Precision Medication Selection in the Long-Term Care Setting

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The Science Behind Better

What Is…………..

- Quite possibly the 4th leading cause of death in the United States?

- Ahead of pulmonary disease, diabetes, AIDS, pneumonia, accidents, auto deaths?

- Leading to as many as 106,000 deaths annually?

- Costing as much as $528 billion annually?

- Largely preventable?

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https://www.fda.gov/drugs/drug-interactions-labeling/preventable-adverse-drug-reactions-focus-drug-interactions

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ADRs

Adverse Drug Reactions and drug-drug interactions

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Objectives

1. Describe the potential negative effects of medication use and identify contributing factors to variability in medication response

2. Define pharmacogenetics (PGx) and state key considerations for use in practice

3. Discuss the clinical and economic benefits of PGx

4. Highlight precision medicine solutions offered by Genomind

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Imprecision Medicine

- 3.8 billion Rxs filled at pharmacies in the United States in 2019

- Medication use:
  - 50% of individuals in the US take at least one prescription medication
  - 24% of individuals ≥3 meds
  - 13% of individuals ≥5 meds

- Number needed to treat (NNT) varies greatly

- Many patients experience negative effects of medication use – inefficacy or ADRs

- ADRs increase *exponentially* with >4 drugs

Kaiser Family Foundation. Available at: https://www.kff.org/health-costs/state-indicator/total-retail-rx-drugs/
Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/nchs/fastats/drug-use-therapeutic.htm
Scharfe et al. Genome Med 2017 (PMID 29273066)

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Potential Medication Harms

50% of patients may be non-adherent to medication regimens	3.2 million hospital and emergency room visits per year due to ADRs
$528 billion annually on drug-related morbidity and mortality	52% of outpatient drug ADRs are preventable

American Society of Pharmacovigilance. Available at: https://www.stopadr.org/
Brown MT et al. Mayo Clin Proc 2011 (PMID 21389250)
Watanabe JH et al. Ann Pharmacother 2018 (PMID 29577766)
Lazarou et al. JAMA 1998 (PMID 9555760)

Considerations for Long-term Care

- Estimated that up to 91% of long-term care residents take ≥5 meds; 65% take ≥ 10 meds
- ADR risk increases with age
- 60% of those in nursing home facilities experience ADRs
- Patients 65+ years of age are 2X as likely to be hospitalized due to ADR
- ADRs can be difficult to assess in an elderly population given non-specific presentations
- Some ADRs more likely in seniors, e.g., falls are associated with antihypertensives, sedatives, antidepressants

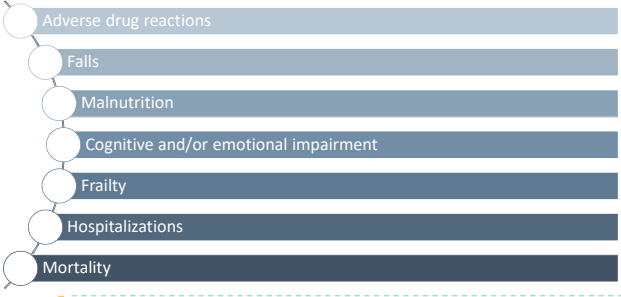Jokanovic et al. J Am Med Dir Assoc 2015 (PMID 25860930) | Lavan et al. Ther Adv Drug Saf 2016 (PMID 26834959)

Other Outcomes Associated with Polypharmacy

- Adverse drug reactions
- Falls
- Malnutrition
- Cognitive and/or emotional impairment
- Frailty
- Hospitalizations
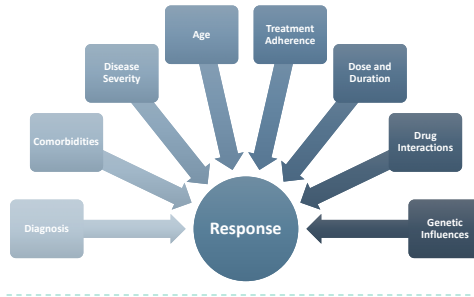- Mortality

Khezrian et al. Ther Adv Drug Saf 2020 (PMID 32587680) |

Variability in Treatment Response and Safety

Age
Treatment Adherence
Disease Severity
Dose and Duration
Comorbidities
Drug Interactions
Diagnosis
Response
Genetic Influences

Ionescu DF et al. Dialogues Clin Neurosci 2015 (PMID 26246787) |
Haga SB. Gender in the Genomic Era 2017;717-732.

Pharmacogenetics (PGx)

One size does not fit all

- Patient's genetic profile
- Drug-Drug interactions
- Drug metabolism
- Gene-Drug interactions
- Response to medications
- Lifestyle impact (ex. caffeine)

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Pharmacogenetic testing

PGx examines how genetic variation affects a person's response to medications

Another tool

Probabilistic and not deterministic

Adds to clinical presentation

Part of the clinical puzzle
Never rely solely on PGx

Safety & tolerability

Better at assessing drug tolerability risk
Field growing rapidly with new guidelines

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Clinical and Economic Utility of PGx Testing

Perlis et al: Pharmacogenetic testing among patients with mood and anxiety disorders is associated with decreased utilization and cost: A propensity-score matched study
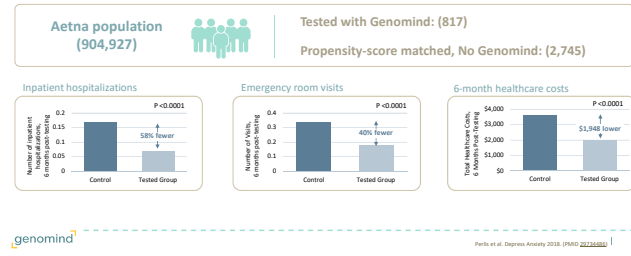
Aetna population (904,927)

Tested with Genomind: (817)

Propensity-score matched, No Genomind: (2,745)

Inpatient hospitalizations — P <0.0001 — 58% fewer

Emergency room visits — P <0.0001 — 40% fewer

6-month healthcare costs — P <0.0001 — $1,948 lower

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Perlis et al. Depress Anxiety 2018. (PMID 29734486)

Jarvis et al: Real-world impact of a pharmacogenomics-enriched comprehensive medication management program

- Retrospective study of the effects of a pharmacogenomics + comprehensive medication management program in 5,288 patients ≥ 65 years old
- Outcomes on direct medical costs and healthcare resource utilization followed over the first 32 months of program initiation
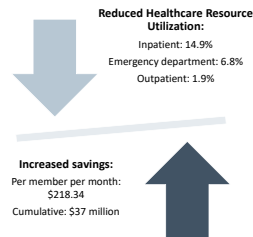
Reduced Healthcare Resource Utilization:
Inpatient: 14.9%
Emergency department: 6.8%
Outpatient: 1.9%

Increased savings:
Per member per month: $218.34
Cumulative: $37 million

Table 2. Risks associated with pre-intervention regimens.

Risks Associated with Pre-Intervention Regimens	
Identified Risk	n (%)
AGS Beers Criteria®	4232 (90%)
Drug-Drug Interaction	4093 (87%)
ADR (FDA Black Box)	3978 (84%)
Genetic	3110 (66%)
Anticholinergic Burden	2645 (56%)
Lifestyle	1171 (25%)
Contraindication	9 (0%)
Total Interventions (MAPs)	4716 (100%)

Abbreviations | ADR, Adverse Drug Reactions; FDA, Food and Drug Administration.

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Jarvis et al. J Pers Med 2022 (PMID 35330421)

David et al: An analysis of pharmacogenomic-guided pathways and their effect on medication changes and hospital admissions: a systematic review and meta-analysis

The effect of PGx on hospitalizations and number of medication changes

Hospitalizations

Study or Subgroup	PGx tested Events	Total	TAU Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Brixner et al. (2016)	20	205	132	820	19.1%	0.56 [0.34, 0.93]
Elliott et al.(2017)	17	57	39	53	13.5%	0.15 [0.07, 0.35]
Epstein et al.(2010)	147	896	685	2688	23.7%	0.57 [0.47, 0.70]
Perlis et al.(2018)	57	817	466	2745	22.6%	0.37 [0.28, 0.49]
Ruano et al.(2020)	99	982	43	477	21.2%	1.13 [0.78, 1.65]
Total (95% CI)		**2957**		**6783**	**100.0%**	**0.50 [0.32, 0.78]**
Total events	340		1365			

Heterogeneity: Tau² = 0.21; Chi² = 31.15, df = 4 (P < 0.00001); I² = 87%
Test for overall effect: Z = 3.01 (P = 0.003)

Favours [PGx tested]   Favours [TAU]

FIGURE 5 | Forest plot showing the effect of PGx testing on hospitalization compared to treatment-as-usual. 95% CI, 95% confidence interval. The number of "events" are the number of participants who were hospitalized during the reporting period of the study.

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David et al. Front Genet 2021 (PMID 34394187)

Medicare local coverage determination (MoIDX)

"PGx testing is considered reasonable and necessary in limited circumstances as described below as an adjunctive personalized medical decision-making tool once a treating clinician has narrowed treatment possibilities to specific medications under consideration for use, or is already using a specified medication, based on other clinical considerations including the patient's diagnosis, the patient's other medical conditions, other medications, professional judgment, clinical science and basic science pertinent to the drug, and the patient's preferences and values.

PGx tests are indicated when medications are being considered for use (or already being administered) that are medically necessary, appropriate, and approved for use in the patient's condition and are known to have a gene(s)-drug interaction that has been demonstrated to be clinically actionable as defined by the FDA (PGx information required for safe drug administration) or Clinical Pharmacogenetic Implementation Consortium (CPIC) guidelines (category A and B).

The selection of the medications in question must be derived from clinical factors/necessity rather than from a PGx test. Once the putative therapeutic agents are selected, and those agents are known to have gene-drug interactions as identified above, then a PGx test may be considered reasonable and necessary when the result of that test is necessary for the physician's decision-making process regarding safely administering or dosing the drug."

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https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=38294&ver=16&DocID=L38294&SearchType=Advanced&bc=EAAAAgAAAA&

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Genomind PGx Report

Variants of 24 pharmacokinetic and pharmacodynamic genes
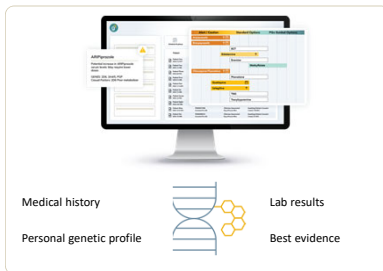
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Genomind PGx Report

Variants of 24 pharmacokinetic and pharmacodynamic genes

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Precision Medicine Software: What is it?

- Precision drug-gene-environment interaction software. Marries drug-drug to drug-gene interactions

- Provides a composite score of all interactions in a profile

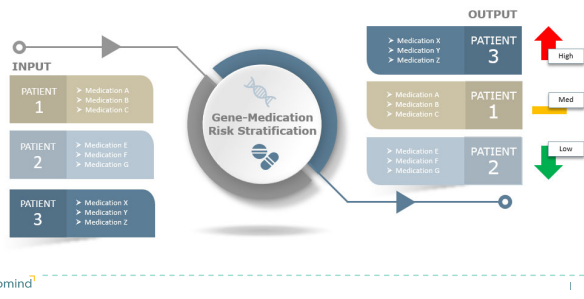- Accounts for the influence of multiple pathways and drug duplications

Medical history

Personal genetic profile

Lab results

Best evidence

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Precision Medicine Software
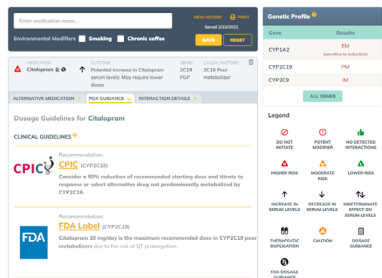
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Population Health Assessment

Integration into Workflow
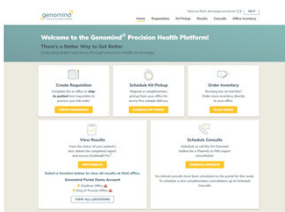
Provider-specific Portal   EMR Integration
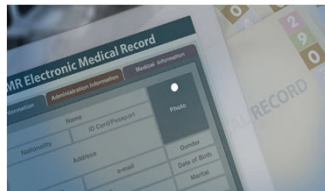
Population and Individual Risk Assessments

- Population Assessments
  - Total interactions per patient
  - Major/moderate/minor interactions
  - Drug-drug vs. drug-drug-gene interactions
  - High risk drug categories
  - Distribution by age

- Individual Score
  - Drug-drug interaction assessment
  - Probability of drug-drug-gene interaction
  - SNaPshot created for each individual

CONCLUSIONS

1. Polypharmacy is common among elderly and long-term care residents
2. It is associated with excess morbidity, mortality and resource utilization
3. PGx is a form of precision medicine that is designed to select meds more likely to be safe and effective
4. PGx has been shown to save resources, including rehospitalization, in multiple settings
5. PGx is covered by Medicare
6. Genomind has multiple tools to facilitate the use of PGx at the individual and population level

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Questions?

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