

Enriched interventions

Introduction

Enriched interventions are treatment paradigms that are specialised for particular illness phases, or comprehensively tailored to a patient's needs. Such intervention paradigms for schizophrenia and psychosis are often combined interventions comprising both pharmaceutical and psychosocial therapies. Enriched interventions are often applied as early intervention programs in first episode psychosis or schizophrenia.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2000 that report results separately for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version was included. Reviews with pooled data are prioritised for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis¹. Reviews rated as having less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent

reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)². The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found one systematic review that met our inclusion criteria³.

- Moderate quality evidence suggests enriched interventions are more effective than standard care for improving symptom severity, with no effect for global functioning.

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Harvey PO, Lepage M, Malla A

Benefits of enriched intervention compared with standard care for patients with recent-onset psychosis: a metaanalytic approach

Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie 2007; 52(7): 464-72

[View review abstract online](#)

<p>Comparison</p>	<p>Enriched intervention programs, comprising high carer to patient ratio and antipsychotic therapy plus psychosocial treatments relevant to this phase of illness plus standard care compared to standard care alone, comprising antipsychotic therapy and case management.</p>
<p>Summary of evidence</p>	<p>Moderate quality evidence (large sample, precise, inconsistent, indirect) suggests enriched interventions is more effective than standard care for improving symptom severity, but not global functioning.</p>

Symptom severity

Measured by the PANSS or BPRS

Enriched intervention programs administered for a minimum of 6 months, or well-identified psychosocial therapy (such as family interventions, social skills training, cognitively oriented therapy, supportive therapy) targeted to the early phase of illness administered for minimum 3 months) and administered for a minimum of 3 months.

Only results from the randomised studies are reported here.

Five enriched intervention trials (EI) were compared with three standard care trials (SC), total N = 875. Follow up duration up to 2 years.

A significant benefit of enriched intervention for reducing symptom severity;

Total symptoms

Effect of EI: $d = -1.79$, 95%CI -1.95 to -1.63

Effect of SC: $d = -1.26$, 95%CI, -1.49 to -1.03

Between group comparison: $Q_B = 13.5$, $p < 0.001$

Positive symptoms

Effect of EI: $d = -1.81$, 95%CI, -1.93 to -1.69

Effect of SC: $d = -1.07$, 95%CI, -1.19 to -1.00

Between group comparison: $Q_B = 74.4$, $p < 0.001$

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<p><u>Negative symptoms</u></p> <p>Effect of EI: $d = -0.67$, 95%CI, -0.80 to -0.55</p> <p>Effect of SC: $d = -0.18$, 95%CI, -0.32 to -0.05</p> <p>Between group comparison: $Q_B = 26.2$, $p < 0.001$</p> <p>An extended sample including non-randomised studies (eleven EI and six SC, total N = 1553) reported similar magnitude and direction of effect and significance.</p>	
<p>Global function</p> <p>Measured by the GAF</p>	
<p><i>No significant difference between EI and SC;</i></p> <p>5 studies, N = 875</p> <p>Effect of EI: $d = 0.78$, 95%CI, 0.61 to 0.95</p> <p>Effect of SC: $d = 0.58$, 95%CI, 0.43 to 0.73</p> <p>Between group comparison: $Q_B = 3.02$, $p = NS$</p> <p>An extended sample including non-randomised studies (eleven EI and six SC, total N = 1,553) reported a significant benefit of EI over SC for improving global function ($p < 0.001$).</p>	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Indirect

Explanation of acronyms

BPRS = Brief Psychiatric Rating Scale, CI = Confidence Interval, d = Cohen's d and g = Hedges' g = standardized mean differences (see below for interpretation of effect size), EI = enriched intervention, GAF = Global Assessment of Function test, N = number of participants, NS = non-significant, p = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), PANSS = Positive and Negative Syndrome Scale, Q = Q statistic for the test of heterogeneity, Q_w = test for within group differences (heterogeneity in study results within a group of studies – measure of study consistency), Q_B = test for between group differences (heterogeneity between groups of studies for an outcome of interest), SC = standard care, vs. = versus

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Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small⁴.

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) which allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect⁴.

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if $RR > 2$ or < 0.5 and a large effect if $RR > 5$ or < 0.2 ⁵. InOR stands for logarithmic OR where a InOR of 0 shows no difference between groups. Hazard ratios

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measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They can provide an indirect indication of prediction, but do not confirm causality due to possible and often unforeseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (b) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula⁴;

$$I^2 = \left(\frac{Q - df}{Q} \right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed⁶.

|| Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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References

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