Prevention of psychosis with a cognitive behavioural intervention in help-seeking young people with an at risk mental state for developing psychosis

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The study aims to reduce the number of transitions into psychosis in a group of people who are in an at risk mental state. This is done with a specialised cognitive behavioural therapy.Other aims are:1) Implementation of screening of all people in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON31359

Source
ToetsingOnline

Brief title
EDIE-NL
Early Detection Intervention Evaluation - Netherlands

Condition

- Other condition

Synonym
at risk mental state, psychosis

Health condition

mensen met een therapievraag bij de ambulante ggz met een hoogrisico op het ontwikkelen van een psychose

Research involving
Human

Sponsors and support

Primary sponsor: Parnassia (Den Haag)
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: CBT, prevention, psychosis

Outcome measures

Primary outcome

Primary outcome:

Rate of transitions to psychosis as defined in with the CAARMS criteria. The prescription of antipsychotic medication will be considered as a transition as well.

At the transition to psychosis the PANSS and the PSYRATS will be administered and the SCID interview to diagnose the patient.

Secondary outcome

Secondary outcome measures and other products:

1) BDI (Beck Depression Inventory)

2) SIAS (Measure of social anxiety)

3) EQ5D (Health Questionnaire)

4) PBIQ-R (personal beliefs about illness)

5) MANSA (quality of life)

6) Medication check

7) Genetic material for genotyping at a later point in development. We expect

higher transitions rates in people with the val/val genotype of the COMTval158met polimorsime, and the BDNFval166met met/met genotype.

The first six measures are identical to the EDIE-2 study that now runs at Manchester, Birmingham, Glasgow, Cambridge and Norfolk. At the transition to psychosis the PANSS and the PSYRATS will be administered and the SCID interview to diagnose the patient.

8) Implementation of screening of all people in the age range from 18 to 35 that seek psychotherapeutic help at the mental health services in The Hague with the Prodromal Questionnaire.
9) Implementation of the CAARMS in the services in The Hague and Amsterdam to discriminate between normal, ARMS, and psychosis.
10) Implementation of a CBT intervention that is specifically adapted to treat ARMS with a co-morbid disorder.
11) Develop materials and training packages to facilitate spread of these kinds of services to other mental health facilities.

Study description

Background summary

Schizophrenia has an unfavourable course in 80 percent of the cases. These patients are either chronically psychotic or have a relapsing course. The relapses cause high costs in mental health services because of multiple rehospitalisation and continuous care. The cognitive deficits and negative symptoms cause an unemployment rate of more than 80 percent and an unmarried status with little offspring. Prior to the first psychotic episode 80 to 90 %

of the patients have experienced retrospectively symptoms of escalating severity over 1 to 2 years; the so called prodromal phase.
Prospective longitudinal studies have found that Psychotic-like experiences (PLEs) are quite prevalent in the population. These PLEs are transient in nature and only develop into florid psychosis when persistent and combined with other risk factor such as urbanisation, trauma or cannabis use.
Studies have examined the possibility of detecting individuals in the prodromal stage, prior to the development of florid psychosis. Mc Gorry and colleagues have developed operational criteria to identify a group among help-seeking young people of an 'at risk mental state' (ARMS). Such an ARMS makes this group at ultra high risk for developing a psychosis within a year time.
This ARMS group is divided into subgroups. The first group is the group with a genetic endowment. When a person declines in social functioning and a first degree relative has schizophrenia or the person itself has the diagnose of schizotypy, then the person is at risk. This group forms about 15% of the total ARMS group. Another small group of about equal size is the group that has had Brief Limited Interval of Psychotic Symptoms (BLIPS). These transient psychotic symptoms lasted less then a week. The largest subgroup of about 70 % is formed by the group with attenuated psychotic symptoms. These groups could well be considered as different endophenotypes and genotyping might be of prognostic value. The ARMS group develops psychosis in 13 to 54 percent of the cases within a year. The average transition rate is 37 percent in a year. The ARMS group comprises many late prodromal patients. The CIDI psychosis section can detect an ARMS group with high transition rates as well. Two PLEs on the CIDI with a emotional disorder has a transition rate of 40 percent. Based on these findings the question arose whether effective interventions could be developed that would prevent or delay the transition into florid psychosis in the late prodromal state.

Three innovative studies have been undertaken to intervene in the ARMS group to reduce the transition rate into psychosis. The Melbourne study compared needs-based intervention with low dose risperidone (1.3 mg/d) and CBT combined (n=67). The results were that 35% of needs-based intervention developed a psychotic episode versus 10% in the risperidone CBT group. The Manchester trial compared treatment as usual with CBT (n=58). In the TAU group 26% developed a DSM-IV psychosis diagnosis while the CBT group showed only 6 % transitions into psychosis. The Copenhagen trial compared integrated treatment with standard treatment (n=79). After 12 months 33% was diagnosed with psychotic disorder in schizophrenia spectrum in the standard care group and 8% in the integrated treatment group. These are encouraging results in the short term. The reduction in relative risk (RRR) varies from 46% to 78% at 9 to 12 month follow-up. The Copenhagen study also has two year follow-up data that show an RRR of 48%. The three year follow-up from the Manchester trial shows a RRR of 34%, which was no longer statistically significant.

As persistence of PLE is a risk factor for psychosis, the reduction of this risk factor could prevent transition to psychosis in future. At this moment,

CBT and other psychological interventions are capable to reduce the risk for a psychosis in the short term. Although this is only a delay for some patients, a health gain of one year of more is a significant finding in a devastating condition such as schizophrenia.

The specificity of the intervention is still not known. Melbourne combined CBT with anti-psychotic medication, so the relative contribution is unclear. The Copenhagen study provides a whole package of interventions which still has to be sorted out. A replication of the Manchester study seems the best option. The intervention has the largest effects sizes reported so far and is directed at thinking styles that form the basis of the development of psychosis. A manualised protocol has been developed.

The innovative part of this study is to examine the effectiveness of a specific intervention targeted at the prevention of florid psychosis in both a population based sample and a clinical sample. This will take place in help-seeking young people from 18 until 35 years of age.

Research has shown that people with ARMS have a current axis 1 disorder in 76 percent of the cases. We will not miss many of the patients with ARMS with our selection strategy to start in help-seeking people. Also the transition rate to psychosis is higher in people with an axis 1 disorder (30%) compared with those who without an comorbid disorder (13%).

Study objective

The study aims to reduce the number of transitions into psychosis in a group of people who are in an at risk mental state. This is done with a specialised cognitive behavioural therapy.
Other aims are:
1) Implementation of screening of all people in the age range from 18 to 35
a. that seek psychotherapeutic help at the mental health services in The Hague and
b. that are referred to a specialised clinic on suspect of development of psychosis with the Prodromal Questionnaire.
2) Implementation of the CAARMS in the services in The Hague and Amsterdam to discriminate between below threshold ARMS, ARMS, and psychosis.
3) Implementation of a CBT intervention that is specifically adapted to treat ARMS with a co-morbid disorder.
4) Test the reduction of persistence of PLEs over an 18 month period.
5) Test the transition rates of different genotypes
6) Develop materials and training packages to facilitate spread of these services to other mental health facilities.

Study design

All consecutive referrals to the mental health services in the age from 18 to 35 years in The Hague (PsyQ) and the referrals from the mental health services of Amsterdam to the specialised Adolescent Clinic in the age of 18 to 35 years will be screened with the Prodromal Questionnaire. In the general population the prevalence of one psychotic feature is about 17 percent. In the help seeking population this prevalence will be higher and is estimated at 25 percent. The prevalence of ARMS is estimated at 3.5 percent. This is a conservative estimate as Yung found 29 percent of the general help-seeking population of young people aged 14 to 25 met the ARMS criteria [10]. During two years about 6000 people in the age range from 18 to 35 years seek help at PsyQ for a psychic problem. About 1500 people will self-report at least one psychotic feature, 210 will be in an ARMS and have a co-morbid disorder. This group will be selected for the intervention study. All estimates are based on relatively small studies and the security intervals are to be regarded as quite large. For this reason the catchment area is elaborated with Amsterdam. The Adolescent Medical Centre has experience in screening people with an at risk mental state as they are involved in the DUPS study.

In the selected group, the transition rate will probably be 35 percent to psychosis over an 18 month period and about 40 percent will have persistent PLEs. The intervention will aim top reduce the transitions to 17 percent and the persistence as an important risk factor for later transition to 20 percent.

Furthermore, measurements have been matched with the EDIE-2 trial. A comparable study in Britain in Manchester, Birmingham, Glasgow, Cambridge and Norfolk. This will allow us to compare the results of the UK trial and the Dutch trial. It would be possible for certain analysis to combine data to allow greater statistical power. We will request permission with the sponsor of the UK study who owns the British data. The next meeting will be end of February 2007.

Power calculation:
The only study that used a help-seeking population fond a 24 percent transition in 12 months[11]. We will calculate power on an expected transition rate of 35 percent over 18 months. To be conservative power we expect a 50% reduction in the transitions which is smaller than the reductions reported thus far. The sample we need for a 2-tailed test of the proportions with an alpha of .05 and a power of .80 is 2 x 93 for reduction of the transition rate from 35 percent to 17 percent over an 18 month period and 2 x 82 for the persistence of PLEs. With 20 percent drop-out over 12 months, we need to include 240 persons into the trial. The refusal rate is expected to be very low as was the case in the Manchester trial as people are seeking help and get an additional help offer. Both research sites will (The Hague and Amsterdam) recruit 60 ARMS patients each year.

Randomisation: The inclusion period will stop after 240 young people have consented to participate in the study. These are randomised over the cognitive behavioural intervention or treatment as usual.

Time table:
Month 0 to 2: Preparation of the sites. Training of the CAARMS raters. Training of the therapists in the targeted CBT protocol.
Month 3 to 26: Inclusion of patients. 6 month intervention stage (targeted CBT or TAU and 18 month since inclusions follow-up).
Months 27 to 44: Last therapies of 6 month envelop and 18 month follow-up period.
Months 45 to 48: Analysis and report.

Intervention

Intervention: The effective intervention is the Dutch translation of the protocol as developed by French and Morrison and was demonstrated to be effective. This is a formulation driven cognitive behavioural intervention directed at reducing symptoms and normalising psychotic-like experiences and preventing that an catastrophising appraisal will occur. Such an appraisal is a next step on the road to psychosis. The control condition is treatment as usual at PsyQ in The Hague and monitoring in Amsterdam.

Study burden and risks

N.A.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

At Risk Mental State (see page 7 and 8 of protocol)
Age 18 to 35 years

Exclusion criteria

current or previous receipt of antipsychotic medication
moderate to severe learning disability; organic impairment
non-Dutch speaking

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-12-2007

Enrollment:	240
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	21-08-2007
Application type:	First submission
Review commission:	METIGG: Medisch Ethische Toetsingscommissie Instellingen Geestelijke Gezondheidszorg (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL17123.097.07