Treatment Adherence & Relapse Prevention in Schizophrenia

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Liverpool

Objectives

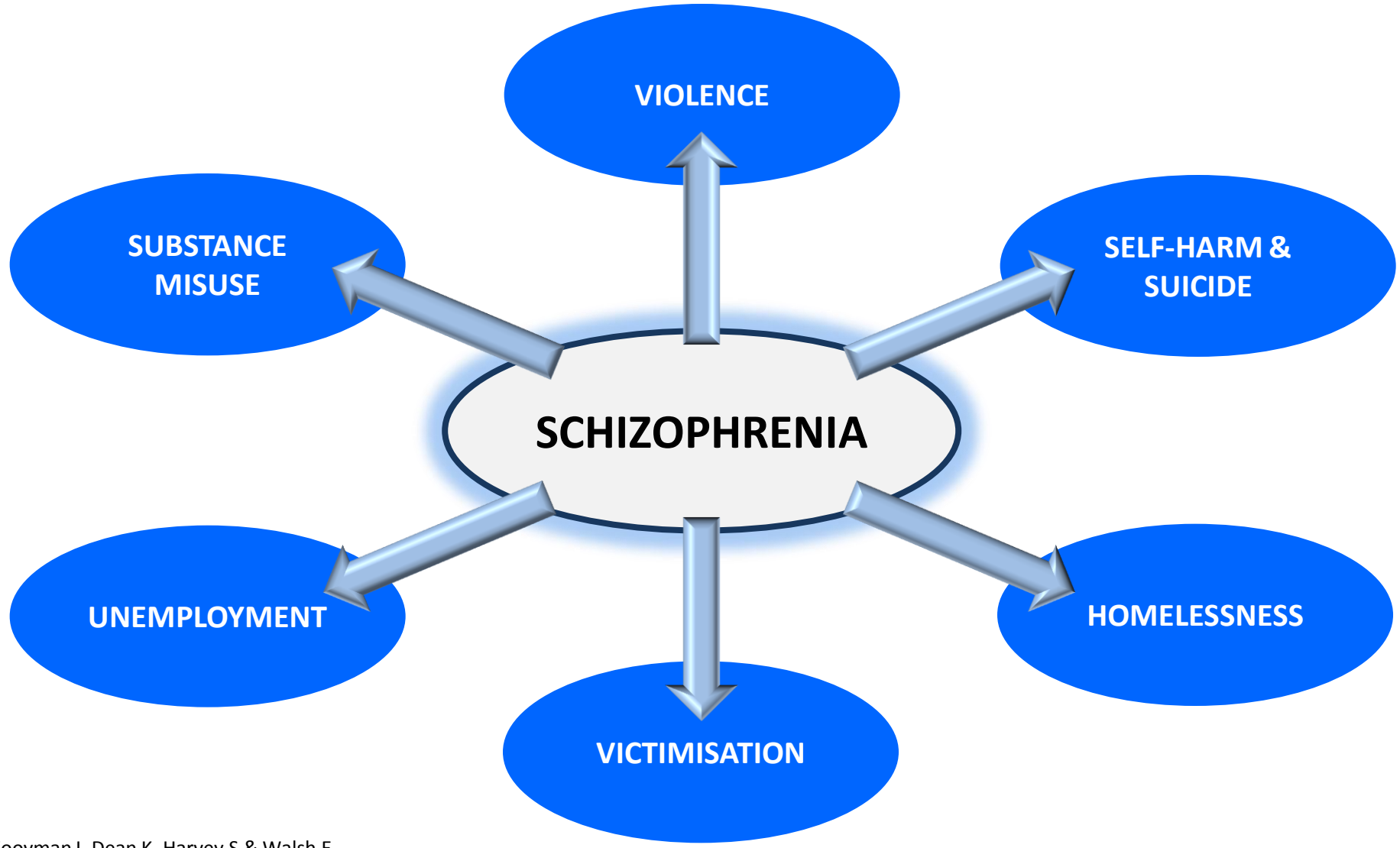
- To review the pivotal relationship between treatment adherence and outcome in schizophrenia
- To consider how better medicines management could aid adherence to treatment with antipsychotic medication
- To review data for relapse prevention with 2nd-generation antipsychotic medicines

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

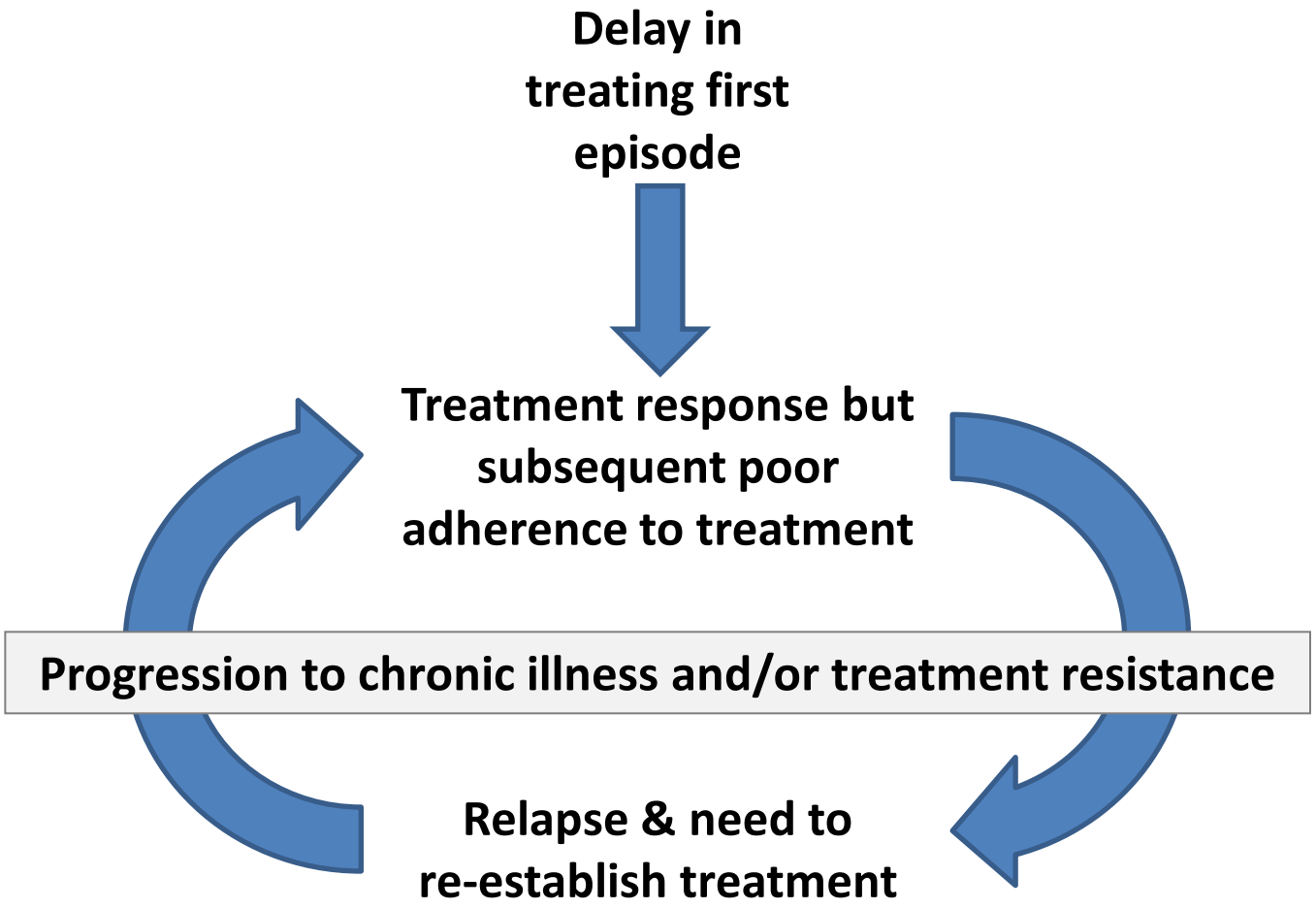
National Collaborating Centre for Mental Health
Core interventions in the management of schizophrenia in primary and secondary care (update).
National Clinical Practice Guideline Number 82, Full Guideline
National Institute of Health and Clinical Excellence, London, March 2009.

Outcomes of public concern



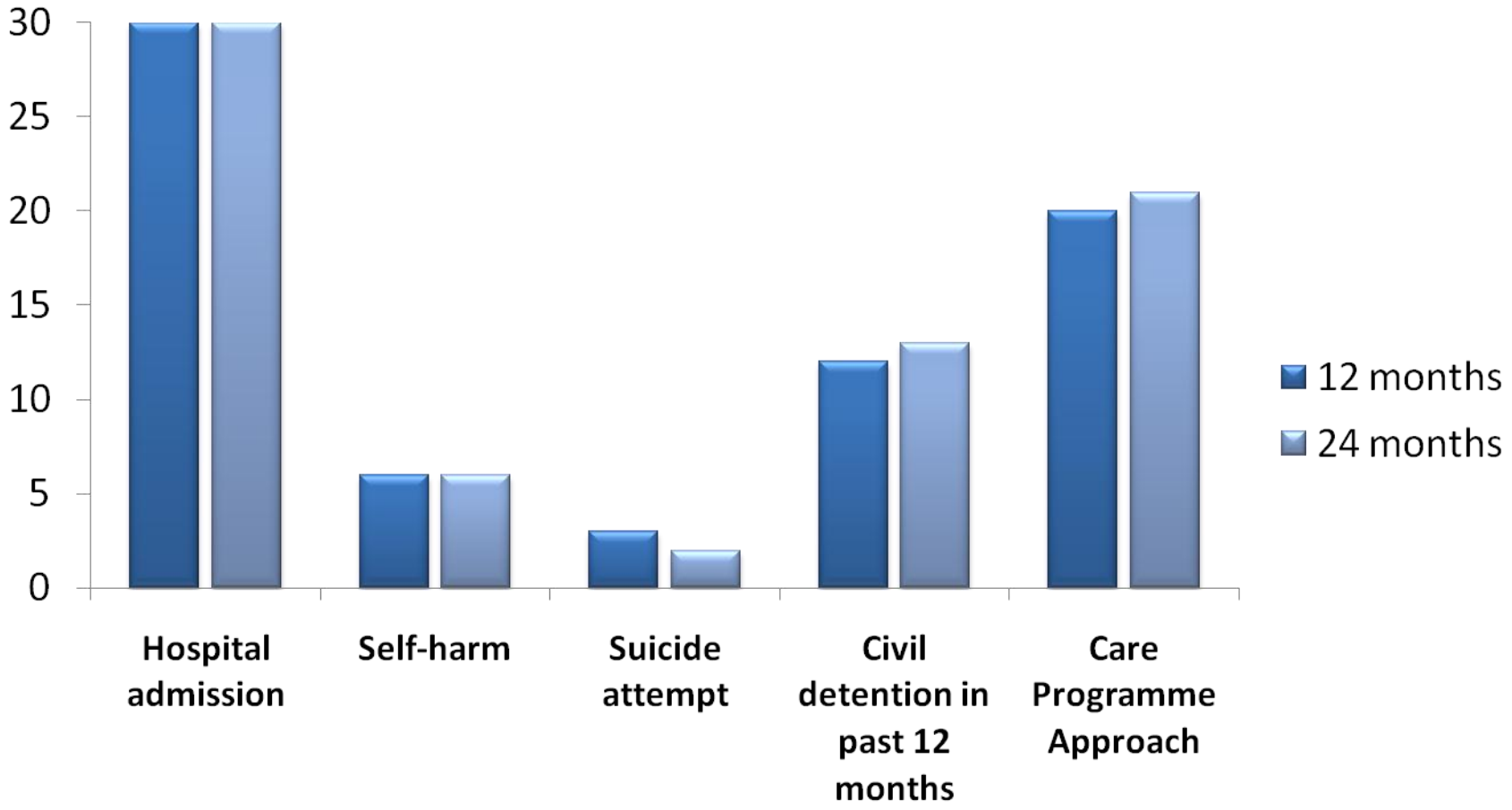
Kooyman I, Dean K, Harvey S & Walsh E
Outcomes of public concern in schizophrenia
Br J Psychiatry 2007;191:29-36

Revolving door = vicious cycle



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

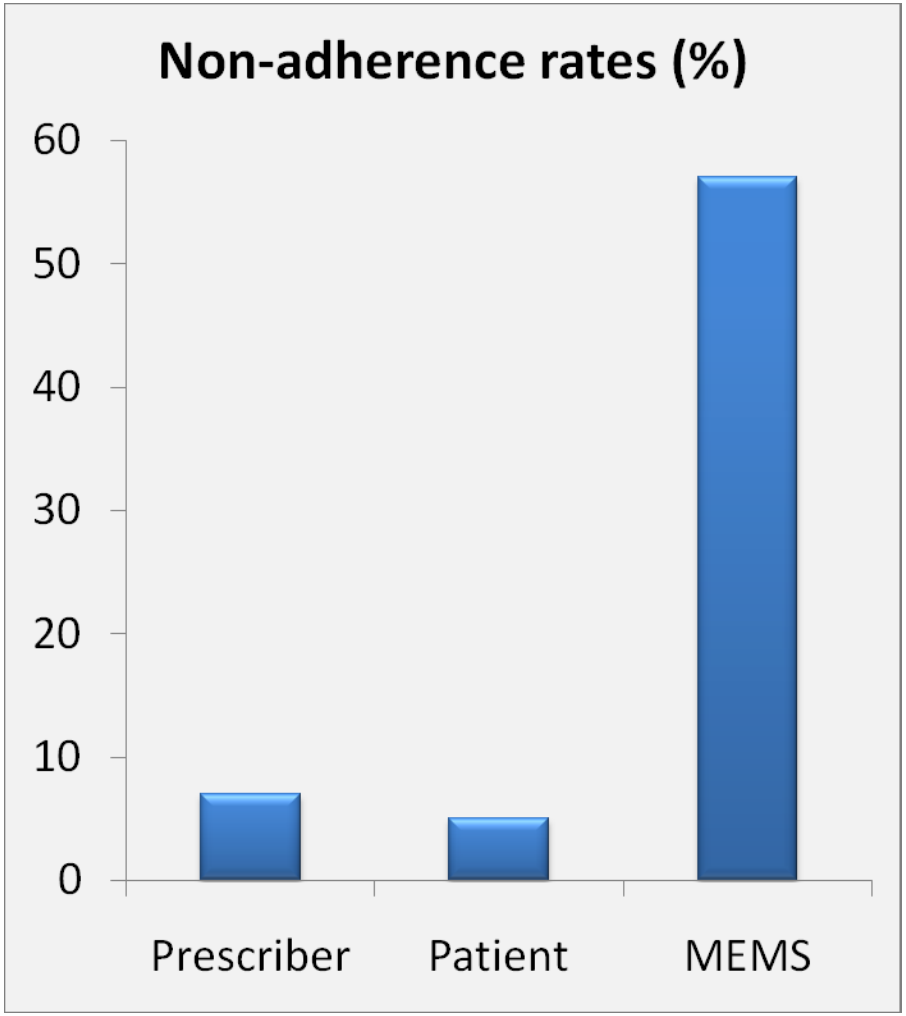
WHO: Conclusions about poor treatment adherence

- A problem of striking magnitude
- Poor health outcomes and increased costs
- Influenced by multiple factors
- Patient-tailored interventions are required

World Health Organization
Adherence to long-term therapies: Evidence for action
Geneva, WHO 2003
http://www.who.int/chp/knowledge/publications/adherence_introduction.pdf

Clinicians often underestimate poor adherence in their patients

- **Electronic medication event monitoring system (MEMS)**
  - Adherence ratings collected from:
    - Clinicians
    - Patients
    - MEMS
  - 6 consecutive monthly visits
  - Non-adherence = <70% adherence for 2 or more months

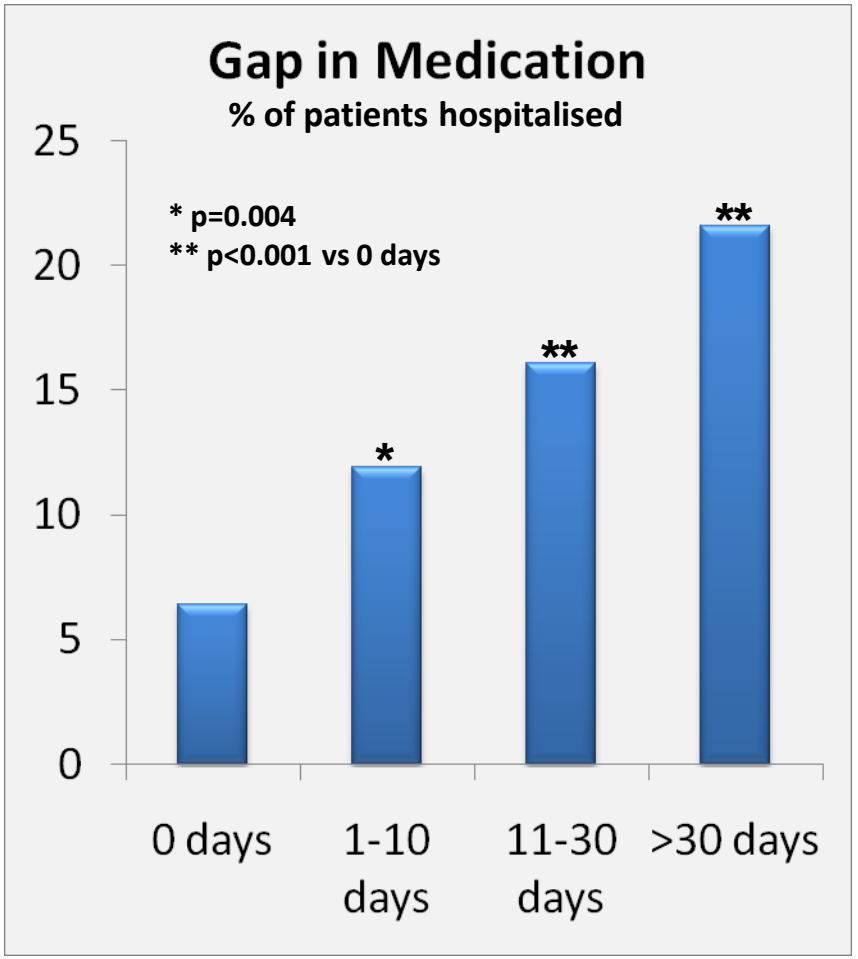


Patient population:
Outpatients with schizophrenia (n=35)
or schizoaffective disorder (n=26)

Byerly MJ, Thompson A, Carmody T et al.
Validity of electronically monitored medication adherence and conventional adherence measures in schizophrenia
Psychiatric Services 2007;58:844-7

When does poor adherence increase hospital admission?

- Retrospective review in USA
  - 4325 Medicaid outpatients with schizophrenia
- Adherence assessed using:
  - Gap in medication
  - Medication consistency
  - Medication possession ratio
- Study duration 1 year



Weiden PJ, Kozma C, Grogg A, Locklear J
Partial compliance and risk of rehospitalisation among California Medicaid patients with schizophrenia
Psychiatric Services 2004;55:886-91

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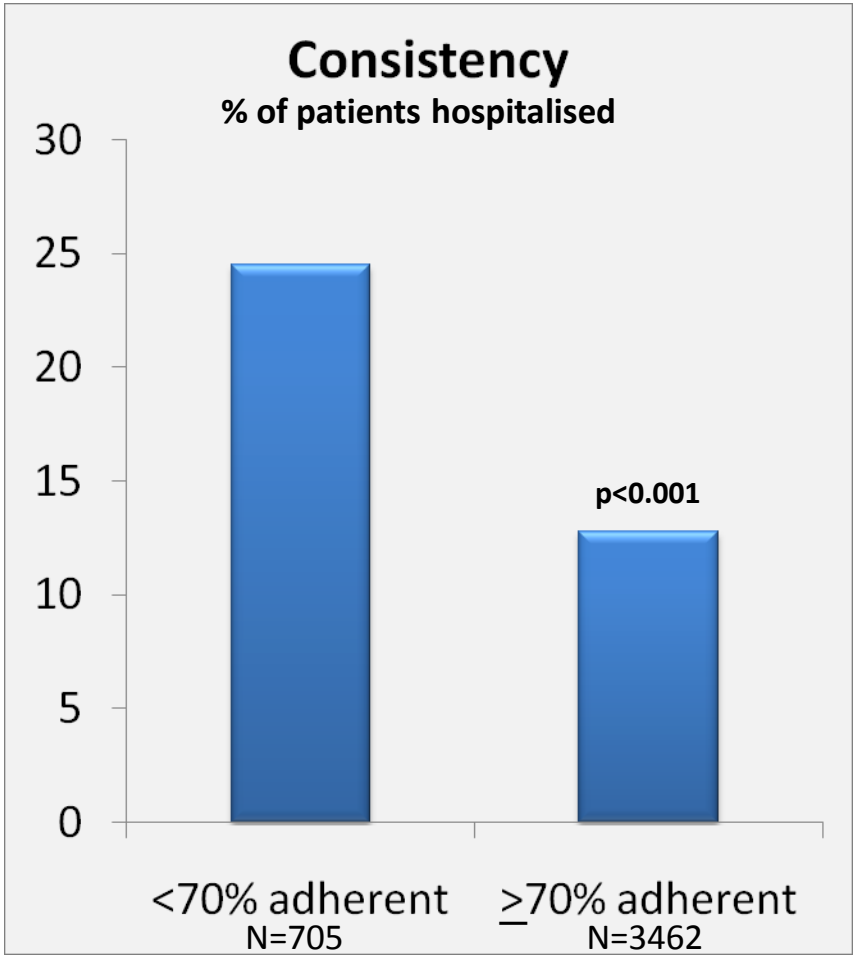

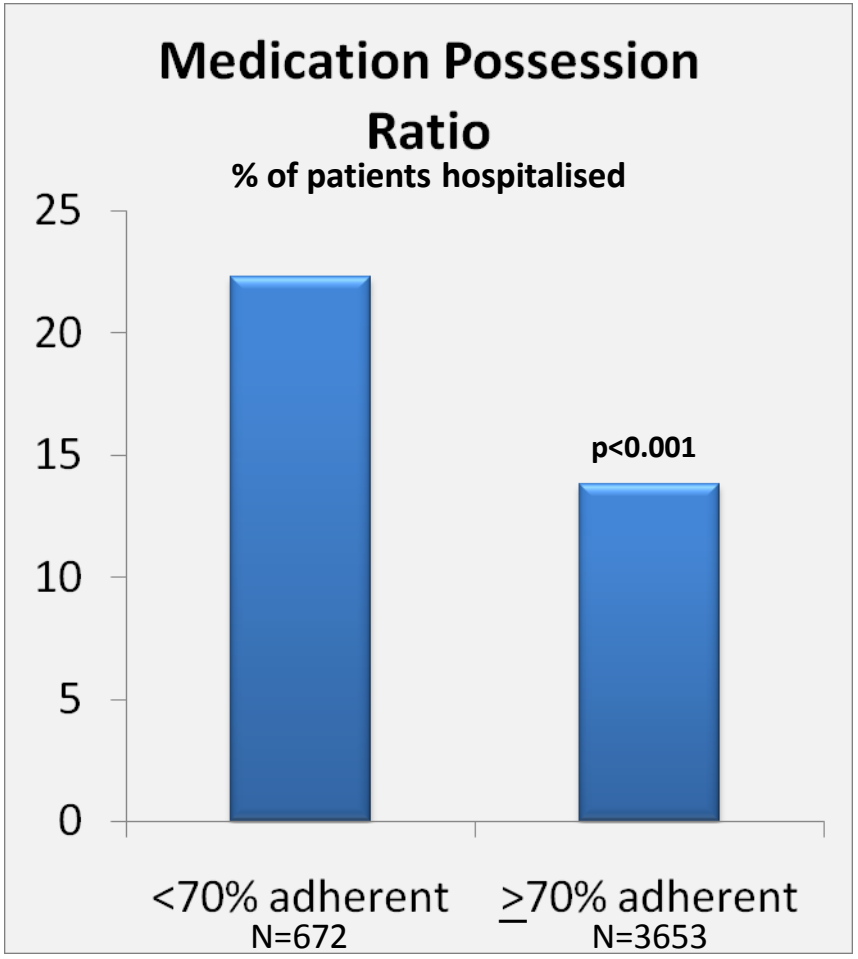

Weiden PJ, Kozma C, Grogg A, Locklear J
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Psychiatric Services 2004;55:886-91

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 10-24 years
- Range of adherence measures
- *"Taking medication as prescribed at least 75% of the time"*

49.5% of patients non-adherent

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.
J Clin Psychiatry 2002;63:892-909

Adherence varies over time

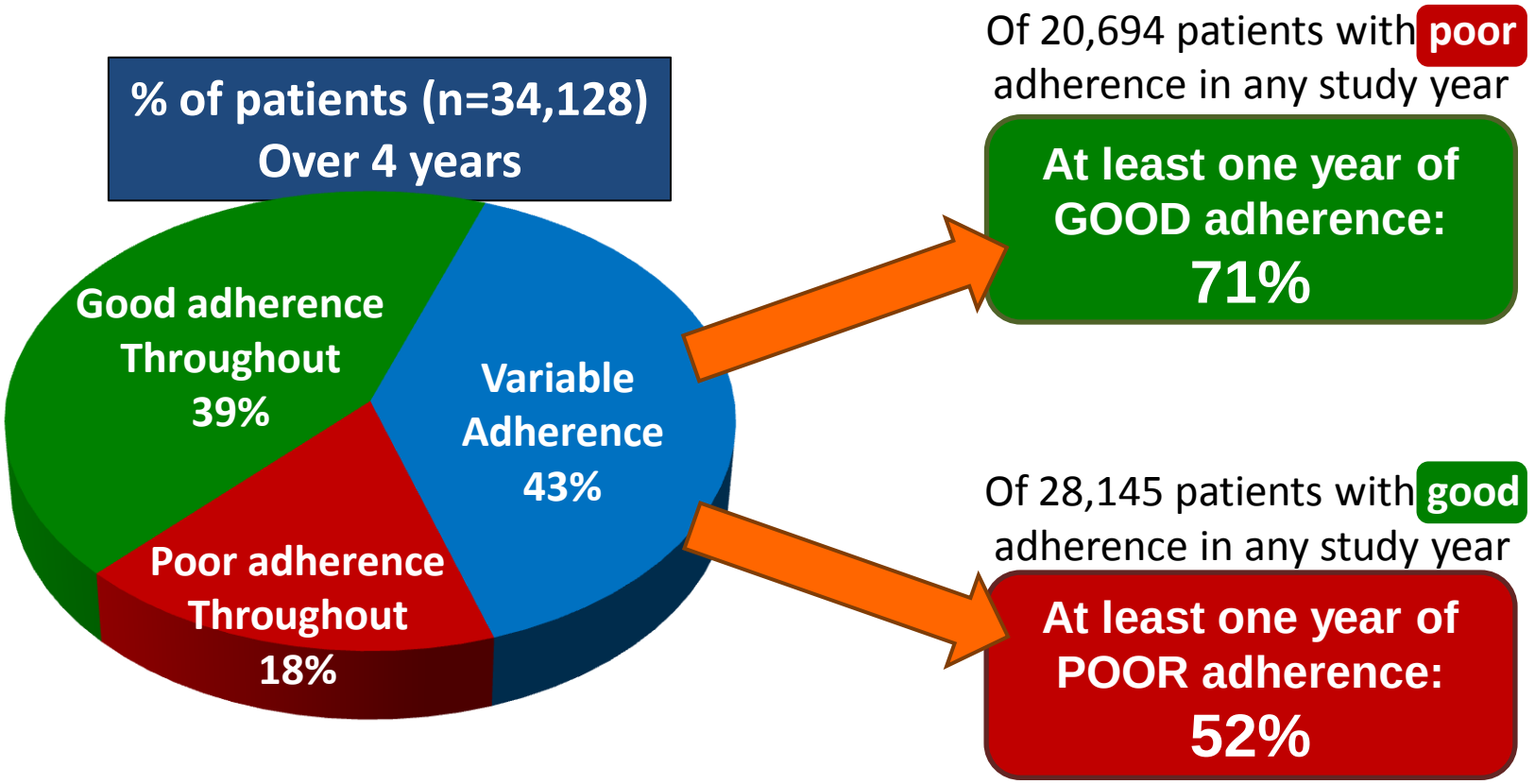
- 4-year study in US Veterans Affairs system
- 34,128 patients with schizophrenia
- 'Medication possession ratio' (MPR) calculated

$$\text{MPR} = \frac{\text{Number of days supply of antipsychotic obtained from pharmacy}}{\text{Number of days supply needed for continuous antipsychotic use}}$$

- MPR <0.8 = poor adherence
- Cross-sectional prevalence of poor adherence was stable: 36%-37%

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

Adherence varies over time



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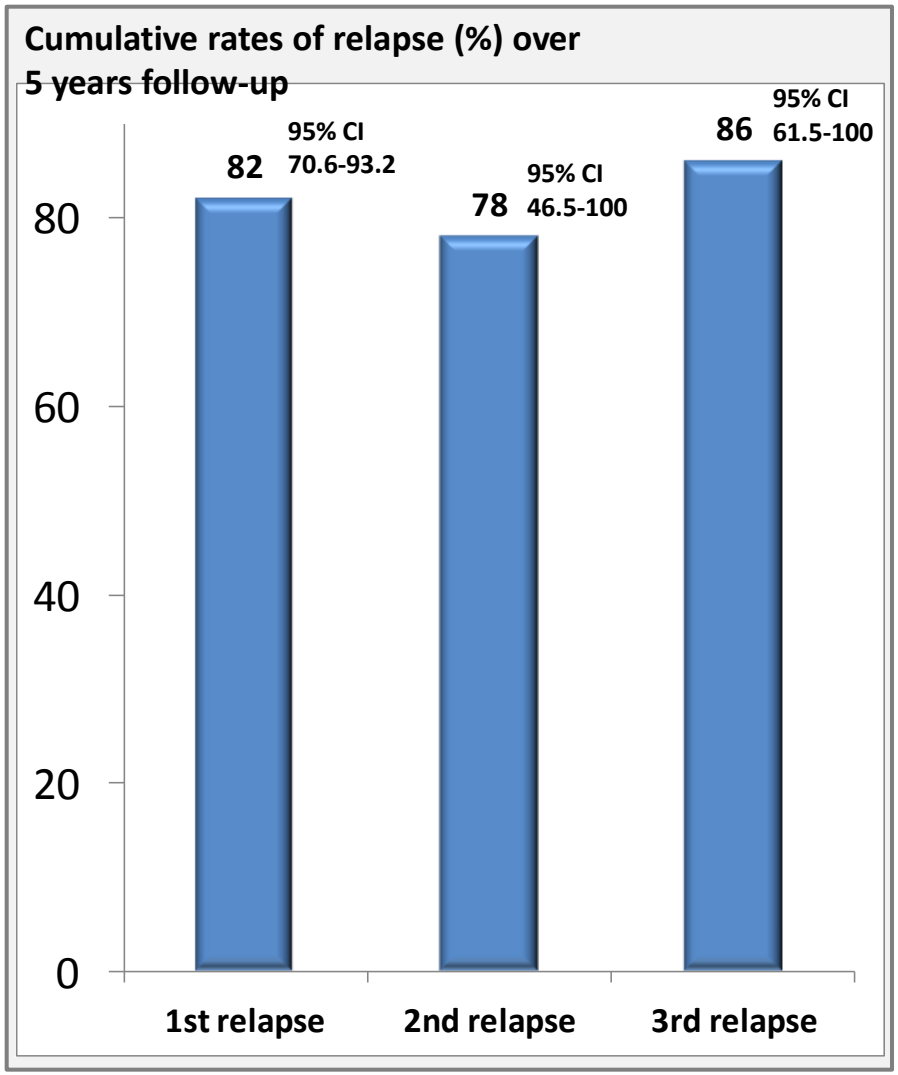
Poor adherence in 1st episode schizophrenia leads to high rates of relapse

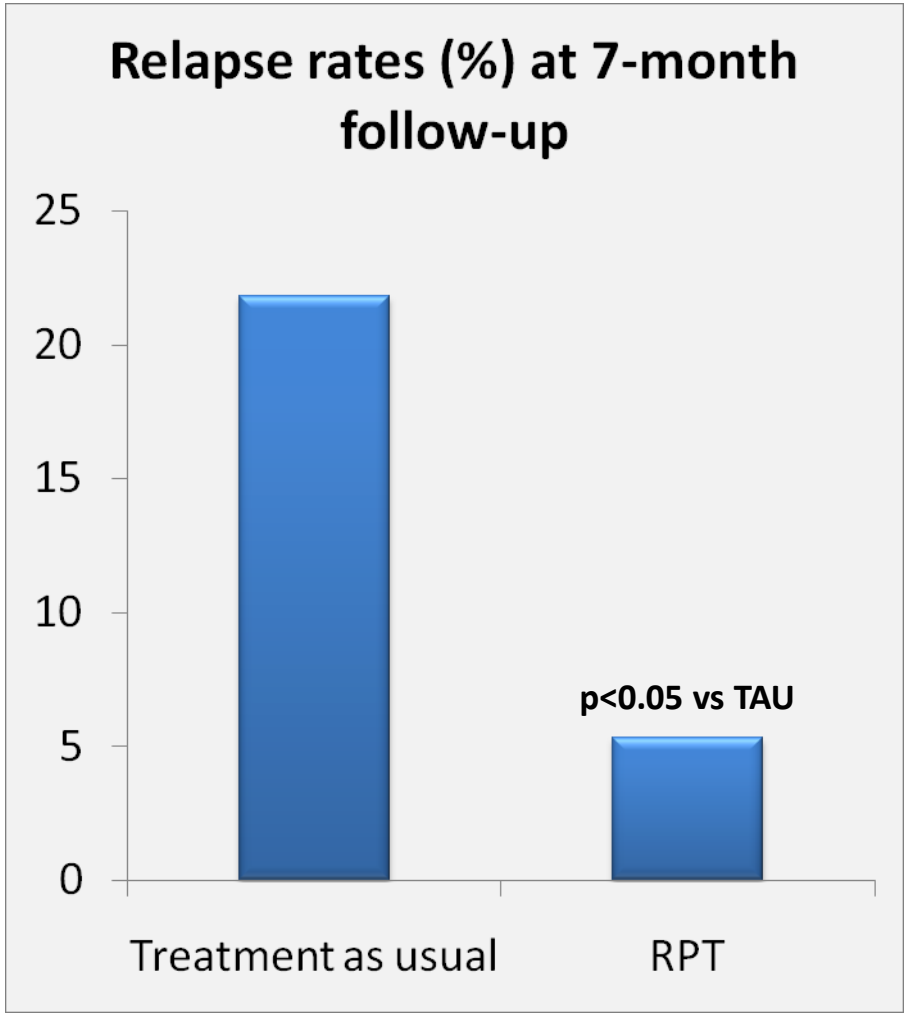
- 5-year follow-up study after initial recovery from first episode of schizophrenia or schizoaffective disorder
- 104 patients
- Discontinuation of antipsychotic medication increased risk of relapse almost 5-fold



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

Preventing relapse in 1st episode psychosis

- **Relapse Prevention Therapy (RPT)**
  - Shared written individual assessment of relapse risk
  - Phased systematic approach to relapse prevention – CBT interventions
  - Parallel individual and family relapse prevention CBT sessions
  - Supervision specifically focused on relapse prevention
- Patients randomised to receive
  - RPT N=41
  - Treatment as usual (TAU) N=40



Gleeson JF, Cotton SM, Alvarez-Jiminez M et al.
A randomized controlled trial of relapse prevention therapy for 1st episode psychosis patients
J Clin Psychiatry 2009;70:477-486

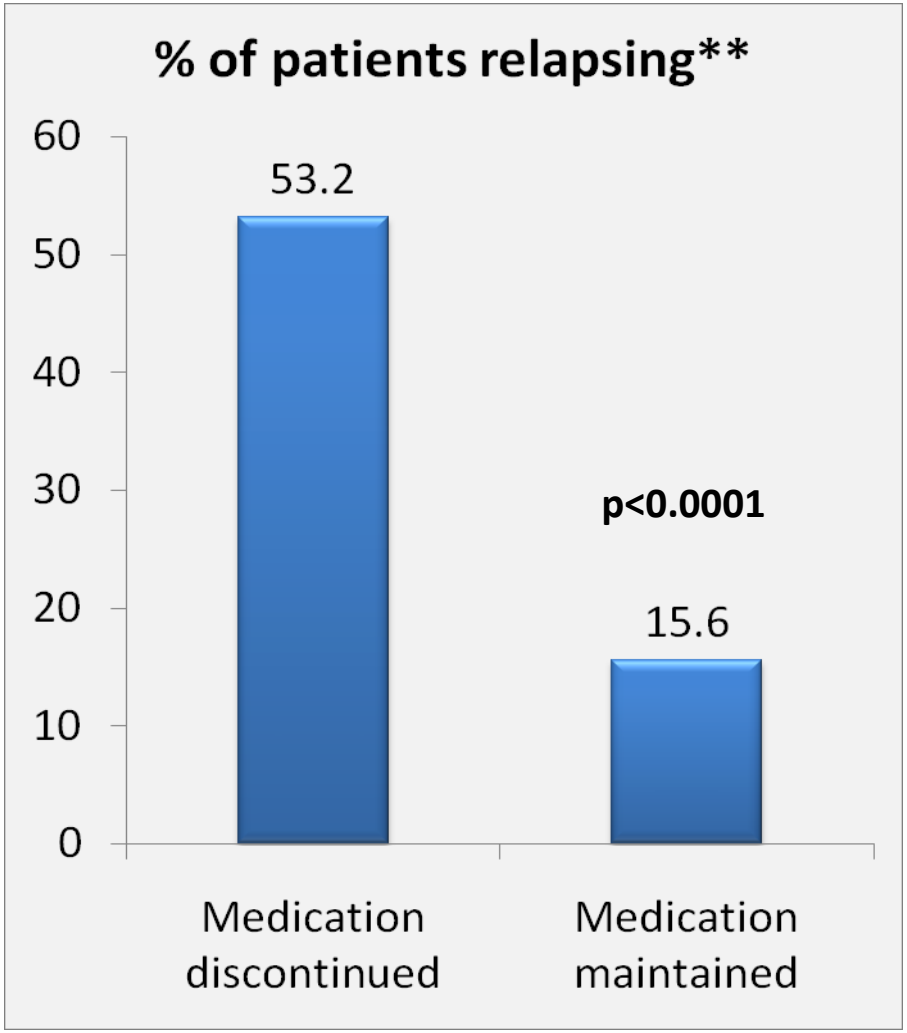
Poor adherence in chronic schizophrenia leads to high rates of relapse

- Pooled analysis of 66 studies with 4365 patients with chronic schizophrenia
- Relapse rates over 10 month period

- Number Needed to Harm for medication withdrawal*

  NNH = 3 (95% CI 2-3)

*** Calculated from the study results**



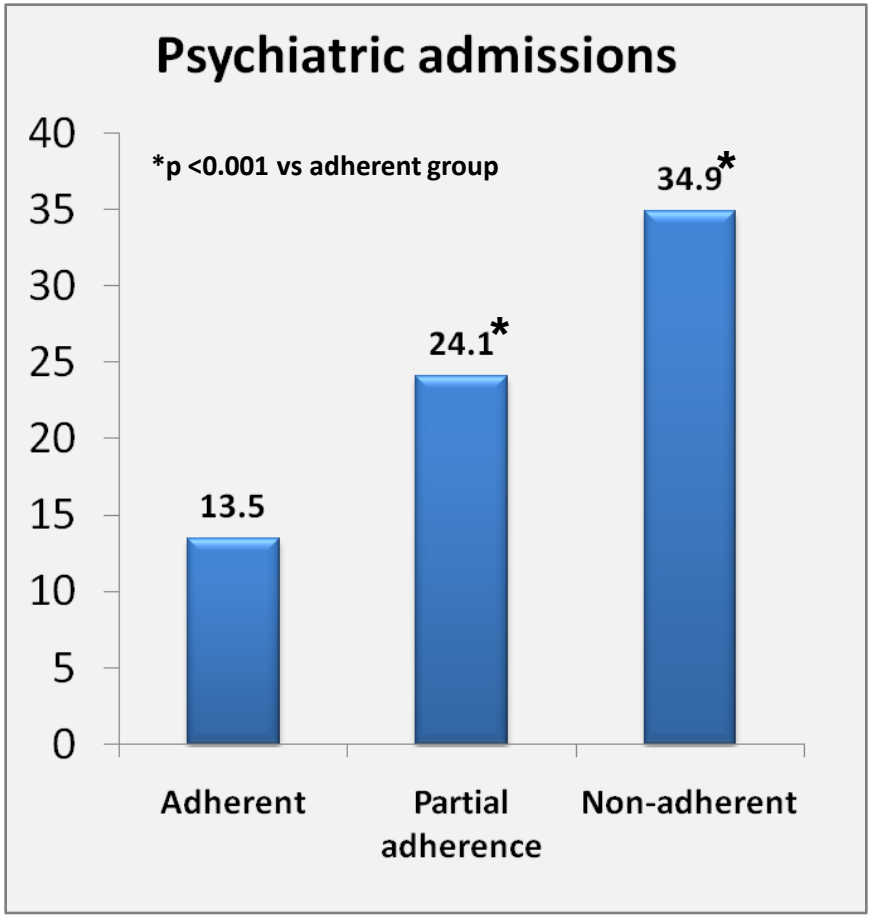
**** Data from 29 of the 66 studies where there were matched withdrawal and treatment maintenance groups**

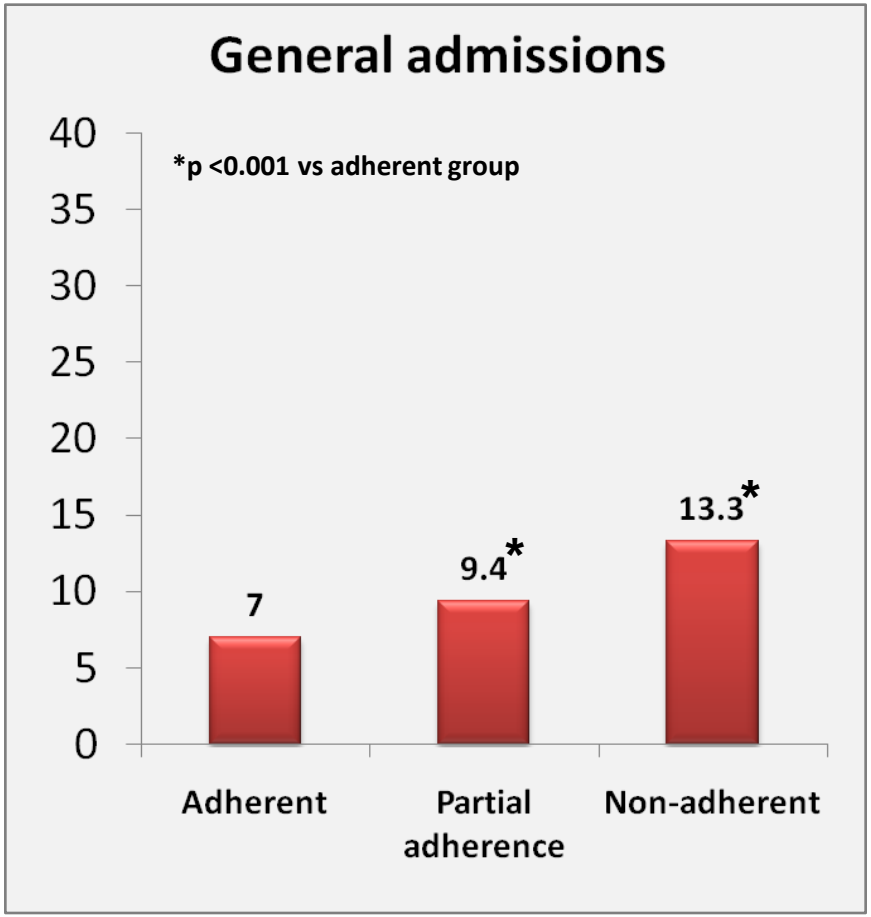
NNT calculation made using University of British Columbia clinical significance calculator (http://spph.ubc.ca/sites/healthcare/files/calc/clinsig.html

Gilbert PL, Harris MJ, McAdams LA, Jeste DV. Neuroleptic withdrawal in schizophrenic patients: a review of the literature. Archives of General Psychiatry 1995;52:173-88

Poor adherence in schizophrenia leads to high rates of hospital admission

Estimates of annual admission rates %





Gilmer TP, Dolder CR, Lacro JP et al
Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia
Am J Psychiatry 2004;161:692-9

Poor adherence in schizophrenia is costly to the NHS

- **UK Health economic study**
- **Data for 1 year (1994) 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

Poor adherence

- 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

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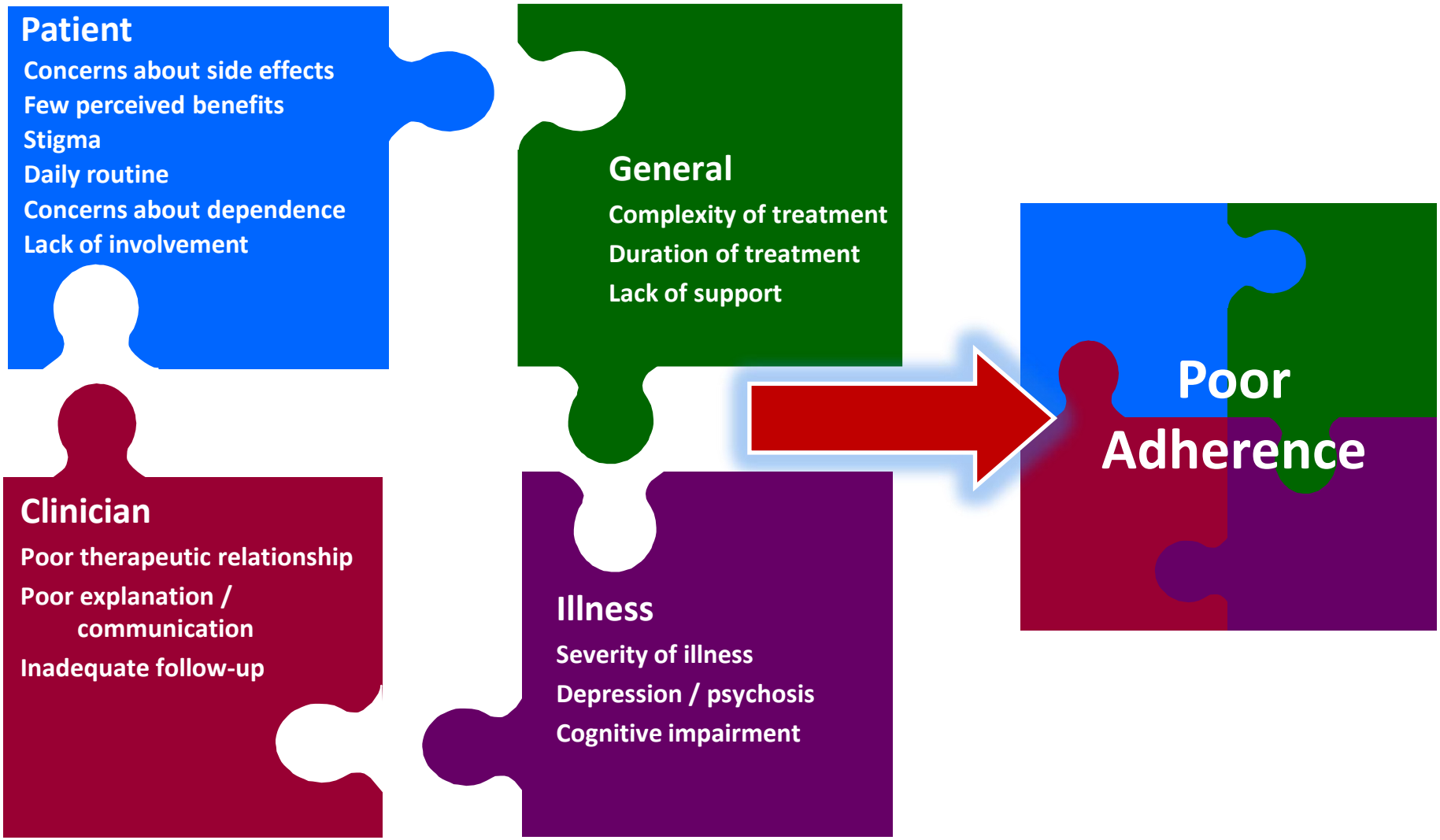
Adherence is influenced by multiple factors



Mitchell AJ, Selmes T
Why don't patients take their medicines? Reasons and solutions in psychiatry.
Advances in Psychiatric Treatment 2007;13:336-346

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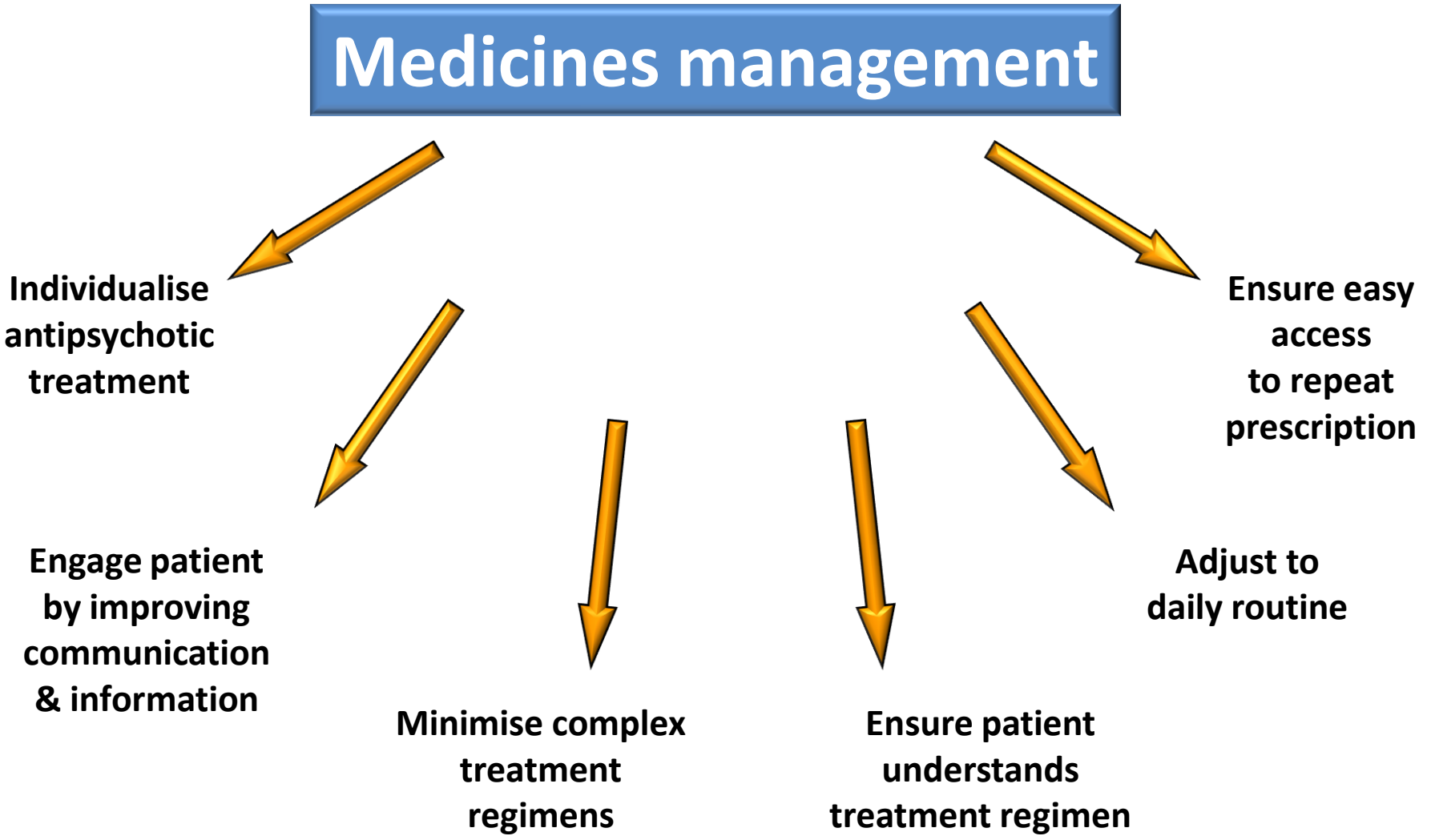
A strategy for preventing relapse



Individualising antipsychotic medication

- Offer oral antipsychotic medication.
- Provide information and discuss the benefits and side-effect profile of each drug with the service user.
- 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)

National Institute for Health and Clinical Excellence.
Core interventions in the treatment and management of schizophrenia in adults in primary and secondary care.
Clinical Guideline 82. March 2009.
National Institute for Health and Clinical Excellence, London, 2009.

Once-daily dosing improves adherence

Systematic review of MEMS literature 1986 – 2007

(Range of chronic physical & neurological illnesses
No psychiatric illnesses were included in this analysis)

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

Dosing frequency and adherence in schizophrenia and schizoaffective patients

Effect of increasing frequency of dose

- 1639 patients with ≥50% dose increase
- 1381 stayed on once-daily dosing before and after dose increase
  - No change in MPR
- 258 patients with increase in frequency of dosing
  - Significant reduction in MPR from 0.89 to 0.79 ($p<0.001$)

Effect of decreasing frequency of dose

- 1370 patients with dosing frequency reduced to once-daily
- Matched to 2740 controls
- OD dosing group
  - Significant improvement in MPR: 0.045
- Control group
  - Small reduction in MPR: -0.018 ($p<0.001$)

Pfeiffer P, Ganoczy D, Valenstein M
Dosing frequency and adherence to antipsychotic medications
Psychiatric Services 2008;59:1207-10

Relapse prevention with 2nd-generation oral antipsychotic medicines (placebo-controlled studies)

- Aripiprazole
- Olanzapine
- Seroquel XL▼ (quetiapine prolonged release)

Data unavailable for oral risperidone

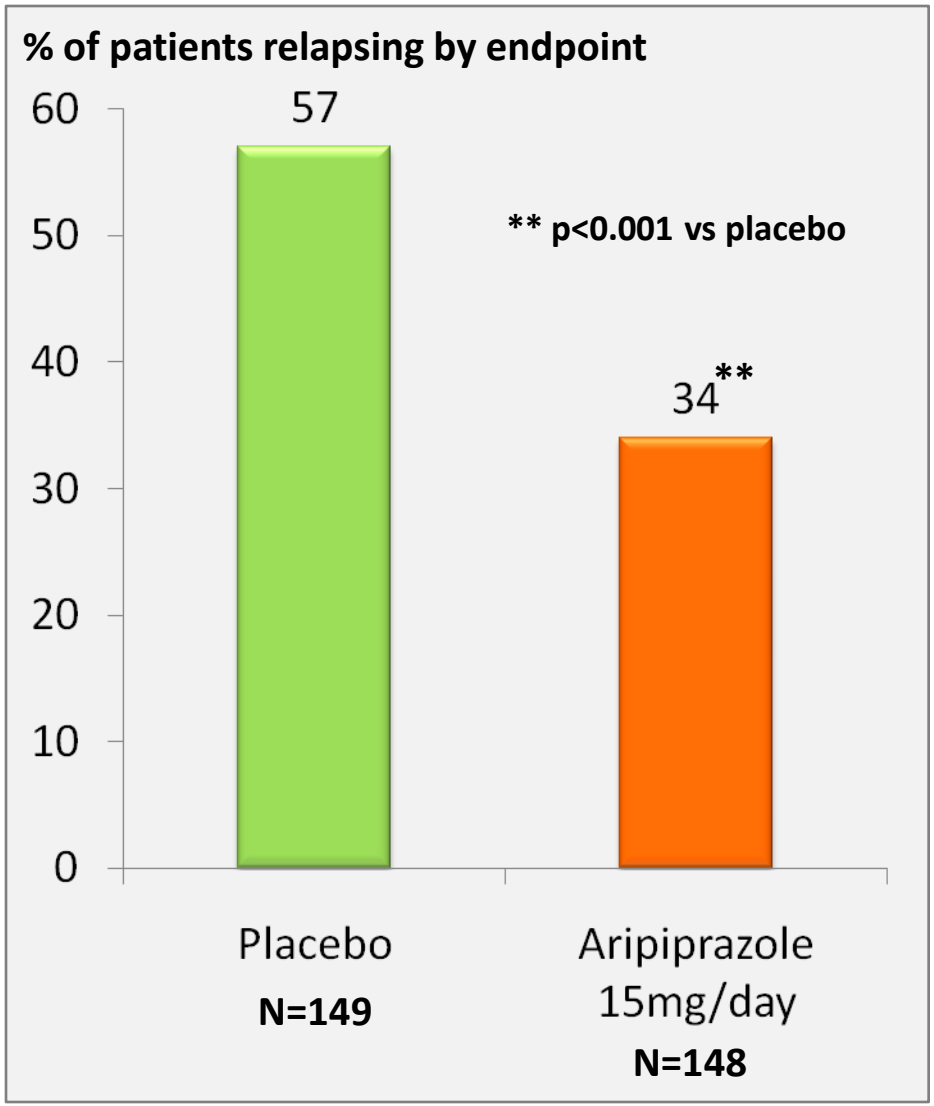
Please refer to individual SmPCs for licensed indications

Aripiprazole: relapse prevention

- 6 month randomised, double-blind, placebo controlled trial
- Patients clinically stable for 3 months prior to randomisation
- Number Needed to Treat* compared with placebo

  NNT = 4 (95% CI 3-8)

*** Calculated from the study results**



NNT calculation made using University of British Columbia clinical significance calculator (http://spph.ubc.ca/sites/healthcare/files/calc/clinsig.html

Please refer to SmPC for licensed indications

Pigott TA, Carson WH, Saha AR et al.
Aripiprazole for the prevention of relapse in stabilized patients with chronic schizophrenia: a placebo-controlled 26 week study
J Clin Psychiatry 2003;64:1048-56

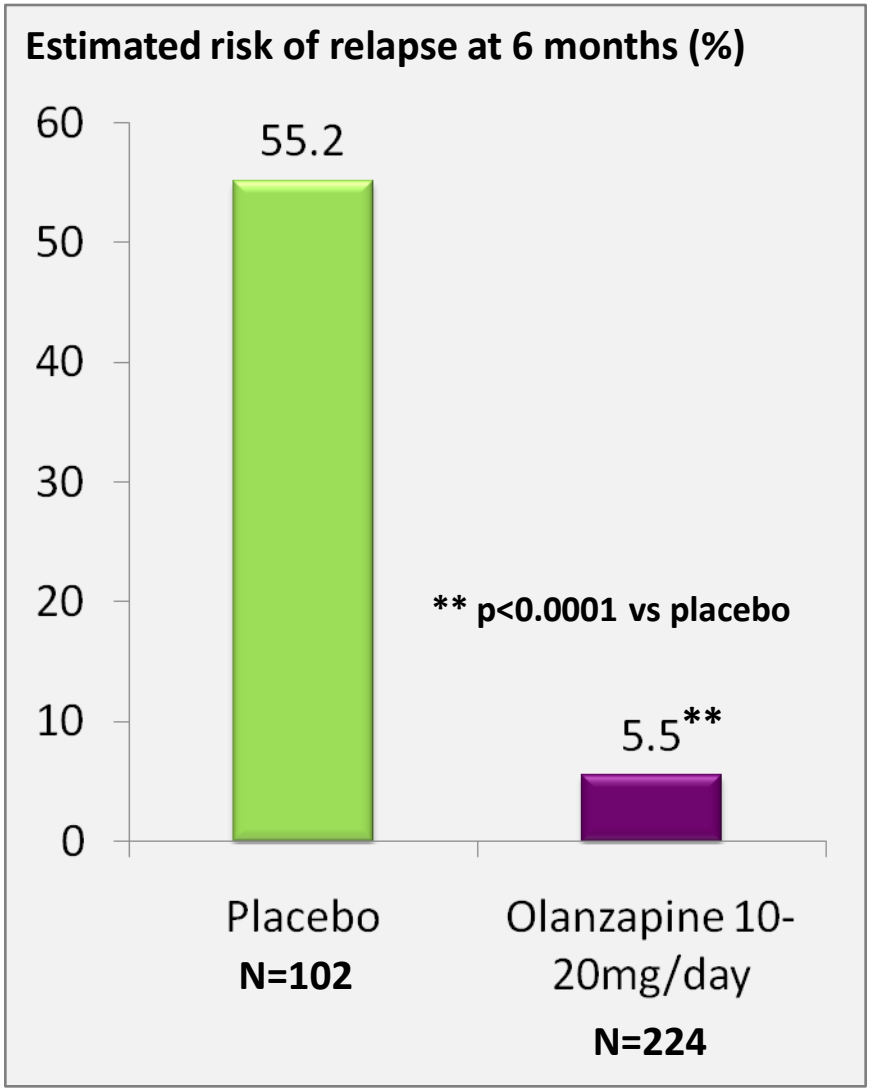
Olanzapine: relapse prevention

- 1 year randomised, double-blind, placebo controlled trial
- Patients stable on olanzapine 10-20mg/day for 2 months prior to randomisation

- Number Needed to Treat* compared with placebo

  NNT = 2 (95% CI 2-2)

*** Calculated from the study results**



NNT calculation made using University of British Columbia clinical significance calculator (http://spph.ubc.ca/sites/healthcare/files/calc/clinsig.html

Please refer to SmPC for licensed indications

Beasley CM, Sutton VK, Hamilton SH,et al
A double-blind, randomized, placebo-controlled trial of olanzapine in the prevention of psychotic relapse.
J Clin Psychopharmacol 2003;23:582-94

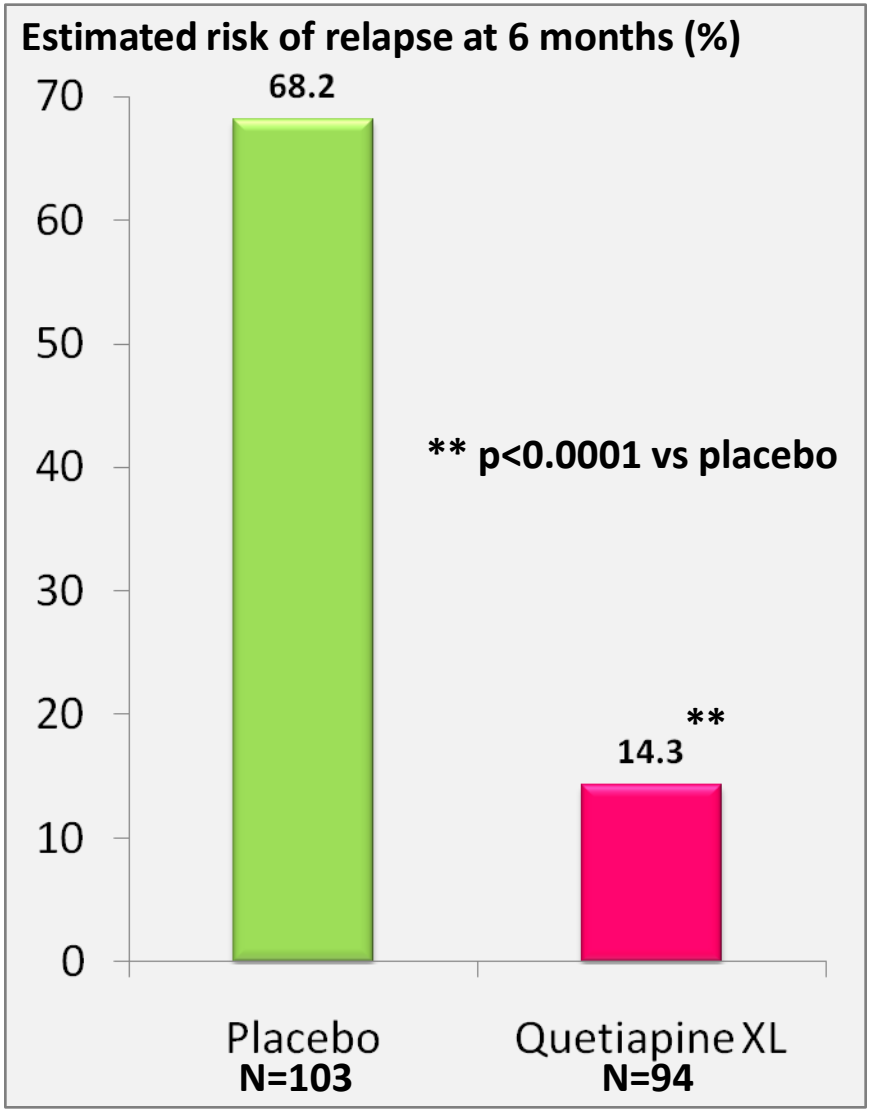
Quetiapine XL: relapse prevention

- 1 year randomised, double-blind, placebo controlled trial

- Number Needed to Treat* compared with placebo

  NNT = 2 (95% CI 2-2)

*** Calculated from the study results**



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Peuskens J, Trivedi J, Malyarov S et al
Prevention of schizophrenia relapse with extended release quetiapine fumarate dosed once daily: a randomized, placebo-controlled trial in clinically stable patients
Psychiatry (Edgmont) 2007;4:34–50

Summary

- Poor adherence in schizophrenia is common and results in
  - High rates of relapse
  - High cost burden for the NHS
- Medicines management may offer a strategy to support adherence and prevent relapse
  - Individualising treatment
  - Minimising complex treatment regimens
- Second-generation antipsychotics are effective in preventing relapse in schizophrenia

www.mentalmeds.co.uk