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# **Randomized Clinical Trials of Nonpharmacological Treatments**

**Edited by  
Isabelle Boutron  
Philippe Ravaud  
David Moher**



**CRC Press**  
Taylor & Francis Group

A CHAPMAN & HALL BOOK

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# Introduction

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**Isabelle Boutron and Philippe Ravaud**

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Nonpharmacological treatments represent a wide range of treatments proposed to patients. They could be defined as all interventions involving not just the administration of pharmacological treatments. Nonpharmacological treatments concern technical interventions such as surgical procedures; technical interventions such as joint lavage and angioplasty; implantable devices such as stents and arthroplasty; nonimplantable devices such as orthoses, ultrasound treatments, and laser treatments; and participative interventions such as rehabilitation, education, behavioral interventions, and psychotherapy.

The number of published randomized controlled trials assessing nonpharmacological treatments is increasing with time. A cross-sectional assessment of randomized trials published in 2000 identified 25% of such trials assessing nonpharmacological treatments (10% surgery or procedures, 11% counseling or lifestyle interventions, and 4% equipment) [1]. A similar recent study showed that randomized trials assessing nonpharmacological treatments concerned 42% of the trials published in 2006 (21% surgery or procedures, 18% counseling or lifestyle interventions, and 3% equipment).

Assessing nonpharmacological treatments raises specific issues. An important issue is the funding source. Most assessments of nonpharmacological treatments, except perhaps implantable and nonimplantable devices, rely on public funding, or more restricted amounts of money [2,3]. Further, the regulatory requirements for nonpharmacological treatments are less stringent than for pharmacological treatments. In most cases, the drug approval process of the U.S. Food and Drug Administration requires demonstrated treatment effectiveness from at least two adequate and well-controlled clinical trials.

In contrast, most nonpharmacological treatments such as surgical procedures or participative interventions have no specific requirements for approval. Consequently, they can be widely proposed in clinical practice but may not have been adequately evaluated. This situation is an important barrier for the evaluation of the beneficial effects of these treatments and the conduct of randomized controlled trials.

Finally, assessing nonpharmacological treatments raises specific methodological issues [3]. First, blinding of patients, care providers, and outcome assessors is frequently not feasible, particularly because of a lack of placebo for most nonpharmacological treatments [4]. Second, nonpharmacological treatments

are usually complex interventions made of several components that may all have an impact on the beneficial effect of the treatment [5]. These interventions are, consequently, difficult to describe, reproduce in the trial, and implement in clinical practice. Finally, care providers' expertise and centers' volume of care can have an important impact on the success of the interventions [6].

Nevertheless, it is essential to overcome these barriers and to adequately evaluate nonpharmacological treatments.

This book is divided in two parts. Part I is dedicated to specific issues when assessing nonpharmacological treatments. It highlights the difficulties of blinding and how these difficulties can be overcome. It discusses the placebos that can be used in such trials. It also addresses how the complexity of the intervention, the learning curve, and the clustering effect should be taken into account in trials. Issues of assessing harm and assessing the applicability of trials in this field are also raised. Different designs that are particularly useful in this context—cluster randomized controlled trials, expertise-based trials, pragmatic trials, and nonrandomized trials, as well as specific issues of systematic reviews in this field—are also presented.

Part II provides several examples of the planning, conduct, analyses, and reporting of trials in different fields. It is obviously impossible to cover all the different clinical areas, but these examples in the field of surgery, technical interventions, devices, rehabilitation, psychotherapy, behavioral interventions, etc., should be very useful for readers to learn and grasp some ideas from various domains.

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## **Part I**

# **Assessing Nonpharmacological Treatments: Theoretical Framework**

