Cost effectiveness of a collaborative stepped care intervention for anxiety disorders in the primary care setting.

Published: 29-04-2008
Last updated: 10-05-2024

Aim of the studyThe aim of this study is to evaluate effects and costs of a collaborative stepped care approach in theprimary care setting for patients with prevalent anxiety disorders PD and GAD compared with treatmentas usual.Question of the study...

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

Summary

ID

NL-OMON31723

Source
ToetsingOnline

Brief title
CC:PAD

Condition

- Psychiatric disorders

Synonym
Generalised anxiety disorder, panic disorder

Research involving
Human

Sponsors and support

Primary sponsor: Zorgonderzoek Nederland (ZON)
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Anxiety disorder, Collaborative stepped care, Cost effectiveness, Primary care

Outcome measures

Primary outcome

*outcome parameters: Baseline measurememts: The mini-International Neuropsychiatric Interview (MINI 28;29) is administered for the classification of symptoms and the BAI for measurement of severity.

Primary outcome measure is reduction of GAD or PD symptoms as measured by the BAI. Secondary outcome measures are remittance of GAD or PD as measured with MINI and the BAI (score below 10; range 0-61), adherence and compliance, and the Patient-Doctor Relationship Questionnaire (PDRQ-9).

The number and intensity of functional somatic complaints a patient is experiencing is assessed with the LKV (Lichamelijke Klachten Vragenlijst),(33) the Somatosensory amplification Scale(34) and the Whitely Index.(35) Health care use is assessed by the Scale for Medical Utilisation of Health Services.

Secondary outcome

*Economic evaluation: The aim of this economic evaluation is to assess the cost effectiveness of collaborative stepped care in primary care of the treatment of GAD/PD. The

results will be expressed as
cost per unit of the BAI and as cost per Quality Adjusted Life Year (QALY). The economic evaluation will
be undertaken from a societal perspective. Hence, all relevant effects and costs due to resource
utilisation within the healthcare (direct medical costs) and costs due to production losses (productivity
costs) will be included. The costs will be estimated in line with the Dutch guidelines for cost calculations
in health care.(38)The TiC-P will be used for collecting data on health care utilisation as well as
production losses.(36,37). The TiC-P is commonly applied in economic evaluations of treatments in
mental health care. For instance, the TiC-P was recently used in a large naturalistic trial on the
cost-utility of brief psychological treatment for depression and anxiety.(69) Furthermore, we will add a
module of the Prodisq, a questionnaire for collecting data on production losses of paid work. Calculating
the total direct medical costs, the total number of medical contacts (GP visits, outpatient visits, use of
medication, etc.) will be multiplied by unit costs of the corresponding health care services. Reference
unit prices of the corresponding health care services will be applied, and

adjusted to the year of the
study according to the consumer price index.(38) Since the collaborative
stepped care model is new kind
of intervention, a unit price per session is currently not available. To
determine a reference price for this
intervention, a micro-costing study will be performed. Therefore, we will
perform measurements of time
for face-to-face contacts with the patient as well as indirect time per
contact. Indirect time per contact
may consist of e.g. mutual consultations contacts between GP, casemanager
and/or psychiatrist.
Furthermore, we will estimate overhead costs based on the financial information
of at least 3 GP
practices. This will result in an estimate of the actual costs per contact. The
unit cost estimate per
contact will be used as a reference price per contact for the collaborative
care intervention. For reasons
of comparison we will also estimate the costs for a GP contact in the CAU
study-arm applying a similar
micro-costing methodology. The number of contacts at the GP will collected at
the participating sites.
The second section of the TiC-P includes a short form of the Health and Labour
questionnaire (HLQ) for
collecting data on productivity losses.(78) The Short-Form HLQ (SF-HLQ)

consists of three modules that
measure productivity losses: absence from work, reduced efficiency at work and difficulties with job
performance. The number of days absent from work and the actual cost of hours missed at work due to health-related problems are valued according to the average value added per worker by age and gender
per day and per hour, respectively. If respondents indicate that they have been absent for the entire
recall period, data will be collected from the time when the period of
long-term absence started. This
additional information will be used to value the production losses according to the friction cost
method.(66,67) The friction cost method takes into account the economic circumstances that limit the
losses of productivity to society, which are related to the fact that a formerly unemployed person may
replace a person who becomes disabled.(67) Data of the Prodisq questionnaire will be used for
assessing job- and branch characteristics. At baseline, several demographic characteristics (e.g. age,
gender, educational level and work status) will be assessed. At all measurements we will assess the
health-related quality of life, use of medical resources and productivity loss using respectively the

EuroQol questionnaire (EQ5D)(44,45) and the *Trimbos and iMTA questionnaire on Costs associated with Psychiatric illness' (TiC-P)(36). This measures costs every three months. Additionally, data concerning costs will be taken from the GP files. Treatment in the CAU group is assessed in patients and GPs with the Scale Assessing Medical Utilization of Health Services. For the economic evaluation, the effects will be measured according to utility scores. Quality of life is assessed by the *EuroQol* (EQ-5D).(79) The EQ-5D is a validated tool for measuring general health*related quality of life. The EQ-5D descriptive system consists of five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with three levels (no problems, some problems, and extreme problems), thus defining 243 (35) distinct health states. A recent study in the Netherlands measured and valuated the EQ-5D, resulting in the *Dutch EQ-5D tariff*, which will be used to calculate utilities for EQ-5D health states for the cost-utility analyses of Dutch health care programmes and treatments.(80) In addition to the clinical outcome parameters, the utility scores will supply information

about the impact on the general health related quality of life of the patients in both treatment groups.

Furthermore, the results can be compared to a broad range of other health care interventions, also outside the field of mental health care. The cost-utility will be evaluated by relating the difference in direct medical costs per patient receiving collaborative care or CAU to the difference in terms of QALYs gained, which yields a cost per QALY estimate. Furthermore, we will also estimate the cost per QALY, including the productivity costs.

Calculating the total direct medical costs the total number of medical contacts (outpatient visits, hospital length of stay, use of medication, etc.) will be multiplied by unit costs of the corresponding health care services. Reference unit prices of health care services will be applied and adjusted to the year of this study by using the consumer price index.(69) As secondary analysis, the cost utility will be evaluated by relating the difference in direct medical costs per patient receiving collaborative care or CAU to the diffe-rence in terms of BAI and Quality Adjusted Life Years gained (QALY), to yield a cost per unit (BAI) and QALY estimate. Furthermore, we will also estimate the cost per unit (BAI)

and QALY including the

productivity costs. Cost utility, next to the improvement of severity of

symptoms, the cost utility of

collaborative care compared to CAU is assessed in this design. Therefore, an

estimation of the direct

medical costs and the costs due to production losses (productivity costs) is

made. In case of missing

data on costs and/or effects, and the additional uncertainty it introduces, we

will use multiple

imputation.(47) We will use the Monte Carlo Markov Chain (MCMC) approach to

impute the missing

values. The uncertainty will be assessed using bootstrapping, and the results

will be presented in

acceptability curves.(82)

Study description

Background summary

*describe the healthcare problem that underlies this proposal: Nowadays the insight has come that common mental disorder should best be approached by a collaborative stepped care approach with evidence based components.(63-65) Evidence based Guidelines have been developed for several mental disorders, including anxiety disorders.(1-5) Although many Dutch GPs have followed courses into the diagnosis and treatment of anxiety disorders, the amount in which these guidelines are followed is insufficient(6) in terms of recognition(7) and treatment of mental disorders in primary care(8) with

consequent overburdening of the health care system.(9,10,59) This problem could be solved with more
efficient treatment according to collaborative stepped care
principles.(11-13,52-59) The aim of this study
is to implement and evaluate an organization of care in the primary care
setting in terms of collaborative stepped care for anxiety disorders and to
evaluate its cost effectiveness. *what is the disease subject of
this proposal: In this proposal Generalized Anxiety Disorder (GAD) and panic disorder (PD) are targeted
because they are the most prevalent and most costly mental disorder in terms of societal impact(60,61)
that can be treated effectively(56,52-53,58)in the primary care
setting,(14,15)if recognition and treatment
is enhanced (1-3,5-7). *what is the group of patients, targeted in this
proposal: The group of patients at
which this study targets is primary care patients diagnosed with GAD and/or PD, aged older than 18, not
under current psychiatric teatment, and having sufficient knowledge of the Dutch language to fill in the
questionnaires. To enhance the external validity of the RCT no other exclusion criteria will be applied. *if
applicable in relation to the target group, indicate how variations in sex, age
or cultural background are
taken into account: Although women suffer from anxiety disorders more often than men,(14-16) both
sexes will be sufficiently represented in the sample to consider gender as a variable in the analysis. The
same holds for age and cultural background. *describe the usual care in the Netherlands for the
(sub)group of patients involved: If the anxiety disorder is recognized, the GP should follow the guideline
of the Dutch College of General Practitioners (NHG standard)(3) for anxiety disorders. Many GPs feel
incapable to deliver the cognitive behavioural interven-tions described in these guidelines.(19) Almost
half of the patients receive antidepressant medication instead or are referred to psychiatric
care.(6,8,9,19)In summary, Care As Usual often implies suboptimal care, including referral to medical
specialists to exclude somatic disease. *who are involved in the usual care, and what is their
participation in this proposal: GPs give the usual care and participate in this proposal via the LUMC (The
Hague region)and VUMC (Amsterdam region) departments of primary care. In The Hague the local GPs
collaborate with the regional mental health care institution Parnassia. The same holds for GPs in the

south/west region of Amsterdam, who collaborate with the regional mental health care institution GGZ
Buiten Amstel. *describe your motivation for the intervention, subject of this proposal and motivate the
effectiveness of the intervention. The intervention is a collaborative stepped care intervention for GAD
and PD in the primary care setting. The algorithm is built up from 3 interventions that have separately
been proven effective and feasible in the primary care setting.(17,19):
manual-guided self help protocol,
three-session cognitive behavioural approach in which the patient scores his symptoms and evaluates
them with the GP, and an algo-rithm of antidepressant medication for anxiety disorders prescribed by
the GP.(17) Globally, minor interventions precede more invasive interventions. All subsequent steps
have been proven effective in randomized clinical trials performed by this research group.(17,19)
Evidence exists that such a stepped collaborative care model for anxiety disorder is cost-effective in the
GP setting.(54,55,57)However, this model is not yet used in the Netherlands. This approach could
improve effectiveness and costs of care for GAD and PD. *if applicable in relation to the intervention, pay
attention to compliance: In the collaborative care framework, compliance and adherence enhancing
techniques are essential(see further). This method has been proven effective in an RCT by the research
group before.(17,20)

Study objective

Aim of the study
The aim of this study is to evaluate effects and costs of a collaborative stepped care approach in the
primary care setting for patients with prevalent anxiety disorders PD and GAD compared with treatment
as usual.
Question of the study is:
Is a 12-24 weeks collaborative stepped care approach applied by the GP in the primary care setting
more (cost-)effective on improvement of GAD and PD compared with care as usual in the primary care
setting in the short term (6 months) and long-term (12 months)?

Study design

Clinical study
*preliminary studies by applicants on the subject of this proposal: By Van der Feltz e.a., a multi center
randomized trial has been performed in primary care in which 3 session cognitive behavioral techniques
and an antidepressant algorithm, both performed by the GP, in a collaborative stepped care framework,
were effective in patients with PD (panic disorder) and/or GAD (generalised anxiety disorder) presenting
with Medically Unexplained Medical Symptoms (MUMS). Effect sizes were between 0.80 and 2.60
Cohen*s delta.(17,20) In another RCT, Van Boeijen e.a. established effectiveness of a manual guided
self help method for patients with PD and/or GAD.(19) In this RCT, the pre-post effect size of the guided
self-help manual was 0.8 on the main outcome measure the STAI. Van der Feltz e.a. set up a
nationwide program in which collaborative care techniques such as contracting and compliance and
adherence improving techniques are implemented in primary care settings.(6) Now is the time to
establish cost effectiveness of the combined collabo-rative stepped care strategy for GAD and PD.
*Design: Two armed cluster-randomized pragmatic clinical trial, with randomization between primary
care practices in order to prevent contamination and thus dilution of the effect.(26)A flow chart is
included in the appendix.
*sample size calculation (motivate assumptions) and feasibility of recruitment. In this study, cluster randomisation between GP practices, and a MLA where GPs are the first hierarchical level and patients
are the second level, is used. The BAI is the primary outcome measure. Power calculation: The power
calculation is for a MLA analysis. sample size calculation/data analysis: In studies examining the effect
size of monotherapy with antidepressants for PD, short term effect sizes of 0.50 and long term effect
sizes of 0.70 were found.(75,76) In the study evaluating effectiveness of a two step protocol, effect sizes
between 0.80 and 2.60 were found depending on the outcome measure.(17) Because in this study the BAI was not used as main outcome measure, an estimate of the clinically relevant difference should be
made. In this study, we would like to be able to detect a clinically relevant difference in terms of a
duplication of the effect of monotherapy, that is an effect of 1.2, as difference with the CAU on the
continuous measure of the BAI. In unpublished NESDA data, 10 points decrease on

the BAI, which is a
difference of * SD, may be considered a clinically relevant difference.(48) A variance of 1.15 as
intraclass correlation would be acceptable as presumption if the contrast between the experimental
conditions would be rather high, that is if the practiced CAU would be different than the collaborative
care intervention as performed in the different practices. Consequently, the sample size should be 1.12 x
60,(31) that is 2 x 67 completers. We estimate a drop out rate of 30% and must include 2 x 87 patients in
the study. (alpha = .05; power 0.90).
*data-analysis and presentation / synthesis: Intention-to-treat analysis will be performed by MLA with
GPs in the primary hierarchical level. If at this level differences in outcome will be found, age, gender
and experience, and practice characteristics will be explored as variables influencing the outcome.
Subsequently, at the secondary hierarchical level, patient characteristics influencing the outcome will be
explored. To control for possible skewness in the randomised groups as far as distribution of
confounders is concerned, propensity scores will be calculated. Possible confounders such as age,
gender, and immigrant status, will be taken as variables in the analysis. In case of missings, two
methods of analysis will be used. The methods that are available to deal with the missing data of
patients who withdraw can be distinguished into so-called naïve and principled methods.(72) Naïve
methods aim to provide an estimate of the mean costs by omitting patients, e.g. complete case analyses
or LOCF. Another method is to use MLA and to cluster the outcome measures per measurement: all T1
measurements are taken together, al T2 measurements, etc, and they are compared to each other as
clustered outcome measures. This is an elegant method to deal with incidental missings that did not lead
to complete loss to follow up.In this trial, this method will be used to account for missings in the
effectiveness analysis. An advantage of multilevel analysis of longitudinal data is the ability to handle
missing data. Because multilevel regression models (in contrast to traditional analysis of variance of
repeated measures) do not assume equal number of observations or even fixed time points all cases
remain in the analysis increasing the precision of the estimates and the power

of the statistical tests.
Attrition in longitudinal designs normally is not random. In longitudinal designs information about the
dropouts from earlier measurements in normally available. It may be assumed that, conditional on these
variables, the missingness is random. It is not assumed that the missingness is completely independent
of all other variables. Multilevel modeling of repeated measures with missing data assumes that the data
are missing at random, provided that Maximum likelihood estimation is used. This is in contrast to the
complete cases method in traditional analysis of variance of repeated measures, which assumes that
data are missing completely at random. Principled methods aim to provide an unbiased estimate of the
variance by taking account of the missing observations. Currently, principled methods e.g. multiple
imputation are the standard to deal with missing data in economic evaluations. The principled methods
take into account the special characteristics of cost data that affects their analysis.(69) Hence, we will
apply a principled method for dealing with missing data in our economic evaluation.
.time schedule: Preparation: 6 months. Subsequent to the approval of the Medical Ethical Board PCP
practises are recruited and GPs are trained. Inclusion and intervention phase: 24 months. Analysis and
writing: 6 months. Expected inclusion: every two months, in both regions 5-6 completers are expected to
be included, leading to 134 completers during the 24 month inclusion phase. The study will last 3 years.
Baseline measurements take place before inclusion (T0), follow up at 3 months,(T1) 6 months (T2), 9
months(T3) and 12 months(T4).

Intervention

*Intervention(s): Evidence exists for effectiveness of stepped care in PD and GAD,(68) more specific for
two of the three proposed steps. The effect size of the combined step 2 and three ranged between 0.80
and 2.60 in a former study of the research group.(17)Evidence exists as well that the combination of self
help with CGT is effective in treatment of PD and/or GAD in primary care.(74)A three-step algorithm is
favoured because of good results with three steps in a large algorithm study on treatment of depressive

disorder (STAR*D trial), in which relatively high remission rates were found for the first three steps, but not for later steps: 36.8%, 30.6%, and 13.7% for the respective steps.(71)Recent publications make a case for a similar stepped care approach for PD and GAD in the primary care setting. The systematic review in the appendix gives an overview. The international consensus group on Depression and Anxiety suggests this approach as well.(50) In this study, the most feasible stepped care intervention that is in line with these recommendations, and has been proven partially effective is chosen. The probability that this intervention, if proven cost effective, would become part of the GP guidelines and would be implemented is deemed high. The approach is expected to yield higher remission rates in primary care, less referral to mental health care, less costs and more health gain. The intervention follows a collaborative stepped care model lasting for at least 12 weeks and maximum 24 weeks. In collaborative care, a casemanager (SPV) and a consultant psychiatrist support the GP. The patient is actively involved in the treatment plan by contracting by the GP. Motivation and monitoring is perfor-med by the casemanager by means of written instructions, regular visits and self report of the patient with the BAI. Adherence to the stepped care protocol is supported by feedback on these by a psychiatrist, as shown effective in prior research.(17)The stepped care approach comprises the following steps: a) manual guided self help by casemanager, a method proven effective in a former study (19); b) three cognitive behavioral sessions by the GP. This consists of 3 sessions in which the GP instructs the patient to score the disturbing symptoms, such as panic attacks or MUMS as symptoms of PD and/or GAD, on a daily basis, and to report this every two weeks to the GP. In 2 sessions, the GP analyses and discusses this with the patient and gives instructions to cope with the symptoms. This approach has been proven effective in a former study(17) with effect sizes 0.80-2.60 depending on the outcome measure; c) antidepressants according to a step-up algorithm, prescribed by GP. He chooses one of two antidepressants, registered for GAD or PD. In two periods of two months, the antidepressant is evaluated and if needed, another antidepressant is prescribed. This algorithm

was used in a former
study with good results.(17)Goal of the intervention is improvement of the
patients, as found in the Beck
Anxiety Inventory(BAI) during the monitoring process of the stepped care
algorithm. During the
intervention period, the patients are monitored every 2 months. Clinically
meaningful improvement is
defined as a decrease of 10 points on the BAI, based on unpublished NESDA data.
If patients relapse,
defined as an increase of 10 points on the BAI during the 12-month period, the
next intervention step is
offered. In case of non-response after all steps have been taken, patients are
referred to the regional
mental health care institution.
Treatment of control group. Half of the PCP practices function as control
group, and within these
practices patients receive CAU. The actual content of the CAU treatment (e.g.
medication, number of
contacts in primary care, and referral policy) will be assessed with the Scale
for Medical Utilisation of
Health Services.

Study burden and risks

Not applicable

Contacts

Public
Zorgonderzoek Nederland (ZON)

Laan van Nieuw Oostindie 334
2593 CE Den Haag
NL
Scientific
Zorgonderzoek Nederland (ZON)

Laan van Nieuw Oostindie 334
2593 CE Den Haag
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients who visit the GP practice and meet the DSM-IV diagnosis for GAD or PD are included in the study.

Exclusion criteria

Suicidal, psychotic, cognitive deterioration.

Study design

Design

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

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	01-05-2008
Enrollment:	174
Type:	Actual

Ethics review

Approved WMO Date:	29-04-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL20106.029.07
Other	volgt