ECNP
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ECNP WORKSHOP
on Clinical Research Methods

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METHODS FOR THE ASSESSMENT OF NON-PHARMACOLOGICAL TREATMENTS

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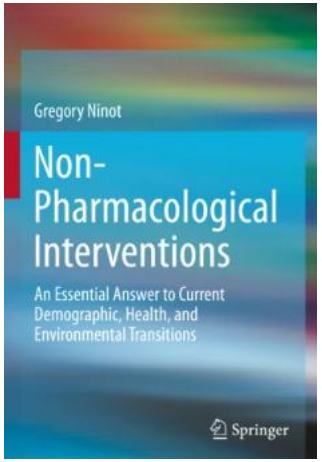
cibersam Centro de Investigación Biomédica en Red Salud Mental

INTRODUCTION

Non-pharmacological interventions

Non-pharmacological interventions in clinical research are any planned therapeutic strategies that do not involve administration of drugs, aiming to influence health outcomes.

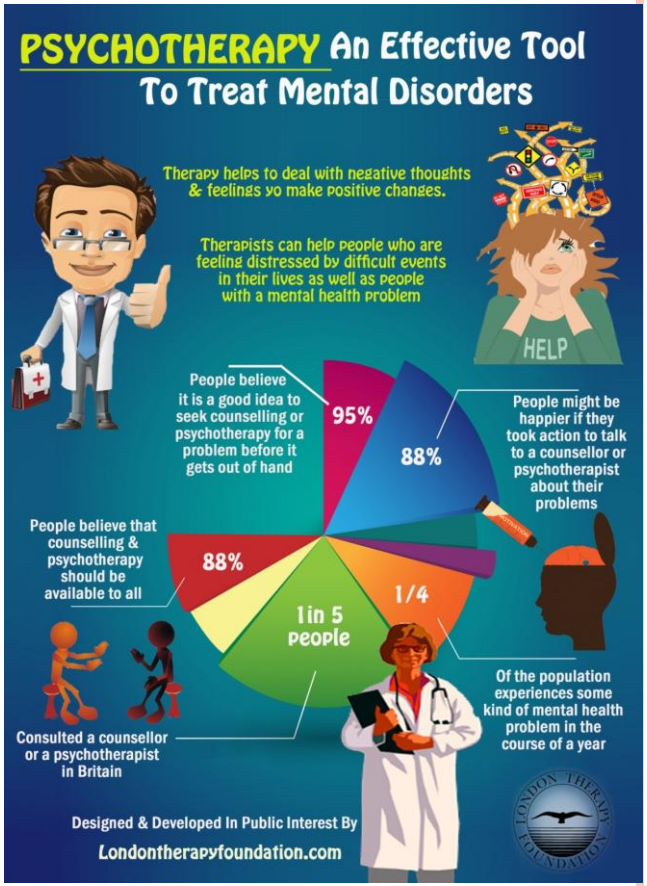
- Psychological/Behavioral
- Lifestyle/Behavioral modification (diet, exercise, sleep hygiene)
- Physical Rehabilitation
- Device/Procedure
- Complementary/Alternative (Acupuncture, yoga..)
- Educational/Psychoeducational



Editorial: Non-pharmacological interventions for mental disorders

Lara Guedes de Pinho[1,2], César Fonseca[1,2], Łukasz Gawęda[3], Manuel Lopes[1,2] and Brooke C. Schneider[4]*

[1]Nursing Department, University of Évora, Évora, Portugal, [2]Comprehensive Health Research Centre (CHRC), University of Évora, Évora, Portugal, [3]Experimental Psychopathology Lab, Institute of Psychology, Polish Academy of Sciences, Warsaw, Poland, [4]Department of Psychiatry and Psychotherapy, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

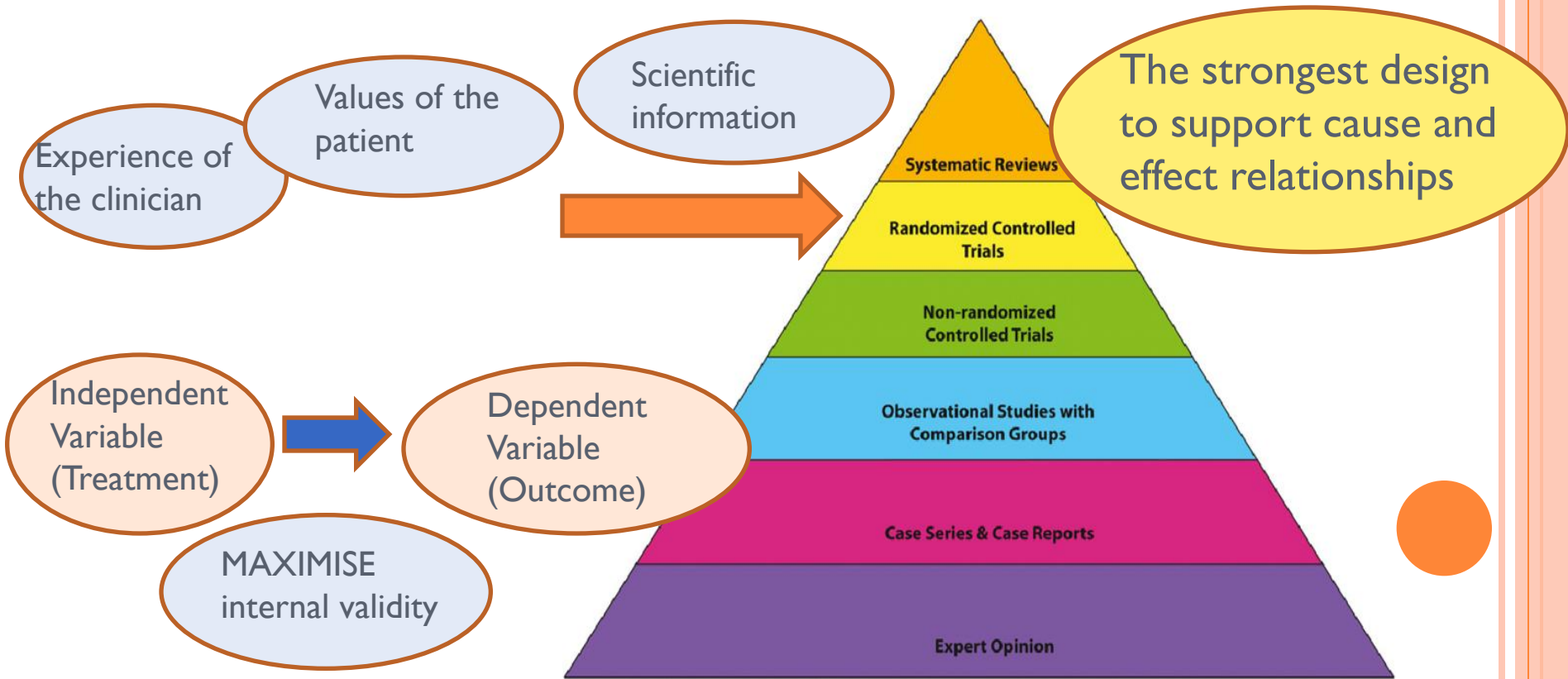


- Non-pharmacological interventions are essential, evidence-based strategies for treatment, prevention, and mental-health promotion, yet remain underutilized worldwide.
- Psychotherapy, psychosocial, mindfulness, lifestyle, and resilience-based interventions are recommended in international guidelines.

Guedes de Pino et al, Frontiers in Psychology, 2024

Evidence -Based medicine (EBM)

- The EBM movement has had a major positive impact in many areas of medicine since it arose in the 1990's.
- Making medical decisions based on solid scientific evidence, guided by professional experience, and tailored to what the patient wants and needs.
- EBM introduced a hierarchy for appraisal of research evidence with the randomized clinical trials (RCT) at the top with regard to original studies.



What research evidence is valid for psychotherapy research?

frontiers in Psychiatry

PERSPECTIVE
published: 11 January 2021
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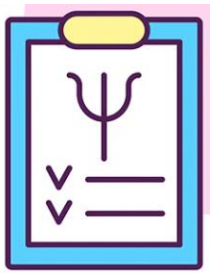


What Research Evidence Is Valid for Psychotherapy Research?

Björn Philips[1]* *and Fredrik Falkenström*[2]

[1] *Department of Psychology, Stockholm University, Stockholm, Sweden,* [2] *Department of Behavioral Sciences and Learning, Linköping University, Linköping, Sweden*

The EBM model is less suitable for psychotherapy research than for pharmacological research or other areas of somatic medicine.

Philips and Falkestrome et al 2021

Types of randomized clinical trials

- By outcome of interest
  - Explanatory. Test efficacy with highly selected participants and under highly controlled conditions
  - Pragmatic. Test effectiveness in everyday practice with relatively unselected participants and under flexible conditions
- By hypothesis
  - Superiority trials. An intervention is hypothesized to be superior to another
  - Noninferiority trials. To determine whether a new treatment is no worse than a reference treatment
  - Equivalence trials. In which the hypothesis is that two interventions are indistinguishable from each other

Efficacy or explanatory studies. Key features

'Can this intervention work'?

- Highly controlled environment: Often conducted in specialized research centers.
- Strict inclusion/exclusion criteria: Only participants who are most likely to respond are enrolled. Homogeneous samples, with restricted range of diagnoses made according to research criteria.
- Standardized intervention: Therapy, procedure, or drug is delivered exactly as per protocol.
- Blinding and randomization rigor: Maximizes internal validity and reduces bias.
- Shorter follow-up periods are common.
- Focus on biological or clinical outcomes rather than real-world application.
- Aim to test whether an intervention can give benefit under ideal circumstances.
- Such studies are often designed to maximize differences between the interventions being tested.

Effectiveness or pragmatic studies. Key features

'Does this intervention work in real clinical setting'?

- Conducted in routine practice settings.
- Setting broad inclusion criteria: includes participants with comorbidities, carrying severity and diverse demographics.
- Therapists who work in the practice setting rather than providing specially trained research therapists.
- The comparator is an alternative treatment strategy which would be considered in real life for a similar patient, rather than placebo.
- Flexibility is allowed in using concomitant medication, complementary care and compliance.
- Longer follow-up periods are common to capture sustained effects.
- Drop-outs: the patients entered into the study are correctly accounted for the end of the study (intention to treat analysis)

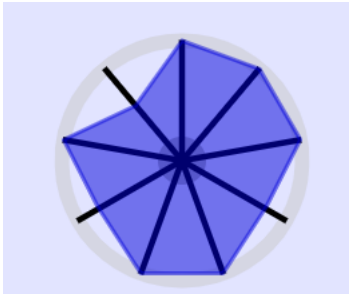
https://www.precis-2.org/

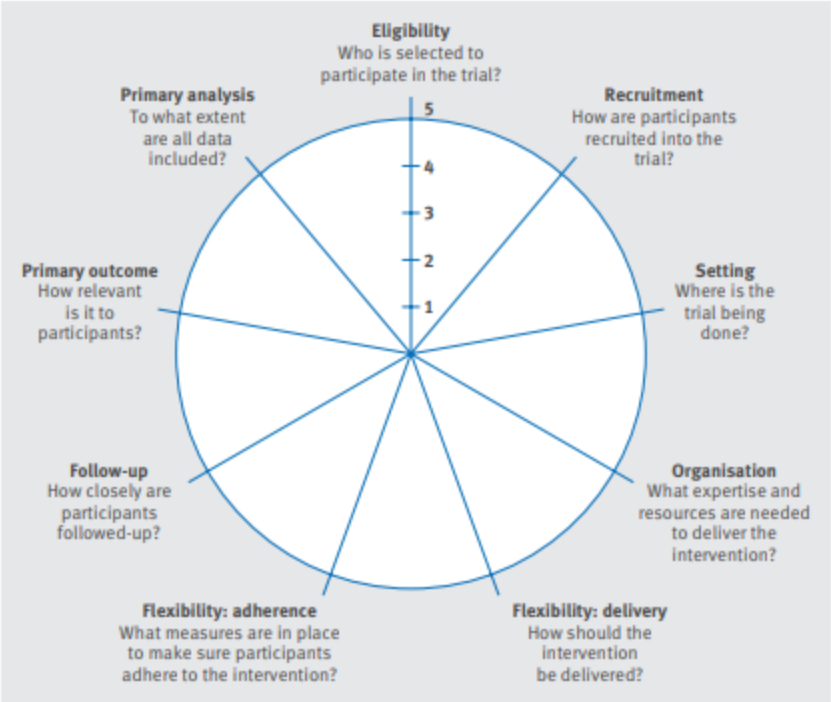
The PRECIS-2 tool: designing trials that are fit for purpose

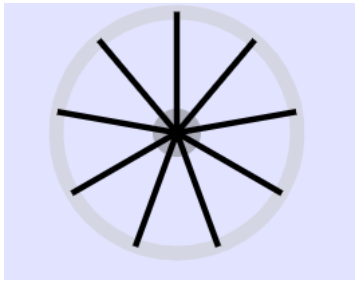
Kirsty Loudon,[1] Shaun Treweek,[1] Frank Sullivan,[2] Peter Donnan,[3] Kevin E Thorpe,[4] Merrick Zwarenstein[5]

Recruitment - how much extra effort is made to recruit participants over and above what that would be used in the usual care setting to engage with patients? For example, score 5 for very pragmatic recruitment through usual appointments or clinic; score 1 for a very explanatory approach with targeted invitation letters, advertising in newspapers, radio plus incentives and other routes that would not be used in usual care.

Setting – how different is the setting of the trial and the usual care setting? For example, score 5 for a very pragmatic choice using identical settings to usual care; score 1, for a very explanatory approach with only a single centre, or only specialised trial or academic centres.







SUMMARY POINTS

PRECIS (2009) was a tool with 10 domains to design clinical trials on a continuum of explanatory attitude (ideal situation) to more pragmatic attitude (usual care)

Cited over 300 times by end of 2014, but weaknesses have been highlighted: no rating scale, problems with some domains, needing better guidance, and not validated

This paper presents PRECIS-2—a validated, improved version of the tool—together with guidance for how to use it

PRECIS-2 has nine domains including three new ones (recruitment, setting, and organisation), each scored on a 5-point Likert continuum (from 1=very explanatory "ideal conditions" to 5=very pragmatic "usual care conditions") so that trialists, clinicians, and policymakers can more easily consider whether design decisions match their intended purpose

PICOT METHOD (TO FORMULATE A GOOD RESEARCH QUESTION)

P Population of interest . Refers to the sample of subjects you wish to recruit for your study.

I Intervention to be studied.

C Comparator intervention. If an existing treatment is considered the 'gold standard' then this should be the comparison group.

O Outcomes to be evaluated

T Time duration for intervention fot the data collection.

THELANCETPSYCH-D-16-00474R1
S2215-0366(16)30302-9
Embargo: Sept 26, 2016—23:30 (BST)
Green OA (NIHR)

Articles
ZN
This version saved: 15:58, 22-Sep-16

Clinical effectiveness and acceptability of structured group psychoeducation versus optimised unstructured peer support for patients with remitted bipolar disorder (PARADES): a pragmatic, multicentre, observer-blind, randomised controlled superiority trial

N=153 PSY
N= 151 unstructured peer support

trial at eight community sites in two regions in England. Participants aged 18 years or older with bipolar disorder and no episode in the preceding 4 weeks were recruited via self-referral or secondary care referral. Participants were individually randomly assigned (1:1), via a computer-generated stochastic allocation sequence, to attend 21 2-h weekly sessions of either structured group psychoeducation or optimised unstructured peer support. Randomisation was minimised by number of previous episodes (one to seven, eight to 19, or ≥20) and stratified by clinical site. Outcome assessors were masked to group allocation. The primary outcome was time from randomisation to next bipolar episode, with planned moderator analysis of number of previous bipolar episodes and qualitative interview of participant experience. We did analysis by intention to treat. This trial is registered

- Methods: multicentre, parallel-group, observer-blind, randomized controlled superiority trial at eight community sites in two regions in England.
- Primary outcome: time to next bipolar episode.
- No differences between the groups (58% vs. 65%), only people with seven or fewer previous bipolar episodes had a greater delay in time to next bipolar episode.

Analysis 'parades'

- The reason may be related to the fact that the study was designed to allow the implementation in the public system by using non-experts therapists by enroling patients with greater morbidity and comorbidity than the unicentric trials.
- The peer-support intervention likely contained therapeutic components.
- Primary outcome (time no any bipolar episode) may diluate domain-speciic effects, combining episode types can mask a true advantadge on one pole.
- 'Pragmatic' studies prioritise feasability and transference to the clinic however often pragmatism derives into ambiguity.
- Sample characteristics: many participants had very long, recurrent ilness.
- The trial failed to separate Psychoeducation from Unstructured Peer Support (time no a new episode) but showed superiority in the same variable in people with seven or fewer episodes.

Vieta & Morilla, Lancet Psychiatry, 2016

Types of randomized clinical trials

- By outcome of interest
- Explanatory. Test efficacy with highly selected participants and under highly controlled conditions
- Pragmatic. Test effectiveness in everyday practice with relatively unselected participants and under flexible conditions
- By hypothesis
- Superiority trials. An intervention is hypothesized to be superior to another
- Noninferiority trials. To determine whether a new treatment is no worse than a reference treatment
- Equivalence trials. In which the hypothesis is that two interventions are indistinguishable from each other

Non-inferiority trial

- To determine whether a new treatment is no worse than a reference treatment.“, therefore the New treatment is at least as good as the Old treatment.
- Non-inferiority studies are used to show that a minimum level of efficacy has been achieved.
- In comparison studies with a current therapy, non-inferiority is used to demonstrate that the new therapy provides at least the same benefit to the patient.

Why non-ineriority trials are helpful?

- They show that a new treatment works almost as well as the standard while offering such as lower cost, shorter duration, easier delivery or fewer side effects. They are useful to:

- Validating practical alternatives when superiority isn't necessary.
- Expanding access through simpler, faster or more scalable treatments.
- Guiding policy and clinical decisions by providing a new option os 'Good enough' whithout compromising patient outcomes.

Open access Protocol

BMJ Open

Study protocol for a single-blind, parallel-group, randomised, controlled non-inferiority trial of 4-day intensive versus standard cognitive behavioural therapy for adults with obsessive–compulsive disorder

Ekaterina Ivanova ,[1] Robin Fondberg,[2] Oskar Flygare ,[1] Max Sannemalm,[1] Sofia Asplund,[3] Sofia Dahlén,[3] Filipa Sampaio ,[4] Erik Andersson ,[5] David Mataix-Cols,[1,6] Volen Z Ivanov,[1] Christian Rück [1]

Non-inferiority trials uses to compare a newer psychotherapy with a traditional one.

The aim is focusing in showing that the new treatment is not significantly worse tnat the standard treatment.

Non-inferiority trials are especially useful when it's ethically or practically challenging to wihthold effective standard treatments in favor of a new one, experimental one

Non-inferior: equally ineffective?

- Non-inferiority trials assume that the chosen reference therapy really is superior to a placebo-intervention, however, this is not self-evident, given that the interventions may fail in one trial and not in another.
- The absence of a «placebo intervention» arm is very common in the psychotherapy literature.
- Ideally, such study should have a third arm with a sort of 'placebo' intervention, with both active arms showing superiority over the third.
- Superiority is the only way to prove actual efficacy when using psychometric outcomes.

Vieta & Sanchez-Moreno, Lancet, 2017

Non-inferior: equally ineffective?

- Without questioning the assay sensitivity of the study and the risk that both interventions might have been not equally effective, but equally ineffective.
- Limitations of non-inferiority designs should be reported.
- The margins are smalller needing a larger sample size in order to get significance
- Non-inferiority designs may not be scientifically powerful enough to be used for regulatory purposes, although they may yield clinically relevant information on comparative safety and cost-effectiveness.

Vieta & Sanchez-Moreno, Lancet, 2017

Key Components to be defined

1.- Non-Inferiority Margin (Δ)
Defines how much worse the new therapy can be before becoming clinically unacceptable.
Should be **clinically justified**, not only statistical.
Example in depression:
Δ = 6 points on MADRS , based on Minimal Clinical Important Difference (6-8 points).

2.- Primary Outcome. Choose a measure sensitive to change:
PHQ-9, HAM-D, MADRS, PTSD Checklist, etc.
Define timing (eg. 12 weeks) and rater (self-report vs clinician)

3. Analysis Plan. Non-inferiority trials require both:
ITT (Intention-to-Treat) and PP (Per-Protocol)
Includes all randomized participants
Conservative for superiority vs Only includes participants who adhered to treatment

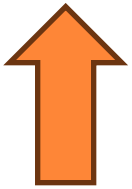
4. Sample Size Analysis Plan. Non-inferiority trials require larger samples than superiority trials

EQUATOR

Enhancing the QUAlity and Transparency Of health Research

- Established in 2006, based in UK (initially funded by the National Library of Medicine, UK Department of Health and other partners)
- Act as a central repository and network for all reporting guidelines initiatives in health research

Randomized and Non-Randomized Clinical trials	Observational studies	Systematic reviews and Evidence Syntheses	Diagnostic and Prognostic studies	Qualitative studies	Reporting interventions and treatment components
CONSORT SPIRIT TIDieR CONSORT	STROBE STREGA	PRISMA PRISMA extensions	STAND TRIPOD	CARE SCARE	TIDieR CReDECI2 GUIDED



CONSORT GUIDELINES

- It is a reporting guideline, internationally recognized set of evidence-based guidelines designed to improve the quality, transparency, and completeness of reporting in randomized controlled trials (RCTs).

CONSORT does not dictate how to conduct a trial but how to report it clearly and transparently so that:

- Readers can understand what was done and why clinicians can interpret the results
- Other researchers can replicate or evaluate the study systematic reviewers can extract accurate data

JAMA. 2025;333(22):1998-2005

CONSORT 2025 checklist of information to include when reporting a randomised trial

Section/topic	No.	CONSORT 2025 checklist item description
Title and abstract		
Title and structured abstract		
	1a	Identification as a randomized trial
	1b	Structured summary of the trial design, methods, results, and conclusions
Open science		
Trial registration	2	Name of trial registry, identifying number (with URL), and date of registration
Protocol and statistical analysis plan	3	Where the trial protocol and statistical analysis plan can be accessed
Data sharing	4	Where and how the individual deidentified participant data (including data dictionary), statistical code, and any other materials can be accessed
Funding and conflicts of interest		
	5a	Sources of funding and other support (eg, supply of drugs), and role of funders in the design, conduct, analysis, and reporting of the trial
	5b	Financial and other conflicts of interest of the manuscript authors
Introduction		
Background and rationale	6	Scientific background and rationale

The **open science dimension** is about *making clinical trial reporting transparent, complete, reproducible, and accessible*, which strengthens the credibility and usefulness of medical research.

CONSORT 2025 checklist of information to include when reporting a randomised trial

Methods		
Patient and public involvement	8	Details of patient or public involvement in the design, conduct, and reporting of the trial
Trial design	9	Description of trial design, including type of trial (eg, parallel group, crossover), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)
Changes to trial protocol	10	Important changes to the trial after it commenced, including any outcomes or analyses that were not prespecified, with reason
Trial setting	11	Settings (eg, community, hospital) and locations (eg, countries, sites) where the trial was conducted
Eligibility criteria		
	12a	Eligibility criteria for participants
	12b	If applicable, eligibility criteria for sites and for individuals delivering the interventions (eg, surgeons, physiotherapists)
Intervention and comparator	13	Intervention and comparator with sufficient details to allow replication; if relevant, where additional materials describing the intervention and comparator (eg, intervention manual) can be accessed
Outcomes	14	Prespecified primary and secondary outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome
Harms	15	How harms were defined and assessed (eg, systematically, nonsystematically)
Sample size		
	16a	How sample size was determined, including all assumptions supporting the sample size calculation
	16b	Explanation of any interim analyses and stopping guidelines

CONSORT 2025 checklist of information to include when reporting a randomised trial

Methods

- **Trial design** (including changes after trial start)
- **Participants** — eligibility criteria, settings, locations
- **Interventions** — detailed description for each group
- **Outcomes** — definitions, measurement, changes after start
- **Sample size** — calculation and assumptions
- **Randomization: sequence generation**
- **Randomization: allocation concealment mechanism**
- **Randomization: implementation**
- **Blinding / masking** — who was blinded and how
- **Statistical methods** — primary and secondary analyses
- **Analysis populations and missing data** (NEW emphasis)
- **Data on harms and unintended effects** (expanded from earlier versions)

The Methods section in ensures that all aspects of trial conduct are fully described, enabling: critical appraisal, replication, assessment of bias, clear interpretation of findings. It is a cornerstone of high-quality clinical trial reporting.

CONSORT 2025 checklist of information to include when reporting a randomised trial

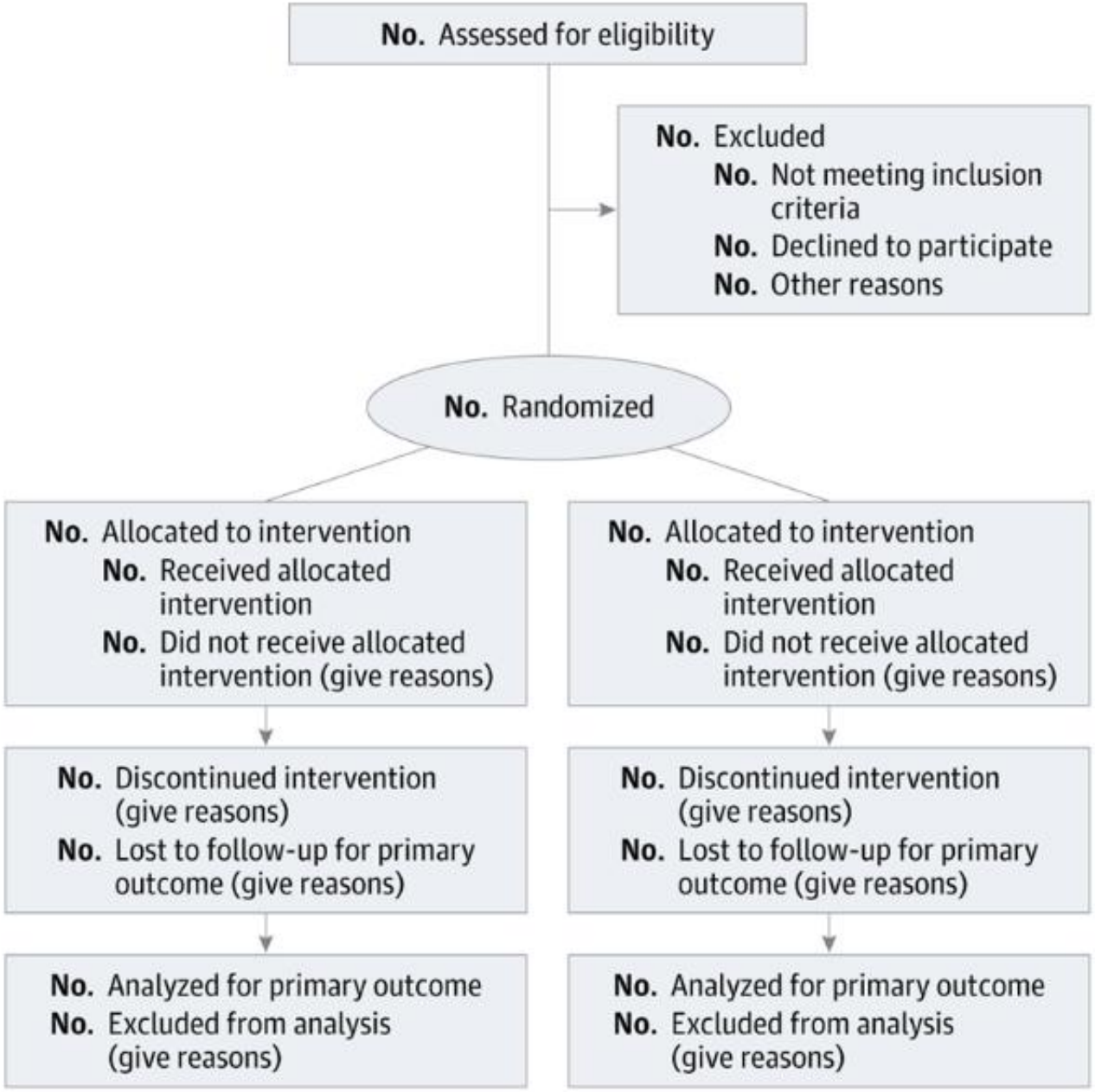
Randomization		
Sequence generation		
	17a	Who generated the random allocation sequence and the method used
	17b	Type of randomization and details of any restriction (eg, stratification, blocking, and block size)
Allocation concealment mechanism	18	Mechanism used to implement the random allocation sequence (eg, central computer/telephone; sequentially numbered, opaque, sealed containers), describing any steps to conceal the sequence until interventions were assigned
Implementation	19	Whether the personnel who enrolled and those who assigned participants to the interventions had access to the random allocation sequence
Blinding		
	20a	Who was blinded after assignment to interventions (eg, participants, clinicians, outcome assessors, data analysts)
	20b	If blinded, how blinding was achieved and description of the similarity of interventions
Statistical methods		
	21a	Statistical methods used to compare groups for primary and secondary outcomes, including harms
	21b	Definition of who is included in each analysis (eg, all randomized participants) and in which group
	21c	How missing data were handled in the analysis
	21d	Methods for any additional analyses (eg, subgroup and sensitivity analyses), distinguishing prespecified from post hoc

CONSORT 2025 checklist of information to include when reporting a randomised trial

Section/topic	No.	CONSORT 2025 checklist item description
Results		
Participant flow, including flow diagram		
	22a	For each group, the numbers of participants who were randomly assigned, received intended intervention, and were analyzed for the primary outcome
	22b	For each group, losses and exclusions after randomization, together with reasons
Recruitment		
	23a	Dates defining the periods of recruitment and follow-up for outcomes of benefits and harms
	23b	If relevant, why the trial ended or was stopped
Intervention and comparator delivery		
	24a	Intervention and comparator as they were actually administered (eg, where appropriate, who delivered the intervention/comparator, how participants adhered, whether they were delivered as intended [fidelity])
	24b	Concomitant care received during the trial for each group
Baseline data	25	A table showing baseline demographic and clinical characteristics for each group
Numbers analyzed, outcomes, and estimation	26	For each primary and secondary outcome, by group: • The number of participants included in the analysis • The number of participants with available data at the outcome time point • Result for each group and the estimated effect size and its precision (such as 95% confidence interval) • For binary outcomes, presentation of both absolute and relative effect size
Harms	27	All harms or unintended events in each group
Ancillary analyses	28	Any other analyses performed, including subgroup and sensitivity analyses, distinguishing prespecified from post hoc
Discussion		
Interpretation	29	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence
Limitations	30	Trial limitations, addressing sources of potential bias, imprecision, generalizability, and, if relevant, multiplicity of analyses

- **Participant flow** — numbers at each stage
- **Recruitment** — dates of recruitment and follow-up
- **Baseline data** — characteristics per group
- **Numbers analyzed** — for each outcome and population
- **Outcomes and estimation** — per group, effect sizes
- **Ancillary analyses** — subgroup, sensitivity, exploratory
- **Harms / unintended effects** (detailed reporting)

Phases from RCT



Flow diagram of the progress through the phases of a randomized trial of 2 groups (ie, enrollment, intervention allocation, follow-up, and data analysis).

Changes compared to CONSORT 2010

Addition of New Checklist Items

- Item 4: Added item on data sharing, including where and how individual deidentified participant data, statistical code, and any other materials can be accessed.
- Item 5b: Added item on financial and other conflicts of interest of manuscript authors.
- Item 8: Added item on how patients and/or the public were involved in the design, conduct, and/or reporting of the trial.
- Item 12b: Added item on eligibility criteria for sites and for b individuals delivering the interventions, where applicable.
- Item 15: Added item on how harms and other unintended effects were assessed.
- Item 21: Added items to define who is included in each analysis (eg, all randomized participants) and in which group (item 21b), and how missing data were handled in the analysis (item 21c).
- Item 24: Added item on intervention delivery, including how the intervention and comparator were actually administered (item 24a) and details of concomitant care received during the trial (item 24b).

Completely Revised Checklist Items

- Item 3: Revised item to include where the statistical analysis plan can be accessed in addition to the trial protocol.
- Item 10: Revised item to include reporting of important changes to the trial after it commenced, including any outcomes or analyses that were not prespecified.
- Item 26: Revised item to specify for each primary and secondary outcome the number of participants included in the analysis and the number of participants with available data at each time point for each treatment group.

Deletion of Checklist Item

- Deleted item on generalizability of trial findings, which is now incorporated under trial limitations (item 30).

Integration of Checklist Items From Key CONSORT Extensions

- Addition of items related to reporting of how harms[25] were assessed and analyzed (items 7, 15, 21a, 23a, and 27), how outcomes[26] were measured and analyzed (items 14 and 26), and how the intervention[28,29] and comparator were actually administered and by whom (item 24).

Structure and Organization of Checklist Items

- Restructuring of checklist, with a new section on open science, which includes items that are conceptually linked, such as trial registration (item 2), where the trial protocol and statistical analysis plan can be accessed (item 3), sharing of deidentified participant-level data (item 4), and funding and conflicts of interest (item 5).
- Aligned wording of some CONSORT checklist items with that of Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist items and vice versa.
- Clarified and simplified wording of some items.

General Changes

Integration of extensions

Extensions for different trial designs, for special types of interventions or outcomes

New focus on open science (major update). Protocol access, trial registration, data sharing statements, acces to analysis coide and materials

More detailed Reporting of Interventions: CONSORT 2025 expands requirements for describing interventeions and comparators, including who delivered them, how and in what context , improving reproducibility

Updated Participants Flow and Results Reporting

→ Increased focus on context, feasibility and implementation

JAMA | Special Communication

SPIRIT 2025 Statement
Updated Guideline for Protocols of Randomized Trials

An-Wen Chan, MD, DPhil; Isabelle Boutron, MD, PhD; Sally Hopewell, DPhil; David Moher, MSc, PhD; Kenneth F. Schulz, PhD, MBA; Gary S. Collins, PhD; Ruth Tunn, DPhil; Rakesh Aggarwal, MD, DM; Michael Berkwits, MD; Jesse A. Berlin, ScD; Nita Bhandari, MD, PhD; Nancy J. Butcher, PhD; Marion K. Campbell, BSc(Hons), MSc, PhD, CStat, FSS; Runcie C. W. Chidebe, Dip, BSc, MSc; Diana R. Elbourne, PhD; Andrew J. Farmer, MA, DM, BM, BCh; Dean A. Fergusson, PhD; Robert M. Golub, MD; Steven N. Goodman, MD, MHS, PhD; Tammy C. Hoffmann, PhD; John P. A. Ioannidis, MD, DSc; Brennan C. Kahan, PhD; Rachel L. Knowles, PhD, MSc, MBChB; Sarah E. Lamb, DPhil, MSc, MA; Steff Lewis, PhD; Elizabeth Loder, MD; Martin Offringa, MD, PhD; Philippe Ravaud, MD, PhD; Dawn P. Richards, PhD; Frank W. Rockhold, PhD; David L. Schriger, MD, MPH; Nandi L. Siegfried, DPhil, MPH(Hons), MBCHB; Sophie Staniszewska, DPhil, BSc(Hons); Rod S. Taylor, PhD; Lehana Thabane, PhD; David J. Torgerson, PhD; Sunita Vohra, MD, MSc; Ian R. White, PhD; Asbjørn Hróbjartsson, MD, PhD

SPIRIT provides the framework for designing a complete and transparent trial protocol, while CONSORT ensures that the results of that trial are reported with the same level of clarity, accuracy, and methodological rigor.

INDEX

Task 2. using the consort 2025 check list

RESEARCH Open Access

Comparative effectiveness of short-term psychodynamic psychotherapy and cognitive behavioral therapy for major depression in psychiatric outpatient clinics: a randomized controlled trial

Anders Malkomsen[1*], Theresa Wilberg[1,2], Bente Bull-Hansen[3], Toril Dammen[1,2], Julie Horgen Evensen[1], Benjamin Hummelen[1], André Løvgren[1], Kåre Osnes[3], Randi Ulberg[2,4] and Jan Ivar Røssberg[1,2]

Section/topic	No	CONSORT 2025 checklist item description	Reported on page no.
Title and abstract			
Title and structured abstract	1a	Identification as a randomised trial	
	1b	Structured summary of the trial design, methods, results, and conclusions	
Open science			
Trial registration	2	Name of trial registry, identifying number (with URL) and date of registration	
Protocol and statistical analysis plan	3	Where the trial protocol and statistical analysis plan can be accessed	
Data sharing	4	Where and how the individual de-identified participant data (including data dictionary), statistical code and any other materials can be accessed	
Funding and conflicts of interest	5a	Sources of funding and other support (eg, supply of drugs), and role of funders in the design, conduct, analysis and reporting of the trial	
	5b	Financial and other conflicts of interest of the manuscript authors	
Introduction			
Background and rationale	6	Scientific background and rationale	
Objectives	7	Specific objectives related to benefits and harms	
Methods			
Patient and public involvement	8	Details of patient or public involvement in the design, conduct and reporting of the trial	
Trial design	9	Description of trial design including type of trial (eg, parallel group, crossover), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	
Changes to trial protocol	10	Important changes to the trial after it commenced including any outcomes or analyses that were not prespecified, with reason	
Trial setting	11	Settings (eg, community, hospital) and locations (eg, countries, sites) where the trial was conducted	
Eligibility criteria	12a	Eligibility criteria for participants	
	12b	If applicable, eligibility criteria for sites and for individuals delivering the interventions (eg, surgeons, physiotherapists)	
Intervention and comparator	13	Intervention and comparator with sufficient details to allow replication. If relevant, where additional materials describing the intervention and comparator (eg, intervention manual) can be accessed	
Outcomes	14	Prespecified primary and secondary outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome	
Harms	15	How harms were defined and assessed (eg, systematically, non-systematically)	
Sample size	16a	How sample size was determined, including all assumptions supporting the sample size calculation	
	16b	Explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	17a	Who generated the random allocation sequence and the method used	

Some questions…

- What is the main finding of this trial?
- What are the key strengths of this RCT?
- What are the main limitations?
- What CONSORT items are illustrated well in the study?
- What CONSORT items are missing or weak?

PSYCHOTERAPY DEFINITION

- Psychotherapy is a collaborative treatment based on the relationship between an individual and a psychologist. Grounded in dialogue, it provides a supportive environment that allows the patient to talk openly with someone who's objective, neutral, and nonjudgmental.

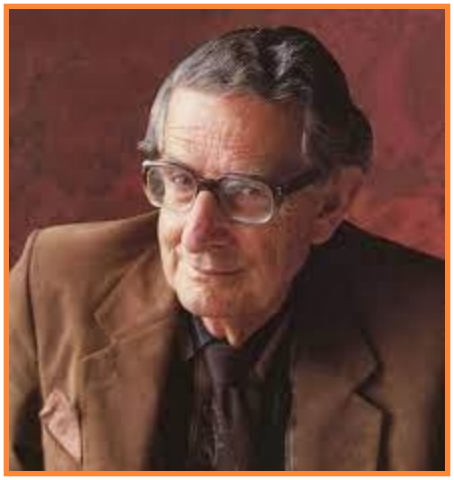
- ✓ Subjectivity
- ✓ Complexity

Why is psychotherapy challenging to evaluate?

American Psychological Association 2016

The Effects of Psychotherapy: An Evaluation

H. J. Eysenck
Institute of Psychiatry, Maudsley Hospital
University of London

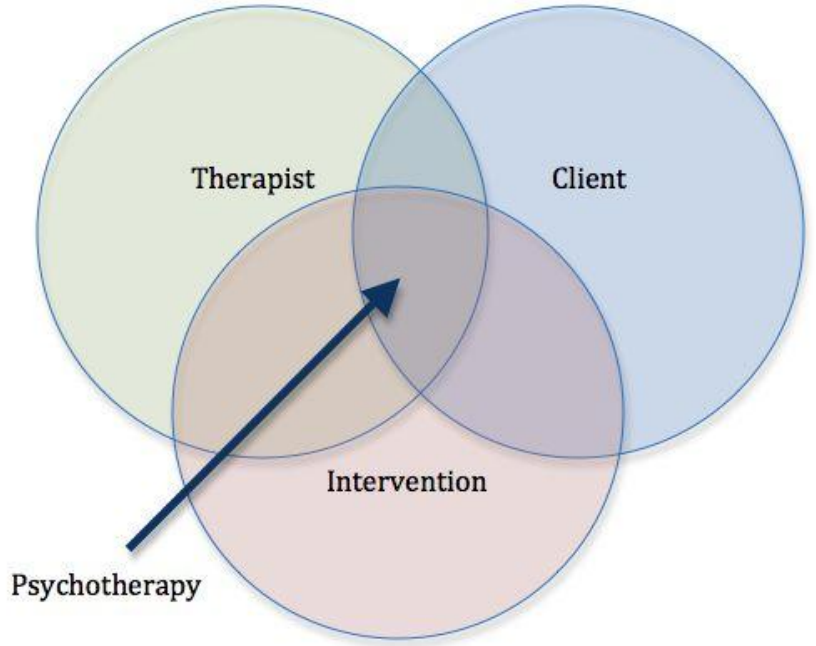


- Eysenck reviewed existing studies and concluded that psychotherapy did nor significantly improve patients outcomes compared to natural recovery.
- He suggested that around 66% of individuals with psychological issues would recover naturally within two years without any formal treatment, whether or not they are treated with psychotherapy.
- He found lack of control groups and objective measures.

IMPACT and CONTROVERSY

Why is psychotherapy challenging to evaluate?

- Interventions are often complex, involving numerous sessions over weeks or months.
- The therapeutic alliance (relationship between therapist and patient) is a key component, which can affect outcomes.



Medical trials:

- Intervention is a drug o medical procedure.
- The effect is often studied through biological mechanisms.
- The intervention is usually standardized (eg. dosage, administration).

COMPLEXITY

Linear Causality

RCTs are based on linear causality, however is highly likely that the human mind and the practice of psychotherapy would better be characterized as complex systems with bi-directional effects as a collaborative work between patient and therapist.

Treatment package

In contrast to a pharmacological treatment, a nonpharmacological treatment rarely consists of a single component.

Complex treatments

The treatments are complex and their core features difficult to define.

Evolution of treatment

Treatments may evolve over time. There may be uncertainty about whether a treatment has changed sufficiently to warrant evaluation.

Dodo solution

- Saul Rozenzweig (1936) introduced the hypothesis that effect of therapy should not be attributed to the specifics of a certain method, but to what all had in common, the so-called 'common factors'.

- 'Dodo solution'. Dodo bird (in *Alice's Adventures in Wonderland*) judging constestants in a race, declares that all have won and all must have prizes. All psychotherapy methods are winners?

Dodo solution

A meta-analysis of outcome studies comparing bona fide psychotherapies: Empiricially, "all must have prizes."

© Solicitar permisos

Wampold, B. E., Mondin, G. W., Moody, M., Stich, F., Benson, K., & Ahn, H.-n. (1997). A meta-analysis of outcome studies comparing bona fide psychotherapies: Empiricially, "all must have prizes." *Psychological Bulletin, 122*(3), 203–215. https://doi.org/10.1037/0033-2909.122.3.203

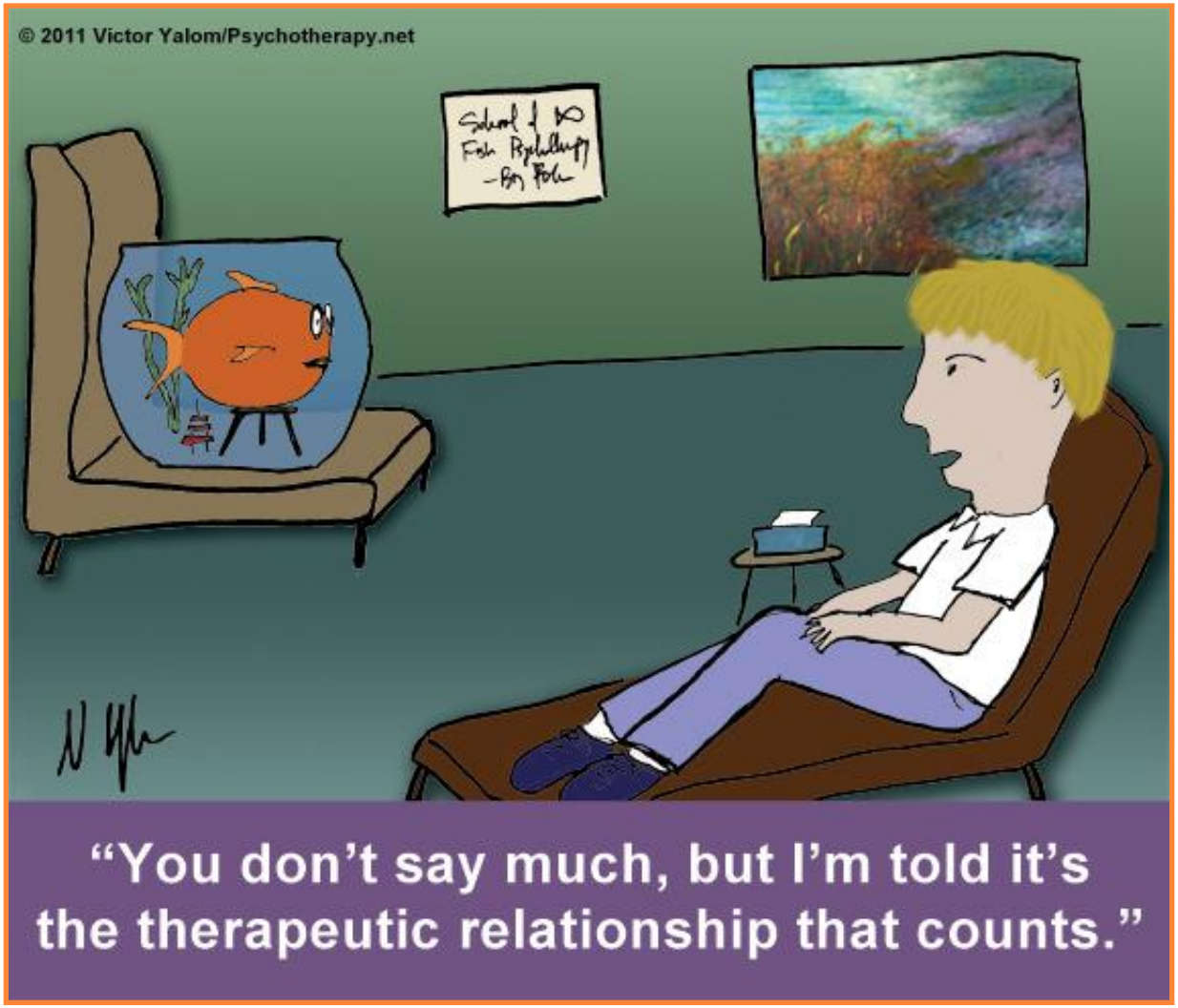
After reviewing more tan 200 scientific studies comparing the effective of mainstream therapies, they did not find many differences between outcomes concluding that the treatments were roughly equivalents.

Aggregation

Support for the Dodo's effect comes from meta-analyses that combine results from multiple treatments and outcomes, but they fail to show therapy effectiveness for specific disorders.

Instead of examining each treatment's effect om each individual disorder, they also combine primary outcomes and secondary outcomes.

Psychotherapy works….



World Psychiatry
The World Psychiatric Association

The efficacy of psychotherapies and pharmacotherapies for mental disorders in adults: an umbrella review and meta-analytic evaluation of recent meta-analyses

Falk Leichsenring, Christiane Steinert, [...], and John P.A. Ioannidis

Leichsenring et al, 2022

102 meta-analyses encompassing 3,782 RCTs and 650,514 patients covering the main mental disorders.

- This research provided an overarching picture of limited additional gain for both psychotherapies and pharmacotherapies over placebo or TAU suggesting a ceiling effect, with an average SMD of 0.35.
- Risk of bias was often high.

A paradigm shift in research seems to be required to achieve further progress.

RESEARCH REPORT

Cognitive behavior therapy vs. control conditions, other psychotherapies, pharmacotherapies and combined treatment for depression: a comprehensive meta-analysis including 409 trials with 52,702 patients

Pim Cuijpers[1-3], Clara Miguel[1], Mathias Harrer[4,5], Constantin Yves Plessen[1,6], Marketa Ciharova[1], David Ebert[4], Eirini Karyotaki[1]

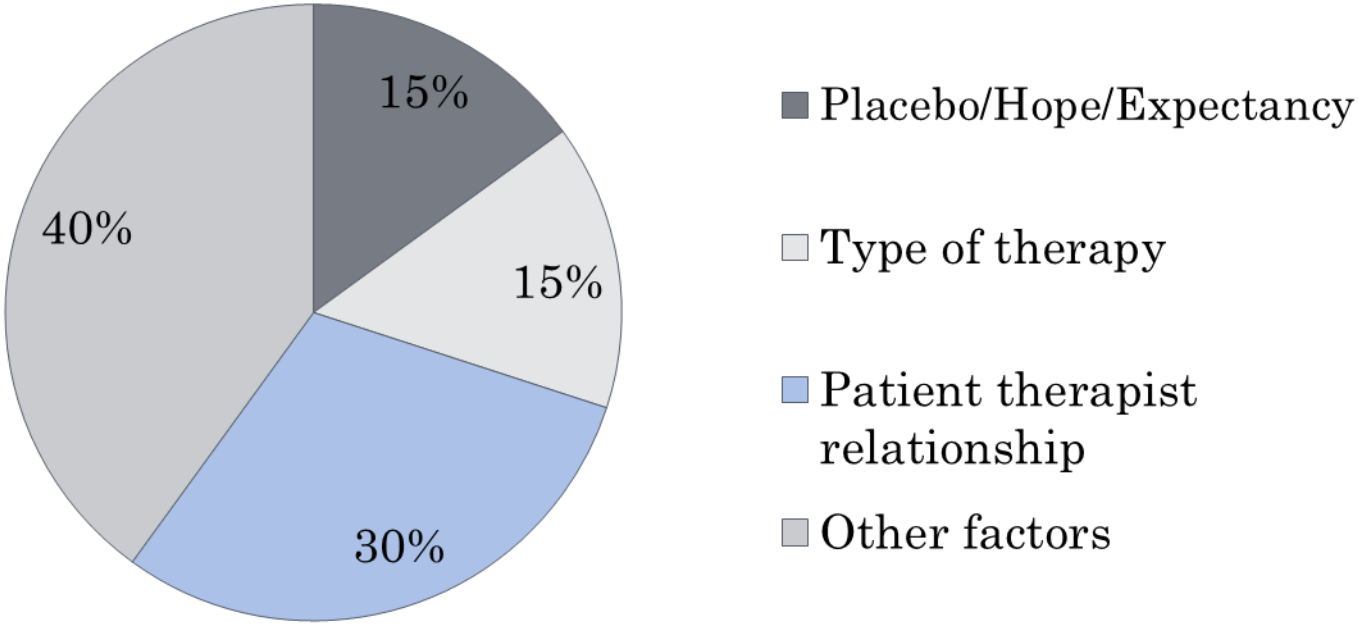
[1]Department of Clinical, Neuro and Developmental Psychology, Amsterdam Public Health Research Institute, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands; [2]Babeş-Bolyai University, International Institute for Psychotherapy, Cluj-Napoca, Romania; [3]WHO Collaborating Centre for Research and Dissemination of Psychological Interventions, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands; [4]Psychology & Digital Mental Health Care, Department of Health Sciences, Technical University Munich, Munich, Germany; [5]Department of Clinical Psychology & Psychotherapy, Friedrich-Alexander-University Erlangen-Nuremberg, Erlangen, Germany; [6]Department of Psychosomatic Medicine, Charité Universitätsmedizin Berlin, Berlin, Germany

Cuijpers et al, 2023

- This is the largest meta-analysis ever of a specific type of psychotherapy for a mental disorder, including 409 RCTs with 52,702 patients.
- CBT was found to be effective in depression when compared to control conditions such as usual care and waitlist, with a moderate to large effect size (g=0.79).
- CBT appears to be as effective as pharmacotherapies at the short term, but more effective at the longer term.
- Combined treatment appears to be superior to pharmacotherapy alone but not to CBT alone.
- The superiority of CBT over other psychotherapies does not emerge clearly from this meta-analysis.

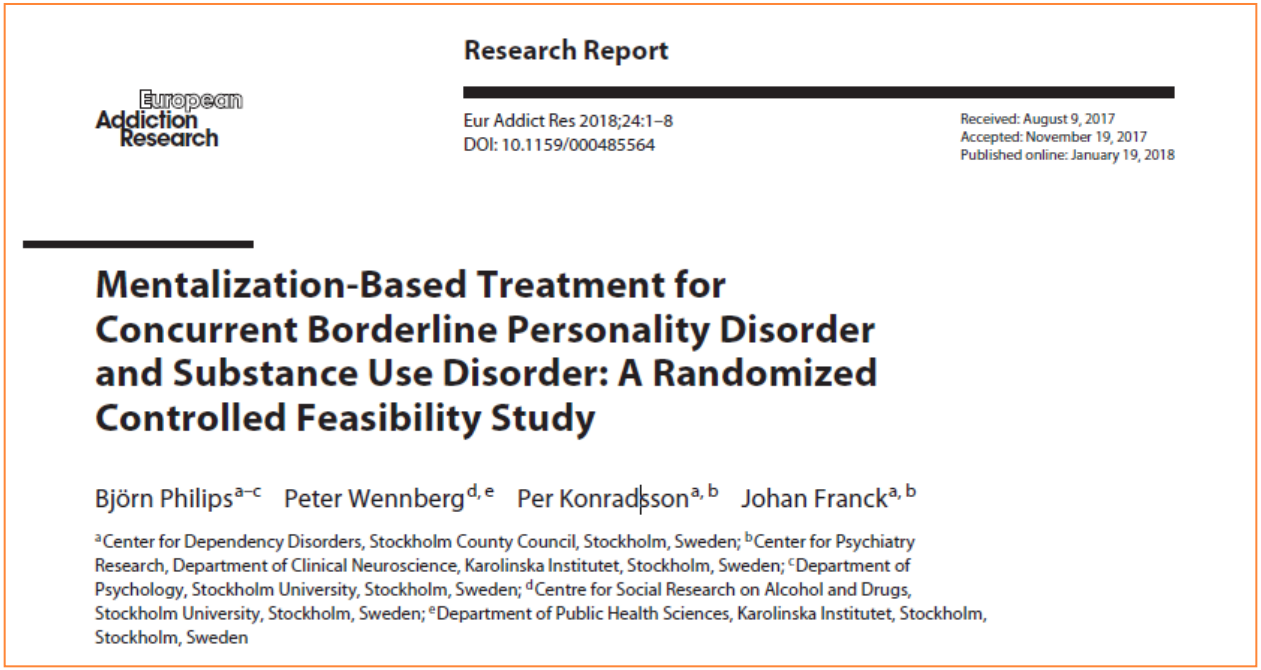
The quality of studies has improved with the increasing number of trials with low risk of bias.
Decrease use of waitlist control groups.
Increase sample sizes and decrease of treatment sessions.

Common factors contributing to success of psychotherapy



Adapted from Lambert et al, 1992

Particular research challenges for complex psychopathology



Research Report

European Addiction Research

Eur Addict Res 2018;24:1–8
DOI: 10.1159/000485564

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Accepted: November 19, 2017
Published online: January 19, 2018

Mentalization-Based Treatment for Concurrent Borderline Personality Disorder and Substance Use Disorder: A Randomized Controlled Feasibility Study

Björn Philips[a–c] Peter Wennberg[d, e] Per Konradsson[a, b] Johan Franck[a, b]

[a]Center for Dependency Disorders, Stockholm County Council, Stockholm, Sweden; [b]Center for Psychiatry Research, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden; [c]Department of Psychology, Stockholm University, Stockholm, Sweden; [d]Centre for Social Research on Alcohol and Drugs, Stockholm University, Stockholm, Sweden; [e]Department of Public Health Sciences, Karolinska Institutet, Stockholm, Stockholm, Sweden

The study was aiming for the inclusion of 80 patients but after 5 years of hard work they stop at N=46.

The study with fragile patients should be studied with research designs other than typical RCt

Study between Borderline Personality Disorder and Substance Use Disorder

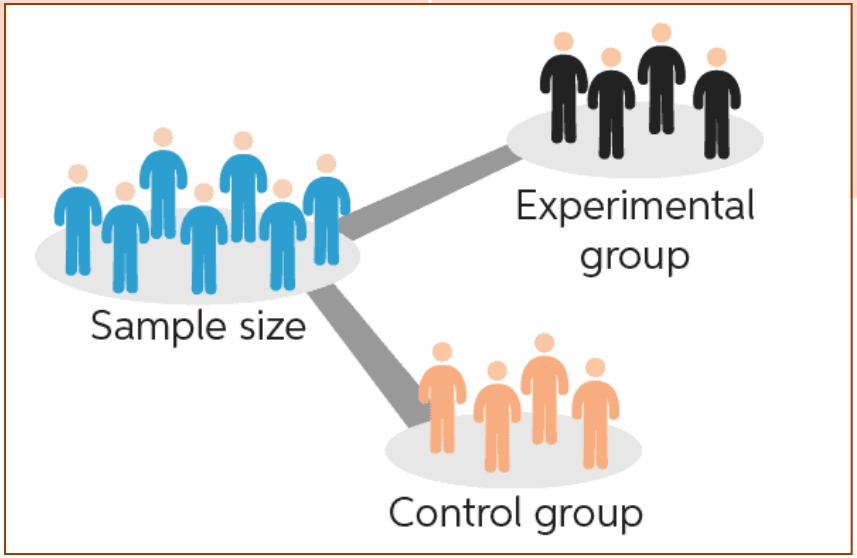
Methods: Patients (n = 46) with concurrent BPD and SUD were randomized either to MBT in combination with SUD treatment (n = 24) or to SUD treatment alone (n = 22). Outcome was measured after 18 months using objective data, as well as interview and self-report measures.

Results: no differences between MBT or SUD treatment for dual diagnosis patients, partly because the staff taking care of the control group helped many of those patients by referring them to some sort of psychotherapy.

Philips et al, 2018

Features of RCTs

Features of RCts	Criticisms
○ RCTs are a methodological procedure that consists in the comparison of the group of patients in whom the usefulness of treatment is being examined with the group of patients who are receiving no active treatment.	○ The non-specific psychological treatments administered to patients in control groups are not 'neutral' in the way that placebo is pharmacologically 'neutral'.



METHODOLOGICAL ISSUES

related to psychotherapy trials

1. RANDOMIZATION. CHALLENGES

High drop out rates: Participants may have strong preferences for certain types of therapy and may drop out if they are assigned to a group they did not want.

Unequal motivation: Participants assigned to less preferred or control groups may be less motivated, potentially affecting the outcomes.

MITIGATIONS

Preference trials or patient-choice design: Allow participants to choose their preferred treatment when feasible, and compare outcomes between those who chose and those who were randomized.

Enhanced informed consent: Educate participants about the value of randomization and the importance of trying new therapies, which can help reduce dropout rates by increasing understanding and buy-in.

RESEARCH ARTICLE

WILEY

The impact of accommodating client preference in psychotherapy: A meta-analysis

Joshua K. Swift[1] | Jennifer L. Callahan[2] | Mick Cooper[3] | Susannah R. Parkin[1]

1) Activity preferences, refer to the activities that clients hope they and their therapists will engage in throughout the course of psychotherapy (confrontation, homeworks, treatment format).
2) Treatment preferences: type of intervention, Psychotherapy vs. medication, between psychotherapies, or between psychotherapies and other interventions (Self-help, peer-support groups).

Expectations represent what clients believe will occur in psychotherapy, whereas preferences represent their desires

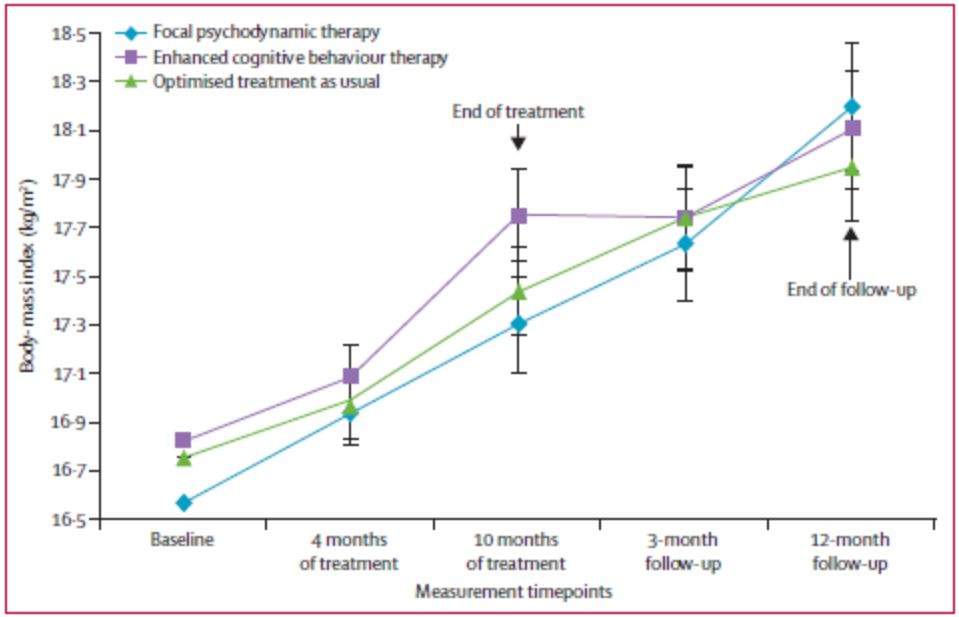
Swift et al, J Clin Psychol, 2018

Features of RCTs and relative criticisms

Features of RCts	Criticisms
○ Strict diagnostic homogeneity	○ Psychotherapy patients are not as diagnostically homogeneous as patients in RCTs
○ Randomization. Process to assign participants to different groups in a way that ensures each participant has an equal chance of being placed in any group. The aim is to reduce bias.	○ Randomization creates and artificial situation

Focal psychodynamic therapy, cognitive behaviour therapy, and optimised treatment as usual in outpatients with anorexia nervosa (ANTOP study): randomised controlled trial

*Stephan Zipfel, Beate Wild, Gaby Groß, Hans-Christoph Friederich, Martin Teufel, Dieter Schellberg, Katrin E Giel, Martina de Zwaan, Andreas Dinkel, Stephan Herpertz, Markus Burgmer, Bernd Löwe, Sefik Tagay, Jörn von Wietersheim, Almut Zeeck, Carmen Schade-Brittinger, Henning Schauenburg, Wolfgang Herzog on behalf of the ANTOP study group**



Course of weight gain during treatment and follow-up by treatment group

- Primary outcome: weight gain measured as increased body mass index at the end of treatment

N=242

N=80 focal psychodynamic therapy

N=80 enhanced CBT

N=82 TAU

No differences between the interventions when the clinical groups not included anorexia patients but also patients with subthreshold anorexia.

2. Generalizability and sample size . Challenges

Psychotherapy trials often struggle with small sample sizes due to the intensive nature of the interventions and limited access to trained therapists.

The specificity of the trial setting can limit the generalizability of the findings.

MITIGATIONS

Multisite trials: Conduct the trial across multiple sites to increase sample size and improve generalizability

Pragmatic designs: With broader inclusion criteria.

General principles and aims of evaluations of effectiveness

- Validity: Studies should be designed to protect against bias.
- Applicability or External validity: They should be designed so that the findings are relevant to, and can be applied to, typical healthcare situations.

Can sometimes be difficult to design a study that is both highly valid and highly applicable and different study designs maybe appropiate to evaluate subtly different research questions.

INTERNAL VALIDITY

- Internal validity refers to the extent that the outcome for a trial can be attributed to the experimental treatment and not to any alternative explanation such as the natural course of the target problem

- The use of control conditions and randomization are the principal methods ensuring that an RCT is 'internally valid'.

To maximize internal validity in a psychoterapy RCT

- The sample is homogeneous and clearly specified (usually in terms of psychiatric diagnosis)

- Specifying the target population, choosing the sampling procedure, and determining the sample size. Sample size is determined by statistical power analysis
- Important to have an unbiased sample that is representative of the target population from which its drawn.
- Specific criteria to allow the identification of participants.
- Exclusion criteria.
- Broad criteria to reflect real-world clinical settings.

  - 1/3-1/2 of people seeking therapy do not meet criteria for any diagnostic category (or show comorbid conditions, not a single diagnosis).
  - 40%-70% of individuals are excluded because do not meet restrictive inclusion criteria required by RCTs designs.

To get a stronger ecological validity

- Including regular patients at the clinic with less strict eligibility criteria.
- Being more flexible regarding lenght and 'dose' of therapy in order to adapt to the particular patient.
- Allowing more freedom to the therapist in how to apply the psychotherapy method.
- Including therapists who work at the clinic who are not handpicked for the research study.

Increase external validity by introducing the concept of pragmatic clinical trials

EXTERNAL VALIDITY

Features of RCTs and relative criticisms

Features of RCts	Criticisms
○ Double blind design	○ A double-blind design is impossible in psychotherapy research. Patients can not be blind because they participate actively and the therapists they know what treatment administer.

3. BLINDING. CHALLENGES

Complete blinding is nearly impossible in psychotherapy trials because both therapists and participants know the nature of the intervention.

Expectation bias: participants who know they are receiving the new treatment may have higher expectations of improvement, influencing self-reported measures.

MITIGATIONS

Blinded outcome assessment: Use independent assessors who are blind to the treatment condition to evalute oucomes.

Blinded data analysis Analysts who handle the data can also be blinded to group assignments to prevent interpretation bias.

4. Control group and placebo effects. Challenge

Difficulty in using placebos. Unlike medical trials where a placebo pill can be used, creating 'placebo' version of psychotherapy is challenging. Ethical concerns with waitlist controls

MITIGATIONS

Use an active control group: Instead of a waitlist or no-treatment control, use an active control group that receives a form of psychological intervention that mimics some aspects of the experimental therapy but is not expected to have the same specific effects.

Add a treatment-as-usual (TAU) group : Participants continue their usual care (e.g. medication or general counselling) to compare the new psychotherapy against standard practice.

Blinded assessment. Use blinder assessors who do not know which intervention the participants received to reduce bias in outcome evaluation.

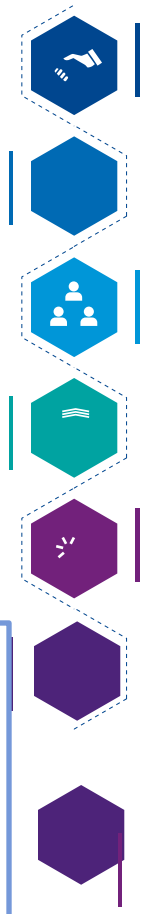
Frequently used control conditions in behavioural intervention trials

Active comparator
A treatment that has an evidence base to support its efficacy but is different from the experimental treatment

Dismantling study
Aim to see what the effective components of a treatment are. The full treatment is compared to a comparison group, which receives the treatment minus one component

Minimal treatment controls
Treatments that entail fewer than four sessions.

Non-specific factor component control. Includes time with a therapist of the same duration and frequency as the experimental treatment, but no exercises or techniques regarded as therapeutic. This control condition often includes educational sessions during which patients are informed only about treatments available or self-aid options.



Treatment as usual. Requires that the trial is done in a clinic where patients have acces to some form of treatment.

No-treatment control: Contains no study treatment and it is not done in a setting in which treatment would be available.

Waitlist control: No treatment is provided during the experimental treatment period, but the experimental treatment is offered after posttreatment assessment

Patient's choice: Patients can choose freely between treatment offered in a trial (e.g one of several types of psychotherapy or between psychotherapy and medication).

Pill placebo: A placebo pill is given to the control group, which does not receive the experimental behavioural treatment.

Treatment as usual

Focal psychodynamic therapy, cognitive behaviour therapy, and optimised treatment as usual in outpatients with anorexia nervosa (ANTOP study): randomised controlled trial

Stephan Zipfel, Beate Wild, Gaby Groß, Hans-Christoph Friederich, Martin Teufel, Dieter Schellberg, Katrin E Giel, Martina de Zwaan, Andreas Dinkel, Stephan Herpertz, Markus Burgmer, Bernd Löwe, Sefik Tagay, Jörn von Wietersheim, Almut Zeeck, Carmen Schade-Brittinger, Henning Schauenburg, Wolfgang Herzog on behalf of the ANTOP study group*

Panel 1: Treatment provided

Overview

We developed a framework of medical ca
the ANTOP study. This framework includ
sessions of specialist assessment at the p
centre. To avoid and reduce medical com
study period, we asked all patients to see
least once a month. Every individual stud
family doctors written instructions on ho
relation to this study. Treatment was pro
doctors and psychologists specialising in
the respective assigned treatment metho
implemented a rigorous system of super
control, and treatment fidelity (appendi

Focal psychodynamic therapy

At the beginning of focal psychodynamic
identified psychodynamic foci with a sta
operationalised, psychodynamic diagnos
psychodynamic treatment manual can b
three treatment phases. The first phase f
therapeutic alliance, pro-anorectic behav
beliefs (attitudes and behaviour viewed
self-esteem. In the second phase of treat
placed on relevant relationships and the
interpersonal relationships and eating (a
The pertinent aspects of the final phase
everyday life, anticipation of treatment t
parting. Before every treatment session,
assessor measured every patient's weigh
or her therapist.[26]

Enhanced cognitive behaviour therapy

The unpublished German version of the m
cognitive behaviour therapy (CBT-E) used
developed in 2007 during initial training.
written by Fairburn before publication of
in enhanced cognitive behaviour therapy
manual since its publication. The cognitiv
plan consists of several modules, of which
well), nutrition, creating a formulation, ar
(ending well) are essential. Other modules

Optimised treatment as usual

Patients assigned to optimised treatment as usual received support in accessing therapy and were given a list of established outpatient psychotherapists with experience in treating eating disorders and who work in accordance with German general psychotherapy guidelines. Patients' family doctors had an active role in treatment and monitoring. In the German health-care system, psychotherapy for patients with eating disorders—in particular, those with anorexia nervosa—is usually covered by health insurance. To further optimise the treatment as usual approach, patients' family doctors had three roles. First, they were asked to take regular weight measurements, do monthly blood tests, and make structured reports to the study centre. Second, they were advised to admit patients to hospital should they fall under a particular weight (body-mass index <14 kg/m^2). Finally, they were informed about physical and psychiatric risks in patients with anorexia nervosa and were instructed to contact the respective study centre should a patient become at risk. In the study protocol, treatment (dosage and type of therapy) in the optimised treatment as usual study group was not regulated. Patients assigned to this group had at least five contact sessions with the study centre, at which their weight, laboratory findings, eating pathology, and psychiatric comorbidity were investigated and monitored.

Waitlist control: No treatment is provided during the experimental treatment period, but the experimental treatment is offered after posttreatment assessment

Some caveats:

- ✓ Assigning a patient to a waiting list is essentially withholding treatment (ethically questionable).
- ✓ Not be used when a gold-standard treatment exists.
- ✓ Not be used if prevention of treatment could result in adverse effects for the participants.
- ✓ Waiting list may overestimate the effect size of a given therapy.

SUMMARY OF CONTROL CONDITIONS IN PSYCHOTERAPY RESEARCH

- Relevant comparators include;

A) ones that reflect existing clinical or public health practices or services (e.g. usual care or standard of care)

B) alternative interventions (e.g., a well-established, evidence-based intervention as a comparator for a newer intervention),.

C) clinically-relevant variations on the experimental intervention (e.g., the same intervention except delivered via an alternative modality, such as when a face-to-face intervention is compared to the same intervention delivered via remote telehealth technology).

5. Therapists variability . Challenges

Differences in therapist skill, experience and adherence to the protocol can introduce variability in treatment effects, making it harder to attribute changes to the therapy itself.

MITIGATIONS

Therapist training and certification: Ensure that all therapists receive standardized training and certification in the specific intervention being tested.

Fidelity checks: Regularly monitor therapy sessions using fidelity checklists, either through direct observation or video/audio recordings, to ensure adherence to the therapeutic model.

Supervision. Provide on-going supervision and feedback to therapists throughout the trial to maintain consistency.

One of the most important differences between psychotherapy trials and other clinical trials is that the treatment is delivered using human communication.

A practitioner unwilling to discuss uncertainty about alternative treatments with patient

The treatment that is most effective when provided by one practitioner may not be the most effective when provided by antoher.

THERAPIST

A practitioner may have a learning curve for a new intervention

Innate skill varies between practitioners/Training

A practitioner may have a strong preference for one treatment rather than another. ALLEGIANCE

It is important to have more than a therapist in the study.

Controversy whether each therapist should be assigned to deliver only a treatment, or if each therapist should deliver all the treatments (**cross-contamination**).

Clinical Psychology Review 33 (2013) 501–511

Contents lists available at SciVerse ScienceDirect

Clinical Psychology Review

Researcher allegiance in psychotherapy outcome research: An overview of reviews

Thomas Munder [a,b,*], Oliver Brütsch [a], Rainer Leonhart [c], Heike Gerger [a], Jürgen Barth [a]

[a] Institute of Social and Preventive Medicine, University of Bern, Switzerland
[b] Institute of Psychology, University of Kassel, Germany
[c] Institute of Psychology, University of Freiburg, Germany

- *Belief in the superiority of a treatment and the superior validity of the theory of change that is associated with the treatment'*
- 30 meta-analysis were included
- Research allegiance –outcome association is substantial and robust.
- Therapist allegiance accounts about 69% of the variance in psychotherapy outcome studies

Munder et al, 2013

How to control the effects of Allegiance?

- Comparative studies shoud be conducted collaboratively by teams with mixed allegiances.
- Study therapists in all treatment conditions should be motivated to learn and deliver their respective treatments.
- Clinicians also tend to arrive with an allegiance to the treatment they are to deliver, or develop one during the trial.

Rigorous clinician training is recommended, but most of the clinical skills and abilities that study clinicians utilize are acquired long before they begin work on a trial.

If clinicians provide a treatment that they are well trained in they will likely be more skilled and enthusiastic in their delivery of that treatment, which in turn may influence the outcome.

OTHER THREATS TO THE INTERNAL VALIDITY

1.- Assessment

2.- Outcome determination

ASSESSMENT

- Measurement of clinical issues (type, severity and sequence of symptoms, staging, severity of comorbidity, problems of functional capacities, reasons for medical decisions, well being and distress)
- Standardization of observer-rated scales
- Self-rated measures
- Evaluation of side effects

- Psychotherapists are biased against recognizing their own treatment's side effects
- Side effects may be related not only to symptoms or course of illness but also to other areas of life and it is difficult to ascertain the relationship between a certain event and a treatment.
- Both interviews and self-rated instruments can be used.

Guidi et al, 2018

Self-reports

Advantages

- It gives you the respondent's own view directly information which is unobtainable in any other way.
- Can be used to obtain information and situations where observational data are not normally available.

Disadvantages

- Potential validity problems (errors due to deception, inaccurate recall or the unavailability of the information to conscious processing).
- The data are personal and idiosyncratic and thus may bear little relationship to 'reality'.
- Lack of insight.
- Research participants may not be able to provide the level of detail, or use the concepts, that the researcher is interested in.

Outcome determination

- Define properly primary and second outcomes
- Remission (categorical variable/comparative category)
- Relapse and recurrence (adequate criteria are not available for all mental health conditions)
- Indicate the number of participants display deterioration after treatment should be noted according to specific cut-off points of the same rating scales
- Include biomarkers as secondary outcome (changes in neutrophins, neuroimage, digital biomarkers…)

Barkler et al, 2014

6. Measure outcomes . Challenges

Outcomes in psychotherapy trials are often subjective, relying heavily on self-report measures, which may be influenced by various biases (eg. Social desirability, psychopathological state, recall bias).
Psychological changes may take time to manifest, making it difficult to measure immediate effects.

MITIGATIONS

Use a combination of outcome measures: Include both self-report scales and clinician-rated scales.

Multiple time points: Assess outcomes at several points to capture changes over time and evaluate the sustainability of the treatment effects.

7. Long-term follow-up. Challenge

Psychotherapy effects may continue to evolve after the active treatment phase ends, making short-term evaluations insufficient.

SOLUTION

Extended follow-up periods Plan follow-up assessments at multiple time points to evaluate the persistence of treatment effects.

Maintenance interventions: If feasible, consider offering booster sessions during the follow-up period.

Length of therapy

- The average number of sessions for published RCTs in psychotherapy research is sixteen.
- Field studies of CBT for depressed patients report an average of 69 sessions.
- Short term therapies produce benefits more quickly than more individually focused therapies.
- Long term therapy is superior than short-term therapies at three and five years follow-up.

LAC Studie

Original Research

The Canadian Journal of Psychiatry / La Revue Canadienne de Psychiatrie
1-12

DOI: 10.1177/0706743718780340
TheCJP.ca | LaRCP.ca
SAGE

Outcome of Psychoanalytic and Cognitive-Behavioural Long-Term Therapy with Chronically Depressed Patients: A Controlled Trial with Preferential and Randomized Allocation

Résultat d'une thérapie psychanalytique et cognitivo-comportementale à long terme chez des patients souffrant de dépression chronique : un essai contrôlé avec allocation préférentielle et randomisée

Marianne Leuzinger-Bohleber, Prof. PhD[1,2], Martin Hautzinger, Prof. PhD[3], Georg Fiedler, Dipl. Psych.[4], Wolfram Keller, Dr. med.[5], Ulrich Bahrke, PD. Dr. med.[6,7], Lisa Kallenbach, Dipl. Psych.[6], Johannes Kaufhold, Dipl. Psych.[6], Mareike Ernst, Dipl. Psych.[2], Alexa Negele, PhD[2], Margerete Schoett, Dipl. Psych.[7], Helmut Küchenhoff, Prof. PhD[8], Felix Günther, PhD[8], Bernhard Rüger, Prof. Dr. rer. nat.[8], and Manfred Beutel, Prof. Dr. med.[2]

LAC Study: Goals

(1) compare outcome of PAT and CBT in reducing depressive symptoms (BDI, QIDS-C) in a controlled, randomized trial
(2) compare remission rates of PAT and CBT
(3) study the influence of patients treatment preference
(4) study the influence of **treatment intensity**
(5) study the influence of early trauma

It was expected that
(a) both treatments lead to positive effects
(b) being treated by preferred treatment results in better outcome
(c) CBT shows faster improvement than PAT
(d) PAT starts slowly but achieves more stable effects.

LAC Studie

Treatment Intensity and Duration

- **PAT** Therapists could meet their patients up to 300 sessions (range 160 – 300) over the 3 years study time:
- First year (t0-t4) 81 sessions
- All three years (t0-t8) 234 sessions
- Duration of PAT: mean of 34 months

- **CBT** therapists could meet their patients up to 80 sessions (range 34 – 60)
- First year (t0-t4) 33 sessions
- All three years (t0-t8) 57 sessions
- Duration of CBT: mean of 17 months

PAT treats twice as long and four times as intensive than **CBT** but without any outcome differences

8. Handling missing data and attrition. Challenge

High drop-out rates and missing data can bias the results and reduce the power of the study

MITIGATION

Intent-to-treat (ITT) analysis: Include all participants who were randomized in the final analysis, regardless of whether they completed treatment. This approach helps to maintain the benefits of randomization and reduces bias.

Imputation methods: Use statistical techniques like multiple imputation to handle missing data without introducing significant bias.

Retention strategies: Enhance participant retention with regular check-ins, flexible scheduling, and compensation for time and travel, as well as reminders about the importance of their participation in the study.

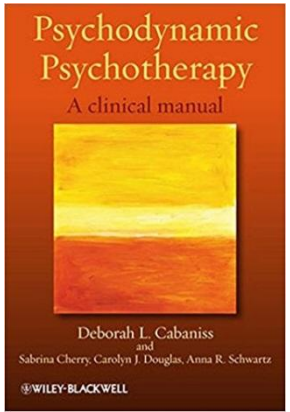
Missing data

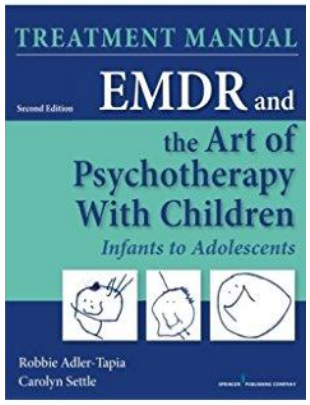
- RCT often suffer from two major complications, i.e., noncompliance and missing outcomes.
- Not all patients who are assigned to treatment complete their participation in the study (Attitrition)
- Attitrition can be problematic for data analysis, some authors estimate that most researchers can expect 20% of their sample to withdraw or be necessarily removed from the study before it is complete
- To adress this matter two sets of analyses:
  - Analyses of outcomes for the completers
  - Analyses for patients included at the time of randomization (ITT)

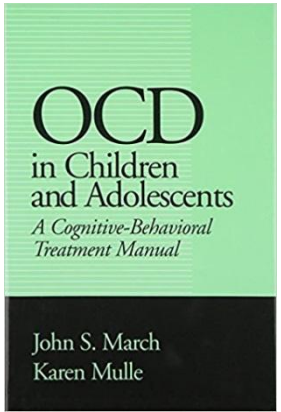
Features of RCTs and relative criticisms

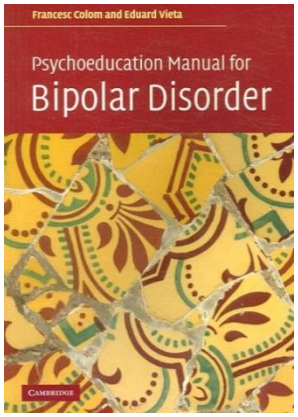
Features of RCts	Criticisms
○ Standarization of treatment procedures	○ Psychoterapy is extremely difficult to 'standardize' so that its procedures and techniques are used in the same way by all therapists.

- The use of manuals biases outcome research in favor of those therapies that can't be operationalized.
- The treatment should be manualized, its implementation monitorized and the interventions trained and supervised.









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REVIEW ARTICLE

To manualize, or not to manualize: Is that still the question? A systematic review of empirical evidence for manual superiority in psychological treatment

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The Alliance in Adult Psychotherapy: A Meta-Analytic Synthesis

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IMPORTANT ISSUES TO INCLUDE IN AN 'IDEAL' PSYCHOTHERAPY TRIAL DESIGN

- Randomized Controlled Trial with three groups:
  - Experimental group: Receives the targeted psychotherapy intervention
  - Active control group: Receives supportive therapy or psychoeducation
  - Treatment-as-Usual Group: Continues their usual care
- Blinding:

Outcome assessors and data analysts blinded to treatment assignment.

- Fidelity checks:

Regular therapist supervision and session recording reviews to ensure adhere
nce to protocol

- Outcome measures:

Use a combination of self-report, clinician-rated, and objective measures.

Why don't clinical psychologists do research?

- Irrelevance
- Emphasis on generalities
- Mistaken paradigm
- Intrusiveness
- Time demands
- Technical expertise
- Ethical concerns
- Bureaucracy
- Bad training experiences
- Disturbing conclusions

Morrow Bradley & Elliot, 1986; Hayes et al, 1999

Thanks for your attention

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