Disclosures

- I have no financial conflicts to disclose.
- Some commercially available products will be discussed or presented for the purposes of example only. I do not recommend or endorse any specific products.

Objectives

- After attending this presentation, the participant should be able to:
  - Describe factors that contribute to medication non-adherence
  - Discuss positive and negative aspects of various tools and strategies designed to improve medication adherence
**Transplant at HMH 2016**

<table>
<thead>
<tr>
<th>2016</th>
<th>New Transplants</th>
<th>Post-tx Actively Managed</th>
<th>Post-tx Outpatient Clinic Visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>211</td>
<td>2081</td>
<td>2168</td>
</tr>
<tr>
<td>Kidney / Pancreas</td>
<td>20</td>
<td>192</td>
<td>638</td>
</tr>
<tr>
<td>Liver</td>
<td>112</td>
<td>580</td>
<td>1432</td>
</tr>
<tr>
<td>Heart</td>
<td>39</td>
<td>302</td>
<td>1099</td>
</tr>
<tr>
<td>Lung / Heart</td>
<td>64</td>
<td>460</td>
<td>1725</td>
</tr>
<tr>
<td>Total</td>
<td>446</td>
<td>3615</td>
<td>7062</td>
</tr>
</tbody>
</table>

- Lung transplant service
  - Surgeons (6)
  - Transplant pulmonologists (5)
  - Mid-level providers (4)
  - Pharmacists (2)
  - Post coordinators (7)
- Pre coordinators (2)
- Clinical assistants (5)
- Case manager
- Social worker
- Financial specialist
- Psychiatrist

**Background**

"Drugs don't work in patients who don't take them."

– C. Everett Koop, M.D.

In the interest of time, let’s assume this to be true...

- For a more elaborate conversation regarding:
  - Theoretical definition of “adherence” vs. “compliance”
  - Characterizations / classifications of adherence
  - Strategies / tests to measure adherence
  - Incidence / epidemiology of non-adherence
  - Outcomes associated with non-adherence

Recommended Reading

Barriers to Adherence

- Access
  - Financial barriers
  - Care coordination issues
  - Insurance barriers
- Communication
  - Lack thereof
  - Misunderstanding
- Carelessness
  - Forgetfulness
  - Patient busyness
- Intentional dissent
  - Side effects
  - Inconvenience / complexity
  - Perceived lack of need / consequences
- Health Literacy
- Support (Lack of)
- Mental Health Issues
  - Depression
  - Cognitive impairment

Key Point

- Transplant environment practically forces prospective assessment of some potential barriers to non-adherence
  - Financial
  - Case management / social work
  - Psych
- This requires effort (and maybe resources), but solving problems early vs. late is usually easier and safer

My Approach...

Access to Medications

Key Point

- Ensure core logistics related to medication access between prescriber, patient, and dispensing pharmacy are in order
  - Ensure active scripts on file with dispensing pharmacy
  - Ensure "prior authorizations" and other information requests completed in a timely manner
  - Ensure final copays reasonable given available resources
- Tip: Just handing/phonign/sending a script is often simply not good enough... Is the patient physically holding the medication in their hands?

My Approach...

- Accuracy of the Med List
- Access to Medications

Key Point

- Ensure patient and team are always working off of the same (or "agreeing") medication lists
  - How many "systems" or "sources of truth" are there?
  - Need a plan to handle adjustments by all providers
  - Need to ensure inpatient admission/discharge process doesn't cause chaos
  - Are changes date/time/user stamped?
  - Does the system allow meds to "fall off" a profile vs. forcing manual removal?
  - Is the EHR primarily designed to generate/maintain a med list or generate scripts?
**My Approach...**

- **Aesthetics / Functionality of the physical Med List**
- **Accuracy of the Med List**
- **Access to Medications**

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**Key Point**

- Paper medication lists should be as detailed and “patient friendly” as necessary - balancing the patient’s level of health literacy, the complexity of the medication regimen, and the logistics of the care team
  - The most “patient friendly” look/feel is the goal
  - However, other programmatic needs must also be considered
    - E.g., accuracy, access, accountability, efficiency, etc...

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**Med List Considerations**

- Patient-friendly?
- Degree of customization?
- Allow for templates for ease of use / consistency?
- Easy foreign language translations?
- Are changes date/time/user stamped?
- Forced ownership amongst users?
- Do all necessary team members have access to make updates? How many users?
- Does the patient also have access / ability to modify?
Example Med List

Microsoft Word

Comments:
- Basic
- Fine for simple med lists
- Potentially exists outside of EHR
- Local/Shared/Cloud file storage?
- Who has access?
- Not date/time/user stamped

Example Med List

Allscripts

Comments:
- Within the EHR
- Not very "pretty"
- Not very customizable

<table>
<thead>
<tr>
<th>Capsules 65 mg oral tablet, chewable</th>
<th>1 x daily, twice a day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folic acid 0.5 mg oral capsule</td>
<td>1 x daily, twice a day</td>
</tr>
<tr>
<td>Metamucil 40 mg oral capsule 4 tablets</td>
<td>1 x daily, twice a day</td>
</tr>
<tr>
<td>Phenazopyridine 40 mg oral tablet</td>
<td>1 x daily, twice a day</td>
</tr>
<tr>
<td>Oxelase 100 mg oral tablet</td>
<td>1 x daily, twice a day</td>
</tr>
</tbody>
</table>
Example Med List

Comments:
Better for complex regimens
Facilitates pillbox usage
Potentially exists outside of EHR
Double work
Conflicts common with EHR
Local/Shared/Cloud drive files?
Who has access?
Not date/time/user stamped

Example Med List

Comments:
Better for complex regimens
Facilitates pillbox usage
Very "patient friendly"
Very customizable
Easy language translation
Web-based interface
Associated mobile app
Patient/team access
Date/time/user stamped
Potentially exists outside of EHR
double work
discrepancies with EHR

Example Med List

Comments:
Better for complex regimens
Facilitates pillbox usage
Date/Time/User stamped
Potentially exists outside of inpatient EHR
double work
discrepancies with EHR
Example Med List

Comments:
- Within the inpatient and outpatient EHR
- Not very customizable
- Interface difficult, discourages use amongst providers
- Data lost during transitions of care
- Thinks in terms of prescriptions vs. as a "med list"

My Approach...

Other Tools
Aesthetics / Functionality of the physical Med List
Accuracy of the Med List
Access to Medications

Key Point
- Encourage novel/creative/advanced adherence tools when necessary
  - Med adherence mobile device applications
  - Behavioral contracts
  - Other med adherence devices
Med Adherence Apps

Considerations:

- Many (but not all) patients use smartphones
- What purpose / functionality are you looking for?
  - Patient: maybe alerts to take a dose, refill reminders?
  - Provider: maybe ability to modify and “push” to patient?
- Cost
- Operating system
- As a program / provider, do you choose a preferred app for the entire program, or let patients choose?
  - Is there a plan to ensure med list on the app is not in disagreement with provider profile?
Disclaimer

- While potential benefits of mobile medication adherence apps are easy to grasp, evidence for beneficial outcomes is still lacking...
  - "Relatively" new area of study
  - Technology constantly changing
  - What is the treatment variable?
    - E.g., the app itself or the dose alarm/notification/reminder?
  - What does the comparator group look like?
    - E.g., not the same app, no alerts, no reminder, no smartphone?

Evidence

- Vervloet M et al. 2012
  - Review of 13 studies
    - Patients with a variety of disease states
    - Variable: SMS messages, pager messages, or use of other electronic reminder devices
    - Frequency of notifications varied
    - Follow-up limited (<6mo) in most studies
    - Most studies suggested benefit of the usage of the reminder device/notification
• Thakkar J et al. 2016
  – Review of 16 studies
    • Patients with a variety of disease states
    • Variable was mobile phone text messaging
    • Short follow up (6 weeks – 6 mo)
    • Some studies personalized messages
    • Frequency of messages varied
    • Definition of “adherence” varied
    • Aggregate adherence rate was 67.8%
      – Typical adherence rate assumed to be ~50% at 1 year for
        patients with chronic diseases
    » Authors concluded benefit vs. 50% threshold

• DeVito Dabs A et al. 2016 – Initial
• Rosenberger EM et al. 2016 – long-term
  – ~200 lung transplant patients, ~5 years of follow-up
    • Variable: use of a mobile app designed to improve adherence to
      self-monitoring plan (e.g., spirometry, vitals, symptoms, etc...)
    • Control group received standard of care
    • Medication adherence was included in a composite endpoint
    • App improved adherence to self-monitoring, adherence to the
      medical plan and communication of critical indicators
    • No difference in clinical outcomes observed between groups
      – E.g., mortality, chronic rejection, hospitalizations, etc...

• Commonly used in transplantation
  – Most often in the pre-tx, eval, listing phase
    • Gist is that patient agrees to do X, Y, and Z or there will be consequences
    • Examples
      • Negative nicotine tests
      • Negative drug screens
      • Keep all clinic/lab appointments
      • Take meds as instructed
      • Define support / care giver team
Behavioral Contracts

- Helps convey just how serious adherence to all aspects of the program really is
- Conveys a mutual agreement where the patient has to “do their part” as well
- The idea that non-adherence pre-transplant could impact a center’s willingness to offer transplantation is usually a good “carrot”
  - Some patients do declare themselves as non-adherent during the pre-tx process

Evidence

Chisholm-Burns MA et al. 2013
- Renal tx patients only (n=150), from multiple tx centers
- All patients > 1 year post transplant prior to enrollment
- Intervention was q 3 month “visits” x 4 for study group
  - Control group was standard of care
- Adherence outcome variable was determined by day on which outpatient meds were filled vs. quantity prescribed
  - Intervention group hospitalized less often than control group
  - Intervention group showed better adherence

Considerations

• HMH kidney transplant experience
  – Recently tried instituting a medication-specific adherence contract in the post environment
    • Not overwhelming success so far
      – Forms get signed (check)
      – Survey questionnaires garnered minimal response

• What are the consequences of a patient not adhering to the contract / program?
  – Are there any? [fired by the MD?, long clinic wait-times?]
  – Does the program do anything different based on the contract?

Considerations

• No threat of de-listing a patient for non-adherence after the transplant already happened
  – Possible impact on likeliness to re-transplant

• What is the “carrot”?
  – Graft may fail with poor adherence
    • Grave, though not always enough...
  – What about in non-transplant patients?
    • Eg. Hypertension, hyperlipidemia, hyperglycemia, etc...

• How do you prevent the behavioral contract from being just another “thing”?
  – We are still working on this...

Evidence

• Dobbels F et al. 2017
  – Heart, Lung, Liver tx recipients (n=205)
  – All patients > 1 year post transplant prior to enrollment
  – Intervention was 5 “visits” for the study group
    • Multicomponent behavioral interventions
    • Control group was standard of care
  – Adherence outcome variable measured using an event monitoring pillbox for tacrolimus
    • Dosing adherence 95% in the intervention group vs. 79% in the control group
Evidence

Behavioral Interventions

Dobbels F et al. J Heart Lung Transplant. 2017 (ahead of print)

Other Devices

Med Adherence

• Smart/Connected electronic pill boxes / bottles
  – Multiple companies offering
  – Features may include event monitoring, tracking of adherence, communication to family members, reminders

• Pillbox cellphone cases
  – Were being pitched, not sure if they really caught on...
  – Awkward / bulky, difficult if lots of meds

Assessment Question 1

1. Which of the following potentially contribute to medication non-adherence?

   a. Access
   b. Communication
   c. Carelessness
   d. Intentional dissent
   e. All of the above
Assessment Question 2

2. True or False – The outcomes evidence for mobile medication adherence apps is strong enough that providers should recommend their use in all patients?

a. True
b. False