Supporting Patients on Oral Anticancer Therapies

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Objectives

- Discuss the impact of poor adherence on cancer outcomes including survival
- Identify 5 barriers to adherence to oral anticancer therapies and describe strategies to mitigate risk.
- Describe methods for monitoring adherence to oral anticancer therapies
- Describe effective strategies to provide patient education that promotes adherence.

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Terminology

- Oral antineoplastic drugs (OADs), oral anticancer agents (OAAs), oral anticancer therapies (OATs)
  - Oral chemotherapy
  - Targeted therapies
  - Hormonal therapies

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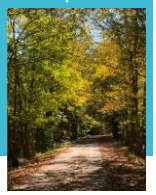
Oral anticancer agent landscape



The total drug expenditure in the USA on targeted therapies (almost exclusively OAA) increased from 26% in 2010 to 40% in 2016.

- More than 50 oral anticancer agents have been FDA approved.
- Estimated that **25–30%** of all hematological oncology drugs currently in development are orally administered, small molecules.
- Number of oral therapies predicted to double over next few years.
- Oral therapies incorporated into treatment of most major disease types.
- 2014-2018: 57 new drugs with 89 indications
  ~30% are oral agents
- 2017-2019: 5 of 7 agents newly approved for acute leukemia are OAAs

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Terminology

Compliance
- One way communication
- Implies that the patient does what the doctor says

Adherence
- Implies active patient involvement and a provider-patient partnership
- Patient and provider mutually agree to a plan
- Dynamic, can change day to day

Persistence
- Continuing treatment for the prescribed duration
  The opposite of discontinuation

Compliance, Adherence, Persistence, Miriam Karmel

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Terminology

Under-adherence
- Taking less medication than prescribed
- Missing a daily dose, not starting on day prescribed, stopping cycle early

Over-adherence
- Taking more medication than prescribed
- Doubling up on doses after a missed dose, taking more pills than prescribed, taking medication when off cycle/for longer than prescribed

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Adherence: What is the right target?

- 80% used most often in clinical trials
  - **This may not be high enough**
- 95% used in HIV

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Oral Chemotherapy Considerations

Advantages

- Autonomy and patient convenience
- Ease of administration
- Improved quality of life
- Reduced burden of care

Challenges

- Education and monitoring requirements
- Self-management responsibilities for patient
- Complex regimens
- Side effect & adherence monitoring
- Financial burden

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Why does adherence matter??

"Adherence is the single most important factor in achieving the best possible outcomes."

Poor adherence associated with:

- Adverse events
- Additional prescriptions (changes to dose and regimen)
- Increased healthcare utilization including unnecessary hospitalization & diagnostic testing, increased outpatient visits
- Increased health care costs
- **Drug resistance**
- **Decreased quality of life**
- **Lower overall survival**
- **Disease progression**

33-67% of all medication related hospitalizations are due to medication non-adherence at a cost of $100 billion annually.

(QOPI® Standards, 2020)

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Examples

Adherence rates in literature are widely variable, some as low as 33%.

- CML: adherence to therapy **>90%** was associated with significantly better probability of achieving both major and complete molecular response.
- Adherence to 6MP at **<90%** was associated with a 3.9-fold increased risk of relapse in a multiracial cohort of children with ALL.
- **<70-80%** adherence to tamoxifen associated with increased risk of death.

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Quality & practice standards that address adherence

- NCCN Guidelines for Adolescent & Young Adult Oncology
- NCCN Guidelines for Older Adult Oncology
- Oncology Nursing Society Oral Chemotherapy Toolkit
- Multinational Association for Supportive Care in Cancer (MASCC)
- 2016 Updated American Society of Clinical Oncology/Oncology Nursing Society Chemotherapy Administration Safety Standards, Including Standards for Pediatric Oncology
- 2018 Hematology/Oncology Pharmacist Association Best Practices for the Management of Oral Oncolytic Therapy: Pharmacy Practice Standard
- **American Society of Clinical Oncology (ASCO) Quality Oncology Practice Initiative (QOPI®, 2020)**
- **Patient-Centered Standards for Medically Integrated Dispensing: ASCO/NCODA (National Community Oncology Dispensing Association) Standards 2019**

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QOPI® Standards

Standard 4.2

The healthcare setting has a policy that outlines the procedure to assess patients' ability to adhere to chemotherapy that is administered outside of the heath care setting.

Documentation of assessment is available in the patient record.

Standard 4.3

The healthcare setting has a policy that requires assessment of each patient's chemotherapy adherence at defined clinically meaningful intervals to address any issues identified when chemotherapy is administered outside of the health care setting.

Documentation of assessment is available in the patient record.

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ASCO/NCODA Standards

What patient-centered interventions improve the quality and safety of medically integrated dispensing* of oral oncology drugs?

- Communicate with patient about dispensing process
- Ensure patients have direct access to dispensing team
- **Provide formal education prior to initiation of treatment**
- Obtain informed consent, provide the patient a copy
- Review parameters for contacting the medical team
- Provide a calendar outlining key information including dates to take medication, refill dates, etc
- **Follow up with patient within 7 days of dispensing**
- Subsequent calls can be tailored based on patient risk factors
- Pill boxes/caddies may be helpful
- **Assess for adherence and toxicity at each encounter**
- **Adherence assessment should include at a minimum: confirmation patient received the prescription, date started medication, verify patient understands how to take medication**
- Discuss financial concerns
- **Visit with the provider 2 weeks after initiation of therapy**
- Review drug interactions at each encounter
- Prescription should not be filled unless the consent and education have been completed

*In-office dispensing

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Key take-aways

- Standardized adherence assessment should be used at key points throughout treatment, including at baseline, regardless of duration of therapy.
- Risks to adherence should be addressed and modified prior to starting therapy.
- Patients should receive education on medication and adherence before starting treatment.
- Drug-drug interactions should be assessed at regular intervals.
- Information should be tailored to the patient.

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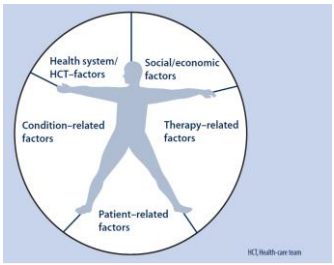
5 Dimensions of Adherence



World Health Organization, 2003. ADHERENCE TO LONG-TERM THERAPIES: EVIDENCE FOR ACTION

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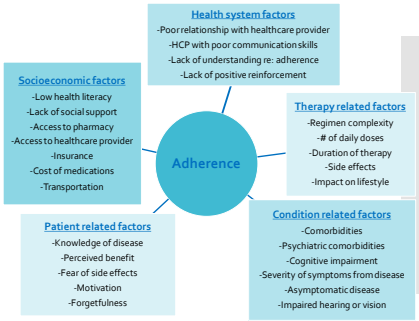
5 Dimensions of Adherence



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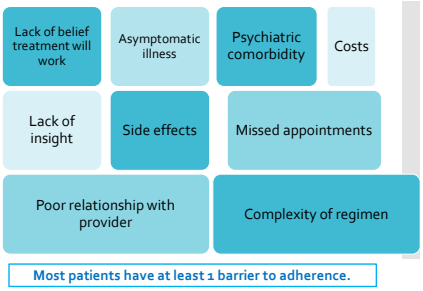
Major predictors of poor adherence



Most patients have at least 1 barrier to adherence.

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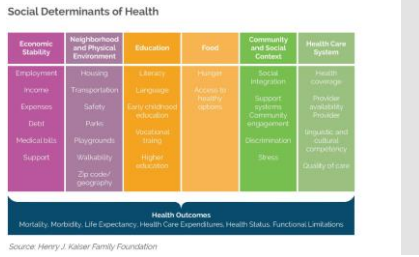
Social Determinants of Health



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Measuring adherence

- Assessing: the act of collecting information to make a judgement
  - **Example: self-reporting of adherence**
- Measurement: the process of measuring or assigning numerical values to an event
  - **Example: 80% rate of adherence**
- Direct measures:
  - Drug assays (limited; 6MP one example)
  - Direct observation
- Indirect measures:
  - Pill counts
  - Electronic medication monitors (MEMs: medication event monitoring systems)
  - Review of prescription records and claims
    - **Proportion of days covered (PDC)**: number of days in a time period "covered" by the medication divided by the number of days in a period. Caps at 100%.
    - **Medication Possession Ratio (MPR)** is calculated as the ratio of the amount of days a patient has their medicine on hand to the amount of days a patient is eligible to have the medicine on hand. The ratio is ideal at 100% or 1:1.

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Assessing adherence

"State of the science on assessment and measurement of oral adherence is poor." (Spoelstra & Rittenberg)

- Self report
- Assessment tool examples:
  - Morisky medication adherence scale (MMAS)
  - Brief Adherence Rating Scale (BARS)
  - ASK-20 (Adherence starts with Knowledge)
  - Adherence Estimator
- Most measures are indirect and include some form of self-report
- Many measures used in research are not realistic in clinical care

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Assessing adherence

Initial assessment
- Goal is to identify risk for non-adherence
- Discuss past experience with taking medications

Ongoing assessment
- Identify key timepoints in treatment course to assess
- Ask every time/every encounter

Because adherence is dynamic, it needs to be measured continually over time.

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ONS Oral Chemotherapy Tooklit Patient Assessment Checklist (2016)

Socioeconomic issues
How will the patient fill the prescription?
Does the patient have insurance?
What copays and out-of-pocket costs are associated with the patient's insurance?
Psychosocial issues
What is the patient's mental status?
Does the patient have social support?
Regulatory or administrative needs
Is the drug on formulary?
Is the drug approved by the FDA?
Health and medication beliefs and preferences
Is the patient ready to accept the necessity of treatment?
Is the patient prepared for safety and adherence concerns?
Have the patient's expectations about treatment been managed?
Lifestyle
Where does the patient live in proximity to the clinic/pharmacy?
Is the treatment regimen a good fit for the patient's lifestyle (i.e., does the patient work, drive, etc.)?
Will a family member or caregiver be available to help with treatment and patient care?
Personal factors
How does the patient learn best?
Does the patient have any cognitive impairment?
Does the patient have the ability to take medications as prescribed (i.e., swallow pills or open packaging)?
Does the patient have comorbidities that could impact or affect the treatment regimen or adherence?
Does the patient use alcohol or drugs?
Treatment factors
How complex is the patient's treatment regimen?
Is there pill burden associated with the treatment regimen?
What is the treatment duration?

https://www.ons.org/sites/default/files/ONS_Toolkit_ONLINE.pdf

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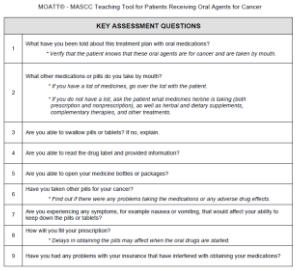
MASCC Oral Agent Teaching Tool (MOATT)



MOATT® - MASCC Teaching Tool for Patients Receiving Oral Agents for Cancer

	KEY ASSESSMENT QUESTIONS
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.
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. * If you do not have a list, ask the patient what medicines he/she is taking (both prescription and nonprescription), as well as herbal and dietary supplements, complementary therapies, and other treatments.
3	Are you able to swallow pills or tablets? If no, explain.
4	Are you able to read the drug label and provided information?
5	Are you able to open your medicine bottles or packages?
6	Have you taken other pills for your cancer? * Find out if there were any problems taking the medications or any adverse drug effects.
7	Are you experiencing any symptoms, for example nausea or vomiting, that would affect your ability to keep down the pills or tablets?
8	How will you fill your prescription? * Delays in obtaining the pills may affect when the oral drugs are started.
9	Have you had any problems with your insurance that have interfered with obtaining your medications?

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Assessing adherence: Ongoing assessment

How many pills did you take in the last week?

Tell me how you are taking your pills.

How many pills/doses have you missed in the last week?

Ask open-ended questions: What questions or concerns do you have about taking your medication as prescribed?

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Strategies to promote adherence

No established gold standard for promoting adherence

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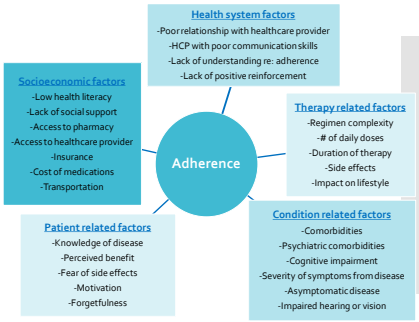
5 Dimensions of Adherence



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Strategies to address

Therapy related factors
-Regimen complexity
-# of daily doses
-Duration of therapy
-Side effects
-Impact on lifestyle

- Incorporate into patient routine
- Simplify schedule whenever possible
- Proactive identification and management of side effects
- Assess for drug-drug interactions with every visit

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Strategies to address

Condition related factors

-Comorbidities
-Psychiatric comorbidities
-Cognitive impairment
-Severity of symptoms from disease
-Asymptomatic disease
-Impaired hearing or vision

- Coordinate with other members of the care team; optimize management of comorbidities
- Partner with psychiatric providers
- Engage resources (ex. Social work)
- Ensure vision and hearing needs are addressed

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Strategies to address

Socioeconomic factors

-Low health literacy
-Lack of social support
-Access to pharmacy
-Access to healthcare provider
-Insurance
-Cost of medications
-Transportation

- Leverage resources (ex. Social work, medication assistance programs, American Cancer Society)
- Take cost into consideration when prescribing
- Synchronize timing of refills; consider 90 day supply for select drugs
- Use telehealth to monitor, limit number of in person visits
- Lobby, advocate, VOTE
- Build community resources, invest in communities

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Assess cultural and religious influences

- **Respectfully ask patients** about their health beliefs and customs, and note their responses in their medical records.
- Address patients' cultural values specifically in the context of their health care.

For example:

  - "Is there anything I should know about your culture, beliefs, or religious practices that would help me take better care of you?"
  - "What do you call your illness and what do you think caused it?"
  - "Do any traditional healers advise you about your health?"

- Avoid stereotyping based on religious or cultural background.
- Understand that each person is an individual and may or may not adhere to certain cultural beliefs or practices common in his or her culture.

Asking patients about their beliefs and way of life is the best way to be sure you know how their values may impact their care.

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Strategies to address

Health system factors
-Poor relationship with healthcare provider
-HCP with poor communication skills
-Lack of understanding re: adherence
-Lack of positive reinforcement

- We spend more time focused on patient related factors
- **Need to focus more time on health system factors**
- Healthcare provider education, communication skills training
- Establish clear, mutual, and realistic expectations

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Health System Factors

"Patients need to be supported, not blamed"

"Despite evidence to the contrary, there continues to be a tendency to focus on patient-related factors as the causes of problems with adherence, to the relative neglect of provider and health system-related determinants. These latter factors, which make up the health care environment in which patients receive care, have a major effect on adherence." (WHO, 2003)

Adherence is a dynamic partnership between a provider and a patient – **patients are more likely to adhere to a treatment plan if they are engaged in the process and decisions with their provider, and if they are supported by the wider system.**

WHO, 2003. Adherence to long-term therapies, Evidence for action.

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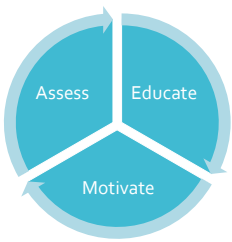
Strategies to address

Patient related factors
-Forgetfulness
-Perceived benefit
-Fear of side effects
-Motivation
-Knowledge of disease



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Interventions that target forgetfulness

- Calendars
- Alarms
- Text based interventions
- Apps
- Smart pill bottles
- Video games
- Calls
- Pillboxes

- Incorporate into routine (brushing teeth)
- Keep in a visible, safe location
- Say out loud "I am taking my pills now" can reinforce the behavior
- Enlist family and friends

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Text based interventions: Examples

- Daily medication reminders
  - "Keep taking your hormonal therapy; it will help prevent your cancer from returning"
  - "If you are having side effects from your hormone therapy, there may be options. Talk to your doctor instead of stopping."
- Ability to reply that medication was taken or missed
- If patient reports missed doses, can communicate reason why
- Patient reported outcomes monitoring with educational intervention.

Henshman et al., 2020;Mougalian et al., 2018; BETA Text, Mougalian et al., 2017; Clinicaltrails.gov NCT03949270

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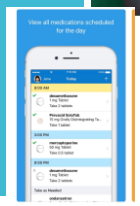
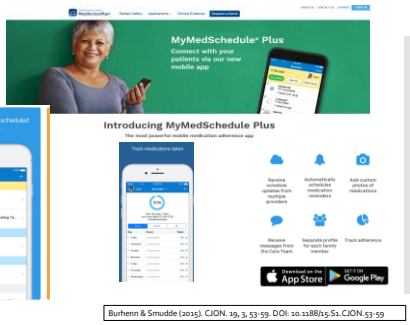
Apps





Burhenn & Smudde (2015). CJON. 19, 3, 53-59. DOI: 10.1188/15.51.CJON.53-59

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Empowering patients with information

Strategies for providing patient education

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IOM Report on Health Literacy

36% of U.S. adults identified as having serious limitations in health literacy skills

Healthy People 2020

- Improve health communication/health literacy

Joint Commission (1993)

- Patients must be given information they understand

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U.S. high school dropout rate is 30%

EPE Research Center (2008). "Cities in Crisis"

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40 to 80% of medical information is forgotten immediately.

Almost half of information is remembered incorrectly.

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Red Flags for Low Literacy

- Frequently missed appointments
- Incomplete registration forms
- Unable to name medications, explain purpose or dosing
- Identifies pills by looking at them, not reading label
- Patient says they are too tired to read, forgot glasses
- Asks family/friend to read for them
- Unable to give coherent, sequential history
- Asks fewer questions
- Lack of follow-through on tests or referrals

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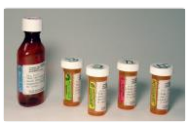
Patient Safety: Medication Errors

"How would you take this medicine?"

395 primary care patients in 3 States



- **46%** did not understand instructions ≥ 1 labels
- **38%** with adequate literacy missed at least 1 label

Davis TC., et al. Annals Int Med 2006

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Use Plain Language

living room conversation

- Speak slowly
- Use non-medical terms
  - Example: Say "blood pressure pill", not "antihypertensive"
- Avoid vague terms
  - Example: Instead of: Take on an empty stomach, say, "take 1 hour before you eat breakfast"
- Use pictures whenever possible

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Use plain language

Say this	Instead of this
Side effect	Adverse reaction
Low blood sugar	Hypoglycemia
When you need it	PRN
Put on your skin	Topical
Do not	Avoid
By mouth	Oral
Prevention	Prophylaxis

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Providers *underestimate* learning needs of patients and *overestimate* their own effectiveness in conveying information.

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We remember:

10% of what we read
20% of what we hear
30% of what we see
50% of what we see and hear
80% of what we say

90% of what we say and apply

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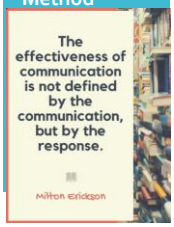
Use Teach-Back Method



"I want to make sure I explained it correctly."

- "Can you tell me in your words how you understand the plan?"
- "Tell me in your own words how you are going to take this medication"

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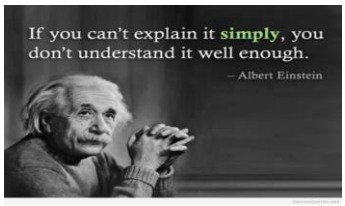

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Tips

Patients prefer receiving key messages from their clinician with accompanying written information.

- **Written materials, when used alone, will not adequately inform**.
- Hand-outs *supplement* verbal information, do not replace verbal information
  - Paper alone does not = patient education
  - Gives patients something to refer to at home
  - Engages other senses
  - Highlight, underline, or circle most important information
- Do not give written materials if the patient can't read English
- Pictures/demonstrations most helpful to patient with low literacy & visual learners
  - Most health drawings too complicated
  - Hand drawing usually simpler

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Tips

- Eye contact (if culturally appropriate); avoid distractions
- Listen carefully, don't interrupt
- Prioritize & Limit information (3-5 key points) **CHUNK & CHECK**
- Be specific and concrete, not general
  - **Example: Instead of staying, "Be sure to drink enough fluids". Say "Drink one liter of water per day" (and show how much 1 liter is)**

- **Use the patient's words**
- Demonstrate, draw pictures, use models
- Repeat/summarize
- Teach-Back (confirm understanding)
- Be positive, hopeful, empowering
- Encourage questions: What questions do you have?

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Setting expectations

- Explain patient's responsibility in adherence, explain your responsibility in their care.
- Why is adherence important to them?
- Outline potential impact on outcomes if they do not take medication.
- Be honest about side effects and what we can do about them.
- Help patient understand when they can expect to see response.
- If asymptomatic, how will we assess response.

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Key components of initial education

- How medication supplied
- Dose and administration
- Timing and schedule, duration
- Storage and handling
- Proper disposal
- Monitoring (labs, visits)
- Expected side effects
- Reportable side effects/when to call
- Management of a missed dose
- Safe handling & storage in the home; medication disposal
  - Sexual activity

- Drug/food interactions
  - What to avoid
- Expected out of pocket costs
- Medication acquisition process
- Contraindications
- Allergies
- Comorbidities
- Barriers to learning/adherence
- Expected outcomes

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Provide positive reinforcement

Support, encourage, and recognize difficulties

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One model: Yale New Haven Health System

- Five Hospitals
  - Yale New Haven Hospital
  - Bridgeport Hospital
  - Greenwich Hospital
  - Lawrence + Memorial Hospital
  - Westerly Hospital
- 2,563 Licensed Beds

- Primary teaching hospital for Yale University School of Medicine and School of Nursing
  - >5,000 medical staff members
  - 1,400 trainees
- System physician foundation: Northeast Medical Group
  - 835 providers

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Smilow Cancer Hospital

- One of 45 National Cancer Institute Designated Comprehensive Cancer Hospitals
  - One of three in Northeast U.S.
- One of 27 National Comprehensive Cancer Network Hospitals (NCCN)
- 15 Cancer Hospital Care Centers located throughout Connecticut
  - Decentralized oncology pharmacists manage infusion and oral chemotherapy
- QOPI Certified in all ambulatory locations

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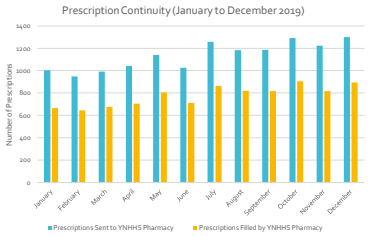
YNHHS Specialty Pharmacy



- 91% clinical continuity of oral chemotherapy prescriptions from health system (N=14,883)
- 68% filled internally (n=9326)

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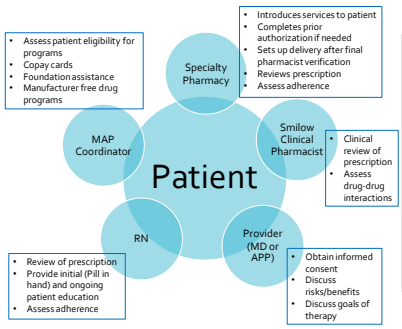
Smilow Cancer Hospital Oral Anticancer Therapies Model



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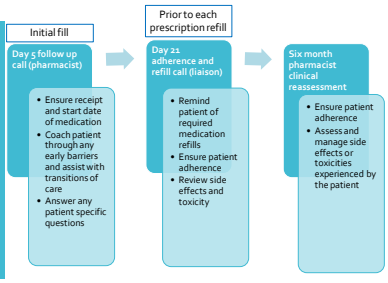
YNHHS Specialty Pharmacy Workflow



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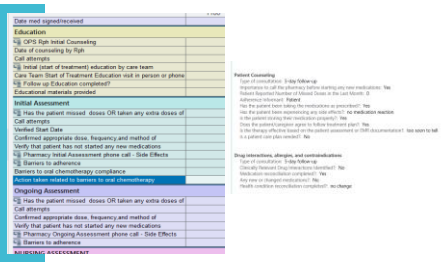
Smilow Cancer Hospital OAA Tools



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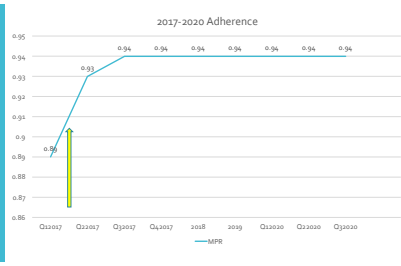
Smilow Cancer Hospital Adherence Rates



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Smilow Cancer Hospital

- Piloting an RN telehealth intervention for initial education
- Next steps: Ongoing nurse-only visits for education and adherence assessments

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Take-home messages

- Adherence is critical to key outcomes including survival
- Adherence is a multidimensional, dynamic construct that can change from day to day
- Requires a systematic, comprehensive strategy to mitigate barriers and promote adherence
- Team approach most successful
- RNs & APRNs are ideal partners to support patients

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Resources

- Oncology Nursing Society (ONS) recommended "Oral Adherence Toolkit" resource (2016). For more information, visit: https://www.ons.org/sites/default/files/ONS_Toolkit_ONLINE.pdf
- Multinational Association of Supportive Care in Cancer (MASCC) Oral Agent Teaching Tool (MOATT)
- Hematology Oncology Pharmacy Association Oral Chemotherapy Resources (hoparx.org)
- AHRQ, Health Literacy Universal Precautions Toolkit, 2nd Edition, 2020 [https://www.ahrq.gov/health-literacy/improve/precautions/tool3a.html]

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Thank you!

"Thank You Our Heroes", an appreciation for our Frontline Workers.
Lyman Orchards, Middlefield, CT

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