The clinical role of pharmacogenetics and drug testing in patients with mental health disorders

Drug Monitoring podcast series—Topics in Drug Testing

June 2021

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Welcome!

Thank you for joining us today

- During today's podcast we will focus on clinical care for patients with mental health disorders

- Will discuss and share information regarding:
  1. Mental health disorder and substance abuse prevalence
  2. The clinical utility of pharmacogenomics in mental health and addiction
  3. Mental health disorders and medication nonadherence

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What are the most common types of mental health disorders?

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Prevalence and occurrence of mental health disorders

44M Americans (18%) age 18+ **experience some form of mental illness**[1]

20M people (8.4%) in the past year **had substance use disorders**[1]

8.1% American adults age 20+ **had depression in a given 2-week period**[1]

7.9M of these people had **BOTH mental disorders & SUDs**[1]

- Mental disorders begin and occur at different stages in life and are more prevalent in certain age groups[2]
- Schizophrenia and other disorders usually emerge in early adulthood[2]

The COVID-19 pandemic has had an extremely significant impact on mental health.

1. https://www.cdc.gov/nchs/data/databriefs/db303.pdf
2. https://www.samhsa.gov/disorders

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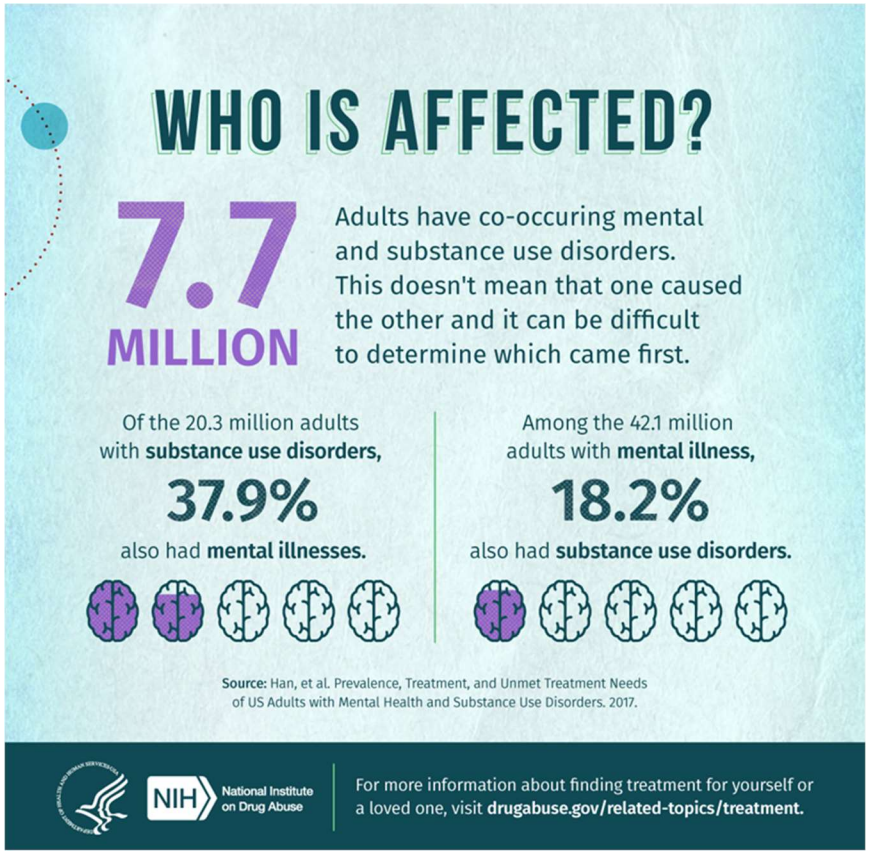
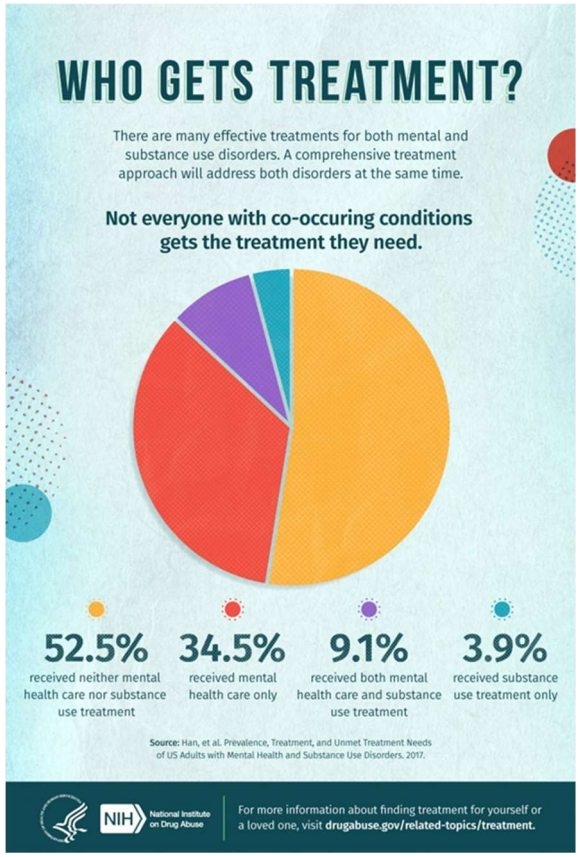
Comorbidity—substance use disorders and other mental health disorders





https://www.drugabuse.gov/drug-topics/trends-statistics/infographics/comorbidity-substance-use-other-mental-disorders

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Pharmacogenomics in mental health and addiction

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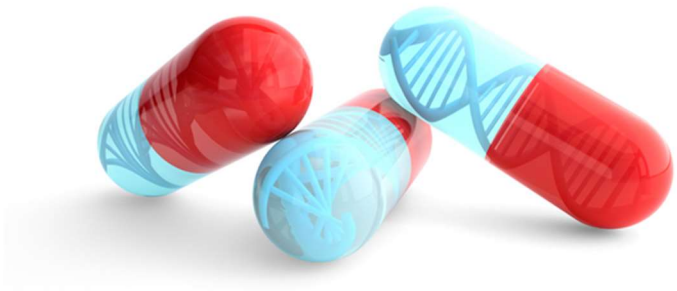
What is pharmacogenomics (PGx)?

- Pharmacogenomics uses information about a person's genetic makeup, or genome, to choose the drugs and drug doses that are likely to work best for that particular person[1]
- Pharmacogenomic testing identifies genetic variations that impact pharmacodynamics and pharmacokinetics
- Certain genetic variations are associated with specific medications and these interactions can help guide prescribing



1. National Institutes of Health. National Human Genome Research Institute

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Variability in efficacy and safety

Pharmacogenomics (PGx) influences how a medication is chosen for a patient

Hicks et al. *Am J Health Syst Pharm*. 2016 Dec 1;73(23):1967-1976.

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Pharmacogenomics clinical utility

- PGx is not used in a vacuum as it is always supplemented by clinical judgment
- PGx does not replace clinicians' clinical experience or supplant evidence-based medicine
- The use of data from pharmacogenomic testing can improve clinical outcomes by:
  - Reducing adverse events
  - Maximizing drug effectiveness
  - Minimizing gaps in care
- These benefits can have a positive effect on quality metrics and financials for healthcare systems

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Specific gene-drug combinations

Mental health

- Metabolism
  - CYP2D6, CYP2C19: antidepressants, antipsychotics, anti-anxiety
  - Able to give guidance on potential concentration of specific medications
  - Poor, intermediate, normal, rapid, ultrarapid
- Pharmacodynamics
  - SLC6A4: SSRIs
    - Serotonin transporter gene, where SSRIs have their effect
    - Presence of short form of promoter can indicate that patients are less likely to respond to SSRIs
  - HLA-B*15:02 and HLA-A*31:01: phenytoin, carbamazepine, oxcarbazepine, lamotrigine
    - Patients with these HLAs have an increased risk of Stevens-Johnson Syndrome
  - MTHFR-methyltetrahydrofolate reductase
    - Enzyme that converts folate to active methylfolate form required as a co-factor in serotonin manufacture
  - Other genes with less evidence: COMT, ABCB1, GRIK4, HTR2A, BDNF

CPIC guidelines

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Specific gene-drug combinations

Opioids and other pain medications

- Metabolism
  - CYP2D6: codeine, tramadol, hydrocodone, oxycodone
  - CYP2B6: methadone
  - CYP3A4: buprenorphine, fentanyl (and possibly derivatives), meperidine
  - CYP2C9: NSAIDs-ibuprofen, celecoxib, flurbiprofen, naproxen, diclofenac
  - Medications not significantly affected by CYP metabolism: tapentadol, morphine, hydromorphone, oxymorphone
- Poor/intermediate metabolizers at CYP2D6
  - Parent compounds are less potent than active metabolites: codeine, tramadol, hydrocodone
  - May lead to poor pain control
- Ultrarapid metabolizers at CYP2D6
  - Active metabolites are produced at a much faster rate than in normal metabolism
  - May lead to serious adverse effects such as respiratory depression

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Specific gene-drug combinations

Opioids

- Pharmacodynamics
  - OPRM1: opioids
    - Mu opioid receptor gene
    - Best studied allele is A118G
    - Patients with G allele are less likely to experience analgesia from opioids
    - May require higher doses
    - Patients with G allele are more likely to have addiction
  - COMT: opioids
    - Catechol-*O*-methyltransferase gene
    - Best studied allele is val158met
    - Patients with met allele may require less opioid doses and are less likely to have addiction
  - OPRD1: opioids
    - Less well-characterized relationship, may be gender related

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Specific gene-drug combinations

Addiction treatment

- Methadone maintenance treatment
  - CYP2B6 metabolism: may influence concentration, mixed evidence on clinical parameters
  - OPRM1: mixed evidence on clinical outcomes
- Suboxone treatment
  - OPRM1, OPRD1, COMT: may influence response to treatment
  - CYP3A4: ultrarapid metabolizers may need higher doses

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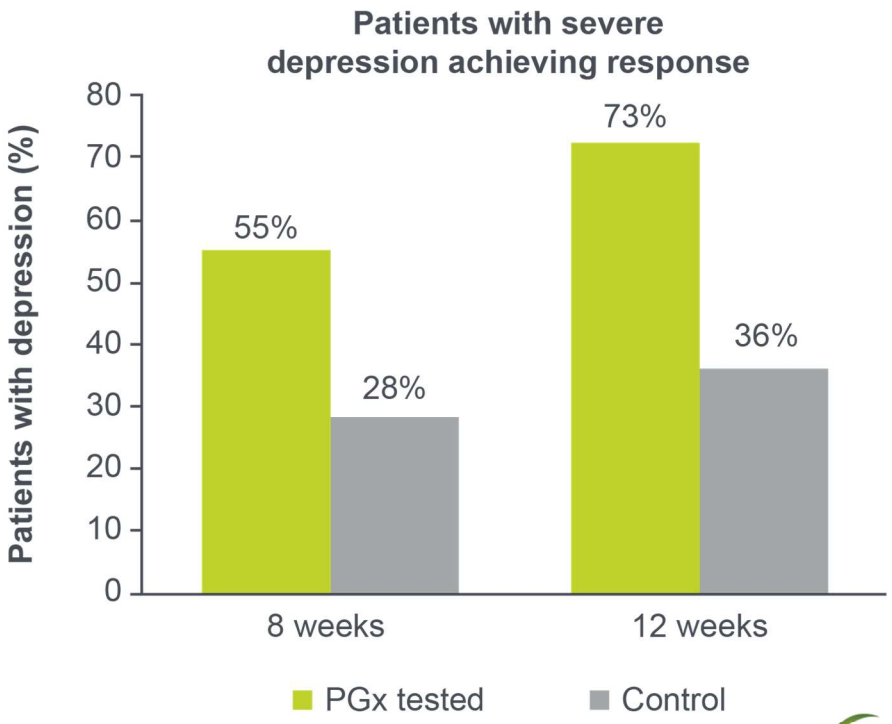
Why pharmacogenomic testing?

Realizing the benefits of more informed prescribing

More effective treatment

- Pharmacogenomic testing has been shown to **increase the number of patients** with major depression **who responded with antidepressant therapy**[1]
- Remission rates were also improved after 12 weeks
  - 35% PGx vs 13% control
- **NNT for additional patient with severe depression to respond after 12 weeks = 3**



1. Bradley 2018.

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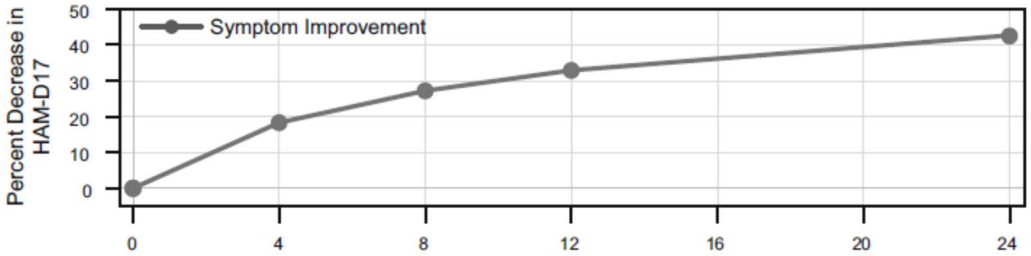
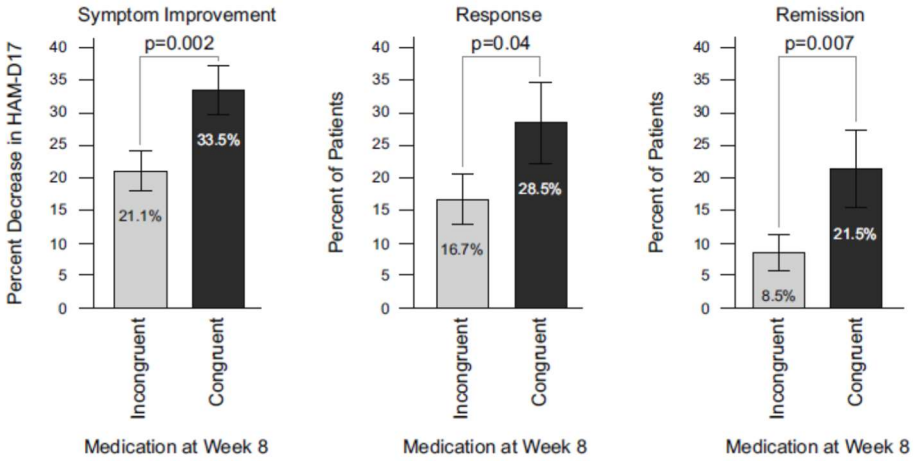
Why pharmacogenomic testing?

Durable and clinically valid outcomes in depression shown in the GUIDED trial (n=1799)



Patients in the GUIDED trial continued to see improvement (>50%) in depression symptoms when using PGx even after trial end at week 8.

Patients also saw greater improvement in depression symptoms when switched from an incongruent medication to a congruent medication based on the PGx report.



Greden et al. 2019

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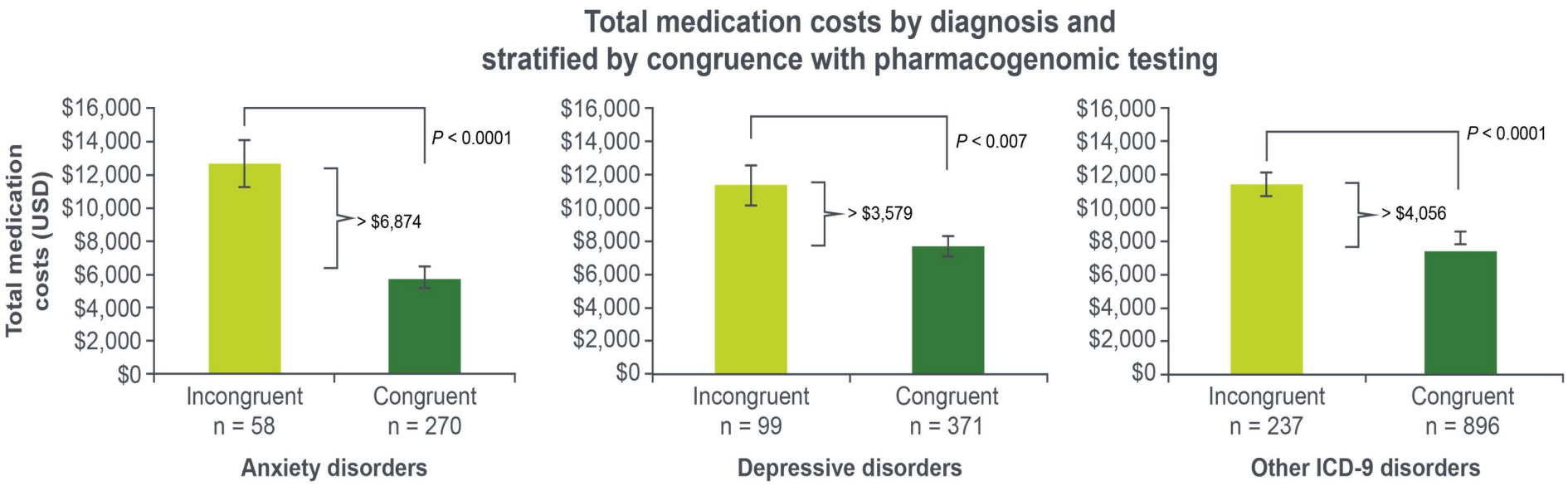
PGx testing informs prescribing and reduces pharmacy costs

- Providers who prescribed medications based on the results of pharmacogenomic testing realized annual pharmacy cost savings when compared with those who did not follow the prescribing recommendations of pharmacogenomic testing[1]



1. Winner 2015. ICD-9, International Classification of Diseases, 9th Revision; USD, United States dollars.

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Mental Health disorders and medication nonadherence

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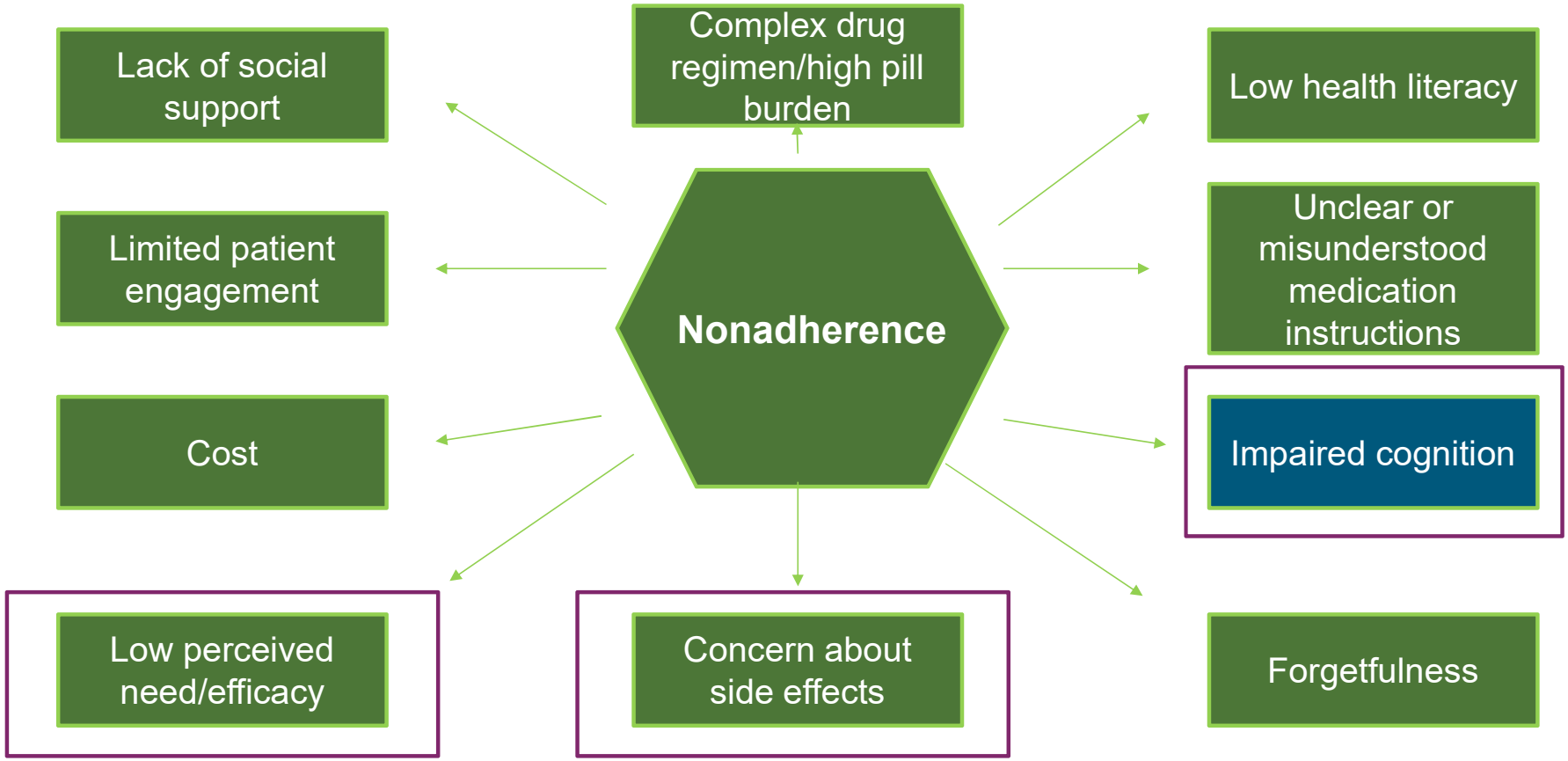
Many reasons for medication nonadherence



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Consequence of nonadherence

- Worsening of symptoms
- Increased risk of relapse
- Rehospitalization
- Suicide attempt
- Increased cost
- Disrupted recovery
- Risk of self-injury or harm to others

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Drug testing considerations for patients with mental health disorders

In addition to controlled substance drug monitoring, clinical decision-making can benefit from testing compliance to medications for mental health disorders

- Reason for testing for antidepressant/antipsychotic is not an abuse issue
  - Medication adherence
  - Potential for mixing these medications with other drugs or substances
- May not need to test as often as SUD
- HCPs tend to acknowledge nonadherence as a global issue and not a local issue (“not my clinic,” “not my patients”)
- **If a patient is experiencing nonadherence, using PGx** to find a different medication that may have a lower side effect burden or be more effective **can be a solution**

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How can Quest help?

- Our offerings
  - Clinical drug monitoring for controlled substances
  - Compliance monitoring for antidepressants, anticonvulsants, and antipsychotics
  - At-home and PSC testing options (when in-office UDT is not an option)
  - Rx Toxline for expert consultation
    - PharmDs and MDs available for clinical consultation
    - Toxicologists for testing details and interpretation

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Moderator close:

Quest Diagnostics® Clinical Drug Monitoring

- Thank you for joining us today and thank you to our speakers
- To learn more about the Quest Diagnostics Clinical Drug Monitoring offering, visit:
  - **www.QuestDrugMonitoring.com**
- For educational resources and insights from our team of toxicology experts, spend some time at our website resources center:
  - **www.QuestDrugMonitoring.com/resources**
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- For a copy of our latest Health Trends study, *The Opioid Epidemic Within the COVID-19 Pandemic: Drug Testing in 2020*, published in *Population Health Management*, go to:
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