Interventions for the prevention of psychosis

Paul French
Mrazek and Haggerty (1994) have discussed the idea of preventative interventions and identified three prevention strategies. These are:

- **Universal**: all of the population
- **Selective**: specific risk factors
- **Indicated**: minimal, but detectable, signs of psychosis
Buckingham Project UK
Falloon 1985

• GP’s trained to identify early psychosis symptoms

• Referred to specialist team for assessment

• Those with positive early symptoms treated with low dose medication, crisis and family intervention

• Outcome: 10 fold reduction in schizophrenia over 4 years

• But several methodological shortcomings (small n)
Prevention of psychosis

McGorry et al 2002 Archives of General Psychiatry

% making transition to psychosis

- 40%
- 35%
- 30%
- 25%
- 20%
- 15%
- 10%
- 5%
- %

Needs based Tx
Specific interventions

n=58

6 Months

12 Months
Prime Study

- A double-blind comparison of olanzapine with placebo
- Prodromal symptoms were measured by the SOPS
- N=60, and the median age was 16 years
- 65% males
- 93% of the patients had mild but definable psychotic symptoms (attenuated symptoms)
- The average GAF was 42.
- The dose of olanzapine included 5, 10, and 15 mg strengths.
- At 1 year, 15 of the 60 patients developed a full psychotic syndrome.
- Of the converters, 8 of 15 converted within the first month from baseline.
A single blind randomised controlled trial Cognitive Therapy vs. Treatment As Usual
Preliminary Results from 12 months Follow-up
Morrison, French et al 2004

Transition rate in % per group

<table>
<thead>
<tr>
<th>Transition criteria</th>
<th>PANSS P-scores</th>
<th>Prescription of antipsychotics</th>
<th>DSM-IV Diagnosis</th>
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<tbody>
<tr>
<td>CT (n=35)</td>
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<td>TAU (n=23)</td>
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A single blind randomised controlled trial
Cognitive Therapy vs. Treatment As Usual
Results from 36 months Follow-up
Morrison, French et al 2006

![Chart showing PANSS P Scores, Antipsychotic Medication, and DSM IV comparison between CT and TAU]
EDIE 2 MRC Funded Clinical Trial

- EDIE 2 - a randomised controlled trial of Cognitive Therapy compared to usual treatment for the prevention of transition to psychosis.
- 288 participants at ultra high risk across 4 centres in the United Kingdom.
- Centres are Manchester, Glasgow & Clyde, Birmingham/Worcester, East Anglia / Cambridge.
Consort Criteria

- Referrals: 634
- Eligable, consenting patients
- Baseline -1
  - Baseline 0
- Randomize: N = 288
- Follow up
- CT up to 6 months Monitoring: 144
- Monitoring: 144
- Exclusions
- Month 1, Month 2, Month 3, Month 4, Month 5, Month 6, Month 9, Month 12, Month 15, Month 18, Month 21, Month 24
Consort Criteria

EXCLUDED (n=346)
Did not meet entry criteria (n=321)
Due to antipsychotic medication = 36
Due to current psychosis at initial baseline = 91
Due to current psychosis at second baseline = 29
Due to being sub-threshold for ARMS = 110
Due to not being help-seeking = 45
Other = 10
Lost contact before assessment complete (n=16)
Declined involvement before assessment complete (n=9)
Clinical features

- 53.8% endorsed feeling moderately anxious or depressed
- 33.6% endorsed feeling extremely anxious or depressed
SCID

- 33% of the cohort did not receive a SCID diagnosis
- 33% received a diagnosis of Major Depressive Disorder
- 20% Panic Disorder
- 15% Social Anxiety Disorder
- 4% Post Traumatic Stress Disorder
- 9% Generalised Anxiety Disorder
- 2% Bipolar Disorder
Cognitive Therapy

- N = 144
- Mean number of sessions = 9.11 sessions (s.d.=6.69; range 0 to 26)
- Adherence to CT
  - 9/144 (6.25%) not attending any sessions
  - 108/144 (75%) receiving at least 4 or more sessions
- Fidelity to the therapy model (assessed using competency and adherence scales in relation to audio recordings of 80 therapy sessions)
  - 90% of rated sessions scored over the threshold for competency and 93.3% met criteria for therapy that was adherent with the manual
Primary outcomes BMJ 2012

• Transition to psychosis
  • Effect of CT was non-significant (proportional odds ratio 0.73, 95% CI 0.32 to 1.68, p=0.45).

• Severity of psychotic symptoms (centred on month 12)
  • Difference between treatment arms at 12 months (CT minus Control) was estimated to be -5.05 (95% CI -9.11 to -0.99), which was statistically significant (p = 0.015)

• Distress from psychotic symptoms (centred on month 12)
  • Estimated difference at 12 months was −3.03 (95% CI -6.95 to +0.94; p=0.14).
Meta analyses
11 trials including 1246 participants and eight comparisons were included. Median sample size of included trials was 81 (range 51-288). Meta-analyses were performed for transition to psychosis, symptoms of psychosis, depression, and mania; quality of life; weight; and discontinuation of treatment. Evidence of moderate quality showed an effect for cognitive behavioural therapy on reducing transition to psychosis at 12 months (risk ratio 0.54 (95% confidence interval 0.34 to 0.86); risk difference −0.07 (−0.14 to −0.01). Very low quality evidence for omega-3 fatty acids and low to very low quality evidence for integrated psychotherapy also indicated that these interventions were associated with reductions in transition to psychosis at 12 months.

• Conclusions Although evidence of benefits for any specific intervention is not conclusive, these findings suggest that it might be possible to delay or prevent transition to psychosis. Further research should be undertaken to establish conclusively the potential for benefit of psychological interventions in the treatment of people at high risk of psychosis.
A search conducted according PRISMA guidelines found 10 studies that reported 12 month follow-up data, and 5 studies with medium-term follow-up varying from 24 to 48 months. 12 month and 24 - 48 month results on transition to psychosis were selected. The trials were assessed for quality. Random and fixed effects meta-analyses were conducted.
The quality of the papers varied from poor to excellent. Overall the risk reduction at 12 months was 54% (RR=0.463 (95%CI:0.33-0.64)) with a Number Needed to Treat of 9 (95%CI:6-15). Although the interventions differed, there was only mild heterogeneity and publication bias was small. All sub analyses showed efficacy. Five studies with 24 to 48-month follow-up still showed a risk reduction of 37% (RR=.635 (95%CI:0.44-0.92)) with a Number Needed to Treat of 12 (95%CI:7-59). Sensitivity analysis excluding the weakest study shows that the findings are quite robust.

Early detection and intervention in people with an ultra-high risk of developing psychosis prevents or postpones first episode psychosis. Antipsychotic medication showed efficacy, but more trials are needed. Omega-3 fatty acid needs replication. Integrated psychological interventions need replication with more methodologically sound studies. The findings regarding CBT seem robust, but the 95 percent confidence interval is still very large.
Meta Analysis
Hutton and Taylor 2013

• The relative risk (RR) of developing psychosis was reduced by more than 50% for those receiving CBT at every time point [RR at 6 months 0.47, 95% confidence interval (CI) 0.27–0.82, p=0.008 (fixed-effects only: six randomized controlled trials, n=800); RR at 12 months 0.45, 95% CI 0.28–0.73, p=0.001 (six RCTs, n=800); RR at 18–24 months 0.41, 95% CI 0.23–0.72, p=0.002 (four RCTs, n=452)].

• Conclusions. CBT-informed treatment is associated with a reduced risk of transition to psychosis at 6, 12 and 18–24 months, and reduced symptoms at 12 months.
Early Detection and Cognitive Therapy for People at High Risk Developing of Psychosis

A TREATMENT MANUAL

Paul French and Anthony P. Morrison
What are the vital factors of CBT?


- The causal effect of each aspect of therapy on outcome at 12 month follow-up is investigated individually. Baseline covariates by randomisation group interactions are considered as instruments. To select the most effective instruments the LASSO (Least Absolute Shrinkage and Selection Operator) method is used, this has been shown to be effective when choosing from a selection of instruments when no instrument has been set prior to the analysis. The analyses allow for a direct effect of randomisation to CBT even if the particular aspect of therapy in question was not received. All analyses are adjusted for the baseline measure of symptom severity and bootstrapped with 1000 replications.

- What it means is that these things are important
- Over 4 sessions
- Homework
- Behavioural experiments
- Formulation
NICE Guidelines for Psychosis 2014
NICE 2014
Psychosis and schizophrenia in adults

• Preventing psychosis
• If a person is considered to be at increased risk of developing psychosis
• offer individual cognitive behavioural therapy (CBT) with or without family intervention and
• offer interventions recommended in NICE guidance for people with any of the anxiety disorders, depression, emerging personality disorder or substance misuse. [new 2014]
Conclusion

- It is feasible to identify people at high risk of psychosis
- At risk of psychosis and definitely struggling
- CBT in ARMS reduces transition
- CBT in ARMS may reduce transition to multiple disorders or minimise long term disability

Thank you