Treatment Adherence in those with Severe Mental Illness

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Learning Objectives
At the end of our session, the observer will be able to:

1. Discuss the link between medication adherence and service utilization.
2. Discuss factors that influence the level of medication adherence in persons with severe mental illness
3. Discuss strategies for improving medication adherence in persons with severe mental illness.

Adherence and Service Utilization

“...nonadherence plays a significant role in psychotic relapse and each relapse contributes to accrued social toxicity and disability.”

Antipsychotic medications are effective in:
- the treatment of acute episodes of psychosis
- the prevention of relapse
- in reducing the risk of relapse for 1st episode AND chronic schizophrenia

--Freudenreich and Cather, 2012
Adherence and Service Utilization

Subotnik and colleagues (2011); in early course schizophrenia, even a mild degree of nonadherence robustly predicted psychotic symptom exacerbation.

Weiden and colleagues (2004) used medicaid pharmacy refill and medicaid claims data to demonstrate: partial adherence predicts rehospitalization risk in a dose dependent manner.

--Freudenreich and Cather, 2012

Poor Adherence is Highly Prevalent

It is estimated that 41% of schizophrenia patients are nonadherent

Insufficient adherence to medications is a pervasive problem in ALL of medicine

Jackevicius CA and colleagues (2002) performed a study looking at 2-year adherence to statins for secondary prevention of cardiac event: it was only 40% in a cohort of elderly patients following acute coronary syndrome

--Freudenreich and Cather, 2012

Poor Adherence is Highly Prevalent

Even with 1st episode patients:

In a study of 171 1st-episode psychosis patients; 24% of subjects were non-adherent at a 4 year follow-up (Kane JM, 2008)

--Freudenreich and Cather, 2012
How poor is “poor”?

A cutoff of < 75 – 80% of prescribed doses is often used, but is not empirically based.

Docherty et al (2003) provided some evidence that there is a dose response relationship between increasing percentage of missed doses and level of active symptomatology.

No “gold standard” seems to exist

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Can we measure it?

Clinical Judgement of Adherence Scale

Medication levels

Pill counts

Electrical monitoring of container opening

“Smart pills”

Prescription / fill ratios.

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Risk Factors for Poor Med Adherence

Multiple factors (Lacro JP et al, 2002)

Poor insight

Negative attitude toward medication

Negative subjective response to medication

Previous nonadherence

Substance abuse

Shorter illness duration

Inadequate discharge planning or aftercare environment

Poorer therapeutic alliance

--Freudenreich and Cather, 2012
**Negative Drug Attitude**

Drug Attitude: correlates with adherence; refers to patient’s overall appraisal of the risks and benefits associated with a particular medication.

Measurable: Drug Attitude Inventory
- Originally a 30-item true / false scale
- Available also as 10-item version

--Freudenreich and Cather, 2012

No differences found in drug attitude for those taking 1st-gener generation antipsychotics vs. 2nd generation
(Freudenreich O et al, 2004)

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**Negative Drug Attitude**

EUFEST (Gaebel E et al, 2010) demonstrated that, in the first episode / early psychosis population, drug attitude was the STRONGEST predictor of later drug discontinuation; sexual side effects and high psychopathology score also predicted nonadherence

--Freudenreich and Cather, 2012

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**Lack of Insight**

Identified by WHO as a pathognomnic, core symptom of schizophrenia (Carpenter WT, 1973)

Retained insight is part of proposed criteria for “Attenuated Psychosis Syndrome” in DSM-V (Woods SW, et al, 2010).

--Freudenreich and Cather, 2012
Lack of Insight

- Insight is a multidimensional construct:
- Awareness of symptoms: capacity to re-label inner experiences as pathological symptoms
- Recognition of mental illness: attributing symptoms to a psychiatric illness
- Acceptance of need for treatment
- Sociocultural dimension: ...the end-result of an intersubjective construction of meaning...clinician and patient bring assumptions, opinions, etc. to the table based on culture, experience and training

--Freudenreich and Cather, 2012

Lack of Insight

Tranulis and colleagues (2009) proposed the term “narrative insight”:

--Posits that insight is developed through a combination of abstract reasoning and introspection as well as concrete interpersonal interactions and actual experiences of illness and treatment.

--Freudenreich and Cather, 2012

Lack of Insight

Lack of insight has been shown to be associated with treatment discontinuation and poor outcomes (Pinenborg GH et al, 2011).

Poor insight can be indicative of a stable, anosognosia-like neurocognitive deficit (Arango C, et al, 2011).

Partial insight also exists and can create difficulties.

--Freudenreich and Cather, 2012
### Risk Factors for Poor Med Adherence

Multiple factors (Lacro JP et al, 2002)

- Poor insight
- Negative attitude toward medication
- Negative subjective response to medication
- Previous nonadherence
- Substance abuse
- Shorter illness duration
- Inadequate discharge planning or aftercare environment
- Poorer therapeutic alliance

--Freudenreich and Cather, 2012

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### Remedies?

1st Step: RECOGNITION!!

Clinicians and patients are NOT good at this!

In one prospective trial of 52 outpatients dx’d with schizophrenia, pill counts and electronic monitoring were strongly correlated; however, pills counts were only weakly correlated with both patient self-report and clinician estimate (Velligan DI et al, 2007)

--Freudenreich and Cather, 2012

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### Can we measure it?

- Clinical Judgement of Adherence Scale
- Medication levels
- Pill counts
- Electrical monitoring of container opening
- “Smart pills”
- Prescription / fill ratios.
Remedies?

Velligan and colleagues (2010): 3-tiered approach!

**Universal Prevention**: psychoeducation, systems-based interventions

**Selective Intervention**: higher level of care for persons at high risk of non-adherence. E.G. implementing pill organizers, enlisting families and friends, behavioral tailoring (take pills at same time as brush teeth), etc.

**Indicated Intervention**: for patients KNOWN to be non-adherent, use higher yield (typically more intensive) interventions, such as directly observed therapy (DOT).

--Freudenreich and Cather, 2012

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Remedy: Improved Therapeutic Alliance

Perceived clinician or physician support is a powerful predictor of adherence

Sample of 228 patients w/ psychotic disorder: negative treatment attitudes predicted by less positive relationship with prescriber, perceived coercion during admission and low insight (Day JC et al, 2005)

Most critical question here: does the patient see the role of psychiatric treatment as at least potentially beneficial

--Freudenreich and Cather, 2012

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Remedy: Improved Attitude Toward Treatment

Beck and colleagues demonstrated that targeting treatment-related attitudes lead to more robust changes in adherence than trying to increase global insight (2011)

Shared decision-making known to be effective

Should work to improve “subjective well-being under neuroleptic treatment” (SWN): target lowest effective doses, show flexibility in altering dosing times or switching medication (Naber D et al, 2005).

Unfortunately, psychiatric meds are often only partially effective and invariably have side effects.

--Freudenreich and Cather, 2012
Remedy: Compliance Therapy (CT)

CT is rooted in CBT and motivational interviewing... attempts to help patients weigh risks and benefits from treatment, similar to how patients would approach their treatment for hypertension or diabetes

In particular: assists the patient in viewing discrepancies between his or her goals and values and his or her current state of function in light of possible benefits from treatment adherence.

--Freudenreich and Cather, 2012

Remedy: Compliance Therapy (CT)

Kemp et al (1996, 1998): CT resulted in significant improvements in compliance, attitudes toward drug treatment, and insight into illness when compared with "standard treatment". Gains were still present at 6 and 18 month follow-up. There were not demonstrable improvements in social functioning or symptomatology.

Two replication studies failed to demonstrate similar benefits:

O'Donnell et al (2003) and Gray et al, 2006 conducted subsequent replication efforts and failed to replicate the benefits seen in the Kemp study

Remedy: Behavioral Tailoring


"The investigator helped each participant tailor his prescribed regimen so that it was better adapted to his personal habits and routines. This involved identifying a highly visible location for the placement of medications and pairing the daily medication intake with specific routine behavior of the participant. Each participant was given a self-monitoring spiral calendar, which featured a dated slip of paper for each dose of the neuroleptic. The participant was instructed to keep the calendar near his medications and tear off a slip each time he took a pill..."
Remedy: Long-Acting Injectables (LAIs)

LAIs are effective medications, however there is no significant proof that they are superior to oral medications, overall, regarding hospitalization rates, symptom improvement or quality of life.

Difficult to study in that those willing to enter a trial comparing injectable vs. oral medication may be more likely to be adherent in the first place

--Freudenreich and Cather, 2012

Remedy: Long-Acting Injectables (LAIs)

Evidence to support advantages of LAIs over oral antipsychotics is limited.

Schooler at colleagues conducted a well-designed (1980) study comparing oral and depot fluphenazine (Prolixin).

No reports from this study identified significant differences between the two treatments on relapse, symptoms or social adjustment.

Remedy: Long-Acting Injectables (LAIs)

Evidence to support advantages of LAIs over oral antipsychotics is limited.

Rifkin et al. (1977): RCT comparing oral fluphenazine vs. depot fluphenazine vs. placebo

Both active meds outperformed placebo for prevention of relapse, but did not differ from each other

More side effects noted with depot form; authors cited high doses of depot in comparison to oral
Remedy: Long-Acting Injectables (LAIs)

Evidence to support advantages of LAIs over oral antipsychotics is limited.

Hogarty et al (1979): oral vs. depot fluphenazine
In the first year: no difference in relapse rates
When looking at 2 – 24 months: large difference in relapse rates (80.8% for depot; 35.6% for oral), but this was not statistically significant

Remedy: Cognition Adaptation Training (CAT)

Velligan and colleagues (2008): designed a multi-pronged intervention called CAT
9 month intervention: tailored environmental support and compensatory strategies lead to significant improvement in adherence vs treatment as usual (TAU)
Benefit extended beyond treatment period (longer term follow-ups needed!)

--Freudenreich and Cather, 2012

Remedy: Directly Observed Therapy (DOT)

As it sounds…directly observe and verify that the patient is adherent to treatment

Farooq and colleagues (2011): randomized 110 patients to family-supervised med administration vs. TAU:
67.3% adherent in intervention group
45.5% in TAU

Spaniel and colleagues (2008): piloted cell-phone based telemonitoring system to detect non-adherence and signs of early relapse in 45 patients.
Reduced hospitalizations by 60% compared with same time period prior to participation

--Freudenreich and Cather, 2012
**Remedy: Financial Incentives**

Paying patients to take meds—can be effective!!

Pilot study in Netherlands: 5 patients; acceptance of injections increased from 44% - 100% and resulted in 10-fold reduction in days spent in the hospital (Staring AB et al, 2010).

FIAT currently underway in Britain: Financial Incentives for Adherence Trial (FIAT) (Priebe S, et al, 2009)

--Freudenreich and Cather, 2012

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**REMEDIES for Nonadherence to Antipsychotic Meds**

<table>
<thead>
<tr>
<th>Type of Nonadherence</th>
<th>Interventions</th>
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<tr>
<td>For intended nonadherence</td>
<td>Optimize overall care experience, Minimize perceived coercion</td>
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<tr>
<td>Negative drug attitude</td>
<td>Prevent in trying to achieve good efficacy, Increase “subjective well-being under neuroleptics”</td>
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<tr>
<td>Poor insight*</td>
<td>Consider long-acting injectable (LAI) antipsychotic, Consider directly observed therapy (DOT), Incentivize taking antipsychotics (e.g., financial), Use motivational principles (e.g. Compliance Therapy)</td>
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<tr>
<td>For unintended nonadherence</td>
<td>Consider Cognitive Adaptation Training (CAT), Consider LAI, Consider DOT</td>
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*Risk factors are not mutually exclusive. These interventions are not specific for just one risk factor. For example, DOT would also be appropriate for patients with a poor therapeutic alliance or negative drug attitude.

In some patients insight per se might not be amenable to change

--Freudenreich and Cather, 2012

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**References**

- Docherty et al. (2003). Schizophr Res. 60 (Suppl): 281.
- Schulszer et al. (1986). Arch Gen Psychiatry. 43: 10-24.