Appendix 25: 2009 Evidence tables for economic studies

Sections of the appendices where the evidence has not been updated from the previous NICE guideline, Schizophrenia in Adults (2002) are shaded in grey.

Access and engagement

Early intervention services

References to included studies (in previous schizophrenia guideline)

Mihalopoulos, C., McGorry, P.D., Carter, R.C. (1999) Is phase-specific, community-oriented treatment of early psychosis an economically viable method of improving outcome? *Acta Psychiatrica Scandinavica, 100,* 47-55.

Study	Methods	Cost data	Interventions	Participants	Primary outcome(s) measured	Cost(s) measured	Results	Comments	Risk of bias (Validity scores
Mihalopoulos et al., 1999	Economic study design: CEA Clinical effect size data source: controlled study with historical controls – McGorry 1996 Perspective: government funding agency – Victoria Dept. of Human Services Time frame: 1 year Setting: Melbourne	Country: Australia Fiscal year: 1993/94 Currency: Australian Dollars	EPPIC (Early Psychosis Prevention and intervention centre) Pre-EPPIC (inpatient ward and local generic community psychiatric services)	66.7% with schizophrenia spectrum disorder N=51 N=51	QLS (Quality of Life Scale) SANS (Scale for the Assessment of Negative Symptoms	1. Inpatient 2. Outpatient 3. Day care 4. Community health care 5. Medication	The weighted average cost was $24,074/participant for intervention 2, and $16,964/participant for intervention 1. Intervention 1 is more effective and less costly. To gain a one-point improvement in SANS is 91% cheaper ($AUD 1,081 versus $AUD 12,671) , and to gain a one-point improvement in QLS is 46% cheaper ($AUD 380 versus $AUD 836) by intervention 1 than intervention 2.	The study was conducted prior to the introduction of atypicals in Australia. Sensitivity analysis proved the robustness of the result.	Low (25/32)

Abbreviations

CEA – Cost-effectiveness analysis N – Number of participants

References to economic studies on psychological interventions for people with schizophrenia, excluded at stage 5 of the systematic review (see Chapter 3 for methods of systematic review of the economic literature)

Goldberg, K., Morman, R., Hoch, J., *et al*. (2006) Impact of a specialised early intervention service for psychotic disorders on patient characteristics, service use, and hospital costs in a defined catchment area. *Canadian Journal of Psychiatry, 51*, 895-903.

Mihalopoulos, C., McGorry. P.D., Carter, R.C. (1999) Is phase-specific, community-oriented treatment of early psychosis an economically viable method of improving outcome? *Acta Psychiatrica Scandinavica, 100*, 47-55.

Pharmacological interventions in the treatment and management of schizophrenia

Initial treatment with antipsychotic medication

References to included studies

Davies, L. & Lewis, S. (2000) Antipsychotic medication for people with first episode schizophrenia: an exploratory economic analysis of alternative treatment algorithms. Discussion Paper 178, 1-51. York: Centre for Health Economics, University of York.

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
Davies & Lewis, 2000 UK Cost-utility analysis	Interventions: Olanzapine Risperidone Chlorpromazine Haloperidol Clozapine 8 scenarios examined, with maximum 4 lines of treatment; switch assumed in the event of intolerance, inadequate response or relapse; clozapine used as 3rd and 4th line treatment only	People with a first episode of schizophrenia Decision-analytic modelling Source of clinical effectiveness data: review of published trials including Cochrane reviews, supplemented by other published literature Source of resource use: literature review, national sources and authors' estimates Source of unit costs: national sources	Costs: Inpatient care, day hospital, outpatient visits, medication, treatment of adverse events Total 3-year costs of first-line treatment per 1000 people (mean values): Olanzapine £22,312,200 Risperidone £20,653,000 Chlorpromazine £17,982,170 Haloperidol £20,160,470 Outcomes: QALYs Total 3-year QALYs of first-line treatment per 1000 people (mean values): Olanzapine 2,326 Risperidone 2,414 Chlorpromazine 2,336 Haloperidol 2,298	1st and 2nd line treatment: Chlorpromazine dominant over olanzapine and haloperidol Risperidone versus chlorpromazine: £34,241/QALY (1st line) £153,600/QALY (2nd line) 3rd and 4th line treatment: Chlorpromazine dominant over olanzapine and haloperidol Clozapine dominant over olanzapine and risperidone Clozapine versus chlorpromazine: £35,689/QALY (3rd line) £47,980/ QALY (4th line) Results robust to sensitivity analysis	Perspective: health and social services Currency: UK£ Cost year: 1997 Time horizon: 3 years Discounting: not reported Quality score: 27/3/5

Oral antipsychotics in the treatment of acute episode

References to included studies

Alexeyeva, I., Mauskopf, J., Earnshaw, S.R., *et al*. (2001) Comparing olanzapine and ziprasidone in the treatment of schizophrenia: a case study in modeling. *Journal of Drug Assessment, 4*, 275-288.

Almond, S. & O'Donnell, O. (2000) Cost analysis of the treatment of schizophrenia in the UK. A simulation model comparing olanzapine, risperidone and haloperidol. *Pharmacoeconomics, 17*, 383-389.

Bagnall, A-M., Jones, L., Ginnelly, L., *et al*. (2003) A systematic review of atypical antipsychotic drugs in schizophrenia. *Health Technology Assessment, 7* (13), 1-193

Beard, S.M., Maciver, F., Clouth, J., *et al.* (2006) A decision model to compare health care costs of olanzapine and risperidone treatment for schizophrenia in Germany. *European Journal of Health Economics, 7*, 165-172.

Bounthavong, M. & Okamoto, M.P. (2007) Decision analysis model evaluating the cost-effectiveness of risperidone, olanzapine and haloperidol in the treatment of schizophrenia. *Journal of Evaluation in Clinical Practice, 13*, 453-460.

Cummins, C., Stevens, A. & Kisely, S. (1998) The use of olanzapine as a first and second choice treatment in schizophrenia. A West Midlands development and Evaluation Committee report. Birmingham: Department of Public Health and Epidemiology, University of Birmingham.

Edgell, E.T., Andersen, S.W., Johnstone, B.M., *et al*. (2000) Olanzapine versus risperidone. A prospective comparison of clinical and economic outcomes in schizophrenia. *Pharmacoeconomics, 18*, 567-579. ***Refers to study ID TRAN1997***

Geitona, M., Kousoulakou, H., Ollandezos, M., *et al.* (2008) Costs and effects of paliperidone extended release compared with alternative oral antipsychotic agents in patients with schizophrenia in Greece: a cost effectiveness study. *Annals of General Psychiatry, 7*, 16.

Hamilton, S.H., Revicki, D.A., Edgell, E.T., *et al.* (1999). Clinical and economic outcomes of olanzapine compared with haloperidol for schizophrenia. Results from a randomised clinical trial. Pharmacoeconomics, 15(5), 469-480. ***Refers to study ID TOLLEFSON1997***

Jerrell, J.M. (2002) Cost-effectiveness of risperidone, olanzapine, and conventional antipsychotic medications. *Schizophrenia Bulletin, 28*, 589-605. ***Refers to study ID JERRELL2002***

Lecomte, P., De Hert, M., van Dijk, M., *et al*. (2000) A 1-year cost-effectiveness model for the treatment of chronic schizophrenia with acute exacerbations in Belgium. *Value in Health, 3*, 1-11.

Nicholls, C.J., Hale, A.S. & Freemantle, N. (2003) Cost-effectiveness of amisulpride compared with risperidone in patients with schizophrenia. *Journal of Drug Assessment, 6*, 79-89. ***Refers to study ID LECRUBIER2000***

Palmer, C.S., Revicki, D.A., Genduso, L.A., *et al.* (1998) A cost-effectiveness clinical decision analysis model for schizophrenia. *American Journal of Managed Care, 4*, 345-355.

Palmer, C.S., Brunner, E., Ruiz-Flores, L.G., *et al.* (2002) A cost-effectiveness clinical decision analysis model for treatment of schizophrenia. *Archives of Medical Research, 33*, 572-580.

Rosenheck, R., Perlick, D., Bingham, S., *et al.* (2003) Effectiveness and cost of olanzapine and haloperidol in the treatment of schizophrenia: a randomized controlled trial. *The Journal of the American Medical Association, 290*, 2693-2702. ***Refers to study ID ROSENHECK2003***

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
Alexeyeva *et al.*, 2001 US Cost-effectiveness analysis	<u>Interventions:</u> Olanzapine 5 to 15mg/day Ziprasidone 40 to 120mg/day Followed by 2nd line treatment in the case of no response (switch between the 2 drugs), and clozapine as 3rd line treatment	People with an acute episode of schizophrenia requiring hospitalisation Decision-analytic modelling Source of clinical effectiveness data: published and unpublished data from placebo-controlled clinical trials (indirect comparisons) and other published literature Source of resource use and unit costs: published data and national sources	<u>Costs:</u> Medication, hospitalisation, outpatient mental health visits, suicide, management of EPS Total costs per person: Olanzapine $48,676 Ziprasidone $48,873 <u>Outcomes:</u> percentage of relapse; number of hospital days; number of days with EPS Percentage of relapse: Olanzapine 23.5% Ziprasidone 25.2% Number of hospital days: Olanzapine 36.7 Ziprasidone: 37.4 Number of days with EPS: Olanzapine 60.0 Ziprasidone 60.1	Olanzapine dominated ziprasidone (more effective than ziprasidone at similar cost) Cost results moderately sensitive to relapse and response rates and changes in drug costs	Perspective: 3rd party payer Currency: US$ Cost year: 2001 Time horizon: 12 months Discounting: not needed Funded by Eli Lilly and Company Quality score: 24/1/10

Almond & O'Donnell, 2000 UK Cost-effectiveness analysis	Interventions: Olanzapine 10mg/day Risperidone 6mg/day Haloperidol 15mg/day	People with schizophrenia who have experienced multiple acute episodes, excluding first episode and treatment-resistant cases; people entered the model on experiencing a new acute episode Decision-analytic modelling Source of clinical effectiveness data: published clinical trials (TOLLEFSON1997 and TRAN1997), other published literature and expert opinion Source of resource use: published data and assumptions Source of unit costs: national data	Costs: direct medical Medication, short- and long-term hospitalisation, outpatient mental health visits, day care, specialist supported accommodation, outpatient contacts with psychiatrists, GPs and community psychiatric nurses, suicide Costs of managing side effects not included Total costs per person: Olanzapine £35,701 Risperidone £36,590 Haloperidol £36,653 Outcomes: percentage of people with BPRS score <18 over 5 years; percentage of people with no relapse over 5 years Percentage of people with BPRS score <18: Olanzapine 63.6% Risperidone 63.0% Haloperidol 52.2% Percentage of people with no relapse: Olanzapine 31.2% Risperidone 29.3% Haloperidol 18.2%	Olanzapine dominant over risperidone (marginally) and haloperidol Cost results sensitive to daily dosages, relapse and drop-out rates; overall cost differences rather insignificant	Perspective: NHS Currency: UK£ Cost year: 1996/1997 Time horizon: 5 years Discounting: 6% for costs Funded by Eli Lilly and Company Ltd Quality score: 25/3/7

Bagnall *et al.*, 2003 UK Cost-utility analysis	<u>Interventions:</u> Olanzapine Quetiapine Risperidone Zotepine Clozapine Ziprasidone Sertindole Amisulpride Haloperidol Chlorpromazine All tested as 1st, 2nd, and 3rd line treatment	People with an acute episode of schizophrenia, schizoaffective or schizophreniform disorder, or psychotic illness Decision-analytic modelling Source of clinical effectiveness data: systematic review and meta-analysis of clinical trials and other published literature Source of resource use: national studies and databases and other published literature Source of unit costs: national data	<u>Costs:</u> Medication, hospitalisation, day-care, outpatient contacts with healthcare professionals, community-based services, management of side effects Total costs per person (for use as 1st line): Olanzapine £10,802 Quetiapine £11,579 Risperidone £13,798 Zotepine £11,840 Clozapine £13,475 Ziprasidone £14,477 Sertindole £12,286 Amisulpride £15,295 Haloperidol £13,238 Chlorpromazine £12,534 <u>Primary outcome:</u> number of QALYs Total QALYs per person (for use as 1st line): Olanzapine 0.42; quetiapine 0.44; risperidone 0.62; zotepine 0.52; clozapine 0.55; ziprasidone 0.66; sertindole 0.53; amisulpride 0.66; haloperidol 0.55; chlorpromazine 0.57	(For 1st line treatment) Quetiapine, risperidone, clozapine, sertindole, amisulpride and haloperidol were dominated by absolute or extended dominance Ziprasidone versus chlorpromazine £21,589/QALY Chlorpromazine versus zotepine £13,880/QALY Zotepine versus olanzapine £10,380/QALY Cost and efficacy data characterised by great uncertainty	Perspective: NHS and local authority social services Currency: UK£ Cost year: not stated Time horizon: 12 months Discounting: not needed Quality score: 26/2/7

Beard *et al.*, 2006 Germany Cost-effectiveness and cost-utility analysis	<u>Interventions:</u> Olanzapine 10mg/day Risperidone 4mg/day Followed by 2nd line treatment in the case of no response (switch between the 2 drugs), and clozapine as 3rd line treatment	People with a long-term history of relapsing schizophrenia, experiencing an acute episode (BPRS score at least 24), and assumed not to have received any form of previous treatment with atypical antipsychotics Decision-analytic modelling Source of clinical effectiveness data: published clinical trial (TRAN1997), other published literature and expert opinion Source of resource use: expert opinion Source of unit costs: national data	<u>Costs:</u> Medication, hospitalisation, outpatient mental health visits, outpatient contacts with psychiatrists and GPs, sheltered housing or home-support, suicide, management of EPS Total costs per person: Olanzapine €3,226 Risperidone €3,261 <u>Outcomes:</u> percentage of acute relapses, number of QALYs gained Percentage of acute relapses: 0.33% fewer for olanzapine versus risperidone (results for each drug not provided) Number of QALYs per person: 0.0005 more for olanzapine versus risperidone (results for each drug not provided)	Costs and effects similar to both drugs – olanzapine marginally dominant over risperidone Results sensitive to hospitalisation rates	Perspective: healthcare system Currency: Euros (€) Cost year: not stated Time horizon: 12 months Discounting: not needed Funded by Eli Lilly Quality score: 20/5/10

Bounthavong & Okamoto, 2007 US Cost-effectiveness analysis	Interventions: Olanzapine 15mg/day Risperidone 6mg/day Haloperidol 20mg/day Followed by clozapine as 2nd line treatment in the case of no response, and ECT as 3rd line treatment	People with schizophrenia or schizoaffective disorders in an acute episode Decision-analytic modelling Source of clinical effectiveness data: systematic review of published clinical trials Source of resource use: published guidelines, other published literature and further assumptions Source of unit costs: national sources	Costs: Medication, hospitalisation, doctor visits, emergency department visits, pharmacy dispensing fees, management of EPS Total costs per person: Olanzapine $13,592 Risperidone $13,410 Haloperidol $15,513 Outcomes: percentage of responders, defined as individuals who achieved a ≥ 20% reduction in the PANSS from baseline Percentage of responders: Olanzapine 60% Risperidone 63% Haloperidol 34%	Risperidone dominant over olanzapine (marginally) and haloperidol Results between risperidone and olanzapine sensitive to response rates and changes in drug costs	Perspective: 3rd party payer Currency: US$ Cost year: 2005 Time horizon: 16 weeks Discounting: not needed Quality score: 25/1/9
Cummins *et al.*, 1998 UK Cost-utility analysis	Interventions: Olanzapine 15mg/day Haloperidol 10mg/day In case of no response or no compliance, olanzapine followed by haloperidol; haloperidol followed by fluphenazine	People with an acute episode of schizophrenia Decision-analytic modelling Source of clinical effectiveness data: published RCT (TOLLEFSON1997) Source of resource use: published literature Source of unit costs: national sources	Costs: Medication, short- and long-term hospitalisation, outpatient visits, day care, community psychiatric visits, management of EPS Total costs per person: Olanzapine £26,200 Haloperidol £31,627 Primary outcome: number of QALYs Number of QALYs per person: Olanzapine 0.833 Haloperidol 0.806	Olanzapine dominated haloperidol Results insensitive to response rates, rates of hospitalisation and intensive community care for non-responders	Perspective: NHS Currency: UK£ Cost year: not stated Time horizon: 1 year Discounting: not needed Quality score: 24/3/8

Edgell *et al.*, 2000 (TRAN1997) US Cost-consequence analysis	<u>Interventions:</u> Olanzapine 10-20 mg/day Risperidone 4-12mg/day	Inpatients or outpatients aged 16-65 years with schizophrenia, schizoaffective or schizophreniform disorder and a BPRS score ≥ 42 Multicentre, double-blind RCT (N=339) Source of clinical effectiveness data: RCT (US sub-sample of N=150) Source of resource use estimates: RCT (N=150) – clinical case report forms verified by hospital records, psychiatric history, medical records or family reports where available Source of unit costs: national and state sources	<u>Costs:</u> direct medical Hospitalisations, emergency department visits, day hospital, outpatient visits to psychiatrists, other physicians or mental health providers, home visits, medication Median cost: Olanzapine $5,141 Risperidone $7,984 (p = 0.342) <u>Outcomes:</u> percentage of clinically important response, defined as 40% improvement in the PANSS total score; survival analysis assessing maintenance of response; rate of treatment-emergent EPS Percentage of clinically important response at 28 weeks: Olanzapine 28.0% Risperidone 20.0% (p=0.251) Survival analysis assessing maintenance of response: p=0.048 favouring olanzapine Rate of treatment-emergent EPS Olanzapine 25.3% Risperidone 45.3% (p=0.016)	Olanzapine more effective than risperidone, with lower EPS rates and a similar cost	Perspective: 3rd party payer Currency: US$ Cost year: 1997 Time horizon: 28 weeks Discounting: not needed Funded by Eli Lilly and Company Quality score: 20/1/14

Geitona *et al*., 2008 Greece Cost-effectiveness analysis	Interventions: Paliperidone Olanzapine Risperidone Quetiapine Ziprasidone Aripiprazole	People with an acute exacerbation of schizophrenia Decision-analytic modelling Source of clinical effectiveness data: selected published RCTs and expert opinion Source of resource use: consensus panel of 10 psychiatrists and 6 health economists Source of unit costs: official reimbursement tariffs, official retail prices and other published sources; price of paliperidone based on assumption according to the highest prices in Europe	Costs: direct medical Hospitalisations, physician consultations, visits to mental health clinics, treatment of side effects (EPS and weight gain), medication Total annual cost: Paliperidone €7,030 Olanzapine €7,034 Risperidone €7,082 Quetiapine €8,321 Ziprasidone €7,713 Aripiprazole €7,807 Measure of outcome: annual number of stable days (i.e. days with no symptoms) Annual number of stable days: Paliperidone 272.5 Olanzapine 272.2 Risperidone 265.5 Quetiapine260.7 Ziprasidone 260.5 Aripiprazole 258.6	Paliperidone dominated all other pharmacological treatments (marginally in the case of olanzapine) Results overall robust to ±10% changes in the duration and frequency of relapses, and ±10% changes in resource use in stable days and during relapse	Perspective: national healthcare system Currency: Euros (€) Cost year: not stated Time horizon: 1 year Discounting: not needed Funded by Janssen-Cilag Pharmaceutical SACI Quality score: 24/2/9

Hamilton *et al.*, 1999 (study ID TOLLEFSON1997) US Cost-consequence analysis	<u>Interventions:</u> Olanzapine 5 to 20 mg/day Haloperidol 5 to 20mg/day	Inpatients or outpatients with schizophrenia, schizoaffective or schizophreniform disorder aged over 18 years with a BPRS score ≥ 18 and/or no longer tolerating current antipsychotic therapy, excluding haloperidol Multicentre, double-blind RCT (N = 1996) Source of clinical effectiveness data: RCT (US sub-sample of N=817 in the acute phase; N=344 in the maintenance phase) Source of resource use estimates: RCT (N=817 in the acute phase; N=344 in the maintenance phase) – clinical case report forms verified by hospital records, psychiatric history, medical records or family reports where available Source of unit costs: national and state sources	<u>Costs:</u> direct medical Hospitalisations, emergency department visits, day hospital, outpatient visits to psychiatrists, other physicians or mental health providers, home visits, medication Laboratory testing costs not considered Mean cost per person: Acute phase: olanzapine $6,114; haloperidol $6,502 (p = 0.033) Maintenance phase: olanzapine $15,594; haloperidol $16,230 (0.128) <u>Outcomes:</u> percentage of people with clinical improvement based on BPRS (minimum 40% improvement from baseline score) and Quality of Life Scale scores (minimum 20% improvement from baseline score) Percentage of people with BPRS-based clinical improvement: Acute phase: olanzapine 38.5%; haloperidol 26.8% (p = 0.002) Maintenance phase: no significant differences Percentage of people with clinical improvement on the Quality of Life Scale: Acute phase: olanzapine 32.7%; haloperidol 24.8% (p = 0.094) Maintenance phase: no significant differences	Olanzapine dominated haloperidol in the acute phase; cost and effectiveness differences insignificant in maintenance phase	Perspective: 3rd party payer Currency: US$ Cost year: 1995 Time horizon: 52 weeks (6 weeks acute phase + 46 weeks maintenance phase) Discounting: not needed Protocol visits included at estimation of costs Funded by Eli Lilly and Company Quality score: 20/1/14

Jerrell 2002 (study ID JERRELL2002) US Cost-consequence analysis	<u>Interventions:</u> Olanzapine average dose 12 to 15 mg/day Risperidone average dose 4 to 6mg/day	Inpatients aged 18-54 years with schizophrenia or schizoaffective disorder who had two or more recent acute hospitalisations and who were noncompliant with their pharmacotherapy interventions or otherwise unstable in their maintenance treatment Open-label RCT (N = 108) Source of clinical effectiveness data: RCT (N=108) Source of resource use estimates: RCT (N=108) – hospital and other medical records, medical databases Source of unit costs: national sources	<u>Costs:</u> direct medical Hospitalisations, outpatient visits to mental health providers, medication Mean cost per person over 12 months: Olanzapine $34,879; risperidone $36,446 (non-significant results) <u>Outcomes:</u> PANSS and BPRS scores, side effects (Dyskinesia Identification System Condensed User Scale [DISCUS] scores), psychosocial functioning (Role Functioning Scale [RFS] score), time to hospital discharge, time to initial rehospitalisation, satisfaction with services No statistically significant differences between interventions in terms of effectiveness at all 3-month time points examined	Olanzapine and risperidone had comparable costs and outcomes (non-significant differences)	Perspective: 3rd party payer Currency: US$ Cost year: not stated Time horizon: 12 months Discounting: not needed Quality score: 15/6/14

Lecomte *et al.*, 2000 Belgium Cost-effectiveness analysis	<u>Interventions:</u> Olanzapine 15mg/day Risperidone 5mg/day Haloperidol 10mg/day Followed by switch to another drug of those assessed as 2nd line treatment in the case of no response or intolerability, and haloperidol depot or clozapine as 3rd line treatment	People with chronic schizophrenia, hospitalised for an acute exacerbation of psychotic symptoms with a PANSS score 60-120 and a CGI score ≥ 5 Decision-analytic modelling Source of clinical effectiveness data: estimates by Delphi panel and literature review Source of resource use: expert opinion Source of unit costs: national sources	<u>Costs:</u> Medication, hospitalisation, health professional consultations (psychiatrists, psychotherapists, GPs, nurses), sheltered housing, normal housing, day hospital, laboratory testing, management of side effects Total costs per person: Olanzapine BEF 1,151,900 (≈£22,839) Risperidone BEF 1,137,700 (≈£22,557) Haloperidol BEF 1,142,000 (≈£22,642) <u>Primary outcome:</u> time with minimum symptoms and minimum toxicity (bearable side effects) Time with minimum symptoms and toxicity: Olanzapine 6.25% Risperidone 6.25% Haloperidol 6.06%	Risperidone dominated olanzapine (marginally) and haloperidol Results sensitive to response rates and changes in drug costs	Perspective: health insurance system Currency: Belgian Francs (BEF) Cost year: 1998 Time horizon: 1 year Discounting: not needed Funded by Janssen Research Foundation Quality score: 23/2/10

Nicholls *et al.*, 2003 (study ID LECRUBIER2000) UK Cost-minimisation analysis	<u>Interventions:</u> Amisulpride 400-1000 mg/day Risperidone 4-10mg/day	People aged 16-65 years with chronic schizophrenia of ≥ 2 years' duration, with a recent worsening of symptoms necessitating modifications to therapeutic management International, multicentre, double-blind RCT (N=309) Source of clinical effectiveness data: international RCT (N=309) Source of resource use estimates: international RCT (N=198) – trial records Source of unit costs: UK national sources	<u>Costs:</u> direct medical Medication, full and part-time hospitalisation, day hospital, visits to healthcare professionals Mean cost per person: Amisulpride £12,673 (95% CI: £10,628 to £14,717) Risperidone £14,818 (95% CI: £12,323 to £17,312) <u>Primary outcome:</u> total PANSS score Total PANSS score: Difference in change scores over 6 months: 0.80 (95% CI: -4.62 to 6.22)	Amisulpride cheaper than risperidone by £2,145, but result not statistically significant (95% CI: -£5,379 to £1,089)	Perspective: NHS Currency: UK£ Cost year: not stated Time horizon: 6 months Discounting: not needed Funded by Sanofi-Synthélabo Quality score: 19/2/14

Palmer *et al.*, 1998 US Cost-effectiveness and cost-utility analysis	<u>Interventions:</u> Olanzapine 10mg/day Risperidone 6mg/day Haloperidol 15mg/day Followed by 2nd line atypical antipsychotics (one of the above options) if treatment failed, and clozapine as 3rd line treatment; all switches made within 6 months	People with experience of multiple episodes of schizophrenia Decision-analytic modelling Source of clinical effectiveness data: 2 international RCTs (TOLLEFSON1997 and TRAN1997), plus other published literature and expert opinion Source of resource use: expert opinion supplemented by published literature Source of unit costs: national data and published literature	<u>Costs:</u> direct medical Medication, hospitalisation, day-hospital, outpatient mental health and physician visits, residential treatment, laboratory tests, treatment of EPS, suicide Total 5-year costs per person: Olanzapine $92,593 Risperidone $94,468 Haloperidol $94,132 <u>Outcomes:</u> Time in disability-free state, defined by a BPRS total scores <18; percentage of people with no relapse over 5 years; number of QALYs Time in disability-free state per person (years) Olanzapine 3.18 Risperidone 3.15 Haloperidol 2.61 Percentage of people with no relapse Olanzapine 31.2% Risperidone 29.3% Haloperidol 18.2% Number of QALYs Olanzapine 3.15 Risperidone 3.12 Haloperidol 2.96	Olanzapine dominated both risperidone and haloperidol Results sensitive to changes in drug costs and shortened hospital stay	Perspective: 3rd party payer Currency: US$ Cost year: 1995 Time horizon: 5 years Discounting: 5% annually Funded by Lilly Research Laboratories, Eli Lilly and Company Quality score: 28/1/6

Palmer *et al.*, 2002 Mexico Cost-effectiveness analysis	Interventions: Olanzapine 10mg/day Risperidone 6mg/day Haloperidol 15mg/day Followed by 2nd line atypical antipsychotics (one of the above options) if treatment failed, and a hypothetical mixture of olanzapine and risperidone as 3rd line treatment; all switches made within 6 months	People with experience of multiple episodes of schizophrenia Decision-analytic modelling Source of clinical effectiveness data: 2 international RCTs (TOLLEFSON1997 and TRAN1997), plus other published literature and expert opinion Source of resource use: expert opinion supplemented by published literature Source of unit costs: national data	Costs: direct medical Medication, hospitalisation, day-hospital, outpatient mental health and physician visits, residential treatment, laboratory tests, treatment of EPS Total 5-year costs per person: Olanzapine 225,100 pesos (≈ £12,000) Risperidone 226,700 pesos (≈ £12,100) Haloperidol 196,620 pesos (≈£10,500) Outcomes: Time in disability-free state, defined by a BPRS total scores <18; percentage of people with no relapse over 5 years Time in disability-free state per person (years) Olanzapine 3.04 Risperidone 3.01 Haloperidol 2.50 Percentage of people with no relapse Olanzapine 28.7% Risperidone 26.8% Haloperidol 15.3%	Olanzapine marginally dominant over risperidone ICERs of olanzapine versus haloperidol: 52,740 pesos (≈ £2,820) per disability-free year; 212,540 pesos (≈ £11,350) per relapse avoided Results sensitive to changes in drug costs and drug dosages	Perspective: 3rd party payer Currency: Mexican pesos Cost year: 2000 Time horizon: 5 years Discounting: 5% annually Funded by Lilly Mexico Quality score: 26/1/8

Rosenheck *et al.*, 2003 (study ID ROSENHECK2003) US Cost-consequence analysis	<u>Interventions:</u> Olanzapine 5-20 mg/day Haloperidol 5-20mg/day	Inpatients or outpatients with schizophrenia or schizoaffective disorder, with serious symptoms (BPRS score ≥ 36) and serious dysfunction for the previous 2 years Multicentre, double-blind RCT in 17 Veterans Affairs Centres (N=309) Source of clinical effectiveness data: RCT (N=309) Source of resource use estimates: RCT (N=309) – Veterans Affairs data systems and treatment records of non-Veterans Affairs providers; for non-healthcare costs: interviews and published data Source of unit costs: national and state sources	<u>Costs:</u> Direct medical: medication, inpatient days, outpatient visits, group treatment, day hospital, domiciliary and nursing home care Non-medical: criminal justice (police contacts and arrests), productivity losses of participants and their carers, administrative costs of transfer payments Mean cost per person: Olanzapine $45,811 Haloperidol $38,439 (p = 0.24) <u>Outcomes:</u> mean PANSS score, mean Quality of Life Scale score, side effect rates Mean PANSS score at 12 months: Average difference -1.1 points favouring olanzapine (p=0.35) Mean Quality of Life Scale score at 12 months: Average difference 0.1 points favouring olanzapine (p=0.71) Side effect rates: Lower scores for olanzapine on the Barnes scale for akathisia (p<0.001) – the only significant difference in side effect rates	Olanzapine more expensive than haloperidol (not statistically significant), equally effective, with lower akathisia rates	Perspective: societal Currency: US$ Cost year: 1998 Time horizon: 52 weeks Discounting: not needed Funded by Eli Lilly Study likely underpowered to detect differences in cost Quality score: 21/2/12

Promoting recovery in people with schizophrenia that is in remission – pharmacological relapse prevention

References to included studies

Davies, A., Langley, P.C., Keks, N., *et al.* (1998) Risperidone versus haloperidol: II. Cost-effectiveness. *Clinical Therapeutics, 20*, 196-213.

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Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
Davies *et al.*, 1998 Australia Cost-effectiveness analysis	Interventions: Risperidone 3mg/day Haloperidol 10mg/day In resistant people, followed by clozapine 400mg/day	People with chronic schizophrenia Decision-analytic modelling Source of clinical effectiveness data: meta-analysis of clinical trials and expert opinion Source of resource use: national statistics, published reports and surveys, and expert opinion Source of unit costs: national data	Costs: direct medical Medication, hospitalisation, health care professional services (psychiatrist, GP, social worker), outpatient visits, laboratory tests, government-subsidised hotel accommodation, management of EPS and depression Total cost per person: Risperidone $15,549 Haloperidol $18,332 Primary outcome: percentage of people in a response phase at the end of the 2-year time horizon Percentage of people in response phase: Risperidone 78.9% Haloperidol 58.9%	Risperidone dominated haloperidol Results sensitive to the difference in clinical response rate	Perspective: healthcare system Currency: Aus$ Cost year: not stated Time horizon: 2 years Discounting: not applied Funded by Janssen-Cilag Pty Ltd Quality score: 22/5/8

Ganguly *et al.*, 2003 US Cost-effectiveness analysis	Interventions: Risperidone 4mg/day Haloperidol 10mg/day	Recently diagnosed or hospital-discharged outpatients with schizophrenia Decision-analytic modelling Source of clinical effectiveness data: literature review including published meta-analyses of clinical trials Source of resource use: published data Source of unit costs: national data	Costs: direct medical Medication, hospitalisation, physician visits, case management, management of EPS and depression Total cost per person: Risperidone $6,422 Haloperidol $4,989 Primary outcome: percentage of employable persons; employability defined by a PANSS score reduction of at least 20% from baseline (expressing clinical stability) and a Wisconsin Card Sorting Test Category (WCST-Cat) score of ≥ 3.5 Percentage of employability: Risperidone 32.58% Haloperidol 25.17%	ICER of risperidone versus haloperidol: $19,609 per employable person Results sensitive to the probability of achieving clinical stability for compliant people and to compliance rates ICER ranging from $2,940 to $1,000,000 per employable person	Perspective: 3rd party payer Currency: US$ Cost year: 2001 Time horizon: 12 months Discounting: not needed Quality score: 25/1/9

Knapp *et al.*, 2008 10 European countries Cost-utility analysis	Interventions: Olanzapine Risperidone Quetiapine Amisulpride Clozapine (plus oral or depot FGAs)	People aged ≥ 18 years, initiating or changing antipsychotic medication for the treatment of schizophrenia, who presented within the normal course of care in the outpatient setting or in the hospital when admission was planned for the initiation of antipsychotic medication and discharge was planned within 2 weeks Prospective observational study in 10 European countries (SOHO) Source of clinical effectiveness data: multi-country observational study (N=9,107) Source of resource use estimates: multi-country observational study (N=9,107) – interviews with study participants at 3, 6 and 12 months Source of unit costs: UK national data	Costs: direct medical Antipsychotic and concomitant medication including necessary blood test monitoring, schizophrenia-related inpatient care, schizophrenia-related day care, schizophrenia-related outpatient psychiatric consultations Total cost per person: Olanzapine £3,259 Risperidone £3,034 Quetiapine £3,780 Amisulpride £3,962 Clozapine £3,247 Primary outcome: number of QALYs Number of QALYs per person: Olanzapine 0.1787 Risperidone 0.1349 Quetiapine 0.1436 Amisulpride 0.1342 Clozapine 0.1620	Olanzapine dominant over quetiapine and amisulpride Olanzapine versus risperidone £5,156/QALY Olanzapine versus clozapine £775/QALY Clozapine dominant over risperidone Probabilistic sensitivity analysis (separate comparisons between olanzapine and each of the remaining drugs): Probability (P) of olanzapine being more cost effective than risperidone and amisulpride: 100% at a willingness-to-pay (WTP) £18,000/QALY; P of olanzapine being more cost effective than quetiapine: 100% at a WTP <£5,000/QALY; P of olanzapine being more cost effective than clozapine: 81% at a WTP £30,000/QALY	Perspective: Health service payer Currency: UK£ Cost year: 2004 Time horizon: 12 months Discounting: not needed QALYs based on EQ-5D scores of participants Epoch analysis performed: data analysed for 0–3 months, 3–6 months and 6–12 months Only comparisons between olanzapine and each of the remaining drugs performed Funded by Eli Lilly and Company Quality score: 22/2/11

Launois *et al*., 1998 France Cost-effectiveness analysis	Interventions: Sertindole 12-24mg/day Olanzapine 10-20mg/day Haloperidol 10-20mg/day	People with chronic schizophrenia Decision-analytic modelling Source of clinical effectiveness data: literature review including published meta-analyses Source of resource use: published local data Source of unit costs: national and local data	Costs: direct medical Medication, hospitalisation, day care, outpatient contacts with healthcare professionals Costs of treating side effects not considered Total 10-year costs per person: Sertindole $198,800 Olanzapine $205,484 Haloperidol $205,300 Primary outcome: mean time spent without relapse Mean time spent without relapse per person: Sertindole 57 months Olanzapine 51.3 months Haloperidol 43.5 months	Sertindole dominated both olanzapine and haloperidol Results robust in sensitivity analysis (no more details provided)	Perspective: healthcare system Currency: US$ Cost year: 1996 Time horizon: 10 years Discounting: not stated Quality score: 20/7/8
Oh *et al*., 2001 Canada Cost-utility analysis	Interventions: Risperidone 6mg/day Haloperidol 20mg/day Haloperidol depot 100mg/3 weeks Fluphenazine depot 25mg/3 weeks	Previously treated, hospitalised people with chronic schizophrenia with moderate symptoms Decision-analytic modelling Source of clinical effectiveness data: synthesis of data taken from meta-analyses and expert opinion Source of resource use: expert opinion Source of unit costs: national and provincial data	Costs: direct medical Medication, laboratory testing, hospitalisation, psychiatrist and nurse visits, case management (nurse or social worker), residential care, management of EPS Total cost per person: Risperidone $69,855 Haloperidol $76,365 Haloperidol depot $78,388 Fluphenazine depot $82,264 Primary outcome: QALYs Number of QALYs gained per person: Risperidone 0.87 Haloperidol 0.83 Haloperidol depot 0.84 Fluphenazine depot 0.83	Risperidone dominated all other treatment options Results sensitive to response rates, hospital discharge rates, and utility scores of mild symptoms for risperidone and haloperidol	Perspective: government Currency: Can$ Cost year: 1997 Time horizon: 12 months Discounting: not needed Compliance not taken into account Funded by Janssen-Ortho Canada Quality score: 24/3/8

Rosenheck *et al.*, 2006 (study ID LIEBERMAN 2005) US Cost-utility analysis	Interventions: Perphenazine Olanzapine Quetiapine Risperidone Ziprasidone	People aged 18-65 years with schizophrenia, excluding people with first episode or treatment-resistant schizophrenia Pragmatic multicentre RCT (N = 1,493) Source of clinical effectiveness data: pragmatic RCT (N=1,424) Source of resource use estimates: pragmatic RCT (N=1,424) – self-report questionnaires Source of unit costs: national sources, published reports and administrative data sets	Costs: direct medical Medication, hospitalisation, emergency room visits, outpatient visits to mental health services, community care visits, nursing facilities, supervised apartments, rehabilitation services Mean monthly cost per person (ITT analysis; analysis for period of initial drug only) Perphenazine $1,131; $959 Olanzapine $1,433; $1,404 Quetiapine $1,657; $1,478 Risperidone $1,534; $1,533 Ziprasidone $1,730; $1,770 ($p<0.0001$ between perphenazine and SGAs in both cases) Primary outcome: number of QALYs (ITT analysis; analysis for period of initial drug only) Total QALYs per person: Perphenazine 0.720; 0.731 Olanzapine 0.717; 0.727 Quetiapine 0.718; 0.727 Risperidone 0.704; 0.713 Ziprasidone 0.716; 0.720 Perphenazine versus risperidone significant in ITT analysis ($p<0.005$)	Perphenazine dominated SGAs (similar effectiveness at a lower cost)	Perspective: 3rd party payer Currency: US$ Cost year: not stated Time horizon: 18 months Discounting: not needed Individuals with dyskinesia on entry into the study excluded from analysis Quality score: 20/3/12
Tunis *et al.*, 2006 (study ID TUNIS2006) US Cost-consequence analysis	Interventions: Olanzapine 10mg/day at initiation Risperidone 2mg/day at initiation	People aged over 18 years with schizophrenia or schizoaffective disorder, and a psychotic symptom threshold BPRS score of at least 18 Open-label multicentre RCT (N = 441)	Costs: direct medical Medication, hospitalisation, emergency room visits, crisis services, outpatient visits to mental health services, primary care visits, nursing facilities, laboratory testing Total costs per person: Olanzapine $20,891	Olanzapine had lower costs and better outcomes than risperidone but results statistically insignificant	Perspective: public payer Currency: US$ Cost year: 2001 Time horizon: 12 months Discounting: not needed Funded by Eli Lilly and Company Quality score: 20/1/14

		Source of clinical effectiveness data: open-label RCT (N=441) Source of resource use estimates: open-label RCT (N=441) – patient reports, medical records, administrative databases Source of unit costs: national sources	Risperidone $21,347 (p=0.862) <u>Outcomes:</u> number of days in response; clinical response defined by a BPRS score <18; social response defined by 33% improvement in the Quality of Life Scale social relations score or by maintaining a high level of satisfaction with social relationships (for individuals reporting a baseline score ≥ 18) Number of days in clinical response: Olanzapine 129.0 Risperidone 127.7 (p=0.868) Number of days in social response: Olanzapine 105.5 Risperidone 96.5 (p=0.305)		
Vera-Llonch *et al.*, 2004 US Cost-consequence analysis	<u>Interventions:</u> Risperidone 4.8mg/day Olanzapine 12.4mg/day	People with chronic schizophrenia or schizoaffective disorders Decision-analytic modelling Source of clinical effectiveness data: mainly unpublished data, some published data, expert opinion and further assumptions Source of resource use: published sources and expert opinion Source of unit costs: national and local data	<u>Costs:</u> direct medical Medication, hospitalisation, residential treatment, case management, day care, outpatient visits, emergency crisis intervention, management of side effects Mean monthly costs per person: Risperidone $2,163 Olanzapine $2,316 <u>Outcomes:</u> incidence of EPS, prolactin-related disorders, and diabetes; change in body weight; percentage of people remaining on initial therapy Incidence of EPS Risperidone 9.2%; olanzapine 7.2% Incidence of prolactin-related	Risperidone led to lower discontinuation rates, had overall lower side effect rates and was less costly than olanzapine Results robust in the majority of sensitivity analyses; results sensitive to changes in body weight and in probability of discontinuation following weight gain more than 5kg	Perspective: 3rd party payer Currency: US$ Cost year: 2003 Time horizon: 12 months Discounting: not needed Funded by Janssen Pharmaceutica Products L.P. Quality score: 21/4/10

			disorders Risperidone 5.4%; olanzapine 2.2% Incidence of diabetes Risperidone 1%; olanzapine 1.7% Percentage of people with ≥ 7% change in body weight Risperidone 3.7%; olanzapine 25.4% Percentage of people remaining on initial therapy Risperidone 76.9%; olanzapine 45.6%		

Depot antipsychotic treatment

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Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
Chue *et al.*, 2005 Canada Cost-effectiveness analysis	Interventions: Long-acting risperidone 2.3mg/day Oral risperidone 4mg/day Haloperidol depot 4.76mg/day All followed by olanzapine 15mg/day as 2nd line treatment and clozapine 384mg/day as 3rd line treatment	High-risk, non-compliant people with schizophrenia; 25% fully recovered people, who suffered multiple episodes with no or minor impairment between episodes and 75% partly recovered people who experienced increasing impairment with each of several episodes and did not become well again between multiple episodes Decision-analytic modelling Source of clinical effectiveness data: literature review and expert opinion Source of resource use: expert opinion and literature review Source of unit costs: national and local data	Costs: direct medical Medication, hospitalisation, day care, sheltered living, outpatient contacts with healthcare professionals Costs of treating side effects not considered Mean annual costs per person: Long-acting risperidone $31,173 Oral risperidone $33,799 Haloperidol depot $32,555 Outcomes: number and duration of psychotic episodes; mean PANSS scores during and between relapses Mean number of relapses per person: Long-acting risperidone 4.54 Oral risperidone 5.08 Haloperidol depot 4.82 Mean time in psychosis per person (years): Long-acting risperidone 3.00 Oral risperidone 3.36 Haloperidol depot 3.18 Mean PANSS score per person during/ between relapses: Long-acting risperidone 137/82 Oral risperidone 149/91 Haloperidol depot 147/91	Long-acting risperidone dominated both oral risperidone and haloperidol depot Long-acting risperidone not cost saving in the subpopulation of people experiencing full recovery Results sensitive to compliance rates	Perspective: healthcare system Currency: Can$ Cost year: 2003 Time horizon: 5 years Discounting: 5% annually Funded by Janssen Pharmaceutica, N.V., Belgium, and Janssen-Ortho, Canada Quality score: 23/4/8
De Graeve *et al.*, 2005 Belgium Cost-	Interventions: Long-acting risperidone 25mg/14 days Olanzapine 10mg/day Haloperidol depot 100-125mg/28 days	Young people with schizophrenia, who had been treated for 1 year and whose disease had not been diagnosed for longer than 5 years	Costs: direct medical Medication, hospitalisation, outpatient contacts with healthcare professionals (psychiatrists, GPs), laboratory testing, sheltered housing, psychiatric care home, management of EPS	Long-acting risperidone dominated both olanzapine and haloperidol depot	Perspective: healthcare system Currency: Euros (€) Cost year: 2003 Time horizon: 2 years Discounting: 3% annually

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
effectiveness analysis	Long-acting risperidone followed by olanzapine, clozapine and haloperidol depot as 2nd, 3rd and 4th line treatments respectively; olanzapine followed by long-acting risperidone, clozapine and haloperidol depot as 2nd, 3rd and 4th line treatments respectively; haloperidol depot followed by long-acting risperidone, olanzapine and clozapine as 2nd, 3rd and 4th line treatments respectively	Decision-analytic modelling Source of clinical effectiveness data: one published non-randomised study, one published RCT (CSERNANSKY2002) and expert opinion Source of resource use: published literature and expert opinion Source of unit costs: national data	Mean cost per person: Long-acting risperidone €16,406 Olanzapine €17,074 Haloperidol depot €21,779 <u>Outcomes:</u> proportion of people successfully treated, defined as those responding to initial treatment and had none to two episodes of clinical deterioration without needing a change of treatment over 2 years Proportion of people successfully treated: Long-acting risperidone 82.7% Olanzapine 74.8% Haloperidol depot 57.3%	Results robust to response rates and dosage	Funded by Janssen-Cilag Quality score: 21/6/8
Edwards *et al.*, 2005 US Cost-effectiveness analysis	<u>Interventions:</u> Long-acting risperidone 32.5mg/14 days Oral risperidone 3.8mg/day Olanzapine 15mg/day Quetiapine 391mg/day Ziprasidone 144mg/day Aripiprazole 19.6mg/day Haloperidol depot 84.5mg/26 days	Community-dwelling people with schizophrenia who had previously experienced a relapse requiring hospitalisation Decision-analytic modelling Source of clinical effectiveness data: literature review, unpublished data, and expert opinion Source of resource use: published literature, national databases, and expert opinion Source of unit costs: national and local data	<u>Costs:</u> direct medical Medication, staff time for injections, hospitalisation, emergency room visits, outpatient mental health visits, physician visits, nutritionist visits, day hospital, social/group therapy, home care, treatment of side effects Mean annual cost per person: Long-acting risperidone $20,769 Oral risperidone $20,929 Olanzapine $22,194 Quetiapine $21,276 Ziprasidone $21,028 Aripiprazole $21,837 Haloperidol depot $28,992 <u>Primary outcomes:</u> percentage of people relapsing; number of days in relapse	Long-acting risperidone dominated all other options Long-acting risperidone not cost saving when hospitalisation costs were reduced by 10% or duration of relapse requiring hospitalisation was reduced by 22% Results sensitive to relative relapse and compliance rates	Perspective: 3rd party payer Currency: US$ Cost year: 2003 Time horizon: 1 year Discounting: not needed Funded by Janssen Medical Affairs, L.L.C. Quality score: 22/3/10

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
			Percentage of people relapsing, who require/do not require hospitalisation: Long-acting risperidone 25.9% - 23.6% Oral risperidone 41.2% - 36.5% Olanzapine, quetiapine, ziprasidone, aripiprazole 41.2% - 36.5% Haloperidol depot 65.8% - 60.4% Number of days in relapse per person: Long-acting risperidone 14.3 Oral risperidone 22.6 Olanzapine, quetiapine, ziprasidone, aripiprazole 22.6 Haloperidol depot 36.3		
Heeg *et al.*, 2008 Portugal Cost-effectiveness analysis	Interventions: Long-acting risperidone 1.8mg/day Oral risperidone 5mg/day Haloperidol depot 3.3mg/day All followed by olanzapine 10mg/day as 2nd line treatment and haloperidol (or oral risperidone in the case of haloperidol) as 3rd line treatment	High-risk, non-compliant people with schizophrenia; 25% fully recovered people who experienced multiple episodes with no or minor impairment between episodes and 75% partly recovered people who experienced increasing impairment with each of several episodes and did not become well again between multiple episodes Decision-analytic modelling Source of clinical effectiveness data: literature review and expert opinion Source of resource use: expert opinion and literature review Source of unit costs: national data	Costs: direct medical Medication, hospitalisation, day care, institution, outpatient contacts with healthcare professionals, staff time for injections, visits to private practices Costs of treating side effects not considered Mean annual costs per person: Long-acting risperidone €58,871 Oral risperidone €63,553 Haloperidol depot €62,474 Outcomes: number and duration of psychotic episodes; mean PANSS scores during and between relapses Mean number of relapses per person: Long-acting risperidone 2.76 Oral risperidone 3.35 Haloperidol depot 3.20 Mean time in psychosis per person (years):	Long-acting risperidone dominated both oral risperidone and haloperidol depot Cost results sensitive to hospitalisation and institutionalisation cost, rate of symptom reduction, and change in probability of people with schizophrenia presenting a risk for society	Perspective: healthcare system Currency: Euros (€) Cost year: 2003 Time horizon: 5 years Discounting: 5% annually Funded by Janssen Pharmaceutica, Belgium, and Janssen-Cilag, Portugal Quality score: 24/3/8

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
			Long-acting risperidone 1.75 Oral risperidone 2.16 Haloperidol depot 2.04 Mean PANSS score per person during/ between relapses: Long-acting risperidone 128/78 Oral risperidone 137/83 Haloperidol depot 140/8		
Laux *et al.*, 2005 Germany Cost-effectiveness and cost-utility analysis	Interventions: Long-acting risperidone 1.8mg/day Olanzapine 10mg/day Haloperidol depot 3.3mg/day Followed by olanzapine 10mg/day as 2nd line treatment (oral risperidone 5mg/d in the case of olanzapine) and clozapine 300mg/d as 3rd line treatment	People with schizophrenia experiencing multiple relapses, with total or partial recovery between acute episodes; subgroups of people with high-risk of non-compliance to oral atypical agents and people with more severe disease considered Decision-analytic modelling Source of clinical effectiveness data: literature review and expert opinion Source of resource use: expert opinion and literature review Source of unit costs: national tariffs, expert opinion and published literature	Costs: direct medical Medication, staff time for injections, physician visits, hospitalisation, day care, sheltered living, outpatient and home contacts with healthcare professionals Costs of treating side effects not considered Mean annual costs per person: Long-acting risperidone €87,284 Olanzapine €92,706 Haloperidol depot €88,892 Outcomes: number of relapses; mean PANSS scores during and between relapses; QALYs Mean number of relapses prevented by long-acting risperidone per person: Versus olanzapine 0.32 Versus haloperidol depot 0.23 Mean time in psychosis per person (years): Long-acting risperidone 1.59 Olanzapine 1.78 Haloperidol depot 1.72 Mean PANSS score per person during/	Long-acting risperidone dominated both olanzapine and haloperidol depot Long-acting risperidone not cost saving in the subpopulation of people with non-severe and medium–severe people experiencing full recovery Results sensitive to relative relapse and compliance rates	Perspective: 3rd party payer (sickness funds and social security) Currency: Euros (€) Cost year: 2004 Time horizon: 5 years Discounting: 5% annually Funded by Janssen Pharmaceutica, N.V., Belgium, and Janssen-Cilag GmbH Germany Quality score: 26/3/6

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
			between relapses: Long-acting risperidone 110/73 Olanzapine 114/76 Haloperidol depot 116/79 Mean QALYs per person: Long-acting risperidone 1.87 Olanzapine 1.79 Haloperidol depot 1.78		
Oh *et al*., 2001 Canada Cost-utility analysis	<u>Interventions:</u> Risperidone 6mg/day Haloperidol 20mg/day Haloperidol depot 100mg/3 weeks Fluphenazine depot 25mg/3 weeks	Previously treated, hospitalised people with chronic schizophrenia with moderate symptoms Decision-analytic modelling Source of clinical effectiveness data: synthesis of data taken from meta-analyses and expert opinion Source of resource use: expert opinion Source of unit costs: national and provincial data	<u>Costs:</u> direct medical Medication, laboratory testing, hospitalisation, psychiatrist and nurse visits, case management (nurse or social worker), residential care, management of EPS Total cost per person: Risperidone $69,855 Haloperidol $76,365 Haloperidol depot $78,388 Fluphenazine depot $82,264 <u>Primary outcome:</u> QALYs Number of QALYs gained per person: Risperidone 0.87 Haloperidol 0.83 Haloperidol depot 0.84 Fluphenazine depot 0.83	Risperidone dominated all other treatment options Results sensitive to response rates, hospital discharge rates, and utility scores of mild symptoms for risperidone and haloperidol	Perspective: government Currency: Can$ Cost year: 1997 Time horizon: 12 months Discounting: not needed Compliance not taken into account Funded by Janssen-Ortho Canada Quality score: 24/3/8

Promoting recovery in people with schizophrenia who have had an inadequate or no response to treatment (treatment resistance)

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Lewis, S.W., Davies, L., Jones, P.B., *et al*. (2006) Randomised controlled trials of conventional antipsychotic versus new atypical drugs, and new atypical drugs versus clozapine, in people with schizophrenia responding poorly to, or intolerant of, current drug treatment. *Health Technology Assessment, 10* (17), 1-165. ***Refers to study ID CUtLASS Bands 1 and 2***

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Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
Rosenheck *et al.*, 1997 [study ID ROSENHECK1997] US Cost-consequence analysis	Interventions: Clozapine 100 to 900mg/day Haloperidol 5 to 30mg/day	People with schizophrenia refractory to treatment and a history of a high level of use of inpatient services defined as 30 to 364 days of hospitalisation for schizophrenia in the previous year Multicentre RCT - 14 Veterans Affairs Centres (N = 423) Source of clinical effectiveness data: RCT (N = 423) Source of resource use: RCT (N = 423) – Veterans Affairs data systems, interviews with participants and treatment records of non-Veterans Affairs providers; for non-healthcare costs: interviews and published data Source of unit costs: Veterans Affairs national data	Costs: Direct medical: medication, laboratory testing, inpatient days, outpatient visits, group treatment, day hospital, domiciliary and nursing home care Non-medical: criminal justice (police contacts and arrests), productivity losses of participants and their carers, administrative costs of transfer payments Total cost per person: Clozapine $58,151; haloperidol $60,885 (p=0.41) Outcomes: compliance rates, mean PANSS score, mean Quality of Life Scale score, side effect rates Compliance rates Clozapine 57%; haloperidol 28% (p<0.001) Mean PANSS score Clozapine 79.1; haloperidol 83.6 (p=0.02) Mean Quality of Life Scale score Clozapine 44.4; haloperidol 40.9 (p=0.17) Mean score on the EPS scale: Clozapine 2.6; haloperidol 4.0 (p<0.001)	Clozapine more effective than haloperidol, with better compliance, fewer side effects and similar overall costs	Perspective: societal Currency: US$ Cost year: 1994 Time horizon: 12 months Discounting: not needed Quality score: 21/2/11
Tilden *et al.*, 2002 UK Cost-effectiveness analysis	Interventions: Quetiapine 600mg/day Haloperidol 20mg/day	People aged ≥ 18 years with schizophrenia, who had a history of persistent positive symptoms while previously taking therapeutic doses of an antipsychotic agent and scores of at least 15 on the PANSS and at least 3 on the CGI	Costs: direct medical Medication, laboratory testing, short- and long-term hospitalisation, sheltered accommodation, outpatient visits, treatment of EPS Total cost per person: Quetiapine £38,106	Quetiapine more effective than haloperidol at a slightly lower total cost Cost results sensitive to	Perspective: NHS Currency: UK£ Cost year: not stated Time horizon: 5 years Discounting: 6% for costs; 1.5% for outcomes Funded by AstraZeneca Quality score: 23/4/8

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
		Decision-analytic modelling Source of clinical effectiveness data: published multicentre RCT (EMSLEY1999), other published literature and expert opinion Source of resource use: expert opinion and published literature Source of unit costs: national data	Haloperidol £38,350 <u>Outcomes:</u> average number of relapses per person; expected duration of time in response health states per person Average number of relapses per person Quetiapine 2.30 Haloperidol 2.49 Expected duration of time in response per person (years): Quetiapine 2.25 Haloperidol 1.90	difference in response rates, risk of relapse in non-responding and non-compliant individuals, and proportion of hospitalisation following relapse	
Lewis *et al.*, 2006 (study ID CUtLASS Band 1) UK Cost-utility analysis	<u>Interventions:</u> SGAs FGAs	People with schizophrenia, aged 18–65 years, responding inadequately to, or having unacceptable side effect from, their current antipsychotic medication Pragmatic RCT conducted in 4 centres (N = 227) Source of clinical effectiveness data: pragmatic trial (N = 227, including imputing values for missing data) Source of resource use: pragmatic trial (N = 227, including imputing values for missing data) - data taken from case-note review and questionnaires completed by the study participants	<u>Costs:</u> Medication, hospital inpatient and outpatient services, primary and community care services, social services Total cost per person: SGAs £20,123 FGAs £18,849 (non-significant difference) <u>Outcomes:</u> number of QALYs SGAs 0.66 FGAs 0.74 (non-significant difference)	FGAs associated with non-significant lower costs and better outcomes compared with SGAs Sensitivity analysis: FGAs dominated SGAs or had an ICER lower than £5,000 per QALY Probabilistic sensitivity analysis: Probability (P) of FGA being cost effective 65% at zero willingness-to-pay (WTP);	Perspective: Health and social care Currency: UK£ Cost year: 2001/02 Time horizon: 12 months Discounting: not needed Quality score: 26/0/9

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
		Source of unit costs: national sources		P of FGA being cost effective 91% at WTP £50,000/QALY P of FGA being cost effective around 80% at WTP £20,000/QALY	
Lewis *et al.*, 2006 Davies *et al.*, 2008 (study ID CUtLASS Band 2) UK Cost-utility analysis	Interventions: Clozapine SGAs	People with schizophrenia responding inadequately to, or having unacceptable side effect from, their current antipsychotic medication Pragmatic RCT conducted in 4 centres (N = 136) Source of clinical effectiveness data: pragmatic trial (N = 136, including imputing values for missing data) Source of resource use: pragmatic trial (N = 136, including imputing values for missing data) - data taken from case-note review and questionnaires completed by the study participants Source of unit costs: national sources	Costs: Medication, hospital inpatient and outpatient services, primary and community care services, social services Total cost per person: Clozapine £33,227 SGAs £28,323 (significant) Outcomes: number of QALYs Clozapine 0.74 SGAs 0.68 (non-significant)	Clozapine versus SGAs: £33,240/QALY Sensitivity analysis: ICER between £23,000-£70,000 per QALY Probabilistic sensitivity analysis: P of clozapine being cost effective 33% at zero WTP; P of FGA being cost effective 50% at WTP between £30,000 and £35,000 per QALY	Perspective: Health and social care Currency: UK£ Cost year: 2005/06 Time horizon: 12 months Discounting: not needed Quality score: 26/0/9

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Psychological therapy and psychosocial interventions in the treatment and management of schizophrenia

Adherence therapy

References to included studies

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Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
Healey *et al.*, 1998 (KEMP1996) UK Cost-consequence analysis	Intervention: CBT + standard care (CBT) Comparator: Supportive counselling (control)	People aged 18-65 years with schizophrenia, affective disorders with psychotic features or schizoaffective disorder, hospitalised for psychosis RCT (N = 70) Source of clinical effectiveness data: RCT and naturalistic follow-up (N=41 at 18 months' follow-up) Source of resource use estimates: RCT and naturalistic follow-up (N=41) – service users' self-reports using the Client Service Receipt Inventory (CSRI) Source of unit costs: national sources and local data	Costs: NHS plus criminal justice system NHS costs: Hospital (psychiatric and non-psychiatric inpatient, psychiatric outpatient, day hospital, A&E) Community (GPs, nurses, psychologists, psychiatrists, social workers, day centres, job centres, etc) Criminal justice system costs: arrests, police, solicitor, court appearances, probation officer, police cell Mean weekly cost per person over 18 months: CBT: £175; Control: £193 (p=0.92) Outcomes: Relapse rates, BPRS and GAF scores, Drug Attitudes Inventory (DAI), Insight scale, compliance CBT showed a significantly effect over control in terms of relapse, GAF scores, DAI, Insight scale and compliance at various time points of follow-up	CBT more effective than supportive counselling at no additional cost	Perspective: NHS and criminal justice system Currency: UK£ Cost year: 1995/1996 Time horizon: 18 months Discounting: not needed Study sample at endpoint sufficient to detect a 30% difference in costs at the 5% level of significance Quality score: 19/2/14

Cognitive behavioural therapy

References to included studies

Kuipers, E., Fowler, D., Garety, P., *et al*. (1998) London–East Anglia randomised controlled trial of cognitive-behavioural therapy for psychosis. III: follow-up and economic evaluation at 18 months. *British Journal of Psychiatry, 173*, 61-68. ***Refers to study ID KUIPERS1997***

Startup, M., Jackson, M.C., Evans, K.E., *et al*. (2005) North Wales randomized controlled trial of cognitive behaviour therapy for acute schizophrenia spectrum disorders: two-year follow-up and economic evaluation. *Psychological Medicine, 35*, 1307-1316. ***Refers to study ID STARTUP2004***

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
Kuipers *et al.*, 1998 (KUIPERS1997) UK Cost-effectiveness analysis	Intervention: CBT + standard care (CBT) Comparator: Standard care (control)	Outpatients aged 18-65 years with medication-resistant psychosis, diagnosed with schizophrenia, schizoaffective or delusional disorder RCT (N = 60) Source of clinical effectiveness data: RCT and naturalistic follow-up (N=47 at 18 months' follow-up) Source of resource use estimates: RCT and naturalistic follow-up (N=32) – case records and service users' self-reports using a variant of CSRI Source of unit costs: national sources	Costs: NHS and specialist, non-domestic accommodation NHS costs: Hospital (psychiatric and non-psychiatric inpatient and outpatient, day hospital) Community (GPs, nurses, social workers, day centres) Medication costs not considered Mean monthly cost per person over 18 months: CBT £1,220 Control £1,403 (p=0.416) Primary outcome: mean change in BPRS score Mean change in BPRS score: CBT: 7.57; Control: 0.46 (p<0.001)	CBT + standard care more effective than standard care alone at no additional cost	Perspective: NHS and PSS Currency: UK£ Cost year: 1996 Time horizon: 18 months Discounting: not needed Lack of some resource use data for the treatment phase Insufficient power for economic analysis Medication prescribing not controlled Quality score: 19/2/14
Startup *et al.*, 2005 (STARTUP2004)	Intervention: CBT + standard care (CBT)	People aged 18-65 years with a schizophrenia spectrum disorder, hospitalised for an acute psychotic episode	Costs: NHS plus residential care NHS costs: hospital, medication, key workers, psychiatrists, GPs, support workers, day hospitals, day centres.	CBT + standard care more effective than standard care at no additional cost	Perspective: NHS and PSS Currency: UK£ Cost year: 2001 Time horizon: 24 months

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
UK Cost-consequence analysis	<u>Comparator:</u> Standard care (control)	RCT (N = 90) Source of clinical effectiveness data: RCT and naturalistic follow-up (N=60 at 24 months' follow-up) Source of resource use estimates: RCT and naturalistic follow-up (N=60) – hospital records and key workers' reports using the Service Utilisation Schedule (SUS) Source of unit costs: national sources and local Trust data	Mean cost per person over 24 months: CBT: £27,535; Control: £27,956 (p=0.94) <u>Outcomes:</u> Scale for the Assessment of Positive Symptoms (SAPS), Scale for the Assessment of Negative Symptoms (SANS), Social Functioning Scale (SFS) and GAF scores CBT showed a significant effect over control in SANS and SFS scores		Discounting: not needed Insufficient power for economic analysis Quality score: 20/1/14

Family interventions

References to included studies (from previous NICE schizophrenia guideline)

Goldstein, M.J. (1996) Psychoeducational family programs in the United States. In *Handbook of Mental Health Economics and Health Policy, Vol. 1: Schizophrenia (*eds. M. Moscarelli, A. Rupp & N. Sartorius). New York, NY: John Wiley & Sons.

Leff, J., Trieman, N. & Gooch, C. (1996) Team for the assessment of psychiatric services (TAPS) project 33: prospective follow-up study of long-stay patients discharged from two psychiatric hospitals. *American Journal of Psychiatry, 153,* 1318-24

Liberman, R .P., Cardin, V., McGill, C.W., *et al*. (1987) Behavioral family management of schizophrenia: clinical outcome and costs. *Psychiatric Annals, 17*, 610-619.

McFarlane, W.R., Lukens, E., Link, B., *et al*. (1995) Multiple-family groups and psychoeducation in the treatment of schizophrenia. *Archives of General Psychiatry, 52,* 679-87.

Tarrier, N., Lownson, K. & Barrowclough, C. (1991) Some aspects of family interventions in schizophrenia. II. Financial considerations. *British Journal of Psychiatry, 159,* 481-4.

Study	Methods	Cost data	Interventions	Participants	Primary outcome(s) measured	Cost(s) measured	Results	Comments	Risk of bias (Validity scores)
Goldstein 1996	Economic study design: COA Clinical effect size data source: RCT – Falloon 1985 Perspective: healthcare provider? Time frame: 9 months Setting: participants' homes for intervention 1, aftercare clinic for intervention 2	Country: US Fiscal year: no mention Currency: US Dollars	1. Behavioural family intervention with antipsychotic medication (21 sessions) 2. Individual supportive therapy with antipsychotic medication	Service users with schizophrenia 1. N=16 2. N=16	None	1. Direct treatment (personnel) 2. Savings by readmissions averted	Cost estimates of one block of intervention 1 were $5,000 by two therapists and $2,500 by one therapist. Intervention 1 could save $6,200 by one averted hospital readmission.	Readmission data used were not original, but it was estimated from relapse data. Unit cost data source was not presented, important cost components (e.g. travel expenses, overheads) were not included. No statistical or sensitivity analyses. Serious methodological flaws. Small sample size.	High (4/18)
Leff *et al*., 2001	Economic study design: COA Clinical effect size data source: RCT-Leff Perspective: unclear Time frame: 12 months Setting: participants' homes	Country: UK Fiscal year: no mention Currency: Pounds Sterling	Family intervention with 2 sessions of psychoeducation by two therapists – bi- weekly then monthly 2 sessions of psychoeducation by one therapist	HEE families of participants with schizophrenia 1. N=16 2. N=14	None	Direct treatment Training of staff Savings on inpatient costs Savings on criminal justice costs	The additional costs of the intervention (£2,566) were offset by the decreased hospital care costs (£10,996 versus £14,938). Although the difference in institutional care costs was not significant.	Small sample size, low power, no sensitivity analysis.	High (8/18)
Liberman et al.,, 1987	Economic study design: CBA Clinical effect size data source: RCT – Falloon 1985 Perspective: unclear Time frame: 12 months Setting: participants' homes for intervention 1, aftercare clinic for intervention 2	Country: US Fiscal year: no mention Currency: US Dollars	1. Behavioural family intervention with antipsychotic medication (21 sessions) 2. Individual supportive therapy with antipsychotic medication	Schizophrenic service users 1. N=16 2. N=16	1. Earnings 2. Well-being 3. Institutional expenditure	1.Direct treatment 2.Inpatient 3. Community care	Direct treatment costs were higher for intervention 1 than for intervention 2, but costs exceeded benefits in both cases. Favoured intervention 1 since net benefit was more (-$2,600) than for intervention 2 (-$6,300).	Medication costs were not included. No information about quantities and unit cost sources. No statistical and sensitivity analyses were carried out. Altogether, very limited details about economic analysis. Small sample size.	High (11/32)
McFarlane *et al*., 1995	Economic study design: CBA Clinical effect size data source: RCT - McFarlane 1995 (mirror image analysis) Perspective: healthcare provider? Time frame: 6 months	Country: US Fiscal year: no mention Currency: US Dollars	1. Psycho-educational multiple-family group (MFG), participants included – biweekly for 2 years 2. Psycho-	Acutely psychotic service users with schizophrenia spectrum disorders 1. N=86 2. N=86	Rehospitalis-ation	Direct treatment (personnel)	The cost-benefit ratio of MFG compared with the period before treatment was 1:34, for SFG it was 1:17. MFG was favoured over SFG.	In the economic analysis, the pre-study rehospitalisation rates of both groups were compared with the study period, and the two differences were used to calculate the cost-benefit ratio. Limited health	High (13/32)

	Setting: public hospitals in New York		educational single-family group (SFG), participants included – biweekly for 2 years					economic methodology. Compared the most favourable study period, so the result is prone to bias. No statistical and sensitivity analyses.	
Tarrier *et al*., 1991	Economic study design: CA Clinical effect size data source: RCT – Tarrier 1988 Perspective: NHS Time frame: 9 months Setting: outpatient	Country: UK Fiscal year: 1987/88 Currency: Pounds Sterling	1. Family intervention (13 sessions) 2. Standard care	HEE families of service users with schizophrenia 1. N=25 2. N=29	None	1. Direct treatment 2. Inpatient 3. Outpatient 4. Day care 5. Community healthcare (CPN) 6. Social care (SW)	Intervention 1 group showed an overall saving of £17,112 compared to the intervention 2 group over 9 months. The mean saving was £432 per service user (27% of the mean cost per service user in intervention 1). Savings made on inpatient and social service costs were significant for int. 1.	Resource use of both groups was costed. Based on a 2-year follow-up, authors predicted that cost savings would continue over time. No sensitivity analysis. Small sample size.	Low (11/18)

Abbreviations:

CA – Cost analysis
CBA – Cost-benefit analysis
CBT – Cognitive behavioural therapy
CCA – Cost-consequence analysis
CEA – Cost-effectiveness analysis
CMA – Cost-minimisation analysis
CPN – Community psychiatric nurse
COA – Cost-offset analysis
CUA – Cost-utility analysis
HEE – High expressed emotions
N – Number of participants
RCT – Randomised controlled trial
SC – Standard care
SW – Social worker

References to economic studies on psychological interventions for people with schizophrenia, excluded at stage 5 of the systematic review (see Chapter 3 for methods of systematic review of the economic literature)

Cullberg, J., Mattsson, M., Levander, S., *et al*. (2006) Treatment costs and clinical outcome for first episode schizophrenia patients: a 3-year follow-up of the Swedish 'Parachute Project' and two comparison groups. *Acta Psychiatrica Scandinavica, 114*, 274-281.

Goldstein, M.J. (1996) Psychoeducational family programs in the United States. In *Handbook of Mental Health Economics and Health Policy, Vol. 1: Schizophrenia (eds. M.* Moscarelli, A. Rupp & N. Sartorius). New York, NY: John Wiley & Sons

Gutierrez-Recacha, P., Chisholm, D., Haro, J.M., *et al.* (2006) Cost-effectiveness of different clinical interventions for reducing the burden of schizophrenia in Spain. *Acta Psychiatrica Scandinavica, 114* (Suppl. 432), 29-38.

Leff, J., Trieman, N. & Gooch, C. (1996) Team for the assessment of psychiatric services (TAPS) project 33: prospective follow-up study of long-stay patients discharged from two psychiatric hospitals. *American Journal of Psychiatry, 153,* 1318-24

Mihalopoulos, C., Magnus, A., Carter, R., *et al.* (2004) Assessing cost-effectiveness in mental health: family interventions for schizophrenia and related conditions. *Australian and New Zealand Journal of Psychiatry, 38*, 511-519.

Mino, Y., Shimodera, S., Inoue, S., *et al*. (2007) Medical cost analysis of family psychoeducation for schizophrenia. *Psychiatry and Clinical Neurosciences, 61*, 20-24.

Service-level interventions

(from previous NICE schizophrenia guideline – not updated)

Community mental health teams

References to included studies

Burns, T. & Raftery, J. (1993) A controlled trial of home-based acute psychiatric services II: treatment patterns and costs. *British Journal of Psychiatry, 163*, 55-61.

Gater, R., Goldberg, D., Jackson, G., *et al.* (1997) The care of patients with chronic schizophrenia: a comparison between two services. *Psychological Medicine, 27*, 1325-1336.

McCrone, P., Thornicroft, G., Phelan, M., *et al*. (1998) Utilisation and costs of community mental health services. PRiSM Psychosis Study. 5. *British Journal of Psychiatry, 173*, 391-398.

Merson, S., Tyrer, P., Carlen, D., *et al*. (1996) The cost of treatment of psychiatric emergencies: a comparison of hospital and community services. *Psychological Medicine, 26*, 727-734.

Tyrer, P., Evans, K., Gandhi, N., *et al*. (1998) Randomised controlled trial of two models of care for discharged psychiatric patients. *British Medical Journal, 316*, 106-109.

Study	Methods	Cost data	Interventions	Participants	Primary outcome(s) measured	Cost(s) measured	Results	Comments	Risk of bias (Validity score)
Burns & Raftery 1993	Economic study design: CMA Clinical effect size data source: RCT – Burns Perspective: societal Time frame: 1 year Setting: suburban London	Country: UK Fiscal year: 1986/87 Currency: Pounds Sterling	1. Home-based psychiatric service (CMHT) 2. Standard care	1. N=94 2. N=78 The proportion of psychotic participants was lower in intervention 1 than 2	Different clinical outcomes	1. Direct treatment 2. Inpatient 3. Outpatient 4. Day care 5. Community health care	Total cost per participant was 39% more in intervention 2 than 1, although the difference is not statistically significant. Outcomes were the same in both groups. Sensitivity analysis confirmed the cost saving characteristic of CMHT.	The proportion of service users with schizophrenia differed in the two groups, but data were adjusted for this condition.	Low (10/18)
Gater *et al.*, 1997	Economic study design: CA Clinical effect size data source: RCT – Gater Perspective: societal Time frame: 12 months Setting: Manchester	Country: UK Fiscal year: not clear Currency: Pounds Sterling	1. CMHT 2. Standard care	All participants had schizophrenia 1. N=92 2. N=47	None	1. Direct treatment 2. Inpatient 3. Outpatient 4. Day care 5. Community healthcare 6. Medication 7. Social care 8. Travel costs 9. Caregiver costs 10. Income foregone due to illness 11. Income foregone due to death 12. Income foregone by caregiver 13. Service user costs	The cost of services was £1,879/patient/year for intervention 1 and £1,634/patient/year for intervention 2. Costs to families were £3,235 and £2,730, respectively. The cost differences were not significant. Savings were not sufficient to offset the cost of the new team. The heavy cost burden raises concern in the shift of services to the community.	Costs varied widely between individuals. No sensitivity analysis.	Low (10/18)
McCrone *et al.*, 1998	Economic study design: CA Clinical effect size data source: controlled study with concurrent controls – Thornicroft 1998 Perspective: not clear Time frame: 2 x 6 months Setting: deprived area in South London	Country: UK Fiscal year: 1995/96 Currency: Pounds Sterling	1. Intensive sector (ICM) 2. Standard sector (CMHT)	Psychotic participants 1. N=62 2. N=61	None	1. Day care 2. Medication 3. Social care 4. Criminal justice 5. Supported, non-supported accommodation 6. Inpatient care 7. Emergency clinic 8. Sheltered work 9. Psychologist, psychiatrist, GP, CPN, occupational therapist 10. General healthcare 11. Employment	The significant total cost difference between the two sectors was likely to be due to the baseline difference between the two populations and not due to the different interventions. The two programmes did not result in significant cost savings compared to the period before the introduction of the new services. Regarding the different components of healthcare cost, inpatient care was the most expensive followed by supported accommodation. GP care was relatively inexpensive (~1%).	Intensive sector clients were on average significantly more disabled than those in the standard sector. Medication was not extensively measured. No sensitivity analysis and no adjustment for group differences.	Low (9/18)

						12. Informal care			
Merson *et al.*, 1996	Economic study design: CA Clinical effect size data source: RCT – Merson 1992 Perspective: healthcare system Time frame: 3 months Setting: Central London	Country: UK Fiscal year: not clear Currency: Pounds Sterling	1. Early intervention service (CMHT) 2. Standard hospital-based psychiatric service	Acute severely mentally ill service users who were not in contact with psychiatric services. 1. N=48 (40% had schizo-phrenia spectrum disorder) 2. N=52 (37% had schizo-phrenia spectrum disorder)	None	1. Inpatient 2. Outpatient 3. Day care 4. Community health care 5. Staff 6. Medication 7. Overheads 8. Capital equipment 9. Real estate 10. Materials 11. Social care 12. Criminal justice	Total cost of intervention 2 over 3 months (£130,100) was more than 2.25 times those of intervention 1 (£55,701). More than 10% of the total cost of intervention 1 arose from failed appointments, as long as the same cost was only less than 2% for intervention 2.	No sensitivity analysis was carried out. No information about whether result is significant or not. Small sample size and short time frame should be treated with caution.	Low (9/18)
Tyrer *et al.*, 1998	Economic study design: CA Clinical effect size data source: RCT – Tyrer 1998 Perspective: healthcare system Time frame: 1 year Setting: Inner and outer London	Country: UK Fiscal year: not clear Currency: Pounds Sterling	1. CMHT 2. Standard hospital-based care	N=82 N=73 55% had schizophrenia Cost data were available for: 1. N=74 2. N=70	None	1. Direct treatment 2. Inpatient 3. Outpatient 4. Day care 5. Community health care 7. Social care	Costs were lower for service users in intervention 1, which had fewer admissions to hospital. Mean cost/service user £16,765 versus £19,125 (or log-transformed: £7,161 versus £8,147). The difference was not significant. Costs were twice as high in outer London compared to inner London, presumably due to insufficient number of beds in the area.	Limited methodology information. No sensitivity analysis. The considerable pressure on psychiatric beds in London during the study period might have biased the results.	High (7/18)

Abbreviations:
CA – Cost analysis
CMA – Cost-minimisation analysis
CMHT – Community mental health team
CPN – Community psychiatric nurse
N – number of participants
RCT – Randomised Controlled Trial

Assertive community treatment

References to included studies

Bond, G.R., Miller, L.D., Krumwied, R.D., *et al*. (1988) Assertive case management in three CMHCs: a controlled study. *Hospital and Community Psychiatry, 39,* 411-418.

Chandler, D., Spicer, G., Wagner, M., *et al.* (1999) Cost-effectiveness of a capitated assertive community treatment program. *Psychiatric Rehabilitation Journal, 22*, 327-336.

De Cangas, J.P.C. (1994) Le 'case management' affirmatif: une evaluation complete d'un programme du genre en milieu hospitalier. *Sante mentale au Quebec*, *19*, 75-92.

Essock, S.M., Frisman, L.K. & Kontos, N.J. (1998) Cost-effectiveness of assertive community treatment teams. *American Journal of Orthopsychiatry, 68,* 179-190.

Hu, T.W. & Jerrell, J.M. (1998). Estimating the cost impact of three case management programmes for treating people with severe mental illness. *British Journal of Psychiatry, Suppl. 36,* 26-32.

Lehman, A.F., Dixon, L., Hoch, J.S., *et al.* (1999) Cost-effectiveness of assertive community treatment for homeless persons with severe mental illness. *British Journal of Psychiatry, 174,* 346-352.

Preston, N.J. & Fazio, S. (2000). Establishing the efficacy and cost effectiveness of community intensive case management of long-term mentally ill: a matched control group study. *Australian and New Zealand Journal of Psychiatry, 34,* 114-121.

Quinlivan, R., Hough, R., Crowell, A., *et al*. (1995) Service utilisation and costs of care for severely mentally ill clients in an intensive case management program. *Psychiatric Services, 46,* 365-371.

Rosenheck, R. A. & Neale, M. S. (1998) Cost-effectiveness of intensive psychiatric community care for high users of inpatient services. *Archives of General Psychiatry, 55*, 459-466.

Salkever, D., Domino, M. E., Burns, B. J., *et al*. (1999) Assertive community treatment for people with severe mental illness: the effect on hospital use and costs. *Health Services Research, 34,* 577-601.

Wolff, N., Helminiak, T. W., Morse, G. A., *et al*. (1997) Cost-effectiveness evaluation of three approaches to case management for homeless mentally ill clients. *American Journal of Psychiatry, 154,* 341-348.

Study	Methods	Cost data	Interventions	Participants	Primary outcome(s) measured	Cost(s) measured	Results	Comments	Risk of bias (Validity scores)
Bond *et al*., 1988	Economic study design: CA Clinical effect size data source: RCT – Bond 1988 Perspective: not clear Time frame: 6 months Setting: 3 urban CMHCs, Indiana	Country: US Fiscal year: not clear Currency: US Dollars	1. PACT 2. Public mental health services	61% had schizophrenia, 14 % had schizoaffective disorders 1. N=84 2. N=83 Economic data obtained from: 1. N=70 2. N=62	None	1. Direct treatment 2. Inpatient 3. Outpatient 4. Day care 5. Community health care 6. Medication 7. Social care 8. Social benefits 9. Criminal justice 10. Income forgone due to death	Intervention 1's cost/client/ 6 months was $4,245, $2,873 and $7,021 for centres A, B and C, respectively. Intervention 1 was cost saving for centre A, where the average cost/client was $5,490 less than that for intervention 2. In centre B, intervention 1 service users incurred more costs than intervention.2 service users, and no cost difference was observable at centre C.	There were baseline differences between the two intervention groups at centres A and B. No statistical or sensitivity analyses. High discrepancy in results between the 3 centres. Short time frame of analysis.	High (6/18)
Chandler *et al*., 1999	Economic study design: CCA Clinical effect size data source: RCT-Chandler (California 2) Perspective: insurer Time frame: 12 months Setting: California, US	Country: US Fiscal year: 1995/96 Currency: US Dollars	1. ACT 2. Usual services	61% schizophrenia, 34% schizoaffective participants 1. N=29 2. N=28	1. QoL 2. Living circumstances 3. Satisfaction 4. Income 5. Homeless-ness 6. Preferences 7. Level of functioning 8. Community tenure	Mental health service costs	Total cost for the intervention 1 group was $946,283 versus $123,3545/year. Intervention 1 is at least as effective as intervention 2 and less costly, therefore intervention 1 is more cost effective.	Limited details of methodology. Significance of cost differences was not investigated. No sensitivity analysis.	High (13/32)
De Cangas, 1994	Economic study design: CCA Clinical effect size data source: RCT – De Cangas 1994 Perspective: societal Time frame: 6 months Setting: Quebec, Canada	Country: Canada Fiscal year: not clear Currency: Canadian Dollars	1. 'Le case management affirmative' – ACT 2. Routine inpatient and community care	1. N=60 2. N=60 Economic data obtained for: 1. N=43 N=42	1. Hospital admission 2, Lost to follow-up 3. Imprison-ment 4. Employment 5. Deviant behaviour 6. Social functioning 7. Family burden 8. QoL 9. Expressed emotion	1. Direct treatment 2. Inpatient 3. Outpatient 4. Day care 5. Community health care 6. Criminal justice 7. Family costs 8. Employment earnings (staff, overheads, real estate)	Net cost per service user was significantly less for intervention 1 ($3,609) than for intervention 2 ($7,792). ACT is more effective and less costly.	Intervention 1 service users were less severely ill than intervention 2 service users. Limited details of methodology. No sensitivity analysis.	High (13/32)

Essock *et al.*, 1998	Economic study design: CEA Clinical effect size data source: RCT – Essock 1995 Perspective: societal / Department of Mental Health (DMH) Time frame: 12 months Setting: 3 study sites, Connecticut	Country: US Fiscal year: 1992 Currency: US Dollars	1. ACT 2. Standard CM	High service users, 67% with schizophrenia spectrum disorder 1. N=131 2. N=131 (Economic data are based only on 234 participant's data)	Days spent in the community	1. Direct treatment 2. Inpatient 3. Outpatient 4. Community health care 5. Emergency room 6. Nursing home 7. Administration of transfer payments	The direct treatment cost of intervention 1 was significantly higher by $8,221 than that of intervention 2, but average inpatient and nursing home costs were significantly lower for intervention 1 than for intervention 2. The mean annual cost per service user to society (or to DMH) was not significantly different between the groups. Intervention 1: Society: $33,473 (DMH $23,155) Intervention 2: Society: 35,656 (DMH: $23,839) The average effectiveness – cost ratio was 9 community days / $1000 for intervention 1 and 7.3 community days / $1000 for intervention 2. There was no significant difference between them.	No sensitivity analysis. Large sample size increases reliability of results.	Low (19/32)
Hu & Jerrell, 1998	Economic study design: COA Clinical effect size data source: RCT – Jerrell 1995 Perspective: societal Time frame: 6 months (pre-treatment) + 18 months (treatment) Setting: large urban mental health system	Country: US Fiscal year: 1990/91 Currency: US Dollars	1. 'Intensive broker model team' (CM) 2. Clinical team programme 3. PACT	1. N=42 (73.8% schizophrenia) 2. N=40 (75.0% schizophrenia) 3. N=40 (77.5% schizophrenia)	None	1. Social benefits 2. Travel costs 3. Caregiver costs 4. Criminal and legal justice 5. Intensive mental health services 6. Supportive mental health services 7. General medical	All three interventions significantly reduced the average societal cost of caring for people with SMI compared with the baseline period (intervention 1: -$12,279 = -49%, intervention 2: -$12,610 = -50%, intervention 3: -$13,809=-62%). Cost savings were primarily due to reduction in inpatient and skilled nursing service costs. In the short-term intervention 2 was considered to be more cost saving, in the long-term intervention 3 was less costly.	No sensitivity analysis, no statistical details.	Low (10/18)
Lehman *et al.*, 1999	Economic study design: CEA Clinical effect size data source: RCT – Lehman 1997 Perspective: healthcare system Time frame: 1 year Setting: Baltimore, US	Country: US Fiscal year: 1994 Currency: US Dollars	1. PACT 2. Standard psychiatric care	Homeless SMI service users, 58% with schizophrenia spectrum disorders 1. N=77 2. N=75	Days of stable housing	1. Fixed costs of ACT 2. Mental health (outpatient, inpatient, emergency room, rehabilitation) 3. Substance misuse: (outpatient, in-patient, emergency room, rehabilitation) 4. General medical (Out-patient, inpatient, emergency room, rehabilitation)	Intervention 1 participants spent significantly more days in stable housing than people having intervention 2. The mean yearly cost per case was less ($50,748) for intervention 1 than for intervention 2 ($66,480). This difference was not of statistical significance. The average CE ratios were $241/day housed for intervention 1 and $415/day housed for intervention 2, although this difference was not significant either.	No sensitivity analysis. The skewed cost data were analysed non-parametrically as well and the conclusions were identical. Only direct treatment costs were included in analysis. Neither housing costs nor legal system costs were measured.	Low (20/32)
Preston &	Economic study	Country:	1. ICM	Matched groups,	None	1.Inpatient	A steady significant reduction in total	No sensitivity	High

Fazio, 2000	design: COA Clinical effect size data source: controlled study with concurrent controls (mirror-image analysis) Perspective: health care provider Time frame: 12 months (pre-treatment) + 12 months (treatment) Setting: metropolitan region, Perth	Australia Fiscal year: not clear Currency: Australian Dollars	2. Standard clinic based community treatment (ACT)	56% with schizophrenia 1. N=80 2. N=80		2. Outpatient	operational costs was observed for intervention 1. The reduction for intervention 2 was not significant. Between the two regions, the total cost differential was $801,475 in favour of intervention 1 for the 24 months. For intervention 1, reduction in inpatient costs far offset the increased outpatient costs.	analysis. Only narrow service use was costed. Intervention 1 had significantly lower outpatient contacts in the baseline period.	(8/18)
Quinlivan *et al.*, 1995	Economic study design: CA Clinical effect size data source: RCT – Quinlivan Perspective: health care provider Time frame: 2 years Setting: San Diego County, US	Country: USA Fiscal year: not clear Currency: US Dollars	1. ACT 2. CM 3. Standard care	High inpatient service users, 67.8% with schizophrenia spectrum disorder 1. N=30 2. N=30 3. N=30	None	1. Inpatient and A&E 2. Outpatient 3. Day care 4. Case management	Intervention 1 had significantly less inpatient costs ($7,232) than intervention 3 ($39,270) and had significantly more outpatient costs ($11,710 versus $2,824) - including CM costs- than intervention 3. Savings outweighed extra treatment costs. Mean yearly participant costs were: intervention. 1: $9,471; intervention 2: $13,043; intervention 3: $21,047. ACT was the least costly alternative, although the total mean cost difference was not significant. Favoured ACT to CM, and CM to standard care.	No sensitivity analysis. High attrition rate. Only direct healthcare costs were analysed. Baseline difference in participant characteristics between the groups.	High (8/18)
Rosenheck & Neale, 1998	Economic study design: CEA Clinical effect size data source: RCT – Rosenheck 1995 Perspective: societal / healthcare system Time frame: 2 years Setting: 4 rural neuropsychiatric hospitals (long-stay), 6 urban general hospitals (acute care)	Country: US Fiscal year: not clear Currency: US Dollars	1. Intensive psychiatric community care (ACT) 2. Standard care	50.5% were participants with schizophrenia 1. N=183 (NH) + 271 (GH) 2. N=162 (NH) + 257 (GH)	1. BPRS 2. GAS	1. Inpatient 2. Outpatient 3. Social benefits 4. Criminal justice 5. Residential care 6. Employment earnings	<u>Societal:</u> At GH, intervention 1 was significantly more expensive by $5,046 than intervention 2, and intervention 1 was significantly more effective. Excluding 2 sites that did not adequately implement intervention 1, clinical outcome difference did not change, but the cost difference disappeared ($44,772 intervention 1 versus $44,810 intervention 2). The incremental CE ratio for GH changed from $1,705 to -$13 per unit of improvement on the BPRS. At NH there was no difference in clinical outcomes, but intervention 1 was significantly	No sensitivity analysis.	Low (19/32)

							cheaper ($82,454 versus. $116,651). Health Care System: Conclusions are exactly the same.		
Salkever *et al*., 1999	Economic study design: CA Clinical effect size data source: RCT Perspective: not clear Time frame: 2 x 18 months Setting: South Carolina	Country: US Fiscal year: not clear Currency: US Dollars	1. PACT 2. Office-based case management programme	Non-emergency SMI service users, 64.6% with schizophrenia spectrum disorder. Randomised: 1. N=104 2. N=69 Economic analysis based on: 1. N=91 2. N=53	None	Inpatient	Inpatient costs were reduced in both groups compared with baseline data, with a higher decline for intervention1 (-56% versus – 33%). The difference was not significant. PACT was more effective in reducing the probability of being hospitalised.	Attrition bias was reported. Higher baseline inpatient care use by intervention 1 could be related to difference in illness severity between the two groups. Very narrow perspective of analysis. Limited health economic methodology. No statistical or sensitivity analysis.	High (7/18)
Wolff *et al.*, 1997	Economic study design: CCA Clinical effect size data source: RCT Perspective: not clear Time frame: 6 months (pre-treatment) + 18 months (treatment) Setting: St. Louis Mental Health Centre	Country: US Fiscal year: 1992 Currency: US Dollars	1. ACT 2. ACT & Community workers 3. Brokered case management	People with a risk of homelessness, 67.1% had schizophrenia. N=165 were randomised. CE study used: 1. N=28 2. N=35 3. N=22	1. Service contact 2. BPRS 3. Client satisfaction 4. Stable housing	1. Direct treatment 2. Inpatient 3. Outpatient 4. Social benefits 5. Vocational/ educational 6. Residential	The total cost/service user estimates over the 18- month study period were: intervention. 1: $49,510, intervention 2: $39,913, intervention 3: $45,076. The cost differences were not significant. ACT approaches are more effective in satisfaction, service contacts and BPRS than intervention 3. In summary, ACT approaches are more cost effective.	Significantly more clients dropped out from intervention 3 than from the other two arms, although the samples were still comparable. The analysis had reduced statistical power, and no sensitivity analysis was carried out. No criminal justice costs were included.	Low (17/32)

Abbreviations:

ACT – Assertive Community Treatment
BPRS – Brief Psychiatric Rating Scale
CA – Cost analysis
CCA – Cost-consequence analysis
CE – Cost effectiveness
CEA – Cost-effectiveness analysis
CM – Case management
COA – Cost-offset analysis
GAS – General Attitude Scale
GH – General hospital
ICM – Intensive case management
N – Number of participants
NH – Neuropsychiatric hospital
PACT – Programme of assertive community treatment
QoL – Quality of Life
RCT – Randomised Controlled Trial
SMI – Severe mental illness

Acute day hospital

References to included studies

Creed, F., Mbaya, P., Lancashire, S., *et al*. (1997) Cost effectiveness of day and in-patient psychiatric treatment. *British Medical Journal, 314,* 1381-1385.

Francois, I., Gadreau, M., Gisselmann, A., *et al*. (1993) Contribution to the economic evaluation in psychiatry: a comparison of two establishments for chronic schizophrenic patients in the C.H.R.U. of Dijon. *Journal D'Economie Medicale, 11,* 185-199.

Sledge, W. H., Tebes, J., Wolff, N., *et al.* (1996) Day hospital/crisis respite care versus inpatient care, part II: service utilization and costs. *American Journal of Psychiatry, 153,* 1074-83.

Abbreviations in table below:
CA – Cost analysis
CCA – Cost-consequence analysis
CMHC – Community mental health centre
N – number of participants
RCT – Randomised controlled trial

Study	Methods	Cost data	Interventions	Participants	Primary outcome(s) measured	Cost(s) measured	Results	Comments	Risk of bias (Validity scores)
Creed *et al.*, 1997	Economic study design: CCA Clinical effect size data source: RCT - Creed 1997 Perspective: Central Manchester Health Trust, societal Time frame: 12 months Setting: Teaching hospital in an inner city area, Manchester	Country: UK Fiscal year: 1994/95 Currency: Pounds Sterling	1. Acute day hospital 2. Routine inpatient treatment	1. N=89 (46% people with schizophrenia) 2. N=90 (40% people with schizophrenia)	1. Mental state 2. Social functioning 3. Burden on relatives	Both perspectives: 1. Inpatient 2. Outpatient 3. Day care 4. Community health care 5. Medication 6. Tests Only societal: 7. Social care 8. Travel costs 9. Caregiver costs 10. Income forgone due to illness 11. Income forgone by caregiver	~40% of potential inpatient admissions could be treated in day hospitals. There was no significant difference in the clinical outcomes between the two groups except burden to caregivers was less for intervention 1 service users. Carers of day hospital service users may bear additional costs. Day hospital treatment was £1,923/service user (95% CI: 750-3,174) cheaper from the Central Manchester Health Care Trust's viewpoint, and £1,994/service user (95% CI: 600-3,543) cheaper from the society's viewpoint. Day hospital is at least as effective as routine inpatient treatment and less costly.	High attrition rate should be taken into account. Service users were not too ill. Housing costs were not included, but there was no significant difference between the groups in this respect. No sensitivity analysis.	Low (27/32)
Francois *et al.*, 1993	Economic study design: CA Clinical effect size data source: controlled study with concurrent controls Perspective: Healthcare provider Time frame: 1 year Setting: Dijon, urban	Country: France Fiscal year: 1989 Currency: French Francs	1. Acute day hospital 2. Standard inpatient care	All participants had schizophrenia, matched groups 1. N=16 2. N=15	None	1. Inpatient 2. Day care (staff, medication, labs/diagnostic, overhead, capital equipment, real estate)	The cost difference/day is 377F between the two programmes; day hospital is cheaper.	Small sample size. Only direct treatment costs were calculated. The cost of hospitalisation was overestimated. No statistical or sensitivity analysis.	Low (10/18)
Sledge *et al.*, 1996	Economic study design: CA Clinical effect size data source: RCT – Sledge 1996 Perspective: CMHC and the crisis residence Time frame: index admission and 10-month follow-up Setting: CMHC, poor urban community	Country: US Fiscal year: 1992/93 Currency: US Dollars	1. Acute day hospital/ Crisis respite care 2. Inpatient care	1. N=93 (39% people with schizophrenia) 2. N=104 (52% people with schizophrenia)	None	1. Inpatient 2. Outpatient 3. Day care (staff, overheads, capital equipment, real estate)	Total cost per service user was significantly less for intervention 1 ($19,521 versus $27,631). The savings were generated during the index period. For psychotic service users the savings by intervention 1 were not significant.	No rehabilitative service use data. Only narrow service use costed. No sensitivity analysis.	Low (11/18)

Vocational rehabilitation

References to included studies

Bell, M. & Lysaker, P. (1995) Paid work activity in schizophrenia: program costs offset by costs of rehospitalizations. *Psychosocial Rehabilitation Journal, 18,* 25-34.

Bond, G.R., Dietzen, L.L., Vogler, K., *et al.* (1995) Toward a framework for evaluating cost and benefits of psychiatric rehabilitation: three case examples. *Journal of Vocational Rehabilitation, 5,* 75-88.

Clark, R.E., Bush, P.W., Becker, D.R., *et al.* (1996) A cost-effectiveness comparison of supported employment and rehabilitative day treatment. *Administration and Policy in Mental Health, 24,* 63-77.

Clark, R.E., Xie, H., Becker, D.R., *et al.* (1998) Benefits and costs of supported employment from three perspectives. *Journal of Behavioral Health Services and Research, 25,* 22-34.

Hallam, A. & Schneider, J. (1999) Sheltered work schemes for people with severe mental health problems: service use and costs. *Journal of Mental Health, 8,* 171-186.

Rogers, S. E., Sciarappa, K., MacDonald-Wilson, K., *et al.* (1995) A benefit-cost analysis of a supported employment model for persons with psychiatric disabilities. *Evaluation and Program Planning, 18,* 105-115.

Warner, R., Huxley, P. & Berg, T. (1999) An evaluation of the impact of clubhouse membership on quality of life and treatment utilization. *International Journal of Social Psychiatry, 45,* 310-320.

References to unavailable papers

Bond, G.R., Dincin, J., Setze, P.J., *et al.* (1984) The effectiveness of psychiatric rehabilitation: a summary of research at thresholds. *Psychosocial Rehabilitation Journal, 7,* 6-22.

Study	Methods	Cost data	Interventions	Participants	Primary outcome(s) measured	Cost(s) measured	Results	Comments	Risk of bias (Validity scores)
Bell & Lysaker, 1995	Economic study design: CBA Clinical effect size data source: RCT – Bell et *al*., 93/94 Perspective: healthcare provider Time frame: 3 years Setting: VA Medical Centre	Country: US Fiscal year: not clear Currency: US Dollars	1. Prevocational training (up to 20 hours/week alongside regular staff of a medical centre and support group for 26 weeks, paid $3.40/hour) 2. As above but unpaid	DSM-III-R diagnoses of schizophrenia or schizoaffective disorder. 100 participants were randomised, but the economic analysis was based on: 1. N=56 2. N=36	Hospitalisation	1. Direct treatment 2. Inpatient 3. Day hospital (Halfway house)	Total cost/participant averaged $1,403.07 for intervention 1 and $97.72 for intervention 2. The incremental cost benefit ratio of the two programmes was 1/5.69 at 3 years, favouring intervention 1. The difference is not statistically significant.	No sensitivity analysis.	Low (17/32)
Bond *et al*., 1995	Economic study design: COA Clinical effect size data source: RCT Perspective: healthcare provider Time frame: 1 year Setting: CMHCs	Country: US Fiscal year: 1994 Currency: US Dollars	1. Supported employment for 12 months 2. Prevocational training for 4 months and then supported employment	66% of the 88 participants had a diagnosis of a schizophrenia spectrum disorder. Cost data based on: N=38 N=35	None	1. Direct treatment 2. Outpatient 3. Day hospital 4. Day care 5. Community care 6. Medication	Intervention.1 participants had lower average CMHC service cost ($3,156/patient/year) than intervention 2 participants ($7,038/patient/year). This cost saving offset the higher direct cost of intervention 1 ($3,020/patient) compared with intervention 2 ($1,584/patient).	Lack of precision in the data collection. No statistical or sensitivity analysis.	Low (9/18)
Clark *et al*., 1996	Economic study design: CA Clinical effect size data source: mirror-image study – Drake 1994 Perspective: healthcare system Time frame: 2 x 1 year periods Setting: 2 CMHCs	Country: US Fiscal year: 1993 Currency: US Dollars	1. Supported employment 2. Rehabilitative day treatment	55% people with schizophrenia N=58 participants	None	1. Direct treatment 2. Inpatient 3. Outpatient 4. Day treatment 5. Community care 6. Medication	At site 1, the mean total treatment costs/participant/year decreased significantly from $16,217 to $10,547 when switching to intervention 1 from intervention 2. At site 2, the two values were not significantly different. ($23,000, $20,920 respectively). The programme conversion improved vocational outcomes without increasing cost.	Overall cost reduction is ambiguous since a great proportion of the reduction is related to decrease in unit costs. No sensitivity analysis.	Low (11/18)

Clark *et al.*, 1998	Economic study design: CBA Clinical effect size data source: RCT – Drake 1996 (mirror-image analysis) Perspective: societal/ participant and participant family Time frame: 2 x 18 months Setting: 2 mental health care centres	Country: US Fiscal year: 1992 Currency: US Dollars	1. Group skills training - prevocational training for 8 weeks 2. Individual placement and support - supported employment	46.9% participants had schizophrenia spectrum disorder. 1. N=69 2. N=74 (Cost data calculated only for N=137 data.)	1. Earnings 2. % participants getting jobs 3. Number of hours worked	1. Direct treatment 2. Inpatient 3. Outpatient 4. Medication	The applied societal perspective is the closest to the perspective of NHS. From this perspective, both interventions had net benefits compared with the period before treatment (intervention. 1: $5,390, intervention 2: $6,736). Intervention 2 is more cost effective than intervention 1 with an average benefit: cost ratio of 2.18 versus 2.07, although the difference is not significant.	No sensitivity analysis was carried out. The statistically non-significant result can originate from the wide variations in both costs and benefits.	Low (20/32)
Hallam & Schneider, 1999	Economic study design: CA Clinical effect size data source: observational study Perspective: societal Time frame: 1 year Setting: Greater London	Country: UK Fiscal year: 1994/95 Currency: Pounds Sterling	7 different work schemes in the UK were compared, two were in the scope of the guideline: 1. VOC (prevocational training) 2. CLB (Clubhouse programme)	Chronically mentally ill participants. Service use of participants with schizophrenia did not differ significantly from the others. N=15 N=20	None	1. Direct treatment 2. Inpatient 3. Outpatient 4. Day care 5. Community care 6. Medication 7. Social care 8. Accommodation 9. Personal expenditure	Work group costs of CLB were significantly higher (£95.12/week) than the same costs for VOC (£54.6/week). The average weekly total cost for all services was also higher (£307.11) for CLB than VOC (£272.93). The net cost/placement was £3,449 for VOC compared with £6,172/placement for CLB.	The two groups were not matched. No indirect costs measured. No sensitivity analysis.	Low (10/18)
Rogers *et al.*, 1995	Economic study design: CBA Clinical effect size data source: mirror-image Perspective: societal Time frame: 2x12 months Setting: working in a university setting	Country: US Fiscal year: 1990 Currency: US Dollars	1. Supported employment for 12 months 2. Period before enrolment	N=19 37% had schizophrenia.	1. Earnings 2. Social benefits 3. Savings on service use	Direct treatment (direct, non-direct, overhead costs)	The average per client cost of the programme was $7,128/year. The average incremental benefit per client was $6,335. The incremental benefit-cost ratio is 0.89. The programme was not cost-efficient.	No statistical or sensitivity analysis. The small sample size needs to be treated with caution. The authors assume that cost effectiveness could be achieved by larger participant number (economies of scale).	Low (24/32)
Warner *et al.*, 1999	Economic study design: CCA Clinical effect size data source: controlled study	Country: US Fiscal year: 1992-1994	1. Regular Clubhouse use (4 times/ month for 6 months)	DSM-III-R diagnosis of schizophrenia spectrum	Quality of life (LQOLP)	1. Direct treatment 2. Inpatient 3. Outpatient	The mean cost per 6 months increased for intervention 2 group from $550 to $1,440 and decreased for intervention 1 ($1,500-$750) during the study period. Intervention 1	The two groups are assumed to differ in disease severity. Details of cost	High (5/18)

	with concurrent controls Perspective: not clear Time frame: 24 months Setting: community setting	Currency: US Dollars	2. Participants without access to Clubhouse service	disorder Groups matched in basic characteristics, although participants in intervention 1 assumed to be more severe than those in intervention 2. N=68 N=38		4. Community care	participants had significantly higher quality of life.	calculation are not given. No statistical or sensitivity analysis.	

Abbreviations:
CA – Cost analysis
CBA – Cost-benefit analysis
CCA – Cost-consequence analysis
CLB – Clubhouse programme
COA – Cost-Offset Analysis
CMHC – Community mental health centre
N – number of participants
RCT – Randomised controlled trial
VOC – Pre-vocational training

Crisis resolution and home treatment teams

References to included studies

Fenton, F.R., Tessler, L. & Struening, E.L. (1984) A two-year follow-up of a comparative trial of the cost-effectiveness of home and hospital psychiatric treatment. *Canadian Journal of Psychiatry, 29*, 205-211.

Ford, R., Minghella, E., Chalmers, C., *et al.* (2001) Cost consequences of home-based and in-patient-based acute psychiatric treatment: results of an implementation study. *Journal of Mental Health, 10,* 467-476.

Knapp, M., Marks, I.M., Wolstenholme, J., *et al*. (1998) Home-based versus hospital-based care for serious mental illness: controlled cost-effectiveness study over four years. *British Journal of Psychiatry, 172,* 506-512.

Weisbrod, B.A., Test, M.A. & Stein, L.I. (1980) Alternative to mental hospital treatment: II Economic benefit-cost analysis. *Archives of General Psychiatry, 37*, 400-405.

Study	Methods	Cost data	Interventions	Participants	Primary outcome(s) measured	Cost(s) measured	Results	Comments	Risk of bias (Validity scores)
Fenton *et al*., 1984	Economic study design: CA Clinical effect size data source: RCT – Fenton 1979 Perspective: healthcare provider Time frame: 2 years Setting: suburban, US	Country: Canada Fiscal year: 1975 Currency: US Dollars	1. Home treatment (crisis intervention) 2. Standard care	Schizophrenia spectrum disorder in 41.9% participants. Cost data are available separately for these participants. 1. N=31 2. N=32	None	1. Inpatient 2. Outpatient	Intervention 1 is significantly cost saving for schizophrenic participants for the 2-year study period (total mean cost: $3,770 versus $4,550 based on cost model 1). However, the cost gap narrows gradually between the two service provisions over time, and during the second year intervention 1 is more expensive ($1310 versus $580).	No sensitivity analysis. The authors question the long-term cost effectiveness of crisis intervention due to the large number of participants 'failed' on home treatment.	Low (9/18)
Ford *et al*., 2001	Economic study design: CBA Clinical effect size data source: controlled study with concurrent controls Perspective: mental health services Time frame: 26 weeks Setting: two different catchment areas in North Birmingham	Country: UK Fiscal year: 1996/97 Currency: Pounds Sterling	1. Home-based acute psychiatric treatment (for 6 weeks) 2. Hospital-based acute psychiatric treatment	23 % participants had schizo-phrenia. The two groups were matched for key variables. 1. N=58 2. N=58	Hospital bed days saved	1. Direct service (overheads, capital included) 2. Outpatient 3. Day care 4. Community healthcare 5. Social care 6. Housing	The annual cost of providing the service was £ 481,000 (4584 contacts/annum). During the first 6 weeks intervention 1 was more cost effective when comparing community service costs with savings on hospitalisation. The incremental cost-benefit ratio was £1,371: £2,283 (1:1.7) . The ratio further decreased to £351: £1,875 (1:5) during the 6-26 week follow-up period. The cost differences were statistically significant. Sensitivity analysis confirmed the result unless the cost of inpatient care per day decreases to £101.	Two different catchment areas are compared which may impose bias.	Low (21/32)

Knapp *et al.*, 1998	Economic study design: CCA Clinical effect size data source: RCT – Marks 1994 Perspective: societal Time frame: 45 months Setting: Maudsley Hospital, London	Country: UK Fiscal year: 1996/97 Currency: Pounds Sterling	1. Daily Living Programme (crisis intervention) 2. Standard in/outpatient care	Diagnosis of schizophrenia or severe affective disorder 1. N=92 2. N=97 Cost data were available at 45 months only for: 1. N=32 still in intervention 1. N=28 finished intervention 1 (ex-int. 1) 2. N=70	1. Participant and relatives' satisfaction 2. GAS 3. BPRS 4. PSE 5. SAS 6. Daily Living Skills Rating	1. Inpatient 2. Outpatient 3. Day care 4. Community healthcare 5. Social care 6. Criminal justice	Weekly cost for those continuing intervention 1 averaged £188 over the 45 months, and was significantly less than the cost of intervention 2 (£288). Intervention 1 is cost effective compared with intervention 2 in the short term (cost savings of £236/week during 1-12 months). However, it appeared to lose its cost effectiveness in the final year of the research period, when there were no further cost and outcome differences compared to ex-int. 1 or intervention 2 participants. Based on subsamples, family burden costs seemed not to differ between the two groups.	Data analysed for biasing effects – robust results.	Low (20/32)
Weisbrod *et al.*, 1980	Economic study design: CBA Clinical effect size data source: RCT – Stein 1975 Perspective: societal Time frame: 12 months Setting: urban / suburban Wisconsin	Country: US Fiscal year: not mentioned Currency: US Dollars	1. Training in Community Living 2. Standard care	Approx. 50% of participants had schizophrenia 1. N=65 2. N=65	Earnings	1. Direct treatment 2. Inpatient 3. Outpatient 4. Day care 5. Community healthcare 6. Social care 7. Social benefits 8. Care-giver costs 9. Criminal justice 10. Income forgone by care-giver	Intervention 1 involved larger direct treatment costs per participant per year ($4,798) than did intervention 2 ($3,138), but it had lower costs in every other cost component. Intervention 1 provided both additional benefits ($1,196) and costs ($797) with a net benefit of $399 per participant per year. Family burden costs did not differ between the two groups significantly.	No statistical and sensitivity analysis.	High (15/32)

Abbreviations:

BPRS – Brief Psychiatric Rating Scale	N – number of participants
CBA – Cost-benefit analysis	PSE – Present State Examination
CCA – Cost-consequence analysis	RCT – Randomised controlled trial
GAS – Global Assessment Scale	SAS – Simpson-Angus Scale

Case management

References to included studies

Byford, S., Fiander, M., Barber, J.A., *et al*. (2000) Cost-effectiveness of intensive v. standard case management for severe psychotic illness. UK700 case management trial. *British Journal of Psychiatry, 176,* 537-543.

Essock, S.M., Frisman, L.K. & Kontos, N.J. (1998) Cost-effectiveness of assertive community treatment teams. *American Journal of Orthopsychiatry, 68,* 179-190.

Ford, R., Raferty, J., Ryan, P., *et al*. (1997) Intensive case management for people with serious mental illness - site 2: cost effectiveness. *Journal of Mental Health, 6,* 191-9.

Galster, G. C., Champney, T. F. & Williams, Y. (1995) Costs of caring for persons with long-term mental illness in alternative residential settings. *Evaluation & Program Planning, 17,* 3.

Hu, T.W. & Jerrell, J.M. (1998) Estimating the cost impact of three case management programmes for treating people with severe mental illness. *British Journal of Psychiatry, (Suppl. 36),* 26-32.

Johnston, S., Salkeld, G., Sanderson, K., *et al.* (1998) Intensive case management: a cost effectiveness analysis. *Australian and New Zealand Journal of Psychiatry, 32,* 551-559.

McCrone, P., Beecham, J. & Knapp, M. (1994) Community psychiatric nurse teams: cost-effectiveness of intensive support versus generic care. *British Journal of Psychiatry, 165,* 218-221.

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Preston, N.J. & Fazio, S. (2000) Establishing the efficacy and cost effectiveness of community intensive case management of long-term mentally ill: a matched control group study. *Australian and New Zealand Journal of Psychiatry, 34,* 114-121.

Quinlivan, R., Hough, R., Crowell, A., *et al*. (1995) Service utilisation and costs of care for severely mentally ill clients in an intensive case management program. *Psychiatric Services, 46,* 365-371.

Salkever, D., Domino, M.E., Burns, B.J., *et al*. (1999) Assertive community treatment for people with severe mental illness: the effect on hospital use and costs. *Health Services Research, 34*, 577-601.

Wolff, N., Helminiak, T. W., Morse, G. A., *et al*. (1997) Cost-effectiveness evaluation of three approaches to case management for homeless mentally ill clients. *American Journal of Psychiatry, 154,* 341-348.

Study	Methods	Cost data	Interventions	Participants	Primary outcome(s) measured	Cost(s) measured	Results	Comments	Risk of bias (Validity score)
Byford *et al.*, 2000	Economic study design: CMA Clinical effect size data source: RCT – Byford 2000 Perspective: not clear Time frame: 2 years Setting: 4 inner city areas	Country: UK Fiscal year: 1997/98 Currency: Pounds Sterling	1. ICM 2. CM	86% had schizophrenia spectrum disorder: 1. N=335 2. N=332	Days in hospital for psychiatric problems (CPRS) (DAS) (QoL)	1. Inpatient 2. Outpatient 3. Day care 4. Medication 5. Social care 6. Criminal justice 7. A&E 8. Case managers/ CMHT 9. GP 10. Practice nurse 11. Accommodation	No significant differences were found in the average overall cost of care per participant between intervention 1 and intervention 2 (mean: £24,553 and £22,704, respectively). Intervention 1 has no clear beneficial effect on clinical outcomes, costs or cost effectiveness in a severely psychotic population.	Very high quality study. Sensitivity analysis confirmed the conclusion. Result is generalisable to the UK.	Low (29/32)
Essock *et al.*, 1998	Economic study design: CEA Clinical effect size data source: RCT – Essock 1995 Perspective: societal / Department of Mental Health (DMH) Time frame: 12 months Setting: 3 study sites, Connecticut	Country: US= Fiscal year: 1992 Currency: US Dollars	1. ACT 2. Standard CM	High service users, 67% with schizophrenia spectrum disorder 1. N=131 2. N=131 (Economic data are based only on 234 participant's data)	Days spent in the community	1. Direct treatment 2. Inpatient 3. Outpatient 4. Community healthcare 5. Emergency room 6. Nursing home 7. Administration of transfer payments	The direct treatment cost of intervention 1 was significantly higher by $8,221 than that of intervention 2, but average inpatient and nursing home costs were significantly lower for intervention 1 than for intervention 2. The mean annual cost per participant to society (or to DMH) was not significantly different between the groups. Intervention 1: Society: $33,473 (DMH: $23,155) Intervention 2: Society: $35,656 (DMH: $23,839) The average effectiveness – cost ratio was 9 community days / $1000 for int. 1 and 7.3 community days / $1000 for int. 2. There was no significant difference between them.	No sensitivity analysis. Large sample size increases reliability of results.	Low (19/32)

Ford *et al.*, 1997	Economic study design: CCA Clinical effect size data source: RCT – Ford (London) Perspective: health and social care system Time frame: 18 months Setting: Southwark, UK	Country: UK Fiscal year: 1990/91 Currency: Pounds Sterling	1. ICM 2. Standard care	82% had schizophrenia 1. N=39 2. N=38	1. Service engagement 2. Compliance with medication 3. QoL 4. Clinical functioning	1. Inpatient 2. Outpatient 3. Day care 4. Community healthcare 5. Social care 6. Case management 7. Residential care (overheads, capital equip-ment, real estate)	Intervention 1 did not show any advantages in QoL or clinical functioning compared with intervention 2, although compliance with medication was better for this group. Programme costs accounted for 43% of the total cost/participant for intervention 1. Total cost/participant was significantly higher for intervention 1 than for intervention 2 (£21,759 versus £8,604). Sensitivity analysis confirmed the result.	Costs could be reduced by higher caseloads. The highly professional skill mix of the study teams could have affected the average cost per client.	Low (21/32)
Galster *et al.*, 1994	Economic study design: CA Clinical effect size data source: controlled study with concurrent controls Perspective: societal Time frame: 29 months Setting: two suburban and rural Ohio counties.	Country: US Fiscal year: 1990 Currency: US Dollars	1. NS/CM 2. S/CM 3. NS/ICM 4. S/ICM 5. CST 6. Inpatient care	All SMI participants: 1. N=11 2. N=24 3. N=11 4. N=16 5. N=20 6. Not clear (ICM and CST participants had more severe illnesses than participants in the other groups)	None	1. Shelter 2. Mental healthcare 3. General medical care 4. Dental care 5. Consumption	Community care was significantly cheaper by $4200-5300/month/client than inpatient treatment. CM was significantly cheaper than ICM, and ICM was significantly cheaper than CST. Housing subsidies significantly increased the total operating costs. Adjusted mean monthly costs per participant were: 1. $748 2. $1,114 3. $1,082 4. $1,434 5. $1,730 6. $5,813-6,681	Indirect costs were not included in the analysis. Non-matched groups, although costs were adjusted for group difference. No sensitivity analysis.	Low (9/18)

Hu & Jerrell, 1998	Economic study design: COA Clinical effect size data source: RCT – Jerrel, 1995 Perspective: societal Time frame: 6 months (pre-treatment) + 18 months (treatment) Setting: large urban mental health system	Country: US Fiscal year: 1990/91 Currency: US Dollars	1. 'Intensive broker model team' (CM) 2. Clinical team programme 3. PACT	1. N=42 (73.8% schizophrenia) 2. N=40 (75.0% schizophrenia) 3. N=40 (77.5% schizophrenia)	None	1. Social benefits 2. Travel costs 3. Caregiver costs 4. Criminal and legal justice 5. Intensive mental health services 6. Supportive mental health services 7. General medical	All three interventions significantly reduced the average societal cost of caring for people with SMI compared with the baseline period (intervention 1: -$12,279=-49%; intervention 2: -$12,610=-50%; intervention 3: -$13,809=-62%). Cost savings were primarily due to reduction in inpatient and skilled nursing service costs. In the short-term intervention 2 was considered to be more cost saving, in the long-term intervention 3 was less costly.	No sensitivity analysis, no statistical details.	Low (10/18)
Johnston *et al.*, 1998	Economic study design: CEA Clinical effect size data source: RCT – Issakidis - Sydney Perspective: not clear Time frame: 12 months Setting: eastern suburb of Sydney	Country: Australia Fiscal year: 1994 Currency: Australian Dollars	1. ICM 2. Standard CM	1. N=37 (92% schizophrenia) 2. N=36 (86% schizophrenia) Outcome and costing data based on: 1. N=33 2. N=25	Level of functioning (life skills profile)	1. Inpatient and A&E 2. Outpatient 3. Day care 4. Community healthcare 5. Medication 6. Case managers 7. Crisis service 8. Rehabilitation services 9. Supported accommodation 10. Voluntary sector 11. Domestic	Significantly more participants in intervention 1 made a clinically significant improvement in functioning, but the mean cost/participant was $7,745 more for intervention 1. The cost difference was not significant. It costed $27,661/year for one additional participant to make a clinically significant improvement in functioning for intervention 1.	Capital costs of hospital facilities, accommodation costs and informal care costs were not included in the analysis. Sensitivity analysis confirmed the result. Small sample size.	Low (24/32)
McCrone *et al.* , 1994	Economic study design: CMA Clinical effect size data source: RCT – Muijen 1994 Perspective: not clear Time frame: 3 months (pre-referral) + 18 months Setting: Greenwich, London	Country: UK Fiscal year: 1992/93 Currency: Pounds Sterling	1. Community support team (CM) 2. Standard CPN support (standard care)	N=82 psychotic participants were randomised. Service use data could not be collected from 24 people over the whole evaluation period.	See Muijen *et al.*, 1994	1. CPN services 2. Hospital inpatient 3. Hospital outpatient 4. Community health services 5. Employment 6. Voluntary sector service 7. Accommodation	Total cost for intervention 2 averaged £110 more per participant than for intervention 1, although this difference was not significant. Intervention 1 was significantly cheaper in the first 6 months compared with the pre-referral period, but not after 6 months. Intervention 1 is cost effective in the short term, but not beyond.	No sensitivity analysis.	High (12/32)

McCrone et al., 1998	Economic study design: CA Clinical effect size data source: controlled study with concurrent controls – Thornicroft, 1998 Perspective: not clear Time frame: 2 x 6 months Setting: deprived area in South London	Country: UK Fiscal year: 1995/96 Currency: Pounds Sterling	1. Intensive sector (ICM) 2. Standard sector (CMHT)	Participants with psychosis 1. N=62 2. N=61	None	Day care Medication Social care Criminal justice Supported, non-supported accommodation Inpatient care Emergency clinic Sheltered work Psychologist, psychiatrist, GP, CPN, occupational therapist General healthcare Employment Informal care	The significant total cost difference between the two sectors was likely to be due to the baseline difference between the two populations and not due to the different interventions. The two programmes did not result in significant cost savings compared with the period before the introduction of the new services. Regarding the different components of healthcare costs, inpatient care was the most expensive followed by supported accommodation. GP care was relatively inexpensive (~1%).	Intensive sector clients were on average more disabled than those in the standard sector. Medication was not extensively measured. No sensitivity analysis and no adjustment for group differences.	Low (9/18)
Preston & Fazio, 2000	Economic study design: COA Clinical effect size data source: controlled study with concurrent controls (mirror-image analysis) Perspective: healthcare provider Time frame: 12 months (pre-treatment) + 12 months (treatment) Setting: metropolitan region, Perth, Australia	Country: Australia Fiscal year: not clear Currency: Australian Dollars	1. ICM 2. Standard clinic based community treatment (ACT)	Matched groups, 56% with schizophrenia 1. N=80 2. N=80	None	1. Inpatient 2. Outpatient	A steady significant reduction in total operational costs was observed for intervention 1. The reduction for intervention 2 was not significant. Between the two regions, the total cost differential was $801,475 in favour of intervention 1 for the 24 months. For intervention 1, reduction in inpatient costs far offset the increased outpatient costs.	No sensitivity analysis. Only narrow service use was costed. Intervention 1 had significantly lower outpatient contacts in the baseline period.	High (8/18)
Quinlivan *et al.*, 1995	Economic study design: CA Clinical effect size data source: RCT - Quinlivan Perspective: healthcare provider Time frame: 2 years Setting: San Diego County, US	Country: US Fiscal year: not clear Currency: US Dollars	1. ACT 2. CM 3. Standard care	High inpatient service users, 67.8% with schizophrenia spectrum disorder 1. N=30 2. N=30 3. N=30	None	1. Inpatient and A&E 2. Outpatient 3. Day care 4. Case management	Intervention 1 had significantly fewer inpatient costs ($7,232) than intervention 3 ($39,270) and had significantly more outpatient costs ($11,710 versus $2,824) - including CM costs- than intervention 3. Savings outweighed extra treatment costs. Mean yearly participant costs were: inter-vention 1: $9,471; intervention 2: $13,043; intervention 3: $21,047. ACT was the least costly alternative, although the total mean cost difference was not significant. Favoured	No sensitivity analysis. High attrition rate. Only direct healthcare costs were analysed. Baseline difference in participant characteristics between the groups.	High (8/18)

							ACT to CM, and CM to standard care.		
Salkever *et al.*, 1999	Economic study design: CA Clinical effect size data source: RCT Perspective: not clear Time frame: 2 x 18 months Setting: South Carolina	Country: US Fiscal year: not clear Currency: US Dollars	1. PACT 2. Office based case management programme	Non-emergency SMI participants, 64.6% with schizophrenia spectrum disorder. Randomised: 1. N=104 2. N=69 Economic analysis based on: 1. N=91 2. N=53	None	Inpatient	Inpatient costs were reduced in both groups compared to baseline data, with a higher decline for intervention 1 (-56% versus – 33%). The difference was not significant. PACT was more effective in reducing the probability of being hospitalised.	Attrition bias was reported. Higher baseline inpatient care use by inter-vention 1 could be related to difference in illness severity between the two groups. Very narrow perspective of analysis. Limited health economic methodology. No statistical or sensitivity analysis.	High (7/18)
Wolff *et al.*, 1997	Economic study design: CCA Clinical effect size data source: RCT Perspective: not clear Time frame: 6 months (pre-treatment) + 18 months (treatment) Setting: St. Louis Mental Health Centre	Country: US Fiscal year: 1992 Currency: US Dollars	1. ACT 2. ACT and community workers 3. Brokered case manage-ment	People with a risk of homelessness, 67.1% had schizophrenia. N=165 were randomised. CE study used: 1. N=28 2. N=35 3. N=22	1. Service contact 2. BPRS 3. Client satisfaction 4. Stable housing	1. Direct treatment 2. Inpatient 3. Outpatient 4. Social benefits 5. Vocational/educational 6. Residential	The total cost/participant estimates over the 18- month study period were: intervention 1: $49,510; intervention 2: $39,913; intervention 3: $45,076. The cost differences were not significant. ACT approaches are more effective in satisfaction, service contacts and BPRS than intervention 3. In summary, ACT approaches are more cost effective.	Significantly more clients dropped out from intervention 3 than from the other two arms, although the samples were still comparable. The analysis had reduced statistical power, and no sensitivity analysis was carried out. No criminal justice costs were included.	Low (17/32)

Abbreviations

ACT – Assertive community treatment
BPRS – Brief Psychiatric Rating Scale
CA – Cost analysis
CCA – Cost-consequence analysis
CE – Cost effectiveness
CEA – Cost-effectiveness analysis
CM – Case management
CMA – Cost-minimisation analysis
CMHT - Community mental health team
COA – Cost-offset analysis
CPN – Community psychiatric nurse
CPRS - Comprehensive Psychopathological Rating Scale
CST - Community service team
DAS – Disability Assessment Schedule
DMH – Department of Mental Health
ICM – Intensive case management
N – number of participants
NS – Non-subsidised housing
QoL – quality of life
RCT – Randomised controlled trial
S – Subsided house

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