

CONSORT Statement for Randomized Trials of Nonpharmacologic Treatments: a 2017 update and a CONSORT extension for nonpharmacologic trial abstracts

Isabelle Boutron (MD/PhD)^{1,2,3}; Douglas G Altman (DSc)⁴, David Moher (PhD)^{5,6}, Kenneth F. Schulz (PhD, MBA)⁷, and Philippe Ravaud (MD/PhD)^{1,2,3,8}; CONSORT NPT group

¹ Centre d'Épidémiologie Clinique, Hôpital Hôtel Dieu, Assistance Publique des Hôpitaux de Paris, Paris, France

² Paris Descartes University, Paris, France

³ INSERM, UMR 1153 Epidemiology and Biostatistics Sorbonne Paris Cité Center (CRESS), METHODS team, Paris, France

⁴ Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, OX3 7LD, UK

⁵ Centre for Journalology, Ottawa Hospital Research Institute, Ottawa, ON, K1H 8L6, Canada

⁶ School of Epidemiology, Public Health and Preventative Medicine, University of Ottawa, Ottawa, ON, K1H 8M5, Canada

⁷ FHI 360, Durham, NC, 27701 and University of North Carolina School of Medicine, USA

⁸ Department of Epidemiology, Columbia University Mailman School of Public Health, New York, NY, USA

CONSORT group

- Virginia Barbour (Office of Research Ethics & Integrity and Division of Research and Commercialisation, Queensland University of Technology, (QUT) Brisbane, Australia)
- Kamaldeep Bhui (Centre for Psychiatry, Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK)
- Nancy Chescheir (University of North Carolina at Chapel Hill Department of Obstetrics and Gynecology Chapel Hill, NC, USA)
- Pierre Alain Clavien Department of surgery, Swiss HPB and Transplantation Center, Department of Surgery, University Hospital Zürich, Switzerland)
- Markus K. Diener (Department of General, Visceral, and Transplantation Surgery; Study Center of the German Surgical Society, University of Heidelberg, Heidelberg, Germany)
- Paul Glasziou (Centre for Research in Evidence Based Practice, Bond University, Robina, QLD, Australia)
- Robert M. Golub (JAMA)
- Jeremy M. Grimshaw (Centre for Practice-Changing Research, Ottawa Hospital Research Institute; Department of Medicine, University of Ottawa, Canada)
- Trish Groves (British Medical Journal)
- Sally Hopewell (Centre for Rehabilitation Research in Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK)
- Sarah E Lamb (Centre for Rehabilitation Research in Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK)
- Peter McCulloch (Nuffield Department of Surgical Sciences, University of Oxford, UK)
- Cynthia Mulrow (Annals of Internal Medicine; University of Texas Health Science Center, San Antonio, TX, USA)
- Daniel Riddle (Virginia Commonwealth University, Richmond, VA, USA)
- Joseph S. Ross (General Internal Medicine, School of Medicine and Health Policy and Management, School of Public Health, Yale University, New Haven, CT, USA)
- Paula P. Schnurr (National Center for PTSD, White River, VT; Geisel School of Medicine at Dartmouth, Hanover, NH, USA)
- David Schriger (University of California Los Angeles, CA, USA)

- Larissa Shamseer (Centre for Practice-Changing Research, Ottawa Hospital Research Institute; School of Epidemiology, Public Health and Preventative Medicine, University of Ottawa, Ottawa, ON, Canada)
- David Torgerson (York Trials Unit, Department of Health Sciences, University of York, York, UK)

Word count: 1995

Abstract: 262

Abstract

Incomplete and inadequate reporting is an avoidable waste that reduces the usefulness of research. The Consolidated Standards of Reporting Trials (CONSORT) Statement is an evidence-based reporting guideline that aims to improve research transparency and reduce waste. In 2008, the CONSORT group developed an extension to the original statement that addressed methodologic issues specific to trials of nonpharmacologic treatments (NPTs) such as surgery, rehabilitation or psychotherapy. This article describes an update of that extension and presents a CONSORT extension for reporting abstracts of NPT trials. To develop these materials, we reviewed pertinent literature published up to July 2016, surveyed authors of NPT trials, and conducted a consensus meeting with editors, trialists and methodologists.

Changes to the CONSORT Statement extension for NPT trials include wording modifications to improve readers' understanding and the addition of 3 new items. New items address whether and how adherence of participants to interventions was assessed or enhanced, the description of any attempts to limit bias if blinding was not possible, and specification of the delay between randomization and the initiation of the intervention. The CONSORT extension for abstracts of NPT trials includes 2 new items that are not specified in the original CONSORT Statement for abstracts. The first addresses the reporting of eligibility criteria for centers where the intervention is performed and for care providers. The second addresses reporting of any important changes to the intervention from what was planned. Both the updated CONSORT extension for NPT trials and CONSORT extension for NPT trial abstracts should help authors, editors, and peer reviewers improve the transparency of NPT trial reports.

INTRODUCTION

Incomplete reporting is responsible for a great deal of avoidable waste in research (1, 2). The Consolidated Standards of Reporting Trials (CONSORT) Statement (3-5), an evidence-based reporting guidelines, was developed to improve research transparency.

Nonpharmacologic treatments (NPTs), such as surgery, rehabilitation, education, psychotherapy and devices, represent a wide range of interventions. However, assessing NPTs raises specific methodological issues related to the complexity of the intervention, influence of care providers, center's expertise, and the difficulties of blinding (6-15). To account for these specific issues, the CONSORT group developed a CONSORT Statement extension for trials of NPTs (hereafter CONSORT NPT extension) (16, 17). This extension (16, 17) was published in the *Annals of Internal Medicine* in 2008.

In 2010, the main CONSORT Statement was updated (5, 18). To take into account this update and methodological developments since publication of the original NPT extension, we aimed to update the CONSORT NPT extension and develop a CONSORT extension for reporting abstracts of NPT trials (19, 20).

METHODS

To update the CONSORT NPT extension, we proceeded in 3 steps.

First, we reviewed the literature to identify up-to-date evidence. The search is detailed in appendix 1.

Second, we surveyed corresponding authors of published articles citing the 2008 CONSORT NPT extension. Of the 1,525 authors invited by email, 194 (13%) participated. For each item of the CONSORT NPT extension, participants were asked to indicate whether they believed the item should be modified, and if so, why and how. The results of the survey are reported in the Appendix tables 1 and 2. From the literature review and the survey, we synthesized some proposals for changes to each item.

Finally, we organized a 2-day consensus meeting in May 2014 in Paris, France with 22 participants (editors (n=9), trialists (n=6) and methodologists (n=7)). During this meeting, the survey results and proposals for change were presented and each item was discussed until consensus was reached. After the meeting, we developed a draft of the current manuscript, which was sent to all participants for comments. The updated checklist was not modified at this stage.

UPDATING THE CONSORT NPT EXTENSION

Main changes to the CONSORT NPT extension

The revision of the CONSORT NPT extension checklist consisted of the deletion of items and the addition of new items, wording changes, and reformatting. The numbering and content of items were adjusted to follow the 2010 CONSORT Statement. Some wording was changed to improve readers' understanding, such as the use of "care providers" instead of "those performing the intervention" in Item 3.

Items 11a and 11b, related to blinding, were modified because these items were incorporated in the 2010 CONSORT Statement. Three new items were added to account for the difficulties in replicating NPTs, the frequent lack of blinding, and the risk of a differential delay between randomization and the initiation of the intervention. These items are dedicated to 1) whether and how adherence of participants to interventions was assessed or enhanced (Item 5d), 2) the description of any attempts to limit bias if blinding was not possible (Item 11c), and 3) the delay between randomization and the initiation of the intervention (Items 13c).

The updated NPT checklist is reported in Table 1, with examples of adequate reporting in the Appendix (table 3 and figure 1). The participant flow diagram is presented in Figure 1.

Development of the CONSORT extension for reporting abstracts of NPT trials

The CONSORT extension for abstracts was published in 2008 (19). We added 2 new items to this extension; one for reporting "eligibility criteria for centers where the intervention is performed and for care providers" and one for "any important changes to the intervention delivered from what was planned" (Table 3). The Appendix (table 4) provides examples of published abstracts that we modified to adhere to the CONSORT extension for abstracts of NPT trials.

Specific methodological issues considered in the update to the CONSORT NPT extension

Complexity of NPTs

NPTs frequently involve multi-component interventions delivered by multiple care providers, and each component or provider may potentially influence the success of the overall intervention (21). NPTs are difficult to describe and standardize, and sometimes the "active ingredients" are difficult to disentangle (22). Furthermore, the intervention actually administered may differ substantially from the one that was planned.

To account for these issues, the updated CONSORT NPT extension recommends providing a description of the different components of the intervention and, when applicable, a description of the procedure for tailoring the intervention to individual participants (Item 5a) in the methods section. We also recommend describing whether and how the interventions were standardized (Item 5b), whether and how adherence of care providers to the protocol was assessed or enhanced (Item 5c), and whether and how adherence of participants to interventions was assessed or enhanced (Item 5d).

In the results section, authors should report details of the experimental treatment and comparator as they were implemented (new item). In the abstract, authors should report “any important changes to the intervention delivered from what was planned.”

These items are consistent with the Template for Intervention Description and Replication (TIDieR) checklist and guidance (23).

Influence of center and care provider expertise

For most NPT trials, the center volume of the intervention and care providers’ expertise can greatly affect treatment effect estimates. Interventions beneficial in one setting may not be as effective or may be even harmful in another setting (24). Furthermore, in NPT trials comparing interventions that could be performed by the same care provider (e.g.; comparison of surgical procedures), different methods for allocating care providers to each group are possible: care providers can deliver the intervention in both groups or in only one group. All these choices can raise specific methodological and logistical issues (shown in the Appendix, Table 5).

The updated CONSORT NPT extension recommends reporting how care providers were allocated to each trial group (Item 3a), eligibility criteria for centers and for care providers (Item 4a), the number of care providers or centers performing each intervention and the number of patients treated by each care provider or in each center (Item 13a) as well as a description of care providers (case volume, qualification, expertise, etc.) and centers (volume) in each group (Item 15).

Furthermore, the flow diagram (Item 13a) now includes a supplementary box to report the number of care providers or centers performing the intervention in each treatment group and the number of patients treated

by each care provider or in each center (Figure 1). The information reported in the flow diagram should report summary statistics, but the detailed description of the number of patients included and treated in each center and each group could be reported in an appendix. This information is particularly important because the interpretation of the results and their applicability vary considerably if, for example, one high-volume surgeon in one high-volume center performs 90% of the interventions or if the interventions are well distributed in all centers and among all surgeons. Finally, authors should discuss the limitations related to any differing expertise of care providers or centers in each group (Item 20) and the generalizability according to the care providers and centers involved in the trial (Item 21). In the abstract, we also recommend reporting eligibility criteria for care providers and centers where the intervention is performed.

Clustering

In individual RCTs, standard sample size calculations and statistical analysis assume that the outcome for each participant is independent. However, this may not be true in individual NPT RCTs in which the outcomes tend to be more similar for patients treated by the same care provider than by other care providers (25). Lack of accounting for this type of clustering by care providers and centers may lead to an underestimation of the sample size required and provide incorrect treatment-effect estimates (26-28). A number of analysis methods such as fixed- and random-effects (or mixed-effects) models and generalized estimating equations are available to account for clustering (29-31).

The updated CONSORT NPT extension recommends reporting details of whether and how the clustering by care providers or centers was addressed in the sample size calculation (Item 7a) and in the statistical analysis (Item 12a).

Difficulties of blinding

Blinding of patients and care providers is frequently impossible in trials assessing NPTs. When possible, it often relies on complex methods (10) (32). Some of these methods rely on the blinding of other care providers who did not perform the intervention but who will care for the patients after the intervention. To account for this situation, Item 11a was slightly modified.

If blinding was not possible in a trial, the updated CONSORT NPT extension recommends reporting this information explicitly and providing a description of any attempts to limit bias, such as the collection of data by an independent researcher (Item 11c). Furthermore, the authors are advised to discuss the limitations related to the lack of blinding when relevant (Item 20).

Delay between randomization and the initiation of the intervention

For most NPT RCTs, a delay may occur between randomization and delivery of the intervention (33). This delay is typically related to logistical issues owing for example to the scheduling of hospitalization or visits with the care provider (34). Such a delay could lead to crossover, loss to follow-up, or nonadherence to the intervention if the participant's status changes between randomization and the time of intervention. The delays can be unequal between trial groups. For example, a trial comparing chemonucleolysis and manipulation had an average delay of 3 weeks in one group and 13 weeks in the other group (35). The updated CONSORT NPT extension recommends reporting “for each group, the delay between randomization and initiation of the intervention” (Item 13c) in the results section.

Adherence to the original CONSORT NPT extension

Several systematic reviews showed a poor adherence to the original CONSORT NPT extension. Only 39% of NPT interventions were adequately described in NPT trial reports (36). A systematic evaluation of surgical RCTs showed that only 6% and 4% reported how clustering was addressed in the sample size calculation and statistical analysis, respectively (37).

Discussion

The updated CONSORT NPT extension should allow authors to increase the transparency of their reports and facilitate an accurate interpretation of trial results. Improving transparency is particularly important in the context of the replication crisis in science (38).

Despite the publication of CONSORT Statement extension to NPT trials, the completeness of reporting of NPT trials remains insufficient (39-41). Space constraints in published articles have been suggested as one reason for inadequate reporting of interventions; however, an online appendix or link to a website where videos and manuals can be accessed can be used to report this essential information. Open-access repositories such as the Open Science Framework (<https://osf.io>) should facilitate the dissemination of this information.

Several initiatives to improve adherence to guidelines have already been implemented (42). Most of them were implemented during the submission and peer review process. More recently, use of writing aid tools based on the CONSORT guidelines have shown promising results (43).

The process for developing these guidelines followed recommended practices (44). The updated checklist results from a consensus, and some specific issues that were discussed during the meeting, such as difficulties in recruiting in NPT RCTs because of strong investigator and patient preferences, did not lead to changes in the checklist.

Some of the issues considered in this extension can be more broadly applicable to the reporting of RCTs assessing some pharmacologic treatments such as complex chemotherapy, a drug treatment whose effectiveness may depend in part on the skill of the care provider. Finally, the updated checklist is consistent with reporting guidelines that were developed since the publication of the 2008 CONSORT extension for NPTs, particularly with the TIDieR checklist for better reporting of interventions (23).

We hope the 2017 update of CONSORT NPT extension improves the reporting of RCTs. The guidelines are not intended to deter authors from publishing imperfect trials, the perfect trial being difficult to achieve, but to ensure transparency and a coherent approach to testing and reporting trials of complex interventions.

References

1. Glasziou P, Altman DG, Bossuyt P, Boutron I, Clarke M, Julious S, et al. Reducing waste from incomplete or unusable reports of biomedical research. *Lancet*. 2014;383(9913):267-76.
2. Chalmers I, Glasziou P. Avoidable waste in the production and reporting of research evidence. *Lancet*. 2009;374(9683):86-9.
3. Begg C, Cho M, Eastwood S, Horton R, Moher D, Olkin I, et al. Improving the quality of reporting of randomized controlled trials. The CONSORT statement. *Jama*. 1996;276(8):637-9.
4. Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. *Ann Intern Med*. 2001;134(8):663-94.
5. Moher D, Hopewell S, Schulz KF, Montori V, Gotzsche PC, Devereaux PJ, et al. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trials. *Bmj*. 2010;340:c869.
6. Ceelen WP. Clinical Research in Surgery: Threats and Opportunities. *European Surgical Research*. 2014;53(1-4):95-107.
7. Evrard S, McKelvie-Sebileau P, van de Velde C, Nordlinger B, Poston G. What can we learn from oncology surgical trials? *Nature Reviews Clinical Oncology*. 2016;13(1):55-62.
8. Boutron I, Tubach F, Giraudeau B, Ravaud P. Methodological differences in clinical trials evaluating nonpharmacological and pharmacological treatments of hip and knee osteoarthritis. *Jama*. 2003;290(8):1062-70.
9. Boutron I, Estellat C, Ravaud P. A review of blinding in randomized controlled trials found results inconsistent and questionable. *J Clin Epidemiol*. 2005;58(12):1220-6.
10. Boutron I, Guittet L, Estellat C, Moher D, Hrobjartsson A, Ravaud P. Reporting methods of blinding in randomized trials assessing nonpharmacological treatments. *PLoS Med*. 2007;4(2):e61.
11. Boutron I, Tubach F, Giraudeau B, Ravaud P. Blinding was judged more difficult to achieve and maintain in nonpharmacologic than pharmacologic trials. *J Clin Epidemiol*. 2004;57(6):543-50.
12. Pibouleau L, Boutron I, Reeves BC, Nizard R, Ravaud P. Applicability and generalisability of published results of randomised controlled trials and non-randomised studies evaluating four orthopaedic procedures: methodological systematic review. *Bmj*. 2009;339:b4538.
13. Ergina PL, Cook JA, Blazeby JM, Boutron I, Clavien PA, Reeves BC, et al. Challenges in evaluating surgical innovation. *Lancet*. 2009;374(9695):1097-104.
14. Cook JA. The challenges faced in the design, conduct and analysis of surgical randomised controlled trials. *Trials*. 2009;10:9.
15. McCulloch P, Altman DG, Campbell WB, Flum DR, Glasziou P, Marshall JC, et al. No surgical innovation without evaluation: the IDEAL recommendations. *Lancet*. 2009;374(9695):1105-12.
16. Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Ann Intern Med*. 2008;148(4):295-309.
17. Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P. Methods and processes of the CONSORT Group: example of an extension for trials assessing nonpharmacologic treatments. *Ann Intern Med*. 2008;148(4):W60-6.
18. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *PLoS Med*. 2010;7(3):e1000251.
19. Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG, et al. CONSORT for reporting randomised trials in journal and conference abstracts. *Lancet*. 2008;371(9609):281-3.
20. Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG, et al. CONSORT for reporting randomized controlled trials in journal and conference abstracts: explanation and elaboration. *PLoS Med*. 2008;5(1):e20.
21. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions: Medical Research Council guidance. *Bmj*. 2015;350:h1258.
22. Blencowe NS, Blazeby JM, Donovan JL, Mills N. Novel ways to explore surgical interventions in randomised controlled trials: applying case study methodology in the operating theatre. *Trials*. 2015;16.

23. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *Bmj*. 2014;348:g1687.
24. Foster JD, Mackenzie H, Nelson H, Hanna GB, Francis NK. Methods of Quality Assurance in Multicenter Trials in Laparoscopic Colorectal Surgery A Systematic Review. *Annals of Surgery*. 2014;260(2):220-9.
25. Cook JA, Bruckner T, MacLennan GS, Seiler CM. Clustering in surgical trials--database of intracluster correlations. *Trials*. 2012;13:2.
26. Roberts C, Roberts SA. Design and analysis of clinical trials with clustering effects due to treatment. *Clin Trials*. 2005;2(2):152-62.
27. Lee KJ, Thompson SG. The use of random effects models to allow for clustering in individually randomized trials. *Clin Trials*. 2005;2(2):163-73.
28. Lee KJ, Thompson SG. Clustering by health professional in individually randomised trials. *Bmj*. 2005;330(7483):142-4.
29. Roberts C, Walwyn R. Design and analysis of non-pharmacological treatment trials with multiple therapists per patient. *Stat Med*. 2013;32(1):81-98.
30. Roberts C. The implications of variation in outcome between health professionals for the design and analysis of randomized controlled trials. *Stat Med*. 1999;18(19):2605-15.
31. Kahan BC, Morris TP. Assessing potential sources of clustering in individually randomised trials. *BMC Med Res Methodol*. 2013;13:58.
32. Wartolowska K, Judge A, Hopewell S, Collins GS, Dean BJ, Rombach I, et al. Use of placebo controls in the evaluation of surgery: systematic review. *Bmj*. 2014;348:g3253.
33. Torgerson D. *Designing Randomised Trials in Health, Education and the Social Sciences*. An Introduction: Palgrave Macmillan UK; 2008.
34. Thornton JG, Hornbuckle J, Vail A, Spiegelhalter DJ, Levene M. Infant wellbeing at 2 years of age in the Growth Restriction Intervention Trial (GRIT): multicentred randomised controlled trial. *Lancet*. 2004;364(9433):513-20.
35. Burton KA, Tillotson MK, Cleary J. Single-blind randomised controlled trial of chemonucleolysis and manipulation in the treatment of symptomatic lumbar disc herniation. *European Spine Journal*. 2000;9(3):202-7.
36. Hoffmann TC, Eructi C, Glasziou PP. Poor description of non-pharmacological interventions: analysis of consecutive sample of randomised trials. *Bmj*. 2013;347:f3755.
37. Nagendran M, Harding D, Teo W, Camm C, Maruthappu M, McCulloch P, et al. Poor adherence of randomised trials in surgery to CONSORT guidelines for non-pharmacological treatments (NPT): a cross-sectional study. *BMJ Open*. 2013;3(12):e003898.
38. Baker M. 1,500 scientists lift the lid on reproducibility. *Nature*. 2016;533(7604):452-4.
39. Dworkin JD, McKeown A, Farrar JT, Gilron I, Hunsinger M, Kerns RD, et al. Deficiencies in reporting of statistical methodology in recent randomized trials of nonpharmacologic pain treatments: ACTTION systematic review. *J Clin Epidemiol*. 2016;72:56-65.
40. Yu J, Li X, Li Y, Sun X. Quality of reporting in surgical randomized clinical trials. *British Journal of Surgery*. 2016.
41. McCleary N, Duncan EM, Stewart F, Francis JJ. Active ingredients are reported more often for pharmacologic than non-pharmacologic interventions: an illustrative review of reporting practices in titles and abstracts. *Trials*. 2013;14:146.
42. Chan L, Heinemann AW, Roberts J. Elevating the quality of disability and rehabilitation research: mandatory use of the reporting guidelines. *Arch Phys Med Rehabil*. 2014;95(3):415-7.
43. Barnes C, Boutron I, Giraudeau B, Porcher R, Altman DG, Ravaud P. Impact of an online writing aid tool for writing a randomized trial report: the COBWEB (Consort-based WEB tool) randomized controlled trial. *BMC Med*. 2015;13:221.
44. Moher D, Schulz KF, Simera I, Altman DG. Guidance for developers of health research reporting guidelines. *PLoS Med*;7(2):e1000217.

Figure legend

Figure 1: Modified CONSORT flow diagram for individual randomized controlled trials of nonpharmacologic treatments.

Address for reprint requests

Isabelle Boutron
Equipe METHODS (CRESS-UMR1153)
Centre d'épidémiologie clinique
Hôpital Hôtel-Dieu,
1 place du Parvis Notre-Dame,
75004 Paris
France

Douglas G Altman
Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences
University of Oxford
Botnar Research Centre
Windmill Road
Oxford, OX3 7LD
UK

David Moher
Centre for Journalology, Ottawa Hospital Research Institute
The Ottawa Hospital - General Campus
501 Smyth Rd, Room L1288
Ottawa, ON K1H 8L6
Canada

Kenneth F. Schulz
FHI 360
359 Blackwell Street, Suite 200
Durham, NC 27701
USA

Philippe Ravaud
Equipe METHODS (CRESS-UMR1153)
Centre d'épidémiologie clinique
Hôpital Hôtel-Dieu,
1 place du Parvis Notre-Dame,
75004 Paris
France

Figure 1: Modified CONSORT flow diagram for individual randomized controlled trials of nonpharmacologic treatments.

An extra box per intervention group relating to care providers and centers has been added.

IQR = interquartile range; max = maximum; min = minimum

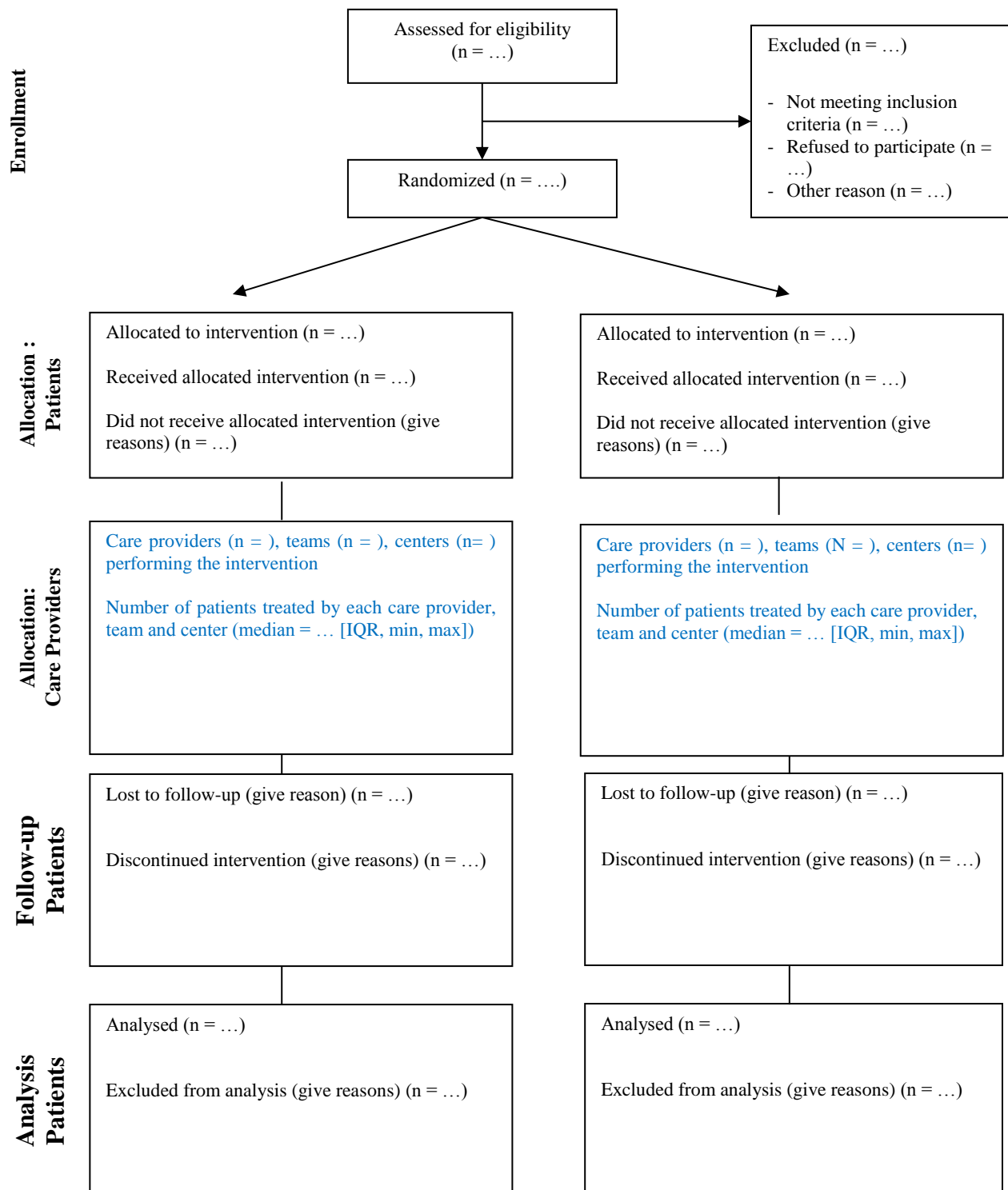


Table 1. 2017 CONSORT checklist of information to include when reporting a randomized trial assessing nonpharmacologic treatments (NPTs)*. Modifications of the extension appear in italics and blue.

Section/Topic Item	Checklist item no.	CONSORT item	Extension for NPT trials
Title and abstract			
	1a	Identification as a randomized trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	<i>Refer to CONSORT extension for abstracts for NPT trials</i>
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	
	2b	Specific objectives or hypotheses	
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	When applicable, how care providers were allocated to each trial group
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	When applicable, eligibility criteria for centers and for <i>care providers</i>
	4b	Settings and locations where the data were collected	
Interventions†	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Precise details of both the experimental treatment and comparator
	5a		Description of the different components of the interventions and, when applicable, description of the procedure for tailoring the interventions to individual participants.
	5b		Details <i>of whether and</i> how the interventions were standardized.
	5c.		Details <i>of whether and</i> how adherence of care providers to the protocol was assessed or enhanced
	5d		<i>Details of whether and how adherence of participants to interventions was assessed or enhanced</i>
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	
	6b	Any changes to trial outcomes after the trial commenced, with reasons	

Section/Topic Item	Checklist item no.	CONSORT item	Extension for NPT trials
Sample size	7a	How sample size was determined	When applicable, details of whether and how the clustering by care providers or centers was addressed
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomization:			
- Sequence generation	8a	Method used to generate the random allocation sequence	
	8b	Type of randomization; details of any restriction (such as blocking and block size)	
- Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
- Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Whether or not those administering co-interventions were blinded to group assignment If done, who was blinded after assignment to interventions (e.g., participants, care providers, <i>those administering co-interventions</i> , those assessing outcomes) and how
	11b	If relevant, description of the similarity of interventions	If blinded, method of blinding and description of the similarity of interventions
	11c		<i>If blinding was not possible, description of any attempts to limit bias</i>
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	When applicable, details of whether and how the clustering by care providers or centers was addressed
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome	The number of care providers or centers performing the intervention in each group and the number of patients treated by each care provider or in each center
	13b	For each group, losses and exclusions after randomization, together with reasons	
	13c		<i>For each group, the delay between randomization and the initiation of the intervention</i>

Section/Topic Item	Checklist item no.	CONSORT item	Extension for NPT trials
	new		Details of the experimental treatment and comparator as they were implemented
Recruitment	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	When applicable, a description of care providers (case volume, qualification, expertise, etc.) and centers (volume) in each group.
Numbers analyzed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	In addition, take into account the choice of the comparator, lack of or partial blinding, and unequal expertise of care providers or centers in each group
Generalizability	21	Generalizability (external validity, applicability) of the trial findings	Generalizability (external validity) of the trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Other information			
Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	

*Additions or modifications to the 2010 CONSORT checklist. CONSORT = Consolidated Standards of Reporting Trials

†The items 5, 5a, 5b, 5c, 5d are consistent with the Template for Intervention Description and Replication (TIDieR) checklist

Table 2: Items to include when reporting an RCT assessing NPT in a journal or conference abstract *

Item	Standard CONSORT abstract item	Extension for NPT trials
Title	Identification of the study as randomized	
Authors *	Contact details for the corresponding author	
Trial design	Description of the trial design (e.g. parallel, cluster, noninferiority)	
Methods		
Participants	Eligibility criteria for participants and the settings where the data were collected	When applicable, report eligibility criteria for centers where the intervention is performed and for care providers
Interventions	Interventions intended for each group	
Objective	Specific objective or hypothesis	
Outcome	Clearly defined primary outcome for this report	
Randomization	How participants were allocated to interventions	
Blinding (masking)	Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment	
Results		
Number randomized	Number of participants randomized to each group	Report any important changes to the intervention delivered from what was planned
Recruitment	Trial status	
Number analyzed	Number of participants analyzed in each group	
Outcome	For the primary outcome, a result for each group and the estimated effect size and its precision	
Harms	Important adverse events or side effects	
Conclusions	General interpretation of the results	
Trial registration	Registration number and name of trial register	
Funding	Source of funding	

Appendices

Appendix 1: Literature search

We searched for studies evaluating adherence to the CONSORT NPT extension and methodological developments that we should consider in the update. We searched Web of Science (search date November 2013, update July 2016) to identify all articles published citing one of the two articles on the 2008 CONSORT NPT extension (1-3). We also searched MEDLINE via PubMed for studies evaluating the reporting of trials assessing NPTs since January 2009 (search date November 2013, update July 2016) by using the following search strategy: (Reporting AND CONSORT)[tiab], with a limitation to articles with an abstract, published in English. Finally, we used a personal collection of reports on new developments related to the specific methodological issues when assessing NPTs (e.g., clustering within individual patient RCTs, complexity of intervention), and other relevant reporting guidelines developed since the publication of the 2008 CONSORT extension for NPTs such as the TIDieR (Template for Intervention Description and Replication) checklist developed to report all types of interventions(4).

Appendix table 1: Characteristics of corresponding authors surveyed* about the CONSORT Statement extension for randomized controlled trials (RCTs) of non-pharmacologic treatments (NPTs).

	N=194
Domain of expertise	
• Surgery	23%
• Devices	4%
• Rehabilitation	24%
• Psychotherapy	8%
• Behavioral interventions	20%
• Others	21%
Location	
• Europe	54%
• USA	22%
• Canada	9%
• South America	3%
• Asia	3%
• Oceania	10%
Number of RCTs participants had been involved in, mean (SD)	9.6 (30.5)
Number of reports of RCTs published, mean (SD)	3.8 (7.0)
Number of reports of RCTs evaluating NPTs published, mean (SD)	2.8 (3.7)
Use of CONSORT extension for NPT trials	40%

* Response rate 13% (194/1525)

Appendix table 2: Results of the survey

	Item	Original CONSORT NPT items	No of participants who agreed to retain the item without modification N=194
Trial design	3a	How care providers were allocated to each trial group	89%
Participants	4a	Eligibility criteria for centers and those performing the interventions	88%
Interventions	5	Precise details of both the experimental treatment and comparator 5a. Description of the different components of the interventions and, when applicable, descriptions of the procedure for tailoring the interventions to individual participants 5b. Details of how the interventions were standardized 5c. Details of how adherence of care providers with the protocol was assessed or enhanced	72%
Sample size	7a	Details of whether and how the clustering by care providers or centers was addressed	89%
Blinding	11a	Whether or not those administering co-interventions were blinded to group assignment	81%
Stats methods	12a	Details of whether and how the clustering by care providers or centers was addressed	88%
Participants Flow	13a	The number of care providers or centers performing the intervention in each group and the number of patients treated by each care provider or in each center	84%
Implementation of intervention	New item	Details of the experimental treatment and comparator as they were implemented	81%
Baseline data	15	When applicable, a description of care providers (case volume, qualification, expertise, etc.) and centers (volume) in each group	88%
Limitations	20	In addition, take into account the choice of the comparator, lack of or partial blinding, and unequal expertise of care providers or centers in each group	89%
Generalizability	21	Generalizability (external validity) of the trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial	89%

Appendix table 3. Extended CONSORT checklist of information to include when reporting a randomized controlled trial (RCT) assessing NPTs with examples for 2 types of interventions: surgery/procedures and participative interventions such as rehabilitation or education. We focused on these 2 types of interventions because they concern very different audiences.

CONSORT item and extension for NPT trials	Examples for RCTs assessing surgery and procedures	Examples for RCTs assessing participative interventions
METHODS		
Trial design		
Item 3a		
<u>Standard CONSORT description</u> Description of trial design (such as parallel, factorial) including allocation ratio <u>Extension for NPT trials</u> When applicable, how care providers were allocated to each trial group	<u>Surgery and procedures</u> “This was a parallel group trial with a 1:1 allocation ratio. The same team of surgeons [...] performed both conventional laparoscopic appendectomy and single-port appendectomy.”(45) “Surgeons were assigned to a group on the basis of the operation that they preferred.”(46)	<u>Participative interventions</u> Recruitment [...] of DBT [dialectical behavior therapy] Therapists “Psychotherapists recommended by colleagues as potentially good DBT therapists were recruited for the study;” [...] “The CTBE [Community Treatment by Experts] therapists were nominated by community mental health leaders. These included heads of inpatient psychiatric units and clinical directors of mental health agencies, who nominated therapists whom they considered experts in treating difficult clients.” (47)
Participants		
Item 4a		
<u>Standard CONSORT description</u> Eligibility criteria for participants <u>Extension for NPT trials</u> When applicable, eligibility criteria for centers and for care providers	<u>Surgery and procedures</u> “All participating centres [...] were major neurosurgical centres, treating large numbers of patients after aneurismal subarachnoid hemorrhage (SAH), each centre treating between 60 and 200 cases annually [...] Centres had to have expertise in both neurosurgical and endovascular management of ruptured aneurysms. Only accredited neurosurgeons with experience of aneurysm surgery were permitted to manage patients in the trial. Endovascular operators had to have done a minimum of 30 aneurysm treatment procedures, before they were permitted to treat patients in the trial.”(48) “The selection of centers for participation in the trial was based on stringent quality assessment by the study management committee to confirm the use of proper surgical technique. Unedited recordings of five consecutive laparoscopic total mesorectal excisions were evaluated. The respective pathology reports of these five consecutive cases were reviewed to confirm completeness of the specimens. Pathologists adhered to standardized processing and assessment of specimens, as described in detail in the trial protocol, to ensure accurate reporting by all participating centers. The circumferential resection margin was defined as “involved” when tumor cells were present within 2 mm from the lateral surface of the mesorectum.”(49)	<u>Participative interventions</u> “Therapists were trained to deliver both the exercise programme and control interventions. All therapists received 4 h of training covering theoretical and practical application of both interventions, and two short update training sessions during the trial. Therapists detailed the content of all treatment sessions in a standardised log book and clinical records. Every therapist received at least one quality-control assessment per intervention type, and all records were reviewed to ascertain attendance and for documentary evidence of assessment, and of progression or regression of exercises.”(51) “The cases were divided between 2 masters-level and 2 doctoral-level therapists, all of whom had prior training and experience with CBT for depression.”(52)

CONSORT item and extension for NPT trials	Examples for RCTs assessing surgery and procedures	Examples for RCTs assessing participative interventions
	“To qualify as a study neurointerventionalist, physicians must have placed an intracranial stent in at least 10 patients (for aneurysm or atherosclerosis) in the 12 months prior to site initiation.”(50)	
Interventions		
Item 5		
<u>Standard CONSORT description</u> The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	See 5a,5b,5c	See 5a,5b,5c,5d
<u>Extension for NPT trials</u> Precise details of both the experimental treatment and comparator		
Interventions		
Item 5a		
Description of the different components of the interventions and, when applicable, description of the procedure for tailoring the interventions to individual participants.	<u>Surgery and procedures</u> “(…) participants were individually randomized to receive surgery or close contact casting (…) Surgery was internal fixation conducted with internationally recognized principles and techniques. ¹² Selection of implants, postoperative splinting, immediate or delayed weight bearing, and clinical follow-up were according to usual local practice and the surgeon’s preference. The close contact cast was applied in an operating room under general or spinal anesthesia by an orthopedic surgeon immediately after closed fracture reduction. Instructions were to achieve joint congruence with no talar shift or tilt. The close contact casting application was first a stockinette bandage (BSN Medical GmbH) and then shaped, self-adhesive foam pads (Fleecy Foam 5 mm; Hapla) placed over prominences (tibial crest, fibular head, calcaneum, Achilles tendon, and metatarsal heads) and medial and lateral sides of the ankle, where molding pressure was applied to hold the fracture reduction. The exact molding points for each participant were at the surgeon’s discretion. Then 2 self-adhesive strips were applied to the full length of the cast (Fleecy web roll 5 cm; Hapla) to prevent plaster saw injury during removal. Finally, a single nonoverlapping synthetic wool layer (Soffban Plus; BSN Medical GmbH), plaster of paris (Gypsona; BSN Medical GmbH), and a reinforcing topcoat of synthetic casting material (Soft Cast Casting Tape; 3M Health Cate Ltd) were applied below the knee. All surgeons who applied casting had completed a 1-hour training session, supplemented with a video	<u>Participative interventions</u> “[...]/Pelvic floor muscle training was provided individually in face-to-face contacts combined with home exercises. The pelvic physiotherapists recorded the treatment modalities and the number of treatment sessions for each participant. For all participants, the intervention started with an explanation of the function of the pelvis and the pelvic floor and about pelvic floor dysfunctions; illustrations and three dimensional models of the pelvis were used. Pelvic floor muscle function was assessed by digital palpation. During this examination, the physiotherapists also checked whether participants were able to correctly contract (“squeeze and lift”) and relax their pelvic floor muscles. If necessary, they used breathing exercises to increase awareness of the pelvic floor. Participants who were not able to contract or relax their pelvic floor muscles were first instructed how to do this by being given feedback during digital palpation or, if necessary, by application of myofeedback or electrical stimulation. Participants who were able to control their pelvic floor consciously but whose pelvic floor muscles were too weak started training their pelvic floor by doing exercises. All participants started with the same basic exercise scheme, to which specific exercises could be added (web appendix 2).

CONSORT item and extension for NPT trials	Examples for RCTs assessing surgery and procedures	Examples for RCTs assessing participative interventions
	<p>(https://www.youtube.com/playlist?list=PL2Gg_an4nwPfiUC9RQV54Y2lbD76HiWcV) or were supervised by a surgeon who had completed training. Joint congruence was monitored with radiographs in the weeks after initial close contact cast application and after any reapplications for cast loosening. Reapplications did not require anesthesia. The protocol specified that if during clinical follow-up there was, in the treating surgeon's opinion, an unacceptable loss of fracture position before clinical union, he or she could remanipulate and reapply a cast in the outpatient clinic or operating room or convert to surgery. Guidance was that the casting group should touch or nonweight bear for 4 weeks and increase to full weight bearing by 6 to 8 weeks from intervention at the surgeon's discretion and patient volition.</p> <p>The treatment protocol anticipated and allowed scenarios in which allocated treatment might have to be modified. Participants in the casting allocation could proceed to surgery when reduction could not be achieved or held with close contact casting in the operating room. Participants in the surgical allocation could proceed to traditional casting or external fixation when incision was considered unsafe, but not to close contact casting. For both allocations, a temporary treatment could be undertaken in the operating room (manipulation and splinting or external fixation) until it was appropriate to receive the allocated treatment. Each hospital followed its own protocols for thromboprophylaxis, surgical antibiotic prophylaxis, and rehabilitation.”(53)</p>	<p>The exercise programme was individualised and was modified at each appointment on the basis of examination findings. In cases of an overactive pelvic floor, the focus of the exercises was on relaxation rather than on contraction and, if necessary, general relaxation exercises were used. All participants were taught to contract their pelvic floor muscles before and during any increases in abdominal pressure (“the knack”), and attention was paid to lifestyle (diet, body weight) and toilet habits (web appendix 2). Initially, participants visited the pelvic physiotherapist on a weekly basis, but when they were able to correctly contract and relax their pelvic floor muscles the intervals between appointments were extended (two to three weeks). Participants were encouraged to continue practising at home three to five times a week, twice or three times each day.” (54)</p> <p>“The exercise programme was individualised and was modified at each appointment on the basis of examination findings. In cases of an overactive pelvic floor, the focus of the exercises was on relaxation rather than on contraction and, if necessary, general relaxation exercises were used”. (54)</p> <p>“The intervention protocols were developed and tested in previous pilot studies. Both interventions were intended to be pragmatic in nature (for example, modified to patient presentation and needs) and were informed by commonly recommended clinical practices, patient preferences, and promising research evidence.”(55)</p> <p>“Four therapists were employed for the study and had the necessary qualifications and experience to be accredited by the British Association for Counselling. They adhered to a Rogerian model of psychotherapy by helping the patient to express feelings, clarify thoughts, and to restate or reframe difficulties; the therapists also suggested alternative understandings. They did not give advice, but used empathy and advanced listening skills to help patients resolve their own difficulties. The therapists complied with a standard code of ethics and practice. Patients were offered six to 12 sessions of brief psychotherapy, which entailed 50 min of therapy once a week over 6 or more weeks. Patients randomised to the brief-psychotherapy intervention were able to see their general practitioners as usual. Therapists asked</p>

CONSORT item and extension for NPT trials	Examples for RCTs assessing surgery and procedures	Examples for RCTs assessing participative interventions
		<p>each patient to consent to the tape-recording of one session of brief psychotherapy. An independent therapist assessed the tapes for adherence to a non-directive, person-centred therapy style.” (56)</p> <p><u>Comparator</u></p> <p>“Participants randomised to watchful waiting received no treatment and no recommendations”(54).</p> <p>“We chose routine general-practitioner care as the control approach. The doctors were able to talk to their patients and discuss their difficulties as they would do in normal practice. They were discouraged, however, from referring the patient to a therapist during the study period, unless absolutely necessary.”(56)</p>
<p>Interventions Item 5b</p>		
<p>Details of whether and how the interventions were standardized.</p>	<p><u>Surgery and procedures</u></p> <p>“A detailed overview of the VAT-PP and talc pleurodesis techniques is described in the appendix. To ensure uniformity of approach, all surgeons discussed the VAT-PP procedure, and from Jan 13, 2009, they also recorded tumour extent and lung re-expansion before and after pleurectomy (appendix). At study outset, talc pleurodesis was done using talc slurry via an intercostal chest drain. From November, 2008, the protocol changed to allow talc pleurodesis by thoracoscopic poudrage.”(57)</p> <p>“All patients underwent standard repairs performed by residents, staff, or attending surgeons, following a detailed protocol. All surgeons participating in the study were personally instructed by the principal investigator and adequately trained in both surgical techniques.”(58)</p> <p>“For subjects assigned to the intraoperative drain group, the specific size, brand, and number of closed-suction drains were at the discretion of the surgeon.”(59)</p> <p>“The usual practices of surgeons performing optic nerve decompression surgery were determined through literature review and through a survey of study surgeons. These practices were described in the protocol as a series of 31 steps, only six of which were required to be performed so as to ensure adequacy of the surgery as well as safety of the patient. The remaining steps could be performed according to surgeon preference as they did not directly affect either patient safety or adequacy of surgery. Each study surgeon signed a written commitment to adhere to the six required steps, which were: general anesthesia, medial approach, no mechanical static traction, subarachnoid dissection if no cerebrospinal fluid release was seen following fenestration of the optic</p>	<p><u>Participative interventions</u></p> <p>“The standardization process including initial training and maintenance throughout the trial is detailed in the Manual of Procedures (MOP). [...] Training of all intervention therapists will occur during the initial six months of the study. The initial training activity will be led by the ASAP Intervention Team. ASAP intervention therapists (clinical site coordinators) will attend a 3-day training workshop in Los Angeles to accomplish Phase I competency in administration and documentation of a complete dose (30 hrs). For Phase II competency, each interventionist will be videoed, off-site during administration of each element (task-specific training; impairment mitigation; motivational enhancements) with study volunteers. Follow-up videotapes of the intervention therapist are required once a month for the first three months after the beginning of participant enrollment, once again three months later, and once every six months for the remainder of the project.”(61)</p>

CONSORT item and extension for NPT trials	Examples for RCTs assessing surgery and procedures	Examples for RCTs assessing participative interventions
	nerve sheath, no more than 7 minutes of sustained traction on the globe at any one time and rest periods of at least 2 minutes following any 7-minute period of globe traction.”(60)	
Interventions		
Item 5c		
Details of whether and how adherence of care providers to the protocol was assessed or enhanced	<p><u>Surgery and procedures</u></p> <p>“In every centre, a gastrointestinal pathologist ensured consistent reporting of resection specimens according to an agreed and established technique that focused on the completeness of resection and extent of the circumferential resection margin (CRM).20 Tumour histology was reviewed centrally.”(62)</p> <p>“For surgical quality assurance, laparoscopic procedures performed on trial patients were videorecorded and members of the COST executive committee audited a randomly selected subset of the first 500 cases.”(63)</p>	<p><u>Participative interventions</u></p> <p>“Counselors’ adherence to treatment protocols was monitored via review of session videos during supervision meetings. Additionally, 20% of treatment sessions were randomly selected and rated by trained adherence raters who were otherwise uninvolved in the study. Raters assessed adherence to essential components of each treatment and monitored protocol violations.”(64)</p> <p>“All therapy sessions are videotaped [...]. A senior clinician who is independent of [...] treatment delivery will rate 10% of the videotapes using measures adapted from several randomized clinical trials of psychotherapy [...]; the 10% figure was chosen arbitrarily in an attempt to ensure an adequate sample of information from each treatment condition.”(65)</p>
Interventions		
Item 5d		
Details of whether and how adherence of participants to the interventions was assessed or enhanced	<u>Surgery and procedures</u> : Not applicable	<p><u>Participative interventions</u></p> <p>“Therapists detailed the content of all treatment sessions in a standardised log book and clinical records. Every therapist received at least one quality-control assessment per intervention type, and all records were reviewed to ascertain attendance and for documentary evidence of assessment, and of progression or regression of exercises. We defined patient compliance with the intervention as attendance at all face-to-face sessions with the therapist. Participants kept a diary record of exercise completion.”(51)</p> <p>“Treatment fidelity was facilitated through standardized training, manuals of operation, and clinical documentation forms that were monitored weekly by research staff.”(55)</p>
Sample size		
Item 7a		
<u>Standard CONSORT description</u>	<p><u>Surgery and procedures</u>:</p> <p>“As all patients randomised to a given surgeon under expertise-based randomisation will</p>	<u>Participative interventions</u>

CONSORT item and extension for NPT trials	Examples for RCTs assessing surgery and procedures	Examples for RCTs assessing participative interventions
How sample size was determined <u>Extension for NPT trials</u> Details of whether and how clustering by care providers or centers was addressed	have had their operations using the same technique, they cannot be regarded as independent of each other. Assuming that 80 surgeons would take part in the trial, the resultant intraclass correlation coefficient (ICC) was estimated from data from Bristol and Oxford cardiac databases to be 0.005. Using these assumptions, a sample size of 5418 patients had 90% power to detect a 30% reduction in RR with 5% significance (two tailed).”(66)	“The original sample size calculation did not include inflation for therapist effects, although we included assessment for these effects in the final analysis.”(51) “Although the treatment will be delivered on an individual basis, observations from the participants treated by the same therapist are likely to be correlated. Assuming each therapist treats m study participants, the sample size needs to be inflated by the following inflation factor f to retain the same power [56] and [57]: $f = 1 + (m - 1)\rho$, where ρ is the intraclass correlation due to therapist, or equivalently, the correlation between the primary outcomes from two individuals receiving treatment from the therapist. (...) The Planning Committee determined that it is reasonable to assume each therapist will deliver either PE or CPT to 8 participants over the course of the study ($m = 8$). It follows that $f = 1 + (8 - 1) * 0.134 = 1.94$. Hence, a total of 878 participants (439 per group) is needed to provide 90% power to detect $\Delta\mu = 5$ in the primary outcome [...]”(67).
Blinding Item 11a <u>Standard CONSORT description</u> If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how <u>Extension for NPT trials</u> If done, who was blinded after assignment to interventions (for example, participants, care providers, those administering co-interventions, those assessing outcomes) and how	<u>Surgery and procedures:</u> “The operating surgeon could not be blind in the trial and, as the Kirschner wires protrude on the back of the wrist and the locking plate require an incision, nor could the patient. All staff involved in checking, entering, and analysing questionnaire responses, however, were blind to allocation”(68)	<u>Participative interventions</u> “Participants were blinded to trial hypothesis. They were informed that the study aimed to compare two computer-assisted interventions in patients admitted to EDs, but they were not informed of all the research hypotheses. Furthermore, to limit bias, the data collection was standardized and performed by phone by independent and trained research assistants, who were blinded to the treatment allocation.”(69) “Using the standard double-blinding procedures employed in medication research is not feasible or desirable in psychotherapy research. Therapists need to be aware of which treatment they are delivering, and patients need to know as well. Blinded assessment is the gold standard in psychotherapy trials. Using centralized phone assessment for the primary outcome in this trial enhances blinding because assessors are not physically located where patients are receiving treatment, which offers an additional layer of protection from accidental unblinding. For secondary outcomes, the Site Coordinator collects patient self-report questionnaires by providing folders containing the

CONSORT item and extension for NPT trials	Examples for RCTs assessing surgery and procedures	Examples for RCTs assessing participative interventions
questionnaire measures to participants and then collecting these folders from participants after completion.”(67)		
Blinding Item 11c		
<u>Extension for NPT trials</u> If blinding was not possible, description of any attempts to limit bias	<u>Surgery and procedures:</u> “A blinded health professional performed outcome assessments at the primary end point (6 months). Before assessments, opaque ankle bandages were applied to obscure the ankle. (...) The assessments at 6 weeks were not blinded because the assessor needed knowledge of postoperative instructions for weight bearing and movement. It was not possible to mask the surgeons or participants because of the nature of the interventions, nor was it possible to mask the radiograph assessors.”(53)	<u>Participative interventions</u> “Blinding was not feasible in this study. However, independent research staff rather than the treating physician performed outcome assessments.”(70)
Statistical methods Item 12a		
<u>Standard CONSORT description</u> Statistical methods used to compare groups for primary and secondary outcomes <u>Extension for NPT trials</u> When applicable, details of whether and how clustering by care providers or centers was addressed	“We compared the on-pump and off-pump procedures for each baseline characteristic using a mixed-effect logistic regression model, fitting the group as the dependent variable and each baseline characteristic as the independent variable. We used an exchangeable covariance structure in the model to account for the clustering effect of surgeons. The analysis was stratified by allocated treatment group. Comparisons of the perioperative data between the two procedures were carried out using a generalized linear mixed-effect model. Similar adjustment for clustering of surgeons was included in the model.” (71)	<u>Participative interventions</u> “We estimated therapist effects from a random effect nested within every centre.” (51) “Although the participants were individually randomized, a clustering of outcomes is potentially possible since a single therapist was treating several patients. If these clustering effects were strong, then this might alter the results. We therefore used multilevel modeling to check for any clustering effects by undertaking an analysis on the primary outcome.”(72) “The difference in the primary outcome between the intervention and comparator groups was evaluated at 12 months by a linear mixed longitudinal model estimating the difference in change from baseline between the 2 groups (coefficient for time × group interaction) and accounting for the correlation in data for the same patient and the same center (random effects).”(69)
RESULTS		
Participant flow (a diagram is strongly recommended) Item 13a		
<u>Standard CONSORT description</u> For each group, the number of participants who were randomly assigned, received intended treatment, and were	See figure 2a	See figure 2b

CONSORT item and extension for NPT trials	Examples for RCTs assessing surgery and procedures	Examples for RCTs assessing participative interventions																																	
<p>analysed for the primary outcome</p> <p><u>Extension for NPT trials</u></p> <p>The number of care providers or centers performing the intervention in each group and the number of patients treated by each care provider or in each center</p>																																			
Item 13c																																			
<p><u>Extension for NPT trials</u></p> <p>For each group, the delay between randomization and the initiation of the intervention</p>	<p><u>Surgery and procedures</u></p> <p>“Patients meeting the clinical and angiographic criteria were randomly assigned 1:1 [...] The stent group underwent the stenting procedure within 48 hours of randomization.”(50)</p> <p>In a study comparing the effect of stent-assisted percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG) in the management of patients with multivessel disease(73): “The index procedure was done within 2 weeks of randomisation in 51% (n=247) of PCI patients and 33% (n=166) of surgery patients, and within 6 weeks in 94% (n=460) of PCI patients and 85% (n=422) of CABG patients. The median delay between randomisation and index procedure was 14 days (IQR 5–29) for PCI and 23 days (11–38) for CABG.”</p>	<p><u>Participative interventions</u></p> <p>“The mean delay before commencement of manipulative treatment in the manipulator’s office practice was 3 weeks (SD 3.6), whilst the mean delay for chemonucleolysis, performed at the hospital, was 12.9 weeks (SD 7.8)”.(35)</p>																																	
New Item																																			
<p><u>Extension for NPT trials</u></p> <p>Details of the experimental treatment and comparator as they were implemented</p>	<p><u>Surgery and procedures</u></p> <p>“Table 2 shows the details of the surgeons and the operations. Of note, the surgical time for the Kirschner wire fixation was shorter than for locking plate, with a median difference of 31 minutes (95% confidence interval 28 to 35 minutes; Mann-Whitney test $P<0.001$) (....)”</p> <table border="1"> <thead> <tr> <th></th><th>Wire (n=230)</th><th>Plate (n=231)</th></tr> </thead> <tbody> <tr> <td>Median (IQR) operation time (min)</td><td>31 (24-45)</td><td>66 (50-85)</td></tr> <tr> <td>Median (IQR) length of stay (days)</td><td>1 (0-1)</td><td>1 (0-1)</td></tr> <tr> <td colspan="3">Wires</td></tr> <tr> <td colspan="3">No of wires used:</td></tr> <tr> <td>1</td><td>1 (0)</td><td>—</td></tr> <tr> <td>2</td><td>96 (42)</td><td>—</td></tr> <tr> <td>3</td><td>105 (46)</td><td>—</td></tr> <tr> <td>>3</td><td>5 (2)</td><td>—</td></tr> <tr> <td colspan="3">Wire size (mm):</td></tr> <tr> <td>1.6</td><td>187 (81)</td><td>—</td></tr> </tbody> </table>		Wire (n=230)	Plate (n=231)	Median (IQR) operation time (min)	31 (24-45)	66 (50-85)	Median (IQR) length of stay (days)	1 (0-1)	1 (0-1)	Wires			No of wires used:			1	1 (0)	—	2	96 (42)	—	3	105 (46)	—	>3	5 (2)	—	Wire size (mm):			1.6	187 (81)	—	<p><u>Participative interventions</u></p> <p>“Overall, 94% of study patients attended their prescribed treatment visits: 98% in the SMT plus HEA group and 91% in the HEA group. The mean number of HEA visits was 3.8 (SD, 0.6; median, 4.0) in the SMT plus HEA group and 3.6 (SD, 1.0; median, 4.0) in the HEA group. The mean number of SMT visits was 14.6 (SD, 3.8; median, 16) in the SMT plus HEA group. Each HEA provider delivered care to approximately the same number of patients in each treatment group (range for SMT plus HEA group, 1 to 38; range for HEA group, 2 to 47); 7 chiropractors who delivered SMT plus HEA also delivered at least 1 HEA session. [...] There were no crossovers of treatment assignments during the trial.”. (55)</p> <p>“Treatment Fidelity of physical therapy (PT). The average number of PT sessions attended was 8.4 (SD, 4.6). Fifty-four patients (66%) attended at least 50% of the prescribed 12</p>
	Wire (n=230)	Plate (n=231)																																	
Median (IQR) operation time (min)	31 (24-45)	66 (50-85)																																	
Median (IQR) length of stay (days)	1 (0-1)	1 (0-1)																																	
Wires																																			
No of wires used:																																			
1	1 (0)	—																																	
2	96 (42)	—																																	
3	105 (46)	—																																	
>3	5 (2)	—																																	
Wire size (mm):																																			
1.6	187 (81)	—																																	

1.1	1 (0)	—
Other	12 (5)	—
Technique		
Kapandji	54 (23)	-
Interfragmentary	78 (34)	—
Mixed technique	71 (31)	—
Plates		
No of distal locking screws used:		
3	—	20 (9)
4	—	62 (27)
5	—	42 (18)
>5	—	88 (38)
Proximal screw		
Locking	—	103 (45)
Non-locking	—	110 (48)

“The rate of peri-operative antibiotic use was higher in the plate group than in the Kirschner wire group; 83% v 71% of study participants were prescribed antibiotics (estimated odds ratio 3.5, 95% confidence interval 2.0 to 6.5; Fisher’s exact test $P<0.001$).”(68)

sessions. Thirteen patients (16%) did not attend at least 1 session, and 77% of them ($n = 10$) had surgery.”(74)

“Table 2 details treatments received. 48 therapists provided treatment. Treatment was initiated after baseline assessment at a median of 20 days (IQR 12–34) for the group assigned to exercise and 19 days (13–33) for the group assigned to usual care. Nearly all participants completed treatment in the usual care group and 184 (75%) participants attended all six sessions in the intervention group. Participants in the exercise group reported greater compliance with daily or any exercise at 4 months; this difference narrowed at 12 months. Comparison of treatment attendance and content across the two trial groups indicated that therapists complied well with the protocol (table 2). No significant therapist effects were recorded (intraclass coefficient <0.0001).”(51)

	Usual care	Exercise
Treatments delivered		
Median number of sessions	1 (1–2)	6 (5–6)
Did not attend any sessions	7/242 (3%)	8/246 (3%)
Attended assessment session only*	135/242 (56%)	8/246 (3%)
Part completion of treatment	10/242 (4%)	46/246 (19%)
Full completion of treatment	225/242 (93%)	184/246 (75%)
Time from randomisation to last treatment (months)	1.1 (0.5–1.7)	3.2 (2.7–4.0)
Self-reported exercise (≥ 1 –2 sessions per week)		
At 4 months	137/222 (62%)	174/216 (81%)
At 12 months	123/216 (57%)	128/206 (62%)
Treatment session components		
Provided joint protection advice	224/235 (95%)	220/238 (92%)
Provided ACR booklets	220/235 (94%)	222/238 (93%)
Provided functional splinting	103/235 (44%)	98/238 (41%)
Modified or reviewed functional splinting?	81/235 (34%)	111/238 (47%)
Helped patient complete exercise diary?	NA	223/238 (94%)
Helped patient complete personal exercise guide?	NA	201/238 (85%)
Median number of exercises progressed	NA	8 (3–10)
Ran through discharge advice	NA	169/238 (71%)
Discussed continuing with exercise programme	NA	169/238 (71%)

Data are median (IQR), or n/N who completed questionnaires or treatment logs (%). ACR=American College of Rheumatology. NA=not applicable. *No follow-up sessions were attended (usual care were expected to have between one and three sessions).

Table 2: Details of the interventions provided in the groups assigned to usual care and to exercise

CONSORT item and extension for NPT trials	Examples for RCTs assessing surgery and procedures	Examples for RCTs assessing participative interventions
<p>Baseline data</p> <p>Item 15</p> <p>A table showing baseline demographic and clinical characteristics for each group</p> <p><u>Extension for NPT trials</u></p> <p>When applicable, a description of care providers (case volume, qualification, expertise, etc.) and centers (volume) in each group.</p>	<p><u>Surgery and procedures</u></p> <p>“We dichotomized surgeon’s experience in laparoscopic repair into greater than 250 repairs (experienced) and less than 250 repairs (inexperienced) [...] Surgeons participating in this trial ranged in age from 27 to 70 with a median of 42 years in the laparoscopic group (55 surgeons) and from 30 to 76 with a median of 42 in the open group (77 surgeons). In the laparoscopic group, 8 surgeons were classified as experienced and 47 as inexperienced.”(75)</p>	<p><u>Participative interventions</u></p> <p>“All therapists were master’s- or doctoral-level clinicians who had at least 2 years of psychotherapy experience and who underwent extensive training and certification in either IPT or CGT. Certification entailed completion of 2 treatment cases in a manner judged competent by K.S. (for CGT) or E.F. (for IPT). Therapists received ongoing group supervision, separately for IPT and CGT, throughout the study period. Selected audiotapes or videotapes were used in supervision sessions as a part of the discussion. Therapy sessions were audiotaped for adherence and competence ratings, performed on a randomly selected subset of sessions.”(76)</p>
<p>DISCUSSION</p> <p>Limitations</p> <p>Item 20</p> <p><u>Standard CONSORT description</u></p> <p>Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses</p> <p><u>Extension for NPT trials</u></p> <p>In addition, take into account the choice of the comparator, lack of or partial blinding, and unequal expertise of care providers or centers in each group</p>	<p><u>Surgery and procedures</u></p> <p>“First, surgeons might not be proficient in one or both treatments. The difference in malunion rates between the two treatment groups was consistent across all four study sites, indicating the difference is due to the procedure and not technical proficiency. Staff from all four centres were experienced in both techniques and, therefore, the results are probably typical of other paediatric centers.”(77)</p>	<p><u>Participative interventions</u></p> <p>“The sham acupuncture intervention in our study was designed to minimize potential physiological effects by needling superficially at points distant from the segments of ‘true’ treatment points and by using fewer needles than in the acupuncture group. However, we cannot rule out that this intervention may have had some physiological effects. The nonspecific physiological effects of needling may include local alteration in circulation and immune function as well as neurophysiological and neurochemical responses. The question investigated in our comparison of acupuncture and sham acupuncture was not whether skin penetration matters but whether adherence to the traditional concepts of acupuncture makes a difference. For this purpose, our minimal acupuncture intervention was clearly an appropriate sham control although it might not be an inert placebo.”(78)</p>
<p>Generalisability</p> <p>Item 21</p> <p><u>Standard CONSORT description</u></p> <p>Generalizability (external validity, applicability) of the trial findings</p> <p><u>Extension for NPT trials</u></p>	<p><u>Surgery and procedures</u></p> <p>“One surgeon performed all the procedures in this study. Consequently, his technical proficiency is critical to the generalisability of our findings. Our study surgeon is board-certified, is fellowship-trained in arthroscopy and sports medicine, and has been in practice for 10 years in an academic medical center. He is currently the orthopaedic</p>	<p><u>Participative interventions</u></p> <p>“As the intervention was implemented for both sexes, all ages, all types of sports, and at different levels of sports, the results indicate that the entire range of athletes, from young elite to intermediate and recreational senior athletes, would benefit from using the presented training programme for the prevention of</p>

CONSORT item and extension for NPT trials	Examples for RCTs assessing surgery and procedures	Examples for RCTs assessing participative interventions
Generalizability (external validity) of the trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial	surgeon for a National Basketball Association team and was the physician for the men's and women's U.S. Olympic basketball teams in 1996.”(79)	recurrences of ankle sprain. By including non-medically treated and medically treated athletes, we covered a broad spectrum of injury severity. This suggests that the present training programme can be implemented in the treatment of all athletes. Furthermore, as it is reasonable to assume that ankle sprains not related to sports are comparable with those in sports, the programme could benefit the general population.”(80)

Appendix table 4. Examples of abstracts compliant with the CONSORT extension for abstracts of NPT trials

Original abstracts were modified to comply with the CONSORT extension for abstracts and the CONSORT extension for abstracts of NPT trials (CONSORT NPT abstracts). Information in bold and red is requested for CONSORT NPT abstracts.

Title and abstract of a participative intervention RCT compliant with CONSORT NPT abstracts	Title and abstract of surgical RCT compliant with CONSORT NPT abstracts
<p>TITLE: Massage therapy versus simple touch to improve pain and mood in patients with advanced cancer: a randomized trial. (81).</p> <p>Background: Small studies of variable quality suggest that massage therapy may relieve pain and other symptoms.</p> <p>Objective: To evaluate the efficacy of massage for decreasing pain and symptom distress and improving quality of life among persons with advanced cancer.</p> <p>Design: 2-arm parallel group single blind multisite, randomized clinical trial using a centralized computer generated randomization process. Only data collectors were blinded to treatment assignment (ClinicalTrials.gov: NCT00065195).</p> <p>Setting: 15 U.S. hospices of the population-based Palliative Care Research Network.</p> <p>Patients: 380 adults with advanced cancer who were experiencing moderate-to-severe pain (188 massage therapy, 192 control).</p> <p>Intervention: Six 30-minute massage sessions by licensed therapists with at least 6 months of experience or simple-touch sessions provided after a standardized training over 2 weeks.</p> <p>Measurements: Primary outcomes were immediate (Memorial Pain Assessment Card, 0- to 10-point scale) and sustained (Brief Pain Inventory [BPI], 0- to 10-point scale) change in pain over 3 weeks. Secondary outcomes were immediate change in mood (Memorial Pain Assessment Card) and 60-second heart and respiratory rates and sustained change in quality of life (McGill Quality of Life Questionnaire, 0- to 10-point scale), symptom distress (Memorial Symptom Assessment Scale, 0- to 4-point scale), and analgesic medication use (parenteral morphine equivalents [mg/dl]). Immediate outcomes were obtained just before and after each treatment session. Sustained outcomes were obtained at baseline and weekly for 3 Weeks.</p> <p>Results: 298 (151 massage therapy, 147 control) patients were included in the immediate outcome analysis and 348 (171 massage therapy, 177control) in the sustained outcome analysis. A total of 82 patients did not receive any allocated study treatments (37 massage patients, 45 control patients). Both groups demonstrated immediate improvement in pain (massage, -1.87 points [95% CI, -2.07 to -1.67 points]; control, -0.97 point [CI, -1.18 to -0.76 points]) and mood (massage, 1.58 points [CI, 1.40 to 1.76 points]; control, 0.97 point [CI, 0.78 to 1.16 points]). Massage was superior for both immediate pain and mood (mean difference, 0.90 and 0.61 points, respectively; $P < 0.001$). No between-group mean differences occurred over time in sustained pain (BPI mean pain, 0.07 point [CI, -0.23 to 0.37 points]; BPI worst pain, -0.14 point [CI, -0.59 to 0.31 points]), quality of life (McGill Quality of Life Questionnaire overall, 0.08 point [CI, -0.37 to 0.53 points]), symptom distress (Memorial Symptom Assessment Scale global distress index, -0.002 point [CI, -0.12 to 0.12 points]), or analgesic medication use (parenteral morphine equivalents, -0.10 mg/d [CI, -0.25 to 0.05 mg/d]). Adverse events were infrequent, were similar in both groups, and did not seem to be related to treatments.</p> <p>Limitations: The immediate outcome measures were obtained by unblinded study therapists, possibly leading to reporting bias and the overestimation of a beneficial effect. The generalizability to all patients with advanced cancer is uncertain. The differential beneficial effect of massage therapy over simple touch is not conclusive without a usual care control group.</p> <p>Conclusion: Massage may have immediately beneficial effects on pain and mood among patients with advanced cancer. Given the lack of sustained effects and the observed improvements in both study groups, the potential benefits of attention and simple touch should also be considered in this patient population.</p> <p>Funding: National Institutes of Health and National Center for Complementary and Alternative Medicine (1R01AT01006-01A2), Mendel/Asarch Lung Cancer Family Foundation Grants Program.</p>	<p>TITLE: Surgery Versus Nonsurgical Treatment of Lumbar Spinal Stenosis: A Randomized Trial (74)</p> <p>Background: Primary care management decisions for patients with symptomatic lumbar spinal stenosis (LSS) are challenging, and nonsurgical guidance is limited by lack of evidence.</p> <p>Objective: To compare surgical decompression with physical therapy (PT) for LSS and evaluate sex differences.</p> <p>Design: Multisite 2-arm parallel group randomized, controlled trial. (ClinicalTrials.gov: NCT00022776). Randomization was computer generated and concealed using sequentially numbered and sealed envelopes.</p> <p>Setting: Neurologic and orthopedic surgery departments and PT clinics.</p> <p>Participants: Surgical candidates with LSS aged 50 years or older who consented to surgery.</p> <p>Intervention: Surgical decompression or PT. All surgical procedures were performed by fellowship-trained spine surgeons or surgeons with more than 20 years of experience dedicated to spine surgery. Physical therapy was prescribed for 6 weeks, with a frequency of 2 visits per week, and was delivered by licensed physical therapists.</p> <p>Measurements: Primary outcome was physical function score on the Short Form-36 Health Survey at 2 years assessed by masked testers.</p> <p>Results: The study took place from November 2000 to September 2007. A total of 169 participants were randomly assigned and stratified by surgeon and sex (87 to surgery and 82 to PT), with 24-month follow-up completed by 74 and 73 participants in the surgery and PT groups, respectively. All but 2 patients assigned to the surgery group received surgery. In contrast, 47 (57%) of the participants in the PT group crossed over to surgery over the 2-year period. Mean improvement in physical function for the surgery and PT groups was 22.4 (95% CI, 16.9 to 27.9) and 19.2 (CI, 13.6 to 24.8), respectively. Intention-to-treat analyses revealed no difference between groups (24-month difference, 0.9 [CI, -7.9 to 9.6]). Sensitivity analyses using causal-effects methods to account for the high proportion of crossovers from PT to surgery (57%) showed no significant differences in physical function between groups. Thirty-three surgery-related complications occurred, 11 of which were in participants who crossed over from PT to surgery. All 9 PT-related complications were reports of worsening symptoms.</p> <p>Limitation: Without a control group, it is not possible to judge success attributable to either intervention.</p> <p>Conclusion: Surgical decompression yielded similar effects to a PT regimen among patients with LSS who were surgical candidates. Patients and health care providers should engage in shared decision-making conversations that include full disclosure of evidence involving surgical and nonsurgical treatments for LSS.</p> <p>Primary Funding Source: National Institutes of Health and National Institute of Arthritis and Musculoskeletal and Skin Diseases.</p>

Appendix table 5: Allocation of care providers to each trial group

Allocation across group

In NPT trials where care providers could perform the intervention in both groups, the allocation of care providers to each trial group raises specific issues. Several situations are possible, all having advantages and drawbacks.

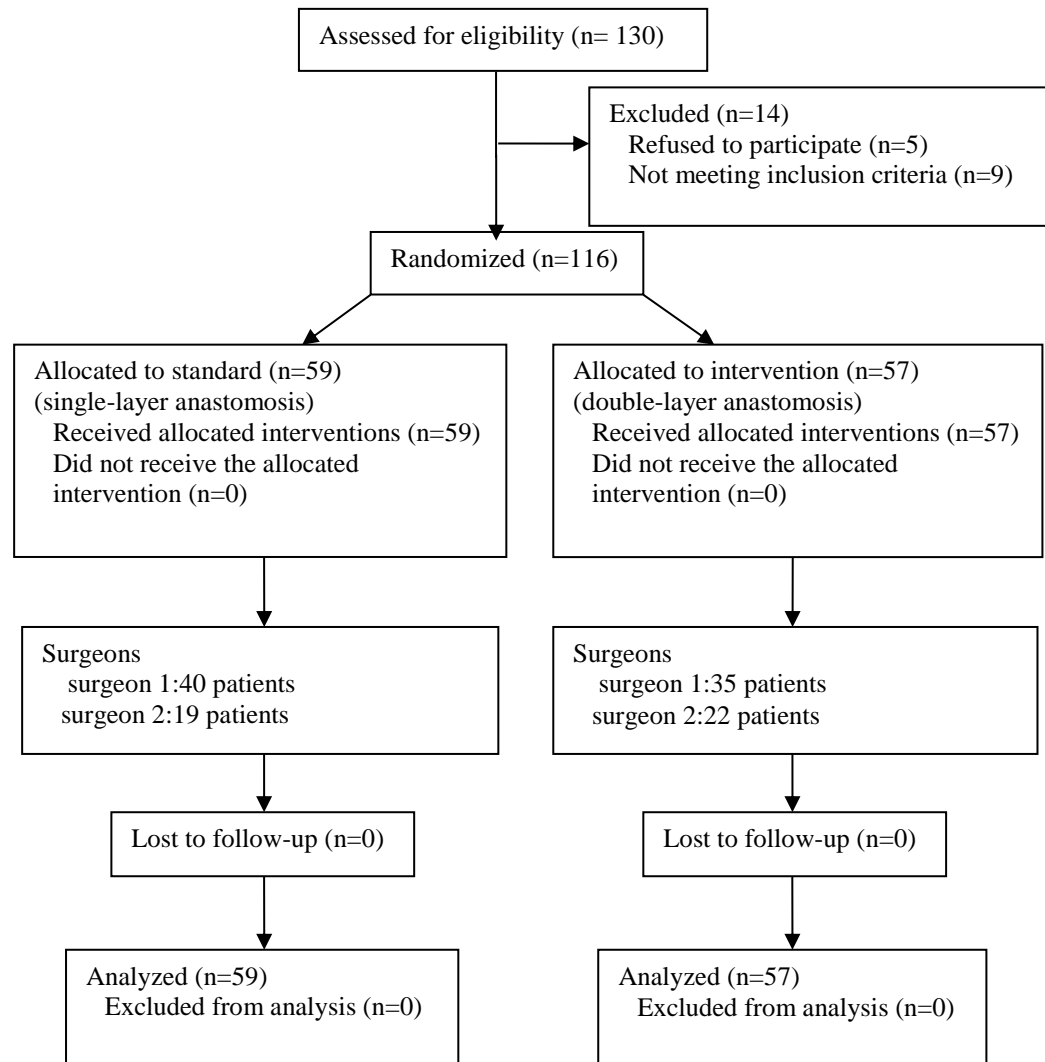
- Care providers deliver the intervention in both groups.
In this situation, care providers may have to administer an intervention they are less confident with or expert in. Consequently, there is a risk of
 - Low adherence to the protocol
 - Contamination (i.e., participants randomized in one group inadvertently receive the intervention [or some component of the intervention] that is allocated to the other group) (82). Contamination may underestimate treatment effect estimates and reduce the study power.
 - Differential expertise bias (i.e., a disproportionate number of patients treated by an expert care provider in one group compared to the other group)
- Care providers could be randomized to perform the intervention in one group.
Care providers may be randomized to an intervention they are not expert in or they are less committed to. This situation would increase the risk of low adherence and contamination.
- Care providers could perform only the intervention they prefer or are expert in. Such choice is also called an “expertise-based randomized controlled trial” (83, 84). This design has several advantages: it should reduce the risk of contamination, take into account the learning curve and avoid the risk of differential expertise bias, and facilitate participation of care providers and patients. However, it also raises some feasibility issues and questions the applicability of the trial results (85, 86).

Allocation within group

In some NPT trials, the care providers can perform the intervention in only one group (e.g., surgery vs drug or surgery vs physiotherapy). The allocation of care providers within groups is frequently determined by logistical considerations. However, in some situations, care providers could be randomized among a pool of eligible care providers.

Appendix Figure 1: Examples of flow diagrams

Figure 1a: Participant flow diagram for single-center trial, surgery



(Modified flow diagram from Menon et al (87))

Figure 1b: Participant flow diagram for multicenter trial, Participative interventions

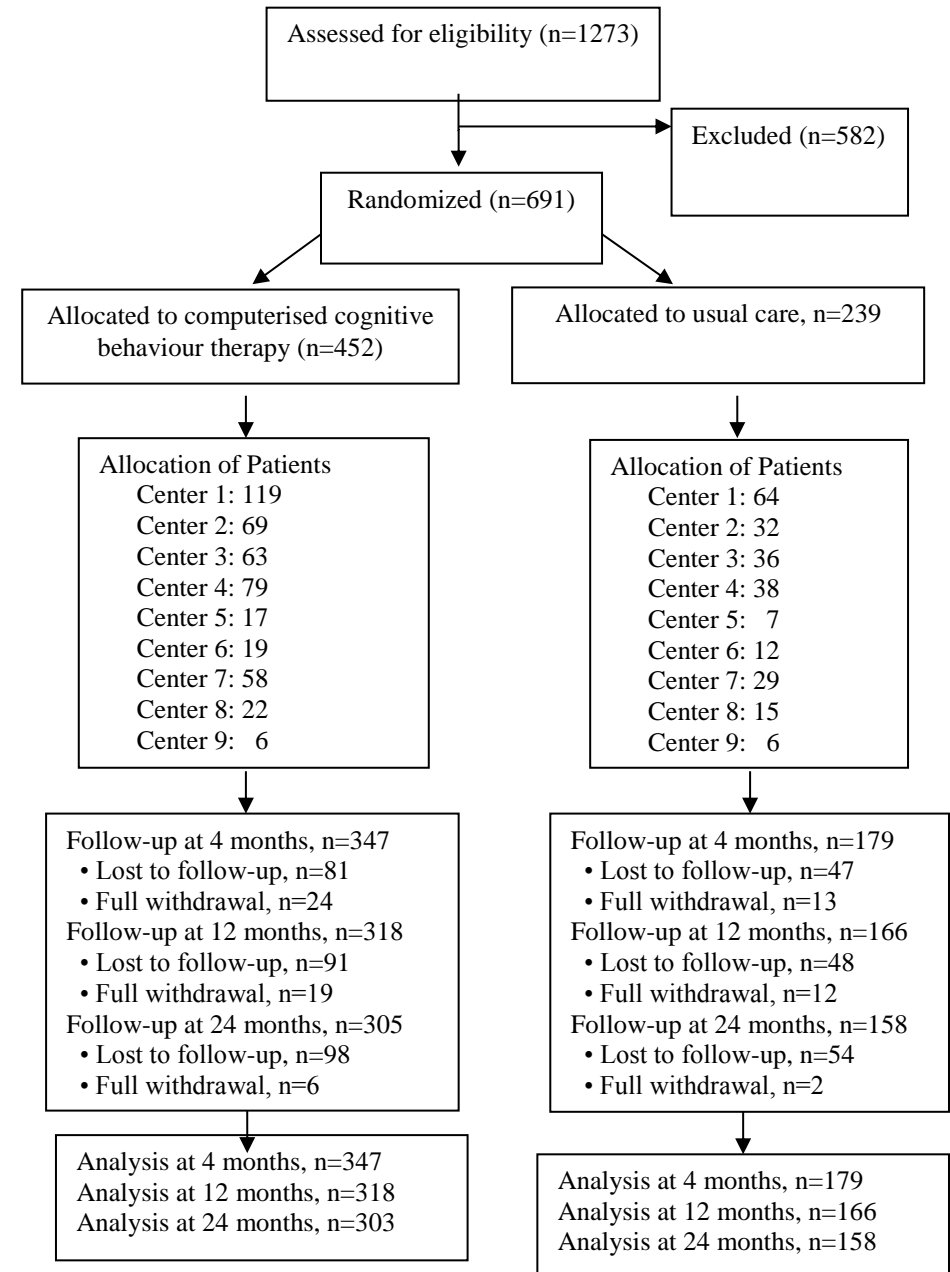
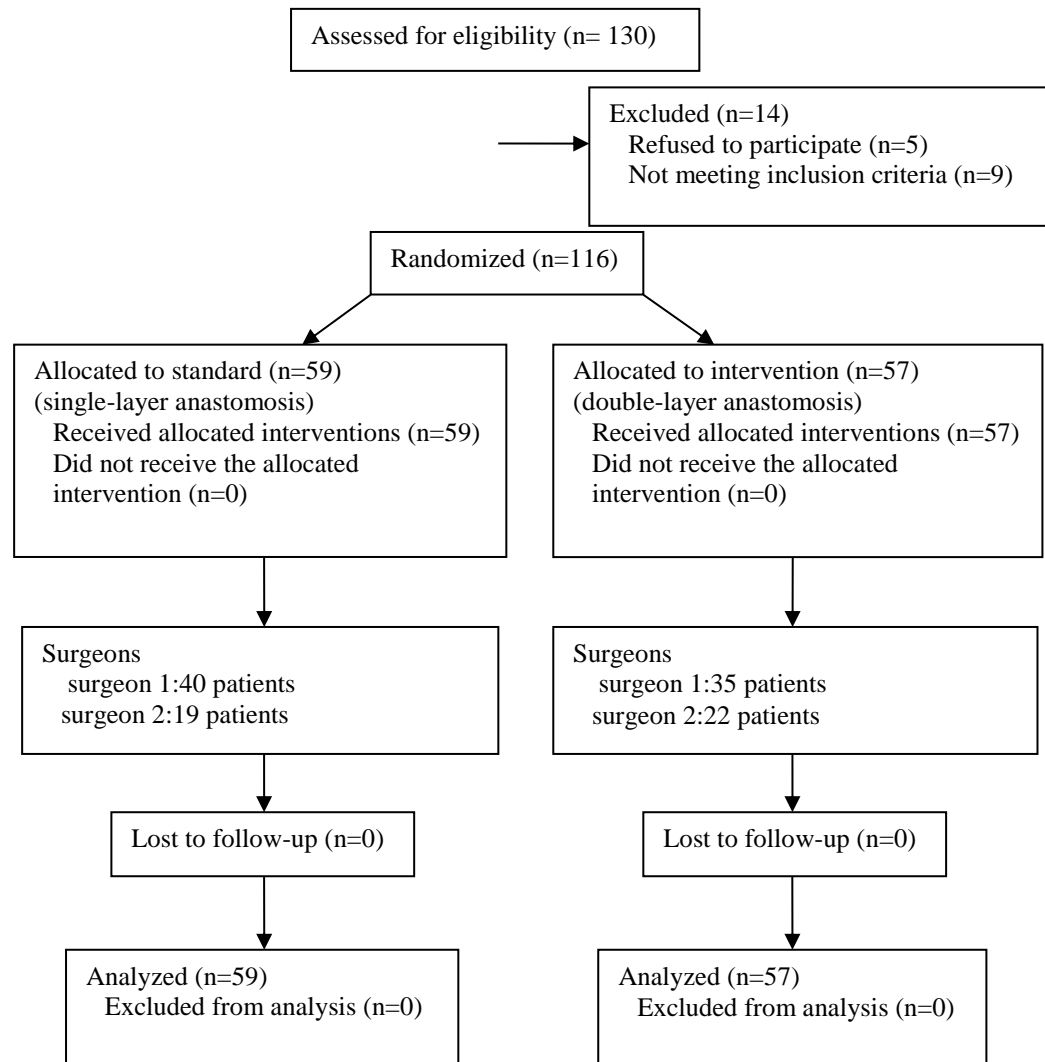
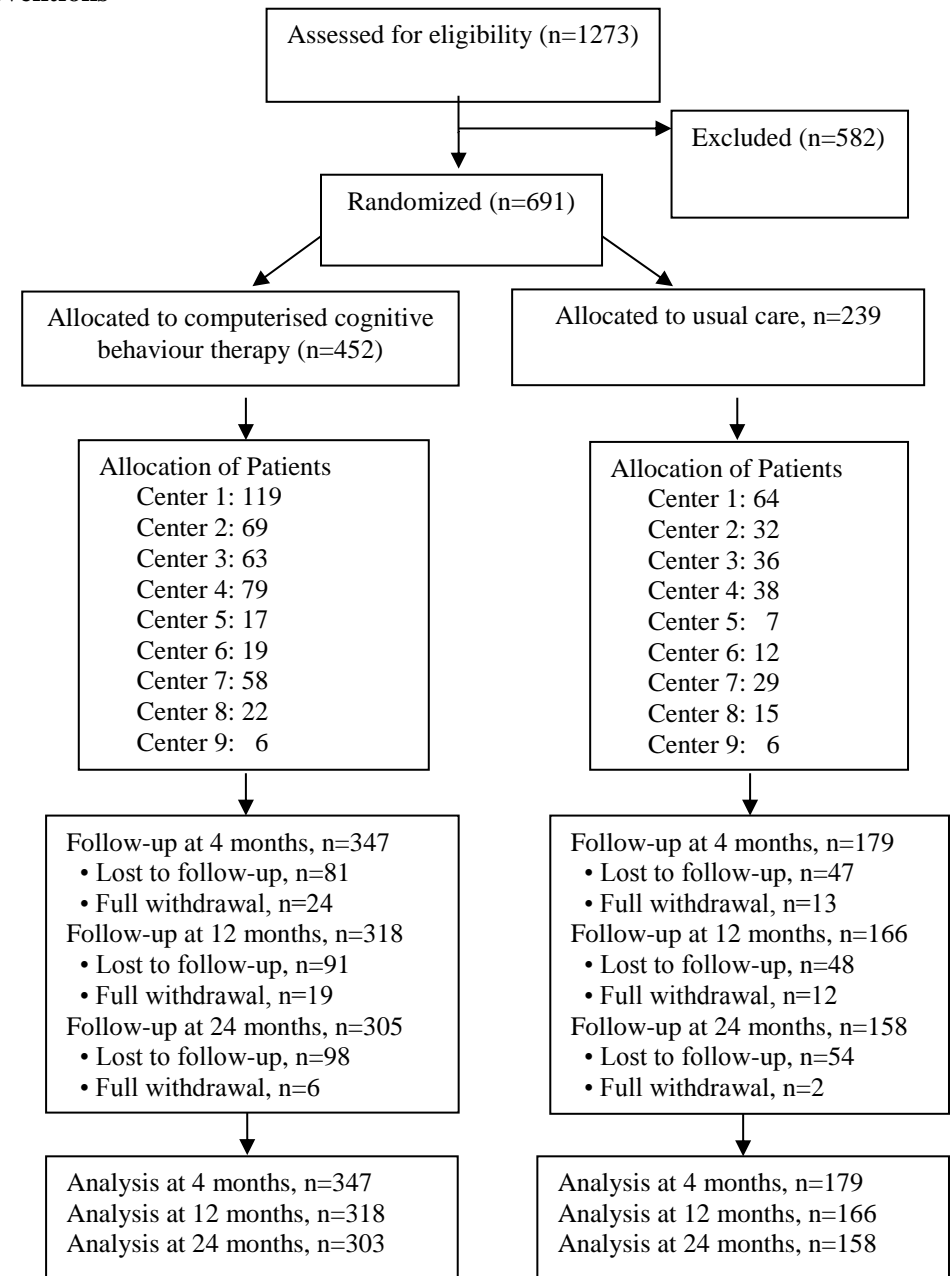


Figure 2: Examples of flow diagrams
Figure 2a: Participant flow diagram for single-center trial, urgency



(Modified flow diagram from Menon et al (43))

Figure 2b: Participant flow diagram for multicenter trial, Participative interventions





(Modified flow diagram from Littlewood et al (10

- 1
- 2
- 3
- 4 1. Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P. Methods and processes of the
- 5 CONSORT Group: example of an extension for trials assessing nonpharmacologic
- 6 treatments. *Ann Intern Med.* 2008;148(4):W60-6.
- 7 2. Chan AW, Altman DG. Epidemiology and reporting of randomised trials published in
- 8 PubMed journals. *Lancet.* 2005;365(9465):1159-62.
- 9 3. Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P. Extending the CONSORT
- 10 statement to randomized trials of nonpharmacologic treatment: explanation and
- 11 elaboration. *Ann Intern Med.* 2008;148(4):295-309.
- 12 4. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better
- 13 reporting of interventions: template for intervention description and replication
- 14 (TIDieR) checklist and guide. *Bmj.* 2014;348:g1687.
- 15 5. Frutos MD, Abrisqueta J, Lujan J, Abellan I, Parrilla P. Randomized prospective study
- 16 to compare laparoscopic appendectomy versus umbilical single-incision
- 17 appendectomy. *Ann Surg.* 2013;257(3):413-8.
- 18 6. Wyrsh B, McFerran MA, McAndrew M, Limbird TJ, Harper MC, Johnson KD, et al.
- 19 Operative treatment of fractures of the tibial plafond. A randomized, prospective
- 20 study. *J Bone Joint Surg Am.* 1996;78(11):1646-57.
- 21 7. Linehan MM, Comtois K, Murray AM, et al. Two-year randomized controlled trial
- 22 and follow-up of dialectical behavior therapy vs therapy by experts for suicidal
- 23 behaviors and borderline personality disorder. *Archives of General Psychiatry.*
- 24 2006;63(7):757-66.
- 25 8. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, et al.
- 26 International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus
- 27 endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a
- 28 randomised trial. *Lancet.* 2002;360(9342):1267-74.
- 29 9. Bonjer HJ, Deijen CL, Abis GA, Cuesta MA, van der Pas MH, de Lange-de Klerk ES,
- 30 et al. A randomized trial of laparoscopic versus open surgery for rectal cancer. *N Engl*
- 31 *J Med.* 2015;372(14):1324-32.
- 32 10. Zaidat OO, Fitzsimmons BF, Woodward BK, Wang Z, Killer-Oberpfalzer M,
- 33 Wakhloo A, et al. Effect of a balloon-expandable intracranial stent vs medical therapy
- 34 on risk of stroke in patients with symptomatic intracranial stenosis: the VISSIT
- 35 randomized clinical trial. *Jama.* 2015;313(12):1240-8.
- 36 11. Lamb SE, Williamson EM, Heine PJ, Adams J, Dosanjh S, Dritsaki M, et al. Exercises
- 37 to improve function of the rheumatoid hand (SARAH): a randomised controlled trial.
- 38 *Lancet.* 2015;385(9966):421-9.
- 39 12. Freedland KE, Carney RM, Rich MW, Steinmeyer BC, Rubin EH. Cognitive Behavior
- 40 Therapy for Depression and Self-Care in Heart Failure Patients: A Randomized
- 41 Clinical Trial. *JAMA Intern Med.* 2015;175(11):1773-82.
- 42 13. Willett K, Keene DJ, Mistry D, Nam J, Tutton E, Handley R, et al. Close Contact
- 43 Casting vs Surgery for Initial Treatment of Unstable Ankle Fractures in Older Adults:
- 44 A Randomized Clinical Trial. *Jama.* 2016;316(14):1455-63.
- 45 14. Wiegersma M, Panman CM, Kollen BJ, Berger MY, Lisman-Van Leeuwen Y, Dekker
- 46 JH. Effect of pelvic floor muscle training compared with watchful waiting in older
- 47 women with symptomatic mild pelvic organ prolapse: randomised controlled trial in
- 48 primary care. *Bmj.* 2014;349:g7378.

15. Bronfort G, Hondras MA, Schulz CA, Evans RL, Long CR, Grimm R. Spinal manipulation and home exercise with advice for subacute and chronic back-related leg pain: a trial with adaptive allocation. *Ann Intern Med.* 2014;161(6):381-91.
16. Friedli K, King MB, Lloyd M, Horder J. Randomised controlled assessment of non-directive psychotherapy versus routine general-practitioner care. *Lancet.* 1997;350(9092):1662-5.
17. Rintoul RC, Ritchie AJ, Edwards JG, Waller DA, Coonar AS, Bennett M, et al. Efficacy and cost of video-assisted thoracoscopic partial pleurectomy versus talc pleurodesis in patients with malignant pleural mesothelioma (MesoVATS): an open-label, randomised, controlled trial. *Lancet.* 2014;384(9948):1118-27.
18. Droezer RA, Dell-Kuster S, Kurmann A, Rosenthal R, Zuber M, Metzger J, et al. Long-term follow-up of a randomized controlled trial of Lichtenstein's operation versus mesh plug repair for inguinal hernia. *Ann Surg.* 2014;259(5):966-72.
19. Van Buren G, 2nd, Bloomston M, Hughes SJ, Winter J, Behrman SW, Zyromski NJ, et al. A randomized prospective multicenter trial of pancreaticoduodenectomy with and without routine intraperitoneal drainage. *Ann Surg.* 2014;259(4):605-12.
20. Feldon SE, Scherer RW, Hooper FJ, Kelman S, Baker RS, Granadier RJ, et al. Surgical quality assurance in the Ischemic Optic Neuropathy Decompression Trial (IONDT). *Control Clin Trials.* 2003;24(3):294-305.
21. Winstein CJ, Wolf SL, Dromerick AW, et al. Effect of a task-oriented rehabilitation program on upper extremity recovery following motor stroke: The icare randomized clinical trial. *JAMA.* 2016;315(6):571-81.
22. Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, Smith AM, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. *Lancet.* 2005;365(9472):1718-26.
23. Weeks JC, Nelson H, Gelber S, Sargent D, Schroeder G, for the Clinical Outcomes of Surgical Therapy Study G. Short-term quality-of-life outcomes following laparoscopic-assisted colectomy vs open colectomy for colon cancer: A randomized trial. *JAMA.* 2002;287(3):321-8.
24. Foa EB, McLean CP, Capaldi S, Rosenfield D. Prolonged exposure vs supportive counseling for sexual abuse-related PTSD in adolescent girls: a randomized clinical trial. *Jama.* 2013;310(24):2650-7.
25. Schnurr PP, Friedman MJ, Engel CC, Foa EB, Shea MT, Resick PM, et al. Issues in the design of multisite clinical trials of psychotherapy: VA Cooperative Study No. 494 as an example. *Contemp Clin Trials.* 2005;26(6):626-36.
26. Rogers CA, Pike K, Campbell H, Reeves BC, Angelini GD, Gray A, et al. Coronary artery bypass grafting in high-RISK patients randomised to off- or on-Pump surgery: a randomised controlled trial (the CRISP trial). *Health Technol Assess.* 2014;18(44):v-xx, 1-157.
27. Schnurr PP, Chard KM, Ruzek JI, Chow BK, Shih MC, Resick PA, et al. Design of VA Cooperative Study #591: CERV-PTSD, comparative effectiveness research in veterans with PTSD. *Contemp Clin Trials.* 2015;41:75-84.
28. Costa ML, Achten J, Parsons NR, Rangan A, Griffin D, Tubeuf S, et al. Percutaneous fixation with Kirschner wires versus volar locking plate fixation in adults with dorsally displaced fracture of distal radius: randomised controlled trial. *BMJ.* 2014;349.
29. Duroy D, Boutron I, Baron G, Ravaud P, Estellat C, Lejoyeux M. Impact of a computer-assisted Screening, Brief Intervention and Referral to Treatment on reducing alcohol consumption among patients with hazardous drinking disorder in hospital

- emergency departments. The randomized BREVALCO trial. *Drug Alcohol Depend.* 2016;165:236-44.
30. Cohen A, Assyag P, Boyer-Chatenet L, Cohen-Solal A, Perdrix C, Dalichampt M, et al. An education program for risk factor management after an acute coronary syndrome: a randomized clinical trial. *JAMA Intern Med.* 2014;174(1):40-8.
31. Taggart DP, Altman DG, Gray AM, Lees B, Nugara F, Yu L-M, et al. Effects of on-pump and off-pump surgery in the Arterial Revascularization Trial. *European Journal of Cardio-Thoracic Surgery.* 2015;47(6):1059-65.
32. Klaber Moffett JA, Jackson DA, Richmond S, Hahn S, Coulton S, Farrin A, et al. Randomised trial of a brief physiotherapy intervention compared with usual physiotherapy for neck pain patients: outcomes and patients' preference. *Bmj.* 2005;330(7482):75.
33. Investigators S. Coronary artery bypass surgery versus percutaneous coronary intervention with stent implantation in patients with multivessel coronary artery disease (the Stent or Surgery trial): a randomised controlled trial. *The Lancet.* 2002;360(9338):965-70.
34. Burton KA, Tillotson MK, Cleary J. Single-blind randomised controlled trial of chemonucleolysis and manipulation in the treatment of symptomatic lumbar disc herniation. *European Spine Journal.* 2000;9(3):202-7.
35. Delitto A, Piva SR, Moore CG, Fritz JM, Wisniewski SR, Josbeno DA, et al. Surgery versus nonsurgical treatment of lumbar spinal stenosis: a randomized trial. *Ann Intern Med.* 2015;162(7):465-73.
36. Neumayer LA, Gawande AA, Wang J, Giobbie-Hurder A, Itani KM, Fitzgibbons RJ, Jr., et al. Proficiency of surgeons in inguinal hernia repair: effect of experience and age. *Ann Surg.* 2005;242(3):344-8; discussion 8-52.
37. Shear K, Frank E, Houck PR, Reynolds CF, 3rd. Treatment of complicated grief: a randomized controlled trial. *Jama.* 2005;293(21):2601-8.
38. Wright JG, Wang EE, Owen JL, Stephens D, Graham HK, Hanlon M, et al. Treatments for paediatric femoral fractures: a randomised trial. *The Lancet.* 2005;365(9465):1153-8.
39. Linde K, Streng A, Jurgens S, Hoppe A, Brinkhaus B, Witt C, et al. Acupuncture for patients with migraine: a randomized controlled trial. *Jama.* 2005;293(17):2118-25.
40. Moseley JB, O'Malley K, Petersen NJ, Menke TJ, Brody BA, Kuykendall DH, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med.* 2002;347(2):81-8.
41. Hupperets MD, Verhagen EA, van Mechelen W. Effect of unsupervised home based proprioceptive training on recurrences of ankle sprain: randomised controlled trial. *Bmj.* 2009;339:b2684.
42. Kutner JS, Smith MC, Corbin L, Hemphill L, Benton K, Mellis BK, et al. Massage therapy versus simple touch to improve pain and mood in patients with advanced cancer: a randomized trial. *Ann Intern Med.* 2008;149(6):369-79.
43. Menon M, Muhletaler F, Campos M, Peabody JO. Assessment of early continence after reconstruction of the periprostatic tissues in patients undergoing computer assisted (robotic) prostatectomy: results of a 2 group parallel randomized controlled trial. *J Urol.* 2008;180(3):1018-23.
44. Keogh-Brown MR, Bachmann MO, Shepstone L, Hewitt C, Howe A, Ramsay CR, et al. Contamination in trials of educational interventions. *Health Technol Assess.* 2007;11(43):iii, ix-107.

- 147 45. Cook JA, Elders A, Boachie C, Bassinga T, Fraser C, Altman DG, et al. A systematic
148 review of the use of an expertise-based randomised controlled trial design. *Trials*.
149 2015;16:241.
- 150 46. Devereaux PJ, Bhandari M, Clarke M, Montori VM, Cook DJ, Yusuf S, et al. Need for
151 expertise based randomised controlled trials. *Bmj*. 2005;330(7482):88.
- 152 47. Walter SD, Ismaila AS, Devereaux PJ. Statistical issues in the design and analysis of
153 expertise-based randomized clinical trials. *Stat Med*. 2008;27(30):6583-96.
- 154 48. Pike K, Angelini G, Reeves B, Taggart D, Rogers C. Recruitment challenges in
155 surgical trials: lessons from the crisp trial. *Trials*. 2013;14(1):1-.
- 156
157
158
159
160