Reporting and Replicating Trials of Exercise-Based Cardiac Rehabilitation
Do We Know What the Researchers Actually Did?

Bridget Abell, MSc; Paul Glasziou, MBBS, FRACGP, PhD; Tammy Hoffmann, PhD

Background—Complete reporting of all components of complex interventions is essential for translation of research evidence into clinical practice. Previous work has highlighted deficiencies in the reporting of nonpharmacological interventions; however, the reporting quality of exercise-based interventions for coronary heart disease has not been examined.

Methods and Results—A systematic search strategy was used to identify randomized controlled trials of exercise-based cardiac rehabilitation published until December 2013. Fifty-seven trials were included, reporting on 74 interventions. Intervention description completeness was assessed using the Template for Intervention Description and Replication checklist. Missing intervention details were then sought from additional published material and also by emailing corresponding authors. Only 6 interventions (8%) sufficiently described all required items within the main publication; this increased to 11 (15%) after searching for additional published material and 32 (43%) after contacting trial authors. Although location/setting and duration were consistently well reported in publications, complete descriptions of the exercise schedule, as well as details about its tailoring and progression, were missing for over half of interventions (complete for 42% and 36% of interventions, respectively). Although some authors (25/61) were able to provide missing intervention details when contacted, others could not be located (20) or did not respond (16).

Conclusions—Inadequate reporting of cardiac rehabilitation interventions is a substantial problem, with essential information frequently missing, and for almost half of all interventions, unobtainable after publication. A conscientious effort to address this problem could facilitate an improvement in the quality of cardiac rehabilitation delivered in clinical practice. (Circ Cardiovasc Qual Outcomes. 2015;8:00-00. DOI: 10.1161/CIRCOUTCOMES.114.001381.)

Key Words: exercise • heart disease • rehabilitation • trials

The existence of evidence demonstrating the effectiveness of interventions is not enough to guarantee that it is used to inform healthcare delivery. The processes and strategies required to integrate evidence into routine care are often lacking, which contributes to gaps between research and clinical practice.1–3 One crucial, but poorly acknowledged, challenge to evidence implementation is the need for clinicians to have sufficient information about the components of an intervention to make informed decisions about how to implement it within their practice. This requires clear, complete, and accessible reporting of the essential components of the intervention.

Despite the need for complete descriptions, the quality of intervention reporting is consistently poor. Studies have found that only 27% of nursing interventions2 and 49% of high quality, clinically relevant primary care interventions3 are described with adequate detail to permit replication, with reporting considerably worse for nonpharmacological interventions. Deficiencies in the reporting of a range of nonpharmacological interventions were further highlighted in a recent study,6 which found that only 39% of 137 interventions were adequately reported. Nonpharmacological interventions are often complex and multifaceted, placing an even greater onus on researchers to facilitate reproducibility by providing clear and complete details.

Exercise-based cardiac rehabilitation for the secondary prevention of coronary heart disease is one such complex nonpharmacological intervention. At its core, it generally involves exercise therapy (the nature of which varies among programs) with or without other components, such as smoking cessation, psychological counseling, and dietary advice. The format of individual cardiac rehabilitation programs, however, varies substantially both within and between countries. Traditionally, these programs began as group sessions based in outpatient centers or hospitals, but subsequent variations have emerged over the last 2 decades, including individual home-based models of care using information manuals, case-managers, phone and Internet support.7–11 The evolution of and variation in what is meant by cardiac rehabilitation therefore highlights the need for clear and precise reporting of the exact intervention used.
WHAT IS KNOWN

- Previous work has highlighted deficiencies in the reporting of a range of nonpharmacological interventions in published trials.
- Despite frequent acknowledgment of this problem and its implications for research and clinical practice, an examination of the completeness of intervention reporting in exercise-based interventions for coronary artery disease has not yet occurred.

WHAT THE STUDY ADDS

- This analysis of published randomized controlled trials of exercise-based cardiac rehabilitation found substantial deficiencies in the reporting of the interventions used.
- Exercise-based interventions may be reported with less clarity than other nonpharmacological treatments, and the reporting of these interventions has not discernibly improved over the last 40 years.
- A conscientious effort is required by authors, journals, and peer reviewers to improve the clarity and completeness of intervention description in order to better facilitate the use of research evidence in clinical practice.

Incomplete descriptions of interventions also hamper an understanding of the relationship between the component parts of cardiac rehabilitation and their effect on clinical outcomes. Although there is a large body of evidence demonstrating the clinical benefits of exercise-based cardiac rehabilitation, authors have frequently reported limitations in interpretation of these results because of missing information about the interventions used in many trials. These missing details essentially render complex interventions, such as cardiac rehabilitation, into black boxes, thus limiting the use of research evidence in practice. It also limits exploration of which components of the intervention may moderate treatment effect. Despite frequent mention of this limitation, examination of the completeness of intervention reporting in cardiac rehabilitation trials has not yet occurred.

Guidance for researchers about how to report the essential details of interventions has been lacking until recently. Although the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement aims to improve the quality of reporting of randomized controlled trials by providing reporting guidelines, it does not provide detailed recommendations for describing interventions. The relevant item in CONSORT has now been supplemented by the Template for Intervention Description and Replication (TIDieR) guide and checklist: an extension of both the CONSORT and Standard Protocol Items for Clinical Trials (SPIRIT) statements. TIDieR has the potential to improve the use of research interventions in clinical practice because it identifies essential details of interventions that should be reported and aims to assist authors communicate the components of these interventions to readers.

This study aims to examine the completeness of reporting of exercise-based interventions for coronary artery disease in published randomized controlled trials (using the TIDieR checklist) and to determine whether incomplete intervention descriptions can be improved by searching additional sources and contacting trial authors.

Methods

Eligibility Criteria

The sample of trials was identified via a systematic search for publications reporting on the effects of exercise-based cardiac rehabilitation on clinical outcomes for coronary artery disease. Studies were included if they were randomized controlled trials comparing exercise-based cardiac rehabilitation to usual care and reported any of the following clinical outcomes: all-cause mortality, cardiovascular mortality, myocardial infarction, or coronary intervention (percutaneous coronary intervention or coronary artery bypass graft). Cardiac rehabilitation could be provided to participants in any setting (eg, outpatient, at home, or in the community) and must have involved the prescription of a supervised or unsupervised exercise program, with or without the addition of lifestyle modification and counseling. Trials of heart failure programs or nonexercise-based interventions were excluded. Where multiple intervention arms were compared with usual care within a single study, each exercise arm was considered a separate intervention.

Search Strategy

A systematic search of multiple electronic databases (EMBASE, PEDro, MEDLINE, SCI expanded, Cochrane Central Register of Controlled Trials, Allied and Complementary Medicine, CINAHL, SPORTDiscus) was performed and included publications up to December 2018. The search strategy comprised both free-text and relevant MeSH terms and was developed in conjunction with a medical librarian experienced in conducting systematic reviews. It used a variety of exercise-based rehabilitation terms combined with coronary artery disease descriptors, with methodological filters to limit results to randomized controlled trials, systematic reviews, and meta-analyses (see MEDLINE strategy in Appendix 1 in the Data Supplement). Reference lists of included studies, existing meta-analyses, systematic reviews, and conference proceedings were also searched, and used along with citation tracking, to identify further trials eligible for inclusion. Any concerns about study eligibility were discussed by the authors and resolved via consensus.

Assessment of Intervention Description

Intervention descriptions in eligible trials were assessed using the TIDieR checklist, which contains guidance on the reporting of 12 intervention items (Table). Items 1 and 2 capture the intervention name and rationale; Items 3 through 9 cover the core procedural and contextual elements of the intervention required for replication, whereas the final items (10–12) record modifications to and fidelity of the intervention. As this study was specifically concerned with exercise interventions, Item 8 of TIDieR (When and How Much) was assessed in its component parts to include the essential elements of the exercise dose: intensity of exercise, session frequency, session length, and overall intervention duration. Each intervention in the included trials was appraised for completeness of reporting of each checklist item. Items missing from the intervention description, or not described in sufficient detail for replication, were considered to be incomplete. For each intervention that was incompletely described, a list of missing items was generated.

Collection of Further Intervention Details

For each trial, reference lists, as well as citation and author tracking, were used to determine whether additional information about the intervention had been published in other sources. If relevant publications were found, these were retrieved and searched for additional description of the exercise intervention. If present, relevant data were extracted.
If no further sources describing the intervention could be located, or if some items were still incomplete, attempts were made to contact the authors of the original trials for further information. For more recent studies, email addresses were generally available within the article. Contacting authors of older studies involved searching for their most recent publications and accompanying contact details, using Google, or workplace staff directories. Corresponding authors were emailed questions specifically related to the missing intervention information. Authors were sent ≤3 reminder emails, each ≈1 month apart. If emails were not delivered because of an incorrect or inactive address, attempts were made to contact coauthors. If authors responded with the requested information, the completeness of the relevant TIDieR item was reassessed.

### Data Analysis

A data extraction form was used to compile the details about each checklist item. An Excel spreadsheet was used to track the completion of missing items, including searches for additional sources and follow-up with email contacts. Data were analyzed using descriptive statistics.

### Results

After deduplication, abstract screening, and full-text review, the final sample comprised 57 eligible trials and a total of 74 individual interventions (Figure 1A). The trials were published between 1975 and 2013 and included various models of exercise-based cardiac rehabilitation (eg, home-based, high intensity interval training, walking programs, case-managed, residential programs, and circuit training). Three of the 56 publications were written in a language other than English (1 in Italian, 1 in Danish, and 1 in Russian). Across the 57 trials, 67 corresponding authors were listed (Figure 1B) because one publication reported outcomes of a collaborative study which involved several individual investigators and participating trialists.
centers. Additionally, one author had published 2 separate trials eligible for inclusion in the analysis.

Figure 2 displays the percentage of interventions for which each checklist item that describes the core intervention items (3 through 9) was assessed as complete in the original publications; after searching for additional sources; and after email contact with authors.

Description of Cardiac Rehabilitation Interventions in Original Publications
A brief intervention description (Item 1) and rationale (Item 2) were found in the original trial publication for all 74 interventions. Only 4 trials,8,18–20 describing 6 different interventions (8% of total sample), provided complete information about all 7 core items required for replication.

Intervention setting (Item 7) was consistently well reported across the original studies and assessed as complete in 89% of interventions. Conversely, items which were described for half or less of all interventions included materials (Item 3; 50%), the when and how much of the intervention dose (Item 8; 42%), and intervention tailoring/progression (Item 9; 36%).

In terms of the component parts of the when and how much of the exercise intervention (Figure 3), program duration was almost always reported (complete in 97% of interventions), whereas the intensity of exercise prescribed (eg, % maximal heart rate, rating of exertion) was missing from half of original publications.

Only 19 interventions (26%), across 6 publications,8,17,19,21,22 reported on planned strategies to enhance intervention fidelity and how this was assessed (Item 11). No mention of intervention modification (Item 10), from the original protocol or during the trial process, was made in any original publication.

Forty-nine interventions (66%) contained information about the level of compliance of participants with the prescribed intervention, in terms of either number/percentage of sessions attended, participants who completed the program, or self-reported exercise levels (Item 12).

Description of Cardiac Rehabilitation Interventions in Additional Sources
Additional information about intervention items was obtained from 16 supplementary sources, including other published trials (12) and study protocols (4). Eleven of these sources were
Description of Cardiac Rehabilitation Interventions After Email Communication

Sixty-one authors (91%) needed to be contacted for additional information about missing intervention components. Contact details were unobtainable for 20 authors (30%), most with publications over 15 years old. Emails requesting additional information were therefore sent to 41 trial authors, with 25 (61%) responding and providing supplementary information about missing items (Figure 1B). Sixteen authors did not respond, despite numerous reminder emails.

Contacts with authors resulted in the completion of the full number of interventions which described all 7 components necessary for study replication to 32 (43%). These responses enabled completion of descriptions about the when and how much of exercise (Item 8) for 13 interventions, as well as procedures (Item 4) and mode of delivery (Item 6) for a further 11 interventions each. Authors also provided details about the exercise intensity for 10 interventions. Eleven authors were additionally able to provide details about participant compliance with the exercise intervention from their records, which were not published in the original study, increasing the number of interventions which reported Item 12 to 81%.

Completeness of intervention reporting was examined by decade across the timeframe of included publications (1975–2013). Figure 4 shows that although more intervention descriptions can be completed via email contact with authors in later decades, the proportion of interventions with complete descriptions in published sources (original trial or other publication) has not increased over time.

Comparison With Other Studies Reporting on the Description of Nonpharmacological Interventions

The high rates of missing intervention information found in cardiac rehabilitation trials are consistent with other examinations of the reporting of nonpharmacological interventions. As in these previous studies, we found the intervention setting/location and mode of delivery to be generally well described and descriptions of materials to be consistently lacking. The extent of missing intervention information in our sample, however, appears to be even greater, with the description of many other key components also missing from reports. Descriptions of materials, providers, schedules, or tailoring remained unknown for one-quarter to one-third of all interventions in our study, even after attempting to ascertain additional information from trial authors.

Previous studies which used a similar checklist have been able to obtain a comparably greater proportion of complete descriptions of nonpharmacological interventions (39% and 31%) from published sources. This result may be partly explained by the difference in the checklist used in these earlier studies. Although similar, it predated the publication of TIDieR and as such did not contain an item about intervention tailoring, one of the worst reported items in our sample (Item 9: complete for only 47% of interventions). However, removing the intervention tailoring item from our analysis only increases the proportion of interventions with all core components described from 15% to 20%; still comparably lower than the results of previous studies. It could additionally be hypothesized that the older age of many publications included in our sample may have contributed to the comparably poorer reporting observed overall. However, this is not likely to be the case, with the proportion of interventions with complete descriptions in published sources varying little over the included decades. It is possible that the findings of our study instead highlight particular reporting deficiencies, which may be more problematic in exercise-based interventions.

The quality of description of exercise-based interventions has not been widely or exclusively studied. In previous examinations of the reporting of nonpharmacological interventions, samples have contained <10% of exercise-based trials, and all types of interventions have been analyzed together when assessing completeness. The specific information needed to provide complete descriptions of items can vary significantly between different types of nonpharmacological interventions. In particular, the when and how much of exercise-based interventions requires the reporting of several components to provide complete knowledge about this item. In a manner
analogous to the prescription of medication, the frequency and length of sessions, intensity of exercise, and overall duration of the exercise program can be adjusted to provide varying exercise doses and each in turn may influence overall training benefit.25 Some other types of nonpharmacological intervention may not require such a specific level of detail to completely report this item. Given the level of detail required to fully complete this item, it is therefore unsurprising that the exercise-based cardiac rehabilitation trials examined in this study displayed comparably worse reporting of the when and how much item compared with other nonpharmacological interventions. A complete description of this item (Item 8) was missing for almost half (47%) of the interventions in our sample compared with 10% to 25% in previous research.26,24 This level of missing information was, however, closer to that observed in an examination of exercise interventions for breast cancer survivors,26 with 34% of included studies failing to report on the intensity, frequency, or length of exercise sessions. Underreporting of these elements is disappointing given that the F.I.T.T principle (frequency, intensity, timing and type), along with the concepts of progression and tailoring captured in Item 9, is well established as a core methodology in exercise prescription.27 It is possible that although these dosing elements are considered during the prescription of exercise throughout the trials, authors remain unaware that details regarding each of these elements should be included in the published report.

**Reporting on the Planned Versus the Delivered Intervention**

Although the TIDieR checklist items about modification and fidelity (Items 10–12) are not essential for replication, reporting of these allows readers to judge the feasibility of the intervention, potential barriers to its successful implementation, and assists with the interpretation of trial results. By reporting on any modifications to the planned intervention which occurred during the trial, authors can highlight aspects which may be difficult to carry out, need to evolve over time, or are context-specific. This information allows readers to judge potential threats to internal and external validity and may also prevent clinicians from repeating mistakes in practice.28 Given the usefulness of this information, it is troubling that it was rarely reported in the cardiac rehabilitation trials examined and not often recalled by authors when contacted. The reporting quality for one of the measures of intervention fidelity (participant adherence) has not been widely examined, yet it is important to consider because the effectiveness of an intervention may depend on the level of participant compliance.29,30 It also helps clinicians to know what level of noncompliance they could reasonably expect in practice and allows for comparison of how participant compliance may vary for similar interventions with differing models of care. In our sample of cardiac rehabilitation trials, it is encouraging to note that compliance with the intervention (Item 12) was the third best reported item in original publications (66% complete), though there is no consistent format in the description of this item. Given that additional information about participant compliance could often be elicited from trial authors, who were able to provide attendance records, exercise logs, or other measures of fidelity on request, authors are encouraged to include this information in their original publications.

**Difficulties in Obtaining Missing Intervention Descriptions**

Restrictive word counts for published articles have been cited as one possible cause of poor intervention reporting.4 Over time, as journals have moved to online or hybrid publishing (with 75% now allowing publication of supplementary information in linked appendices and websites31) and with an increased recognition of the importance of publishing trial protocols, an improvement in intervention reporting quality could be expected. Our findings suggest that this is not the case, with all trials published within the last 5 years missing information about ≥1 intervention item, and no discernable improvement over the last 40 years in the proportion of publications reporting complete intervention descriptions.

Obtaining details missing from interventions after their publication is not a simple task. Only a few studies made reference to intervention information in protocols or other publications, and even when available, these additional sources completed the description of very few interventions. Much more information can be gained by contacting authors directly, although this process has several limitations. The major limiting factor we encountered was an inability to locate contact details for trial authors. Despite an extensive search for contact details of any author listed on the original publication, a current working email address could not be located for one-third of authors. This problem may be because a lot of evidence about the effectiveness of cardiac rehabilitation is now decades old. Others have experienced similar issues when trying to contact authors of older publications, with Vines et al33 finding 40% of authors to be nonlocatable in a set of randomized controlled trials published ≤40 years earlier.

The routine inclusion of corresponding author email addresses in publications, combined with an increase in the number of authors listed per publication since the year 200034 has been purported to make it easier to contact trial authors of more recently published studies. Although in our study, contact details were accessible for all authors with papers published after 2001, it did not necessarily make obtaining information about intervention descriptions any easier. A substantial proportion of authors (40%) did not respond to emails even after repeated reminders; a nonresponse rate comparable with that of others attempting to contact authors via email for additional data or information.6,32,33 Like Vines et al,32 we also found authors of more recent publications to be no more likely to respond to our requests than those of much older trials. Fortunately, we did not experience the same difficulties as others6 (eg, copyright restrictions, missing files, denied access) when requesting intervention information from authors who did respond. In fact, most authors who responded offered additional details readily.

**Strengths and Limitations**

A strength of this study is the use of a systematic search strategy to identify all eligible cardiac rehabilitation trials for inclusion, with no restrictions on type of journal, year of
Implications of Poor Intervention Reporting in Cardiac Rehabilitation Trials

The inadequate reporting of cardiac rehabilitation interventions in this sample, coupled with limited success in retrieving this missing information from trial authors, has important implications for the translation of these interventions into practice and consequently the extent to which evidence-based cardiac rehabilitation can be provided. Cardiac rehabilitation is a complex nonpharmacological intervention and as such it is important for researchers to provide sufficient details about each component of the intervention to enable readers to consider the relevance and reproducibility of the intervention in their own clinical context. If descriptions are incomplete or imprecise, replication in practice may not only be limited, but additionally the beneficial clinical outcomes seen in trials may not be achieved. In particular, the lack of information about exercise intensity in the included trials is concerning, given that there is currently much debate as to the optimal threshold of exercise intensity for cardiac patients to produce beneficial effects. Additionally, the growing impetus to move away from traditional center-based models of care to more flexible modular programs places an even greater importance on understanding the contribution of component parts of cardiac rehabilitation interventions. This process remains encumbered if authors of systematic reviews and meta-analyses are limited in the synthesis and interpretation of their findings because of incomplete intervention descriptions. Conscientious efforts to improve intervention reporting will not only allow for these black box interventions to be assessed in their component parts, but may also have benefits on health service delivery and in reducing wasted research investment. The large proportion of missing information reported in this study, including that in recent trials, demonstrates that more direct actions need to be taken to improve this problem. Authors, journal editors, and peer reviewers all have a role in ensuring that intervention reporting is complete and detailed. Authors should follow the TIDieR guide when writing both their protocol and trial report. Journals should require reviewers to assess the adequacy of intervention reporting as part of the review process, and journals should make complete intervention reporting an explicit requirement for publication. Although this may have been more difficult in the past, with the CONSORT statement offering little guidance about the level of intervention description required, the recent TIDieR guide now provides a common language for reporting interventions, regardless of type. Additionally, although the majority of journals have the means to include online supplementary materials, few require, or even encourage, authors to use this option to assist with intervention reporting. This is an underused feature of online publishing, which has the potential to improve access to intervention descriptions without affecting the already limited word counts available to authors. Furthermore, the introduction of a standardized, central repository to retain intervention protocols, materials, and descriptions as suggested by Hoffman and Conn would aid authors and users of trials. Access to the description in the original article, supplementary material, or other referenced published source is essential for use of the intervention in practice because contacting authors for missing details can be a frustrating and lengthy process which many clinicians are unlikely to undertake.

Conclusions

We have demonstrated a substantial problem, with incomplete reporting of interventions, in the majority of exercise-based cardiac rehabilitation trials. Being able to obtain the complete description of interventions within published material is crucial because attempts to contact authors after publication to obtain missing details are often unsuccessful. For almost half of all interventions, no additional information could be added after publication. Although much of this information from older publications is now lost to science, a more conscientious effort to improve the reporting of interventions going ahead could reduce the likelihood of this occurring in the future and facilitate the delivery of evidence-based care in cardiac rehabilitation.

Acknowledgments

We thank Sarah Thorning (Medical Librarian, Centre for Research in Evidence-Based Practice, Bond University, Queensland, Australia) for assistance with designing search strategies for this study. We also kindly thank all authors of included trials who responded to our requests for intervention descriptions.

Sources of Funding

B. Abell is supported by an Australian Postgraduate Award, which is funded by the Australian Federal Government, to undertake PhD studies. P. Glasziou is supported by the National Health and Medical Research Council of Australia (Australia Fellowship; 527500). T. Hoffmann is supported by the National Health and Medical Research Council of Australia/Primary Healthcare Research Evaluation and Development Career Development Fellowship (1033038), with funding provided by the Australian Department of Health and Ageing. The funders had no role in the design and conduct of the study, data collection, and analysis or in article preparation and approval.

Disclosures

T. Hoffmann and P. Glasziou were on the steering committee that developed the Template for Intervention Description and Replication (TIDieR) guide and checklist and are both authors of that publication. There are no financial relationships or conflicts of interest to declare which may have influenced the results of this research.

References


34. Wren JD, Grissom JE, Conway T. E-mail decay rates among corresponding authors in MEDLINE. The ability to communicate with and request materials from authors is being eroded by the expiration of e-mail addresses. EMBR Rep. 2006;7:122–127. doi: 10.1038/embj.2006031.


Reporting and Replicating Trials of Exercise-Based Cardiac Rehabilitation: Do We Know What the Researchers Actually Did?
Bridget Abell, Paul Glasziou and Tammy Hoffmann

Circ Cardiovasc Qual Outcomes. published online March 3, 2015;
Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7705. Online ISSN: 1941-7713

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circoutcomes.ahajournals.org/content/early/2015/03/03/CIRCOUTCOMES.114.001381

Data Supplement (unedited) at:
http://circoutcomes.ahajournals.org/content/suppl/2015/03/03/CIRCOUTCOMES.114.001381.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Quality and Outcomes can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Quality and Outcomes is online at:
http://circoutcomes.ahajournals.org//subscriptions/
SUPPLEMENTAL MATERIAL

Supplemental methods. Appendix 1. MEDLINE Search Strategy (performed via OVID)

1. exp Myocardial Ischemia/
2. (myocard* adj5 ischaemia or ischemia).tw.
4. exp Coronary Artery Bypass/
5. (myocard* adj5 infarct*).tw.
6. (heart adj5 infarct*).tw.
7. angina.tw.
8. (coronary adj5 (disease* or bypass or thrombo* or angioplast*)).tw.
9. PTCA.tw.
10. PCI.tw.
11. exp Rehabilitation/
12. exp exercise/
13. exp sports/
14. exp exercise therapy/
15. exp physical exertion/
16. rehabilitat*.mp.
17. (physical* adj5 (fit* or train* or therap* or activit*)).mp.
18. (train* adj5 (strength* or aerobic* or exercise* or resistance*)).tw.
19. (aerobic* adj5 exercise*).tw.
20. (train* adj5 (strength* or aerobic* or exercise* or resistance* or interval*)).tw.
21. ((exercise* or fitness) adj3 (treatment or intervent* or program*)).tw.
22. kinesiotherap*.tw.
23. physiotherapy*.tw.
24. ((singl$ or double$ or triple$ or treble$) and (blind$ or mask$)).tw,sh.
25. Randomized controlled trial.pt.
26. meta-analysis.pt.
27. randomized controlled trial/
28. (random$ or placebo$).ti,ab,sh.
30. (retraction of publication or retracted publication).pt.
31. trial.tw.
32. groups.tw.
33. drug therapy.sh.
34. single-blind method.tw.
35. double-blind method.tw.
36. metaanalysis.tw.
37. random allocation.tw.
38. random*.tw.
39. placebo*.tw.
40. RCT.tw.
41. control* stud*.tw.
42. control* trial*.tw.
43. or/1-10
44. or/11-23
45. 43 and 44
46. or/24-42
47. 45 and 46
48. (animals not humans).sh.
49. 47 not 48