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The Importance of Adherence to Long-term Success in Schizophrenia
Adherence is a multidimensional phenomenon determined by the interplay of five sets of factors termed ‘dimensions.’ Patient-related factors are just one determinant. Other factors, including health system, social-economic, treatment-related, and disease-related, affect people’s behavior and capacity to adhere to their treatment.\textsuperscript{WHO 2003 B}

How does adherence differ from the perspective of the patient versus that of the physician? Why is this important?

Reference
Potential predictors for nonadherence have been studied in numerous studies of various medical conditions.
Patients’ adherence levels in schizophrenia have been found to affect:

- Hospitalizations (eg, 17.1% of patients [adherent] vs. 29.6% [non-adherent]; p<0.05)\(^2\)\(^{Ascher-Svanum 2009 A}\) \(^1\)\(^A\)\(^n\)\(^2\)\(^{Sun 2007 A}\)
- Total days hospitalized (eg, 8.8 days [totally adherent] vs. 32.0 [partially adherent]; p<0.05)\(^2\)\(^{Ascher-Svanum 2009 B}\) \(^A\)\(^n\)\(^2\)\(^{Sun 2007 A}\)
- Suicide attempts (eg, 1% [non-adherent] vs. 0% [adherent]; p=.004)\(^3\)\(^{Ahn 2008 A}\)
- Rate of >4 annualized episodes (eg, 23% of patients [non-adherent] vs. 10% [adherent]; p<0.001)\(^2\)\(^{Ahn 2008 A}\)
- Recovery (eg, OR for adherent patients: 2.25)\(^4\)\(^{Novick 2009 A}\)
- Relapse (eg, OR for non-adherent patients: 10.27)\(^2\)\(^5\)\(^{Sun 2007 A}\) \(^{Morken 2008 A}\)

Note: This is not a hierarchical or exhaustive list.

References
Multiple metrics indicating poor adherence were associated with an increased rate of having ≥1 mental health hospitalization.¹{Kozma 2009 A}

Patients who had gaps of >30 days were associated with a 4.7 times greater risk of hospitalization than patients in the 0–10 day group.¹{Kozma 2009 B}

The mean cost of a hospital stay for a patient with schizophrenia in the United States is $7500.²{Wier 2008 A}

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References
Gaps in treatment as short as 1 to 10 days have been found to double the risk of hospitalization. In this study, adherence behavior was estimated by using a retrospective review of California Medicaid pharmacy refill and medical claims for 4325 outpatients for whom antipsychotics had been prescribed for the treatment of schizophrenia between 1999 and 2001.\textsuperscript{(Weiden 2004 B)} Adherence behavior was estimated by using 4 different definitions: gaps in medication therapy, medication consistency, medication persistence, and a medication possession ratio (MPR) and patients were followed for 1 year.\textsuperscript{(Weiden 2004 C)}

Mental health hospitalizations were identified by using “mental health” International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes in the first (primary) diagnosis field. \textsuperscript{(Weiden 2004 D)}

\textbf{Reference}
In clinical practice, defining and assessing adherence may not be a straightforward process. There are many ways by which adherence has been defined and measured in clinical studies. This article reviewed adherence measures in 161 studies that enrolled patients with schizophrenia.\textsuperscript{(Velligan 2006 B)} Patient self-report measures of adherence were by far the most common. These included unstructured or semistructured interviews, a variety of standardized rating scales, medication checklists, patient attitudes and insight into their use of medication in recent weeks, medication refusal by patients, and other self-report methods.\textsuperscript{(Velligan 2006 D)} Other methods included provider report, family or significant other report, chart review, pill count, electronic refill information, electronic monitoring, blood level, urine analysis of medication, and urine analysis of a tracer substance.\textsuperscript{(Velligan 2006 D)} An important observation of this study is that although blood levels provide the most objective assessment of the amount of drug taken by the patient, only 5 of the 161 studies reviewed used blood levels to assess adherence. Nearly all of the studies included in this analysis used subjective measures that rely on the accuracy of the patient’s self-reported adherence.

In addition to the types of measures, these studies also differed in the specific ways in which adherence was defined. Some definitions of poor adherence were based on the patient stopping medication for a specified period of time (eg, stopping for 1 week), various percentage cut-offs (eg, taking at least 75% of medication doses), active refusal to take medication, and whether the patient passively accepted or actively participated in treatment.\textsuperscript{(Velligan 2006 C)}
Consider how adherence is defined and assessed in your clinical setting.

*Figure reproduced from Velligan DI, Lam YW, Glahn DC, et al. Defining and assessing adherence to oral antipsychotics: a review of the literature. Schizophr Bull. 2006;32:724-742, by permission of Oxford University Press.*

**Reference**

Potential Indirect Effects of Adherence on Outcomes

- **Indirect effects: Poor information**
  - May result in wrong medication, inadvertent overmedication, or too many medications prescribed
  - Mistaking lack of efficacy for nonadherence (or vice versa) may result in an incorrect treatment plan

- **Indirect effects: Harming the therapeutic relationship**
  - Tension over ‘obedience’ can hurt the therapeutic relationship
  - Failure to embrace a “harm reduction” approach if nonadherence happens

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Speak to slide.
• In order to discuss the clinical impact of nonadherence you must consider the complex relationship between symptom presentation/exacerbation and deviation from adherence.\textit{(Weiden 2007 A)}

• Which occurs first? Both. Nonadherence to antipsychotic medications results in symptom exacerbation, and vice versa, and both increase the risk of relapse in patients with schizophrenia.\textit{(Weiden 2007 A)}

\textbf{Reference}

• Communication is considered essential to help improve adherence, and several recommendations are shown here.
• Other approaches that may improve the adherence interview in clinical practice include the following:
  • Start with efficacy and goals, bring up adherence later {Weiden 2011 A}
  • Always maintain alliance even when there are differences in opinion about adherence {Weiden 2011 E}
  • Ask about attitudes about medication—both for and against—and if you get new information, be interested and do not contradict, at least for now {Weiden 2011 F}
  • Do not get angry or annoyed if the patient discloses nonadherence, or that will be the end of honest disclosure. Rather, use the discussion to strengthen rather than harm the therapeutic relationship {Weiden 2011 B} {Weiden 2011 C}

Reference
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