The Impact of Polypharmacy, PIMs, and Pharmacotherapy for AUD and HCV

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COMpAAAS Observational Study

Toward Prioritization of Co Medication Among HIV Infected Individuals Who Drink
Prior Work

• Alcohol use is common among HIV+ on ART
  – Commonly co-occurs with tobacco and depression
  – Lower levels associated with frailty and mortality among HIV+ on ART than uninfected
  – Alcohol & HIV-1 viremia accelerate liver cirrhosis
  – (Alcohol increases potentially inappropriate meds, PIMs)
• Polypharmacy 10 years earlier among HIV+ on ART and associated with greater mortality
• Pharmacotherapy for AUD and HCV is under utilized among HIV+ on ART who drink
Terms

• ART: combination antiretroviral therapy
• Co medication: non CART medications
• Polypharmacy: being on 5+ medications
• HCV: hepatitis C infection
• AUD: alcohol use disorder
• PIMs: potentially inappropriate medications
• PSOs: patient salient outcomes
  – Mortality
  – Hospitalization
  – Medically significant falls
  – Pneumonia
  – Delirium
Polypharmacy and PIMs

• Polypharmacy is:
  – Increasing with time (doubled from 2000-2012)
  – 3 times more common among HIV+

• Potentially inappropriate medications (PIMs):
  – Drugs that interact or have increased toxicity in a specified context
  – Increase with polypharmacy
  – Likely contribute to harm from polypharmacy
  – Increase with ART, alcohol, and aging
ART, Alcohol, & Aging PIMs

• ART: 71% of HIV+ on ART are on 1+ ART PIM
  – Interfere with metabolism: CNS/CVD drugs (statins), methadone
  – More common with age, substance use, HCV coinfection

• Alcohol: 48% of those who drink take 1+ alcohol PIM
  – Pharmacodynamic: enhances CNS effect of benzodiazepines, antipsychotics, antidepressants, opioids, muscle relaxants
  – Pharmacokinetic: interferes with drug or alcohol metabolism including H2 blockers, CVD drugs, OTC pain meds, DM meds

• Aging: 54% of uninfected Veterans 65+ take 1+ aging PIM
  – Beer’s Criteria, more if consider STOPP as well
  – Interactions and metabolic limitations with age
HIV and Alcohol May Also Be a Barrier to Beneficial Pharmacotherapy

• Providers may be reluctant to prescribe pharmacotherapy for AUD among HIV+
  – Concern about interactions with ART
  – Pre-existing and rapidly progressing liver injury

• HCV is common among HIV+ who drink and exacerbates harm from alcohol and HIV
  – New direct acting agents (DAAs) can cure HCV
  – Alcohol may be a barrier to receipt
Current cohort consists of ~50K HIV+ demographically matched to ~100K uninfected veterans. VACS is predominantly male but includes ~3,500 (1000 HIV+) women. We have 3 times the national proportion of 65+ year old individuals.
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<th>Patient Salient Outcomes (PSOs) in VACS 2008-2015</th>
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Aim 1: Among those with AUD, characterize AUD pharmacotherapies used and estimate their effects

• AUD will be associated with PSOs; risk will be greater among HIV+ than uninfected.

• HIV+ will be less likely to receive AUD pharmacotherapy than uninfected.

• Receipt of AUD pharmacotherapy will decrease risk of PSOs more for HIV+ than uninfected.
Aim 2: Fully characterize impact of polypharmacy and alcohol on PSOs by HIV status

- Polypharmacy will increase risk which will be greater among HIV+ and current drinkers.

- Controlling for polypharmacy,
  - Drinkers taking Alcohol PIMs will have greater risk compared with unexposed drinkers and risk will be greater among HIV+.
  - HIV+ taking ART PIMs will have greater risk, compared with unexposed HIV+.

- Polypharmacy/PIMs will increase risk of ART discontinuity.

- All associations will increase with better measures (medication reconciliation and PEth).
Aim 3: Compare AUDIT-C vs. PEth estimates as measures of exposure in determining DAA treatment and response (HIV+/HCV+ and HCV+)

- Self report of alcohol use via AUDIT-C will be a greater barrier to DAA initiation than equivalent biomarker (PEth) levels.
- PEth will be a greater barrier to virologic response (SVR) than equivalent self report via AUDIT-C.
- HIV will enhance associations between alcohol use and poorer access/response to DAAs.
Methodologic Issues

• Measurement of exposure
  – Exposures likely measured with error:
    • Alcohol (self-report)
    • Polypharmacy and PIMs (outside care, OTC)
    • AUD and HCV pharmacotherapy (outside care)
  – Measurement error correction (with regression)

• Confounding by indication
  – Pharmacotherapy subject to confounding:
    • Polypharmacy
    • AUD and HCV treatments
  – Propensity adjustment
Innovation

• First to analyze impact of PIMs (ART, alcohol, aging) on a panel of outcomes by HIV status
• First to analyze alcohol as a barrier to DAA receipt/response among HIV+ or uninfected
• First to analyze benefits of pharmacotherapy for AUD by HIV
• First large scale study of all these questions that will adjust for propensity and correct for measurement error
Impact

• Inform the prioritization of co medications among those aging with HIV by identifying medications that:
  – Cause more harm than benefit
    • Which PIMs matter
    • To what extent is pure polypharmacy to blame
  – Cause more benefit than harm
    • Which AUD pharmacotherapies are effective
    • Do drinkers benefit from DAAs
National Team