# *Pragmatic vs explanatory trials: the Pragmascope tool to help measure differences in protocols of mental health randomized controlled trials*

*Graeme Tosh, MD; Karla Soares-Weiser, MD, PhD; Clive E. Adams, MD*

*In the pragmatic-explanatory continuum, a randomized controlled trial (RCT) can at one extreme investigate whether a treatment could work in ideal circumstances (explanatory), or at the other extreme, whether it would work in everyday practice (pragmatic). How explanatory or pragmatic a study is can have implications for clinicians, policy makers, patients, researchers, funding bodies, and the public. There is an increasing need for studies to be open and pragmatic; however, explanatory trials are also needed. The previously developed Pragmatic-explanatory continuum indicator summary (PRECIS) was adapted into the Pragmascope tool to assist mental health researchers in designing RCTs, taking the pragmatic-explanatory continuum into account. Ten mental health trial protocols were randomly chosen and scored using the tool by three independent raters. Their results were compared for consistency and the tool was found to be reliable and practical. This preliminary work suggests that evaluating different domains of an RCT at the protocol level is useful, and suggests that using the Pragmascope tool presented here might be a practical way of doing this.*

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## Background

The randomized controlled trial (RCT) has long been recognized as the most robust technique for evaluating the effects of mental health care interventions.[1] Sometimes these trials are impossible, sometimes unethical, and sometimes impractical. The first RCT was the 1948 Medical Research Council Streptomycin Trial.[2] In the austere times of bankrupt, post-war England, just as the National Health Service was being established, it was suggested that a new drug would be of value for treatment of tuberculosis. The only equitable way to distribute this scarce resource was through randomization and then, by the establishment of good evidence, to encourage those funding health care to support its use. There are many interesting and important examples preceding this date,[3] but this landmark and courageous trial radically changed the pathway of evaluation of medical treatments.

Mental health has a fine tradition of using trials to evaluate treatments.[4] The MRC Streptomycin trial coincided with the discovery of psychoactive compounds that were potentially therapeutic, as well as an increasing push

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towards deinstitutionalization. Mental health professionals discovered, discussed, and, largely, embraced the use of RCTs. Up to the advent of antipsychotic drugs such as chlorpromazine, psychiatric care had been likened to "little more than zoo keeping"[5] and, perhaps because of that stinging criticism, those undertaking the trials did not necessarily follow the path of that first tuberculosis trial. Factors combined to largely direct mental health trials along another route. There was the yearning for rigorous science, collective subspecialty insecurity, and also the needs of regulatory authorities. Mental health trials drifted towards use of as rigorous diagnoses as possible, rather rigid regimens of care and use of fine-grained outcome measures that are not usually part of routine practice. This planted the RCT firmly in the realm of researchers, and there it has stayed. The needs of regulatory authorities did have to be met, but there was less consideration of needs of clinicians and of recipients of care and their families.

This was not at all unique to mental health, but it took leaders in the fields of cancer care,[6] heart disease,[7] and perinatal medicine[8] to recall and refine the techniques of generous inclusion, simple treatment, and routine data collection that underpinned the MRC trial of 1948. Many examples now exist in these areas of RCTs where entry criteria are broad and encompass as many relevant people as possible, the treatment packages are those that would be given in everyday care, and outcomes are essentially routinely recorded data. Examples of such open work were rare in mental health until relatively recently. The description of "pragmatic" or "practical" is increasingly employed of trials in psychiatry or psychology but there are clearly different interpretations of what this really means.

A recent series of papers has highlighted the problems in interpretation of the explanatory/pragmatic domains in trials and presented some practical solutions.[9] It is not a simple continuum from explanatory through to pragmatic. There are many elements of design that should be considered to allow a judgment to take place about whether a randomized trial is investigating whether, in ideal circumstances, a treatment could work (explanatory) or, at the other extreme, whether this accessible treatment would work in everyday practice (pragmatic). This is not a purely academic exercise. There are good reasons to make these judgments. To use one example, funders, on receiving a proposal, may wish to consider whether the proposed trial fits with the ethos in which that support was proffered. For example one funding body may be interested in discovering potentially new treatments. In this instance, explanatory studies, undertaken in very rigorous circumstances with fine measures of outcome to highlight any—even modest—effects, may be best. On the other hand, another funder, using public money, may wish to consider whether the study is likely to produce evidence of practical importance regarding accessible treatments relevant to the majority of people suffering with the condition in that community.[10] Here a much more pragmatic study would be desired. How explanatory or pragmatic a study (or a group of studies) is has also obvious and direct implications for clinicians, policymakers, patients, and the public.

The main goal of this study is to adapt the instrument described by Thorpe et al[9] (PRECIS) to assist researchers in making those judgments in the protocol stage of RCTs in mental health (the Pragmascope tool).

## Methods

### The Pragmascope tool

This tool is based on the ten domains described in the development of the Pragmatic-explanatory continuum indicator summary (PRECIS).[9] It can be used to assess applicability of results from any given RCT, based on what was planned at the protocol stage.

Each included RCT protocol[11-19] was scored in ten domains by three independent reviewers (GT, KSW, CEA). The reviewers made a judgment and rated the protocol from 1 (most explanatory) to 5 (most pragmatic) by reading the details of the protocol. If the protocol did not contain any information on which to base the decision, these domains were rated as zero. The average scores for each included protocol were placed on the wheel diagram and the dots joined for visual clarity *(Figure 1)*.

### Selection of RCT protocols

We searched the Cochrane Schizophrenia Group Trials Register and Medline (November 2010) for references of RCT protocols and chose a random sample of 10 protocols dealing with schizophrenia, depression, post-traumatic stress disorders, and psychiatric rehabilitation.[11-19]

### Scoring the Pragmascope tool

Three independent reviewers (GT, KSW, CEA) scored each included RCT protocol. The overall score can be from 0 to 50 and a diagram illustrating how open (pragmatic) or restrictive (explanatory) the study is likely to be was created using the average score of the three independent reviewers.
Our initial interpretation of the scores was of 0 to 30 for an explanatory study investigating whether the experimental intervention will work in ideal circumstances and a total score >35 for a more pragmatic study focusing mostly on whether, in routine practice, an intervention has a meaningful effect. A total score between 31 and 39 were interpreted as an interim where trial design balances pragmatic and explanatory domains.

### Data analysis

Mean and variance were calculated for each domain of the Pragmascope tool for each included RCT protocol using STATA (version 10). In addition, a weighted kappa for the domains was calculated using R.

## Results

*Table I* presents the average score of the three raters in each one of the domains for each RCT protocols with a judgment based on the scores. Reliability among the three independent raters was high (weighted Kappa =0.72 for categories 0-30, 31-39, 40-50) suggesting that this cluster of judgments might be useful to highlight and quantify important issues during the protocol stage of an RCT.
We recognize that validity is a more problematic issue, as this does depend on the rater's perspective, but work is ongoing involving raters from very different backgrounds. In any case, we concur that consideration of these domains is useful[9] and suggest that the Pragmascope is one practical way of doing this.

## Discussion

The world of RCTs has changed remarkably in the last 10 years. Systematic reviewing of trials, now industrially undertaken through initiatives like the Cochrane Collaboration,[20] has highlighted issues with poor design and inconsistent reporting. These systematic reviews are

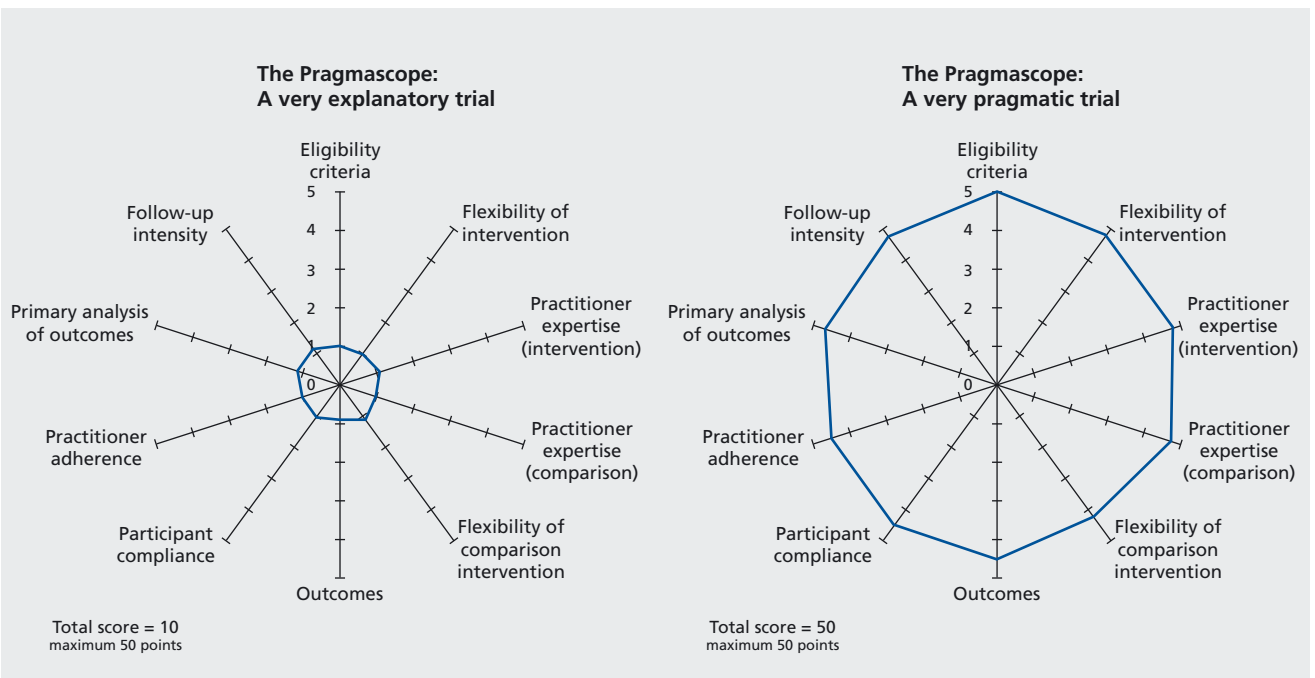


**Figure 1.** Examples of output.
Reproduced from ref 9: Thorpe KE, Zwarenstein M, Oxman AD, Treweek S, Furberg CD, Altman DG, et al. A pragmatic-explanatory continuum indicator summary (PRECIS): a tool to help trial designers. *J Clin Epidemiol*. 2009;62:464-475. Copyright ©2009 Elsevier

potent to guide care but are undermined by trial evidence that is difficult or impossible to apply in the real world. For mental health, studies of increasing pragmatism are now being designed and undertaken.[21-23] Such pragmatic, real-world, practical design can be dovetailed within explanatory studies or sit independently. With maintained systematic reviews guiding practice,[21] transparent priority setting for research funding for evaluative research,[3] and the push towards defining core outcome measures of agreed relevance in trials,[24] a great increase in pragmatic trial activity is likely. Of course explanatory trials have an important place in the portfolio of research, but the rigorously undertaken but highly pragmatic trial will give us the opportunity to learn much more about the real effects of the potent treatments we give. ❑

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| Domain | ACHIEVE[14] (Low) | CATIE[11] (Low) | CCEST[17] (Low) | DYD[18] (Low) | ERP[16] (Low) | FIAT[19] (High) | PTSD- Yoga[20] (Moderate) | ROMT[15] (Moderate) | SPCCD[13] (Low) | TREC –SAVE (High) (unpublished) |
|---|---|---|---|---|---|---|---|---|---|---|
| Eligibility criteria | 1 | 2 | 2 | 2 | 2 | 3 | 2 | 3 | 2 | 5 |
| Flexibility of intervention | 2 | 3 | 3 | 3 | 1 | 4 | 2 | 3 | 3 | 4 |
| Practitioner expertise (intervention) | 1 | 3 | 2 | 2 | 2 | 5 | 2 | 2 | 2 | 4 |
| Practitioner expertise (comparison) | 4 | 3 | 4 | 2 | 5 | 5 | 5 | 5 | 5 | 5 |
| Flexibility of comparison intervention | 3 | 3 | 3 | 3 | 5 | 5 | 5 | 5 | 4 | 5 |
| Outcomes | 3 | 2 | 3 | 3 | 2 | 4 | 4 | 3 | 2 | 4 |
| Participant compliance | 4 | 2 | 4 | 3 | 2 | 4 | 5 | 5 | 3 | 4 |
| Practitioner adherence | 3 | 2 | 3 | 3 | 2 | 4 | 5 | 4 | 3 | 5 |
| Primary analysis of outcomes | 1 | 2 | 1 | 3 | 5 | 4 | 4 | 4 | 5 | 4 |
| Follow-up intensity | 1 | 2 | 3 | 5 | 2 | 4 | 2 | 2 | 2 | 5 |
| Total Average score | 23 | 25 | 29 | 28 | 27 | 43 | 34 | 34 | 28 | 45 |

**Table I.** Average score of three raters for each one of the domains of the RCT protocol.

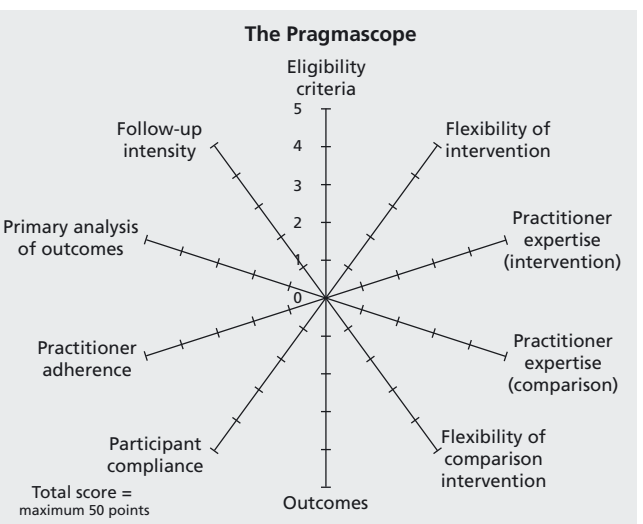
## **Appendix.** The Pragmascope *(Figures 2 and 3)*

*Explanation:* This tool is based on ten domains described in the development of the Pragmatic-explanatory continuum indicator summary (PRECIS).[9] It can be used to assess applicability of results from any given randomized controlled trial.

*Instructions:* For each of the ten domains please make a judgement and rate the protocol from 1 (most explanatory) to 5 (most pragmatic). Your score should be based on a thorough reading of the protocol. If the protocol does not contain any information on which to base your decision we advise a default score of zero. If you feel your scores require justification - please make comments in box provided. Mark score on relevant part of the diagram and join the dots.

*Results:* The scoring can give you an overall score (0-50) and a diagram illustrating how open (pragmatic) or restrictive (explanatory) the study is likely to be.

*Interpretation: Figure 1* (see main text) demonstrates an explanatory study investigating whether the experimental intervention will work in ideal circumstances (total score 0-15) and a more pragmatic study focusing mostly on whether, in routine practice, an intervention has a meaningful effect (total score >35). A total score between 16 and 35 suggest an interim where trail design balances pragmatic and explanatory domains.



**1. Eligibility criteria**
- Does the study population represent the people who will really be treated with the experimental intervention?
- Think about restrictions to participation - such as a pre-determined number of participants or any exclusion criteria which make the trial less real-world.
- Consider any selection bias toward high risk people or those without co-morbidity.
- Trials open to the entire target population are more pragmatic, those which have exclusion criteria become progressively less so as exclusions become more rigid.

Explanatory pragmatic
0 1 2 3 4 5

**2. Flexibility of experimental intervention**
- Does application of the intervention allow for variation and adaptability which exists in everyday life?
- Think about rigidity of protocol application and strict, extensive or complex instructions - these make a study less pragmatic.
- Less pragmatic still are trials which closely monitor application of intervention and make exclusions based on this.
- If creativity is allowed or encouraged in applying the intervention and/or it is tailored to fit the individual - this is more representative of real life and more pragmatic.

Explanatory pragmatic
0 1 2 3 4 5

**3. Practitioner expertise - for experimental intervention**
- Can the experimental intervention be carried out by people ordinarily involved with the care of participants?
- Less pragmatic interventions require higher levels of practitioner expertise – this can mean staff education or training (intensity is important) or bringing in others not normally involved in the care of participants.
- Sometimes the intervention requires involvement of an external expert - particularly non-pragmatic.

Explanatory pragmatic
0 1 2 3 4 5

**4. Practitioner expertise - for comparison intervention**
- Can the comparison be carried out by people ordinarily involved with the care of participants?
- Less pragmatic interventions require higher levels of practitioner expertise – this can mean staff education or training (intensity is important) or bringing in others not normally involved in the care of participants.
- Sometimes the intervention requires involvement of an external expert - particularly non-pragmatic.

Explanatory pragmatic
0 1 2 3 4 5

**5. Flexibility of comparison**
- Is the intervention being compared with what is currently happening in everyday practice? The level of pragmatism is reduced by comparing the experimental intervention to other structured or regulated comparisons.
- The ideal pragmatic comparison is unregulated treatment as usual.
- The more a comparison diverges from this by introducing regulation, instruction or monitoring - the more explanatory the trial becomes.

Explanatory pragmatic
0 1 2 3 4 5

**6. Outcomes**
- Are outcomes important to the health/needs of participants (pragmatic) or the needs/profits of the researcher (explanatory)?
- How complex is the measurement of outcomes?
- How much does measurement of outcome require input from participants?
- More pragmatic trials will look at outcomes in the long term and no specific training will be required for measurement.
- Pragmatism should also avoid the need for central adjudication of outcome measurement.
The outcome should be positive for the participant.

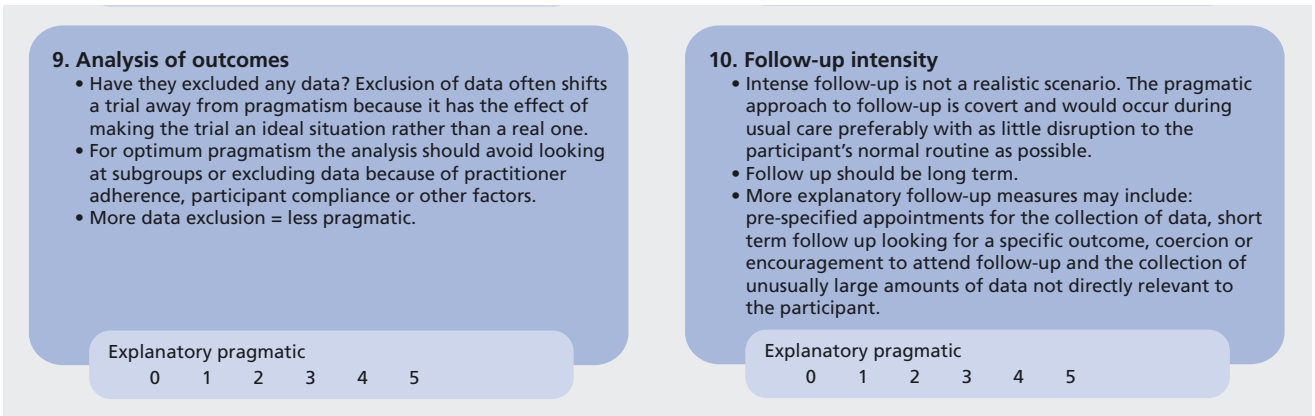
Explanatory pragmatic
0 1 2 3 4 5

**7. Participant compliance**
- In real life compliance with treatment is highly variable, does this trial falsely eliminate non-compliance by monitoring or by excluding those who falter in compliance?
- Pragmatic trials accept that non-compliance is a fact of life and therefore avoid monitoring, or trying to improve compliance.
- Ideally pragmatic trials should avoid measuring compliance altogether since any information obtained could be used in future trials to falsely improve compliance.

Explanatory pragmatic
0 1 2 3 4 5

**8. Practitioner adherence**
- Does this study regulate adherence to treatment to a degree which would not be replicated in real life?
- Pragmatic trials should avoid monitoring practitioner adherence to the study protocol, explanatory trials would try to identify practitioners with poor compliance and possibly eliminate their data from the study.
- Between these two extremes trials which try to improve adherence are less pragmatic and those which allow for individual creativity and flexibility are more so.

Explanatory pragmatic
0 1 2 3 4 5




## *Ensayos pragmáticos versus explicativos: Pragmascope, el instrumento que ayudar a medir las diferencias en los protocolos de ensayos controlados randomizados de salud mental*

*En el continuo pragmático-explicativo, un ensayo controlado randomizado (ECR) puede investigar por una parte si un tratamiento podría funcionar en circunstancias ideales (explicativas) y por otra si podría funcionar en la práctica diaria (pragmático). Cuan explicativo o pragmático sea un estudio, puede tener repercusiones para los clínicos, los políticos, los pacientes, los investigadores, los organismos de financiamiento y el público. Hay una necesidad creciente de que los estudios sean abiertos y pragmáticos; sin embargo, también son necesarios los ensayos explicativos. PRECIS, el resumen del indicador del continuo pragmático-explicativo que se había desarrollado con anterioridad, se adaptó al instrumento Pragmascope para ayudar a los investigadores de salud mental en los diseños de ECR, tomando en consideración el continuo pragmático-explicativo. Se eligieron randomizadamente diez protocolos de ensayos de salud mental y se les asignó puntaje mediante el instrumento por tres evaluadores independientes. Sus resultados se compararon en cuanto a consistencia y se encontró que el instrumento fue confiable y práctico. Este trabajo preliminar sugiere que es útil la evaluación de diferentes aspectos de un ECR a nivel del protocolo y propone que el empleo del instrumento Pragmascope presentado aquí sería una forma práctica de hacerlo.*

## *Études pragmatiques* versus *explicatives : l'outil Pragmascope de mesure pour mesurer les différences dans les protocoles d'études contrôlées randomisées sur la santé mentale*

*Dans le continuum pragmatique-explicatif, une étude contrôlée randomisée (ECR) peut d'un côté analyser l'efficacité d'un traitement en circonstances idéales (explicatives) ou d'un autre côté son efficacité dans la pratique quotidienne (pragmatique). Qu'une étude soit explicative ou pragmatique, elle peut avoir des implications pour les médecins, les responsables politiques, les patients, les chercheurs, les organismes de financement et le public. Les études doivent de plus en plus être ouvertes et pragmatiques, mais les études explicatives sont aussi nécessaires. L'indicateur de continuum pragmatique - explicatif PRECIS (*Pragmatic-explanatory continuum indicator summary*) développé antérieurement a été adapté sous forme de l'outil PRAGMASCOPE pour aider les chercheurs en santé mentale à concevoir des ECR, en prenant en compte ledit continuum. Dix protocoles d'études en santé mentale ont été choisis et cotés au hasard grâce à l'outil, par trois évaluateurs indépendants. Leurs résultats ont été comparés pour évaluer leur cohérence et l'outil s'est avéré fiable et pratique. Ce travail préliminaire suggère que l'évaluation des différents domaines des ECR au niveau du protocole est utile et que l'utilisation du PRAGMASCOPE présenté ici pourrait être un moyen pratique de le faire.*

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