Greater than half of newly approved cancer drugs are administered orally. Oral oncolytics make therapy more manageable and convenient for patients, but they also pose potential challenges in regard to adherence. Take an in-depth look at the issues surrounding adherence, including evidence-based interventions and research gaps. You’ll come away with tools to improve outcomes for your patients.

**Target Audience:** Registered Nurses, Advanced Practice Nurses, Advanced Nurse Researchers

**Level of Content:** Intermediate

**Speaker:**
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**Full Disclosure:**  
Nothing to Disclose

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**Full Disclosure:**  
Nothing to Disclose

**Objectives:**
At the end of this session, participants will be able to:
1. Identify issues impacting adherence to prescribed oral cancer agents.
2. Describe innovative strategies to promote medication adherence.
3. Discuss patient cases in which there are barriers to adherence and suggest ways to support those individuals in taking medications as prescribed.

**Bibliography:**


Oral Therapy: Underadherence, Overadherence and Everything in Between

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and
Susan M. Schneider, PhD, RN, AOCN, FAAN
Associate Professor
Duke University School of Nursing

“Drugs don’t work if people don’t take them.”
C. Everett Koop, Former US Surgeon General

Objectives

- Identify issues impacting adherence to prescribed oral cancer agents
- Describe innovative strategies to promote medication adherence
- Discuss patient cases where there are barriers to adherence and suggest ways to support those individuals in taking their medications as prescribed.

History of Oral Chemotherapy

- First agents introduced 1940-50’s
- Discovery of signaling pathways
- Changes in drug delivery process
- Significant increase in the number of agents approved in an oral form
- Research related to adherence

Shift to oral cancer treatments

- **Advantages**
  - Patient convenience
  - No need for IV access
  - Can achieve sustained drug levels
  - Minimal disruption in daily life
  - Patient preference
- **Disadvantages**
  - Distances patient from provider
  - Changes the way patients are monitored
  - Safeguards for prescription or administration may be lacking
  - Patients have more responsibility for their own care

State of the Problem

- For all medications:
  - One third to one half of all patients do not take medications as prescribed
  - Improving adherence to all medications can save as much as $300 billion in health care costs
- For oral cancer treatment:
  - Rates of adherence remain unknown but some studies in breast cancer have documented rates of 53-93%
  - The number of agents and the number of patients taking these agents will only increase.
  - 50% of therapies in development are oral.
  - Many patient taking oral agents are in the late stage of disease when other therapy has failed. Due to the gravity of a cancer diagnosis our goal should be as close to 100% adherence as possible.

References:
Bedell, 2003; Moore, 2007, 2009; Schneider, S. et al. 2011

Saturday, April 25
Quick Facts...
- Not unique to cancer alone.
- 49% of adults reported taking a Rx medication that they were only "Fairly Confident", "Somewhat Confident", or "Not at all Confident" in their knowledge about the medication.
- 27% of adults have decided not to fill a Rx because they had a concern about potential adverse reaction/s.
- Acute vs chronic disease

Consequence of non-adherence
- Side effects and/or adverse events due to toxicities
- Compromised healthcare provider communication
- Increased ER use or hospitalization
- Severely impede the efficacy of oral regimens leading to tumor growth and decreased survival
- The problem is serious for cancer patients because poor medication adherence can lead to unnecessary disease progression, complications, reduced functional abilities, lower quality of life, & premature death.
- Given the increasing use of oral agents & the unknown nature of what an optimal dose needs to be, adherence is critical to successful treatment outcomes.

Definitions
- Adherence/Compliance
  - Adherence is preferred but both terms are imperfect, and unfortunately, can stigmatize patients
- Definitions of adherence
  - World Health Organization
    - "the extent to which a patient’s behavior coincides with medical advice"
    - International Society for Pharmacoeconomics and Outcomes Research
    - "the degree or extent of conformity to the recommendation about day-to-day treatment by the provider with respect to the timing, dosage, frequency and duration of time from the initiation to discontinuation of therapy"  
    - Adherence is often defined to be taking 80% or more of a medication as prescribed
    - This is an arbitrary number
    - Adherence is impacted by multiple factors

Definitions
- Persistence
  - Duration of time a person takes medication, from initiation to discontinuation
- Overadherence
  - Defined as taking more than the prescribed amount of a medication
  - Reasons can include taking longer than prescribed or taking extra doses on a single day
  - One study found that overadherence was more likely than underadherence (20% compared to 13%)
  - More complex regimens were more likely to have overadherence

World Health Organization Framework
Proposes five factors the may impede adherence:
- Patient related
- Condition related
- Therapy related
- Social/economic related
- Clinician related

Why didn’t you take your meds today?
It’s not just about . . . forgetfulness
Factors influencing adherence

Patient Related Factors
- Language
- Culture
- Religious beliefs
- Cognitive impairment
- Comorbidities
- Other medications
- Gender
- Psychopathology
- Knowledge
  - Most studies have found inconsistencies & weak associations (< 0.15 r) with non-adherence (Choudry 2008; Chen 2010).


Condition/Therapy Related Factors
- Disease Type and Stage
- Knowledge of treatment
- Side effects of disease or treatment


Socioeconomic-related factors
- Attitude towards treatment
- Cost of treatment
- Financial support
- Difficulty accessing pharmacy
- Distance to treatment center
- Social rank of illness
- Social support
- Cultural beliefs

Clinician Related Factors
- Belief in treatment
- Provider and patient relationship
- Use guidelines
- Continuity of care/patient follow-up
- Providing education and information
- Communication and decision-making

Why are some patients adherent to therapy despite many challenges while others struggle despite optimal circumstances?

**Predictors of poor adherence**

- Presence of psychological problems, particularly depression
- Cognitive impairment
- Inadequate follow up or discharge planning
- Side effects
- Patient lack of belief in treatment
- Poor provider-patient relationship
- Barriers to care or medications
- Missed appointments
- Complexity of treatment
- Cost of medication, copayments

Ruddy, Skipper, Partridge, CA: A cancer journal for clinicians, 2009

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**Measuring Adherence**

- A clear definition of what adherence entails must be identified (i.e., percentage of adherence based on number of pills & days to be taken [80%, 90%, 100%])
- If timing of the dosage is required, the window of time that must elapse before a patient is considered to be nonadherent (i.e., 1-hour; or 30-minutes) must be identified.
- The majority of adherence measures are indirect & include some form of self-report & cannot truly capture if the medication was actually taken.
- Strict attention must paid to under & overdosing, so that missed doses & additional doses are assessed.

Spoelstra & Given (2012, Seminars in Oncology)

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**Narrow Index for Oral Agents**

Molecularly targeted oral agents are highly selective for molecules that establish & maintain malignant cell expression.

Pharmacokinetic literature suggests a narrow anti-neoplastic index for oral cancer agents.

What is not known is what level of adherence is required to achieve an anti-neoplastic dose. Thus, the need for increased emphasis on adherence to oral cancer therapies.

(Talpaz 2002; DeMario 1998)

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**Methods of Measuring Adherence**

<table>
<thead>
<tr>
<th>Direct</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observe</td>
<td>Most accurate</td>
<td>Hide in mouth</td>
</tr>
<tr>
<td>Measure metabolite</td>
<td>Objective</td>
<td>Variations</td>
</tr>
<tr>
<td>Measure biomarker</td>
<td>Objective</td>
<td>Expensive</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Indirect</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient reports</td>
<td>Simple</td>
<td>Risk of error</td>
</tr>
<tr>
<td>Pill counts</td>
<td>Objective</td>
<td>Easily altered</td>
</tr>
<tr>
<td>Prescription refill</td>
<td>Objective</td>
<td>Not equal to ingestion</td>
</tr>
<tr>
<td>Clinical response</td>
<td>Simple</td>
<td>Other factors</td>
</tr>
<tr>
<td>Electronic monitor</td>
<td>Precise</td>
<td>Expensive</td>
</tr>
<tr>
<td>Patient diaries</td>
<td>Correct for poor recall</td>
<td>Easily altered</td>
</tr>
</tbody>
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Adapted from: Osterberg, 2005.

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**What does all of this tell us?**

*There needs to be a nursing presence in all phases of oral cancer treatment.*

We need to be PROACTIVE and not reactive

(Yagasaki & Komatsu, 2013)
What can oncology nurses do?

1. Rethink how we practice
2. Remember that Education and Communication are key
3. Intervene

Recommendations to Improve Adherence

<table>
<thead>
<tr>
<th>Knowledge</th>
<th>Support</th>
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</thead>
<tbody>
<tr>
<td>Medication education</td>
<td>Evaluation of Adherence</td>
</tr>
<tr>
<td>Symptom Management</td>
<td>Communication</td>
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<tr>
<td>When to call</td>
<td>Reassurance</td>
</tr>
<tr>
<td>Newsletter</td>
<td>Monitor for depression</td>
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<tr>
<td>Education programs</td>
<td>Primary care provider</td>
</tr>
<tr>
<td>Peer educators</td>
<td>Follow up</td>
</tr>
<tr>
<td>Home safety</td>
<td>Use resources</td>
</tr>
</tbody>
</table>

Behavioral

- Alarm systems
- Cell phones
- Calendar, diary, pill boxes
- Convenience and regimen scheduling
- Avoid complexity, minimize dosing/scheduling changes

Interventions- Knowledge

- MASCC teaching tool (www.mascc.org)
- Develop in response to a nurse from Turkey who completed a study that showed nurses were lacking teaching tools and guidelines for oral cancer treatment.
- This teaching tool has been prepared to assist health care providers in the assessment and education of patients receiving oral agents as treatment for their cancer.
- The goal is to ensure that patients know and understand their treatment and the importance of taking the pills/tablets as prescribed.

Rethink our practice patterns

- What are current practices in the US regarding care and safety of patients on oral cancer treatment?
  - Survey of 577 oncology nurses
    - 53% of nurses had specific policies, procedures and resources for patients on oral chemotherapy
    - Barriers included cost (81%) and adverse effects (27%)
    - Many practices had erratic procedures and inadequate communication
  - Implications
    - Nurses should provide thorough education and repeated teaching to improve patient safety, adherence and self-monitoring for adverse effects

(KEY ASSESSMENT QUESTIONS from the MASCC teaching tool)

1. What have you been told about this treatment plan with oral medications? *Verify that the patient knows that these oral agents are for cancer and are taken by mouth for their cancer.
2. What other medications or pills do you take by mouth? *If you have a list of medicines, go over the list with the patient.
3. Are you able to swallow pills or tablets? If no, explain.
4. Are you able to read the drug label/information?
5. Have you taken other pills for your cancer? *Find out if there were any problems, for example, taking the medications or any adverse drug effects.
6. Are you experiencing any symptoms that would affect your ability to keep down the pills, for example nausea or vomiting?
7. How will you fill your prescription? *Delays in obtaining the pills may affect when the oral drugs are started.
8. Have you had any problems with your insurance that has interfered with obtaining your medications?
ONS adherence toolkit

- 12 tools for nurses
- Provides strategies and resources that nurses can use to facilitate adherence among patients with cancer related to:
  - Safety concerns: drug-drug and food-drug interactions, adverse effects
  - Pharmacy and reimbursement/financial resources
  - Monitoring of adherence
  - Motivational interviewing and counseling
  - Change theory and helping patients to change nonadherence into adherence.


Publications.USA.gov

- Free Resources Help People Stick to Their Prescriptions
- More than 125,000 Americans die each year from not taking their medications properly. Many others experience worsening chronic health conditions because of it.
- Free educational tools from the FDA and the Script Your Future campaign can help people take their medicine as directed.
- Display holders are also available without charge.
- Available in English and Spanish
- Script Your Future Wallet Card
- Stop, Learn, Go Tips for talking to your Pharmacist
- My Medicines - Take Time to Care
- My Medicines: Women’s Health - Take Time to Care

http://promotions.usa.gov/script-your-future.html

Interventions - Knowledge

- Teach back
  - “I want to be sure that I explained your medication correctly. Can you tell me how you are going to take this medicine?”
  - “We covered a lot today about your treatment, and I want to make sure that I explained things clearly. So let’s review what we discussed. What are some strategies that will help you take your chemo correctly?”
  - “What are you going to do when you get home?”

Interventions - Behavior

- Reminder triggers
  - Pill diaries, pill boxes, calendar or spreadsheet, checklist
  - Postcard reminder for refills
  - Blister packs
  - Cell phones, alarms - message texting when doses are due

Interventions - Support

- Communication
- Reassurance
- Monitor for depression
- Primary care provider
- Follow up
- Family support
- Use resources

Electronic Reminders

- Apps
- Text Messaging
- Automated Voice Recording
Paradigm Shift in Delivery of Chemotherapy

Delivery of chemotherapy from a safe, controlled process monitored on a regular basis by oncologists and nurses in hospitals or outpatient clinics to patients’ homes.

Conclusion: Appropriate Administration of Oral Agents Requires

- Patient centered approach
- Collaborative relationship
  - Communication/Coaching
  - Shared understanding
- Education assessment and needs
  - Literacy
  - Safe handling
  - Knowledge of disease and treatment
- Symptoms/side effects monitoring and management
- Patient, provider, system coordination

How are Nurses Promoting Adherence?

- Sample Programs
- Nurse Coaching