMACISTS?

CDC – A Guide for Pharmacists

Creating Community-Clinical Linkages Between Community Pharmacists and Physicians. Atlanta, GA: Centers for Disease Control and Prevention, U.S. Department of Health and Human Services; 2017

In collaboration with APhA and AMA

NATIONAL ASSOCIATION OF BOARDS OF PHARMACY 1904

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PHARMACISTS AS PART OF THE TEAM

What does the research say?

- Demonstrates the ability to **improve health outcomes**
- Demonstrates the ability to **improve medication use**
- Demonstrates the ability to **reduce overall healthcare costs**

Can these proven benefits be integrated into the healthcare system?

THEY MUST!!!!

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TEAM BASED CARE

Challenges are really just Opportunities

- **Medicine is an art as much as a science**
  - The role of professionalism in team based care
- **Different disciplines not trained together**
  - ACPE standards for inter-professional training
- **Hierarchy**
  - Medical School Training
- **Fiscal and technologic limitations**
  - RHIOs, Value Based Contracting and Reimbursement
- **Lack of continuity in many healthcare models**
  - Systems and Culture historically slow to change but the marketplace is driving adaptation

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DRUG TOPICS

September 24, 2018

Pharmacists Help Meet Value-Based Targets

NATIONAL ASSOCIATION OF BOARDS OF PHARMACY 1904 NABP®

IS THIS COLLABORATIVE PRACTICE?

- NABP MODEL ACT

  "Collaborative Pharmacy Practice" is that Practice of Pharmacy whereby one or more Pharmacists have jointly agreed, on a voluntary basis, to work in conjunction with one or more Practitioners under protocol and in collaboration with Practitioner(s) to provide patient care services to achieve optimal medication use and desired patient outcomes.

COLLABORATIVE PRACTICE AGREEMENT

A Pharmacist planning to engage in Collaborative Pharmacy Practice shall have on file at his or her place of practice the written Collaborative Pharmacy Practice Agreement. The initial existence and subsequent termination of any such agreement and any additional information the Board may require concerning the Collaborative Pharmacy Practice Agreement, including the agreement itself, shall be made available to the Board for review upon request. The Agreement may allow the Pharmacist, within the Pharmacist's Scope of Practice Pursuant to the Collaborative Pharmacy Practice Agreement, to conduct activities approved by the Practitioner, and as defined by law and by the Rules of the Board. The collaboration that the Practitioner agrees to conduct with the Pharmacist must be within the scope of the Practitioner's current practice. Patients or caregivers shall be advised of such agreement.

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COLLABORATIVE PRACTICE

2018 Survey of Pharmacy Law

- 47 states allow for some form of collaborative practice
- Prescriptive; defined by activities
  - ❑ Medication Therapy Management
  - ❑ Initiate, Modify or Discontinue Drug Therapy
  - ❑ Immunizations
  - ❑ Order/Administer/Interpret Tests
  - ❑ Naloxone

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5 CORE PRINCIPLES OF TEAM-BASED HEALTHCARE[1]

- **Shared goals**

  The team – including the patient and, where appropriate, family members or other support persons – works to establish shared goals that reflect patient and family priorities and that can be clearly articulated, understood and supported by all team members.

[1]Core Principles & Values of Effective Team-Based Health Care, IOM, Oct. 2012

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5 CORE PRINCIPLES OF TEAM-BASED HEALTHCARE

- **Clear roles**

  There are clear expectations for each team member's functions, responsibilities and accountabilities, which optimize the team's efficiency and often make it possible for the team to take advantage of division of labor, thereby accomplishing more than the sum

  of its parts.

5 CORE PRINCIPLES OF TEAM-BASED HEALTHCARE

- **Mutual trust**

  Team members earn each other's trust,

  creating strong norms of reciprocity and

  greater opportunities for shared achievement.

5 CORE PRINCIPLES OF TEAM-BASED HEALTHCARE

- **Effective communication**

  The team prioritizes and continuously refines its communication skills. It has consistent channels for candid and complete communication, which are accessed and used by all team members across all settings.

5 CORE PRINCIPLES OF TEAM-BASED HEALTHCARE

- **Measurable processes and outcomes**
  - The team agrees on and implements reliable and timely feedback on successes and failures in both the functioning of the team and achievement of the team's goals. These are used to track and improve performance immediately and over time.

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ATTRIBUTES VALUED IN TEAM BASED CARE

- ACCP White Paper 2008

Figure 1. Conceptualizing professionalism in pharmacy.

ATTRIBUTES VALUED IN TEAM BASED CARE

- AACP Professionalism Task Force 2011
  - AACP Council of Deans/APhA-ASP Task Force on Professionalism
    - Knowledge and Skills
    - Commitment to self-improvement and lifelong learning
    - A service-minded orientation
    - Pride in the profession and dedication to advance its value to society
    - Create a covenantal relationship with those served
    - Alertness, creativity, initiative and innovation
    - Conscientiousness, integrity and trustworthiness
    - Flexibility and punctuality
    - Accountability
    - Ethical
    - Leadership

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REGULATING TEAM BASED CARE

- Tri-Regulator Collaborative
  - Federation of State Medical Boards (FSMB)
  - National Council of State Boards of Nursing (NCSBN)
  - National Association of Boards of Pharmacy (NABP)
- Tri-Regulator Position Statement on Team Based Care 2013
- Regulatory Questions and Opportunities explored at the 2015 Tri-Regulator Symposium

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TRI-REGULATOR CONSENSUS

- Regulatory bodies need to work in concert
  - Ensure regulations align
    - If a state grants prescriptive authority to pharmacists must ensure nursing regulations allow for the acceptance of such orders
  - Explore new methods for discipline cases
    - Just Culture Approach
    - Joint Case Review
    - Standards of Care

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REGULATING PHARMACY IN TEAM BASED CARE MODELS

- Supervision of staff
- Dispensing Errors
- Continuing Education Requirements
- MTM/Collaborative Practice
- Team Based Care
- Continuing Professional Development
- Standards of Care
- Use of Artificial Intelligence
- Role for Pharmacy Technicians

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TEAM BASED CARE

NABP's exploration of current and evolving models:

- **2017 NABP Task Force on the Definition of a Patient-Pharmacist Relationship**
- **2018 NABP Task Force to Develop Regulations based on Standards of Care**
  - Invited guests include FSMB and NCSBN

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POST TEST QUESTION 1

Research has shown that pharmacist participation in team based care consistently reduces overall medication costs

- True
- False

Some studies show an increase in medication costs, as the most appropriate drug for the indication may be necessary to reduce consumption of healthcare resources, thereby reducing overall healthcare costs.

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POST TEST QUESTION 2

Collaborative Practice is a more prescriptive form of team based care

- *True*
- *False*

The regulations for collaborative practice in most states clearly define written relationships, requirements to file with the board of pharmacy and are confined to specific activities

POST TEST QUESTION 3

EHR connectivity and inter-operability are critical to the participation of both medical specialists and community pharmacists in team based care.

- True
- False

Access to information and multi-directional electronic communication are necessary for team based care to be efficient, effective and safe.