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ARTICLE

Interpretation of composite endpoints in urology: an analysis of citation quality

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ABSTRACT

Objective: To investigate how urological studies using composite endpoints as the primary outcome were cited.

Materials and methods: In this quality analysis of citations, three randomized clinical trials each investigating oncological and non-oncological urology were selected for citation analysis based on predefined criteria. In total, 531 papers citing the selected studies were reviewed; citations were evaluated based on whether they correctly referred to the composite endpoint and if singleton endpoints were defined and/or discussed.

Results: Among the citations, 223/531 (42%) referred to the composite endpoint, of which 217/223 (97.3%) correctly cited the composite endpoint. However, only 91/217 (41.9%) defined and/or discussed the singleton endpoints of the composite endpoint. The lack of a validated instrument for citation analysis was a limitation of this study. Meanwhile, the main strength is the large number of individually analyzed citations.

Conclusions: The composite endpoints of urological randomized clinical trials are generally cited without referring to the composite endpoint; when cited, the composite endpoints are described correctly. However, in most cases, without defining or discussing the singleton endpoints.

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Introduction

A randomized clinical trial (RCT) can combine several singleton endpoints into one composite endpoint (CE). For example, studies investigating cancer treatment often use the CE 'progression-free survival' as the primary endpoint. This CE is commonly composed of the following singleton endpoints: The time from randomization until the first documentation of disease progression or all-cause death. Patients experiencing one of the singleton endpoints experienced the CE. Using the CE as the primary endpoint in an RCT can provide a broader perspective of the clinical benefit in relation to the potential harm of a treatment. The concrete advantages of combining singleton endpoints in a CE include potentially achieving a higher event rate, thus decreasing the need for long follow-up periods for rare events [1–3]. The combination of singleton endpoints needs to be well rationalized and of similar clinical and interventional importance; otherwise, CEs can be misleading [4,5]. A hypothetical example is a trial investigating the outcome of a treatment for prostate cancer using a CE consisting of death and erectile function preservation. If the study found a significant effect of the treatment on the CE, it would be difficult to interpret because of the variation in the relevance of each of the singleton endpoints.

Correct interpretation of CEs is important for correct and precise clinical decision-making and patient information [6,7]. Authors intending to cite a CE of RCTs should correctly describe and interpret both the CE and singleton endpoints to avoid misinterpretation.

To our knowledge, no study has investigated the interpretation and citation of CEs in urological studies. We hypothesized that CEs in urological research might be misinterpreted by the authors. Therefore, we aimed to investigate how urological RCTs using CEs as the primary outcome were cited.

Materials and methods

Study selection

We included three RCTs representing oncological urology (prostate cancer, bladder cancer and renal cell carcinoma) and three RCTs on non-oncological urology (lower urinary tract symptoms [LUTS], urolithiasis and andrology) for citation quality analysis to cover different areas of urology. Text and reference lists of relevant European Association of Urology (EAU) guidelines [8–14] were screened by three authors (FMJ, KKT and CFSJ) to select RCTs representing major urological disease classifications with a CE as the primary endpoint. The RCTs had to be cited more than 30 times

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on PubMed to be eligible for citation analysis. No requirements were set for the composition of the CE or the individual singleton endpoints, but the RCTs were required to report all results for both the CE and singleton endpoints in either the manuscript or the supplementary material of the paper (Figure 1). If multiple RCTs for each subtopic met the inclusion criteria, the most cited RCT was analyzed.

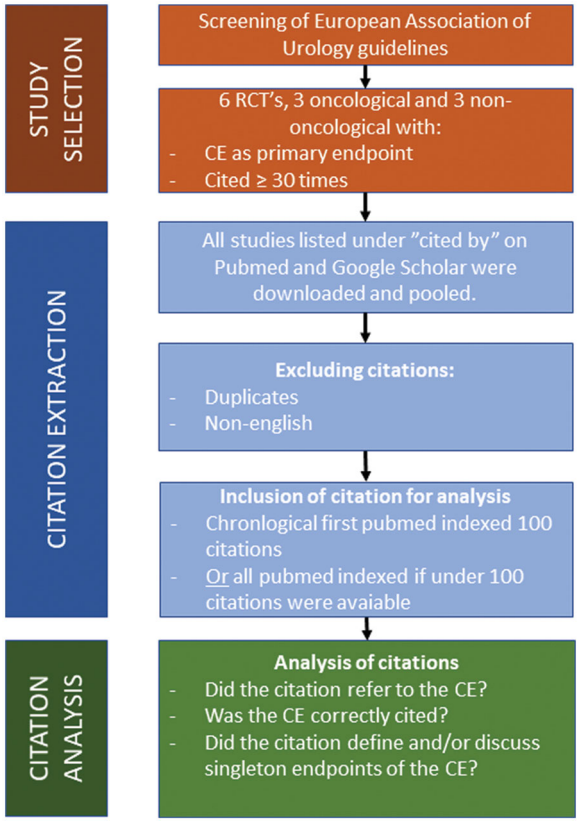

Figure 1. Method flowchart.

Citation extraction

Data extraction and citation analysis were performed by the authors (FMJ, KKT and CFSJ) and any potential incorrect citations were discussed among the authors. For each study, all citations listed under 'cited by' on PubMed were downloaded on 20 November 2020. The same was done in Google Scholar (Figure 2). After downloading all citations, duplicates, citations from journals without peer review and non-English citations were excluded. The remaining citations were sorted by date, with the oldest first and the first 100 citations included in the citation analysis. All PubMed indexed citations were included for further analysis if less than 100 citations were available.

Citation analysis

The citation analysis was performed made in three steps: First, if the citation referred to the CE; second, if the CE was correctly cited, which is if it presented original data and/or conclusions; and third, if the citation defined and/or discussed the singleton endpoints.

If the citation did not refer to the CE, it was assessed whether the citation referred to at least one singleton endpoints or if the citations did not refer to singleton endpoints or CE.

The results were analyzed using descriptive statistics.

Results

After screening the EAU guidelines, the following RCTs were selected for citation analysis: Study 1 by Smith et al. [15] compared denosumab with placebo in men with non-metastatic castration-resistant prostate cancer using the CE 'Bone metastasis-free survival' composed of the first occurrence of bone metastasis and all-cause death. Study 2 by Parekh et al. [16] compared two surgical treatments (robotic cystectomy vs. open cystectomy) for invasive bladder cancer with the CE '2-year progression-free survival' composed of the proportion of patients without disease progression and all-cause death within 2 years of surgery. Disease progression was defined as any documented recurrence including pathological or radiographic evidence of disease as per the Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1.) criteria or disease-specific deaths. Study 3 by Motzer et al. [17] compared medical treatments (lenvatinib, everolimus and combined lenvatinib and everolimus) for metastatic renal-cell carcinoma with the CE 'progression-free survival' composed of the time from the date of randomization to the date of the first documentation of disease progression or death. Disease progression was based on an investigator review and the RECIST version 1.1. Study 4 by McConnell et al. [18] was on the topic of lower urinary tract symptoms (LUTS). They compared doxazosin, finasteride, combined doxazosin and finasteride and placebo in men with benign prostatic hyperplasia (BPH) and LUTS with the CE 'clinical progression of benign prostatic hyperplasia'. This CE was composed of six singleton endpoints: increase in the American Urological Association Symptom Score $\geq$ 4, acute urinary retention, urinary incontinence, recurrent urinary tract infections or renal insufficiency due to BPH. Study 5 by Pace et al. [19] compared two shock wave lithotripsy treatment regimens for urinary stones (60 vs. 120 shocks per minute), with the primary endpoint 'Success rate' consisting of one-free status and asymptomatic fragments $<$ 5 mm at 3 months after treatment. Study 6 by Sønksen et al. [20] compared two surgical treatments (prostatic urethral lift vs. transurethral resection of the prostate) for LUTS in BPH patients. The study had the CE 'BPH6' which was achieved by patients who fulfilled all of the six singleton endpoints at 12 months postoperatively: International Prostate Symptom Score reduction $\geq$ 30%, quality of recovery based on a Visual Analog Scale after 1 month, maintained erectile function (reduction of $<$ 6 points on the Sexual Health Inventory for Men), maintained ejaculatory function (no answer of 'zero' on the Male Sexual Health Questionnaire for Ejaculatory Dysfunction), maintained continence (Incontinence Severity Index score of $\leq$ 4 points

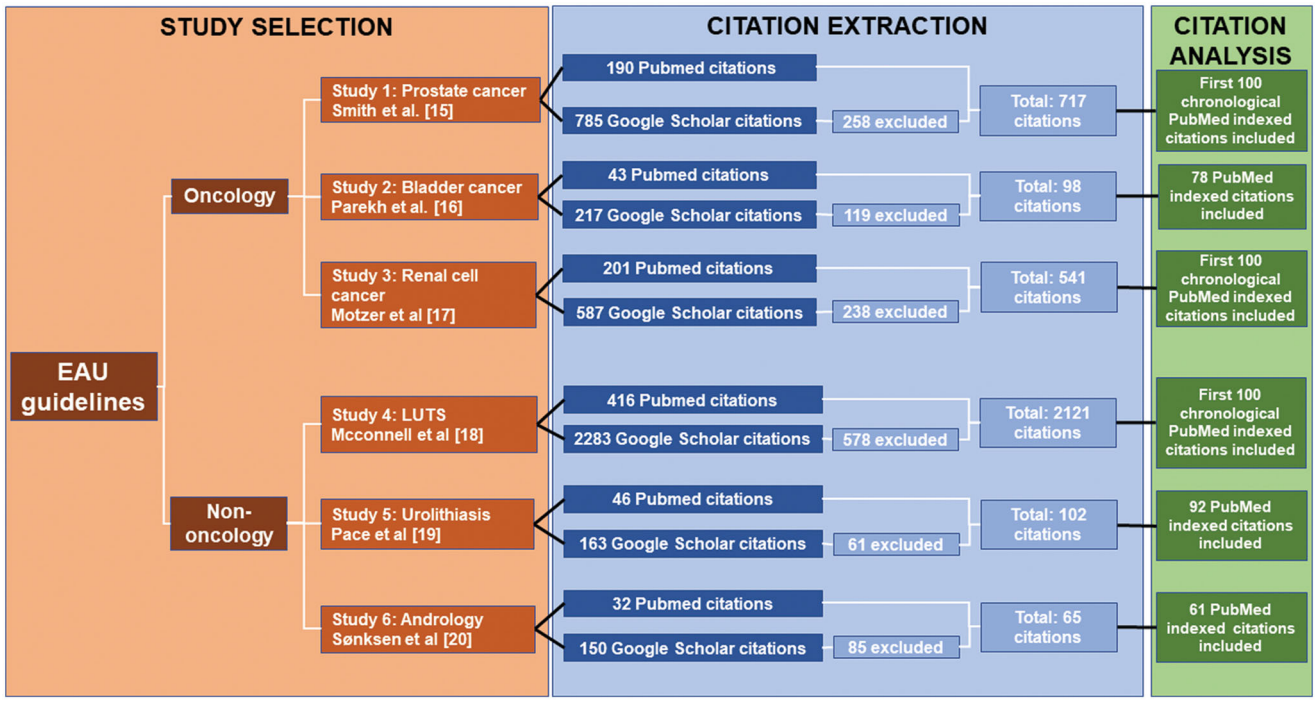

Figure 2. Study selection and citation extraction results.

at all follow-up intervals) and safety (no treatment-related adverse event greater than Clavien-Dindo grade I) (Table 1).

Citation extraction and analysis were performed in November 2020. Across the six included studies, a total of 928 citations and 4,185 citations were listed as 'cited by' on PubMed and Google Scholar, respectively. After excluding duplicates, citations from sources or journals without peer review and non-English citations, 531 citations were reviewed. Finally, citations that were not PubMed indexed were excluded (Figure 2). For studies 1 through 6, we reviewed 100, 78, 100, 100, 92, and 61 citations, respectively. Among the 531 citations, 223 (42%) referred to the CE, of which 217 (97.3%) had correctly cited CEs. However, only 91/217 (41.9%) defined and/or discussed the singleton endpoints. In total, 58/531 (10.9%) citations referred to the singleton endpoints, but not the CE, and 250/531 (47.1%) did not refer to any endpoint.

For study 1, 73/100 (73%) citations referred to CE and 69/73 (94.5%) citations were correct. Four incorrect citations were identified. Two cited a singleton endpoint of the CE while referring to data for the entire CE; one did not define the CE correctly, and one incorrectly cited a treatment effect on a singleton endpoint of the CE. For study 2, 25/78 (32%) citations referred to the CE, and they were all correct. In study 3, 34/100 (34%) citations referred to the CE, of which 33/34 (97.1%) were correct. The incorrect citations did not correctly define the CE. For study 4, 57/100 (57%) citations referred to the CE, and all were correct. In study 5, 20/92 (21.7%) citations referred to the CE, of which 19/20 (95%) were correct. The incorrect citation stated that the intervention had a significant effect on pancreatic cancer. For study 6, 14/61 (22.9%) citations referred to the CE, all of which were correct. The results of the citation analysis for the individual RCTs are presented in Table 2.

Discussion

This is the first study to investigate how RCTs with CEs as primary endpoints are cited and interpreted in the urological literature. From six RCTs on different urological topics, we found that over 50% of the citations did not refer to the CEs, and less than half of these defined or discussed the singleton endpoints. When citations referred to CEs, they were generally correct.

The first part of our citation analysis found that most citations did not refer to CEs. These citations were often part of multiple references used to present an augment or validate a statement when cited. An example of such is a citation of study 3 on renal cell cancer; 'New drugs were also developed for the treatment of renal cell cancer, including pazopanib (Votrient R), vandetanib (Caprelsa R), or lenvatinib (Lenvima R) (Llovet *et al.*, 2008; Escudier *et al.*, 2014; Motzer *et al.*, 2015; Rizzo and Porta, 2017)'. In this citation, study 3 is used among multiple other references without mentioning the CE or singleton endpoints. Furthermore, an example of validating a statement can be seen in this citation of study 5 on urolithiasis 'The efficacy of stone comminution for shock wave lithotripsy is strongly rate dependent [10,14–20]'. Citing studies, as was done in the examples, is a common practice in the scientific literature. However, citing RCTs with a CE does not always provide conclusive evidence and a detailed description of the CE is often necessary to avoid misleading readers. For this reason, the authors should be careful when citing RCTs without mentioning the CE or singleton endpoints.

Incorrect citations were primarily present when citations were more specific.

Overall, we found very few incorrect CE citations. An example is one of study 1 on prostate cancer 'In a

Table 1. Overview of studies included for citation analysis.

Study 1 (prostate cancer, 2012): denosumab and bone metastasis-free survival in men with castration-resistant prostate cancer: results of a global phase 3, randomized, placebo-controlled trial	
Purpose	Evaluate the effect of denosumab to placebo in randomized men with non-metastatic castration-resistant prostate cancer at high risk of bone metastasis.
Composite endpoint	Bone metastasis-free survival was first occurrence of: (1) time to first bone metastasis, (2) death from any cause.
Results: CE	Denosumab significantly increased bone-metastasis-free survival by a median of 4.2 months compared with placebo (median 29.5 [95% confidence interval (CI) 25.4–33.3] vs 25.2 [22.2–29.5] months; hazard ratio 0.85, 95% CI 0.73–0.98, $p = 0.028$)
Results: Singleton endpoints	Denosumab significantly delayed time to first bone metastasis, (33.2 [95% CI 29.5–38.0] vs 29.5 [95% CI 22.4–33.1] months; hazard ratio 0.84, 95% CI 0.71–0.98, $p = 0.032$). Overall survival did not differ between groups (denosumab, 43.9 [95% CI 40.1–not estimable] months vs placebo, 44.8 [95% CI 40.1–not estimable] months; hazard ratio 1.01, 95% CI 0.85–1.20, $p = 0.91$).
Conclusion	In men with castration resistant prostate cancer, denosumab significantly prolonged bone metastasis-free survival and delayed time to bone metastasis.
Study 2 (bladder cancer, 2018): Robot-assisted radical cystectomy versus open radical cystectomy in patients with bladder cancer (RAZOR): an open-label, randomized, phase 3, non-inferiority trial	
Purpose	Compare progression-free survival in patients with bladder cancer undergoing an open cystectomy or robot-assisted cystectomy.
Composite endpoint	Progression-free survival: (1) The time from date of randomization to date of first documentation of disease progression, (2) death.
Results: CE	2-Year progression-free survival was 72.3% (95% CI 64.3–78.8) in the robotic cystectomy group and 71.6% (95% CI 63.6–78.2) in the open cystectomy group (difference 0.7%, 95% CI 9.6–10.9, p non-inferiority = 0.001), indicating non-inferiority of robotic cystectomy.
Results: Singleton endpoints	The proportion of patients with local recurrences was similar between the treatment groups (six [4%] of 150 patients in the robotic cystectomy group vs four [3%] of 152 patients in the open cystectomy group; $p = 0.54$) and local recurrence in the cystectomy bed was also similar (six [4%] patients in the robotic cystectomy group vs two [1%] patients in the open cystectomy group; $p = 0.17$). Death: 28 (19%) of 150 patients in robotic cystectomy group died of bladder cancer and 32 (21%) of 152 patients in the open cystectomy group died of bladder cancer.
Conclusion	In patients with bladder cancer, robotic cystectomy was non-inferior to open cystectomy for 2-year progression-free survival.
Study 3 (renal cell cancer, 2015): Lenvatinib, everolimus and the combination in patients with metastatic renal cell carcinoma: a randomized, phase 2, open-label, multicentre trial	
Purpose	Assess lenvatinib, everolimus or their combination as second-line treatment in patients with metastatic renal cell carcinoma.
Composite endpoint	Progression-free survival: (1) The time from date of randomization to date of first documentation of disease progression, (2) death.
Results: CE	Lenvatinib plus everolimus significantly prolonged progression-free survival compared with everolimus alone (median 14.6 months, 95% CI 5.9–20.1 vs 5.5 months, 95% CI 3.5–7.1; hazard ratio 0.40, 95% CI 0.24–0.68; $p = 0.0005$), but not compared with lenvatinib alone (7.4 months, 95% CI 5.6–10.2; hazard ratio 0.66, 95% CI 0.30–1.10; $p = 0.12$).
Results: Singleton endpoints	The time from date of randomization to date of first documentation of disease progression: An objective response was achieved by 22 (43%) of 51 patients allocated lenvatinib plus everolimus compared with three (6%) of 50 who received single-agent everolimus (rate ratio 7.2, 95% CI 2.3–22.5; vs single-agent everolimus, rate ratio 4.5, 95% CI 1.4–14.7; $p = 0.0067$). The median duration of response was 13.0 months (95% CI 3.7 to not evaluable) for patients allocated lenvatinib plus everolimus, 7.5 months (95% CI 3.8–not evaluable) for those assigned single-agent lenvatinib, and 8.5 months (7.5–9.4) for those on everolimus alone. Overall survival did not differ significantly between patients assigned lenvatinib plus everolimus and those allocated single-agent everolimus (hazard ratio 0.55, 95% CI 0.30–1.01; $p = 0.062$) or single-agent lenvatinib (hazard ratio 0.74, 95% CI 0.40–1.36; $p = 0{\cdot}30$; single-agent lenvatinib vs single-agent everolimus, hazard ratio 0.74, 95% CI 0.42–1.31; $p = 0.29$).
Conclusion	Lenvatinib plus everolimus and lenvatinib alone resulted in a progression-free survival benefit for patients with metastatic renal cell carcinoma who have progressed after one previous VEGF-targeted therapy.
Study 4 (LUTS, 2003) The long-term effect of doxazosin, finasteride and combination therapy on the clinical progression of benign prostatic hyperplasia	
Purpose	Compare the effect of doxazosin, finasteride, doxazosin + finasteride or placebo on clinical progression in men with benign prostatic hyperplasia.
Composite endpoint	Clinical progression: (1) at least 4-point increase in IPSS above baseline, (2) acute urinary retention, (3) urinary incontinence, (4) recurrent urinary tract infections, (5) renal insufficiency due to BPH.
Results: CE	Significant reduction in clinical progression of BPH (39% risk reduction, $p < 0.001$) and finasteride (34% risk reduction, $p = 0.002$), as compared with placebo. The reduction in risk associated with combination therapy (66% for the comparison with placebo, $p < 0.001$) was significantly greater than that associated with doxazosin ($p < 0.001$) or finasteride ($p < 0.001$) alone.
Results: Singleton endpoints	An increase in the AUA symptom score of more than 4 points above base-line values was the most common individual event included in the composite end point of progression. As compared with the risk in the placebo group (3.6 per 100 person-years), the risk was reduced by 45% in the doxazosin group as compared with the rate of acute urinary retention in the placebo group (18 events; rate, 0.6 per 100 person-years), the rate in both the finasteride group (6 events; rate, 0.2 per 100 person-years; risk reduction, 68%; $p = 0.009$) and the combination-therapy group (4 events; rate, 0.1 per 100 person-years; risk reduction, 81%). The rates of urinary incontinence and recurrent urinary tract infection or urosepsis were too low in each of the groups to permit meaningful analyses, in comparison either with placebo or with one another. There were no cases of renal insufficiency related to benign prostatic hyperplasia in any of the groups.
Conclusion	Long-term combination therapy was safe and reduced the risk of overall clinical progression of benign prostatic hyperplasia significantly more than did treatment with either drug alone.
Study 5 (urolithiasis, 2005): Shock wave lithotripsy at 60 or 120 shocks per minute: A randomized, double-blind trial	
Purpose	To examine the effect of decreased shock wave frequency in patients with renal stones.
Composite endpoint	Success rate: (1) stone-free status, (2) asymptomatic fragments less than 5 mm 3 months after treatment.
Results: CE	The success rate was higher for 60 shocks per minute (75% vs 61%, $p = 0.027$). Patients with larger stones (stone area 100 mm^2 or greater) experienced a greater benefit with treatment at 60 shocks per minute. The success rate was 71% for 60 shocks per minute vs 32% ($p = 0.002$) and the stone-free rate was 60% vs 28% ($p = 0.015$).

(*continued*)

Results: Singleton endpoints	Stone-free rates were higher at 3 months in the 60 shocks per minute arm (56.4% vs 44.4%, $p = 0.064$). As with the treatment success rate, a more dramatic difference in the stone-free rate was seen for stones larger than 100 mm^2 in favor of the 60 shocks per minute arm (59.5% vs 28.0%, $p = 0.015$).
Conclusion	Shock wave lithotripsy treatment at 60 shocks per minute yields better outcomes than at 120 shocks per minute, particularly for stones 100 mm^2 or greater, without any increase in morbidity and with an acceptable increase in treatment time.
Study 6 (andrology, 2015): Prospective, randomized, multinational study of prostatic urethral lift versus transurethral resection of the prostate: 12-month results from the BPH6 study	
Purpose	To compare PUL to TURP with regard to LUTS improvement, recovery, worsening of erectile and ejaculatory function, continence and safety.
Composite endpoint	BPH6: (1) Symptom relief, (2) quality of recovery, (3) erectile function preservation, (4) ejaculatory function preservation, (5) continence preservation or (6) safety.
Results: CE	The proportion of patients achieving the BPH6 recovery endpoint by 1 month was 82% in the PUL group, which was significantly better than the 53% in the TURP group ($p = 0.008$).
Results: Singleton endpoints	Quality of recovery as defined by at least a score of 70 on the quality of recovery VAS (0–100 scale), was superior for prostatic urethral lift compared with transurethral resection of the prostate, with 82% of patients in the prostatic urethral lift arm achieving the recovery endpoint by 1 month compared with 53% of patients in the transurethral resection of the prostate arm ($p = 0.008$). Erectile function was preserved in both arms as assessed by sexual health inventory for men, with the vast majority of patients meeting the erectile function criterion of the BPH6 endpoint at 2 years (98% for PUL, 94% for transurethral resection of the prostate). Ejaculatory function was superior for prostatic urethral lift compared with transurethral resection of the prostate ($p < 0.001$), with patients in the transurethral resection of the prostate arm experiencing a significant decline ($p < 0.001$) in Male sexual health questionnaire for ejaculatory dysfunction score from 1 month after the procedure and onwards. Continence function, as assessed by average incontinence severity index score, was maintained throughout follow-up for the PUL arm and did not change significantly from baseline at any time point.
Conclusion	Participants who underwent prostatic urethral lift responded significantly better than those who underwent transurethral resection of the prostate as therapy for benign prostatic hyperplasia with regard to important aspects of quality-of-life.

CE, Composite endpoint; BPH, benign prostate hyperplasia; PUL, prostatic urolift; TURP, transurethral resection of prostate; AUA, American Urological Association; PCa, prostate cancer; RCT, randomized clinical trial.

Table 2. Citation analysis results.

	Study 1 [15]	Study 2 [16]	Study 3 [17]	Study 4 [18]	Study 5 [19]	Study 6 [20]	Total
PubMed citations (*n*)	190	43	201	416	46	32	928
Google scholar citations	785	217	587	2283	163	150	4185
Citations referring to CE	73/100 (73%)	25/78 (32%)	34/100 (34%)	57/100 (57%)	20/92 (21.7%)	14/61 (22.9%)	223/531 (42%)
Correct citations of CE	69/73 (94.5%)	25/25 (100%)	33/34 (97.1%)	57/57 (100%)	19/20 (95%)	14/14 (100%)	217/223 (97.3%)
Correct citation of CE that also defines and/or discuss singleton endpoints	36/69 (52.2%)	8/25 (32%)	5/33 (15.1%)	21/57 (36.8%)	7/19 (36.8%)	14/14 (100%)	91/217 (41.9%)
Citations only referring to singleton endpoints	0/100 (0%)	13/78 (16.7%)	8/100 (8%)	14/100 (14%)	4/92 (4.3%)	19/61 (31.1%)	58/531 (10.9%)
Citations not referring to CE or singleton endpoints	27/100 (27%)	40/78 (51.3%)	58/100 (58%)	29/100 (29%)	68/92 (73.9%)	28/61 (45.9%)	250/531 (47.1%)

CE, Composite endpoint.

randomized phase III study of more than 1,400 men with non-metastatic castration prostate cancer, denosumab delayed metastasis by 4.2 months (HR 0.85; $p = 0.028$)' [21]. While the statement is true and part of the conclusion of Study 1, the citation is incorrect because it states that denosumab delayed the metastasis but referred to results of bone metastasis-free survival (Table 1). Another example of mixing up results is again from study 1, as follows: '… recent publication has reported that the median time to development of skeletal metastasis in castration resistant prostate cancer patients is 25.2 months (Smith *et al*, 2012)' [22]. Here, the authors refer to the results of median bone metastasis-free survival of the placebo group and not time to first bone metastasis. Moreover, in this example, the citation was used to validate a statement and not to discuss the effect of denosumab, which was the purpose of the study. The incorrect citations primarily misinterpreted the RCT by mixing the results from the CE and singleton endpoints.

In the final step of the citation analysis, we found that when the citations referred to the CE, under half of them defined/discussed the singleton endpoints, which may be the result of how RCTs present results and conclusions. For instance, the oncological studies (studies 1–3) more often referred to the CE compared to the non-oncological studies (studies 4–6). In general, the oncological studies focused on the results of CE, with the singleton endpoints less important. Interestingly, study 6 in our citation analysis had very few citations mentioning the CE but, when they did, all of them defined and discussed the singleton endpoints, possibly because the study mainly focused on the singleton endpoints. This highlights that RCTs vary in how they present results and conclusions for singleton endpoints and the CE, potentially making them difficult to cite.

The use and reporting of CEs in RCTs have been widely debated, showing that the conclusions and results of such studies can be difficult to interpret. This was discussed in a research letter by Lavallée et al. [6]. The letter revolved around a study by McConnell et al. [18], which is also included in our analysis (Table 1, study 4). The McConnell et al. study showed a significant reduction in the CE 'clinical

progression' of BPH in patients treated with doxazosin and finasteride. The authors of the research letter noted that a statistically significant reduction in the relative risk was associated with a decreased risk of IPSS score progression and a reduced risk of acute urinary retention; however, the other singleton endpoints had too few events to demonstrate a difference. Therefore, little information can be derived from the treatment effect on the remaining singleton endpoints: incontinence, recurrent infection, and renal insufficiency. Readers should understand the composition of the CE and the relative risk reduction of the singleton endpoints with the treatment, as this indicates which endpoint was affected most by the treatment and thus how patients might benefit from the treatment. Thus, readers and clinicians should be careful when evaluating treatment effects based on RCTs using CEs.

In general, literature on CEs in RCTs in urology is scarce. However, research has been conducted on cardiological RCTs where CEs are very common [4,23–25]. In a systematic review by Cordoba et al. [26], 40 cardiological RCTs were analyzed for how they defined, reported, and interpreted the primary CE. In 22 trials, the authors did not specify that the outcome was a CE, which was only indicated in the method section or other parts of the paper. In 33 RCTs, the effect of the intervention on the most important singleton endpoint was not reported in the conclusion of the study. Furthermore, in 28/40 trials, the singleton endpoints were not of similar importance. The authors concluded that CE use in cardiological trials is problematic and that inconsistencies in defining the CE and inadequate reporting confused readers, leaving them with an exaggerated perception of how well the intervention works. These results highlight the limitations of the CEs in RCTs.

The main limitation of this study was that no validated instruments for citation analysis exist. However, all incorrect citations were carefully discussed by the authors until a consensus was reached. This limitation is further mitigated by the high number of reviewed citations, making a basis for a more robust analysis. Further, the included studies were on different urological topics using different CEs to cover a broad perspective of CEs in urological literature. The study is also limited by not including SCOPUS for citation extraction.

In conclusion, urological RCTs using a CE as the primary endpoint are often cited without referring to the CE. When this is done, the CEs are generally correctly cited, but mostly without defining or discussing the singleton endpoints. The CE and its singleton endpoints should be carefully defined and described to avoid misleading interpretations and citations.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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