Network Analysis of Information Needs to Identify Safe and Effective prescriptions for an Individual.

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The Problem(s)

- 53% of adults have MM2+
- 33% of adults have MM3+
- If you are treating someone with diabetes, depression, and arthritis it is hard to follow the EB guidelines

- 13% of patients have “high risk” prescriptions even with ”good” electronic medical records
  - 10% if taking 2-4 drugs
  - 80% if taking > 14 drugs

- Adverse Drug Events
  - Within 4 weeks of receiving a primary care prescription, 25% of patients experience an adverse drug event
  - Up to 70% of ADRs leading to ED visits are preventable
Aim: Using Network Analysis explore the potential interactions for a hypothetical patient

- Hypothetical comorbid MM5 patient
  - Osteoarthritis (12 drug options)
  - Depression (12 drug options)
  - Hypertension (34 drug options)
  - Diabetes (18 drug options)
  - Hyperlipidemia (4 drug options)

Total of 80 drugs used commonly in primary care available for this patient – no combinations included

- Liver & Renal
- Total of 82 nodes of a network
- That is 3,321 combinations to check for interactions (N*(N-1)/2)
Identify actual potential drug-drug, drug-liver, drug-renal interactions

• Drug Drug Interactions identified using a drug-drug interaction database (Lexicomp)
• Renal interactions identified using a renal drug interaction database and North American product monographs
• Liver Function interactions checked using North American product monographs
• Results: 1,113 described potential interactions
Results:
Types of Interaction

• Interactions were identified as
  • No Action Needed (n=189),
  • Monitor Therapy (n=777),
  • Consider therapy modification (n=144),
  • Avoid combination (n=3).
  • *No Action Needed example: Benazepril and Canagliflozin -SGLT2 inhibitor*
    • Canagliflozin may enhance the hyperkalemic effect of Angiotensin II Receptor Blockers. Canagliflozin may enhance the hypotensive effect of Angiotensin II Receptor

• The mean number of drug-drug, drug-liver, and drug-renal interactions was 27.1 (Range 1 to 56).
• The frequency of interactions was not normally distributed
• Renal dosing information was identified for 50 drugs,
• Liver dosing information was identified for 46 of the drugs.
Renal cocoon of a Cyna moth pupa

non-steroidal anti-inflammatory drugs, diuretics, morphine and duloxetine, were the drugs with most interactions.
Force Atlas Analysis
Weighting appears to highlight diuretics

<table>
<thead>
<tr>
<th>Drug Interaction</th>
<th>Weighting</th>
</tr>
</thead>
<tbody>
<tr>
<td>B: No action needed</td>
<td>0</td>
</tr>
<tr>
<td>C: Monitor therapy</td>
<td>1</td>
</tr>
<tr>
<td>D: Consider therapy modification</td>
<td>2</td>
</tr>
<tr>
<td>X: Avoid combination</td>
<td>3</td>
</tr>
<tr>
<td>Liver Dosing</td>
<td>2</td>
</tr>
<tr>
<td>Renal Dosing</td>
<td>2</td>
</tr>
</tbody>
</table>
Clustering Coefficient
0.243

- Size and colors of nodes is clustering coefficient
- Clear groupings of drugs by mechanism of action, and interaction
Network Analysis

- Takes highly complex data sets
  Combine all these features into one picture
- Clear groupings of drugs
Summary

• Findings
  • There are clearly identified groups of drugs that are potentially more harmful than others (Diuretics, NSAIDs, Hypoglycemics)
  • The size these effects and their relationships can be identified and described using network analysis

• Limitations
  • Only commonly used drugs in primary are included
  • Only Drug-Drug, Liver and Renal interactions included
  • Only Lexicomp used
  • Does not take into account what the patient may be taking already – that reduces the network

• Next Steps
  • Start adding more information from the examples above
  • Explore whether and how guidelines/protocols can manage MM2+ to MM5+
  • Can Network Analysis help clinicians manage prescribing for patients with MM
Conclusions for EBHC guidance about medications

• For a patient with multimorbidity the complexity and volume of potential interactions identified using Network Analysis approach is staggering

• Class effects are significant but not universal

• Rational Prescribing approaches such as Deprescribing systems and Choosing Wisely need to take into account MM, perhaps using Network Analysis.

• “can I just click on the disease for my patient and see the Network Analysis?”

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## Medication Decision Support

### Medication Options

#### Psychotherapy and anti-anxiety medication

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Class</th>
<th>Initial Dose</th>
<th>Titrating</th>
<th>Usual Dose</th>
<th>Maximum Dose</th>
<th>Dose adjusted for renal function</th>
<th>Brands</th>
<th>Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escitalopram</td>
<td>Antidepressant, SSRI</td>
<td>10 mg PO once daily</td>
<td>Increase daily dose by 10 mg every 1-2 weeks as needed and tolerated</td>
<td>20-40 mg PO once daily</td>
<td>40 mg PO per day</td>
<td></td>
<td>Paxil, generics</td>
<td>Acetylsalicylic acid</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Antidepressant, SSRI, CYP2C19 Inhibitor</td>
<td>10 mg PO once daily</td>
<td>Increase daily dose by 10 mg every 1-2 weeks as needed and tolerated</td>
<td>20-40 mg PO once daily</td>
<td>40 mg PO per day</td>
<td></td>
<td></td>
<td>Acetylsalicylic acid</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Antidepressant, SSRI, CYP2C19 Inhibitor</td>
<td>50 mg PO once daily</td>
<td>Increase daily dose by 25 mg at 1 week intervals as needed and tolerated</td>
<td>50-150 mg PO once daily</td>
<td>200 mg PO per day</td>
<td></td>
<td>Zoloft, generics</td>
<td>Acetylsalicylic acid</td>
</tr>
</tbody>
</table>

*Sertraline may increase the antiplatelet activities of Acetylsalicylic acid.*

Duloxetine is not included as an option due to contraindications, drug interactions or previous trial.

Venlafaxine is not included as an option due to contraindications, drug interactions or previous trial.

### Additional Features

- **Management of Drug-Drug Interactions**
- **Drug-Gene Interactions**
- **Specific Dosing** (initial, titration, maximum, target)
- **Dose Adjustment for Renal & Hepatic Impairment**
- **Price Comparison**
- **Brand Names**
- **Drug-Drug Interactions**
- **Excluded Medications**