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Review article

The use of waitlists as control conditions in anxiety disorders research

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ABSTRACT

Current evidence suggests that the strength of the psychological control condition greatly impacts treatment outcomes. Psychological controls can be grouped into three general classes: no-treatment or waitlist (delayed treatment), attention placebo or the best available treatment comparison. Of these three, the use of the waitlist condition is the most common and is used in up to 73% of published psychological treatment studies. Many psychological interventions are in use today based on the efficacy demonstrated in waitlist controlled trials. In the field of anxiety disorders, cognitive behavioural therapy (CBT) is considered a first-line treatment. Meta-analyses in anxiety disorders have revealed that effect sizes for CBT compared to waitlist controls are much higher than those found using psychological placebos as comparators. Furthermore, waitlists have been associated with deleterious effects and have been described as "no-cebos" in related conditions such as major depressive disorder. Despite these findings, the use of waitlist controls continues to be a mainstay in the psychological anxiety disorders literature. The purpose of this paper is to examine the use of waitlists with a focus on the anxiety disorders. Methodological and ethical issues associated with waitlist controls will be explored, as well the use of alternative psychological placebos.

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1. Introduction

Clinical research has evolved exponentially over the past 50 years as clinicians of all types strive to deliver treatments based on the best evidence. Although there are many different study designs which have the capacity to answer diverse research questions, randomized, controlled trial (RCT) designs are considered to be near the top in terms of producing the strongest evidence for or against a particular therapeutic intervention (Devereaux and Yusuf, 2003; Hulley et al., 2013). RCTs are considered second only to the meta-analysis, which itself is a combination of several RCTs. Therefore, evidence-based clinical decisions should be based on multiple individual RCTs or meta-analyses (Devereaux and Yusuf, 2003). In order to maintain the internal validity of a study (the extent to which the outcome of a given intervention can be attributed to that intervention and not to any other explanation, bias or confounder), a great deal of control over various factors is required. Ideally, investigators strive to control for the natural regression towards the mean, the course of the disease, the "Hawthorne Effect" (effect of being evaluated and observed) and the effect of expectancy of being treated for benefit (Furukawa et al., 2014). Historically, one of the most common methods employed to control for some of these variables has been the use of placebo. In pill form, a placebo is pharmacologically inert but is visually indistinguishable from the pharmacological treatment being tested, enabling investigators and study participants to be "blind" to the assigned treatment condition. This has the benefit of allowing the active component of the investigative treatment to be isolated, limiting the effect expectancy and other biases (Sackett et al., 2005). "Psychological placebos" or control conditions are defined as 'treatments' in which the participants have equal faith, but which would not be expected to lead to behavioural changes on any other grounds (Paul, 1966). The use of placebos in clinical research has successfully isolated some of the potential biases and threats to internal validity. In particular, ascertainment bias (where patients may actively look for mild changes in their physical or mental state, if they know they are receiving a particular treatment) and information bias (where patients may be more likely to report mild side effects, improvements, or deteriorations if they are aware of what they are taking) are meaningfully reduced with the use of placebo (Sackett et al., 2005). However, there are many biases which continue to lurk in RCT study methodology regardless of the condition (experimental or control) the participant is in.

1.1. The "placebo effect"

In his influential "The Powerful Placebo" paper published in 1955, Beecher described the use of a placebo as an indispensible tool for testing the efficacy of an intervention, as a "placebo effect" accounts for significant improvement in nearly 35% of cases (Beecher, 1955). Placebo response rates as high as 50–71% have been found in pharmacotherapy RCTs in depression and anxiety disorders (Reinhold and Mandos, 2011; Kirsch and Low, 2013). However, these response rates in psychotherapy trials vary considerably by the type of control or placebo condition used. Although there are many definitions of the placebo effect, it is important for investigators to understand that clinical improvements seen over the course of a clinical trial are equally likely to occur in patients randomized to both treatment and placebo/control conditions (Table 1).

Despite the common acceptance of a placebo effect, very little is known about its mechanism of action (for a good theoretical review, see Stewart-Williams and Podd, 2004). Placebos are purported to operate through the constructs of hope, expectation, remoralization, therapeutic relationship, and other psychological processes (Wampold et al., 2005). Some researchers have also argued that a placebo effect does not actually exist. Although widely criticized, this belief is supported by results of at least one meta-analysis of placebo conditions in clinical research (Hróbjartsson and Gøtzsche, 2001).

Psychological treatment RCTs pose additional challenges to achieving the same degree of control as that produced by pharmacological studies, leading some to argue that a psychological placebo is not equal to a pill placebo (Borkovec and Sibrava, 2005; Bandelow et al., 2015). One of the primary problems with psychological RCTs is that true blinding of the therapists who administer the treatments is impossible (Mohr et al., 2009). Consequently, investigator and patient expectation bias and patient appreciation bias become major confounding factors. Nevertheless, "control" conditions continue to be the mainstay in psychological research, including research in anxiety disorders. Although it is widely accepted that RCTs are the gold-standard study methodology, there is little agreement on how to design or select an appropriate psychological treatment for the necessary comparator condition (Mohr et al., 2009). The current literature reveals significant heterogeneity in the types of psychological placebos or controls used. While diverse, they can be grouped into three general classes: no-treatment or delayed treatment, attention placebo or the best available treatment comparison (Heimberg and Liebowitz, 1996). Of the three types of controls, the use of a waitlist condition (delayed treatment) is the most common. The purpose of this paper is to examine the use of waitlists as control conditions with a focus on the anxiety disorder literature. This issue will be explored in terms of potential practical advantages of waitlists, concerns associated with waitlist controls, alternatives to waitlists and recommendations for future psychological treatment studies.

1.2. Waitlists as a control condition in psychotherapy trials

While placebos attempt to provide a 'zero-dose' of an intervention and control for non-specifics, waitlists attempt to control for the passage of time and assessment in the population of interest (Devilly and McFarlane, 2009). Typically, following a standardized study assessment, consenting participants are randomized to either receive the experimental intervention or to wait for a set period of time. It is commonly accepted that waitlist participants are now functionally similar to a no-treatment control group (control and comparison groups) (Kazdin, 2003). The length of treatment determines the length of time the waitlist group goes without treatment (e.g. two weeks or two months); following this period both treatment and waitlist participants complete a post-treatment assessment (Kazdin, 2003). Only after this post-assessment will waitlist participants be able to receive treatment. There may be variations in this basic design in which participants may have contact with therapists over the waitlist period, allowing therapists to monitor their health, and whether they engage in other help-seeking behaviours (Mohr et al., 2009).

Many psychological interventions are in use today based on evidence from waitlist controlled studies. Conversely, there may be other psychological treatments that are not in use today due to the same evidence. In the anxiety disorders literature, cognitive behavioural therapy (CBT) is considered to be the first-line psychological treatment for all disorders in this category: social anxiety disorder (SAD), generalized anxiety disorder (GAD), panic disorder (PD), agoraphobia (Ag) and specific phobia (APA, 2014). The efficacy of CBT is supported by both RCT and meta-analytic evidence in adults, children, adolescents and the elderly (Haby et al., 2006; Smits and Hofmann, 2009; James et al., 2007; Otte, 2011; Cuijpers et al., 2014).

Waitlists are very common comparators in psychological