Treatment Adherence & Relapse Prevention in Schizophrenia

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Professional Standards for Hospital Pharmacy Services

Optimising patient outcomes from medicines

For pharmacy services in acute, mental health, private and community service providers

1.3 Adherence to medicines

Systems are in place to identify patients who may need adherence support, or to allow patients to request support.

- Patients' ability to adhere to their medicines is routinely assessed by healthcare professionals. Where difficulties are identified further specialist input is provided by the pharmacy team.
- Medicines regimes are simplified as far as possible and/or appropriate aids and charts are made available to support patients.
- Liaison with other healthcare professions or agencies outside the organisation is undertaken where ongoing support is needed.
- Patients are signposted to a community pharmacy of their choice post discharge, for follow-up e.g. if high risk medicines are changed during admission (e.g. Targeted Medicines Use Review, Chronic Medication Service, Discharge Medicines Review Service³) or new medicines are started (New Medicine Service).
Objectives

- To review the pivotal relationship between adherence to antipsychotic treatment and outcome in schizophrenia.

- To consider pragmatic interventions to prevent relapse by minimising the barriers to adherence.
Schizophrenia

- Most common form of psychotic disorder
- Lifetime prevalence 0.4% to 1.4%
- Over 80% of adults have persistent problems with social functioning
- Mortality approx 50% above that of the general population

National Collaborating Centre for Mental Health
Core interventions in the management of schizophrenia in primary and secondary care (update).
National Clinical Practice Guideline Number 82, Full Guideline
Revolving door = vicious cycle

Delay in treating first episode

Treatment response but subsequent poor adherence to treatment

Relapse & need to re-establish treatment

Progression to chronic illness and/or treatment resistance
“A problem of striking magnitude”
Poor adherence in schizophrenia: a large and persistent problem

Systematic review of literature

- 39 studies from 1980 onwards
  - 10 retrospective, 15 cross-sectional, 14 prospective
- Mean duration of illness 9-24 years
- Range of adherence measures
- “Taking medication as prescribed at least 75% of the time”

49.5% of patients non-adherent

Make a note of this number!

Lacro JP, Dunn LB, Dolder CR et al.
Prevalence of and risk factors for medication non-adherence in patients with schizophrenia: a comprehensive review of recent literature.
Of 28,145 patients with good adherence in any study year

- Good adherence throughout: 39%
- Persistently poor adherence: 18%
- Variable adherence: 43%

At least one year of GOOD adherence: 71%

Of 20,694 patients with poor adherence in any study year

- Persistently poor adherence: 18%
- Variable adherence: 43%

At least one year of POOR adherence: 52%

% of patients (n=34,128) Over 4 years

Valenstein M, Ganoczy D, McCarthy JF et al.
Antipsychotic adherence over time among patients receiving treatment for schizophrenia: a retrospective review
J Clin Psychiatry 2006;67:1542-50
Poor health outcomes & increased costs
1st episode schizophrenia: Poor adherence leads to high relapse rates

- 5-year follow-up study after initial recovery from first episode of schizophrenia or schizoaffective disorder
- Discontinuation of antipsychotic medication increased risk of relapse almost 5-fold

Robinson D, Woerner MG, Alvir JMJ et al. Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. Arch Gen Psychiatry 1999;56:241-47
Chronic schizophrenia: Poor adherence leads to high relapse rates

- Pooled analysis of 66 studies with 4365 patients with chronic schizophrenia
- Relapse rates over 10 month period
- Number needed to harm for antipsychotic withdrawal

**NNH = 3** (95% CI 2-3)

What would be predicted annual relapse / admission rates?

If:
50% of patients don't take treatment regularly and
Relapse rates in these patients are about 50% in 1st year

Schizophrenia: 2-year Outcomes in UK

% of patients (N=1,015)

Hunter R, Cameron R, Norrie J.
Using patient-reported outcomes in schizophrenia: The Scottish Schizophrenia Outcomes Study
Psychiatric Services 2009;60:240-245
Poor adherence in schizophrenia is costly to the NHS

- UK Health economic study
- Data for 1 year from Office of Population Censuses and Surveys (OPCS)
- 658 patients taking antipsychotics identified

- Measures included frequency of use of:
  - In-patient care
  - Out-patient care
  - Community-based services
  - Day care / sheltered employment

- 1.5-fold increase in use of in-patient care
- 3-fold increase in costs of community-based services
- Increased in-patient cost of £2500 per patient
- Increased total cost of £5000 per patient

Knapp M, King D, Pugner K, Lapuerta P
Non-adherence to antipsychotic medication regimens: associations with resource use and costs
Br J Psychiatry 2004;184:509-16
Adherence is simultaneously influenced by several factors
Adherence is influenced by multiple factors

**Patient**
- Concerns about side effects
- Few perceived benefits
- Stigma
- Daily routine
- Concerns about dependence
- Lack of involvement

**Illness**
- Severity of illness
- Depression / psychosis
- Cognitive impairment

**Clinician / Service**
- Poor therapeutic relationship
- Poor explanation / communication
- Inadequate follow-up

**General**
- Complexity of treatment
- Duration of treatment
- Lack of support

Mitchell AJ, Selmes T
Why don’t patients take their medicines? Reasons and solutions in psychiatry.
Advances in Psychiatric Treatment 2007;13:336-346
Patient-centred interventions are required
Clinical interventions for treatment non-adherence in psychosis: meta-analysis

MICHELA NOSÉ, CORRADO BARBUI, RICHARD GRAY and MICHELE TANSELLA

Systematic review of interventions to aid adherence

- 24 studies
- Follow-up 2–72 weeks (median 24 weeks)
- Number of patients 21660 (mean 149)
- 14 studies evaluated educational programmes
- 5 studies evaluated service provision
- Pre-discharge contact between patients & community team
- Pre-discharge education about antipsychotics
- 3 studies evaluated psychotherapeutic interventions
- 2 studies evaluated effect of telephone prompts

Table 2 Odds ratios of subgroup analyses of studies assessing the effect of interventions for reducing non-adherence

<table>
<thead>
<tr>
<th>Study characteristic</th>
<th>Patients (n)</th>
<th>Studies (n)</th>
<th>Peto OR lor (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>895</td>
<td>7</td>
<td>2.41 (1.72–3.37)</td>
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<tr>
<td>Psychotherapy</td>
<td>170</td>
<td>2</td>
<td>2.83 (1.36–5.87)</td>
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<tr>
<td>Prompts</td>
<td>1029</td>
<td>2</td>
<td>1.87 (1.45–2.42)</td>
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<tr>
<td>Service policies</td>
<td>863</td>
<td>4</td>
<td>3.63 (2.68–4.92)</td>
</tr>
<tr>
<td>Family therapy</td>
<td>192</td>
<td>4</td>
<td>4.45 (2.52–7.83)</td>
</tr>
</tbody>
</table>

Adherence to

| Appointments | 2211 | 9 | 2.52 (2.10–3.02) |
| Medication   | 938  | 10| 2.81 (2.03–3.88) |

1. Studies using dichotomous outcome data (n=19).
2. Odds ratio: OR > 1 favours experimental interventions; OR < 1 favours usual care.
Adherence (compliance) Therapy

- Meta-analysis of 5 RCTs
- 649 patients

8.2.7 From evidence to recommendations

The current review found no consistent evidence to suggest that adherence therapy is effective in improving the critical outcomes of schizophrenia when compared to any other control.
Addressing **preventable barriers to adherence**

**Patient**
- Concerns about side effects
- Few perceived benefits
- Adjustment to suit daily routine
- Concerns about dependence

**Clinician**
- Poor therapeutic relationship
- Poor explanation / communication

**Illness**
- Cognitive impairment

**General**
- Complexity of treatment

- Be aware of key side effects
- Educate / inform patient about side effects
- Work to avoid side effects
- Involve patient in treatment decisions
- Educate / inform patient about illness and treatment
- Optimise treatment response
- Simplify treatment regimen & Adjust dose timing to suit patient
Necessity / Concerns model for understanding adherence

Necessity = understanding and accepting necessity of treatment
Concerns = concerns about accepting treatment

Necessity
Concerns

Necessity
Concerns

= poor adherence
= adherence
A strategy for preventing relapse

Medicines management

Individualise antipsychotic treatment
The choice of drug should be made by the service user and healthcare professional together, considering the relative potential of individual antipsychotic drugs to cause:

- extrapyramidal side effects (including akathisia)
- metabolic side effects (including weight gain)
- other side effects (including unpleasant subjective experiences)
A strategy for preventing relapse

Medicines management

- Individualise antipsychotic treatment
- Engage patient by improving communication & information
- Avoid complex treatment regimens
Once-daily dosing improves adherence significantly

Systematic review of MEMS literature 1986 – 2007
(Range of chronic physical & neurological illnesses)

**Once daily dosing:**
- 13%-26% better adherence than bd dosing
- 22%-41% better adherence than tid dosing

Saini SD, Schoenfeld P, Kaulback K, Dubinsky MC.
Effect of medication dosing frequency on adherence in chronic diseases
Am J Manag Care 2009;15:e22-33
A strategy for preventing relapse

Medicines management

- Individualise antipsychotic treatment
- Avoid complex treatment regimens
- Adjust to daily routine
- Ensure patient understands treatment regimen
- Ensure easy access to repeat prescription
- Consider depot antipsychotic

Engage patient by improving communication & information
Potential solutions

Medicines management

Patient & carer information

Patient and carer education

Therapeutic relationship
Improving the therapeutic relationship

- Provide accessible & meaningful information
- Involve patient in treatment decisions
- Take patient concerns seriously
Potential solutions

Adherence

- Medicines management
- Therapeutic relationship
- Patient & carer information
- Patient and carer education
Information “... is fundamental to choice and making informed decisions. Without information there is no choice. Information helps knowledge and understanding. It gives patients the power and confidence to engage as partners with their health service.”
5 tests for patient information

• It must be intuitive and easily understood
• It must be evidence-based
• It must address issues that are important to patients
• Both patients and health professionals must be involved in its development locally
• It should be accessible and easily available during all patient-facing interactions

Donoghue JM
www.mentalmeds.co.uk/patient-information.php
Potential solutions

Adherence

- Medicines management
- Patient & carer information
- Therapeutic relationship
- Patient and carer education
Relapse prevention in schizophrenia: Does group family psychoeducation matter? One-year prospective follow-up field study

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Number of in-patient days at 1-year follow-up

- Participants: 5.89
- Non-participants: 17.78

p=0.045
Educational intervention: 7-year follow-up

- 4 weekly group sessions of 60 minutes
- Followed by 4 monthly sessions
- Sessions for relatives
  - 8 bi-weekly sessions lasting 90-120 minutes

- Schizophrenic psychoses provoked by both biological factors and psychosocial stress
- Long-term consistent treatment is necessary with combination of medication and psycho-therapeutic interventions
- Medication is usually necessary to enable psychotherapeutic progress
- Pragmatic coping strategies
- Patients able to discuss openly their concerns about their illness and its treatment & develop solidarity with other patients
- Information booklet

Bauml J, Pitschel-Walz G, Volz A et al
Psychoeducation in schizophrenia: 7-year follow-up concerning rehospitalisation and days in hospital in the Munich Psychosis Information Project Study
Persistence of effect of education

Re-admission rates

Education: 54%
TX as usual: 88%

Bauml J, Pitschel-Walz G, Volz A et al
Psychoeducation in schizophrenia: 7-year follow-up concerning rehospitalisation and days in hospital in the Munich Psychosis Information Project Study
Summary

• Poor adherence in schizophrenia is common and results in
  – Severe psychiatric morbidity
  – High cost burden for the NHS

• Pragmatic interventions could remove barriers to adherence and prevent relapse
  – Medicines management
  – Improving therapeutic alliance
  – Patient / carer information
  – Patient / carer education
Final thoughts:

- Patients should be supported, not blamed
- Health systems must evolve to meet new challenges
- Health professionals need training in supporting adherence
- A multidisciplinary approach is needed
- Improving adherence may have a far greater impact on health than incremental improvements in medical treatments
Improving the use of medicines in severe mental illness

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