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Completion and Publication Rates of Randomized Controlled Trials in Surgery: An Empirical Study. — Source link

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Completion and publication rates of randomized controlled trials in surgery: an empirical study

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Abstract: OBJECTIVE:To investigate the prevalence of discontinuation and nonpublication of surgical versus medical randomized controlled trials (RCTs) and to explore risk factors for discontinuation and nonpublication of surgical RCTs. BACKGROUND:Trial discontinuation has significant scientific, ethical, and economic implications. To date, the prevalence of discontinuation of surgical RCTs is unknown. METHODS:All RCT protocols approved between 2000 and 2003 by 6 ethics committees in Canada, Germany, and Switzerland were screened. Baseline characteristics were collected and, if published, full reports retrieved. Risk factors for early discontinuation for slow recruitment and nonpublication were explored using multivariable logistic regression analyses. RESULTS:In total, 863 RCT protocols involving adult patients were identified, 127 in surgery (15%) and 736 in medicine (85%). Surgical trials were discontinued for any reason more often than medical trials [43% vs 27%, risk difference 16% (95% confidence interval [CI]: 5%-26%); P = 0.001] and more often discontinued for slow recruitment [18% vs 11%, risk difference 8% (95% CI: 0.1%-16%); P = 0.020]. The percentage of trials not published as full journal article was similar in surgical and medical trials (44% vs 40%, risk difference 4% (95% CI: -5% to 14%); P = 0.373). Discontinuation of surgical trials was a strong risk factor for nonpublication (odds ratio = 4.18, 95% CI: 1.45-12.06; P = 0.008). CONCLUSIONS:Discontinuation and nonpublication rates were substantial in surgical RCTs and trial discontinuation was strongly associated with nonpublication. These findings need to be taken into account when interpreting surgical literature. Surgical trialists should consider feasibility studies before embarking on full-scale trials.

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Completion and Publication Rates of Randomized Controlled Trials in Surgery

An Empirical Study

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Methods: All RCT protocols approved between 2000 and 2003 by 6 ethics committees in Canada, Germany, and Switzerland were screened. Baseline characteristics were collected and, if published, full reports retrieved. Risk factors for early discontinuation for slow recruitment and nonpublication were explored using multivariable logistic regression analyses.

Results: In total, 863 RCT protocols involving adult patients were identified, 127 in surgery (15%) and 736 in medicine (85%). Surgical trials were discontinued for any reason more often than medical trials [43% vs 27%, risk difference 16% (95% confidence interval [CI]: 5%–26%); $P = 0.001$] and more often discontinued for slow recruitment [18% vs 11%, risk difference 8% (95% CI: 0.1%–16%); $P = 0.020$]. The percentage of trials not published as full journal article was similar in surgical and medical trials (44% vs 40%, risk difference 4% (95% CI: −5% to 14%); $P = 0.373$). Discontinuation of

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surgical trials was a strong risk factor for nonpublication (odds ratio = 4.18, 95% CI: 1.45–12.06; $P = 0.008$).

Conclusions: Discontinuation and nonpublication rates were substantial in surgical RCTs and trial discontinuation was strongly associated with nonpublication. These findings need to be taken into account when interpreting surgical literature. Surgical trialists should consider feasibility studies before embarking on full-scale trials.

Keywords: discontinuation, publication, randomized controlled trial, recruitment

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Randomized controlled trials (RCTs) can provide high-level evidence about safety and efficacy of interventions. Conducting RCTs involving surgical interventions presents challenges distinct from RCTs investigating pharmacological interventions. Examples are standardization of operative and perioperative interventions, surgeon and team experience, blinding of study personnel, and participants and recruitment (eg, due to patient preference).[1–3]

Trials may be discontinued earlier than planned for various reasons, including compelling evidence of treatment benefit or harm, futility, slow recruitment, commercial reasons, or the emergence of new evidence from other trials that negates the need for another study.[4,5] When there is no early evidence of harm or irrefutable benefit, trial discontinuation has a significant scientific, ethical, and economic impact. The involvement of steering committees and Data and Safety Monitoring Boards with members independent of the sponsor is of utmost importance when deciding to stop a trial early. Moreover, reasons for early trial termination should be transparently communicated. To the best of our knowledge, discontinuation of surgical trials and the associated risk factors have not yet been investigated.

We determined the prevalence of, and reasons for, discontinuation of surgical trials. We further explored differences in the prevalence of discontinuation between medical and surgical trials and risk factors for nonpublication of surgical trials.

METHODS

Included Studies

We identified RCTs conducted in adult patients from a large empirical study investigating trial protocols approved between 2000 and 2003 by 6 research ethics committees (RECs) in Canada, Germany, and Switzerland.[6] Details of the study design have been previously described.[7] For the current analysis, we used the following prespecified definitions: all RCTs conducted among adult patients in clinical areas with surgical or perioperative activities were classified as "surgical." These included anesthesiology, general surgery, vascular surgery, transplantation, orthopedics traumatology, cardiothoracic surgery, cardiovascular surgery, neurosurgery, urology, plastic surgery, maxillofacial surgery, ear-nose-throat surgery, obstetrics/gynecology, ophthalmology, and dentistry. All RCTs conducted among adult patients in clinical areas primarily relying on nonsurgical activities were classified as "medical". Examples are cardiology, gastroenterology, infectious diseases, neurology, and oncology (for full details see Supplemental Digital Content Table 1, available at http://links.lww.com/SLA/A585). In both groups, study interventions were classified as noninvasive (eg, disinfection with antiseptic agent in a "surgical" trial, antihypertensive medication in a "medical" trial) or invasive (eg, colon resection in a "surgical" trial, colonoscopy in a "medical" trial).

Data Extraction

We used a web-based password-protected database for data extraction (http://www.squiekero.org/). Collaborators trained in trial methodology signed confidentiality declarations for the participating RECs; completed a calibration process; and then extracted study characteristics such as information concerning the study population, intervention, control, sample size, and funding from the included RCT protocols. The first 310 (30%) trial protocols were extracted independently and in duplicate; disagreements were resolved by discussion. For pragmatic reasons, the remaining protocols were extracted by a single investigator with regular agreement checks using double data extraction We determined completion status and publication history of RCTs as of April 2013 by using information from REC files if available, by conducting comprehensive searches of electronic databases for corresponding publications, and directly contacting trialists as described previously.[7] Two investigators independently assessed whether the publications identified by electronic searches matched the corresponding protocol.[7]

An RCT was considered as discontinued if the investigators indicated discontinuation with a reason in the correspondence with the REC, in a journal publication, or their response to our survey. If we could not elucidate the reason for trial discontinuation or if poor participant recruitment was mentioned, we used a prespecified cutoff of less than 90% of achieved target sample size to determine discontinuation.[7] In the rare case that several reasons per study were indicated, the primary reason reported was used. Results were regarded as not published at all if the REC files, the contacted investigators, and the electronic database search yielded no evidence that the data were published in any format. In addition, it was evaluated whether results were published as full journal article. We defined sponsorship depending on who took responsibility for the trial: We considered protocols as industry sponsored, if they were written by industry employees, prominently displayed a company logo or name, reported full funding by the industry without any indication that the trial was investigator sponsored, or mentioned a specific policy with respect to data ownership and publication rights suggesting sponsorship by the industry.

In surgical trials, we explored whether authors reported a primary outcome for harm. One investigator coded this information based on the previously extracted information, and any ambiguity was discussed with a second investigator. The rationale to include this variable is the fact that adverse events may be rare or occur late in the sequence of the trial, thus adequately powered studies reaching the targeted sample size and the defined follow-up are of utmost importance.

Statistical Analysis

We used descriptive statistics to report the prevalence of and reasons for discontinuation. We compared features of surgical and medical RCTs using the χ^2 test or the Fisher exact test, as appropriate, and calculated a risk difference and its 95% confidence interval (CI). We excluded trials that never started (according to REC files or our investigator survey) or that were still ongoing when calculating rates of trial completion and publication status.

We built multivariable logistic regression models to identify predictors for discontinuation due to slow recruitment. Because there are well-justified reasons for trial discontinuation, we did not explore reasons for discontinuation overall, but for discontinuation due to slow recruitment only, which we estimated to be an inappropriate reason for early termination. To avoid overfitting, the number of included covariates was limited to one per 10 events/nonevents, whichever was the smaller number in all multivariable regression analyses.[8] Covariates were chosen a priori to explore the following

2 hypotheses: trial discontinuation due to slow recruitment is (1) less likely with industry-sponsored trials than with trials sponsored by an academic investigator, due to differences in the amount of financial and organizational resources between industry and academic sponsors; and (2) less likely with adverse events being the primary outcome than with efficacy outcomes only, due to more patient and health care provider preference for 1 treatment arm in the latter case hampering recruitment.

Using a multivariable hierarchical logistic regression model, we examined the following prespecified predictors for nonjournal publication of RCTs: "industry-sponsorship (vs investigator-sponsorship)," "primary outcome being an adverse event (yes vs no)," and "trial discontinuation for any reason (yes vs no)." We hypothesized (1) that nonpublication was more likely in industry-sponsored trials, as suggested by previous literature[9]; (2) that trial nonpublication was more likely in discontinued trials (assuming that only few trials were discontinued because of compelling evidence of treatment benefit or harm); and (3) that trial nonpublication was more likely with adverse events being the primary outcome than with efficacy outcomes only, due to the high interest in efficacy outcomes. We accounted for clustering by the approving REC using a random effect estimator.

We conducted 2 sensitivity analyses. First, we conducted the multivariable analyses disregarding the clustering by the approving REC. Second, we used multiple imputation to replace missing data for independent and dependent variables.[10]

We conducted 1 posthoc analysis: Because trial comparisons (surgical vs medical) refer to the a priori defined clinical areas and not to study interventions, we compared trials with invasive interventions versus trials without invasive interventions using descriptive analyses (Supplemental Digital Content Figure S1, available at http://links.lww.com/SLA/A586). Analyses were conducted using Stata Version 12.1 (StataCorp LP, College Station, TX).

RESULTS

Baseline Characteristics of Included Studies

We identified 863 protocols for RCTs involving 680,019 adult patients; 127 RCTs in the field of surgery (15%) and 736 in medicine (85%) (Fig. 1). We excluded 39 (5%) trials that were never started and 8 (1%) that were still recruiting. A total of 816 trials (95%) involving 666,760 adult patients remained for the evaluation of completion and publication status [surgery: 115 (14%), medicine: 701 (86%); Fig. 1]. The specialties contributing to at least 10% of the trials were anesthesiology (13%), cardiothoracic surgery (13%), obstetrics/gynecology (16%), ophthalmology (14%), and orthopedics (10%) in surgical trials (Supplemental Digital Content Table S1a, available at http://links.lww.com/SLA/A585) and oncology (21%), cardiovascular (15%), and infectious diseases (11%) in medical trials (Supplemental Digital Content Table S1b, available at http://links.lww.com/SLA/A585). Table 1 presents an overview of RCT characteristics by clinical area.

TABLE 1. Baseline Characteristics by Clinical Area

Characteristic	Clinical Area	
	Surgery 127 (100%)	Medicine 736 (100%)
Intervention, n (%)		
Medication	85 (67)	618 (84)
Invasive procedure	31 (24)	25 (3)
Rehabilitation	2 (2)	14 (2)
Behavioral	0 (0)	18 (3)
Diagnostic test	1 (1)	14 (2)
Other	8 (6)	47 (6)
Sample size,* median (IQR)	150 (60, 450)	288 (105, 628)
Industry funding, n (%)		
Yes	76 (60)	552 (75)
No	51 (40)	184 (25)
Trial sponsor, n (%)		
Industry	59 (46)	470 (64)
Academic investigator	71 (56)	276 (38)
Center status,† n (%)		
Single center	50 (40)	99 (14)
Multicenter	75 (60)	633 (86)
Planned interim analysis, n (%)		
Yes	30 (24)	249 (34)
No	97 (76)	487 (66)
Presence of DSMB, n (%)		
Yes	24 (19)	223 (30)
No	103 (81)	513 (70)
Planned stopping rule, n (%)		
Yes	10 (8)	142 (19)
No	117 (92)	594 (81)

In categorical variables, numbers (column percentages) are displayed.
*Surgery: 4 missings; Medicine: 5 missings.
†Surgery: 2 missings, Medicine: 4 missings.
DSMB indicates Data and Safety Monitoring Board; IQR, interquartile range.

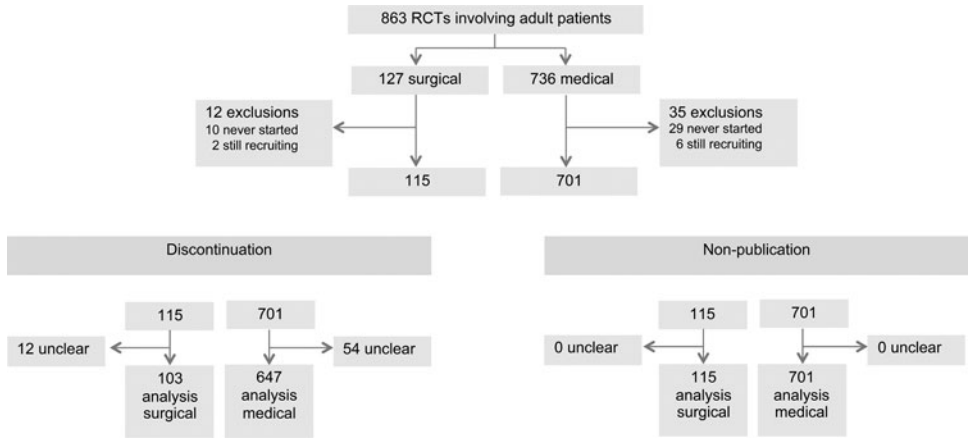

FIGURE 1. Flow chart of included studies: Studies eligible for assessment of discontinuation and of nonpublication, respectively.

Discontinuation of Trials

We excluded 66 trials (12 surgical, 54 medical) with unclear completion status (Fig. 1). In the remaining 750 trials (103 surgical, 647 medical), the overall proportion of discontinued trials was 43% (44/103) in surgical trials and 27% (176/647) in medical trials with a risk difference of 16% (95% CI: 5%–26%; $P = 0.001$; Table 2).

Reasons for RCT discontinuation by clinical area are presented in Table 3. Slow recruitment was the most frequent reason for discontinuation in both surgical (19/44, 43%) and medical (68/176, 39%) trials. Stopping for slow recruitment was more frequent in surgical than in medical trials [19/103 (18%) vs 68/647 (11%), risk difference 8%, 95% CI: 0.1%–16%; $P = 0.020$].

Results of our exploratory analysis comparing invasive with noninvasive trials suggested that RCTs with invasive interventions were more often discontinued for slow recruitment than RCTs with noninvasive interventions (Supplemental Digital Content Figure S1, available at http://links.lww.com/SLA/A586).

Publication of Trials

No trials had to be excluded for unclear publication status (Fig. 1). The overall percentage of trials not published in any format was 40% (46/115) among surgical trials and 34% (235/701) among medical trials with a risk difference of 6% (95% CI: −3% to 16%; $P = 0.176$; Table 2). Most trials were published as full journal articles [surgical 64/115 (56%), medical 421/701 (60%)] as opposed to abstracts, letters, or other short forms of publication [surgical 5/115 (4%), medical 45/701 (6%)]. The overall percentage of trials not published as full journal article was 44% (51/115) among surgical trials and 40% (280/701) among medical trials with a risk difference of 4% (95% CI: −5% to 14%; $P = 0.373$).

Of completed surgical trials 76% (45/59) and of completed medical trials 79% (371/471) were published in any format. Of discontinued surgical trials 55% (24/44) and of discontinued medical trials 52% (92/176) were published.

Results of the supplementary exploratory analysis comparing invasive to noninvasive trials suggested no relevant differences in publication rates (Supplemental Digital Content Figure S1, available at http://links.lww.com/SLA/A586).

TABLE 2. Trial Completion and Publication Status by Clinical Area

	Clinical Area	
	Surgery 115 (100)	**Medicine 701 (100)**
Completion status		
Completed	59 (51)	471 (67)
Discontinued	44 (38)	176 (25)
Unclear	12 (11)	54 (8)
Publication status		
Published	69 (60)	466 (66)
Abstract	5 (4)	31 (4)
Journal	64 (56)	421 (60)
Letter	0 (0)	7 (1)
Other	0 (0)	7 (1)
Not published	46 (40)	235 (34)

Numbers (column percentages) are displayed. Exclusion of never started trials (surgery 10/127, 8%; medicine 29/736, 4%) and of still recruiting trials (surgery 2/127, 2%; medicine 6/736, 1%).

TABLE 3. Reasons for Discontinuation by Clinical Area

	Clinical Area	
Reason	**Surgery 44 (100)**	**Medicine 76 (100)**
Benefit	1 (2)	6 (3)
Futility	5 (12)	28 (16)
Harm	4 (9)	17 (10)
Slow recruitment	19 (43)	68 (39)
External evidence	1 (2)	7 (4)
Lack of funding	0 (0)	4 (2)
Administrative	7 (16)	27 (15)
Other	0 (0)	7 (4)
Unclear	7 (16)	12 (7)

Numbers of studies (column percentages) are displayed.

Risk Factors for Surgical Trial Discontinuation Due to Slow Recruitment

Study discontinuation due to slow recruitment was neither influenced by the type of sponsor [industry vs academic investigator, adjusted odds ratio (OR) = 0.60, 95% CI: 0.20–1.85, $P = 0.377$ (Table 4)] nor by the type of primary outcome (ie, efficacy or harm) (adjusted OR = 0.51, 95% CI: 0.14–1.85, $P = 0.302$). Sensitivity analyses did not affect these findings (Supplemental Digital Content Table S2, available at http://links.lww.com/SLA/A585).

Risk Factors for Nonpublication of Surgical Trials as Full Journal Article

In multivariable analysis, trials discontinued for any reason were significantly more likely to remain unpublished than completed trials (adjusted OR = 4.18, 95% CI: 1.45–12.06, $P = 0.008$) (Table 5). Industry-sponsored trials were significantly more likely to remain unpublished than trials sponsored by an academic investigator (adjusted OR = 2.99, 95% CI: 1.05–8.58, $P = 0.041$). Trials with a primary harm outcome were less likely to remain unpublished than trials with primary efficacy outcomes only (adjusted OR = 0.28, 95% CI: 0.09–0.92, $P = 0.035$).

Sensitivity analyses did not affect these findings with the exception of the effect of the sponsor, which did not remain statistically significant in the model with multiple imputations (Supplemental Digital Content Table S3, available at http://links.lww.com/SLA/A585).

DISCUSSION

This study suggests that the discontinuation rate is substantial in surgical RCTs and that discontinuation is more frequent in surgical than in medical RCTs. This applies to discontinuation for any reason as well as to discontinuation for slow recruitment, which is the predominant reason for discontinuation. Trial discontinuation was found to be a strong predictor for nonpublication.

Relation to Other Studies Investigating Trial Discontinuation

Slow recruitment is an important problem in clinical trials. In a cohort of 114 publicly funded multicenter trials, only 31% reached their initial recruitment target, an additional 24% reached 80% of their recruitment target and 53% of the trials were extended.[11] The target recruitment size was revised in 34% of trials, of which 86% downward.[11] Slow recruitment may occur because of a variety of reasons, such as organizational failure, inadequate funding, or unrealistic projections regarding the number of eligible participants.[12] It may lead to longer study duration and increased resource consumption

TABLE 4. Univariable and Multivariable Logistic Regression for Trial Discontinuation of Surgical Trials for Slow Recruitment (Using a Random Effect Estimator to Account for Clustering by the Approving Research Ethics Committee)

	Univariable			Multivariable		
Potential Predictor	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Industry sponsor, yes *vs* no	0.66	0.22–1.97	0.457	0.60	0.20–1.85	0.377
Primary harm outcome, yes *vs* no	0.55	0.15–1.96	0.354	0.51	0.14–1.85	0.302

Of 115 trials, 12 had an unclear completion status and 14 had at least 1 missing covariate. Of the remaining 89 trials, included in the regression analysis, 19 were discontinued and 70 completed or discontinued for other reasons.

TABLE 5. Univariable and Multivariable Logistic Regression for Nonpublication as Full Journal Article of Surgical Trials (Using a Random Effect Estimator to Account for Clustering by the Approving Research Ethics Committee)

	Univariable			Multivariable		
Potential Predictor	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Industry sponsor, yes *vs* no	2.02	0.84–4.88	0.119	2.99	1.05–8.58	0.041
Primary harm outcome, yes *vs* no	0.32	0.11–0.96	0.043	0.28	0.09–0.92	0.035
Trial discontinuation for any reason, yes *vs* no	2.26	0.94–5.44	0.068	4.18	1.45–12.06	0.008

Out of 115 trials, 26 had at least 1 missing covariate. Of the remaining 89 trials included in the regression analysis, 56 trials were published as full journal article and 33 not published as full journal article.

and early trial discontinuation with less precise study findings.[13] In a Cochrane review investigating methods to improve recruitment, a number of promising strategies have been described, such as telephone reminders and opt-out policies.[13] Most importantly, pilot studies may allow to estimate eligibility and consent rates more precisely and thus should be considered when planning a RCT.[14]

Our exploratory analysis showed that trials with invasive interventions tended to be more frequently discontinued for any reason and were significantly more often discontinued for slow recruitment. This result suggests that the type of intervention (invasive vs noninvasive) rather than the setting (surgery vs medicine) represents a barrier to successful recruitment.[1]

We found trial discontinuation to be more frequent in surgical than in medical trials, both overall and for slow recruitment. Potential explanations may be surgery-specific aspects and challenges with clinical trials such as requirements concerning surgeon experience, standardization of the intervention, and recruitment (eg, due to patient or caregiver preference).[1–3] In addition, there are some fundamental differences concerning the premarket review and approval process of devices versus drugs. Whereas for US Food and Drug Administration approval, safety and efficacy have to be demonstrated in humans for all drugs, this is only required for high-risk devices.[15] Similarly in Europe, clinical data are not required for lower risk devices.[16] Thus, depending on the risk class of surgical devices, regulatory approval may not be based on clinical evidence, which potentially impacts resource investment and other efforts to achieve trial completion.

Relation to Other Studies Investigating Trial Nonpublication

In this study, 60% of surgical and 66% of medical trials were published in any format and 56% and 60%, respectively, as full journal articles. These proportions are slightly higher than a previous investigation of study protocols submitted to a Swiss REC with 52% of trials getting published (233/451).[9] In this previous Swiss study, the odds for publication was higher with noncommercial funding, which is in line with our results, higher with multicenter trials, international collaboration, and a high sample size as assessed by median split.[9] This investigation comprised, however, mostly medical specialties and thus is not strictly comparable to the surgical trials evaluated in our sample. In a Cochrane review of 79 studies investigating the subsequent publication of abstracts presented at meetings, the weighted full publication rate was 44.5% (95% CI: 43.9–45.1) and an estimated cumulative publication rate after 9 years was 52.6% overall and 63.1% for RCTs or controlled clinical trials.[17] Abstract acceptance for presentation at a meeting was found to be associated with subsequent publication with an OR of 1.78 (95% CI: 1.50–2.12).[17]

We found trial discontinuation to be an independent risk factor for nonpublication. This may be explained by the fact that the most frequent reasons of discontinuation of surgical RCTs were slow recruitment, futility, or administrative reasons. These trials were thus potentially more difficult to publish than the few trials stopped early for benefit. Generally, in trials stopped early for benefit, treatment effects tend to be large,[18,19] increasing the chance of a trial to be published. This is supported by a review of such trials in which the majority of RCTs (92/143) were published in 5 high-impact medical journals.[19]

Strengths and Limitations

The collaborating RECs granted us unrestricted access to trial protocols. As outlined previously,[20] this reduced the risk of selection bias; asking trialists or sponsors for permission would almost certainly have led to oversampling of successfully completed and published trials. However, some investigators may not have provided useful information about reasons for trial discontinuation. In addition, our approach allowed us to collect more detailed information about trial characteristics than investigations relying on trial registry entries only.[21] Moreover, we obtained study protocols from several RECs in 3 countries, increasing the generalizability of our findings.[4] In addition, our data extractions were based on a priori definitions[7] and validated through regular quality assessments. Finally, our sensitivity analyses support the robustness of the conducted statistical analyses.

Our investigation has some limitations. Although we included a large number of approved RCTs, we were unable to adjust for additional confounders because of the low number of surgical trials and outcome events.[8] We thus refrained from adjusting for trial characteristics such as sample size and center status (single center vs multicenter).

Implication for Daily Practice and Further Research

These findings of our study raise ethical concerns, as many patients who consent to enroll in surgical trials do not contribute to scientific knowledge, and suggest that considerable resources are being wasted. Thus, our findings may have the following implications during the different phases of a research pathway:

1. Trial conception and design. Strategies to prevent discontinuation should be adopted already during the trial design phase, including training in research methodology, realistic resource estimation (eg, time of personnel), creating research infrastructures, and working in networks and interdisciplinary teams involving trial methodologists, statisticians, data managers, and trial managers. Pilot studies either as part of the trial (internal pilot) or stand-alone (external pilot),[14] that is, a small version of the full-scale study or feasibility studies, are effective means to evaluate particular aspects such as recruitment, resource utilization, and protocol feasibility.[22] This especially applies to trials involving surgical interventions, where recruitment may be more challenging due to patient preferences. Moreover, pilot studies may identify other challenges such as feasibility of standardization of the surgical interventions. Pilot studies should thus be considered when allocating sparse resources to surgical RCTs. In addition, trials should be registered before enrolment of the first patient. This enhances transparency regarding the targeted sample size and additionally allows identifying the study while ongoing or after close-up before publication.
2. Trial conduct. Recruitment should be closely monitored and early modification of trial methods foreseen to enhance recruitment if necessary. The decision to discontinue a trial should be made by an independent Data and Safety Monitoring Board based on predefined criteria.
3. Trial reporting. Reasons for discontinuation and results of discontinued RCTs should be transparently communicated and thus made publicly available.
4. Health care decision making. When interpreting surgical literature, be it primary studies or systematic reviews, potential biases introduced by discontinued RCTs or by nonpublication of trials need to be considered.

CONCLUSIONS

More than 1 in 3 surgical RCTs is discontinued. Discontinuation is more frequent among surgical than among medical RCTs. Slow recruitment is the predominant reason for early termination. Furthermore, results from discontinued trials are more likely to remain unpublished. Rigorous planning within a multidisciplinary research framework, supported by pilot and feasibility studies, predefined criteria for stopping a trial, applied by independent boards, and transparent communication with stakeholders of surgical research and the public could help achieve the ultimate goal of high-quality research that improves the evidence base of surgical interventions.

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