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Subjective and objective outcomes in randomized clinical trials: definitions differed in methods publications and were often absent from trial reports

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Abstract

Objectives: The degree of bias in randomized clinical trials varies depending on whether the outcome is subjective or objective. Assessment of the risk of bias in a clinical trial will therefore often involve categorization of the type of outcome. Our primary aim was to examine how the concepts ''subjective outcome'' and ''objective outcome'' are defined in methodological publications and clinical trial reports. To put this examination into perspective, we also provide an overview of how outcomes are classified more broadly.

Study Design and Setting: A systematic review of methodological publications providing a classification of clinical trial outcomes and a descriptive study of how outcomes were classified in 200 PubMed indexed clinical trial reports published in 2012.

Results: We identified 90 methodological publications with some form of a classification of outcomes. Three distinct definitions were provided for subjective outcome: (1) dependent on assessor judgment, (2) patient-reported outcome, or (3) private phenomena (ie, phenomena only assessable by the patient). Of the 200 clinical trial reports, 12 used the term ''subjective'' and/or ''objective'' about outcomes, but no clinical trial reports explicitly defined the terms.

Conclusion: The terms ''subjective'' and ''objective'' are ambiguous when used to describe outcomes in randomized clinical trials. We suggest that the terms should be defined explicitly when used in connection with the assessment of risk of bias in a clinical trial, in meta-epidemiological research, and generally in the reporting of clinical trials. We also suggest that adding an explicit clarification of the terms in future versions of the Cochrane Handbook might further strengthen its important role in guiding review authors.

Keywords: Subjective outcomes; Objective outcomes; Types of outcomes; Endpoints; Risk of bias; Randomized clinical trials

1. Introduction

In a randomized clinical trial, the type of outcomes investigated is of fundamental importance. The formulation of a meaningful research question for a clinical trial involves careful considerations of outcomes, reflected in the PICO acronym: *p*atients, *i*ntervention, *c*ontrol, and *o*utcomes [1]. The choice of which outcomes to measure is challenging but will often involve a trade-off between risk of bias, relevance to patients, tradition, and practicality of clinical trial logistics.

Clinical trial outcomes differ in a number of important ways and may be categorized accordingly. For instance, outcomes may be categorized based on clinical relevance into surrogate and clinical outcomes. The categorization of outcomes into ''subjective'' and ''objective,'' and the related dichotomy between ''hard'' and ''soft'' outcomes, is particularly important because it is directly linked to formal and informal assessments of the risk of bias in a clinical trial. Large metaepidemiological studies have found that the degree of bias depends on whether the outcome is subjective or objective [2]. In clinical trials with subjective outcomes, lack of double-blinding exaggerated odds ratios by 22% (95% confidence interval: 8, 35), but in clinical trials with objective outcomes, the exaggeration was only approximately 8%, with confidence intervals overlapping the neutral result. A similar tendency was reported for concealment of allocation [2]. Accordingly, the Cochrane Collaboration's tool for assessing risk of bias recommends that risk of bias is assessed for each outcome, or class of outcomes, separately [3].

The opinions expressed are the views of the author and do not necessarily reflect the policy of the National Institutes of Health, the Public Health Service, or the U.S. Department of Health and Human Services.

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What is new?

Key findings

- The terms "subjective" and "objective" are ambiguous when used to describe outcomes in clinical trials.
- We identified three distinct definitions of "subjective outcome" in methods publications. In randomized clinical trial publications, whenever the terms "subjective outcome" or "objective outcome" were used, no explanation was given as to the intended meaning.

What this adds to what was known?

- The classification of outcomes as subjective or objective is central to formal and informal assessments of the risk of bias in individual trials.
- Empirical evidence from metaepidemiological studies shows that the degree of bias in randomized clinical trials varies depending on whether the outcome is subjective or objective, but this division proves to be ambiguous.

What is the implication and what should change now?

- We suggest that the terms "subjective" and "objective" should be defined explicitly when used in connection with the assessment of risk of bias in a trial, in metaepidemiological research, and generally in the reporting of trials.

In assessing the risk of bias in a randomized clinical trial, either informally when studying a single clinical trial report or formally when including a number of clinical trials in a systematic review, the categorization into subjective and objective outcomes becomes essential. If the criteria for judging outcomes to be "subjective" or "objective" are unclear, because of ambiguity of the terms, communication regarding outcomes and risk of bias will be impeded. This may cause inconsistencies in judgments on the risk of bias in clinical trials and may complicate considerations on choice of outcome measures in the planning of clinical trials. Furthermore, a clearer understanding of what outcomes count as "subjective" or "objective" will be crucial for the planning and interpretation of future metaepidemiological studies. Greater clarity regarding the meaning of the terms "subjective outcomes" and "objective outcomes" will be relevant for both clinicians reading individual clinical trial reports, authors of systematic reviews, and methodological researchers. We therefore wanted to provide an overview of how the concepts "subjective outcomes" and "objective outcomes" are defined in methods publications and clinical trial reports. To provide context, and to not miss any closely related terms in use, we searched for outcome classification systems and descriptive terms more broadly.

2. Methods

We conducted a systematic review of methodological publications that provided a classification of clinical trial outcomes and a descriptive study of how outcomes were classified in a random sample of 200 published reports of randomized clinical trials. An unpublished protocol for both parts of the study was prepared before the work was commenced.

2.1. Systematic review of methodological publications

We included scientific journal articles and book chapters attempting to classify clinical trial outcomes. We included articles and books that, as a minimum, contained an explicit description/definition of some type of outcome (eg, "Surrogate outcomes are those outcomes that are not directly clinically relevant") or set up an explicit division of outcomes into two or more groups (eg, "Outcomes may be divided into clinical and surrogate outcomes"). We did not include articles or book chapters that merely *used* terms such as "surrogate" or "composite" outcomes. Categorizations according to the specific subject matter of the outcomes were not included (eg, "joint function outcomes" or "adverse event outcomes"). We excluded articles and books in languages other than English and Danish.

We searched PubMed (1966–April 2013) and the Cochrane Methodology Register (from inception to July 2012 [ie, last update]) (see Appendix A at www.jclinepi.com). All titles and abstracts were screened by one author (H.M.), and in case of doubt about eligibility, the full text was retrieved. We further searched the full-text online database Google Scholar, using a variety of terms and phrases, mostly in English (see Appendix A at www.jclinepi.com). We read the title and text extract for each Google Scholar record, and if there was any indication of a possibly eligible article first the abstract, and if judged relevant, the full text was retrieved. Reference lists in the included articles and book chapters were read, and we searched our personal collections of methodological publications gathered independently of the current review (see Figure A/Appendix A at www.jclinepi.com). Furthermore, we defined a sample of textbooks on clinical epidemiology and clinical trial methodology, respectively, published within the last 10 years and held at the Copenhagen University Library (see Appendix B at www.jclinepi.com). Sections of the books judged potentially to contain discussions of outcomes were read. Textbooks containing outcome classifications were included in the review.

From each article, book, or textbook chapter ("methods publication" hereafter), we extracted the following information: the categorizations used (eg, "patient-reported," "clinical vs. surrogate," etc.), including exact terms used.

From those publications that categorized outcomes as "subjective" or "objective," further details were extracted on any definitions or characterizations offered for the terms and any examples given of outcomes falling into these categories. Expecting a certain overlap between the intended meaning of the distinction "subjective" vs. "objective" and "hard" vs. "soft" based on previous experience of how these terms are used in connection with clinical trials, we similarly extracted details from those publications that categorized outcomes as "hard" or "soft."

We took "subjective" and "objective" to be logical opposites, implying that from any definition of "subjective," a definition of "objective" (ie, "nonsubjective") could be deduced, and vice versa.

Different terms were used for what were essentially the same categories. We grouped publications that categorized outcomes using terms that we judged to be roughly synonymous, based on the terms alone. For instance, "surrogate" vs. "patient-important" was grouped with "surrogate" vs. "clinical." Information on categorizations used was extracted by two of the authors (H.M. and A.H.) independently for a random subsample of 18 of the methods publications (20%) identified for the systematic review (perfect agreement in 16 cases and minor disagreements in the remaining two).

2.2. Descriptive study of randomized clinical trials

We randomly sampled 200 publications indexed in PubMed and published in 2012, describing randomized clinical trials. We noted any occurrences of descriptive terms used about clinical trial outcomes in the publications (see Appendix C at www.jclinepi.com).

Two authors (S.B. and H.M.) read the full text of all articles and independently extracted data using a pretested data extraction sheet. Disagreements were resolved by discussion. For each article, descriptive/classifying terms prefixed to the word "outcome" (or synonyms) were recorded (eg, "surrogate outcome").

Descriptive terms were only included if they might, in principle, be used about outcomes in any type of clinical trial. We thereby excluded descriptive terms that were tied closely to the specific content/subject matter of the clinical trial, for example, "*fertility* endpoints" or "*angiographic* outcomes," whereas terms such as "*mortality* endpoints" and "*adverse event* outcomes" were included.

We further extracted information on type of journal, speciality, intervention, clinical trial design, use of blinding, adequacy of concealment of allocation, and number of patients randomized. One author (H.M.) extracted supplementary data from those articles containing any of the descriptive terms "subjective," "objective," "hard," or "soft." Quotes containing the relevant term or terms were recorded, including any definitions or characterizations of the terms, and any examples of outcomes implied or stated to be "subjective" or "objective," and so on.

2.3. Analyses

We compiled the categories used to describe outcomes in methods publications and clinical trial reports. Equivalent categories from the methods publications were collapsed. Results were tabulated descriptively with actual numbers, and proportions were presented.

3. Results

3.1. Systematic review of methods publications

About 2,772 search records were screened and 2,708 excluded, leaving 64 eligible publications. A further three were identified from the reference lists of included articles, 13 from our personal collections of publications, and 10 from the sample of textbooks. In total, we identified 90 methods publications containing attempts at classification systems for outcomes (Table 1, see Appendix D at www.jclinepi.com).

There were seven main pairs of categorizing concepts, with subjective–objective being the fourth most prevalent, occurring in 14 methods publications (Table 2).

Of the 14 methods publications providing a characterization of subjective and/or objective outcomes, eight contained an explicit definition (Table 3). For the remaining six articles, clues as to the intended meaning of the terms could be found in the context or from the examples given.

We identified three distinct definitions of the subjective outcome–objective outcome division. Subjective was taken to mean: (1) dependent on judgment of assessor, (2) patient-reported outcome, or (3) concerning private phenomena. According to (1), an outcome was considered subjective if based on an observer who exercises judgment while assessing an event or state (objective outcomes being those determined without exercising judgment). According to (2), an outcome was considered subjective if patient reported (objective outcomes being those reported by an observer other than the patient). According to (3), an

Table 1. Systematic review: general characteristics of methods publications with outcome classification systems ($N = 90$)

Publication characteristic	*n* (%)
Publication type	
Journal article	75 (83)
Book chapter	15 (17)
Overall topic	
General methodology	50 (56)
Methodology of specific clinical field	40 (44)
Medicine	27
Surgery	9
Psychiatry	4
Year of publication	
1980–1989	5 (6)
1990–1999	11 (12)
2000–2010	54 (60)
2010–2013	20 (22)
Median (range)	2007 (1982–2013)

Table 2. Systematic review: classification of outcomes in methods publications ($N = 90$)

Classifying concepts	N[a](%)
Surrogate vs. clinical	49 (54)
Patient-reported vs. other	17 (19)
Composite vs. single	15 (17)
Subjective vs. objective	14 (16)
Other content-based divisions (eg, generic vs. specific)	12 (13)
Primary vs. secondary	10 (11)
Hard vs. soft	7 (8)
Continuous vs. discrete	6 (7)
Other	11 (12)

[a] Number of articles categorizing outcomes using the terms listed (or what we consider to be synonymous terms). Publications are counted irrespective of whether they use both terms in the opposed pairs, or just one of them, and may be counted more than once because they may contain more than one of the concept pairs, or for instance use the terms "subjective" vs. "hard," in which case they are counted under both subjective vs. objective and hard vs. soft.

outcome was considered subjective if assessable by no one but the patient (objective outcomes being those assessable by others).

Some outcomes, such as pain or anxiety, are subjective according to all three interpretations, and others, such as all-cause mortality, are objective according to all three interpretations. However, an outcome may be subjective according to one of the aforementioned definitions and not be subjective according to the others. For instance, a patient-reported outcome may be assessable, in principle, by others and may be determined by the patient without any significant degree of personal judgment (eg, bladder diary outcomes such as measurements of volume of urine per voiding), making the outcome objective according to (1), subjective according to (2), and objective according to (3).

A patient-reported outcome may also be assessable by others in principle but involves personal judgment by the patient as it would have involved personal judgment by an external observer had there been one (eg, difficulty in performing activities of daily living), making the outcome subjective according to (1), subjective according to (2), but objective according to (3). Conversely, an outcome may be assessor reported yet determined exercising personal judgment (eg, cause-specific mortality), in which case the outcome would be subjective according to (1) and objective according to (2) and (3).

Table 3. Systematic review of methods publications: definitions of subjective vs. objective outcomes ($N = 14$)

Definition	n (%)	References
Type of explanation given in publication of intended meaning of terms		
Explicit definition[a]	8 (57)	
Explanation other than explicit definition[b]	6 (43)	
Contents of definition		
1. Involves judgment by assessor vs. does not involve judgment	4 (29)	[4–7]
2. Patient-reported vs. assessor reported	1 (7)	[8]
3. Private phenomena vs. public phenomena	2 (14)	[9,10]
Unclear definition ($n = 1$) or no definition[c]	7 (50)	
Total	14 (100)	

[a] For example, "subjective outcomes are those that are based on the patient's experience and report."

[b] Some explanation given but no explicit definition of terms.

[c] One publication attempted an explicit definition, but the definition was unclear, and the publication is counted here with the six publications not offering an explicit definition.

Of the eight articles offering explicit definitions, four understood the distinction "objective" vs. "subjective" in accordance with the aforementioned (1) [4–7], for instance giving the following definition: "The definition of objective and subjective outcomes was based on the extent to which outcome assessment could be influenced by investigators' judgment" [7]. One article offered an explicit definition in accordance with (2) [8], defining "subjective outcomes" as "using questionnaires and interviews to document the opinions and attitudes of the patient" and "objective outcomes" as "using empirical data to verify improvements in performance." Finally, two articles defined the distinction in accordance with (3) [9,10], for instance defining "subjective outcomes" as outcomes that the "physician cannot assess directly with confidence—have to rely on patient (eg, pain, physical, social, and emotional function)" [10] and "objective outcomes" as outcomes that the "physician can assess directly with confidence (eg, tender joint, x-ray erosion)" [10]. One article offered an ambiguous definition of the subjective–objective dichotomy because the definition of "subjective" was in accordance with (2) and the definition of "objective" was in accordance with (3) [11]. The remaining six articles did not offer explicit definitions, although clues could be found to the intended meaning in some of the articles (see Appendix E at www.jclinepi.com). For example, one article divided outcomes into all-cause mortality, semiobjective outcomes, and subjective outcomes [12]. This probably reflects an interpretation according to the aforementioned (1) but viewed as a matter of *degrees*, judgment by the observer being involved to a greater or lesser extent.

Seven methods publications classified outcomes as "hard" vs. "soft," five offering an explicit definition for the terms. Of the five publications, two used the terms "hard"/"soft" outcomes as synonymous with "objective" vs. "subjective," as interpreted according to (1), that is, outcomes determined with or without the personal judgment of the observer [4,13]. Two methods publications offered a definition for "hard"/"soft" [6,14] that combined the characteristics of subjectivity/objectivity as interpreted according to (1) with the characteristic of surrogacy. For instance, "soft" outcomes were interpreted as subjective and not directly clinically relevant outcomes. Finally, one methods publication categorized outcomes as "hard" vs. "surrogate" and defined "hard" outcomes as what might otherwise be termed clinical outcomes ("the real efficacy measures of clinical studies" as opposed to measures that may substitute for those) [15]. Our expectation of some overlap of intended meaning between the "hard" vs. "soft" and "objective"

vs. "subjective" distinction was confirmed for some of the interpretations, although there was also an overlap with "surrogate" vs. "clinical." The overlap of intended meaning is also reflected in Table 2, where two of the seven publications in the hard vs. soft row are also counted in the subjective vs. objective row [4,6] because they used, for example, the pair of terms "subjective vs. hard." One of the publications in the hard vs. soft row is also counted in the surrogate vs. clinical row because the publication used the terms "hard" vs. "surrogate" [15]. (No publications used concept pairs such as "subjective" vs. "surrogate" or "objective" vs. "clinical".) Overall, there was no consensus on the meaning of the distinction between "hard" and "soft" outcomes.

3.2. Descriptive study of 200 clinical trials

The general characteristics of the included clinical trials are shown in Table 4. About 155 clinical trial reports contained terms used to characterize outcomes, and we identified 46 different descriptive terms. "Objective outcome" occurred in nine clinical trial reports and "subjective outcome" in five clinical trial reports (Table 5).

Twelve clinical trial publications used the descriptive terms "subjective" and/or "objective" about outcomes. None of these articles offered a definition of the terms used nor were their meaning explained indirectly (Table 6). Three clinical trial publications used the term "hard" or "harder" about outcomes but gave no clues as to the intended meaning of the terms.

Table 4. Descriptive study: general characteristics of randomized clinical trial publications ($N = 200$)[a]

Publication characteristic	*n* (%)
Journal	
General	30 (15)
Speciality	170 (85)
Speciality	
Medicine	112 (56)
Surgery	67 (33)
Psychiatry	3 (2)
Other	18 (9)
Intervention	
Pharmacological	108 (54)
Nonpharmacological	92 (46)
Design	
Parallel	186 (93)
Crossover/split body	14 (7)
Use of blinding	
Yes	115 (57)
No	85 (43)
Concealment of allocation	
Adequate	38 (19)
Unclear	155 (77)
Inadequate	7 (4)
Number of patients randomized per trial	
Median (interquartile range)	110 (45–321)

[a] A random sample of 200 of an initial sample of 366 randomized clinical trial publications published November–December 2012 and indexed in PubMed.

Table 5. Descriptive study of 200 randomized trials publications: descriptive terms for outcomes[a]

Descriptive term	*N*[b] (%[c])
Primary	122 (61)
Secondary	94 (47)
Main	32 (16)
Clinical	30 (15)
Efficacy	25 (13)
Composite	16 (8)
Safety	11 (6)
Exploratory	10 (5)
Continuous	9 (5)
Objective	9 (5)
Long-term	6 (3)
Patient-reported	6 (3)
Subjective	5 (3)
Co-primary	4 (2)
Functional	4 (2)
Surrogate	4 (2)
Binary	3 (2)
Dichotomous	3 (2)
Patient-centered	3 (2)
Tertiary	3 (2)

[a] A random sample of trial publications from 2012, indexed in PubMed.
[b] The 20 terms occurring in the largest number of publications.
[c] Percentage of the 200 publications containing the term.

In all cases, the use of the terms was consistent with more than one of the interpretations identified in the methods publications.

4. Discussion

The difference between subjective and objective outcomes in randomized clinical trials was addressed in 14 methods publications, providing three distinct characterizations of the term "subjective outcome": dependent on judgment of assessor, patient-reported outcome, or private phenomena. In clinical trial publications, the terms "subjective" and "objective" were in all cases used without a clarification of intended meaning.

4.1. Strengths and weaknesses of the study

To our knowledge, this is the first overview of the methodological literature on outcomes in clinical trials and the

Table 6. Descriptive study of 200 randomized trials publications: use of the terms subjective outcome or objective outcome and accompanying definitions

Definition	*n* (%)
Use of either "subjective outcome" or "objective outcome"	12
Type of explanation given in publication of intended meaning of terms	
Explicit definition	0 (0)
Characterization other than explicit definition	0 (0)
No characterization and judgment on interpretation not possible based on examples/context	12 (100)
Total	12 (100)

first systematic examination of the meaning and use of the terms "subjective" and "objective" in this context. Our search for methodological publications included full-text database searches and textbooks, and the clinical trial publications were recent and randomly sampled.

We have not analyzed the variation in meaning of other terms used to describe outcomes, for example, surrogate, primary, and patient reported. We suspect that there might be some relevant variation in meaning and use of the terms, especially "surrogate." To explore this, however, was not the objective of our study.

The different interpretations of the distinction between subjective and objective are not necessarily exhaustive. For instance, we might speculate that the label "subjective" could hypothetically be used about quality-of-life outcomes to mean "dependent on personal values" rather than merely dependent on personal judgment. Generally, the term "subjective" might also be used in a pejorative sense, as a label simply meaning "inappropriate for use as outcome" or "bias laden." Other interpretations may be imagined. Similarly, the distinction between hard and soft could conceivably be given other interpretations than those discussed here.

4.2. Relation to other studies

Physician interpretations and textbook definitions of the terms "single blind" and "double blind" vary considerably [16,17]. Also, the interpretation of the term "intention to treat" has been shown to vary greatly [18]. It appears that the meaning of many standard terms used to describe central methodological aspects of randomized clinical trials may not be very stable. This may partly reflect the fact that there is no widespread tradition within clinical epidemiology for precise conceptual analysis.

4.3. Subjective vs. objective outcomes and assessment of risk of bias

The Cochrane Handbook for Systematic Reviews of Interventions (ie, Cochrane Handbook) [3] provides important guidance to authors conducting Cochrane reviews and is also widely consulted by reviewers conducting other systematic reviews. The terms "subjective outcomes" and "objective outcomes" occur repeatedly in the Cochrane Handbook in connection with assessment of risk of bias in clinical trials, but we neither found explicit characterization of the terms (The Cochrane Handbook was included in the review because of an explicit description of the category "patient reported outcomes") nor is "subjective outcome" or "objective outcome" defined in the online Cochrane Glossary [3,19].

Many of the passages in the Cochrane Handbook that include the terms "subjective" or "objective" outcomes concern the risk of *detection bias*, that is, systematic differences between groups in how outcomes are determined. For instance, "All outcome assessments can be influenced by lack of blinding, although there are particular risks of bias with more subjective outcomes (eg, pain or number of days with a common cold)." The Cochrane Handbook recommends that the risk of detection bias is assessed for "subjective" and "objective" outcomes separately. This recommendation suggests an interpretation of "objective" and "subjective" that is coherent with the methodological literature more broadly, which primarily anchors the distinction between subjective and objective outcomes to how outcomes are detected or reported.

However, the Cochrane Handbook also suggests assessing the risk of *performance bias* separately for subjective and objective outcomes. This suggests that aspects other than those connected to the detection and reporting of outcomes may be implied by the distinction between subjective and objective outcomes, as used in the Cochrane Handbook. Performance bias implies a systematic difference between groups in the care that is provided or in exposure to factors other than the interventions of interest. In a paragraph on the assessment of risk of bias in relation to adequate or inadequate blinding of participants and personnel, mechanisms of performance bias are explained, and it is stated that it is convenient to group outcomes with similar risks of bias, "For example, there may be a common assessment of risk of bias for all subjective outcomes that is different from a common assessment of blinding for all objective outcomes." No characterization of subjective vs. objective outcomes relevant to risk of performance bias is given explicitly in the Cochrane Handbook nor did we find it in the methodological articles or the clinical trial reports we reviewed.

The mechanism of performance bias is multifaceted, involving both differences in the quality and content of the patient–provider interaction, which may cause different degrees of placebo effect, and differences in the basic care, for example, differences in supplementary pain medication. How to interpret "subjective" in this context is not clear. One possibility is that a "subjective" outcome is one that is susceptible to effect modification by psychological factors, such as placebo interventions or other aspects of the patient–provider dynamics. An example of a subjective outcome in terms of performance bias would be weight loss as successful eating restriction is partly dependent on the patient's psychological stamina (although weight loss can be precisely measured and thus may be perceived as an "objective" outcome when discussing detection bias). This interpretation is consistent with a systematic review of the effects of placebo interventions, which found an association between effects of placebo and type of outcome [20]. In relation to performance bias, an "objective" outcome may thus be one that is presumed to be unaffected by psychological factors, for example, bone healing. However, all outcomes may potentially be affected by cointerventions and other differences in basic care and the distinction between subjective and objective outcomes thus seems less relevant when discussing risk of bias because of cointerventions. Still, these

reflections are speculative, and in the context of performance bias, the meaning of "subjective" and "objective" outcomes remains somewhat obscure.

The Cochrane risk of bias tool has been found to have a moderate interobserver agreement rate [21]. Interobserver agreement will hopefully improve once assessors become more familiar with the tool, are offered better training, and the tool is refined. One likely contributing factor to the modest agreement rates is the different interpretations of what is meant by subjective and objective outcomes.

The fact that bias seems to differ according to type of outcome implies that the concordance in effect between correlated outcomes of different type can become important. In a clinical trial where the blinding of patients and care providers is not possible but no improvement is found for an "objective outcome" (eg, peak flow), it seems reasonable to be less confident in an improvement of a "subjective outcome" (eg, quality of life) as this may not be caused by the intervention as such.

4.4. Risk of bias vs. clinical relevance

From a clinical and patient perspective, the important outcomes in a randomized clinical trial are those directly linked to patients' symptoms, function, and quality of life. There is an increasing awareness of the importance and relevance of patient-reported outcomes [22,23]. Similarly, there has been a considerable focus on the problematic role of surrogate outcomes [24] and on the historical tradition within medicine to discount patient-reported outcomes.

Unfortunately, both patient-reported outcomes and judgment-dependent observer-based outcomes are vulnerable to bias because of inadequate blinding. Comparisons of substudies with blind and nonblind patients within the same clinical trial reported a considerable exaggeration of effect sizes because of lack of patient blinding [25]. Similar comparisons of clinical trials with both blind and nonblind assessors of judgment-dependent (ie, "subjective") outcomes also found a marked exaggeration of the effect [5,26,27]. In clinical trials with binary outcomes, odds ratios based on assessments by nonblind assessors were exaggerated by approximately 36% [5].

From a research perspective, the important outcomes are those that are clinically relevant and can be assessed with low risk of bias. In clinical trials where blinding of patients, treatment providers, and outcome assessors is feasible, it is possible to combine clinical relevance and the scientific ideal of internal validity. However, in clinical trials where blinding is not possible, we are forced to weight against each other considerations of risk of bias and considerations of clinical relevance. Low susceptibility of an outcome to bias may thus often come at the cost of less direct clinical relevance and ultimately less relevance to patients. A notable exception to this dilemma in nonblinded clinical trials is all-cause mortality, which is of clear relevance to patients and has little risk of bias, at least of detection bias. It should also be noted that some outcomes that have generally been considered "objective" may in fact leave considerable room for judgment by the assessor, for instance, blood pressure, ultrasonic measurements, radiographic outcomes, and so on.

4.5. Implications

Clearly, which terms are relevant to use to describe an outcome in a randomized clinical trial or when assessing the risk of bias in a clinical trial depend on the clinical and methodological settings. Our study indicates that central methodological terms may be understood differently by different readers, and we suggest that authors of clinical trial reports explicitly explain the intended meaning of the terms "subjective" and "objective" outcomes (as well as other terms that may be considered ambiguous). Journal editors might contribute to greater clarity by requiring that authors provide such explicit explanations.

We also suggest that adding an explicit clarification of the intended meaning of "subjective" and "objective" outcomes in future versions of the Cochrane Handbook might further strengthen its important role in guiding review authors.

No metaepidemiological study has addressed the risk of performance bias independently from detection bias. Such a study would be worthwhile, although the type of outcome needs careful attention, especially the distinction between subjective and objective outcomes.

5. Conclusion

The terms "subjective" and "objective" are ambiguous when used to describe outcomes in randomized clinical trials. We suggest that the terms should be defined explicitly when used in connection with the assessment of risk of bias in a clinical trial, in metaepidemiological research, and generally in the reporting of clinical trials.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jclinepi.2014.06.020.

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