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Reporting and Guidelines in Propensity Score Analysis: A Systematic Review of Cancer and Cancer Surgical Studies

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Abstract

Propensity score (PS) analysis is increasingly being used in observational studies, especially in some cancer studies where randomization is not feasible. This review evaluated the use and reporting quality of PS analysis in oncology studies. We searched PubMed to identify the use of PS methods in cancer studies (CS) and cancer surgical studies (CSS) in major medical, cancer, and surgical journals over time, and critically evaluated 33 CS published in top medical and cancer journals in 2014-2015 and 306 CSS published up to 11/26/2015, without earlier date limits. The quality of reporting in PS analysis was evaluated. It was also compared over time and among journals with differing impact factors. 50% of the publications with PS analysis from the past decade occurred within the past two years. Of the studies critically evaluated, a considerable proportion did not clearly provide the variables used to estimate PS (CS 12.1%, CSS 8.8%), incorrectly included non-baseline variables (CS 3.4%, CSS 9.3%), neglected the comparison of baseline characteristics (CS 21.9%, CSS 15.6%), or did not report the matching algorithm utilized (CS 19.0%, CSS 36.1%). In CSS, the reporting of the matching algorithm improved in 2014-2015 ($P = 0.043$), and the reporting of variables used to estimate PS was better in top surgery journals ($P = 0.008$). However, there were no significant differences for the inclusion of non-baseline variables and reporting of comparability of baseline characteristics. The use of PS in cancer studies has dramatically increased recently, but there is substantial room for improvement in the quality of reporting even in top journals. Herein we have proposed reporting guidelines for PS analyses that are broadly applicable to different areas of medical research which will allow better evaluation and comparison across studies applying this approach.

INTRODUCTION

Randomized controlled trials are the gold standard in clinical research but are difficult to conduct due to many practical considerations, particularly for treatments that include surgical interventions. Propensity score (PS) analysis of observational studies is an alternative method of estimating causal treatment effects for clinically important questions in observational studies, and well-designed observational studies can also help enhance and complement the findings of randomized studies [1]. Although it cannot be regarded as a replacement for randomized studies, data generated from large observational cohorts have been used to evaluate important clinical questions where data from randomized trials are limited or do not exist (Black 1996; Silverman 2009) [2, 3]. Observational studies also tend to have lower barriers and cost to subject recruitment which may accelerate participation and accrual.

PS analysis is a causal inference technique for treatment effect estimation in observational studies by accounting for the conditional probability of treatment-selection, thus allowing for reduction of bias when comparing interventions between treatment arms [4, 5]. This approach offers researchers the ability to better understand the potential effect of medical interventions and treatments. The use of PS analysis has grown dramatically in the last decade with wider availability of large databases such as Surveillance, Epidemiology, and End Results-Medicare (SEER-Medicare), Centers for Medicare & Medicaid Services (CMS), and the National Cancer Data Base (NCDB).

Despite its practicality, PS analysis also presents analytical and interpretation challenges [6-9]. Importantly, the quality of reporting in PS analysis by studies can be variable, particularly since there are currently no standard reporting guidelines. Proper analyses and reporting can ensure that published results of PS analyses are reproducible,

which in recent years has been recognized as a crucial element for high quality research [10]. Lack of consistency in reporting study results also has implications for those who plan to perform systematic review or meta-analyses [11].

The purpose of this study was to evaluate the reporting quality of PS analysis in cancer and cancer surgical studies by performing a systematic review of publications in top medical and surgery journals. We sought to highlight the challenges and issues associated with reporting PS analyses, and to investigate evolving trends by publication year. Finally, we aimed to develop a set of reporting guidelines that could be used to help standardize future work.

METHODS

Search Strategy and Study Selection

A three-part literature search of PS analysis in cancer and cancer surgical studies was conducted in the MEDLINE database using PubMed. Two primary cohorts of publications were created. The first cohort of Propensity Score Cancer Studies (CS) was created using a systematic search using the key words cancer and propensity score, propensity matched, or propensity analysis across the top 10 general medical journals and top 15 cancer journals (based on Web of Knowledge impact factors, listing in Supplementary Method, and searched on December 28 2015). Articles reported between 2014 and 2015 were identified. Publication of comments, meta-analysis, or reviews, and studies not focusing on cancer were excluded. The second cohort of Propensity Score Cancer Surgical Studies (CSS) was created with a similar search using the same key words but with an additional key word ‘surgery’ among

studies published through November 26 2015, and without date and journal limits (date of search: December 11 2015). A broader criteria for CSS cohort would allow us to compare the quality of reporting over time and among surgery journals of differing impact factors. Studies were eligible for inclusion if their primary question involved surgery among cancer patients, including both comparisons between surgical and non-surgical treatment as well as comparisons between different types of surgery. Studies that involved quality of life or cost burden as the primary outcome, did not have full-text available for review, or were classified as comments, meta-analysis, reviews, or protocols were excluded. A third analysis was then performed examining time trends of cancer studies and cancer surgical studies utilizing PS analysis among high impact journals between 2000 and 2015, using similar search criteria applied to the top 10 general medical journals, top 15 cancer journals, and top 15 surgery journals.

Titles and abstracts for all articles were screened in duplicate by two of the authors (XIY and PC) to independently render decisions regarding inclusion of each article. When consensus could not be reached, the two investigators reconciled the difference through reappraisal of the full text or after review by a third investigator (HP).

Data Extraction

Articles meeting eligibility criteria were included for data abstraction. Study characteristics recorded were cancer type, number of patients enrolled, number and type of treatments, study design, study endpoint and analysis, publication date, and journal. PS elements extracted included PS methods used in the estimation of treatment effect, variables used in PS estimation, whether any non-baseline variables were included, the comparability of baseline characteristics in PS analyses, and the total number of subjects included in the matched

analysis and matching algorithm utilized (if PS matching study). The evaluation of matching algorithm was abstracted, including distance metric (greedy nearest neighbor matching, greedy matching within specified caliper distances, greedy matching by digit, greedy matching without distance metric specified, and optimal matching), matching ratio, the use of replacement, and the method used to assess comparability of baseline characteristics between matched groups [12, 13]. The reporting of the assumptions of no unmeasured confounders and sufficient overlap in the propensity scores distribution, and goodness-of-fit of the model were also abstracted [4, 14, 15]. The reporting of variables used in PS estimation was classified as "Yes", "No", or "Unclear". Studies were classified as "Yes" if the variables were listed out or clearly defined and were classified as "No" if the variables were neither mentioned in text, tables, nor appendices/supplementary materials. Otherwise, the study was classified as "Unclear" if the variables were not clearly reported (e.g., the variables were reported as "all relevant covariates" or "all covariates potentially predictive of treatment" without any clear definition or statement). If the answer of reporting of variables used in PS estimation was "No" or "Unclear", the item whether non-baseline variables were included was defined as "Not evaluable". The reporting of matching algorithm was recorded as "Yes" when the method used to form matched sets of subjects was stated (e.g. greedy matching, optimal matching). Other aspects such as completeness of follow-up and accuracy of endpoint assessment were not taken into consideration.

Variables related to reporting of PS estimation, comparability of baseline characteristics, and matching algorithm were collected and verified by two authors (XIY and PC) and then confirmed by a third author (HP). Interrater agreement was assessed for four variables (PS methods used in the estimation of treatment effect, cancer type, variables used to estimate the PS, and matching algorithm) with sixty randomly selected articles by two data extractors XIY and PC separately. The corresponding Cohen's κ coefficients for these four

variables were 0.95, 1.00, 0.82, and 1.00, respectively, which indicated substantial to perfect interrater agreement [16]. No important discrepancies were observed.

Statistical Methods

Categorical variables for characteristics and reporting of CS and CSS were described with frequencies and percentages. Median and interquartile range were used for number of patients enrolled. To investigate evolving trends by publication year and reporting quality in differently ranked journals, Fisher's exact tests were used to compare the reporting of CSS published on or before 2013 versus 2014/2015, and to compare the reporting quality of top 15 versus non-top 15 surgery journals from CSS. 95% confidence intervals for difference in proportions were also reported. All reported P values were two-sided, and $P< 0.05$ was considered statistically significant. Statistical analysis was performed using R version 3.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Selection and Time Trends

We identified 37 cancer-focused studies involving PS methods reported in top medical/cancer journals between 2014 and 2015, of which 33 met the inclusion criteria (18 in JCO, 6 in JNCI, 4 in BMJ, 3 in The Lancet Oncology, and 2 in JAMA [Fig 1A]). For cancer surgical studies, 505 citations were identified via PubMed (Fig 1B). 480 articles were selected after screening titles and abstracts, and 306 eligible articles were included on the basis of their full text. The

most common reason for exclusion among these publications was that the primary question did not involve surgery.

Time trends of cancer studies reporting use of PS analysis between 2000 and 2015 among the top medical/cancer and surgery journals are presented in Fig 2. The number of cancer studies using PS has grown markedly in recent years. The last two years alone accounted for more than 50% of the total papers published in the past decade. The top three journals were Journal of Clinical Oncology (N = 37), Journal of Thoracic and Cardiovascular Surgery (N = 29), and Annals of Surgical Oncology (N = 28). A fairly similar time trend was also found in CSS cohort (Supplementary Fig S1) with 172 articles published in 2014 and 2015 and 134 articles published up through 2013.

Characteristics of Included Studies

Table 1 describes the main characteristics of studies reviewed. The top three cancer types in CS and CSS were gastrointestinal cancer, followed by lung cancer, then genitourinary cancer. CS tended to enroll more patients than CSS, with a median of 4515 (Q1 to Q3, 1392 to 20600) versus 699 (Q1 to Q3, 307 to 2783). Among the PS matching papers, 19.0% of CS did not mention the proportion of matched sample size, i.e. sample size after matching over sample size before matching, while it was only 5.5% for CSS. In addition, the overall matched proportion was less than 50% in 8 CS (38.1%) and 115 CSS (52.5%). For the matched proportion of the targeted treatment group, see Supplementary Table S2. Most of the articles reviewed compared two treatments (97.0% and 90.5%, respectively). There was only one CS (3%) involving more than two treatment groups, compared to 29 CSS (9.5%). The frequencies of different PS methods (i.e. propensity score matching (PSM), propensity score weighting (PSW), propensity score stratification (PSS), covariate adjustment using

propensity score (CAPS) and more than one type of PS methods) as reported across the studies are available in Table 1. Overall, 16 CS (48.5%) and 207 CSS (67.6%) utilized PSM; 6 CS (18.2%) and 21 CSS (6.9%) utilized more than one type of PS methods, for example both PSM and PSW. A summary on the study design and the study endpoint and analysis can be found in Supplementary Tables S3 and S4. Majority of the articles focused on survival or time-to-event outcomes (81.8% and 73.2%, respectively), followed by dichotomous or discrete outcomes (18.2% and 31.4%, respectively) and continuous outcomes (3.0% and 12.7%, respectively). More than one primary outcomes were of interest in some studies, therefore the total percentages are over 100.

Reporting of PS Methodology

There were 4 CS (12.1%) and 27 CSS (8.8%) that did not provide the variables used in PS estimation clearly (Table 2). In addition, 1 CS (3.4%) and 26 (9.3%) CSS incorrectly included non-baseline variables. In 32 CS and 275 CSS, which involved PSM, PSW, or PSS methods, 7 (21.9%) and 43 (15.6%) of the studies, respectively, did not report the comparability of baseline characteristics between treated and untreated subjects in the matched, weighted, or stratified sample. For those 25 CS and 232 CSS that did report baseline comparisons, 2 CS (8.0%) and 31 CSS (13.4%) found imbalanced characteristics. Among the 21 CS and 219 CSS that utilized PSM, 4 CS (19.0%) and 79 CSS (36.1%) did not report the matching algorithm. 4 CS (19.0%) and 97 CSS (44.3%) did not report the distance metric. The matching ratio was reported by all CS, but not reported in 8 CSS (3.7%). 15 CS (71.4%) and 188 CSS (85.8%) did not report whether replacement was used. 16 CS (76.2%) and 195 CSS (89.0%) assessed the comparability of baseline characteristics between matched groups, while 4 CS (19.0%) and 93 CSS (42.5%) did not clearly state the method used. 13 CS (39.4%) and 73 CSS (23.9%) discussed or mentioned the assumption of no unmeasured

confounders. 4 CS (12.1%) and 14 CSS (4.6%) described the distribution of propensity scores among the compared treatment groups. 1 CS (3.0%) and 28 CSS (9.2%) assessed the goodness-of-fit of the PS estimation model, while 2 CS (6.1%) and 14 CSS (4.6%) assessed the goodness-of-fit of the outcome model.

The reporting of matching algorithm in CSS improved in the last two years (P = 0.043) (Table 3). However, there were no significant improvements for the reporting of variables used (P = 0.226), inclusion of non-baseline variables (P = 0.219), and reporting of comparability of baseline characteristics (P = 0.135). The reporting of variables used to estimate PS was better in top 15 surgery journals (P = 0.008) (Table 3). However, there were no significant differences for the inclusion of non-baseline variables (P = 0.487), reporting of comparability of baseline characteristics (P = 0.424), and reporting of matching algorithm (P = 0.308).

DISCUSSION

The number of manuscripts utilizing PS methods in cancer and cancer surgical journals has rapidly increased in recent years, likely driven in large part by the increasing availability of large databases, such as SEER-Medicare, CMS, and NCDB. In this evaluation of the quality of PS reporting in over 300 cancer-related observational studies, we demonstrate that essential methodological information is often not reported. Our results indicate that the quality of PS reporting in cancer studies requires substantial improvement, even in high-impact factor journals. Our findings clearly support the need for reporting guidelines for PS analyses.

Inadequate reporting of PS analyses could have significant consequences on the interpretation of a study's findings, and potentially impact either subsequent research or even clinical care. First, the design of future clinical studies and patient management can be informed by the results of these large PS analyses. Second, inadequate reporting of variables included in the PS model, not reporting the matching algorithm utilized, and inconsistent reporting of variables in the method and result sections, represents poor data provenance and can result in problems with study reproducibility and interpretation. For example, a considerable number of studies included in our analysis, 21.9% CS and 15.6% CSS, did not report the comparability of measured baseline characteristics after the application of the PS methods, which makes it difficult to judge the appropriateness and effectiveness of the PS analysis and its results [17]. Moreover, comparisons of balance among measured baseline variables should be performed with proper methods for matched samples [8, 9]. The recommended methods to assess the comparability of baseline characteristics between matched groups include the standardized difference (< 10%) and the C-statistic (close to 0.5) [13, 18].

Another area of concern that we identified relates to limited reporting of matched sample size proportions. Incomplete matching can bias the research findings, especially when a sizable proportion of subjects in the treatment group are excluded after matching. The inference of treatment effects derived from a limited subset of subjects can systematically differ from the target population for inference, which means that the estimated average treatment effect on the treated can be biased. When choosing the best matching algorithm (as well as the distance metric, ratio, and the use of replacement), there usually exists a trade-off between the bias from sizable sample loss and residual confounding from the inclusion of poorly matched subjects [19]. Therefore, the reporting of matched sample size proportions

and whether the covariate distribution after matching is subsequently retained for the treatment comparison have important implications regarding the interpretation of results.

Despite the broad usage, PS analysis is limited by its inability to control for unmeasured confounders and variables measured with error [14, 15]. However, as we have noted in the results section these assumptions were often not reported. Also, a low proportion of studies reported the amount of overlap in the propensity scores distributions among the matched treatment groups. Sufficient overlap in the distribution of propensity scores among the comparison groups is also an important assumption in PS analysis to ensure valid causal inference [20-22].

Finally, lack of consistency in reporting study methods and results gives rise to difficulty in performing systematic reviews or meta-analyses. Prior studies have shown that inappropriate and poor reporting can lead to misleading results and can waste valuable resources [10, 23-25]. The lack of consistency across the reporting of PS analyses calls for a more standardized and reproducible reporting of study methods and results, especially considering the dramatic increase in the recent use of these statistical methods in studies of cancer patients.

To improve consistency and reproducibility, we propose a set of guidelines and recommendations (a concise list shown in Table 4 with an expanded version in Supplementary Table S5) to ensure comprehensive, complete, and clear reporting in PS analyses. Based on the systematic review, items that could impact the reproducibility and interpretability of a PS analysis were generated. These items were then integrated with the STROBE categories for reporting observational studies [26]. We believe that following the proposed guidelines should substantially improve the reporting quality of PS analysis. While

cancer and cancer surgery studies were used to generate these guidelines because of the authors combined expertise and the growing use of PS analyses in the oncology literature in recent years (Supplementary Fig S2), the recommendations put forward apply to a broad range of observational research. Of these recommendations, perhaps the most important include the need to state the specific PS method(s) used, to specify the model used in PS estimation including the variables used, to describe comparisons of baseline characteristics, and to explicitly specify the method used to form matched sets of subjects, if matching is used. The set of guidelines should not be viewed as a comprehensive manual for conducting proper statistical analyses using PS methods, but it should be viewed as a tool for consistent reporting, reproducibility and interpretation of PS analysis. These guidelines are a first step toward improving PS analysis reporting and can be further refined.

While consistent reporting, reproducibility and interpretation of PS analysis are our primary focuses, we would like to highlight a few references related to the proper use of PS analysis. A few studies reviewed made comparisons among more than two treatment groups. In this instance, special approaches are needed to fit propensity scores. Investigators should, for example, use a multinomial logistic regression, a multinomial probit model, or a series of binary probits to estimate propensity scores [19, 27]. PS analysis has been occasionally used in case-control studies. In this review we have one example of this study design. When applying PS analysis to case-control study, the investigator should consider the impact of artifactual effect modification and residual confounding on the study findings. More complete discussion on this topic can be found in Månsson et al. (2007) [28]. In this paper, the studies investigated did not involve the effect of time-varying treatment. If the effect of time-varying treatment is of interest, special considerations of time-varying covariates for PS estimation will be necessary [29, 30]. When using PSS method, the number of strata should be chosen based on an analysis of the rate at which the number of strata should increase with sample

size to reduce residual confounding [6]. In general, it has been found that PSW is less prone to model misspecification than CAPS [31]. In addition, when the numbers of outcomes are low relative to the number of confounders, confounder control through use of PS analysis provides less biased and more precise estimated treatment effects than multivariable logistic regression [32]. PS analysis allows for the estimation of marginal treatment effect, an average effect at the population level, whereas multivariable regression yields conditional treatment effect, an average effect at the individual level [33]. When outcomes are binary or time-to-event in nature, which are of primary interest in most studies in this review, the marginal odds ratio or hazard ratio would generally be closer to the null than the conditional effect, while the statistical significance of the estimates was usually similar [34-36]. Moreover, Knol et al. (2012) offered some suggestions in reporting the effect interaction and modification [37].

In this study, we analyze the existing oncology literature to develop a set of novel guidelines for reporting PS analyses. In an era of rapidly increasing use of PS techniques, such guidelines are essential to promote study reproducibility and to responsibly inform patient care and future prospective research. This is a large scale study to scrutinize and evaluate the reporting of PS analyses. Importantly, the descriptions and analyses of the quality of PS reporting are not unique to cancer studies, but our guidelines serve as a framework for evaluating the quality of reporting in PS analyses in other areas as well. Our reporting guidelines can also serve as an evaluation tool in the peer-review process for assessing future research involving PS analysis. Our study closely followed the PRISMA checklist as illustrated in Supplementary Table S6.

Despite notable strengths, our study has some limitations. First, the literature search utilized was based only on literature contained within the MEDLINE database and reported

in PubMed. However, recent studies have shown that using data sources beyond PubMed has only modest impact on the results of systematic reviews [38, 39]. Second, the cancer studies in top journals included in this review were limited to those published between 2014 and 2015. Despite this, the studies included accounted for more than half of the literature utilizing PS methods published to date, and represent the most contemporary use of PS methods in the current literature.

In conclusion, propensity score analysis is a statistical technique commonly used to estimate causal treatment effects for clinical interventions in observational studies. The use of this analytical approach has particularly increased in clinical research involving surgical interventions. We find that current reporting is often inadequate and ambiguous, even in high impact medical journals. Accordingly, we propose rational reporting guidelines to foster transparency, consistency and to facilitate interpretation by readers. The purpose of these guidelines is to set forth a comprehensive and clear checklist to maximize the value of research that leverages PS techniques.

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Figure Legends

Fig 1. Process of literature search (A) cancer studies in top medical and cancer journals (B) cancer surgical studies

Fig 2. Publication trends in cancer studies reporting use of propensity score analysis in high impact medical/cancer and surgery journals

Supplementary Fig S1. Published surgical studies in cancer using propensity score analysis

Supplementary Fig S2. Publication trends of studies reporting use of propensity score analysis in cancer, cardiovascular disease, and diabetes

Table Legends

Table 1. Characteristics of included studies

Table 2. Reporting of propensity score analysis in included studies

Table 3. Reporting quality of cancer surgical studies by publication year (on or before 2013 versus 2014/15) and by journal ranking (non-top 15 versus top 15)

Table 4. Brief guidelines for reporting propensity score analysis

Supplementary Table S1. List of reasons for exclusion in the process of literature search of cancer surgical studies

Supplementary Table S2. The matched proportion of the targeted treatment group of included studies

Supplementary Table S3. Study design and endpoint of included studies

Supplementary Table S4. Analysis of included studies

Supplementary Table S5. Full guidelines for reporting propensity score analysis

Supplementary Table S6. Completed PRISMA Checklist

Table 1. Characteristics of included studies

Variables	**Cancer Studies*** No. of Studies / Total No. (%)	**Cancer Surgical Studies** No. of Studies / Total No. (%)
Cancer type		
Gastrointestinal cancer	7/33 (21.2)	118/306 (38.6)
Lung cancer	7/33 (21.2)	89/306 (29.1)
Genitourinary cancer	6/33 (18.2)	67/306 (21.9)
Breast cancer	5/33 (15.2)	20/306 (6.5)
Thyroid cancer	0	5/306 (1.6)
Head and neck cancers	0	3/306 (1.0)
Hematopoietic and lymphoid cancers	3/33 (9.1)	0
Skin cancer	1/33 (3.0)	0
Nervous system cancer	0	1/306 (0.3)
Advanced/metastatic cancer	3/33 (9.1)	0
Others	1/33 (3.0)	3/306 (1.0)
No. of treatment groups		
2	32/33 (97.0)	277/306 (90.5)
3	1/33 (3.0)	21/306 (6.9)
≥4	0	8/306 (2.6)
No. of patients enrolled		
Median	4515	699
Q1 to Q3	1392 to 20600	307 to 2783
Not mentioned	0	3/306 (1.0)
Propensity score methods type		
Propensity score matching	16/33 (48.5)	207/306 (67.6)
Propensity score weighting	9/33 (27.3)	20/306 (6.5)
Propensity score stratification	1/33 (3.0)	27/306 (8.8)
Covariate adjustment using propensity score	1/33 (3.0)	31/306 (10.1)
More than one type	6/33 (18.2)	21/306 (6.9)
The proportion of matched sample size†		
<25%	2/21 (9.5)	35/219 (16.0)
25%-<50%	6/21 (28.6)	80/219 (36.5)
50%-<75%	3/21 (14.3)	53/219 (24.2)
75%-<100%	6/21 (28.6)	14/219 (6.4)
Not mentioned	4/21 (19.0)	12/219 (5.5)
Only reported the matched sample	0	25/219 (11.4)

* cancer studies in top medical and cancer journals in 2014/15

† The reporting of the proportion of matched sample size was evaluated in studies utilizing matching.

Nine studies were included in both cancer studies and cancer surgical studies.

Table 2. Reporting of propensity score analysis in included studies

Variables	**Cancer Studies*** No. of Studies / Total No. (%)	**Cancer Surgical Studies** No. of Studies / Total No. (%)
Variables used to estimate the PS		
Yes	29/33 (87.9)	279/306 (91.2)
No/Unclear	4/33 (12.1)	27/306 (8.8)
Inclusion of non-baseline variables†		
Yes	1/29 (3.4)	26/279 (9.3)
No	28/29 (96.6)	253/279 (90.7)
Comparability of baseline characteristics‡		
Yes	25/32 (78.1)	232/275 (84.4)
No	7/32 (21.9)	43/275 (15.6)
Matching algorithm§		
Yes	17/21 (81.0)	140/219 (63.9)
No	4/21 (19.0)	79/219 (36.1)
Distance metric§		
Greedy nearest neighbor matching	4/21 (19.0)	46/219 (21.0)
Greedy matching within specified caliper distances	8/21 (38.1)	49/219 (22.4)
Greedy matching by digit	4/21 (19.0)	19/219 (8.7)
Greedy matching without distance metric specified	0	18/219 (8.2)
Optimal matching	1/21 (4.8)	8/219 (3.7)
Not reported	4/21 (19.0)	79/219 (36.1)
Matching ratio§		
Yes	21/21 (100)	211/219 (96.3)
No	0	8/219 (3.7)
Use of replacement§		
With replacement	1/21 (4.8)	4/219 (1.8)
Without replacement	5/21 (23.8)	27/219 (12.3)
Not reported	15/21 (71.4)	188/219 (85.8)
Method to assess comparability of baseline characteristics between matched groups§		
Standardized difference	6/21 (28.6)	31/219 (14.2)
C-statistic	0	17/219 (7.8)
Absolute difference	1/21 (4.8)	1/219 (0.5)
Paired test‖	2/21 (9.5)	20/219 (9.1)
Independent sample test¶	3/21 (14.3)	31/219 (14.2)
Regression	0	2/219 (1.0)
Assessed but method not reported	4/21 (19.0)	93/219 (42.5)
Not assessed	5/21 (23.8)	24/219 (11.0)
Imbalanced baseline characteristics#		
Yes	2/25 (8.0)	31/232 (13.4)
No	23/25 (92.0)	201/232 (86.6)

* cancer studies in top medical and cancer journals in 2014/15

† The reporting of whether non-baseline variables were included was not evaluable if the answer of reporting of variables used to estimate the PS was "No/Unclear".
‡ The reporting of comparability of baseline characteristics in PS analyses was evaluated in studies utilizing matching, weighting, or stratification.
§ The reporting was evaluated in studies utilizing matching.
|| The statistical test for paired or matched sample, e.g. paired t-tests, Wilcoxon signed rank test, and McNemar's test
¶ The statistical test for independent sample, e.g. unpaired t-tests, Wilcoxon rank sum test, chi-squared test, and Fisher's exact test
# The reporting of whether baseline characteristics were imbalanced was evaluated in studies reporting comparability of baseline characteristics.
Nine studies were included in both cancer studies and cancer surgical studies.

Table 3. Reporting quality of cancer surgical studies by publication year (on or before 2013 versus 2014/15) and by journal ranking (non-top 15 versus top 15)

Variables	**Cancer Surgical Studies**		P value	**Cancer Surgical Studies**		P value
	On or before 2013	2014/15		Non-Top 15 journals	Top 15 journals	
Variables used to estimate the PS						
Yes	119 (88.8%)	160 (93.0%)	0.226	208 (88.9%)	71 (98.6%)	0.008
No/Unclear	15 (11.2%)	12 (7.0%)		26 (11.1%)	1 (1.4%)	
Difference in proportions (95% CI)	-	4.2 (-2.7, 11.8)		-	9.7 (1.7, 14.8)	
Inclusion of non-baseline variables						
Yes	8 (6.7%)	18 (11.3%)	0.219	18 (8.7%)	8 (11.3%)	0.487
No	111 (93.3%)	142 (88.8%)		190 (91.3%)	63 (88.7%)	
Difference in proportions (95% CI)	-	4.5 (-3.3, 11.7)		-	2.6 (-5.1, 13.4)	
Comparability of baseline characteristics						
Yes	95 (80.5%)	137 (87.3%)	0.135	179 (83.3%)	53 (88.3%)	0.424
No	23 (19.5%)	20 (12.7%)		36 (16.7%)	7 (11.7%)	
Difference in proportions (95% CI)	-	6.8 (-2.4, 16.4)		-	5.1 (-7.3, 13.8)	
Matching algorithm						
Yes	47 (55.3%)	93 (69.4%)	0.043	113 (65.7%)	27 (57.4%)	0.308
No	38 (44.7%)	41 (30.6%)		59 (34.3%)	20 (42.6%)	
Difference in proportions (95% CI)	-	14.1 (0.4, 27.6)		-	-8.3 (-25.0, 7.7)	

CI = confidence interval

Table 4. Brief guidelines for reporting propensity score analysis

	Item	No.*	Recommendation
Title and abstract	□	1	Indicate the use of propensity analysis with a commonly used term in the title or the abstract
Methods			
Bias	□	9	Describe how propensity score analysis was used to address bias
Statistical analyses	□	12	Describe all the analytic methods, including the propensity score methods, e.g. PSM, PSW, PSS, CAPS
	□	13	Indicate the model used to estimate propensity score
	□	14	State the variables included in the propensity score model
	□	15	Explain the variable selection procedure for propensity score model
	□	16	PSM: explicitly state the matching algorithm and distance metric, indicate matching ratio (1:m matching), indicate whether sampling with or without replacement was used, describe the statistical methods for the analysis of matched data, report the package used to create matched sample, and describe methods for assessing the comparability of baseline characteristics in the matched groups
	□	17	PSW: describe methods for assessing the comparability of baseline characteristics in the weighted groups
	□	18	PSS: give the number of strata and describe methods for assessing the comparability of baseline characteristics in each stratum
	□	19	Explain how assumption of propensity score analysis was examined
	□	20	Explain how missing data in propensity score estimation were addressed
Results			
Participants	□	25.4	PSM: report the sample size for each treatment group before and after matching
Patient characteristics	□	28	Describe the distribution of baseline characteristics for each group before propensity score analysis
	□	29	PSM, PSW, PSS: describe the distribution of baseline characteristics in the matched/weighted groups or in each stratum, and describe the results of the comparability of baseline characteristics
	□	30	Indicate number of patients with missing data for each variable of interest, especially the variables used in propensity score model
Main results	□	32	Give propensity score analysis estimates and their precision, e.g. 95% confidence interval
	□	33	If applicable, give unadjusted estimates and/or adjusted estimates and their precision, e.g. 95% confidence interval. Make clear which additional factors were adjusted for
Discussion			
Interpretation	□	38	Discuss whether imbalance of baseline characteristics still exists, and give a cautious interpretation
Generalizability	□	40	PSM: discuss the possibility and potential influence of incomplete matching, especially the studies in which the matched sample size is less than 50%

PSM = propensity score matching, PSW = propensity score weighting, PSS = propensity score stratification, CAPS = covariate adjustment using propensity score

* For full guidelines, refer to the Supplementary Table S5

Figure 1 A

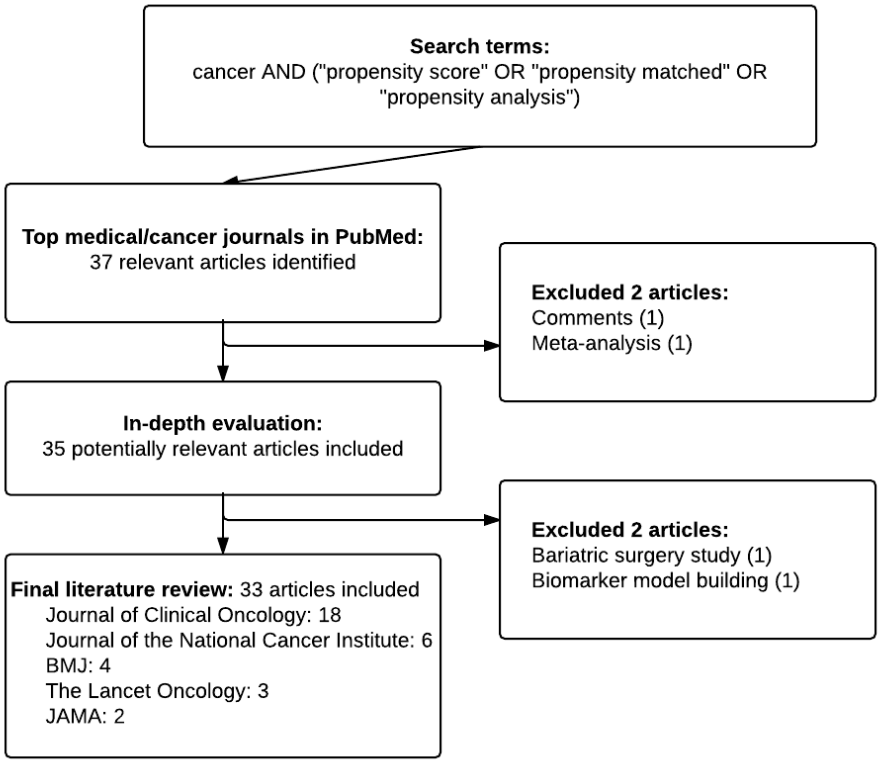
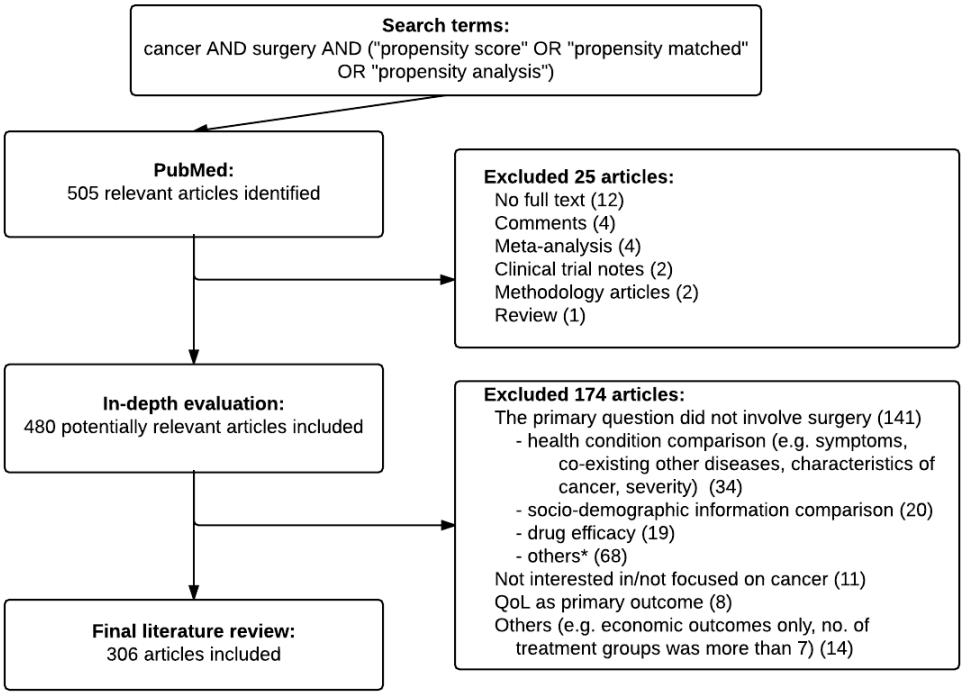
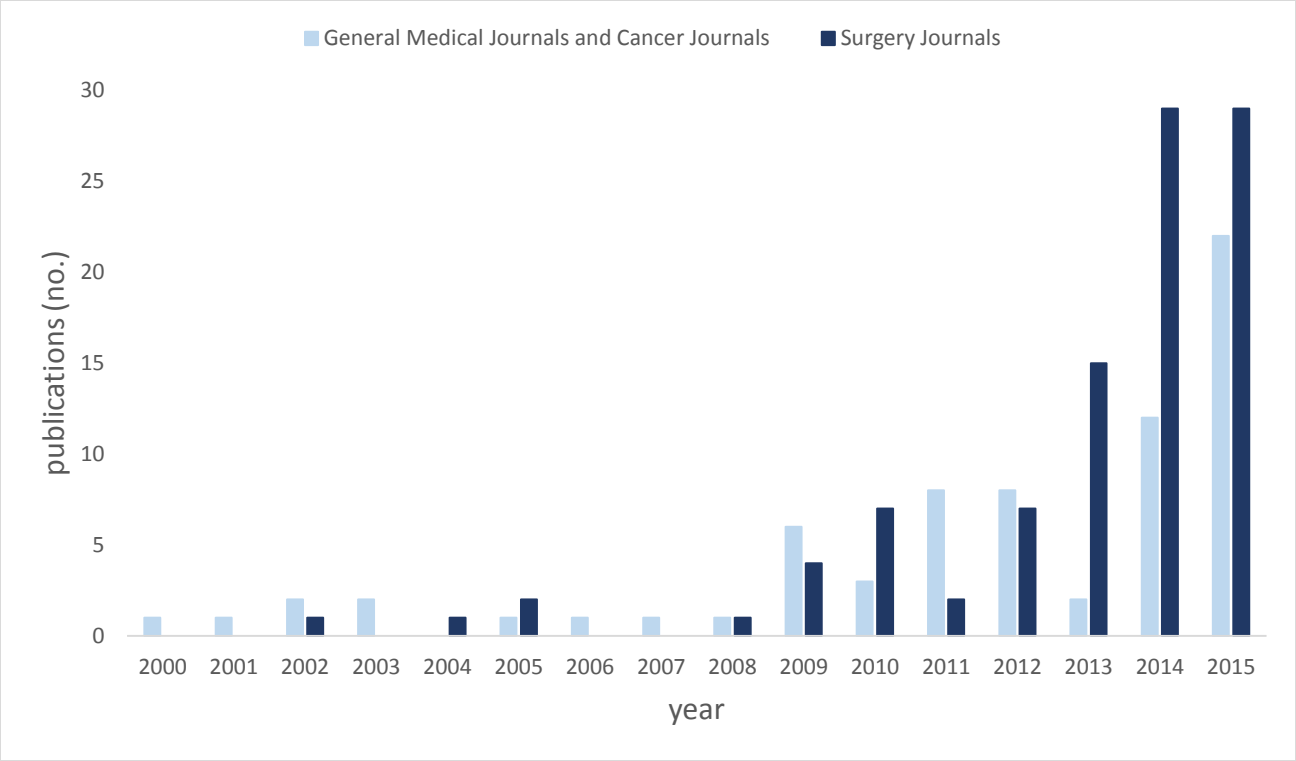


Figure 1 B



* Other reasons are given in Supplementary Table S1.

Figure 2



SUPPLEMENTARY MATERIALS

Reporting and Guidelines in Propensity Score Analysis: A Systematic Review of Cancer and Cancer Surgical Studies

Xiaoxin I. Yao[1,#], Xiaofei Wang[2,#,*], Paul J. Speicher[3], E. Shelley Hwang[3], Perry Cheng[1], David H. Harpole[3], Mark F. Berry[4], Deborah Schrag[5], Herbert H. Pang[1,2]

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Supplementary Methods

Top 10 general medical journals, top 15 cancer journals, and top 15 surgery journals, based on Web of Knowledge impact factors 2014 (http://admin-apps.webofknowledge.com/JCR/JCR)

Top 10 general medical journals

1	NEW ENGL J MED
2	LANCET
3	JAMA
4	ANN INTERN MED
5	BMJ
6	ARCH INTERN MED
7	PLOS MED
8	JAMA INTERN MED
9	BMC MED
10	J CACHEXIA SARCOPENI

Top 15 cancer journals

1	CA-CANCER J CLIN
2	NAT REV CANCER
3	LANCET ONCOL
4	CANCER CELL
5	CANCER DISCOV
6	J CLIN ONCOL
7	NAT REV CLIN ONCOL
8	J Natl Cancer Inst
9	LEUKEMIA
10	SEMIN CANCER BIOL
11	CANCER RES
12	CLIN CANCER RES
13	ONCOGENE
14	BBA-REV CANCER
15	CANCER TREAT REV

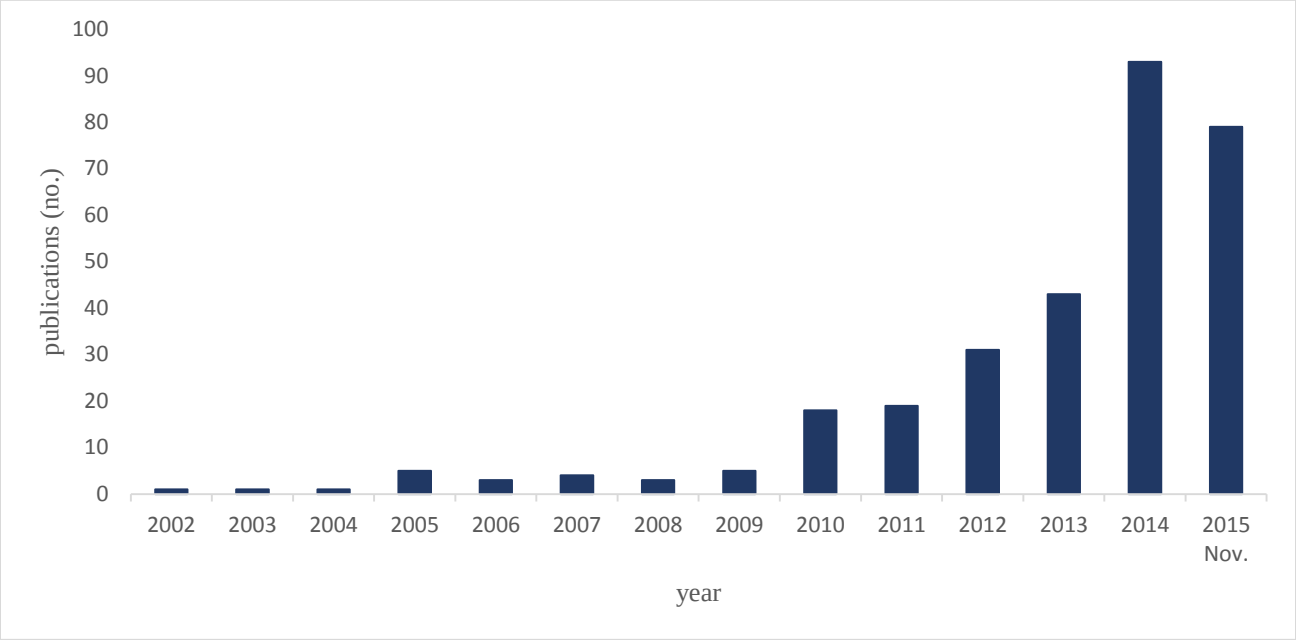
Top 15 surgery journals

1	ANN SURG
2	J NEUROL NEUROSUR PS
3	J HEART LUNG TRANSPL
4	AM J TRANSPLANT
5	BRIT J SURG
6	J BONE JOINT SURG AM
7	AM J SURG PATHOL
8	J AM COLL SURGEONS

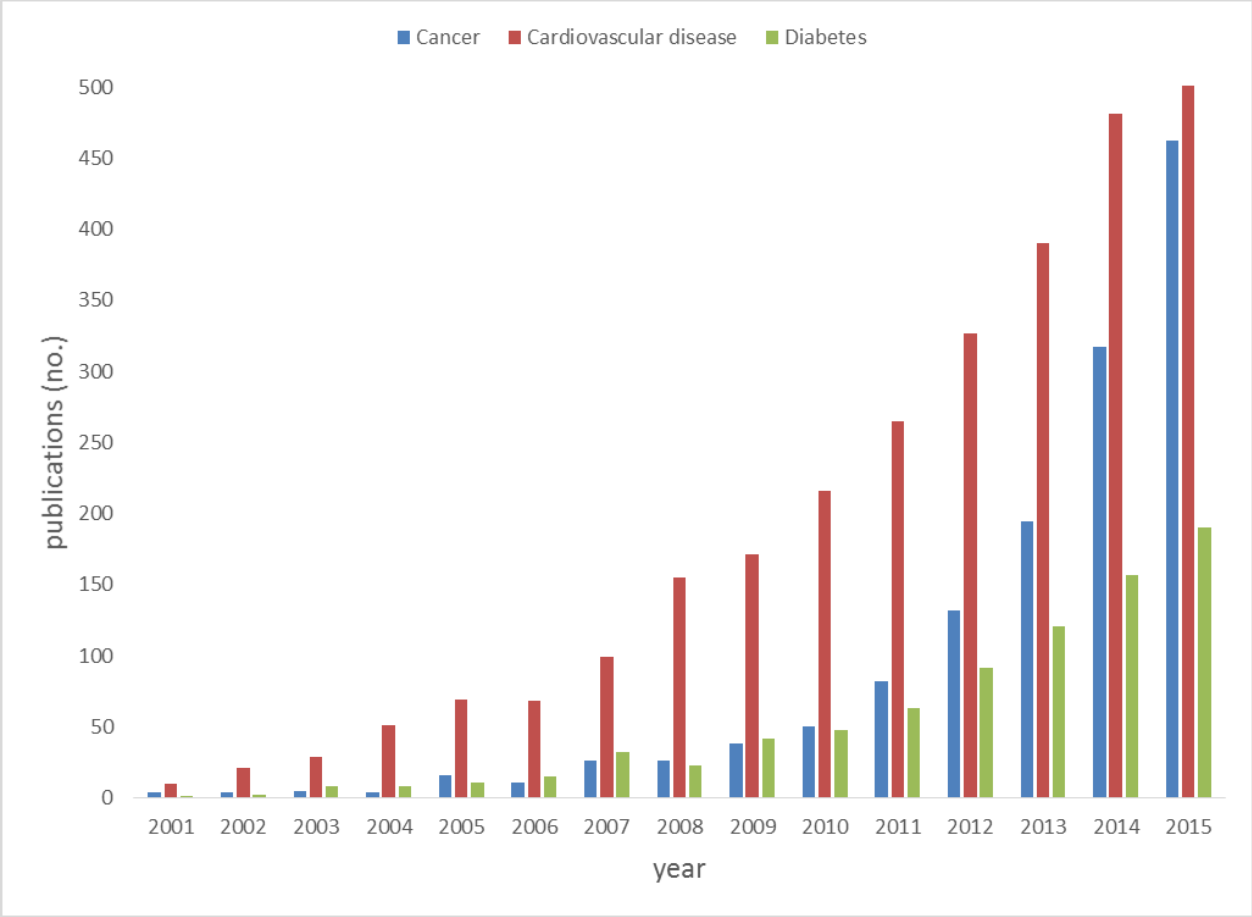
9	ENDOSCOPY
10	ARCH SURG-CHICAGO
11	LIVER TRANSPLANT
12	J THORAC CARDIOV SUR
13	SURG OBES RELAT DIS
14	JAMA SURG
15	ANN SURG ONCOL

Supplementary Figures

Supplementary Figure 1. Published surgical studies in cancer using propensity score analysis



Supplementary Figure 2. Publication trends of studies reporting use of propensity score analysis in cancer, cardiovascular disease, and diabetes



Supplementary Tables

Supplementary Table 1. List of reasons for exclusion in the process of literature search of cancer surgical studies - The primary question did not involve surgery

Primary question	No. of Studies
Health condition comparison (e.g. symptoms, co-existing other diseases, characteristics of cancer, severity)	34
Socio-demographic information comparison	20
Drug efficacy	19
Characteristics of hospital (e.g. hospital volume)	9
Radiation	8
Analgesia/anesthesia	7
Blood transfusion	6
Characteristics of medical practitioner (e.g. surgeon specialization, surgeon volume, changing urologists)	5
Chemotherapy	5
Diagnostic methods (e.g. CT, MRI)	5
Hormone therapy	4
The standard of care	4
Implant	4
Adherence to treatment guideline	3
An oral enzyme	1
Anal decompression	1
Association between utility and treatment	1
Length of interval	1
Physiotherapy	1
Preoperative mechanical bowel preparation	1
Self-referral	1
Skin closure methods	1

Supplementary Table 2. Completed PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3,4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	no
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4,5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4,5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4,5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4,5

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5,6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5,6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7; figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8,9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9,10
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			

Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10-15
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	15

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Supplementary Table 3. The matched proportion of the targeted treatment group of included studies *

Proportion	Cancer Studies†	Cancer Surgical Studies
	No. of Studies/Total No. (%)	No. of Studies/Total No. (%)
<25%	1/21 (4.8)	5/219 (2.3)
25%-<50%	2/21 (9.5)	32/219 (14.6)
50%-<75%	2/21 (9.5)	28/219 (12.8)
75%-<100%	10/21 (47.6)	93/219 (42.5)
Not mentioned	4/21 (19.0)	13/219 (5.9)
Not evaluable‡	2/21 (9.5)	23/219 (10.5)
Only reported the matched sample	0	25/219 (11.4)

* The reporting was evaluated in studies utilizing matching. Nine studies were included in both cancer studies and cancer surgical studies.
† Cancer studies in top medical and cancer journals in 2014/15
‡ The proportion was not evaluable if there is no clear definition of which arm is the targeted treatment group.

Supplementary Table 4. Study design and endpoint of included studies

Variables	Cancer Studies*	Cancer Surgical Studies
	No. of Studies/Total No. (%)	No. of Studies/Total No. (%)
Study design		
Cohort	32/33 (97.0)	306/306 (100.0)
Case-control	1/33 (3.0)	0
Study endpoint		
Continuous outcome	1/33 (3.0)	39/306 (12.7)
Dichotomous/discrete outcome	6/33 (18.2)	96/306 (31.4)
Survival/time-to-event outcome	27/33 (81.8)	224/306 (73.2)

* Cancer studies in top medical and cancer journals in 2014/15. Nine studies were included in both cancer studies and cancer surgical studies.

Supplementary Table 5. Analysis of included studies

Analysis used in:	Cancer Studies*	Cancer Surgical Studies
	No. of Studies/ Total No. (%)	No. of Studies/ Total No. (%)
Studies with continuous outcome	N = 1	N = 39
Independent sample test†	0	23/39 (59.0)
Paired test‡	0	9/39 (23.1)
Linear regression	1/1 (100.0)	6/39 (15.4)
Not reported	0	1/39 (2.6)
Studies with dichotomous/discrete outcome	N = 6	N = 96
Independent sample test§	0	27/96 (28.1)
Paired test‖	0	12/96 (12.5)
Logistic regression	6/6 (100.0)	56/96 (58.3)
Not reported	0	1/96 (1.0)
Studies with survival/time-to-event outcome	N = 27	N = 224
Log-rank test/Tarone-Ware test	2/27 (7.4)	55/224 (24.6)
Cox regression/flexible parametric survival model	20/27 (74.1)	89/224 (39.7)
Both log-rank test and Cox regression	4/27 (14.8)	72/224 (32.1)
Competing risks regression	1/27 (3.7)	8/224 (3.6)

* Cancer studies in top medical and cancer journals in 2014/15. Nine studies were included in both cancer studies and cancer surgical studies
† e.g. unpaired t-tests and Mann-Whitney U test
‡ e.g. paired t-tests and Wilcoxon signed-rank test
§ e.g. chi-squared test and Fisher's exact test
‖ e.g. McNemar's test and Cochran's Q test

Supplementary Table 6. Full guidelines for reporting propensity score analysis, modified From the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) Statement*

Section/topic	Item No		Recommendation
Title and abstract	□	1	Indicate the use of propensity analysis with a commonly used term in the title or the abstract
	□	2	Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction			
Background/rationale	□	3	Explain the scientific background and rationale for the investigation being reported
Objectives	□	4	State specific objectives, including any prespecified hypotheses
Methods			
Setting	□	5	Describe the setting, locations, and relevant dates, including periods of recruitment, treatment, follow-up, and data collection
Patient selection	□	6	Give the eligibility criteria, and the sources and methods of subject ascertainment and selection
Variables	□	7	Clearly define all outcomes, treatments, predictors. Give diagnostic criteria, if applicable
Data sources/ measurement	□	8	For each variable of interest, give sources of data and details of methods of assessment (measurement)
Bias	□	9	Describe how propensity score analysis was used to address bias
	□	10	Describe any other methods to address potential sources of bias, e.g. sensitivity analysis
Sample size	□	11	Explain how the study size was arrived at
Statistical analyses	□	12	Describe all the analytic methods, including the propensity score methods, e.g. matching, weighting, stratification, or covariate adjustment using propensity score
	□	13	Indicate the model used to estimate propensity score, e.g. logistic model, boosting (meta-classifiers), decision trees
	□	14	State the variables included in the propensity score model
	□	15	Explain the variable selection procedure for propensity score model
		16	For propensity score matching:
	□	16.1	Explicitly state the matching algorithm and distance metric
	□	16.2	Indicate matching ratio (1:m matching)
	□	16.3	Indicate whether sampling with or without replacement was used
	□	16.4	Describe the statistical methods for the analysis of matched data

	□	16.5	Describe methods for assessing the comparability of baseline characteristics in the matched groups
	□	17	For propensity score weighting, describe methods for assessing the comparability of baseline characteristics in the weighted groups
		18	For propensity score stratification:
	□	18.1	Give the number of strata
	□	18.2	Describe methods for assessing the comparability of baseline characteristics in each stratum
	□	19	Explain how assumption of propensity score analysis was examined
	□	20	Explain how missing data were addressed, including missing data in propensity score estimation
	□	21	If applicable, describe any methods used to examine subgroups and interactions
	□	22	Describe any sensitivity analyses
	□	23	Indicate the software used for analysis
	□	24	If applicable, report the package used to create matched sample, e.g. GMATCH macro in SAS, MatchIt package®, Optmatch package ®
Results			
Participants		25	Report numbers of participants at each stage of study:
	□	25.1	sample size of patients potentially eligible
	□	25.2	sample size of patients confirmed eligible and included
	□	25.3	sample size of patients analyzed
	□	25.4	for propensity score matching, sample size for each treatment group before and after matching
	□	26	Explain reasons for exclusion at each stage
	□	27	Consider use of a flow diagram
Patient characteristics	□	28	Describe the distribution of baseline characteristics for each group before propensity score analysis
		29	For propensity score matching, weighting, or stratification:
	□	29.1	Describe the distribution of baseline characteristics in the matched/weighted groups or in each stratum
	□	29.2	Describe the results of the comparability of baseline characteristics, whether there are still systematic differences between treatment groups
	□	30	Indicate number of patients with missing data for each variable of interest, especially the variables used in propensity score model
Outcome data	□	31	Report outcomes of each treatment group
Main results	□	32	Give propensity score analysis estimates and their precision, e.g. 95% confidence interval

	□	33	If applicable, give unadjusted estimates and/or adjusted estimates and their precision, e.g. 95% confidence interval. Make clear which additional factors were adjusted for
Other analyses	□	34	Report other analyses done, e.g. analyses of subgroups and interactions, and sensitivity analyses
Discussion			
Key results	□	35	Summarize key results with reference to study objectives
Limitations	□	36	Discuss limitations of the study, taking into account sources of potential bias or imprecision
	□	37	Discuss both direction and magnitude of any potential bias
Interpretation	□	38	Discuss whether imbalance of baseline characteristics still exists, and give a cautious interpretation
	□	39	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalizability	□	40	For propensity score matching, discuss the possibility and potential influence of incomplete matching, especially the studies in which the matched sample size is less than 50%
Other information			
Funding	□	41	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

* von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008;61(4):344-9.

This guideline can be downloaded at:

https://sites.duke.edu/xiaofeiwang/files/2017/03/Supplementary-Table-6.pdf