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CCPP
COMMITTEE ON CLINICAL PHARMACOLOGY AND PHARMACOGENOMICS

Analysis of Clinically Actionable Preemptive Pharmacogenomic (PGx) Information to Impact In-Hospital Prescribing

Yee Ming Lee[1], PharmD,

Keith Danahey[1,2] MS, Mark J. Ratain[1,3,4], MD, David O. Meltzer[5], MD, PhD, Peter H. O'Donnell[1,3,4], MD

[1]Center for Personalized Therapeutics, [2]Center for Research Informatics, [3]Committee on Clinical Pharmacology and Pharmacogenomics, [4]Department of Medicine, [5]Departments of Medicine and Economics, and Harris School of Public Policy, The University of Chicago, IL

BACKGROUND

- Traditional "one size fits all" vs Precision medicine
- Pharmacogenomics (PGx) goal: ↓adverse drug response, ↑drug efficacy
- Various institutions have begun implementing PGx [1]

3 issues on implementation
a.   Test approach: Reactive vs preemptive
b.   Standard for clinical actionable information: **CPIC**,**FDA**, DPWG — **CPIC: Clinical Pharmacogenetics Implementation Consortium** — **FDA: table of PGx biomarkers in drug labels** — DPWG: Dutch Pharmacogenetics Working Group
c.   Genotype population: Everyone vs high-risk groups[2]

1. Dunnenberger et al. Ann Rev Pharmacol Toxicol. 2015
2. Johnson et al. Pharmacogenomics 2013

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HIGH STAKES SETTING

- At University of Chicago, 1200 Patients Project[1]
  - Preemptively genotype patients seen by MD at outpatient clinic
  - Literature for clinically actionable pharmacogenes
  - Risk signals in **U of Chicago Genomic Prescribing System (GPS)**

- Stakes are high in the hospital
  - ~35 million hospital admissions per year in US [2]
  - Average 45% of discharge medications newly started in hospital[3]
  - Acutely ill patients – at risk of adverse drug reactions (ADR)
  - ADR – 5.3% hospitalizations; higher rates in elderly[4]

1. O'Donnell et al. Am J Med Genet C Semin Med Genet. 2014
2. Health Forum LLC; American Hospital Association 2014
3. Thompson-Moore, AJHP 2012
4. Kongkaew et al. Ann Pharmacother. 2008
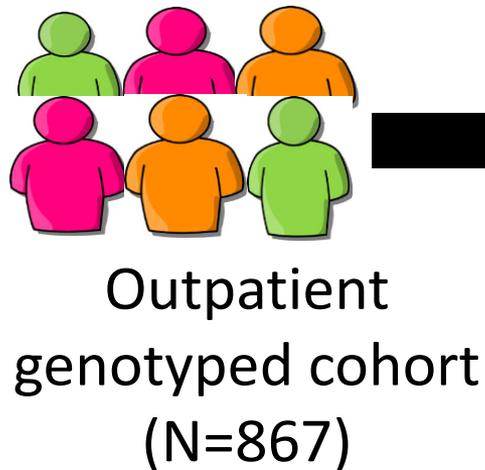
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HYPOTHESIS & AIM

- HYPOTHESIS: Clinically actionable preemptive PGx information made available in high volume and high stakes in-hospital setting, can significantly influence drug prescribing

- AIM: Pilot study to determine the potential opportunities for PGx information to influence drug prescribing

METHODS

- Retrospective analysis of outpatient genotyped cohort

Outpatient genotyped cohort (N=867)

Hospitalizations at University of Chicago Medical Center 2012 to 2015

Medication changes: Compare admission and discharge med list

Germline PGx information
- **CPIC-A list (35 drugs)**
- **FDA list (104 drugs)**
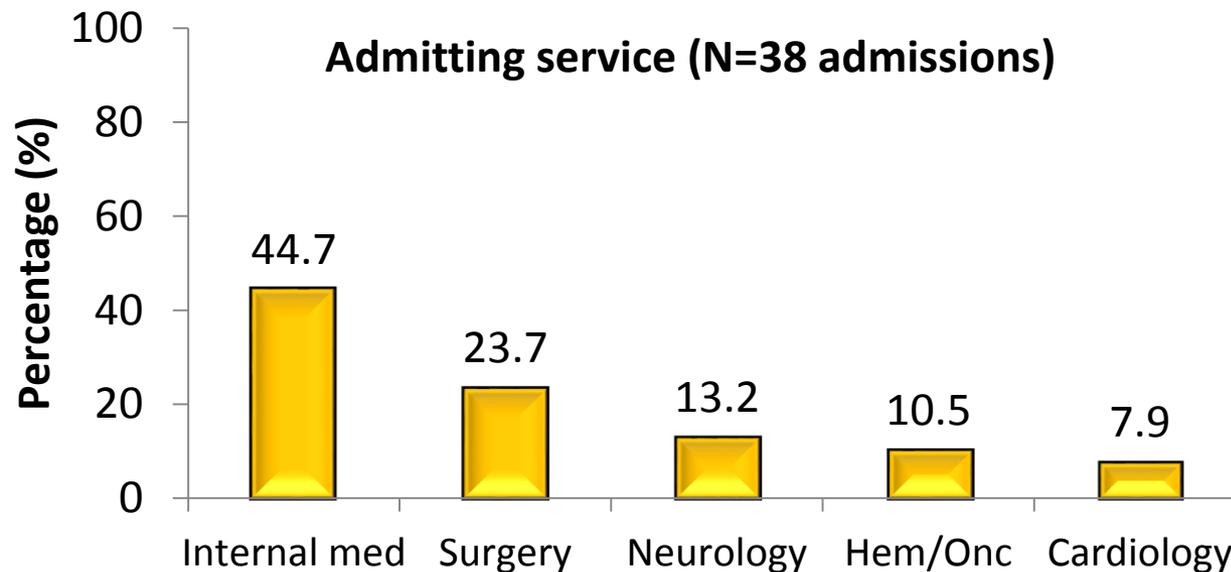- **U Chicago GPS list (46 drugs)**

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RESULTS: PATIENT DEMOGRAPHICS

CHARACTERISTICS – NO. (%)	OUTPATIENT GENOTYPED (N=867)	HOSPITALIZED (N=20)
Age (mean ± SD, years)	61.3 ± 15.5	78.2 ± 12.3*
Male	394 (45.4)	13 (65.0)
Caucasian	536 (58.8)	12 (60.0)
African-American	290 (31.8)	7 (35.0)
Asian	29 (3.2)	0 (0)
More than one race/other	27 (3.0)	0 (0)
Unknown	26 (2.9)	1 (5.0)
American Indian/Alaska native/ Pacific islander	4 (0.4)	0 (0)
No. of medications (mean ± SD)	5.0 ± 3.2	8.8 ± 3.9 *

*P<0.0001

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HOSPITALIZATION DETAILS

CHARACTERISTIC	HOSPITALIZED, N=20
Total no. of hospitalizations	38
Hospitalization rate per patient	1.9 (range 1 − 6)
Length of stay in hospital (days)	4.3 (range 0 − 22.6)
No. of baseline comorbidities (mean ± SD)	7.4 ± 4.8

Admitting service (N=38 admissions)

Percentage (%)

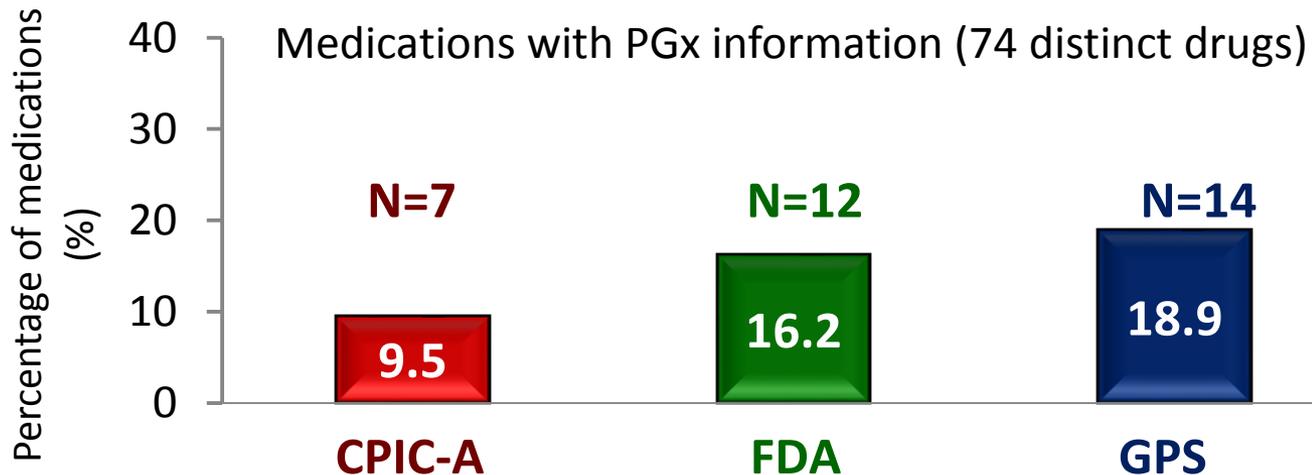| Internal med	Surgery	Neurology	Hem/Onc	Cardiology
44.7	23.7	13.2	10.5	7.9

MEDICATIONS WITH PGx INFORMATION

53% of the Hospitalizations involved PGx drug
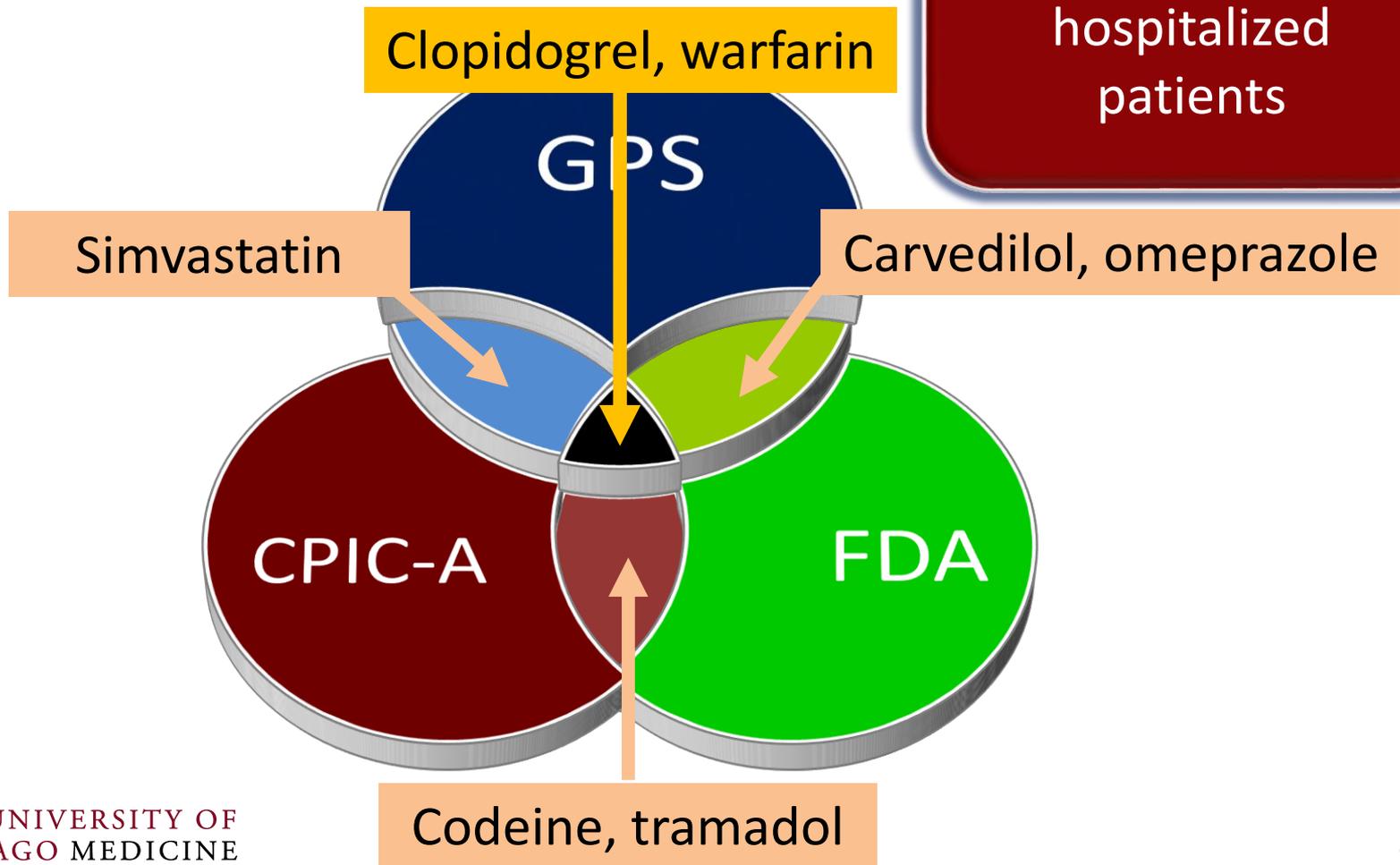
Total 159 medications changed (74 distinct drugs)

- Per hospital visit: average 3.8 medications changed
  - 30% medications changed involved PGx drug

Medications with PGx information (74 distinct drugs)

	CPIC-A	FDA	GPS
N	N=7	N=12	N=14
Percentage of medications (%)	9.5	16.2	18.9

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NEW MEDICATIONS WITH PGx INFORMATION

- Out of 74 distinct drugs changed, 66% were ne
- 7 (14%) new medications had PGx info from at

7 new PGx drugs affected 45% hospitalized patients

Clopidogrel, warfarin

GPS

Simvastatin

Carvedilol, omeprazole

CPIC-A

FDA

Codeine, tramadol

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CONCLUSIONS

1. Majority of hospitalized patients undergo medication changes

2. Having PGx information from broad preemptive genotyping made available could significantly impact in-hospital prescribing

3. Preemptive genotype population: elderly, multiple medications

Future: Prospective study of broad preemptive PGx implementation among hospitalized patients

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