

# Quality of Reporting in Systematic Reviews of Implantable Medical Devices



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## **Quality of Reporting in Systematic Reviews of Implantable Medical Devices**

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This report is based on research conducted by the Tufts Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2007-10055-I). The findings and conclusions in this document are those of the author(s), who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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## Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To improve the scientific rigor of these evidence reports, AHRQ supports empiric research by the EPCs to help understand or improve complex methodologic issues in systematic reviews. These methods research projects are intended to contribute to the research base and be used to improve the science of systematic reviews. They are not intended to be guidance to the EPC program, although they may be considered by EPCs along with other scientific research when determining EPC program methods guidance.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality. The reports undergo peer review prior to their release as a final report.

We welcome comments on this Methods Research Project. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to [epc@ahrq.hhs.gov](mailto:epc@ahrq.hhs.gov).

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# Quality of Reporting in Systematic Reviews of Implantable Medical Devices

## Structured Abstract

**Background:** Despite a significant number of published systematic reviews of implantable medical devices, no empirical evaluation of the reviews has been performed. We conducted a critical appraisal of the quality of reporting in systematic reviews of implantable medical devices to understand the methodologies used; identify current strengths, limitations, deficiencies, and unique challenges; and make recommendations to improve future conduct and reporting.

**Methods:** A Technical Expert Panel (TEP) of private and public payers, industry, and U.S. Food and Drug Administration representatives helped to refine the scope of the project, identified device categories, and provided feedback on the methodological approach. Five device categories were reviewed: cardiac implantable devices (e.g., defibrillators), vascular interventional devices (e.g., stents), orthopedic implants (e.g., prosthetic discs), skin-replacement grafts (e.g., wound care products), and neurostimulators (e.g., deep brain neurostimulators). Searches were conducted in MEDLINE<sup>®</sup> and the Cochrane Database of Systematic Reviews for systematic reviews published from January 2009 to December 2010. The search was repeated to cover January 2004 to January 2009 to identify additional eligible reviews for skin-replacement grafts and cardiac implantable devices. We addressed 30 items about quality of reporting in systematic reviews from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines. With input from the TEP, we developed eight device- and procedure-specific items relevant to the evaluation of implantable medical devices.

**Results:** Our searches yielded 467 citations, of which 181 met the eligibility criteria: 19 (10 percent) evaluated cardiac implantable devices, 124 (69 percent) evaluated vascular interventional devices, 16 (9 percent) evaluated orthopedic implants, 8 (4 percent) evaluated skin-replacement grafts, and 14 (8 percent) evaluated neurostimulators. Of the 181 systematic reviews included, 123 (68 percent) involved meta-analyses and the remaining 58 (32 percent) involved no meta-analyses; 66 (36 percent) reviewed randomized trials only, 51 (28 percent) reviewed nonrandomized studies only, 56 (31 percent) reviewed both, and 8 (4 percent) did not explicitly report the study designs included. Twenty of 30 PRISMA and MOOSE items we ascertained were commonly reported in greater than 50 percent of the reviews. Device-specific information was less commonly reported in reviews—differences in characteristics across devices (47 percent), differences in characteristics within a device (36 percent), and evolution of technology and its potential effects (21 percent). Operator-specific information was rarely reported in reviews—including training of providers (1 percent), ramp-up in provider technique or learning curve (7 percent), evaluation of team expertise (9 percent), practitioner variability (10 percent), and volume at each study site (8 percent).

**Conclusion:** Our evaluation of 181 systematic reviews on implantable medical devices reveals a lack of reporting of some important generic items applicable to any systematic review as well as device- and operator-specific information. We identified eight device- or operator-specific items

that might be of value in reporting on systematic reviews of implantable devices and could be incorporated into reporting guidelines.

# Contents

<b>Background</b> .....	1
Key Questions .....	2
<b>Methods</b> .....	5
Technical Expert Panel .....	5
Literature Search .....	5
Eligibility Criteria and Citation Screening .....	5
Data Extraction .....	6
Data Synthesis .....	7
<b>Results</b> .....	8
Key Question 1. How are items such as literature searches, study selection, and results reported in published systematic reviews of implantable medical devices? .....	10
Reporting of Literature Searches, Study Selection, and Results .....	10
Key Question 2. How do published systematic reviews of implantable medical devices report device- or operator-specific information? .....	12
Reporting of Device-Specific Information .....	12
Reporting of Operator-Specific Information .....	13
Reporting of Device- or Operator-Specific Information by Device Categories .....	14
Key Question 3. Handling of Heterogeneity .....	17
How is the reporting of heterogeneity handled in published systematic reviews of implantable medical devices? .....	17
generalizability in published systematic reviews of implantable medical devices? .....	19
Reporting of Validity, Limitations, and Future Research Recommendations .....	19
Other Subgroup Analyses .....	20
Comparison Between Reviews by Author Affiliation to Industry .....	20
Comparison Between Reviews That Conducted a Meta-Analysis and Reviews That Did Not .....	20
Comparison Between Reviews by Included Study Designs .....	21
Comparison Between Reviews by Type of Journal .....	21
<b>Discussion</b> .....	22
Limitations .....	23
Recommendations of Reporting Items for Systematic Reviews of Implantable Medical Devices .....	24
Reporting of Device- or Procedure-Specific Data .....	24
Reporting of Generic Items as Suggested in the PRISMA and the MOOSE Statements .....	25
<b>Conclusions</b> .....	28
<b>References</b> .....	29

## Tables

Table 1. Reporting Items for Systematic Reviews of Implantable Medical Devices .....	4
Table 2. Reporting of Literature Searches, Study Selection, and Results in Systematic Reviews of Implantable Medical Devices .....	10
Table 3. Reporting of Literature Searches, Study Selection, and Results in Systematic Reviews by Device Categories .....	11
Table 4. Reporting of Device- or Operator-Specific Variables in Systematic Reviews of Implantable Medical Devices .....	12
Table 5. Examples of Device-Specific Information That Appeared in the Discussion Section of Systematic Reviews .....	13
Table 6. Examples of Operator-Specific Information That Appeared in the Discussion Section of Systematic Reviews .....	14
Table 7. Reporting of Device- or Operator-Specific Variables and Handling of Heterogeneity in Systematic Reviews by Device Categories .....	16
Table 8. Reporting of Handling of Heterogeneity in Systematic Reviews .....	17
Table 9. Reporting of Handling of Heterogeneity in Systematic Reviews by Device Categories .....	18
Table 10. Reporting of Validity and Generalizability Information in Systematic Reviews of Implantable Medical Devices .....	19
Table 11. Reporting of Validity and Generalizability Information in Systematic Reviews by Device Categories .....	20

## Figure

Figure 1. Flow Diagram of Systematic Review Selection Criteria .....	9
----------------------------------------------------------------------	---

## Appendixes

Appendix A. Search Strategy	
Appendix B. Data Extraction Form	
Appendix C. List of Included Studies in the Analyses	
Appendix D. Excluded Studies After Full-Text Screening	
Appendix E. Tables 1-4 Subgroup Analyses	
Appendix F. A Critical Appraisal of Primary Studies of Implantable Medical Devices	

# Background

Over the past decade, advances in the technologies used in medical devices have profoundly transformed clinical practice and patient management.<sup>1</sup> According to a recent position paper, studies of medical devices typically do not address in sufficient detail study design features and factors that affect safety and effectiveness, including standardization of outcomes and endpoints, evaluation of device–operator interactions, and evaluation of characteristics of the clinical practice setting.<sup>2</sup> The evaluation of medical devices poses a number of methodological challenges, and empirical research evaluating such devices has not been performed. The challenges in conducting assessments of medical devices are secondary to the rapid evolution of technology, practitioner input into design, operator learning curve, and variation in the skill with which they are used.<sup>2</sup> These features can potentially impact study outcomes.

Systematic reviews have an established role in medical practice and research. Clinicians use systematic reviews to keep abreast of current research and to provide information on the effectiveness of competing interventions. Agencies including the Centers for Medicare and Medicaid in the United States and the National Institute of Clinical Excellence in the United Kingdom use systematic reviews to prioritize funding or coverage decisions. Health care organizations use systematic reviews to shape policy and inform clinical practice guidelines.<sup>3,4</sup> Despite there being many published systematic reviews of medical devices, no empirical evaluation of the reviews has been performed. A thorough empirical appraisal of systematic reviews is needed to critically assess current practices and identify issues and gaps in reporting. The information generated from an empirical appraisal of systematic reviews of medical devices could be used to develop new items in reporting guidelines and improve the conduct and the quality of reporting of systematic reviews of medical devices.

The strength of systematic reviews and meta-analyses relies in part on the clarity of the reporting. Reporting standards may serve to improve the quality of systematic reviews and ultimately to benefit evidence-based patient management and treatment decisions. There have been attempts to improve the general quality of reporting of systematic reviews through guidelines.<sup>5,6</sup> Current reviews indicate that adherence to existing systematic review reporting guidelines has generally been low in systematic reviews published in high-impact journals or leading medical journals.<sup>7,8</sup> Existing systematic review reporting guidelines include the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines.<sup>5,6</sup> While these represent consensus guidelines to improve the quality of reporting in systematic reviews in general, they do not provide guidance for reporting or analyses of variables unique to the field of medical devices. Standardized guidance for researchers conducting systematic reviews on device-related topics could benefit the users of these reviews.

Recently, the Consolidated Standards of Reporting Trials (CONSORT) Statement was modified to extend to trials of nonpharmacological treatments,<sup>9,10</sup> but guidelines specific to systematic review of medical devices are still lacking. The rigor of systematic review methods and the clarity with which they are described are as critical as the conduct and validity of the included primary studies. Issues and gaps in reporting of systematic reviews of medical devices can also directly reflect limitations pertaining to primary data. Therefore, a critical appraisal of systematic reviews could also target what must be done to address issues and gaps in primary data.

One large body of devices of interest is implantable medical devices. The Food and Drug Administration (FDA) defines these as devices that are partly or completely inserted into the body or a natural orifice using surgical or medical procedures and are expected to remain in the body or orifice for at least 30 days (or permanently).<sup>11</sup> Such devices can be removed only surgically or deactivated medically. Implantable devices also include those that are used to replace an epithelial or eye surface.<sup>11</sup> The demand for implantable medical devices in the United States and the cost is projected to increase 8.3 percent annually to \$49 billion in 2014, with the fastest-growing categories being spinal implants, cardiac implants, and orthobiologics (substances that accelerate healing of injured bones).<sup>12</sup> These increases in device implantation are a result of the aging population, new and expanded indications, easier-to-implant devices, better functioning products, and minimally invasive procedures. For example, an estimated 200,000 hip-replacement surgeries are performed in the U.S. each year in elderly patients.<sup>13</sup> The prevalence of functioning cardiac devices, such as permanent pacemakers, is estimated to be over 3 million worldwide.<sup>14</sup>

As the Evidence-based Practice Center (EPC) designated for the crosscutting concentration of diagnostic testing, imaging technologies, and medical and assistive devices, we conducted a critical appraisal of the quality of reporting in systematic reviews of implantable medical devices. The goals of this project were to evaluate published systematic reviews and meta-analyses to understand the methodologies used; identify current strengths, limitations, deficiencies, and unique challenges; and make recommendations to improve future conduct and reporting. Our findings could be used to inform a broad range of stakeholders, including researchers, clinicians, guideline developers, policymakers, and payers. On the basis of the recommendations of the Technical Expert Panel (TEP), and to ensure inclusion of the most frequently used and expensive devices, we chose to focus on five broad categories of implantable medical devices: cardiac implantable devices, vascular interventional devices, orthopedic implants, skin-replacement grafts, and neurostimulators.

## Key Questions

The following Key Questions were formulated in consultation with the TEP and AHRQ. For each of the proposed Key Questions, with input from the TEP, we operationalized our analysis by creating specific items that could be answered by the systematic reviews (Table 1).

1. How are items such as literature searches, study selection, and results reported in published systematic reviews of implantable medical devices?
2. How do published systematic reviews of implantable medical devices report device- or operator-specific information?
3. How is the reporting of heterogeneity handled in published systematic reviews of implantable medical devices?
4. What are the limitations and issues related to reporting of the quality and generalizability in published systematic reviews of implantable medical devices?

**Table 1. Reporting items for systematic reviews of implantable medical devices**

<b>Reporting Item</b>	<b>Definition for Adequate Reporting</b>
<b>Items for Key Question 1</b>	
Search terms	Keywords for identifying relevant studies for the research questions (i.e., population, interventions, comparator, outcomes, and study design [PICOD]), or complete search strategy (e.g., keywords, medical subject headings) were described or referred to elsewhere.
Searches in multiple databases	Search was conducted in more than one electronic database.
Search years	Time period of the articles searched and included was explicitly described.
Searches in multiple languages	Search was conducted in English and other languages.
Searching for unpublished data	Authors explicitly stated the efforts to include unpublished data (e.g., contact with study authors, searching meeting abstracts or conference preceding, dissertations, etc.[also known as a “grey literature” search]).
Inclusion or exclusion criteria	Definitions of at least two of the PICOD criteria (e.g., randomized controlled trials of drug-eluting stents were included) were reported.
Baseline description of the population	Health status of the population at baseline (i.e., hypertension, diabetes, or coronary artery disease).
Types of interventions/exposures	Interventions or exposures were described (usually includes device name, or a brief description, or type of device).
Types of comparators	Comparators were described (can include another device, or medical treatment, or surgical treatment).
Types of outcomes	Outcomes or endpoints were defined.
Types of study designs	Design of the included studies was described.
Number of included and excluded studies	Number of eligible and ineligible studies identified from the search was reported.
Reasons for exclusion	Reasons for exclusions were described.
Flow diagram for the number of included and excluded studies	A flow diagram showing the progress of study selection was presented.
The total number of primary studies included in the systematic review/meta-analysis	The total number of studies that met inclusion criteria (often reported in the text, tables, or figures).
Graphical presentation of the results	Graphics (e.g., forest plots, trends in outcomes over time, and regression plots) summarizing individual study estimates and overall estimates were presented.
Meta-analyses were performed	Description of whether a meta-analysis was performed.
Costs or cost-effectiveness	Specific discussion of costs of devices or analyses of cost-effectiveness.
<b>Items for Key Question 2</b>	
<b>Device or operator-specific</b>	
Data on differences across device characteristics were discussed	When multiple devices are used, the differences among devices (e.g., sirolimus-eluting stents, paclitaxel-eluting stents, or bare-metal stents) were discussed across primary studies included.
Data on differences within device characteristics were discussed	Differences within devices (e.g., differences in programming within implantable cardiac defibrillator) were discussed across primary studies included.
Evolution of devices over time were discussed	Discussions within systematic reviews about evolution (change or development) of devices across primary studies evaluated.
Details of training/certification of operator were reported	Details within systematic reviews can include training, prior experience in procedures performed, or any other performance standards.
Ramp-up in provider technique (i.e. learning curve) was discussed	There was a relevant discussion about how the surgeon’s experience with the device may affect outcomes.
Level of expertise of team/site were considered	Discussions were made related to the levels of expertise of a team within hospital where operators practice that may impact outcomes.

**Table 1. Reporting items for systematic reviews of implantable medical devices (continued)**

<b>Reporting Item</b>	<b>Definition for Adequate Reporting</b>
<b>Items for Key Question 2 (continued)</b>	
Practitioner variability were discussed	Variability among operators because different sets of operators are involved in each arm of the trial was discussed.
"Volume at sites" effect were discussed	There was a relevant discussion about how site experience with the device may affect outcomes.
<b>Items for Key Question 3</b>	
<b>Handling of heterogeneity</b>	
Models for meta-analyses were reported	The methods of combining estimates (e.g., fixed- or random-effects models) were reported.
Meta-analyses used accepted methodology	Accepted methods were used when two or more studies were combined in meta-analysis or five studies or more studies were included in meta-regression analyses. Additionally studies were grouped by design or studies were grouped across similar interventions.
Heterogeneity was assessed or discussed	Sources of heterogeneity within population or among devices were discussed or quantified using statistical methods.
Sensitivity analyses were assessed	Details of the range of treatment estimates and confidence intervals resulting from the various sensitivity analyses were described.
Results by subgroups were considered or quantified	Potentially important subgroup results were discussed (qualitatively) or quantified using accepted methods.
<b>Items for Key Question 4</b>	
Assessment of risk of bias	Potential impacts of the biases present in included primary studies were evaluated.
Publication bias was assessed	Quantitative assessment of publication bias (e.g., funnel plot, Begg and Egger tests) was used.
Use of specific checklist for quality items	The list of quality items for the validity (or quality) assessment of studies were applied and reported for each included study.
Study limitations were described	Specific limitations either relating to primary studies or relating to the systematic review methodology were described.
Overall strength of the body of evidence was assessed	Specific methods were used to assess the overall body of evidence (i.e., other than for example "strong evidence").
Specific future research recommendations were made	Specific suggestions for future research agenda (i.e., other than "more research is needed") were made.
Funding source was declared	Specific funding source to conduct the systematic review was identified or absence of funding was made explicit.
Sub-item: Authors' affiliation to industry was reported	Whether authors of the systematic review were on the board or employees of a device industry or had received current or previous funding from an industry relevant to the device reviewed was reported.

PICOD = Population, intervention, comparator, outcome, and study design

## Methods

We conducted a critical appraisal of the reporting of information in published systematic reviews and meta-analyses of implantable medical devices. We convened a Technical Expert Panel (TEP) to help identify device categories, refine Key Questions, and to comment on the methodological approach.

### Technical Expert Panel

The TEP, a group of eight national experts, was assembled to provide advice regarding the scope of the project. Members included private and public payers, industry representatives, an FDA representative, and the Task Order Officer from AHRQ. The Tufts EPC held teleconferences with the TEP and discussed the goals of the project. The TEP served strictly in an advisory capacity to identify the device categories (the most frequently used and expensive devices or those with broad implications for policy decisionmaking), to assist in the development of project's scope and Key Questions, and to define parameters for the methodology of the critical appraisal. After discussions with the TEP and AHRQ, the following five implantable medical device categories were selected for analyses: cardiac implantable devices (e.g., defibrillators), vascular interventional devices (e.g., stents), orthopedic implants (e.g., disc replacement), skin-replacement grafts (e.g., wound care products), and neurostimulators (e.g., deep brain neurostimulator).

### Literature Search

Critical appraisal of large numbers of implantable medical devices can be challenging since there are many published systematic reviews. Our objective was to evaluate approximately 200 recently published systematic reviews (deemed a priori as a feasible number). To reach this target, we limited our search to recent reviews as they are more likely to be relevant and adhere to reporting standards. Searches were conducted in MEDLINE® and the Cochrane Database of Systematic Reviews to identify systematic reviews published from January 2009 to December 2010, using key words for each of the five categories of implantable medical devices (Appendix A). No language restriction was applied.

Potentially relevant reviews were those articles in which the abstracts described searches or eligibility criteria for study identification or included terms such as “systematic,” “evidence,” “evidence-based,” “meta-analysis,” or “pooled analysis.” We included all eligible systematic reviews published within 2 years (from January 2009 to December 2010) for all topics. Our initial search identified a limited number of reviews for two of the five groups, namely skin-replacement grafts (2 reviews) and cardiac implantable defibrillators (9 reviews). In consultation with the Task Order Officer at AHRQ, we searched back to 2004 to identify additional eligible reviews related to these topics.

### Eligibility Criteria and Citation Screening

For the purpose of this report, a systematic review was defined as a publication that contained at least two of the following three components: a statement of the research questions (or aims or objectives), a description of the literature search, and a list of study-eligibility criteria. This approach was used in a previous empirical paper that considers these three components to identify a systematic review.<sup>15</sup> During full-text screening, we noted that many

published systematic reviews of implantable medical devices did not clearly report all three basic components. We did not contact authors for clarifications of these three components. Therefore, we used a liberal definition (at least two of the three components) in order to include a maximum number of current systematic reviews.

Since the objective was evaluation of reporting characteristics, we included reviews that were of any type of implantable device within each of the five categories and that reviewed a recent publication. For example, the cardiac implantable device category could include a review of a pacemaker, a review of a defibrillator, or a review of both a pacemaker and a defibrillator. We included systematic reviews of any design (randomized trials, nonrandomized comparative studies, or observational studies) and methodology for synthesis (qualitative or quantitative synthesis including meta-analyses of individual patient data). We included all reviews published within this time period, which could potentially include multiple reviews on the same topic or different reviews published by the same team of researchers. However, we did not include duplicate publications or similar reviews by the same team of researchers. We did not restrict our evaluation to any particular devices or uses of an implantable device for any particular conditions.

There were no specific sampling criteria per device category; this approach is reasonable because it reflects the proportion of relevant articles in the published literature. Though an even distribution of reviews across the five implantable medical device categories would be preferable, this could not be achieved because of a large number of articles reviewing vascular interventional devices, in particular stents. The TEP concurred with the approach of selection of reviews without specific sampling criteria, as our primary objective was to make an overall inference about devices.

We assessed titles and/or abstracts of citations identified from literature searches for potentially relevant systematic reviews. Reviewers with prior experience in conducting systematic reviews and data extractions participated in abstract and full-text article screening and data extraction. All participating reviewers had to have no conflict of interest and were required sign disclosure statements. The titles and/or abstracts were screened by one reviewer. Abstracts tagged “reject” by a reviewer were rescreened by a second reviewer. Full-text articles of abstracts that met screening criteria were retrieved and examined by two independent reviewers to confirm their eligibility according to predetermined criteria. All disagreements were resolved in consultation with a senior reviewer. The reasons for excluding systematic reviews (e.g., narrative reviews, reviews of ineligible topics, and other reviews) were tabulated. In this report, we did not evaluate the primary studies included within the systematic reviews. A list of included and excluded full-text articles is available at the end of the text.

## **Data Extraction**

We used the current guidelines of reporting of systematic reviews and meta-analyses (PRISMA and MOOSE)<sup>5,6</sup> to come up with a list of information items to collect from the published systematic reviews to answer the Key Questions 1, 3, and 4. We did not use a measurement tool to evaluate methodological quality of systematic reviews (for example, AMSTAR<sup>16</sup>) because our objective was to assess the reporting of validity and generalizability in systematic reviews of implantable medical devices in particular. The operational definitions of each item are described in Table 1.

Currently, there are no specific tools or checklists to evaluate the reporting quality of systematic reviews of implantable medical devices. We consulted the TEP to identify device-

and operator-specific information that is relevant and important to the evaluation of these devices. We identified eight device- and operator-specific information items in addition to the 30 systematic review-specific information items identified in the MOOSE and PRISMA guidelines (Table 1 under items reported for Key Question 2).

A standardized form using Google™ docs was used for data extraction.<sup>a</sup> The basic elements and design of the form were customized to capture all the relevant elements of the Key Questions. We tested the form on several reviews and revised it as necessary before beginning full data extraction of all articles. The data-extraction fields are presented in Appendix B. Each systematic review was extracted by one reviewer, then reviewed and confirmed by at least one other reviewer. Disagreements were resolved through consensus in consultation with a third reviewer. Extracted data were exported to Microsoft Excel®.

## Data Synthesis

Results and data in the tables were organized on the basis of reporting items for each Key Question. The unit of analysis was the systematic review article. Descriptive analyses were performed and summary statistics calculated regarding the reporting characteristics of systematic reviews. Analyses include whether the reporting followed published guidelines for reporting of systematic reviews and meta-analyses, the reporting of device- or procedure-specific information, the number and types of primary studies analyzed, quality assessment of primary studies, methods for quantitative syntheses, descriptions of heterogeneity (variability in results owing to clinical factors, study design, device-related characteristics) and generalizability, and protocols for reporting of results. Handling of heterogeneity included items that were evaluated within systematic reviews included models for meta-analyses, discussions of statistical heterogeneity, and sensitivity analyses, explicit discussions of clinical heterogeneity, and assessment of heterogeneity and results by subgroups.

We compared key methodological and reporting aspects of reviews pertaining to the five groups of implantable medical devices. These comparisons were performed using the Fisher exact test for categorical variables or the Kruskal-Wallis test for continuous and count variables. Additional a priori subgroup analyses of key methodological and reporting aspects of reviews were conducted comparing systematic reviews of nonrandomized studies to those of randomized trials, comparing reviews that conducted a meta-analysis with those that did not, comparing reviews that reported authors' affiliations to the device industry with those that did not, and comparing reviews published in general medical journals with reviews published in specialty journals. Since some of these variables were recorded on the basis of reporting, it is possible that our classification of variables lacks sensitivity. All quantitative analyses were performed with Excel® and Stata 11® (Stata Corp., College Station, TX). All P-values are two-tailed and considered to indicate significance if less than 0.05; no adjustments for multiple comparisons were performed. In general, a P-value of <0.05 indicates that there are statistically significant differences in reporting items between the groups compared. Additional subgroup analyses were conducted for each of the five groups of implantable medical devices.

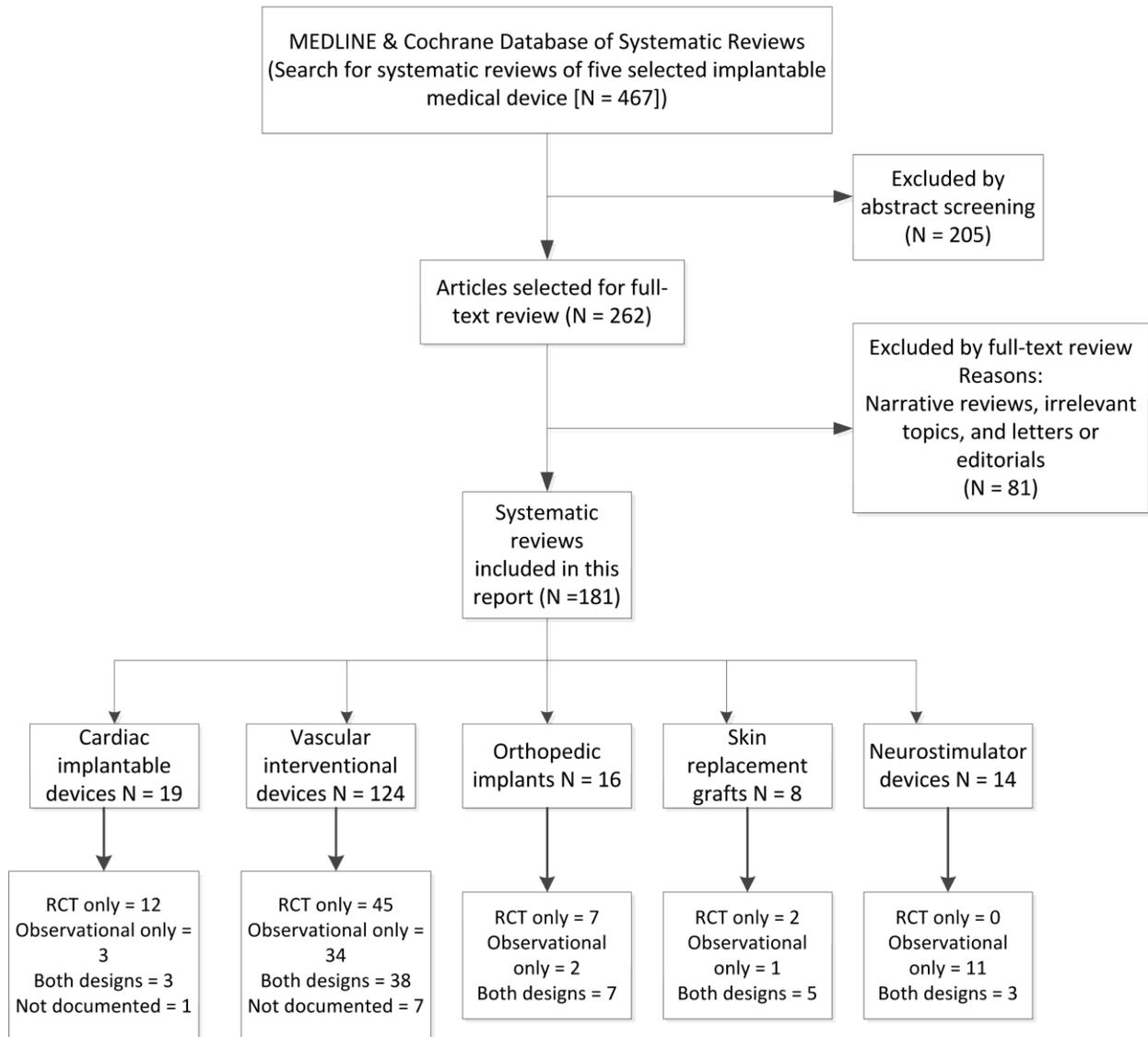
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<sup>a</sup> The live form can be viewed and tested here: <http://bit.ly/nhK0gl> (last accessed on 1/30/2012).

## Results

The searches in MEDLINE® and Cochrane Database of Systematic Reviews identified 467 citations, of which 262 (56 percent) full-text articles were retrieved and evaluated for their eligibility. Included and excluded articles are listed in Appendix C and D. Of these, 181 reviews met the eligibility criteria (Figure 1); 19 (10 percent) evaluated cardiac implantable devices, 124 (69 percent) evaluated vascular devices, 16 (9 percent) evaluated orthopedic implants, 8 (4 percent) evaluated skin-replacement grafts, and 14 (8 percent) evaluated neurostimulators. Among eligible systematic reviews, 66 reviewed only randomized trials, 51 reviewed nonrandomized studies, 56 reviewed both, and 8 reviews did not explicitly mention the study designs of primary studies included.

**Figure 1. Flow diagram of systematic review selection criteria**



Key Question 1. How are items such as literature searches, study selection, and results reported in published systematic reviews of implantable medical devices?

## Reporting of Literature Searches, Study Selection, and Results

This Key Question pertains to generic reporting aspects of reviews—items applicable to any systematic review including reviews of implantable medical devices. Overall results are presented in Table 2. Characteristics reported by nearly all (> 85 percent [median] of) reviews were search terms, years searched, inclusion or exclusion criteria, population at baseline, description of intervention, and types of studies included. These may be considered the core characteristics that are frequently reported within published systematic reviews of implantable medical devices. Among eligible reviews, infrequently reported items (less than 50 percent) were searches or inclusion of studies in more than one language (34 percent) and whether a grey literature search (search for unpublished literature) was performed (44 percent). No reviews reported on all 13 items relevant to search and selection criteria. Infrequently reported items for results included use of study flow diagram (44 percent) and a description of costs or cost-effectiveness of implantable medical devices (23 percent).

**Table 2. Reporting of literature searches, study selection, and results in systematic reviews of implantable medical devices**

Reporting Item	Total N=181 n (%)
<b>Search</b>	
Search terms were described or referred to elsewhere	165 (91)
Multiple databases were searched	144 (79)
Years searched were described	162 (89)
Multiple languages were included in search	62 (34)
Authors explicitly stated searching for unpublished data	80 (44)
<b>Selection</b>	
Inclusion or exclusion criteria were stated	175 (96)
Population at baseline was reported	181 (100)
Interventions/exposures were described	181 (100)
Comparators were described	178 (98)
Outcomes were described	178 (98)
Types of studies included were reported	174 (96)
Number of studies included and excluded were reported	116 (61)
Reasons for exclusion were described	139 (76)
<b>Results</b>	
A flow diagram for the number of studies included and excluded was used	80 (44)
The total number of primary studies included across systematic reviews	4288
Results were presented graphically	117 (64)
Reviews that conducted a meta-analysis	124 (69)
Costs or cost-effectiveness were described	42(23)

## Reporting of Items for Key Question 1 by Device Categories

The quality of reporting of literature searches, study selection, and results was generally uniform across device categories (Table 3). The items relevant to searches (done in three of five reporting items), study selection (in one of eight reporting items), and results (in three of five reporting items) were different across categories. These included performing searches in multiple databases, reporting of search dates, reporting of searches for unpublished data, and reporting of included and excluded studies. The differences across device categories for reporting items evaluating results included use of study flow diagram, graphical plots in meta-analyses, and description of costs (Table 3).

**Table 3. Reporting of literature searches, study selection, and results in systematic reviews by device categories**

Reporting Item	Vascular N=124	Cardiac N=19	Orthopedic N=16	Neurostimulator N=14	Skin Grafts N=8	P- Value
<b>Search</b>						
Search terms were described	113 (91)	17 (89)	16 (100)	12 (86)	7 (88)	0.12
Multiple databases were searched	102 (82)	17 (84)	13 (81)	5 (36)	7 (89)	0.003
Years searched were described	89 (72)	4 (20)	11 (69)	8 (57)	6 (75)	0.002
Multiple languages were included in search	40 (32)	9 (47)	4 (25)	4 (29)	5 (63)	0.39
Searching for unpublished data	58 (47)	15 (79)	2 (13)	2 (14)	3 (38)	<0.001
<b>Selection</b>						
Inclusion or exclusion criteria were stated	119 (96)	19 (100)	15 (94)	13 (93)	8 (100)	0.31
Population at baseline was reported	124 (100)	19 (100)	12 (75)	13 (93)	8 (100)	0.09
Interventions/exposures were described	124 (100)	19 (100)	16 (100)	13 (93)	8 (100)	0.10
Comparators were described	117 (94)	16 (84)	14 (88)	7 (50)	7 (89)	0.06
Outcomes were described	124 (100)	19 (100)	16 (100)	13 (93)	8 (100)	0.10
Types of studies included were reported	117 (94)	18 (95)	16 (100)	14 (100)	8 (100)	0.11
Studies included and excluded were reported	84 (68)	14 (74)	10 (63)	4 (29)	4 (50)	0.03
Reasons for exclusion were described	98 (79)	16 (84)	11 (69)	8 (57)	6 (75)	0.30
<b>Results</b>						
A study flow diagram was used	59 (48)	13 (68)	5 (31)	1 (7)	2 (25)	0.008
The number of primary studies included	2978	248	300	478	284	NA
Reviews that conducted meta-analyses	99 (80)	15 (79)	7 (44)	3 (21)	1 (13)	0.06
Results were presented graphically (among those that conducted a meta-analysis)	91 (73)	15 (79)	6 (38)	3 (21)	2 (25)	<0.001
Costs or cost-effectiveness were described	19 (15)	10 (58)	5 (31)	3 (21)	6 (75)	0.001

Key Question 2. How do published systematic reviews of implantable medical devices report device- or operator-specific information?

## Reporting of Device-Specific Information

Device-specific information was infrequently reported (Table 4). Data on differences across devices were reported the most frequently, 47 percent of the time; about two thirds of reviews had no data differentiating within-device characteristics. A review would typically report data on devices (e.g., type of device and other device information) in a table describing their study and patient characteristics.

Evolution of devices was discussed in the reviews as one of the factors that may have affected the outcome of procedures. For example, the discussion section of a review would attribute evolution in angioplasty and stent catheters as one of the factors to positively influence procedural outcomes in recent primary studies as compared with “older” studies. However, this information was seldom directly assessed or reported in the results section of a systematic review. Additional examples of device-specific information that appeared in the discussion section of systematic reviews are provided in Table 5.

**Table 4. Reporting of device- or operator-specific variables in systematic reviews of implantable medical devices**

Reporting Area	Reporting Item	Total N=181 n (%)
Device-Specific Variables	Data on differences across device characteristics were discussed	85 (47)
	Data on differences within device characteristics were discussed	64 (36)
	Evolution of devices over time were discussed	38 (21)
Operator-Specific Variables	Details of training/certification of provider were reported	2 (1)
	Ramp-up in provider technique (i.e. learning curve) was discussed	13 (7)
	Level of expertise of team/site were considered	16 (9)
	Practitioner variability were discussed	18 (10)
	Volume at sites effect were discussed	14 (8)

**Table 5. Examples of device-specific information that appeared in the discussion section of systematic reviews**

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**Device-Specific Information**

“These findings could be explained by the difference in drug-release kinetics, with the sirolimus-eluting stent releasing almost all the sirolimus in the first 6 months, while more than 80% of the paclitaxel remains unreleased from the polymer coating of the paclitaxel-eluting stent, potentially resulting in more prolonged endothelial dysfunction and delayed healing with the latter.” (Roukoz 2009 PMID 19486720)

**Evolution of Devices Over Time**

“However, it is premature to consider this conclusion definitive for several reasons. [Carotid artery stenting] technology and the technical expertise of operators currently performing the procedure are improving and are superior to those in the studies thus far reported.” (Paraskevas 2009 PMID 19698297)

“Since the last review was published 5 years ago and conducted over 9 years ago, new dressings may have been introduced and higher quality data published....It remains unclear which type of dressing is superior in terms of infection rate, healing quality, quality of life, and cost. It was difficult to compare moist and nonmoist dressings in this review because of the heterogeneity of the included articles.” (Voineskos 2009 PMID 19568092)

“Using meta-regression analysis, we found that the risks of CAS have decreased over time from 1993 to 2006. This may result from improvements in CAS technique, devices, or training and/or a better selection of CAS candidates over time. The development of devices to protect against embolism during the CAS procedure potentially constitutes an important advance.... However, there was significant heterogeneity across studies in this analysis. In fact, the apparent advantage of cerebral protection devices may be illusory. Indeed, the use of such protection devices has increased over time, and the apparent protective effect of those devices may have been confounded by advances in stenting technique and patient selection over time.” (Touze 2009 PMID 19892997)

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CAS = carotid artery stenting, PMID = PubMed Identifier

## **Reporting of Operator-Specific Information**

Data on operator-specific information were rarely reported among included systematic reviews. When reported, they appeared most often in the discussion section. For example, only two reviews of vascular intervention category mentioned data regarding training or certification of the operator in their discussion section. The reviews described these as one of the factors influencing outcomes of the procedures. Table 6 lists selected examples of operator-specific information in systematic reviews of implantable medical devices.

Reviews frequently discussed operators’ learning curve and experience with device implantation as one of the factors that may be associated with temporal improvement in outcomes. Operator’s learning curve or experience with device implantation was also discussed as a confounding variable that may have influenced outcomes. In order to allow sufficient experience with device implantation, some reviews restricted their eligibility criteria to studies that were published in later years. While most of the reviews discussed operators’ experience and volume of the centers impacting outcome data, they rarely explored this variable in subgroup analyses.

**Table 6. Examples of operator-specific information that appeared in the discussion section of systematic reviews**

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“The reason for the lower mortality rate in the DES group seen in our metaanalysis is unclear. It may be that DES, with known lower rates of restenosis, provides a true advantage over BMS....An alternative explanation may relate to a procedural learning curve, as operators may have become more technically proficient at unprotected LMCA PCI by the time DES were favored.” (Pandaya 2010 PMID 20630453)

“As a confounding variable, EPDs have been used more recently and therefore likely at a later stage of the operator’s learning curve.” (Roffi 2009 PMID 19861324)

“Our analysis suggests that centers with an experience of more than 16 stent graft procedures had a significantly higher success rate and a lower rate of complications than less experienced centers.” (Xiong 2009 PMID 19660348)

“These cases were done by a widely varied population of surgeons with varying skill and widely varied surgical technique. It is difficult to standardize the ability of these many surgeons and apply the results to the general population of surgeons practicing today.” (Winegar 2010 PMID 20594011)

“Most centers which have reported, as shown in our reference list, on their experience of surgical correction of thoracic scoliosis with pedicle screws come from very experienced surgeons. Therefore, this literature review may not reflect the reality of what happens in less-experienced centers or with surgeons going through their learning curve.” (Hicks 2010 PMID 20473117)

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BMS = bare-metal stents, DES = drug-eluting stents, EPD = embolic protection device, LMCA = left main coronary artery, PCI = percutaneous coronary intervention, PMID = PubMed Identifier

## **Reporting of Device- or Operator-Specific Information by Device Categories**

### **Device-Specific Information**

In particular, these two items—discussions on differences across devices and discussions within devices—varied significantly according to device category (Table 7). This information appeared most often in the tables describing study and patient characteristics or in the discussion section rather than in the results or analyses section.

### **Cardiac Implantable Devices**

Differences across devices and within devices were rarely reported across reviews of cardiac implantable devices. When reported, one or more of the device-specific information such as device type, method of implant, pacing mode, and position of the electrode were reported under study characteristics. Data related to evolution of devices and their role on applicability of trial results were mostly mentioned in the discussion section.

### **Vascular Interventional Devices**

Compared with other device categories, reviews of vascular interventional devices more frequently reported device type or generation of device in the results or discussion sections. Few reviews conducted exploratory subgroup analyses to evaluate their short- and long-term efficacy. In addition to the discussions related to evolution of devices to explain heterogeneity in outcomes, some reviews used evolution of devices to define their eligibility criteria by excluding trials or data relating to “older” trials.

## **Orthopedic Implants**

In addition to the vascular interventional devices, systematic reviews of orthopedic implants reported device-specific information more frequently in the results or discussion sections than other device categories included. Details of devices were reported under study characteristics or the results section. Device-specific information included was one or more of the following: type of device, type of coating on the device number and location of device, surgical technique or approach, and extraction and insertion torque. Only one review conducted exploratory subgroup analyses of these variables to evaluate their effect on treatment. Evolution of devices was often mentioned in the discussion or conclusion sections to explain good outcome data and progress achieved in clinical management.

## **Skin Replacement Grafts**

Compared with other device categories, differences across devices were less frequently reported across systematic reviews of skin-replacement grafts. When reported device-specific information were frequently available in the results under device characteristics section. Data on differences within devices were reported in one-half of the reviews. Data on skin-replacement grafts reported were type of skin grafts, composition, and bioabsorbability or if they required removal. Only one review mentioned evolution of devices as the objective to conduct a new systematic review.

## **Neurostimulator Devices**

Compared with other device categories, differences across devices and within devices were less frequently reported across systematic reviews of neurostimulator devices. Information on differences within devices included stimulation parameter (frequency, intensity, and pulse width) and location of electrode placement across primary studies included. Data on differences across devices included only a mention of different types of devices without many details about different types of devices used across primary studies. Evolution of devices was discussed to explain differences in outcomes across primary studies included.

## **Operator-Specific Information**

Only reviews of vascular interventional and orthopedic implants reported operator-specific information, while the other three categories did not (Table 7). Only two vascular interventional reviews mentioned training or certification of the operator. In both these reviews, data relevant to training or certification of the operator were reported in the discussion section as one of the factors influencing outcomes of the procedures.

Reviews of vascular interventional noted that some primary studies included data only from centers with experienced operators or excluded data from first few patients due to a significant learning curve observed early in the study. In order to mitigate the impact of technical refinements and the procedural learning curve, one review defined their eligibility criteria by including studies that were published in later years.

While most of the reviews discussed operators' experience and volume in the centers impacting outcome data, reviews rarely explored this variable in subgroup analyses. Reviews that included observational studies discussed practitioner variability as one of the biases inherent to observational data.

**Table 7. Reporting of device- or operator-specific variables and handling of heterogeneity in systematic reviews by device categories**

Reporting Item	Vascular N=124	Cardiac N=19	Orthopedic N=16	Neurostimulator N=14	Skin Grafts N=8	P- value
<b>Device-Specific Variables</b>						
Differences across device characteristics were discussed	68 (55)	4 (21)	9 (56)	5 (36)	2 (25)	0.002
Differences within device characteristics were available	48 (39)	1 (5)	9 (56)	3 (21)	4 (50)	0.002
Evolution of devices over time were discussed	27 (22)	2 (10)	5 (31)	3 (21)	1 (13)	0.30
<b>Operator-Specific Variables</b>						
Details of training/certification of operator were reported	2 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1.00
Learning curve of operator was discussed	12 (10)	0 (0)	1 (6)	0 (0)	0 (0)	0.60
Level of expertise of team were considered	12 (10)	0 (0)	5 (31)	0 (0)	0 (0)	0.14
Practitioner variability were discussed	16 (13)	0 (0)	2 (13)	0 (0)	0 (0)	0.35
Volume at sites effect were discussed	12 (10)	0 (0)	2 (13)	0 (0)	0 (0)	0.47

### Key Question 3. How is the reporting of heterogeneity handled in published systematic reviews of implantable medical devices?

Overall, items infrequently reported were the assessment or discussion of a sensitivity analysis (52 percent), and presentation of results by subgroups (51 percent) (Table 8). The majority of the meta-analyses utilized accepted methodologies (92 percent). The remaining 8 percent of the meta-analyses were performed by combining studies across designs. There were considerable differences across device categories for all reporting items of handling of heterogeneity (Table 9).

**Table 8. Reporting of handling of heterogeneity in systematic reviews**

Reporting Item	Total N=181* n (%)
<b>Handling of heterogeneity</b>	
Models for meta-analyses were reported	123 (99)*
Meta-analyses used accepted methodology (e.g. studies grouped by design or similar interventions)	114 (92)*
Heterogeneity was assessed or discussed	139 (76)
Sensitivity analyses were assessed or discussed	64 (52)
Results by subgroups were considered or quantified	92 (51)

\*Among 181 eligible systematic reviews, 124 conducted a meta-analysis

**Table 9. Reporting of handling of heterogeneity in systematic reviews by device categories**

Reporting Item	Vascular N=124	Cardiac N=19	Orthopedic N=16	Neurostimulator N=14	Skin Grafts N=8	P- Value
<b>Handling of heterogeneity</b>						
Models for meta-analyses were reported	99 (100)	15 (100)	5 (71)	3 (21)	1 (100)	0.03
Meta-analyses used accepted methodology (e.g. studies grouped by design)*	89 (90)	15 (100)	7 (44)	3 (100)	1 (100)	0.62
Heterogeneity was assessed or discussed	88 (71)	8 (42)	6 (38)	1 (7)	3 (38)	0.10
Sensitivity analyses were assessed or discussed	46 (46)	12 (80)	4 (57)	1 (33)	1 (100)	0.008
Results by subgroups were considered or quantified	65 (52)	15 (75)	8 (50)	2 (14)	2 (25)	0.007

\* Results were analyzed based on 124 reviews that conducted meta-analyses

Key Question 4. What are the limitations and issues related to reporting of quality and generalizability in published systematic reviews of implantable medical devices?

## Reporting of Validity, Limitations, and Future Research Recommendations

Outcomes evaluated were mostly clinical outcomes (e.g., stroke, death) in 165 reviews (91 percent), surrogate outcomes (e.g., stent restenosis, wound epithelialization) in 66 reviews (36 percent), and 45 reviews (25 percent) evaluated both.

The items describing validity of primary studies—evaluation of risk of bias (43 percent), the assessment for publication bias (48 percent), and methodological quality using checklists (40 percent)—were infrequently reported among eligible systematic reviews. Study limitations were given in 96 percent of reviews; 82 percent provided specific future research recommendations (i.e., more than stating that future research is simply needed) (Table 10). The reporting of quality items varied significantly across device categories (Table 11). The overall strength of the body of evidence was assessed in only 33 reviews (18 percent); this quality item varied considerably across device categories (Table 11).

Identification of a specific funding source and reporting of author ties to industry were less frequently reported. Of the 76 reviews that declared funding source, 8 (11 percent) reported receiving industry funding, 16 (21 percent) reported receiving professional society funding, 21 (28) reported receiving government agency funding, and the remaining 31 (41 percent) reported receiving no funding. Reporting of specific funding varied significantly across device categories.

**Table 10. Reporting of validity and generalizability information in systematic reviews of implantable medical devices**

Reporting Item	Total N=181 n (%)
<b>Validity</b>	
Risk of bias was assessed	79 (43)
Publication bias was assessed*	59 (48)*
Quality items or checklists were applied and reported	72 (40)
<b>Discussion</b>	
Study limitations were described	175 (96)
Overall strength of the body of evidence was assessed	33 (18)
Specific future research recommendations were made	149 (82)
Funding source was identified	76 (42)
Authors' affiliation to industry was reported	38 (21)

\* Results were analyzed based on 124 reviews that conducted meta-analyses

**Table 11. Reporting of validity and generalizability information in systematic reviews by device categories**

Reporting Item	Vascular N=124	Cardiac N=19	Orthopedic N=16	Neurostimulator N=14	Skin Grafts N=8	P- Value
<b>Validity</b>						
Risk of bias was assessed	56 (45)	14 (74)	6 (38)	2 (14)	5 (63)	0.01
Publication bias was assessed*	45 (45)	12 (73)	3 (43)	0 (0)	0 (0)	0.001
Quality items or checklists were applied and reported	42 (34)	13 (68)	9 (56)	3 (21)	5 (63)	0.02
<b>Discussion</b>						
Study limitations were described	116 (94)	18 (95)	15 (94)	12 (86)	8 (100)	0.89
Overall strength of the body of evidence was assessed	13 (11)	2 (11)	10 (63)	4 (29)	4 (50)	<0.001
Future research recommendations were made	100 (81)	14 (74)	13 (81)	13 (93)	8 (100)	0.66
Funding source was reported	54 (44)	12 (63)	3 (19)	5 (36)	2 (25)	0.04
Authors' affiliation to industry reported	27 (22)	5 (26)	1 (6)	4 (29)	1 (13)	0.33

\* Results were analyzed based on 124 reviews that conducted meta-analyses

## Other Subgroup Analyses

### Comparison Between Reviews by Author Affiliation to Industry

Among 181 eligible systematic reviews, 38 reviews reported that authors conducting systematic reviews had affiliations to industry, and the remaining 143 reviews did not report this information (Appendix E, Table E1). Seventy-six reviews (42 percent) identified their funding.

Reviews that reported whether authors had industry affiliations were more likely to conduct a meta-analysis than reviews that did not disclose this information. For all other items, there were no differences across all reporting characteristics between reviews that reported authors' affiliations to industry and those that did not report this information, except for one item of conducting a meta-analysis.

### Comparison Between Reviews That Conducted a Meta-Analysis and Reviews That Did Not

Of the eligible systematic reviews, 124 conducted meta-analyses and the remaining 57 did not conduct a meta-analysis. Compared with reviews that conducted meta-analyses, reviews without meta-analyses were less likely to report whether searches were conducted in multiple databases or to look for unpublished data, explicitly report eligibility criteria or eligible studies, handling of heterogeneity, assessment of risk of bias, and specific future research

recommendations (Appendix E, Table E2). Device and operator-specific characteristics across both subgroups were infrequently reported without any differences. Reviews without a meta-analysis were more likely to assess overall strength of evidence than reviews that conducted a meta-analysis.

### **Comparison Between Reviews by Included Study Designs**

Systematic reviews that included nonrandomized or observational study designs alone were less likely to identify unpublished data, or to conduct a meta-analysis, or to assess risk of bias. Data on differences within devices were less frequently reported in systematic reviews that included nonrandomized or observational studies alone. Similarly, quality items were less frequently reported in systematic reviews that included nonrandomized or observational studies alone. However, reviews that included nonrandomized or observational studies alone frequently reported specific future research recommendations (Appendix E, Table E3).

### **Comparison Between Reviews by Type of Journal**

Systematic reviews were analyzed by type of journal publication (general medical journals vs. specialty journals). Reviews published in specialty journals were less likely to identify unpublished data, conduct a meta-analysis, or assess risk of bias. However, there were no differences in reporting of device- or operator-specific data between reviews published in general medical journals and reviews published in specialty journals (Appendix E, Table E4).

## Discussion

We identified 30 items from the PRISMA and MOOSE checklists that were relevant to our Key Questions,<sup>5,6</sup> along with 8 new device-specific and operator-specific items (see final list in Table 1). To our knowledge, there has been no prior empirical evaluation of systematic reviews of implantable medical devices. Although the deficiencies in reporting regarding some of items in systematic reviews of implantable medical devices are similar to those seen in reviews of drug-therapy studies,<sup>17,18</sup> our findings highlight types of deficiencies that should be remedied. In particular, reviewers should a priori adhere to a specific guideline (e.g., those described in this report) when conducting a systematic review in order to avoid neglecting to report relevant characteristics within primary studies. Secondly, when conducting a review (and transitively, a primary study), it is essential that variation within the intervention with potential to influence or confound outcomes is reported or at least identified and acknowledged as a possible limitation. Consequently, heterogeneity should be adequately evaluated through subgroup or sensitivity analyses.

Our analyses of a large sample of systematic reviews of implantable medical devices found that about 20 of 30 recommended items were commonly reported (as defined by reporting in at least 50 percent of the reviews). However, eight items identified as specific to the field of medical devices were all infrequently reported across device categories. We also identified inadequate reporting of 9 of 17 items that represented the clarity or transparency of methods and results. There were no significant differences in quality of reporting when reviews were stratified by their reporting of authors' affiliations (vs. not reporting affiliations) to industry, except for one item of conducting a meta-analysis. It is possible that journals mandating disclosure of authors' affiliation were more likely to accept systematic reviews with a meta-analysis than those without a meta-analysis.

Our review also shows that the majority of the meta-analyses were conducted by applying accepted methodologies (92 percent). The remaining eight percent of the meta-analyses were performed in the presence of heterogeneity among device groups (e.g., by combining data across drug-eluting stents and bare-metal stents) or among studies combined across designs (e.g., by combining data across study designs of randomized trials and observational studies). In the presence of such heterogeneity, and by combining such studies into meta-analyses, the meaning of the result is unclear. For example, the utility of assessing outcomes of studies confounded by type of drug-eluting stent or performance of different operators at different sites is unclear.

The number of systematic reviews of implantable medical devices has grown rapidly in recent years, with reviews being published in a broad range of journals. Our results indicate that current systematic reviews of implantable medical devices generally lack data on the reporting of some important items applicable to any systematic review, as well as data relevant to device- and operator-specific items that are specific to review of implantable medical devices. The device-specific factors—including evolution of technology, generalization of results from one device to a similar device, evaluation of device-operator interactions, and evaluation of team expertise—are important characteristics that should be examined in systematic reviews of implantable medical devices. Since there is no widely accepted guidance for reporting of information unique to implantable medical device studies, failure to report data on procedures and devices could potentially lead to invalid synthesis or interpretation of results.

Failure to report the variation in device specifics and operator techniques can potentially confound results. For example, several reviews of stent studies combined sirolimus- and paclitaxel-eluting stents together into a generic category of “drug-eluting stents” when compared to bare-metal stents, without additional subgroup analyses. This highlights a need for the identification and inclusion of items to address device-specific information in a systematic review. The lack of reporting of these potentially important variables may stem from the fact that most reviews focused on evaluating clinical outcomes rather than whether device- or operator-specific variables influenced the clinical outcomes. While this critical appraisal was under peer review, we evaluated 100 primary studies for quality of reporting of device- or operator-specific details (detailed methodology in Appendix F). Our review identified that primary studies frequently report device-specific data but infrequently report operator-specific data (Appendix F). Our findings do emphasize the need for improving quality of reporting in both primary studies and systematic reviews.

Systematic reviews have gained acceptance as a useful way to summarize data and are also helpful in identifying knowledge gaps within primary studies as well as reviews of those studies. Findings from systematic reviews can help target current and identify future specific research needs. Therefore, good-quality reporting and well-conducted systematic reviews can minimize the likelihood of bias or misinterpretation of results. Systematic reviews and meta-analyses represent a very high level within a hierarchy of evidence, making it all the more important that they are conducted as methodologically rigorous as possible.

## **Limitations**

The quality of reporting within the available primary literature is always a limitation, but these limitations ought to be systematically acknowledged and managed. Some of the generic items were observed to be reported in 100 percent of the reviews, while other items were rarely reported. Our examination relied on reporting by the authors of these reviews. It is possible that the authors of these reviews conducted comprehensive evaluations but we cannot comment on this unless authors clearly report their methods in journal publications. We did not check for data-extraction errors within the systematic reviews, contact review authors, or conduct any reanalysis of primary data from those reviews, as none of these was the primary purpose of our review. We did not conduct searches of grey literature to identify unpublished data. Thus, we cannot comment on the quality of reporting in grey literature. Our TEP panel did not include clinical experts. While inclusion of clinical experts as TEP members was desirable, it would have required a large panel of members (one for each device category) and was therefore not pursued. Finally, we used liberal criteria for reporting an item (either in the analyses or descriptively in the discussion). By using a very low threshold for reporting of device- and operator-specific information, our results may have inflated the numbers with regard to reporting of these important variables.

# Recommendations of Reporting Items for Systematic Reviews of Implantable Medical Devices

## Reporting of Device- or Procedure-Specific Data

Our report indicates that the reporting of study characteristics with regard to device- or procedure-specific data needs to be improved. Differences within devices or across device groups were reported in less than half of the reviews and less than one-tenth of the systematic reviews providing information on operator- or procedure-specific data. It is unclear whether the space allotted or word count of the journal is the reason for this poor reporting; if so, journal editors and reviewers should encourage authors to provide supplementary material for posting on a Web page. Information that should be reported includes the device characteristics, evolution of the device during the study period, details of training or certification of the operator, the operator learning curve, the level of expertise of the operating team or site, variations among practitioners, and volume at the sites that conducted the study.

In addition, PROSPERO—the International Prospective Register of Systematic Reviews—provides guidance on reporting, conduct, scientific writing, and publication of systematic reviews through a formal protocol registration process. We suggest incorporation of eight new device- and operator-specific items unique to implantable medical device studies at the time of registration of systematic reviews' protocols. Such an effort would encourage researchers to practice accurate and transparent reporting of systematic reviews of implantable medical devices. We also suggest incorporation of eight new device- and operator-specific items unique to implantable medical device studies into the extension guidelines of PRISMA.

Herein, we describe a list of device-specific characteristics within each of the five device categories that could be considered in future systematic reviews of implantable medical devices. The characteristics in this list are in no particular order but are limited to those that were described in systematic reviews of implantable devices evaluated in this report. Our TEP panel did not include clinical experts, and therefore, to identify additional device-specific characteristics, we encourage review authors to consult domain experts before embarking on future systematic reviews.

Cardiac defibrillators with or without pacemakers:

- Device type
- Method of implantation
- Position of the electrode
- Description of microprocessor technology and programmable features
- Alert features that monitor lead impedance

Vascular interventional devices (e.g., stents)

- Type of stent and stenting technique
- Generation of stent (e.g., first or second generation)
- Type of antiproliferative drug used
- Delivery system
- Polymer layer
- Stent frame

#### Orthopedic implants

- Type of device
- Surgical technique or approach
- Number and location of devices
- Fixation and supplementary materials such as plates and screws
- Type of device coating

#### Skin-replacement grafts

- Type of skin graft required
- Composition of graft
- Graft type: bioabsorbable or requiring removal

#### Neurostimulators

- Stimulation parameters
  - frequency
  - intensity
  - pulse width
- Electrode location

## **Reporting of Generic Items as Suggested in the PRISMA and the MOOSE Statements**

Expert panels have identified guidelines for the conduct and reporting of systematic reviews resulting in statements such as the PRISMA and the MOOSE. These statements have been adopted by many major journals as a tool to ensure appropriate conduct and reporting standards for systematic reviews. Journal editors and reviewers should encourage publication of systematic reviews of implantable medical devices that adhere to the conduct and reporting standards as outlined in these statements.

## **Systematic Reviews of Implantable Devices Should Clearly State the Objective or Rationale For Conducting a Review**

We found that the objective or rationale for conducting a systematic review of implantable medical devices was often not stated clearly. A systematic review is often conducted to confirm a result from a primary study, or a meta-analysis may be conducted to increase the sample size and to determine whether the result from a primary study holds in other populations when combined with evidence from other studies. Another objective may be to evaluate sources of heterogeneity. Without stating an objective it is often difficult for readers to understand the exact reason for which a systematic review was conducted or whether the new review would add any new information to existing knowledge base.

## **Systematic Reviews of Implantable Devices Should Explicitly Report Search and Study-Selection Criteria**

The majority of reviews of implantable medical devices explicitly reported search criteria and selection of studies. However, only a few conducted searches in languages other than English or attempted to include unpublished data. Moreover, in our review, less than one-half of the reviews reported the numbers of papers identified using a flow diagram, as is suggested in the PRISMA and the MOOSE statements. As compared with published trials, unpublished trials

tend to show less beneficial effect, but non–English-language trials and nonindexed trials tend to show larger treatment effects.<sup>19</sup> Therefore, emphasis should be placed on identifying all available evidence by performing a comprehensive literature search (including unpublished studies and non–English-language studies). In addition, comparing unpublished data with published data can be useful in evaluating the potential impact of publication bias.

### **Systematic Reviews of Implantable Devices Should Explore Heterogeneity Through Subgroup and Sensitivity Analyses**

Systematic reviews often explore the degree to which data from individual studies (e.g., from sensitivity analyses) or any variation in relation to specific clinical characteristics of the included studies (e.g., from subgroup analyses) affect the main findings. Our report shows that only half of the reviews used subgroup analyses and used sensitivity analyses to test whether the results of their review are robust. Authors usually perform a variety of analyses and they should publish all their analyses.

### **Systematic Reviews of Implantable Devices Should Assess the Risk of Bias of the Primary Studies Included**

In our review, only 40 percent of systematic reviews of implantable medical devices assessed the risk of bias or used quality scales or checklists to assess the methodological quality of the primary studies included. Without these assessments, the internal validity of the included primary studies is unknown and therefore the impact of the potential biases in the primary studies on the conclusions of a systematic review remains unclear. Furthermore, transparent reporting of the risk of bias ensures more accurate, less biased summaries of the overall evidence that allow users of the systematic reviews to have a better understanding of the summarized evidence and what biases may exist.

### **Systematic Reviews of Implantable Devices Should List Funding Sources and Authors' Conflicts of Interest as Part of Their Standard Reporting**

We found that only 42 percent of systematic reviews reported the funding source, and about 20 percent reported authors' financial affiliation to industry. Some empirical evidence from drug-therapy trials has shown an association between the reporting of favorable results and industry funding and financial ties between authors and industry. Systematic reviews of implantable medical devices should, as part of their standard reporting, disclose device industry funding and authors' affiliation with the device industry.

### **Systematic Reviews of Implantable Devices Should Formally Assess the Overall Body of Evidence**

Only 18 percent of the reviews assessed the overall body of evidence. Rating or evaluating the overall body of evidence allows systematic reviews to link the quality of the overall evidence to the strength of their conclusions. A formal rating system such as the GRADE (Grades of Recommendation Assessment, Development, and Evaluation) allows systematic reviewers to carefully examine the benefits and harms and draw reasoned conclusions by considering the uncertainty of efficacy or effectiveness of an intervention of interest. Formal assessment of the overall body of evidence is a relatively new step in systematic reviews, and the proportion of

studies performing such an assessment may increase as the methods around it are adopted more widely.

## Conclusions

We critically appraised 181 systematic reviews of implantable medical devices, most of which were published in recent years. After evaluating these reviews according to the 30 items from the PRISMA and MOOSE guidelines, we observed that 20 items were commonly reported in more than 50 percent of the reviews. On the basis of input from the TEP, we developed eight items specific to evaluating implantable medical devices. These included device-specific items such as differences in characteristics across devices, differences in characteristics within a device, and the evolution of the device over time; as well as operator-specific information included training of providers, ramp-up in provider technique or learning curve, evaluation of team expertise, practitioner variability, and volume at each study site. Device-specific information was less commonly reported in reviews—differences in characteristics across devices (47 percent), differences in characteristics within a device (36 percent), and evolution of technology and its potential effects (21 percent). Operator-specific information were rarely reported in reviews—including training of providers (1 percent), ramp-up in provider technique or learning curve (7 percent), evaluation of team expertise (9 percent), practitioner variability (10 percent), and volume at each study site (8 percent).

Our evaluation of 181 systematic reviews on implantable medical devices reveals a lack of reporting of some important generic items applicable to any systematic review as well as device- and operator-specific information. We identified eight device- or operator-specific items that might be of value in reporting on systematic reviews of implantable devices and could be incorporated into reporting guidelines.

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## Appendix A. Search Strategy

1 defibrillators, implantable/ or pacemaker, artificial/ or cardiac resynchronization therapy devices/ or heart, artificial/ or heart-assist devices/ or Heart Valve Prosthesis/ (26457)

2 (defibrillator\* or pacemaker\* or cardiac resynchronization therapy device\* or artificial heart or heart assist device\* or heart valve prosthesis\*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (42310)

3 implantable neurostimulators/ or neural prostheses/ or auditory brain stem implants/ or cochlear implants/ or Deep Brain Stimulation/ (5661)

4 (neurostimulator\* or neural prosthesis\* or brain stem implant\* or cochlear implant\* or deep brain stimulator\*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (10382)

5 "prostheses and implants"/ or absorbable implants/ or artificial limbs/ or bioprosthesis/ or orthopedic fixation devices/ or external fixators/ or internal fixators/ (28244)

6 (artificial limb\* or bioprosthesis\* or orthopedic fixation device\* or external fixator\* or internal fixator\*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (13888)

7 blood vessel prosthesis/ or stents/ or drug-eluting stents/ (40837)

8 (blood vessel prosthesis\* or stent\* or drug-eluting stent\*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (57375)

9 (skin graft\* or wound care or skin replacement\*).mp. or Skin, Artificial/ [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (9349)

10 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 (142446)

11 meta-analysis.pt. (24009)

12 meta-analysis.sh. (24009)

- 13 (meta-analys\$ or meta analys\$ or metaanalys\$).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (43475)
- 14 (systematic\$ adj9 review\$).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (29696)
- 15 (systematic\$ adj9 overview\$).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (615)
- 16 (quantitativ\$ adj9 review\$).mp. (2098)
- 17 (quantitativ\$ adj9 overview\$).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (161)
- 18 (quantitativ\$ adj9 synthesis\$).mp. (907)
- 19 (methodologic\$ adj9 review\$).mp. (3153)
- 20 (methodologic\$ adj9 overview\$).mp. (173)
- 21 (integrative research review\$ or research integration).mp. (48)
- 22 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (67875)
- 23 10 and 22 (1385)
- 24 limit 23 to yr="2009 - 2010" (467)

## Appendix B. Data Extraction Form

The live form can be viewed and tested here: <http://bit.ly/nhK0gl> (last accessed on 1/30/2012)

Timestamp

Author Year PMID

Extractor initials

Was the funding source declared?

\* Industry support?

Do the authors have industry ties?

\* Employed by Industry?

Objective elements of PICO stated?

Study Design(s) Included

Search Terms Included in Full-text?

>1 database searched?

Search Year Start

Search Year End

Searched in >1 Language?

Searched grey literature?

Study Flow Diagram Included?

Number of Excluded full-texts given?

Inclusion criteria given?

Reason(s) for exclusions given?

Data extraction checked, or method described?

Total number of included full-texts in SR:

Any meta-analysis performed?

If meta-analysis/es performed, how many unique studies included in MA in total?

Describe the patient population

Intervention/exposure

Comparator

Type(s) of outcomes

\* Efficacy

\* Safety

Is control group defined as Standard of Care or Optimized Care?

Adverse events reported?

If adverse events reported, length of follow up is:

\* < 2 years

\* ≥ 2 years

Was there heterogeneity in follow-up times across studies?

Was there any discussion or evaluation at procedural and/or device level?

Data on differences across device characteristics available or discussed?

Data on differences within device characteristics available or discussed?

Were the evolution of devices over time discussed?

Other descriptions of device characteristics

Any details included on background experience of implant team or surgeon?

Training/certification of provider reported?

Ramp-up in provider technique (ie learning curve) discussed?

Level of expertise of team/site considered when full-texts were evaluated?

Practitioner variability discussed?  
"Volume at sites" effect discussed?  
At least one subgroup analysis considered?  
If subgroup analysis/es considered, quantified?  
Was a meta-analysis performed?  
If meta-analysis performed, was accepted methodology used?  
If meta-analysis performed, what model(s) was used?

Which of the following were reported?

- \* Simple summary data for each group
- \* Effect estimates
- \* Confidence intervals
- \*  $I^2$
- \* Forest plot
- \* Other

Was there a quantitative assessment for heterogeneity in at least one of the meta-analyses?  
Was there an assessment for risk of bias?  
Graphical representation of results?  
Was a sensitivity analysis proposed? (Methods)  
Reporting of concurrent / co-medications in the study population?  
Was there heterogeneity within each device group?  
If there was heterogeneity within each device group, was it analyzed?  
Were studies grouped according to study design?  
Cost-effectiveness discussed?  
Future research recommendations made?  
Specific quality checklist used?  
Was an overall rating for the body of evidence given?  
Were the results of a sensitivity analysis reported or discussed?  
What are some of the limitations of the primary studies identified in the review?  
By outcome, which treatment is favored?  
General notes or comments  
Category of device

## Appendix C. List of Included Studies in the Analyses Cardiac Implants

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## Neurostimulators

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- (2) Andrade P, Noblesse LH, Temel Y et al. Neurostimulatory and ablative treatment options in major depressive disorder: a systematic review. *Acta Neurochir (Wien)*. 2010;152:565-577.PM:20101419
- (3) Andrews C, viles-Olmos I, Hariz M, Foltynie T. Which patients with dystonia benefit from deep brain stimulation? A metaregression of individual patient outcomes. *J Neurol Neurosurg Psychiatry*. 2010;81:1383-1389.PM:20841370
- (4) Benabid AL, Chabardes S, Mitrofanis J, Pollak P. Deep brain stimulation of the subthalamic nucleus for the treatment of Parkinson's disease. *Lancet Neurol*. 2009;8:67-81.PM:19081516
- (5) Clarke CE, Worth P, Grosset D, Stewart D. Systematic review of apomorphine infusion, levodopa infusion and deep brain stimulation in advanced Parkinson's disease. *Parkinsonism Relat Disord*. 2009;15:728-741.PM:19805000
- (6) Flora ED, Perera CL, Cameron AL, Maddern GJ. Deep brain stimulation for essential tremor: a systematic review. *Mov Disord*. 2010;25:1550-1559.PM:20623768
- (7) Fontaine D, Hamani C, Lozano A. Efficacy and safety of motor cortex stimulation for chronic neuropathic pain: critical review of the literature. *J Neurosurg*. 2009;110:251-256.PM:18991496
- (8) Fountas KN, Kapsalaki E, Hadjigeorgiou G. Cerebellar stimulation in the management of medically intractable epilepsy: a systematic and critical review. *Neurosurg Focus*. 2010;29:E8.PM:20672925
- (9) Georgiopoulos M, Katsakiori P, Kefalopoulou Z, Ellul J, Chroni E, Constantoyannis C. Vegetative state and minimally conscious state: a review of the therapeutic interventions. *Stereotact Funct Neurosurg*. 2010;88:199-207.PM:20460949

- (10) Halpern CH, Rick JH, Danish SF, Grossman M, Baltuch GH. Cognition following bilateral deep brain stimulation surgery of the subthalamic nucleus for Parkinson's disease. *Int J Geriatr Psychiatry*. 2009;24:443-451.PM:19016252
- (11) Kennedy SH, Milev R, Giacobbe P et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) Clinical guidelines for the management of major depressive disorder in adults. IV. Neurostimulation therapies. *J Affect Disord*. 2009;117 Suppl 1:S44-S53.PM:19656575
- (12) Lakhan SE, Callaway E. Deep brain stimulation for obsessive-compulsive disorder and treatment-resistant depression: systematic review. *BMC Res Notes*. 2010;3:60.PM:20202203
- (13) Previnaire JG, Nguyen JP, Perrouin-Verbe B, Fattal C. Chronic neuropathic pain in spinal cord injury: efficiency of deep brain and motor cortex stimulation therapies for neuropathic pain in spinal cord injury patients. *Ann Phys Rehabil Med*. 2009;52:188-193.PM:19909709
- (14) St George RJ, Nutt JG, Burchiel KJ, Horak FB. A meta-regression of the long-term effects of deep brain stimulation on balance and gait in PD. *Neurology*. 2010;75:1292-1299.PM:20921515

## Appendix D. Excluded Studies After Full-Text Screening

- (1) Takagi H, Manabe H, Umemoto T. Drug-eluting versus bare metal stents for saphenous vein graft intervention. *Am J Cardiol.* 2010;106:1522-1524.PM:21059450  
(Reject reason: Letter)
- (2) Antoniucci D. JETSTENT trial results: impact on ST-segment elevation myocardial infarction interventions. *J Invasive Cardiol.* 2010;22:23B-25B.PM:20947933  
(Reject reason: Not a systematic review)
- (3) Van Den Broek KC, Habibovic M, Pedersen SS. Emotional distress in partners of patients with an implantable cardioverter defibrillator: a systematic review and recommendations for future research. *Pacing Clin Electrophysiol.* 2010;33:1442-1450.PM:20946298  
(Reject reason: Population not of interest)
- (4) Campbell JE, Stone PA, Bates MC. Efficacy of embolic protection devices in renal artery stenting. *J Cardiovasc Surg (Torino).* 2010;51:747-754.PM:20924334 (Reject reason: No study search methods or eligibility criteria were reported)
- (5) Neschis DG, Scalea TM. Endovascular repair of traumatic aortic injuries. *Adv Surg.* 2010;44:281-292.PM:20919527 (Reject reason: Not a systematic review)
- (6) Mazaki T, Masuda H, Takayama T. Prophylactic pancreatic stent placement and post-ERCP pancreatitis: a systematic review and meta-analysis. *Endoscopy.* 2010;42:842-853.PM:20886403 (Reject reason: Topic not of interest)
- (7) Amarenco P, Labreuche J, Mazighi M. Lessons from carotid endarterectomy and stenting trials. *Lancet.* 2010;376:1028-1031.PM:20870079 (Reject reason: Editorial)
- (8) Naylor AR. Managing patients with symptomatic coronary and carotid artery disease. *Perspect Vasc Surg Endovasc Ther.* 2010;22:70-76.PM:20858607 (Reject reason: Not a systematic review)
- (9) Knepper J, Upchurch GR, Jr. A review of clinical trials and registries in descending thoracic aortic aneurysms. *Semin Vasc Surg.* 2010;23:170-175.PM:20826294 (Reject reason: Not a systematic review)
- (10) Takagi H, Goto SN, Matsui M, Manabe H, Umemoto T. Regarding "preoperative statin therapy is associated with improved outcomes and resource utilization in patients

- undergoing aortic aneurysm repair". *J Vasc Surg.* 2010;52:820-822.PM:20816327 (*Reject reason: Not a systematic review*)
- (11) Klein-Weigel P. [Spinal cord stimulation - evidence and personal experience]. *Zentralbl Chir.* 2010;135:359-362.PM:20806142 (*Reject reason: Not a systematic review*)
- (12) Beattie MJ, Lee MS. Safety and efficacy of drug-eluting stents compared with bare metal stents in ST-elevation myocardial infarction. *Rev Cardiovasc Med.* 2010;11:57-73.PM:20700088 (*Reject reason: Not a systematic review*)
- (13) Navarese EP, Buffon A, De LG, De SS. Effectiveness and safety of drug-eluting stents in vein grafts: a meta-analysis. *Am Heart J.* 2010;160:e9.PM:20691822 (*Reject reason: Letter*)
- (14) Beno M, Rumenapf G. [Comparison between hybrid surgical procedure--intraoperative angioplasty and cross-over bypass with aorto-bifemoral bypass in revascularization of iliac arteries]. *Rozhl Chir.* 2009;88:720-724.PM:20662436 (*Reject reason: Not a systematic review*)
- (15) Lanjewar C, Jolly S, Mehta SR. Effects of aspiration thrombectomy on mortality in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention: a meta-analysis of the randomized trials. *Indian Heart J.* 2009;61:335-340.PM:20635735 (*Reject reason: Intervention not of interest*)
- (16) Vermeulen H, Westerbos SJ, Ubbink DT. Benefit and harm of iodine in wound care: a systematic review. *J Hosp Infect.* 2010;76:191-199.PM:20619933 (*Reject reason: Intervention not of interest*)
- (17) Sparreboom M, van SJ, van Zanten BG et al. The effectiveness of bilateral cochlear implants for severe-to-profound deafness in children: a systematic review. *Otol Neurotol.* 2010;31:1062-1071.PM:20601922 (*Reject reason: Topic not of interest*)
- (18) Ellis E, III. Discussion. Internal fixation of mandibular angle fractures: a meta-analysis. *Plast Reconstr Surg.* 2010;125:1761-1762.PM:20517102 (*Reject reason: Discussion of an included paper*)
- (19) Cevik C, Nugent K, Perez-Verdia A, Fish RD. Prophylactic implantation of cardioverter defibrillators in idiopathic nonischemic cardiomyopathy for the primary prevention of death: a Not a systematic review. *Clin Cardiol.* 2010;33:254-260.PM:20513063 (*Reject reason: Not a systematic review*)

- (20) Seidl K, Strauss M, Kleemann T. [ICD therapy as secondary prevention]. *Herzschrittmacherther Elektrophysiol.* 2010;21:96-101.PM:20505945 (*Reject reason: Not a systematic review*)
- (21) Dorr R. [Bypass surgery versus percutaneous coronary intervention in patients with diabetes mellitus]. *Herz.* 2010;35:182-190.PM:20467930 (*Reject reason: No study search methods or eligibility criteria were reported*)
- (22) Balzer JO, Thalhammer A, Khan V, Zangos S, Vogl TJ, Lehnert T. Angioplasty of the pelvic and femoral arteries in PAOD: results and review of the literature. *Eur J Radiol.* 2010;75:48-56.PM:20451340 (*Reject reason: Not a systematic review*)
- (23) Bellabarba C, Fisher C, Chapman JR, Dettori JR, Norvell DC. Does early fracture fixation of thoracolumbar spine fractures decrease morbidity or mortality? *Spine (Phila Pa 1976)*. 2010;35:S138-S145.PM:20407345 (*Reject reason: No implantable device used*)
- (24) Fiehler J, Bakke SJ, Clifton A et al. Plea of the defence-critical comments on the interpretation of EVA3S, SPACE and ICSS. *Neuroradiology.* 2010;52:601-610.PM:20440484 (*Reject reason: Not a systematic review*)
- (25) Shi ZS, Loh Y, Walker G, Duckwiler GR. Endovascular thrombectomy for acute ischemic stroke in failed intravenous tissue plasminogen activator versus non-intravenous tissue plasminogen activator patients: revascularization and outcomes stratified by the site of arterial occlusions. *Stroke.* 2010;41:1185-1192.PM:20431084 (*Reject reason: No implantable device used*)
- (26) Carter MJ. Evidence-based medicine: an overview of key concepts. *Ostomy Wound Manage.* 2010;56:68-85.PM:20424294 (*Reject reason: Review of concepts*)
- (27) Bizzarri F, Tudisco A, Ricci M, Rose D, Frati G. Different ways to repair the mitral valve with artificial chordae: a systematic review. *J Cardiothorac Surg.* 2010;5:22.PM:20377866 (*Reject reason: No study objectives or eligibility criteria were reported*)
- (28) Movahed MR. Re.: Provisional vs. complex stenting strategy for coronary bifurcation lesions: meta-analysis of randomized trials. *J Invasive Cardiol.* 2010;22:148-149.PM:20197585 (*Reject reason: Letter*)

- (29) Tamhane UU, Chetcuti S, Hameed I, Grossman PM, Moscucci M, Gurm HS. Safety and efficacy of thrombectomy in patients undergoing primary percutaneous coronary intervention for acute ST elevation MI: a meta-analysis of randomized controlled trials. *BMC Cardiovasc Disord.* 2010;10:10.PM:20187958 (*Reject reason: Intervention not of interest*)
- (30) Pendyala LK, Yin X, Li J, Chen JP, Chronos N, Hou D. The first-generation drug-eluting stents and coronary endothelial dysfunction. *JACC Cardiovasc Interv.* 2009;2:1169-1177.PM:20129542 (*Reject reason: Not a systematic review*)
- (31) Mongeon FP, Belisle P, Joseph L, Eisenberg MJ, Rinfret S. Adjunctive thrombectomy for acute myocardial infarction: A bayesian meta-analysis. *Circ Cardiovasc Interv.* 2010;3:6-16.PM:20118149 (*Reject reason: Intervention not of interest*)
- (32) Marazziti D, Consoli G. Treatment strategies for obsessive-compulsive disorder. *Expert Opin Pharmacother.* 2010;11:331-343.PM:20102301 (*Reject reason: Not a systematic review*)
- (33) Jennings DL, Kalus JS. Addition of cilostazol to aspirin and a thienopyridine for prevention of restenosis after coronary artery stenting: a meta-analysis. *J Clin Pharmacol.* 2010;50:415-421.PM:20081227 (*Reject reason: Intervention not of interest*)
- (34) Ramsey S, Robertson A, Ablett MJ, Meddings RN, Hollins GW, Little B. Evidence-based drainage of infected hydronephrosis secondary to ureteric calculi. *J Endourol.* 2010;24:185-189.PM:20063999 (*Reject reason: Topic not of interest*)
- (35) Knur R. Carotid artery stenting: a systematic review of randomized clinical trials. *Vasa.* 2009;38:281-291.PM:19998249 (*Reject reason: Study objectives and search methodology were not reported*)
- (36) Chen SF, El-Bialy A, Matthews R, Clavijo L. Use of drug-eluting versus bare-metal stents in ST-segment elevation myocardial infarction. *J Invasive Cardiol.* 2009;21:E206-E212.PM:19901420 (*Reject reason: Not a systematic review*)
- (37) Diehm N, Baumgartner I. Routine stent implantation vs. percutaneous transluminal angioplasty in femoropopliteal artery disease: a meta-analysis of randomized controlled trials. *Eur Heart J.* 2009;30:3083-3084.PM:19880846 (*Reject reason: Letter*)
- (38) Matsumura JS, Lee WA, Mitchell RS et al. The Society for Vascular Surgery Practice Guidelines: management of the left subclavian artery with thoracic endovascular aortic

- repair. *J Vasc Surg.* 2009;50:1155-1158.PM:19878791 (*Reject reason: Guideline document developed from an included paper*)
- (39) Gorenai V, Dintsios CM, Schonemark MP, Hagen A. [Intravascular brachytherapy for peripheral arterial occlusive disease: systematic review of medical efficacy and health economic modelling]. *Z Evid Fortbild Qual Gesundheitswes.* 2009;103:331-340.PM:19839205 (*Reject reason: Intervention not of interest*)
- (40) Ehdaie A, Lee MS. Drug-eluting stents in primary percutaneous coronary intervention for ST-elevation myocardial infarction: an up-to-date review of the literature. *Minerva Cardioangiol.* 2009;57:645-655.PM:19838154 (*Reject reason: Not a systematic review*)
- (41) Quenneville SP, Xie X, Brophy JM. The cost-effectiveness of Maze procedures using ablation techniques at the time of mitral valve surgery. *Int J Technol Assess Health Care.* 2009;25:485-496.PM:19818194 (*Reject reason: Topic not of interest*)
- (42) Parrish LC, Miyamoto T, Fong N, Mattson JS, Cerutis DR. Non-bioabsorbable vs. bioabsorbable membrane: assessment of their clinical efficacy in guided tissue regeneration technique. A systematic review. *J Oral Sci.* 2009;51:383-400.PM:19776505 (*Reject reason: Topic not of interest*)
- (43) Tjardes T, Shafizadeh S, Rixen D et al. Image-guided spine surgery: state of the art and future directions. *Eur Spine J.* 2010;19:25-45.PM:19763640 (*Reject reason: Intervention not of interest*)
- (44) Eeckhout E. Thrombectomy in acute ST-elevation myocardial infarction: keep it simple. *Eur Heart J.* 2009;30:2180-2181.PM:19726438 (*Reject reason: Intervention not of interest*)
- (45) Burzotta F, De VM, Gu YL et al. Clinical impact of thrombectomy in acute ST-elevation myocardial infarction: an individual patient-data pooled analysis of 11 trials. *Eur Heart J.* 2009;30:2193-2203.PM:19726437 (*Reject reason: Intervention not of interest*)
- (46) Kingston GT, Darby CR, Roberts IS. The pathology of depopulated bovine ureter xenografts utilized for vascular access in haemodialysis patients. *Histopathology.* 2009;55:154-160.PM:19694822 (*Reject reason: Topic not of interest*)
- (47) Byrne RA, Sarafoff N, Kastrati A, Schomig A. Drug-eluting stents in percutaneous coronary intervention: a benefit-risk assessment. *Drug Saf.* 2009;32:749-770.PM:19670915 (*Reject reason: Not a systematic review*)

- (48) Pedersen SS, van den BM, Theuns DA. A viewpoint on the impact of device advisories on patient-centered outcomes. *Pacing Clin Electrophysiol.* 2009;32:1006-1011.PM:19659620 (*Reject reason: Not a systematic review*)
- (49) Noordeen MH, Garrido E, Tucker SK, Elsebaie HB. The surgical treatment of congenital kyphosis. *Spine (Phila Pa 1976).* 2009;34:1808-1814.PM:19644332 (*Reject reason: Not a systematic review*)
- (50) Hedequist DJ. Instrumentation and fusion for congenital spine deformities. *Spine (Phila Pa 1976).* 2009;34:1783-1790.PM:19644329 (*Reject reason: Not a systematic review*)
- (51) Garg S, Serruys P. Drug-eluting stents are safe. *Clin Pharmacol Ther.* 2009;86:130-132.PM:19621006 (*Reject reason: Not a systematic review*)
- (52) Nicolaou G. Endovascular treatment of blunt traumatic thoracic aortic injury. *Semin Cardiothorac Vasc Anesth.* 2009;13:106-112.PM:19617250 (*Reject reason: Not a systematic review*)
- (53) Drug-eluting coronary stents: many meta-analyses, little benefit. *Prescrire Int.* 2009;18:70-74.PM:19585727 (*Reject reason: Not a systematic review*)
- (54) Chung KC, Ghorri AK. Discussion. Systematic review of skin graft donor-site dressings. *Plast Reconstr Surg.* 2009;124:307-308.PM:19568093 (*Reject reason: A review of systematic reviews*)
- (55) Sears SF, Matchett M, Conti JB. Effective management of ICD patient psychosocial issues and patient critical events. *J Cardiovasc Electrophysiol.* 2009;20:1297-1304.PM:19563356 (*Reject reason: Not a systematic review*)
- (56) Ojike NI, Roberts CS, Giannoudis PV. Compartment syndrome of the thigh: a systematic review. *Injury.* 2010;41:133-136.PM:19555950 (*Reject reason: Topic not of interest*)
- (57) Karpov I, Samko AN, Buza VV. [Drug-eluting stents: long-term safety]. *Ter Arkh.* 2009;81:36-41.PM:19537584 (*Reject reason: Not a systematic review*)
- (58) Ilahi OA, Nolla JM, Ho DM. Intra-tunnel fixation versus extra-tunnel fixation of hamstring anterior cruciate ligament reconstruction: a meta-analysis. *J Knee Surg.* 2009;22:120-129.PM:19476176 (*Reject reason: No implantable devices, comparison of autografts*)
- (59) Geissler HJ, Schlensak C, Sudkamp M, Beyersdorf F. Heart valve surgery today: indications, operative technique, and selected aspects of postoperative care in acquired

- valvular heart disease. *Dtsch Arztebl Int.* 2009;106:224-233.PM:19471589 (*Reject reason: Not a systematic review*)
- (60) De VM, Burzotta F, Biondi-Zoccai GG et al. Individual patient-data meta-analysis comparing clinical outcome in patients with ST-elevation myocardial infarction treated with percutaneous coronary intervention with or without prior thrombectomy. ATTEMPT study: a pooled Analysis of Trials on ThrombEctomy in acute Myocardial infarction based on individual Patient data. *Vasc Health Risk Manag.* 2009;5:243-247.PM:19436647 (*Reject reason: Intervention not of interest*)
- (61) Ertas G, van Beusekom HM, van der Giessen WJ. Late stent thrombosis, endothelialisation and drug-eluting stents. *Neth Heart J.* 2009;17:177-180.PM:19421365 (*Reject reason: Not a systematic review*)
- (62) Digby GC, Daubney ME, Baggs J et al. Physiotherapy and cardiac rhythm devices: a review of the current scope of practice. *Europace.* 2009;11:850-859.PM:19411677 (*Reject reason: Not a systematic review*)
- (63) Ng VG, Stone GW. Diabetics and drug-eluting stents in ST segment elevation myocardial infarction: confidence in numbers. *Rev Esp Cardiol.* 2009;62:343-346.PM:19401117 (*Reject reason: Editorial*)
- (64) Yokochi F. [Deep brain stimulation for Parkinson's disease and dystonia]. *Brain Nerve.* 2009;61:473-483.PM:19378817 (*Reject reason: Not a systematic review*)
- (65) Sakhuja R, Keebler M, Lai TS, McLaughlin GC, Thakur R, Bhatt DL. Meta-analysis of mortality in dialysis patients with an implantable cardioverter defibrillator. *Am J Cardiol.* 2009;103:735-741.PM:19231344 (*Reject reason: Duplicate retrieval*)
- (66) Oswald H, Klein G, Struber M, Gardiwal A. Implantable defibrillator with left ventricular assist device compatibility. *Interact Cardiovasc Thorac Surg.* 2009;8:579-580.PM:19223309 (*Reject reason: Primary study*)
- (67) Mandava P, Kent TA. Percutaneous clot removal in acute ischemic stroke. *Arch Neurol.* 2009;66:283-284.PM:19204174 (*Reject reason: Commentary*)
- (68) Naylor AR. Does the risk of post-CABG stroke merit staged or synchronous reconstruction in patients with symptomatic or asymptomatic carotid disease? *J Cardiovasc Surg (Torino).* 2009;50:71-81.PM:19179993 (*Reject reason: Not a systematic review*)

- (69) Amin AP, Mamtani MR, Kulkarni H. Factors influencing the benefit of adjunctive devices during percutaneous coronary intervention in ST-segment elevation myocardial infarction: meta-analysis and meta-regression. *J Interv Cardiol.* 2009;22:49-60.PM:19141090 (*Reject reason: Intervention not of interest*)
- (70) Takkenberg JJ, Klieverik LM, Schoof PH et al. The Ross procedure: a systematic review and meta-analysis. *Circulation.* 2009;119:222-228.PM:19118260 (*Reject reason: Evaluation of autograft*)
- (71) Jolly SS, Amlani S, Hamon M, Yusuf S, Mehta SR. Radial versus femoral access for coronary angiography or intervention and the impact on major bleeding and ischemic events: a systematic review and meta-analysis of randomized trials. *Am Heart J.* 2009;157:132-140.PM:19081409 (*Reject reason: Topic not of interest*)
- (72) Sleilaty G, Achouh P, Fabiani JN. [Stenting or coronary artery bypass surgery for triple vessel disease?]. *Ann Cardiol Angeiol (Paris).* 2009;58:104-112.PM:18930176 (*Reject reason: Not a systematic review*)
- (73) Patel TR, Bulsara KR. Current strategies for the treatment of intracranial atherosclerotic internal carotid artery stenosis. *Neurosurg Rev.* 2009;32:23-27.PM:18818960 (*Reject reason: Narrative review*)
- (74) Hanson MD, Gauld M, Wathen CN, Macmillan HL. Nonpharmacological interventions for acute wound care distress in pediatric patients with burn injury: a systematic review. *J Burn Care Res.* 2008;29:730-741.PM:18695617 (*Reject reason: Intervention not of interest*)
- (75) De LG, Casseti E, Marino P. Impact of duration of clopidogrel prescription on outcome of DES as compared to BMS in primary angioplasty: a meta-regression analysis of randomized trials. *J Thromb Thrombolysis.* 2009;27:365-378.PM:18498003 (*Reject reason: Intervention not of interest*)
- (76) Tomaske M, Bauersfeld U. Experience with implantable cardioverter-defibrillator therapy in grown-ups with congenital heart disease. *Pacing Clin Electrophysiol.* 2008;31 Suppl 1:S35-S37.PM:18226033 (*Reject reason: Narrative review*)
- (77) Celik T, Iyisoy A, Yuksel UC, Isik E. Optimal revascularization strategy for diabetic patients with multivessel coronary artery disease: the duel between old hero and young warrior. *Int J Cardiol.* 2009;131:269-270.PM:17692947 (*Reject reason: Editorial*)

- (78) Bryant J, Brodin H, Loveman E, Payne E, Clegg A. The clinical and cost-effectiveness of implantable cardioverter defibrillators: a systematic review. *Health Technol Assess.* 2005;9:1-150, iii.PM:16153353 (*Reject reason: Duplication publication*)
- (79) Pourati I, Hyder M, Rosenthal L. Indications for implantable cardiac defibrillators in patients with congestive heart failure: implications of the sudden cardiac death in heart failure trial. *Curr Cardiol Rep.* 2005;7:223-228.PM:15865865 (*Reject reason: Narrative review*)
- (80) Nanthakumar K, Epstein AE, Kay GN, Plumb VJ, Lee DS. Prophylactic implantable cardioverter-defibrillator therapy in patients with left ventricular systolic dysfunction: a pooled analysis of 10 primary prevention trials. *J Am Coll Cardiol.* 2004;44:2166-2172.PM:15582314 (*Reject reason: Met sufficient number of reviews*)
- (81) Seidl K, Strauss M, Kleemann T. [ICD therapy as secondary prevention]. *Herzschrittmacherther Elektrophysiol.* 2010;21:96-101.PM:20505945 (*Reject reason: Narrative review*)

**Appendix E. Tables 1–4 Subgroup Analyses**

**Appendix Table E1. Reporting of characteristics in systematic reviews of implantable medical devices according to reported author affiliation.**

Reporting Item	Systematic reviews n (%)	Systematic reviews n (%)	P-value	Total N=181 n (%)
	Authors affiliation to industry: reported N=38	Author affiliation to industry: not reported N=143		
<b>Search</b>				
Search terms were described or referred to elsewhere	33 (87)	132 (92)	0.36	165 (91)
Multiple databases were searched	30 (79)	114 (79)	1.0	144 (79)
Years searched were described	33 (87)	129 (90)	0.57	162 (89)
Multiple languages were included in search	9 (24)	53 (37)	0.18	62 (34)
Authors explicitly stated searching for unpublished data	17 (44)	63 (44)	1.0	80 (44)
<b>Selection</b>				
Inclusion or exclusion criteria were stated	37 (97)	138 (96)	1.00	175 (96)
Population at baseline was reported	38 (100)	143 (100)	NA	181 (100)
Interventions/exposures were described	38 (100)	143 (100)	NA	181 (100)
Comparators were described	38 (100)	140 (98)	1.0	178 (98)
Outcomes were described	38 (100)	143 (100)	NA	154 (85)
Types of studies included were reported	37 (97)	138 (96)	1.00	175 (96)
Number of studies included and excluded were reported	25 (64)	91 (63)	0.49	116 (61)
Reasons for exclusion were described	30 (79)	109 (76)	0.83	139 (76)
<b>Results</b>				
A flow diagram for the number of studies included and excluded was used	20 (53)	60 (42)	0.27	80 (44)
The number of primary studies included	1031	3257	NA	4288
Results were presented graphically	29 (76)	88 (61)	0.09	117 (64)
Meta-analyses were performed	32 (84)	92 (64)	0.02	124 (68)
Costs or cost-effectiveness were described	5 (13)	37 (26)	0.13	42 (23)
<b>Device-specific Variables</b>				
Data on differences across device characteristics were discussed	16 (42)	70 (49)	0.58	86 (47)
Data on differences within device characteristics were discussed	14 (37)	51 (35)	0.85	65 (36)
Evolution of devices over time were discussed	6 (16)	26 (18)	1.0	32 (18)

Continued.

Appendix Table E1 . Continued

Reporting items	Systematic reviews n (%) Authors affiliation to industry: reported N=38	Systematic reviews n (%) Author affiliation to industry: not reported N=143	P-value	Total N=181 n (%)
<b>Operator-specific Variables</b>				
Details of training/certification of provider were reported	2 (5)	0 (0)	0.04	2 (1)
Ramp-up in provider technique (i.e. learning curve) was discussed	2 (5)	11 (8)	1.0	13 (7)
Level of expertise of team/site were considered	2 (5)	14 (10)	0.53	16 (9)
Practitioner variability were discussed	5 (13)	13 (9)	0.54	18 (10)
"Volume at sites" effect were discussed	3 (8)	11 (8)	1.0	14 (8)
<b>Handling of heterogeneity</b>				
Models for meta-analyses were reported	37 (97)	86 (70)	0.50	123 (99)
Meta-analyses used accepted methodologies (e.g. studies grouped by design)	27 (71)	87 (60)	0.35	114 (62)
Heterogeneity was assessed or discussed?	32 (84)	107 (74)	0.28	139 (76)
Sensitivity analyses were assessed or discussed	14 (37)	51 (35)	0.85	65 (36)
Results by subgroups were considered or quantified	11 (29)	29 (20)	0.27	40 (22)
<b>Validity</b>				
Risk of bias was assessed	17 (45)	62 (43)	0.85	79 (43)
Publication bias was assessed	13 (34)	46 (32)	0.85	59 (48)
Quality items or checklists were applied and reported	14 (37)	58 (40)	0.85	72 (40)
<b>Discussion</b>				
Study limitations were described	37 (97)	138 (96)	1.0	175 (96)
Overall strength of the body of evidence was assessed	5 (13)	28 (19)	0.48	33 (18)
Specific future research recommendations were made	30 (79)	119 (83)	0.64	149 (82)
Funding source was identified	20 (53)	56 (39)	0.14	76 (42)

**Appendix Table E2. Reporting characteristics in systematic reviews (with or without meta-analyses) of implantable medical devices**

<b>Reporting Item</b>	<b>Systematic reviews n (%)</b>	<b>Systematic reviews n (%)</b>		
	<b>Meta-analysis conducted N=124</b>	<b>No meta-analyses conducted N=57</b>	<b>P-value</b>	<b>Total N=181 n (%)</b>
<b>Search</b>				
Search terms were described or referred to elsewhere	115 (92)	50 (88)	0.41	165 (91)
Multiple databases were searched	105 (84)	39 (68)	0.02	144 (79)
Years searched were described	113 (91)	49 (84)	0.21	162 (89)
Multiple languages were included in search	48 (38)	14 (25)	0.09	62 (34)
Authors explicitly stated searching for unpublished data	66 (53)	14 (25)	<0.001	80 (44)
<b>Selection</b>				
Inclusion or exclusion criteria were stated	122 (98)	53 (91)	0.03	175 (96)
Population at baseline was reported	124 (100)	57 (100)	NA	181 (100)
Interventions/exposures were described	124 (100)	57 (100)	NA	181 (100)
Comparators were described	123 (99)	55 (99)	0.24	178 (98)
Outcomes were described	121 (98)	57 (100)	0.55	178 (98)
Types of studies included were reported	121 (98)	55 (95)		176 (96)
Number of studies included and excluded were reported	91 (73)	25 (44)	<0.001	116 (61)
Reasons for exclusion were described	105 (85)	34 (59)	<0.001	139 (76)
<b>Results</b>				
A flow diagram for the number of studies included and excluded was used	66 (53)	14 (25)	<0.001	80 (44)
The total number of primary studies included	2876	1412	NA	4288
Results were presented graphically	114 (91)	3 (5)	<0.001	117 (64)
Costs or cost-effectiveness were described	24 (19)	18 (32)	0.09	42(23)
<b>Device-specific Variables</b>				
Data on differences across device characteristics were discussed	61 (49)	25 (44)	0.63	86 (47)
Data on differences within device characteristics were discussed	48 (38)	17 (30)	0.32	65 (36)
Evolution of devices over time were discussed	23 (18)	15 (26)	0.24	38 (21)

Continued.

Appendix Table E2. Continued

Reporting Item	Systematic reviews n (%)	Systematic reviews n (%)	P-value	Total N=181 n (%)
	Meta-analysis N=124	No meta- analyses N=57		
<b>Operator-specific Variables</b>				
Details of training/certification of provider were reported	2 (2)	0 (0)	0.47	2 (1)
Ramp-up in provider technique (i.e. learning curve) was discussed	9 (7)	4 (7)	0.62	13 (7)
Level of expertise of team/site were considered	10 (8)	6 (11)	0.58	16 (9)
Practitioner variability were discussed	13 (11)	5 (9)	0.50	18 (10)
"Volume at sites" effect were discussed	7 (6)	7 (12)	0.14	14 (8)
<b>Handling of heterogeneity</b>				
Models for meta-analyses were reported	121 (97)	NA	NA	123 (99) <sup>a</sup>
Meta-analyses used accepted methodologies (e.g. studies grouped by design)	114 (92)	NA	NA	114 (62) <sup>a</sup>
Heterogeneity was assessed or discussed?	112 (90)	27 (48)	<0.001	139 (76)
Sensitivity analyses were assessed or discussed	60 (48)	5 (9)	<0.001	65 (36)
Results by subgroups were considered or quantified	77 (62)	15 (26)	<0.001	92 (51)
<b>Validity</b>				
Risk of bias was assessed	71 (57)	8 (14)	<0.001	79 (43)
Publication bias was assessed	59 (46)	NA	NA	59 (46) <sup>a</sup>
Quality items or checklists were applied and reported	53 (43)	19 (33)	0.26	72 (40)
<b>Discussion</b>				
Study limitations were described	56 (97)	119 (96)	1.0	175 (96)
Overall strength of the body of evidence was assessed	14 (11)	19 (33)	0.001	33 (18)
Specific future research recommendations were made	96 (77)	53 (93)	0.007	149 (82)
Funding source was identified	57 (42)	19 (33)	0.15	76 (42)
----- Authors' affiliation to industry was reported	32 (26)	6 (10)	0.03	38 (21)

a. Among 181 eligible systematic reviews, 124 conducted a meta-analysis. One of 124 studies did not report a model for meta-analysis

**Appendix Table E3. Reporting characteristics in systematic reviews of implantable medical devices by study types**

Reporting Item	Systematic reviews n (%)			P-value
	Randomized trials N=66	Nonrandomized/observational studies N=51	Both N=64	
<b>Search</b>				
Search terms were described or referred to elsewhere	58 (88)	48 (94)	59 (92)	0.59
Multiple databases were searched	57 (86)	32 (63)	55 (86)	0.005
Years searched were described	60 (91)	44 (86)	58 (90)	0.76
Multiple languages were included in search	31 (47)	11 (22)	20 (31)	0.01
Authors explicitly stated searching for unpublished data	43 (65)	15 (29)	22 (34)	<0.001
<b>Selection</b>				
Inclusion or exclusion criteria were stated	63 (96)	50 (98)	62 (97)	0.79
Population at baseline was reported	66 (100)	51 (100)	64 (100)	NA
Interventions/exposures were described	66 (100)	51 (100)	64 (100)	NA
Comparators were described	66 (100)	49 (96)	64 (99)	0.20
Outcomes were described	66 (100)	51 (100)	64 (100)	NA
Number of studies included and excluded were reported	44 (66)	31 (61)	41 (61)	0.53
Reasons for exclusion were described	48 (73)	39 (77)	52 (80)	0.61
<b>Results</b>				
A flow diagram for the number of studies included and excluded was used	31 (47)	18 (35)	31 (48)	0.36
The number of primary studies included	962	1288	2038	NA
Results were presented graphically	58 (88)	21 (41)	38 (58)	<0.001
Costs or cost-effectiveness were described	17 (26)	6 (12)	19 (29)	0.06
Meta-analyses were performed	59 (89)	23 (45)	42 (64)	<0.001
<b>Device-specific Variables</b>				
Data on differences across device characteristics were discussed	29 (44)	23 (45)	34 (55)	0.60
Data on differences within device characteristics were discussed	32 (48)	11 (22)	22 (34)	0.01
Evolution of devices over time were discussed	12 (18)	11 (22)	15 (23)	0.76

Continued.

Appendix Table E3. Continued

Reporting item	Systematic reviews n (%)			P-value
	Randomized trials N=66	Nonrandomized / observational studies N=51	Both N=64	
<b>Operator-specific Variables</b>				
Details of training/certification of provider were reported	1 (2)	0 (0)	1 (2)	1.0
Ramp-up in provider technique (i.e. learning curve) was discussed	3 (5)	6 (12)	4 (6)	0.31
Level of expertise of team/site were considered	3 (5)	7 (14)	6 (9)	0.20
Practitioner variability were discussed	6 (9)	6 (12)	6 (9)	0.86
"Volume at sites" effect were discussed	2 (3)	6 (12)	6 (9)	0.15
<b>Handling of heterogeneity</b>				
Models for meta-analyses were reported	59 (89)	23 (45)	42 (64)	<0.001
Meta-analyses used accepted methodologies (e.g. studies grouped by design)	59 (89)	20 (39)	36 (56)	<0.001
Heterogeneity was assessed or discussed?	42 (63)	24 (47)	37 (57)	0.20
Sensitivity analyses were assessed	32 (48)	10 (20)	23 (35)	0.005
Results by subgroups were considered or quantified	19 (29)	8 (16)	13 (20)	0.22
<b>Validity</b>				
Risk of bias was assessed	39 (59)	15 (29)	25 (36)	0.003
Publication bias was assessed	34 (52)	8 (16)	17 (26)	<0.001
Quality items or checklists were applied and reported	33 (50)	12 (23)	27 (42)	0.01
<b>Discussion</b>				
Study limitations were described	63 (96)	50 (98)	62 (97)	0.79
Overall strength of the body of evidence was assessed	10 (15)	10 (19)	13 (20)	0.79
Specific future research recommendations were made	48 (73)	47 (92)	54 (84)	0.03
Funding source was declared	33 (50)	22 (43)	21 (32)	0.12
Authors' affiliation to industry was reported	16 (24)	8 (16)	14 (22)	0.55

**Appendix Table E4. Reporting of characteristics in systematic reviews of implantable medical devices according to journal type**

<b>Reporting Item</b>	<b>Published in general medical journals N=34</b>	<b>Systematic reviews n (%) Published in specialty medical journals N=147</b>	<b>P-value</b>	<b>Total N=181 n (%)</b>
<b>Search</b>				
Search terms were described or referred to elsewhere	30 (88)	135 (92)	0.51	165 (91)
Multiple databases were searched	30 (88)	114 (78)	0.36	143 (79)
Years searched were described	30 (88)	132 (90)	0.51	162 (90)
Multiple languages were included in search	15 (44)	47 (32)	0.23	62 (34)
Authors explicitly stated searching for unpublished data	24 (71)	56 (38)	0.001	80 (44)
<b>Selection</b>				
Inclusion or exclusion criteria were stated	34 (100)	141 (96)	1.0	175 (96)
Population at baseline was reported	34 (100)	147 (100)	1.0	181 (100)
Interventions/exposures were described	34 (100)	147 (100)	1.0	181 (100)
Comparators were described	34 (100)	144 (98.0)	1.0	178 (98)
Outcomes were described	34 (100)	144 (98)	1.0	178 (98)
Types of studies included were reported	34 (100)	147 (100)	1.0	181 (100)
Number of studies included and excluded were reported	22 (64.71)	94 (64.0)	0.65	116 (63)
Reasons for exclusion were described	27 (79)	112 (76)	0.82	139 (76.8)
<b>Results</b>				
A flow diagram for the number of studies included and excluded was used	18 (52.9)	62 (42.2)	0.34	80 (44.2)
The number of primary studies included	852	3436	NA	4288
Results were presented graphically	24 (70.6)	93 (63.3)	0.55	117 (64.6)
Meta-analyses were performed	27 (79.4)	97 (66.0)	0.15	124 (68.5)
Costs or cost-effectiveness were described	16 (47)	26 (18)	0.001	42 (23)
<b>Device-specific Variables</b>				
Data on differences across device characteristics were discussed	18 (53)	68 (46)	0.57	86 (48)
Data on differences within device characteristics were discussed	11 (32)	54 (37)	0.78	65 (36)
Evolution of devices over time were discussed	9 (27)	29 (20)	0.48	38 (21)

Continued.

Appendix Table E4. Continued

Reporting items	Published in general medical journals N=34	Systematic reviews n (%) Published in specialty medical journals N=147	P-value	Total n (%) N=181
<b>Operator-specific Variables</b>				
Details of training/certification of provider were reported	1 (3)	1 (1)	0.34	2 (1)
Ramp-up in provider technique (i.e. learning curve) was discussed	2 (6)	11 (8)	1.0	13 (7)
Level of expertise of team/site were considered	1 (3)	15 (10)	0.31	16 (9)
Practitioner variability were discussed	1 (3)	17 (12)	0.20	18 (10)
"Volume at sites" effect were discussed	2 (6)	12 (8)	1.0	14 (8)
<b>Handling of heterogeneity</b>				
Models for meta-analyses were reported	27 (79.4)	97 (66.0)	0.15	123 (69)
Meta-analyses used accepted methodologies (e.g. studies grouped by design)	27 (79)	87 (60)	0.05	114 (63)
Heterogeneity was assessed or discussed?	30 (88)	109 (74)	0.002	139 (76)
Sensitivity analyses were assessed or discussed	20 (59)	45 (31)	0.003	65 (36)
Results by subgroups were considered or quantified	22 (65)	70 (48)	0.08	92 (51)
<b>Validity</b>				
Risk of bias was assessed	21 (62)	58 (40)	0.02	79 (43)
Publication bias was assessed	17 (50)	42 (29)	0.03	59 (33)
Quality items or checklists were applied and reported	21 (62)	51 (35)	0.006	72 (40)
<b>Discussion</b>				
Study limitations were described	33 (97)	142 (96)	1.0	175 (96)
Overall strength of the body of evidence was assessed				
Specific future research recommendations were made	26 (76.5)	122 (83.0)	0.46	148 (81.8)
Funding source was identified	24 (71)	52 (35)	0.0	76 (42)
Authors' affiliation to industry was reported.	8 (24)	30 (21)	0.81	38 (21)

# **Appendix F. A Critical Appraisal of Primary Studies of Implantable Medical Devices**

## **Background**

Despite a significant number of published studies in the field of medical devices, empirical research evaluating medical devices has lagged behind the innovations. As the designated evidenced-based practice center (EPC) for the cross-cutting concentration of diagnostic testing, imaging technologies, and medical and assistive devices, we recently conducted a critical appraisal of reporting of systematic reviews of implantable medical devices. Technical experts identified the following five groups of implantable medical devices as topics of interest for evaluating published systematic reviews: cardiovascular, vascular interventional, orthopedic implants, skin replacement grafts, and neurostimulators.

The technical expert panel opined that the device-specific factors including generation of technology, generalizing results from one device to a similar device, evaluation of device-operator interactions, and evaluation of team are important characteristics in the evaluation of systematic reviews of implantable medical devices. This critical appraisal has evaluated 181 systematic reviews of five selected groups of implantable devices, most of which were published within the last 2 years. Of these reviews, 19 evaluated cardiac implantable devices, 124 evaluated vascular devices, 16 evaluated orthopedic implants, 8 evaluated skin-replacement grafts, and 14 evaluated neurostimulators. We identified that many of the device- or operator-specific information are not reported in the systematic reviews. From reviewing systematic reviews alone, it is unclear whether systematic reviews ignored reporting of device-specific characteristics or if they were not adequately reported in the primary studies.

## **Objective**

The objective of the project is to conduct a critical appraisal of reporting of published primary studies of implantable medical devices that were incorporated in randomly selected systematic reviews. The specific aims of this work assignment are as follows:

- Aim 1. Evaluate the frequency of reporting of device-specific or operator-specific information in a randomly selected subset of primary studies of implantable medical devices.
- Aim 2. Assess the association of reporting of device- or operator-specific information in primary studies with study design and outcomes characteristics reported.
- Aim 3. Compare reporting of device- or operator-specific characteristics between primary studies and the systematic review that incorporated these studies.

## **Methods**

### **Study Selection and Eligibility Criteria**

We sought to evaluate the reporting of device- or operator-specific information in approximately 100 nonoverlapping primary studies of implantable medical devices to compare if

reporting in systematic reviews mirror reporting in primary studies. This sample was identified from 181 systematic reviews of implantable medical devices included in an empirical project. We first selected a random subset of 10 systematic reviews, two reviews for each of the five device categories. For each device category, one review had to have reported or discussed at least one of the three device-specific items and the second could not have reported or discussed any. We based the selection of one review with device-specific information and the other without device-specific information because operator-specific information was rarely reported among reviews. For pragmatic reasons we could select only two systematic reviews from each of the five device categories, and a limited number of primary studies incorporated in these reviews. Albeit a small sample, within each of the device categories, we selected one review that reported device-specific information and the other without to get an indication of whether the lack of reporting of device or operator specific information in SRs is related to lack of reporting of these information in primary studies. In order to achieve a feasible number of at least 100 nonoverlapping primary studies, each of the randomly selected systematic reviews had to have a minimum of 9 and a maximum of 20 primary studies. A minimum threshold of less than 9 primary studies in the review would result in fewer than 100 primary studies, while a maximum threshold of more than 20 studies would result in a much larger number of primary studies. Using these thresholds, 62 of the 181 reviews were eligible for review of the primary studies included, of which we selected the random subset of 10 systematic reviews (two per device category).

All primary studies included in the systematic reviews were eligible, irrespective of design or duration of followup. We excluded primary studies reported only in abstract form, because of the limited space provided to report the information we were interested in. We also excluded cost-effective analyses and those not reporting on an implantable device.

## **Data Fields and Extraction**

For each primary study, the following data was recorded: author and year of publication, description of the population (yes/no for reporting of the disease stage or severity, basic demographics, and inclusion/exclusion criteria), center characteristics (single vs. multi-center), type of study design, source of funding (industry vs. no industry and reporting of author affiliation to industry), device category, concomitant medications, device-specific information (yes/no for reporting of the following items: adequate description of device characteristics, name of model or manufacturer, methods of implantation, and generation of device or modification to the algorithm), operator-specific information (yes/no for reporting of the following items: training/certification of the operator, learning curve, experience of the team, volume at the center, and practitioner variability), primary outcome (yes/no for definition, time points and description of assessment), and type of primary outcome (yes/no for reporting of clinical vs. surrogate). A detailed description of data elements is given in the Additional Information section. Reviewers with expertise in conducting systematic reviews participated in data extraction. All reviewers had to have no conflict of interest and were required to sign a disclosure statement. The selection and data extraction of all eligible papers was carried out by a single reviewer and verified by a second reviewer. Any disagreements were resolved through discussion and consensus among the data extractors or with the help of a third reviewer.

## Data Synthesis and Analyses

All included primary studies were summarized in narrative form and in summary tables that tabulate the important features of each of the three aims. Descriptive analyses were conducted to evaluate reporting characteristics of randomly selected primary studies within each of the five groups of implantable medical devices. All comparisons were performed using the Fisher exact test for categorical variables or the Kruskal-Wallis test for continuous variables.

For Aim 1, the reporting of device- or operator-specific information was additionally extracted as binary data (yes/no). We calculated the proportion of studies that reported analyses of device-specific characteristics.

For Aim 2, subgroup analyses were conducted to examine reporting versus no reporting of device- or operator-specific information in the primary studies for the following study-level characteristics: year of publication, population, intervention, comparator, type of study design, and source of funding. All comparisons were performed using the Fisher exact test for categorical variables or the Kruskal-Wallis test for continuous variables.

For Aim 3, we calculated the proportion of primary studies that reported device-specific characteristics and compared these proportions to the quality of reporting of corresponding items in their respective systematic reviews.

## Results

We identified 111 eligible primary studies included in 10 systematic reviews of implantable medical devices (available in Appendix Table F6 in the Additional Information section as well as in the References).

### Aim 1

*Evaluate the frequency of reporting of device-specific or operator-specific information in a randomly selected subset of primary studies of implantable medical devices.*

At the primary study level, data were considered to be “frequently reported” when they were reported in 50 percent or more of the primary studies. Most of the items relevant to device characteristics were frequently reported in the primary studies (Appendix Table F1). Less consistently reported were evolution of technology or modifications in device during study period (23 percent) and all five operator-/site-specific items including training of providers (4 percent), ramp-up in provider technique or learning curve (5 percent), evaluation of team expertise (10 percent), practitioner variability (24 percent), and volume at each study site (2 percent).

**Appendix Table F1. Reporting characteristics in 111 selected primary studies of implantable medical devices**

Device-specific Variables	Categories	Number of studies (%)
Name of the model or manufacturer mentioned	Yes	75 (68)
	No	36 (33)
Methods of implantation or surgical techniques mentioned	Yes	82 (74)
	No	29 (26)
Generation of device, when applicable, or modifications to algorithm described	Yes	25 (23)
	No	86 (78)
Description of use of concomitant medications	Yes	76 (69)
	No	35 (32)
<b>Operator-/site-specific Variables</b>		
Details of training/certification of provider	Yes	4 (4)
	No	107 (96)
Details of ramp-up in provider technique (i.e., learning curve)	Yes	5 (5)
	No	106 (96)
Details of level of expertise of team/site	Yes	11 (10)
	No	100 (90)
Practitioner variability were discussed	Yes	27 (24)
	No	84 (76)
Volume at sites effect were discussed	Yes	2 (2)
	No	109 (98)

## Aim 2

*Assess the association of reporting of device- or operator-specific information in primary studies with study design and outcomes characteristics reported.*

The description of device-specific information—including name of the model or manufacturer of the device, device implantation techniques, and description of use of concomitant medications—was significantly more frequently reported in studies that reported disease stages (Appendix Table F2). Other variables such as study design and outcome reporting were not associated with reporting of device-specific information (Appendix Tables F3 and F4).

Because of less consistent reporting of operator-specific information, we did not evaluate this variable with characteristics related to study design and outcomes.

**Appendix Table F2. Reporting of device characteristics by whether disease stage or severity was reported**

Variables in primary studies	Categories	Number of studies (%)	Disease stage/severity reported N (%)	Disease stage/severity not reported N (%)	P-value for comparison
Name of the model or manufacturer mentioned	Yes	75 (68)	69 (92)	6 (8)	0.004
	No	36 (33)	25 (69)	11 (31)	
Methods of implantation or surgical techniques mentioned	Yes	82 (74)	78 (85)	4 (5)	0.0
	No	29 (26)	16 (55)	13 (45)	
Generation of device, when applicable, or modifications to algorithm described	Yes	25 (23)	24 (96)	1 (4)	0.11
	No	86 (78)	70 (81)	16 (19)	
Description of use of concomitant medications	Yes	76 (69)	68 (89)	8 (11)	0.05
	No	35 (32)	26 (74)	9 (26)	

N = number

**Appendix Table F3. Reporting of device characteristics by study design**

Variables in primary studies	Categories	Number of studies (%)	RCT design N (%)	Nonrandomized or observational N (%)	P-value for comparison
Name of the model or manufacturer mentioned	Yes	75 (68)	38 (51)	37 (49)	0.16
	No	36 (33)	13 (36)	23 (64)	
Methods of implantation or surgical techniques mentioned	Yes	82 (74)	42 (51)	40 (49)	0.08
	No	29 (26)	9 (31)	20 (69)	
Generation of device, when applicable, or modifications to algorithm described	Yes	25 (23)	15 (60)	10 (40)	0.65
	No	86 (78)	45 (52)	41 (48)	
Description of use of concomitant medications	Yes	76 (69)	43 (57)	33 (43)	0.54
	No	35 (32)	17 (49)	18 (51)	

N = number, RCT = randomized controlled trial

**Appendix Table F4. Reporting of device characteristics by reporting of outcome definition**

Variables in primary studies	Categories	Number of studies (%)	Outcome definition reported N (%)	Outcome definition not reported N (%)	P-value for comparison
Name of the model or manufacturer mentioned	Yes	75 (68)	38 (51)	37 (49)	0.16
	No	36 (33)	13 (36)	23 (64)	
Methods of implantation or surgical techniques mentioned	Yes	82 (74)	78 (95)	4 (5)	0.65
	No	29 (26)	27 (93)	2 (7)	
Generation of device, when applicable, or modifications to algorithm described	Yes	25 (23)	24 (96)	1 (4)	1.0
	No	86 (78)	81 (94)	5 (6)	
Description of use of concomitant medications	Yes	76 (69)	72 (95)	4 (5)	1.0
	No	35 (32)	33 (94)	2 (5)	

N = number

### **Aim 3**

*Compare reporting of device- or operator-specific characteristics between primary studies and the systematic reviews that incorporated these studies.*

We compared reporting of device- and operator-specific characteristics between the 10 systematic reviews and the 111 primary studies incorporated in those 10 reviews (Appendix Table F5).

Initially, we had selected 8 device- or operator-specific reporting items of systematic review — three device-specific and five operator-specific — to compare with corresponding items in the 111 primary studies. Comparisons between systematic reviews and primary studies incorporated in these reviews were possible for all five operator-specific characteristics. However, there were limitations in comparing three device-specific items (within-device differences, across-device differences, and evolution of devices) between systematic reviews and primary studies incorporated in these reviews. We found that the three device-specific items were more relevant to systematic reviews as they inherently examined multiple studies published over a period of time that often evaluated multiple devices. For example, a systematic review description of devices can include “Three trials use nitinol stents while the other trials used stainless steel. There is speculation that nitinol stents may perform differently to stainless steel, however this is not apparent in these data.” Such device differences comparisons were not possible in primary studies. Therefore, in primary studies, we assessed whether devices were adequately described using one or more of the following items: name of a device model, methods of implantation, and generation of device. We compared the descriptions of device information in primary studies against the reporting of device-specific information in the corresponding systematic review (Table 5). Descriptions of devices were adequately described in almost three-quarters (81/111) of the primary studies. However, within the cardiac implantable device category, only 14 percent (3/22) of primary studies adequately described devices.

Operator-specific characteristics were rarely discussed across all primary studies with reporting for the five items; reporting varied between approximately one percent (1/111) and 24 percent (27/111). As expected, this observation is generally consistent across the four systematic reviews that lacked reporting on device/operator-specific characteristics. However, despite lack of reporting in the systematic reviews, within the vascular interventional and orthopedic device categories, practitioner variability is discussed in over 50 percent (9/15) of the corresponding primary studies. Nevertheless, level of expertise is considered in almost 45 percent (4/9) of the primary studies for the vascular interventional and the corresponding systematic review also reported the item of level of expertise.

**Appendix Table F5. Comparisons of reporting characteristics in selected primary studies of implantable medical devices with reporting in systematic reviews that incorporated these studies**

Categories	Cardiac (SR 1)	Cardiac (SR 2)	Vasc (SR 1)	Vasc (SR 2)	Neuro (SR 1)	Neuro (SR 2)	Ortho (SR 1)	Ortho (SR 2)	Skin (SR 1)*	Skin (SR 2)*	Total N Primary studies
N Primary studies per SR	11	11	12	9	15	16	9	6	3	19	111
<b>DEVICE-SPECIFIC</b>											
SR reporting device information	Reported	NR	Reported	NR	Reported	NR	Reported	NR	Reported	Reported	Not applicable
Device information in Primary studies N (%)	0 (0)	3 (27)	12 (100)	6 (67)	13 (87)	13 (81)	8 (89)	5 (83)	3 (100)	18 (95)	81 (73)
<b>OPERATOR-SPECIFIC</b>											
SR reporting operator/team expertise	NR	NR	NR	Reported	NR	NR	NR	NR	NR	NR	Not applicable
Primary studies reporting operator/team expertise N (%)	0 (0)	0 (0)	2 (17)	4 (44)	1 (7)	2 (13)	0 (0)	0 (0)	0 (0)	3 (16)	12 (11)
SR reporting details of training	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	Not applicable
Primary studies reporting operator training N (%)	0 (0)	0 (0)	1 (8)	1 (11)	0 (0)	0 (0)	1 (11)	1 (17)	0 (0)	0 (0)	4 (4)
SR reporting learning curve	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	Not applicable
Primary studies reporting learning curve N (%)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	1 (33)	2 (11)	5 (5)
SR reporting practitioner variability	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	Not applicable
Primary studies reporting practitioner variability N (%)	1 (9)	9 (1)	5 (42)	4 (44)	1 (7)	3 (19)	4 (44)	5 (83)	0 (0)	3 (16)	27 (24)
SR reporting volume at sites	NR	NR	NR	Reported	NR	NR	NR	NR	NR	NR	Not applicable
Primary studies reporting volume at sites N (%)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)

N = number; NR = not reported; SR = systematic reviews

SR 1: Reviews that reported device-specific information, but provided no operator-specific information.

SR 2: Reviews that did not report any device-specific information.

\* All skin-replacement reviews reported device-specific information but did not report operator-specific information.

## Conclusion

Most of the items relevant to device characteristics were frequently described in 111 eligible primary studies. Less consistently reported were evolution of technology or modifications in device during study period, as well as all five operator-/site-specific characteristics. Reporting of device- and operator-specific characteristics from 10 systematic reviews were compared to their reporting in the corresponding primary studies. Frequency of reporting at the primary study level was tallied and items were considered to have been frequently reported when they were described in 50 percent or more of the studies. Within all but five of the systematic reviews, the review reported an item when it was frequently reported at the primary study-level. Whenever an item was infrequently reported at the primary level, it was not reported at the review level. The same result was found for averages across all studies: those items that were frequently reported were also reported on the review level in at least one review; infrequently reported items were found in no reviews.

We identified eight device- or operator-specific items that might be of value in reporting in primary studies and systematic reviews of implantable devices that should be incorporated into reporting guidelines.

## Additional Information

### **Data Extraction Form is available at the following link:**

[https://docs.google.com/spreadsheet/viewform?hl=en\\_US&formkey=dGFjZG5YZFAyclg4amlhcnExS0JYWUE6MA#gid=0](https://docs.google.com/spreadsheet/viewform?hl=en_US&formkey=dGFjZG5YZFAyclg4amlhcnExS0JYWUE6MA#gid=0)

### **Population: Description of the following**

Disease mentioned (Yes/No)

Stage or severity (Yes/No)

Basic demographics such as age, gender, co-morbid conditions (Yes/No)

Inclusion or exclusion criteria reported (Yes/No)

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### **Outcomes: Description of the following**

Definition of outcomes (at least primary outcome) stated (Yes/No)

The time points of outcome measurement described (Yes/No)

How the outcomes assessed were described (Yes/No)

Clinical outcomes / surrogate outcomes /both

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Study design: RCT/n-RCT/Registry/ observational/other

Where the population was recruited (single /multi-center)

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Funding source identified (Yes/No)

If yes, Industry funded (in full or part) (Yes/No)

Did one or more authors have industry ties? (Yes/No/Not reported)

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Device category: Cardiac implantable / vascular interventional / orthopedic / skin-replacement /neurostimulator

Concomitant medications described (Yes/No)

### **Intervention (single device): Description of the following**

Adequate description of device characteristics? (Yes/No)

Level of detail of description of device (High/Low)

Name of the model or manufacturer mentioned (Yes/No)

Methods of implantation or surgical techniques mentioned (Yes/No)

Generation of device, when applicable, or modifications to algorithm described (Yes/No)

### **Intervention (multiple devices): Description of the following for all devices**

Adequate description of device characteristics? (Yes/No)

Level of detail of description of device (High/Low)

Name of the model or manufacturer mentioned (Yes/No)

Methods of implantation or surgical techniques mentioned (Yes/No)

Generation of device, when applicable, or modifications to algorithm described

(Yes/No)Separate analyses or data separately presented for multiple devices? (Yes/No)

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Is comparator a/an: other device?/medical intervention?/other (describe)

Comparator, if it is another device(s): **Description of the following**

Adequate description of device characteristics? (Yes/No)

Level of detail of description of device (High/Low)

Name of the model or manufacturer mentioned (Yes/No)

Methods of implantation or surgical techniques mentioned (Yes/No)

Generation of device, when applicable, or modifications to algorithm described (Yes/No)

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Comparator is medical or surgical therapy: **Description of the following:** Medication type  
and dosage were provided (Yes/No) Surgical therapy  
technique was described (Yes/No )

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Any reporting of device modification during study period (Yes/No)

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Details of training/certification of operator were reported (Yes/No)

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Learning curve of operator was discussed (Yes/No) Criteria: either the word “learning curve” was used or exclusion of data collected in the early phase of the study to account for issues related to learning curve

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Level of expertise of team were considered (Yes/No) Criteria: Any explicit discussions or analyses related to “experienced team or experienced center”

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Practitioner variability discussed (Yes/No) Criteria: Any discussion related to use of a device or adjunct technique was at the discretion of the operator.

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"Volume at sites" effect was discussed (Yes/No) Criteria: Any discussion related to how the results differ due to volume of patients. This could be results or discussions comparing different centers within a study, if it was multi-center or it could comparing to another study that reported better or worse results

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**Appendix Table F6. Primary studies description**

<b>Variables in primary studies</b>	<b>Categories</b>	<b>N studies (%)</b>
<b>Population</b>		
Description of disease for which an implant was used	Yes	106 (96)
	No	5 (5)
Description of severity of disease for which an implant was used	Yes	94 (85)
	No	17 (15)
Description of demographics or baseline characteristics	Yes	105 (95)
	No	6 (5)
Description of eligibility criteria	Yes	102 (92)
	No	9 (8)
Number of devices used	Single	97 (87)
	Multiple	14 (13)
<b>Outcome</b>		
Definition of outcome (at least primary outcome)	Yes	105 (95)
	No	6 (5)
Description of outcome assessment method	Yes	108 (97)
	No	3 (3)
Types of outcomes evaluated	Clinical only	38 (34)
	Surrogate only	8 (7)
	Both	65 (59)
<b>Other study characteristics</b>		
Types of study design	RCT	51 (46)
	Nonrandomized / observational	60 (54)
Funding source declared	Yes	59 (53)
	No	52 (47)
N centers where the study was conducted	Single	68 (61)
	Multiple	39 (35)
	Unclear	4 (4)
<b>Types of Comparator</b>		
Studies with a medical comparator	Yes	9 (8)
Studies with a surgical comparator	Yes	22 (19)
Studies with device comparator	Yes	31 (28)
Studies without comparator	Yes	49 (44)
Description of device comparator (n = 31)		N = 31
Name of the model or manufacturer mentioned	Yes	24 (77)
	No	7 (23)
Methods of implantation or surgical techniques mentioned	Yes	24 (77)
	No	7 (23)
Generation of device, when applicable, or modifications to algorithm described	Yes	5 (16)
	No	25 (84)

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