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Igor Vuković

THE CONSISTENCY OF THE REPORTING OF DATA FROM RANDOMIZED CONTROLLED TRIALS IN ANESTHESIOLOGY ON CLINICALTRIALS.GOV

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Prof. Shelly Melissa Pranić, PhD

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It is said that it takes a village to raise a child. Something along these lines could be applicable to PhD students. I would first like to acknowledge my gratitude to the multitude of people over the years who encouraged me to start this journey, culminating in my beloved wife declaring, “You are enrolling and stop rethinking it!” way back in 2017.

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“A road forks into two pathways, one true and one dangerous.

At the crossroads, two twin brothers stand.

One always tells the truth, the other always lies...”

(Old logical theorem)

ABBREVIATIONS

(in order of appearance)

PB – publication bias

IF – impact factor

CQR – clinical quality registry

ICTRP - International Clinical Trial Registry Platform

WHO - World Health Organization

CTSP - Clinical Trial Search Portal

WMA - World Medical Association

ICMJE - International Committee of Medical Journal Editors

FDA - Food and Drug Administration

NIH - National Institute of Health

FDAAA Food and Drug Administration Amendment Act

ACT - Applicable clinical trial

RCT - randomized controlled trial

PONV - postoperative nausea and vomiting

SAE – serious adverse event

OAE - other adverse event

JCR – Journal Citation Reports

STROBE - Strengthening the Reporting of Observational Studies in Epidemiology

NCT - National Clinical Trial

OR - odds ratio

VIF – variance inflation factor

CI - confidence interval

EUCTR – European Union Clinical Trials Register

RWE – real-world evidence

RWD – real-world data

LLM – large language model

AI – artificial intelligence

Table of Contents

1. INTRODUCTION

1.1. Positive publication bias

Ensuring the reliability and credibility of evidence from clinical trials is essential. Accordingly, methodologically sound and ethically conducted research requires transparent reporting of patient-centered and study design elements (1,2).

A paramount challenge to the concepts of open science and unobstructed data and knowledge dissemination is the phenomenon of selective publication, or publication bias (PB) (3). Selective publication itself could originate at multiple levels, ranging from journal editors to study sponsors or investigators themselves (4). In essence, the root cause for publication bias can be expressed as various forms of conflict of interest, with editors viewing the null-studies as less valuable and thereby protecting their respective journal's impact factor (IF) (3), while industry sponsors could be susceptible to withholding the information if it would undermine the commercial viability of the researched product (5). A recent study investigating publication bias in anesthesiology research found that it was identified in 17.9% of articles from 2016 to 2024 (6).

Ultimately, the core issues that enable publication bias are a lack of transparency and the unavailability of trial data. In response to these issues, the concept of clinical trial registries emerged as a potential solution to alleviate the downstream impact of publication bias on clinical practice (7). Improved accessibility of data in a specific subtype of data registry, clinical quality registries (CQR), was recently even assigned quantifiable economic value in a study by Lee et al. (8)

1.2. Historical background of the trial registration process

According to Tonks (9), a register listing clinical trials registers was established in 1987 at Brown University in the United States and contained over 500 entries, predominantly dedicated to topics of AIDS or cancer.

The year 2004 is the pivot point in the history of the trial registration process. A strong *casus* for wide trial registration endorsement campaign happened in June 2004 when the state of New York launched a lawsuit against the GlaxoSmithKline pharmaceutical company following a case that attracted particular public attention (10). At the time, there was an ongoing scientific debate about the safety profile of selective serotonin-reuptake inhibitor drugs regarding the potential for suicidal behaviour in children (11). An internal document from the company was leaked showing that they conducted two trials that showed no treatment benefit for their marketed drug paroxetine, but chose not to disclose results due to

expected commercial consequences (12). In the aftermath of the public backlash, GlaxoSmithKline announced that they would, from that moment, form a register of clinical trials under their sponsorship, with trial protocol summaries and publicly available results (13). Soon after, in October 2004, during the Cochrane Colloquium in Ottawa, Canada, a group composed of systematic reviewers and pharmaceutical industry representatives discussed the necessity and possible forms of clinical trial registration, which would later be known as the “Ottawa group” (14). In November 2004, ministers and health representatives from 59 countries met in Mexico City for the Summit on Health Research (15) and, in conclusion, called for the establishment of a framework for a network of international clinical trial registries that could be available from a single access point (16). The World Health Assembly followed through with endorsement of this initiative. leading to the establishment of the International Clinical Trial Registry Platform (ICTRP) of the World Health Organization (WHO) in 2005 (5). The platform was launched in 2006 and further supported by the creation of the Clinical Trial Search Portal (CTSP) to fulfill the second part of the Mexico Summit’s resolution and provide a unified data search and access point. Table 1 lists all of the registries currently part of the ICTRP.

Table 1. List of trial registers that are part of ICTRP. Created with information presented in the ICTRP website (17,18)

ICTRP Primary registry	Acronym	Year of establishment
Australian New Zealand Clinical Trials Registry	ANZCTR	2005
Brazilian Clinical Trials Registry	ReBec	2011
Chinese Clinical Trial Registry	ChiCTR	2005
Clinical Research Information Service (Republic of Korea)	CRiS	2010
Clinical Trials Information System (EU/EEA)	CTIS	2022
Clinical Trials Registry - India	CTRI	2007
Cuban Public Registry of Clinical Trials	RPCEC	2007
EU Clinical Trials Register	EU-CTR	2004
German Clinical Trials Register	DRKS	2008
Iranian Registry of Clinical Trials	IRCT	2008
International Standard Randomised Controlled Trial Number	ISRCTN	2000
International Traditional Medicine Clinical Trial Registry	ITMCTR	2022
Japan Registry of Clinical Trials	jRCT	2018
Lebanese Clinical Trials Registry	LBCTR	2019
Thai Clinical Trials Registry	TCTR	2009

Pan African Clinical Trial Registry	PACTR	2009
Peruvian Clinical Trial Registry	REPEC	1995
Sri Lanka Clinical Trials Registry	SLCTR	2006

Subsequently, the World Medical Association (WMA) general assembly included the following article in the 2008 version of the Declaration of Helsinki, guiding the ethical principles for medical research involving human subjects:

"Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject." (19)

The scientific validity of data available on registers is reflected in the recommendations of the Cochrane Collaboration. The Cochrane Handbook for Systematic Reviews of Interventions states that "*Cochrane Reviews of interventions should search relevant trials registers and repositories of results… It is important to note that trials registers are an important source of information about completed, terminated, and ongoing trials, and an increasingly important source of results for completed and terminated trials, especially those whose results have not been published." (20)*

A timeline of key milestones in establishing the clinical trial registration process is presented in Figure 1.

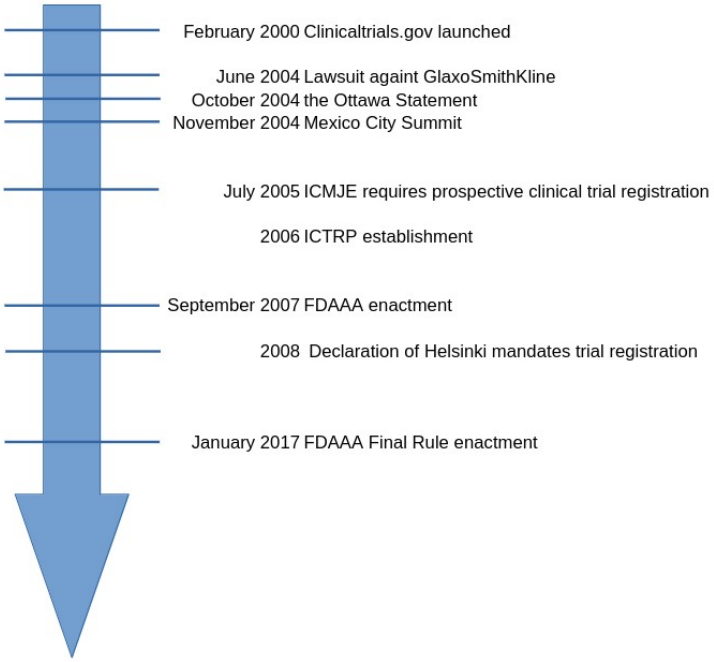


Figure 1. A timeline overview of some of the notable events in the history of clinical trial registrations. Image by Author.

1.3. The role of the International Committee of Medical Journal Editors in endorsing the trial registration

The International Committee of Medical Journal Editors (ICMJE) gradually evolved from informal meetings of a group of medical journal editors that first met in 1978 in Vancouver, British Columbia, to propose a set of uniform guidelines for submission of papers to their journals (21). Determined to address the problem of selective reporting, ICMJE communicated a firm stance on the issue of necessity for establishment of the trial registration practices in the 2004 statement (22), announcing that "*The ICMJE member journals will require, as a condition of consideration for publication, registration in a public trials registry. Trials must register at or before the onset of patient enrollment. This policy applies to any clinical trial starting enrollment after July 1, 2005."* A list of criteria necessary to accept the chosen public registry as a valid registration option was provided, aligning closely with the similar requirements for trial data transparency as the Ottawa group. At the time, the only public registry that met the stated conditions was www.clinicaltrials.gov. Today, more than two decades later, the policy enforced (23) requires pre-registration of trials in any designated primary registry of the ICTRP before publication submission to their member journals. A total of 24 standardized data items created by the WHO are endorsed by the ICMJE and are the minimum required for registries in the ICTRP (see Table 2 for a list of data items) (24).

Table 2. List of 24 items in the current version (1.3.1) of the WHO Trial Registration Data Set (TRDS).

	WHO data set item
1.	**Primary Registry and Trial Identifying Number**
2.	**Date of Registration in Primary Registry**
3.	**Secondary Identifying Numbers**
4.	**Source(s) of Monetary or Material Support**
5.	**Primary Sponsor**
6.	**Secondary Sponsor(s)**
7.	**Contact for Public Queries**
8.	**Contact for Scientific Queries**
9.	**Public Title**
10.	**Scientific Title**
11.	**Countries of Recruitment**
12.	**Health Condition(s) or Problem(s) Studied**

13. **Intervention(s)**
14. **Key Inclusion and Exclusion Criteria**
15. **Study Type**
16. **Date of First Enrollment**
17. **Sample Size**
18. **Recruitment Status**
19. **Primary Outcome(s)**
20. **Key Secondary Outcomes**
21. **Ethics Review**
22. **Completion date**
23, **Summary Results**
24. **IPD sharing statement**

1.4. ClinicalTrials.gov as the implementation of the Food and Drug Administration legislation

The Food and Drug Administration (FDA) is a part of the United States Department of Health and Human Services that regulates drugs, biologics, and medical devices in the biomedical field (25). The importance of the FDA in the context of clinical trial registration starts with the enactment of the Food and Drug Administration Modernization Act of 1997 by the United States Congress, mandating that the National Institute of Health (NIH) create a public registry for clinical trials involving human subjects (26). The design of the system began in September 1998, and the site was publicly available in February 2000, containing more than 4,000 registry entries (27). Today the ClinicalTrials.gov is the world's largest clinical trial registry platform with 583,713 registered studies as of May 06, 2026. (Figure 2).

ClinicalTrials.gov includes studies conducted in over 200 countries, with US-only studies representing only 29% of the total number of registered trials, indicating that ClinicalTrials.gov has outgrown its initial context of national importance (Figure 3).

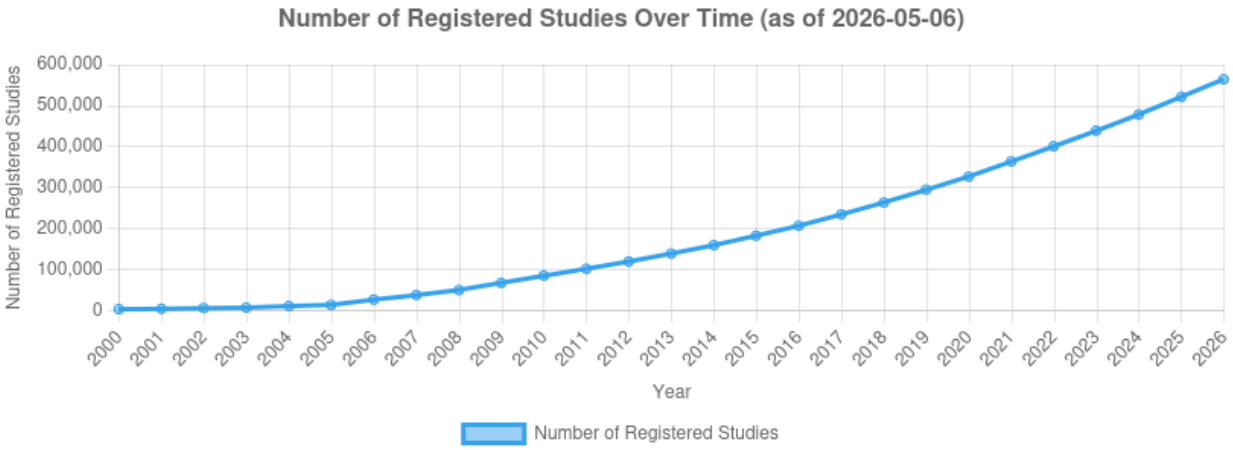
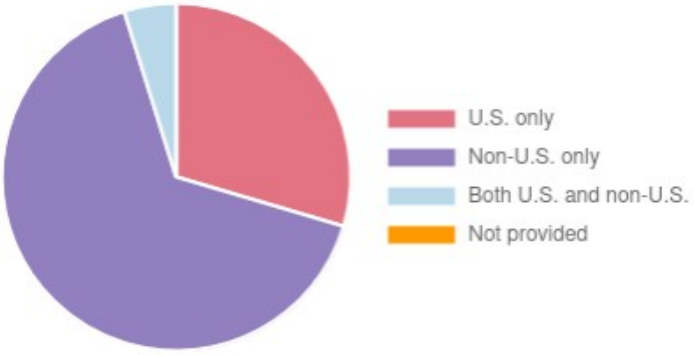


Figure 2. Number of registered studies on ClinicalTrials.gov over time (Official website diagram, accessed on May 05, 2026) (28).

Percentage of recruiting studies by location (as of 2026-05-06)

Total of 64,767 studies



Location	Number of Recruiting Studies and Percentage of Total (as of 2026-05-06)
U.S. only	19,158 (30%)
Non-U.S. only	42,489 (66%)
Both U.S. and non-U.S.	3,120 (5%)
Not provided	0 (0%)
Total	64,767 (100%)

Figure 3. Percentage of recruiting studies on ClinicalTrials.gov by location (Official website diagram, accessed on May 05, 2026) (28).

Further refinement of the legislation (and the ones essential to the design of this dissertation) came with the 2007 Food and Drug Administration Amendment Act (FDAAA). The registration to the ClinicalTrials.gov registry with mandatory disclosure of results and adverse events is required of studies that meet the definition of an "applicable clinical trial" (ACT) and either were initiated after September 27, 2007, or initiated on or before that date and were still ongoing as of December 26, 2007. ACTs were all interventional clinical trials, other than phase 1, about FDA-regulated drugs, biological products, or devices (29,30).

The FDAAA was revised in 2016, and the Final Rule, effective from January 18, 2017, established additional requirements to facilitate researchers' reporting of study design elements (29).

The definition of ACTs was updated in the Final rule:

"ACTs generally include interventional studies (with one or more arms) of FDA-regulated drug, biological, or device products that meet one of the following conditions:

- *The trial has one or more sites in the United States*
- *The trial is conducted under an FDA investigational new drug application or investigational device exemption*
- *The trial involves a drug, biological, or device product that is manufactured in the United States or its territories and is exported for research".*

The ACT checklist is presented in Figure 4.

ClinicalTrials.gov

ClinicalTrials.gov is a service of the National Institutes of Health.

Checklist for Evaluating Whether a Clinical Trial or Study is an Applicable Clinical Trial (ACT) Under 42 CFR 11.22(b) for Clinical Trials Initiated on or After January 18, 2017[1] (NOT FOR SUBMISSION[2])

Instructions: Answer the following questions to evaluate whether the study is an applicable clinical trial (ACT). Use the accompanying "Elaboration" for additional information to help answer the questions.

Question	Yes	No
1. Is the study interventional (a clinical trial)? *Study Type* data element is "Interventional"	☐	☐
2. Do ANY of the following apply (is the answer "Yes" to at least one of the following sub-questions: 2a, 2b, OR 2c)? **a. Is at least one study facility located in the United States or a U.S. territory?** *Facility Location – Country* data element is "United States," "American Samoa," "Guam," "Northern Mariana Islands," "Puerto Rico," "U.S. Virgin Islands," or other U.S. territory. **b. Is the study conducted under a U.S. FDA Investigational New Drug application (IND) or Investigational Device Exemption (IDE)?** *U.S. Food and Drug Administration IND or IDE Number* data element is "Yes." **c. Does the study involve a drug, biological, or device product that is manufactured in and exported from the U.S. (or a U.S. territory) for study in another country?** *Product Manufactured in and Exported from the U.S.* data element is "Yes."	☐	☐
3. Does the study evaluate at least one drug, biological, or device product regulated by the United States Food and Drug Administration (U.S. FDA)? *Studies a U.S. FDA-regulated Device Product* data element is "Yes" and/or *Studies a U.S. FDA-regulated Drug Product* data element is "Yes."	☐	☐
4. Is the study other than a Phase 1 trial of a drug and/or biological product or is the study other than a device feasibility study? For drug product trials, *Study Phase* data element is NOT "Phase 1" and for device product trials, *Primary Purpose* is NOT "Device Feasibility."	☐	☐

If "Yes" is answered to all 4 questions, and the study was initiated on or after January 18, 2017, the trial would meet the definition of an ACT that is required to be registered under 42 CFR 11.22.

Figure 4. Checklist for evaluation of ACTs provided by the FDA (Official website, accessed on March 13, 2026) (31).

This legislation stipulates a trial registration deadline of 21 days after the enrollment of the first trial participant (32). The deadline is to be observed by the responsible party, either the study sponsor or the designated principal investigator.

1.5. Adherence to the trial registration policies

Although the FDAAA, ICMJE, and WHO clearly stated these requirements in order to encourage complete trial data reporting, the underreporting and inconsistencies in trial data are persistently present, especially regarding the adverse events reporting data items (33,34). Furthermore, discrepancies between trial registry data and corresponding publications have been reported in other studies (35–37).

Even though these measures are tools specifically designed to reduce the instances of biased reporting in trial publications, they are overall not recognized as useful tools by study reviewers, the majority of whom do not use the possibility of trial registry – publication comparison as a tool to validate the integrity of trial data while considering the manuscripts for publication (38).

Registration deadline policies are not adhered to any better; recent studies (39,40) found that at least one-third of randomized controlled trials (RCTs) were retrospectively registered.

1.6. Previous research on trial data reporting quality in anesthesiology

In a December 2025 study, Kantheti et al. established that anesthesiology-related trials represent 2.4% of the total ClinicalTrials.gov pool (41). Highlighting the underreporting of essential data in anesthesiology RCTs is warranted, given the severity of cases and potential complications in this field (42,43). Although RCTs are key to advancing the progress of anesthesiology methods and practices, the quality of trials evaluating drugs used in anesthesiology has so far been insufficiently studied. The paucity of existing studies mostly focused on investigating discrepant outcome reporting as a possible indicator of publication bias (44–47). Both Jones et al. (44) and De Oliveira et al. (45) used impact factor to select highest-ranking anesthesiology peer-reviewed journals and investigated the reporting quality of a few selected study design elements. Riemer et al. (47) determined that only 8% of trials on postoperative nausea and vomiting (PONV) prevention drugs were prospectively registered, and then compared the outcome reporting in registered and published versions of those trials. They found that 26% of prospectively registered trials had an added primary outcome, 32% had a demoted primary outcome, and 26% had outcomes with altered assessment times. Their methodology did not include a direct comparison of prospectively and retroactively registered trials, except for the Cochrane Risk of Bias assessment tool score.

Selective reporting of anesthesiology trial data has the potential to lead to adverse consequences when translating trial data and conclusions into clinical practice (48). Therefore, unfortunately, although the practice of evidence-based decision-making aims to reduce the incidence of anesthesia-related morbidity and mortality, in real-world conditions it may not achieve the desired effect (49).

2. AIMS AND HYPOTHESES

2.1. Study objectives

Since the evidence about the reliability of data reporting from anesthesiology clinical trials is scarce, and motivated by the potential negative impact of misreported trial data, we created a cohort of anesthetic-related RCTs subject to the FDAAA and aimed to investigate the consistency of the reporting of WHO Data Set Items, trial results, and adverse events between data reported in ClinicalTrials.gov and corresponding publications.
Our study is the first to form a cohort using the ClinicalTrials.gov registry, examine a broad spectrum of study data items, and perform a subgroup analysis.

2.2. Primary outcomes

A) We used descriptive statistics to examine discrepancies and inadequacies in data item reporting. Analogous to the FDAAA reporting requirements, among the WHO Data Set Items we selected the following data categories due to their intrinsic special importance in conveying relevant patient and study design information:

(1) results and outcome probability measures (reported statistical methods, p-values, interquartile ranges, and confidence intervals);
(2) adverse events (stratified into serious (SAE) and other adverse events (OAE);
(3) all-cause mortality;
(4) study size;
(5) study outcome;
(6) study arm;
(7) selection criteria;
(8) date of enrollment; and
(9) frequencies of compliance with the ClinicalTrials.gov trial registration deadline (one month after the study start date).

B) We selected a set of independent variables to test for frequencies in data misreporting between the most recent ClinicalTrials.gov registered version and corresponding publications:

(a) trial funding type
(b) whether or not the trial was published in a journal claiming to follow ICMJE recommendations
(c) whether or not the trial complied with ClinicalTrials.gov legislation regarding the deadline for trial registration
(d) whether the trial was conducted by a single research center or multicentric;
(e) whether the trial belongs to older (stratified into two groups: 2009-2012 and 2013-2016) or more recent (2017-2020) publications in our cohort based on the updated FDAAA legislation in 2017.
(f) whether the trial was published in an anesthesiology journal.
(g) whether the trial was published in a journal indexed by JCR.

Criteria for classification of the trials into our predictor subgroup variables are explained in section 3.4.4.

2.3. Secondary outcomes

A) Acknowledging the significance of the Final Rule's implications, a subgroup analysis within our cohort compared the All-cause mortality reporting in trials registered before and after the Final Rule compliance deadline.

B) We created a binary logistic regression model utilizing the same (a)-(e) subgroups as predictor variables, with the exception that subgroup (e) was instead stratified in the same manner as in the secondary outcome A). We formed a composite dependent variable that indicated the presence of a reporting discrepancy across the following study data elements: results, SAE, OAE, and mortality. The variable is therefore dichotomous, with a single misreporting instance indicating a positive value for data misreporting, while all selected data categories must be reported adequately to deem the trial consistently reported. Initially, we planned to use any reporting discrepancies in the data categories (1)-(9). However, we could identify no single RCT in our cohort that did not contain reporting discrepancies in at least one data item. Instead, we selected the patient-relevant data items that share a thematic link and are of special importance for both the clinical application and for downstream translation into meta-research.

C) We also conducted a univariable binary logistic regression analysis that used the IF of each trial's publication journal as a predictor variable to test against the consistency of reporting of the chosen data categories (1) – (9). Trials were removed from the analysis if they were published in a journal that was not indexed in the JCR at the time of publication.

3. METHODS AND DATA SOURCES

3.1. Study design

This is a cross-sectional study. While preparing the dissertation we adhered to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional observational studies (50). An overview of the methods implementation process is available in Figure 5.

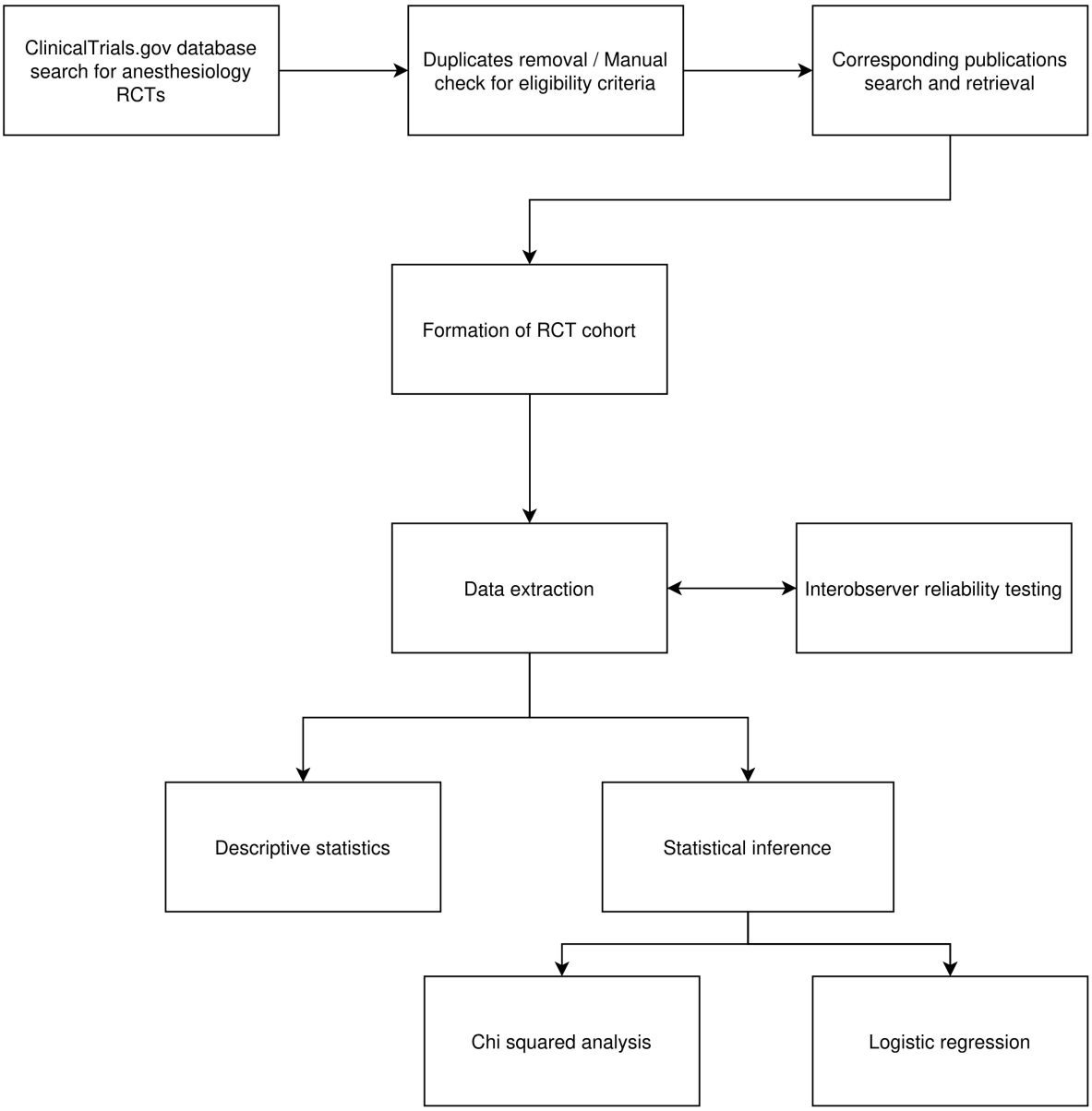


Figure 5. Study flowchart.

3.2. Study eligibility criteria

The inclusion criteria were: RCTs having
(a) ClinicalTrials.gov registration number; and
(b) investigated 29 drugs used in anesthesiology (51):
- intravenous anesthetics: propofol, thiopental, midazolam, etomidate, ketamine
- inhalational anesthetics: sevoflurane, isoflurane, desflurane, enflurane, halothane, xenon, nitrous oxide
- opioids: fentanyl, alfentanyl, sulfentanyl, remifentanyl, morphine
- muscle relaxants and reversal drugs: succinylcholine, rocuronium, vecuronium, pancuronium, atracurium, cisatracurium, mivacurium, suggamadex
- local anesthetics: bupivacaine, levobupivacaine, ropivacaine
- sedatives: dexmedetomidine.

We excluded trials that
a) were first posted on ClinicalTrials.gov two years after the FDAAA mandate (September 27, 2009), allowing a period of two years for trials to publish and post results;
(b) were last updated on ClinicalTrials.gov after the day of our search, May 6, 2022;
(c) non-interventional studies;
(d) phase 1 clinical trials;
(e) trials that were not designated as completed by the time of the search;
(f) trials that have not disclosed results to ClinicalTrials.gov
(g) trials that are not subject to the FDAAA New Rule
(h) trials that did not have a corresponding publication and
(i) trials with published results that were pooled with the results of other trials.

3.3 Trial and publication search and retrieval

The anesthetic drug names were used one at a time as the primary search term in the ClinicalTrials.gov advanced search, while the exclusion criteria (a)-(f) served as search filters. First author (IV) downloaded the search results in the form of a spreadsheet file to be used in subsequent data analysis.

As a result of this action, duplicate versions of the same trial were often created in the spreadsheet, since a single National Clinical Trial (NCT) number could be returned for multiple chosen drugs. The same NCT identifier numbers were utilized to mark duplicates for removal from the spreadsheet by using the Microsoft Excel built-in “Remove duplicates” function.

A trial’s ClinicalTrials.gov entry provides links to associated publications of studies cited in MEDLINE but to reduce accessing potentially non-relevant publications that did not report current data from our selected trials (52), we also searched MEDLINE via PubMed using the NCT number from ClinicalTrials.gov along with the PubMed secondary source identification tag [si] (e.g., NCT01068600 [si]) for trials that did not contain links to publications. A Google Scholar search query using the NCT study identifier was also performed. We also searched PubMed and Google Scholar manually for publications using the provided author's name and the study title from ClinicalTrials.gov.

3.4. Data extraction from ClinicalTrials.gov and publications

3.4.1. Data reporting discrepancy types

We deemed any quantitative or qualitative differences between ClinicalTrials.gov’s most recent available trial entries and the corresponding data in publications to be discrepant.

Numeric discrepancies were defined as differences in quantitative data, such as a rating scale value or the number of patients affected.

Qualitative data discrepancies changed the meaning or interpretation of the reported data. Qualitative discrepancies included trial outcome data or specific selection criteria presented in one version and completely omitted in another, data in publications not presented in a comprehensible manner (purely graphically), lacking adverse events categories in the published or the registered version that are present in the other data source, or even missing any mention of adverse events.

All of the specific instances of misreporting were recorded. Recorded data extracted from ClinicalTrials.gov were numerically coded according to a previously calibrated coding manual based on consensus discussions between the authors and presented in tabular format.

3.4.2. Identification of discrepant reporting of All-Cause Mortality

Subsequent to the enactment of the Final Rule, an All-Cause Mortality field to trial records was added to ClinicalTrials.gov trial entries. This created a specific issue that needed to be addressed to preserve the intrinsic validity of our methodology, because trials completed prior to this period could only report deaths as adverse events or study outcomes, due to the absence of a designated field to report participant deaths (53). Therefore, we deemed trials completed prior to January 18, 2017 (deadline for compliance with the Final Rule) as reporting participant death adequately when explicitly reported in any part of the Results section in ClinicalTrials.gov. For trials completed on or after January 18, 2017, we assessed the reporting of participant death in the designated All-Cause Mortality field of the Results section in ClinicalTrials.gov. All-Cause Mortality was deemed not reported if the trialists did not assign a numerical value to the number of patients affected, either explicitly zero or frequencies ≥1, in the All-Cause Mortality field on ClinicalTrials.gov for trials completed after January 18, 2017. For the pre-Final Rule trials, we considered All-Cause Mortality reported when data were presented on ClinicalTrials.gov and in publications as adverse events, outcome, results, or as part of participant flow data.

Applying the same principle, serious and other adverse events were deemed as reported when explicitly assigned a numerical value either as zero or as frequencies ≥1 on ClinicalTrials.gov and in publications; therefore, trials that did not list zero in the field were treated as not explicitly reporting zero deaths.

3.4.3. Identification of trials that started before registration

Since the retrospective registration functionally served both as a subgroup assignment in our cohort and as an outcome, a critical aspect of our study design was precise identification of RCTs that started before registration in ClinicalTrials.gov. ClinicalTrials.gov trial entry provides the exact date (MM/DD/YYYY) when the trial was first posted. However, the same entry provides only the month and year of the trial start, lacking the specific date. Therefore, the exact calculation and evaluation of whether or not trialists complied with the 21-day deadline for registration after the enrollment of the first participant is impossible (39). With the goal of avoiding bias while categorizing the trials as starting before or after registration, we allowed a one-month reporting period “buffer window” to reduce deeming trials as non-compliant with the registration deadline. This methodology was similarly

used by Zarin et al. (54), but we slightly adjusted the tolerance window to align with our study objectives.

3.4.4. Classification of trials into chosen subgroups

Industry or non-industry funding was identified from funding details in ClinicalTrials.gov records. Publication in a journal claiming ICMJE recommendations was verified by cross-checking with the ICMJE's official list at the time of data extraction (55). The ICMJE no longer maintains this list as of April 2025 due to concerns that many journals do not actually follow ICMJE recommendations (56), but this was still the current practice during our study. Single-center or multicenter status was determined using the ClinicalTrials.gov "Locations" field and by manually checking the publication. Publication in an anesthesiology journal was determined by its classification under the category "anesthesiology" in Journal Citation Reports (JCR) (57). If not indexed by JCR, a journal one investigator (IV) considered an anesthesiology journal if its name included synonyms for "anesthesiology," "anesthesia," "pain medicine," or "perioperative medicine." In parallel, the IF value assigned to each journal by the JCR at the time of publication for the respective RCT was recorded for use as the sole predictor variable in the univariate logistic regression analysis. .

3.5 Inter-observer reliability

The authors' independent extractions were reliability-tested to assess the possibility of subjective interpretation of discrepancies between the registered and published data, potentially inducing a data collector bias. The test was conducted on a 10% random sample of the eligible RCTs. A high inter-observer reliability was obtained, ranging from the lowest kappa of 0.65 (95% CI 0.02-1.00) for study size and study arm reporting to the highest kappa of 1.00 for study size and mortality reporting. For the outcome assessment reliability, we first achieved a high reliability score (kappa=0.83, 95% CI 0.61-1.00) and then, through consensus discussions, reached an agreement concerning separate primary and secondary outcome assessments. For the serious and other adverse events, kappa scores were high (kappa=0.92, 95% CI 0.77-1.00 and kappa=0.91, 95% CI 0.75-1.00). The agreement in ratings of the results and probability measures reporting was also good (kappa =0.89 – 0.93, 95% CI 0.67-1.00). The senior author (SP) reviewed all the remaining extractions by IV.

3.6. Statistical Analysis

No sample size calculation or power analysis was necessary.

We reported descriptive data using frequencies and percentages for categorical variables. Afterward, we performed Chi-square analyses to determine differences in the frequencies of discrepant data reporting between the registry and publications, using Cramér's V (φc) as an effect size measure.

We used binary logistic regression to test for the association between the dependent and independent variables in secondary outcome B). The relationships were examined in a single model. We performed and reported goodness-of-fit and explained-variance metrics based on the Chi-square omnibus tests of model coefficients, the Hosmer-Lemeshow test, Nagelkerke R2, and Cox & Snell outputs, and used the variance inflation factor (VIF) for collinearity diagnostics. Regression results were reported as odds ratios (OR) with 95% confidence intervals (CI).

We used univariate logistic regression analysis to determine the association between any discrepancy in reporting of data items (1) – (9) and the publication journal's IF, a continuous variable, as an independent variable. Goodness-of-fit and explained variance were assessed using the Chi-square omnibus tests of model coefficients, the Hosmer-Lemeshow tests, Nagelkerke R2, and Cox & Snell outputs, and the results were reported. Regression results were reported as odds ratios (OR) with 95% confidence intervals (CI).

For all the statistical analyses, we used IBM SPSS Statistics for Windows, version 26 (IBM Corp., Chicago, IL, USA). Statistical tests with P-values below 0.05 were considered as significant.

4. RESULTS

4.1. Trial selection

The search for trials through the ClinicalTrials.gov database was performed on May 6, 2022. The search initially returned 1264 entries, of which 487 were duplicates. We removed further 162 trials after the manual search since they did not meet our eligibility criteria and were (a) presented in the search yield due to mislabeling, or (b) they were linked to publications that pooled the results of multiple trials; a case which requires manual identification and selection since ClinicalTrials.gov search engine does not provide the option of filtering trials that are part of pooled research process. A further 247 trials were removed because they could not be linked to any publication by the process described in section 3.3. Finally, we removed 110 trials that were not subject to the FDAAA New Rule. 258 trials were therefore selected as our cohort. The trial selection flowchart is shown in Figure 6.

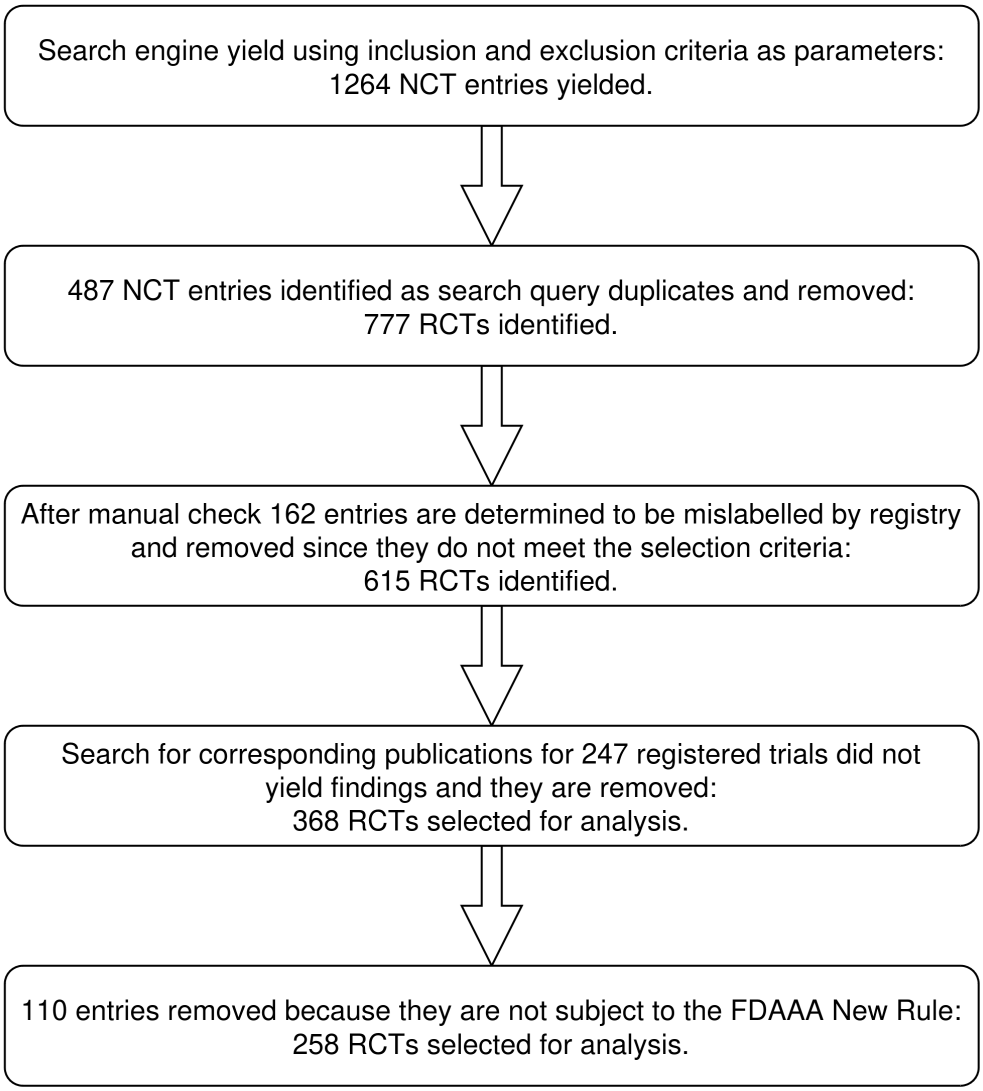


Figure 6. RCT selection flowchart.

4.2 Trial characteristics

Study characteristics are presented in Table 3. Most trials were phase 4 (63.6%), non-industry funded (79.1%), and had at least one site in the United States (98.8%). Plain bupivacaine was the most frequently studied drug (27.9%), followed by ketamine (16.3%) and ropivacaine (14.0%). The number of bupivacaine trials is even higher if we do not discern between trials performed on plain and liposomal bupivacaine (overall 40.7%). We did not identify trials matching our selection criteria for the following nine drugs: thiopental, enflurane, halothane, xenon, pancuronium, atracurium, mivacurium, levobupivacaine, dexmedetomidine. 28.7% of trials failed to register within 21 days of starting.

Table 3. Study characteristics

Total number of trials: 258			
Trial corresponding publications by year (n, %)			
2009	3 (1.2%)	2015	44 (17.1%)
2010	15 (5.8%)	2016	35 (13.6%)
2011	20 (7.8%)	2017	40 (15.5%)
2012	26 (10.1%)	2018	15 (5.8%)
2013	26 (10.1%)	2019	6 (2.3%)
2014	27 (10.5%)	2020	1 (0.4%)
Study size			
Median		Range	
80		1554	
Number of trial study arms			
Median		Range	
2.00		6.00	
Number of trial primary outcomes			
Median		Range	
1.00		8.00	
Study funding source (n)			
Industry		54	
Non - industry		204	

Trials location			
United States of America:	255	Turkey	2
Austria: Belgium Denmark Germany	4	Australia Czechia Finland Lithuania South Korea Taiwan	1
Spain	3		
Trial clinical phase (n, %)			
Phase 1| Phase 2	4 (1.6%)		
Phase 2	35 (13.6%)		
Phase 2| Phase 3	12 (4.7%)		
Phase 3	43 (16.7%)		
Phase 4	164 (63.6%)		
Trials by studied anesthetic **(n, %)**			
Bupivacaine	72 (27.9%)	Desflurane	5 (1.9%)
Ketamine	42 (16.3%)	Remifentanyl	
Ropivacaine	36 (14.0%)	Sulfentanyl	4 (1.6%)
Morphine	33 (12.8%)	N2O	
Liposomal bupivacaine	33 (12.8%)	Vecuronium	3 (1.2%)
Fentanyl Midazolam	28 (10.9%)	Alfentanyl Cisatracurium	2 (0.8%)
Propofol	26 (10.1%)	Etomidate	
Suggamadex	12 (4.7%)	Isoflurane	
Sevoflurane	8 (3.1%)	Succinylcholine	1 (0.4%)
Rocuronium	6 (2.3%)		

4.3 Descriptive statistics

All of the trials in our cohort contained at least one type of data misreporting. Figure 7 presents the quantities of reporting inadequacies for the selected data set items. 28.7% of trials were registered retroactively. Study size and study arm reporting were the most consistent in our study, 90.3% and 95.7%, respectively. Selection criteria were consistently reported in 24% of trials, and study enrollment dates in 29.5%.

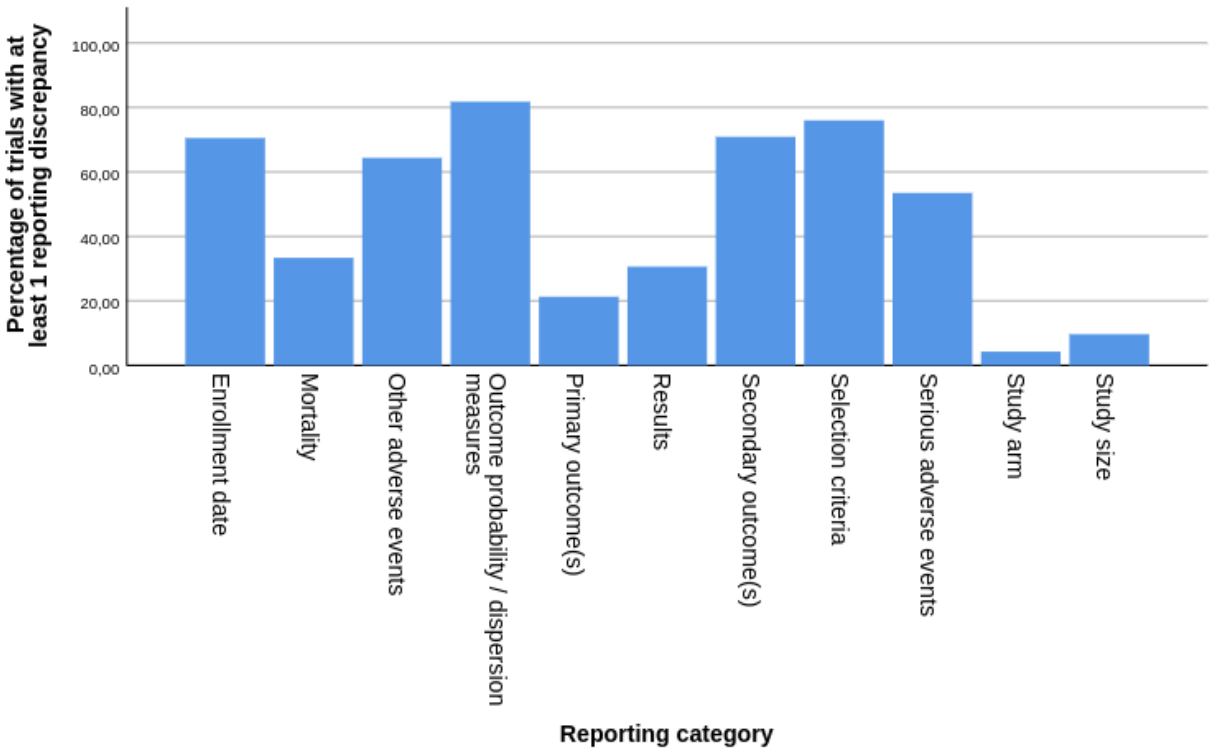


Figure 7. Proportion of trials with reporting discrepancies and/or inadequacies for each data item category examined in our study.

4.3.1. Study results and results probability measures reporting

About two-thirds of the trials in our cohort reported results flawlessly. Publications were a slightly more informative data source (see Table 4). This is in stark contrast to the overall quality of the results probability and dispersion measures quality, where two-thirds of the trialists did not disclose p-values and/or statistical method to the registry (see Table 5).

Table 4. Types and frequencies of results reporting discrepancies between the ClinicalTrials.gov registered version and the publication of the same trial.

Study results reporting discrepancies between ClinicalTrials.gov and publications, n (%)	
Consistent reporting	172 (66.7 %)
Registered primary outcome not designated as primary in the publication[a]	7 (2.7 %)
Quantities of assessments greater in the publication	22 (8.5%)
Quantities of assessments greater in the registry	12 (4.7%)
Assessed parameters reported only in the registry	1 (0.4 %)
Results data expanded in publication with more timepoints for collected data	1 (0.4 %)
Results data reduced in publication with less timepoints for collected data	1 (0.4 %)
Results data presented inconsistently making it impossible to compare[b]	17 (6.6 %)
Results presented with different method or timeframe for outcome assessment	4 (1.6 %)
Quantities of assessments differ in either study arm	8 (3.1 %)
Incomparable because outcomes were completely different between sources	5 (1.9%)
Results data swapped between two study arms	1 (0.4 %)
Difference in measure of central tendency between sources	1 (0.4 %)
Difference in measures of dispersion between sources	1 (0.4 %)

[a]For the purposes of statistical evaluation these discrepancies were reported as outcome discrepancies (see Table 9), not determined as a results reporting discrepancy input in the statistical analysis.
[b]Incomparable due to adverse events presented in a graph or figure in publications while specific values were described in ClinicalTrials.gov. *Percentages have been rounded and do not total 100.

Table 5. Types and frequencies of results probability measures reporting discrepancies between the ClinicalTrials.gov registered version and the publication of the same trial.

Study results probability measures reporting discrepancies, n (%)*	
Consistent reporting	47 (18.2%)
p-value and/or statistical method not presented in registry	179 (69.4%)
p-value and/or statistical method presented in registry but not in publication	1 (0.4%)
Statistical method discrepancy	7 (2.7%)
Statistical method discrepancy, but statistical measure (*p*-value) numerically the same	2 (0.8%)
Probability measure (*p*-value or CI[†]) discrepancy	10 (3.9%)
Discrepant statistical method and probability measure	2 (0.8%)
Either source presented the *p*-value or CI	2 (0.8%)
p-value possibly incorrectly rounded up in the publication	1 (0.4%)
Probability measures (*p*-value or CI) differ due to a quantitative results reporting discrepancy	2 (0.8%)
Probability measures (*p*-value or CI) differ due to qualitative results reporting discrepancy (method of evaluation and timeframe are changed in publication)	1 (0.4%)

[a] For the purposes of statistical evaluation these discrepancies were reported as outcome discrepancies (see Table 9), not determined as a results reporting discrepancy input in the statistical analysis. [b]Incomparable due to adverse events presented in a graph or figure in publications while specific values were described in ClinicalTrials.gov. *Percentages have been rounded and do not total 100.
[†]CI, confidence interval

4.3.2. Adverse events reporting

62.4% of trials in our group contained some sort of serious adverse event reporting inadequacy. Data is presented in Table 6. While more trials reported SAEs only in publications than vice versa, 40.4% of trials cumulatively either did not mention AEs at all or omitted stating that these were the only AEs that occurred during the trial. Due to the less severe nature of the discrepancy, we chose to treat trials that provided consistent reporting but in the wrong input field in the registry platform as adequate reporting during the statistical analysis part of our study.

Table 6. Types and frequencies of serious adverse events reporting discrepancies between the ClinicalTrials.gov registered version and the publication of the same trial.

Study SAE* reporting discrepancies	n (%)
Consistent reporting	97 (37.6%)
Consistent reporting but data provided in wrong data input field in ClinicalTrials.gov[a]	3 (1.2%)
Quantity greater in the registry	4 (1.6 %)
Quantity greater in the publication	2 (0.8%)
At least one adverse event description reported only in the registry	20 (7.8%)
At least one adverse event category reported only in the publication	33 (12.8 %)
Textual descriptions only that are absent in ClinicalTrials.gov	1 (0.4%)
Adverse events data not stated at all in the publication while reported as "0" in the registry	84 (32.6 %)
No explicit statement in the publication about the reported adverse events being all that occurred[a]	20 (7.8 %)
SAE** misclassified as OAE	3 (1.2%)

[a]Despite inadequacies, not counted as discrepant reporting input in the statistical analysis.

Abbreviations: *SAE, serious adverse event; **OAE, other adverse event

Similar to SAE, 67.4% of trials had at least one OAE reporting inadequacy. Types of OAE misreporting are listed in Table 7 along with the frequencies. Registry and publications were similarly informative data sources, except for the tendency of some trials that reported adverse events as zero in the registry to ignore them altogether in the publication; this was a less frequent occurrence than in SAE reporting (Figure 8).

Table 7. Types and frequencies of other adverse events reporting discrepancies between the ClinicalTrials.gov registered version and the publication of the same trial.

Study OAE* reporting discrepancies	**n (%)**
Consistent reporting	84 (32.6%)
Consistent reporting but data provided in wrong data input field in ClinicalTrials.gov[a]	4 (1.6%)
Quantity greater in the registry	13 (5 %)
Quantity greater in the publication	12 (4.7 %)
At least one adverse event description reported only in the registry	50 (19.4%)
At least one adverse event reported only in the registry but using surrogate measures with no quantification provided	3 (1.2%)
Higher threshold percentages reported in the publication than in the registry	13 (5 %)
At least one adverse event category reported only in the publication	58 (22.5 %)
Textual descriptions only that are absent in ClinicalTrials.gov	7 (2.7%)
Adverse events data presented inconsistently making it impossible to compare[b]	1 (0.4 %)
Adverse events data not stated at all in the publication while reported as "0" in the registry	45 (17.4 %)
No explicit statement in the publication about the reported adverse events being all that occurred[a]	3 (1.2 %)
OAE** misclassified as SAE in the registry[a]	1 (0.4 %)

[a]Despite inadequacies, not counted as discrepant reporting input in the statistical analysis.

[b]Incomparable due to adverse events presented in a graph or figure in publications while specific values were described in ClinicalTrials.gov. Abbreviations: *OAE, other adverse event; **SAE, serious adverse event

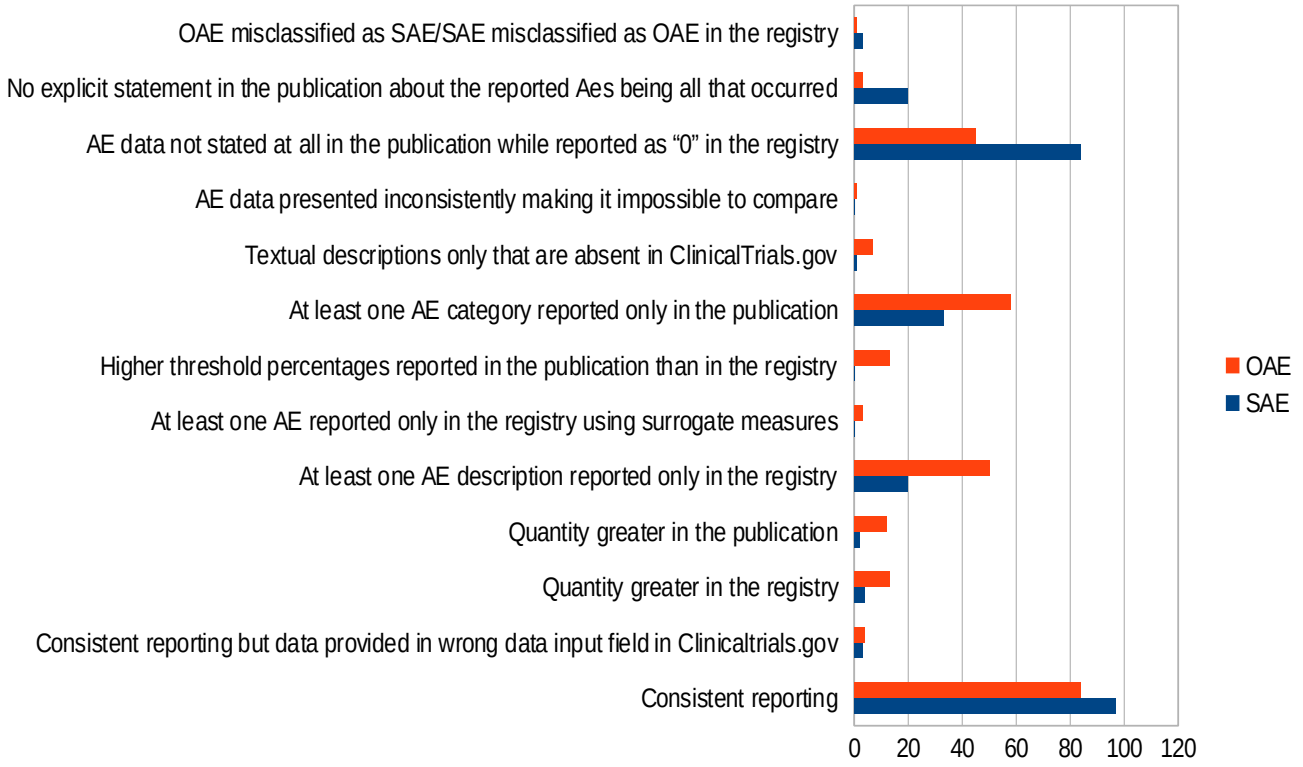


Figure 8. A comparison of the frequencies of identified types of discrepant AE reporting between SAE and OAE reporting in our study.

4.3.3. The all-cause mortality reporting

Overall, the instances of all-cause mortality quantitative discrepant reporting were low, cumulatively 3.6% (see Table 8). Two-thirds of the trials reported mortality correctly. An important instance of reporting inadequacy was leaving blank fields for this category in the registry, a case that happened exclusively in trials that preceded the New Rule.

Table 8. Types and frequencies of mortality reporting discrepancies between the ClinicalTrials.gov registered version and the publication of the same trial.

All-cause mortality reporting discrepancies, n (%)	
Consistent reporting	172 (66.7 %)
Lower frequency in publication	1 (0.4 %)
Lower frequency in registry	2 (0.8 %)
Reported in registry and omitted completely in publication	3 (1.2 %)
Reported in publication and omitted completely in registry	3 (1.2 %)
Reported in the SAE* table in ClinicalTrials.gov	1 (0.4 %)
Not reported in ClinicalTrials.gov**	76 (29.5%)

*Abbreviations: SAE, serious adverse event ** Trialists left blank fields for All-cause mortality reporting in the registry. All of the instances where trials that are not required to be New Rule compliant.

4.3.4. Study outcomes reporting

Primary outcomes were reported much more consistently than secondary outcomes (77.5% vs 22.9%, see Table 9). Registry and publication were similarly informative data sources for primary outcomes, but secondary publications were more often reported in publications. Outcome hierarchy underwent changes in 8.5% of the trials and was insufficiently demarcated in 3.9%.

Table 9. Types and frequencies of study primary and secondary outcomes reporting discrepancies between the ClinicalTrials.gov registered version and the publication of the same trial.

Study outcome reporting discrepancies, n (%)	
Primary outcome reported consistently	200 (77.5 %)
Primary outcome detail reported inconsistently (timeframe or method of evaluation)	17 (6.6 %)
Timeframe	12 (4.7 %)
Methods	7 (2.7 %)
Primary outcome present solely in the registry	9 (3.5 %)

Primary outcome present solely in the publication	16 (6.2 %)
Registered secondary outcome promoted to primary in publication	13 (5 %)
Registered primary outcome demoted to secondary in publication	9 (3.5 %)
Unclear whether the newly added outcome in the publication is primary or secondary	7 (2.7 %)
Publication did not explicitly differentiate outcomes as primary or secondary[a]	3 (1.2 %)
Secondary outcome reported consistently	72 (27.9 %)
Secondary outcome detail reported inconsistently (timeframe, method of evaluation etc.)	13 (5 %)
Timeframe	11 (4.3%)
Methods	4 (1.6%)
Secondary outcome present solely in the registry	77 (29.9 %)
Secondary outcome present solely in the publication	133 (51.6 %)

[a]Despite inadequacy reported but not deemed as a discrepancy input in the statistical analysis. * A single RCT could have multiple outcome reporting discrepancies.

4.3.5. Study eligibility criteria reporting

Selection criteria were the least consistently reported data item in our cohort (Table 10). ClinicalTrials.gov was the data source with more information.

Table 10. Types and frequencies of eligibility criteria reporting discrepancies between the ClinicalTrials.gov registered version and the publication of the same trial.

Eligibility criteria reporting discrepancy	**n (%)**
Selection criteria reported consistently	62 (24 %)
Minimum or maximum values in specific criterion range changed	51 (19.8%)
Selection criteria are present only in registry	137 (53.1 %)
Selection criteria are present only in publication	105 (41 %)

4.3.6. Study enrollment date reporting

Consistency of enrollment date reporting was the second lowest in our cohort (Table 11). Approximately half of the studies reported different dates across sources, while a significant number of authors did not disclose a trial start date in publication.

Table 11. Types and frequencies of enrollment date reporting discrepancies between the ClinicalTrials.gov registered version and the publication of the same trial.

Study enrollment date reporting discrepancies	**n (%)**
Consistent reporting	76 (29.5 %)
Consistent reporting but data provided in wrong data field in ClinicalTrials.gov	1 (0.4 %)
Mismatching date between sources	130 (50.4 %)
Omitted in publication	51 (19.8 %)

4.4 Data reporting consistency predictors

4.4.1. Trial funding source

There were several significant differences between industry- and non-industry-funded trials (Table 12). Industry-funded trials reported outcome probability or dispersion measures and secondary outcomes more consistently, while being more compliant with the trial registration deadline. Non-industry trials reported other adverse events more consistently. It should be noted that they also had a higher frequency of consistent study-size reporting, with the p-value only missing crossing the threshold of statistical significance by a minimal margin.

Table 12. Association between trial funding source and discrepant trial data reporting between data registered on ClinicalTrials.gov and in the publication of the same trial.

Reporting category	Reporting consistency	Industry funded trials (N=54)	Non-industry funded trials (N=204)	p value [a]	Cramer's V
Results	consistent	34	145	0.250	0.072
	discrepant	20	59		
Outcome probability / dispersion measures	consistent	16	31	**0.015**	0.152
	discrepant	38	173		
SAE [b]	consistent	25	95	0.972	0.002
	discrepant	29	109		
OAE [c]	consistent	9	83	**0.001**	0.204
	discrepant	45	121		
Mortality	consistent	38	134	0.516	0.040
	discrepant	16	70		
Study size	consistent	45	188	0.051	0.121
	discrepant	9	16		
Study primary outcome(s)	consistent	44	159	0.572	0.035
	discrepant	10	45		
Study secondary outcome	consistent	22	53	**0.034**	0.132
	discrepant	32	151		
Selection criteria	consistent	11	51	0.479	0.044
	discrepant	43	153		
Study arm	consistent	53	194	0.324	0.061
	discrepant	1	10		
Enrollment date	consistent	15	61	0.761	0.019
	discrepant	39	143		
Registration deadline	compliant	49	135	**0.000**	0.221
	late	5	69		

[a]We used chi-squared analysis and considered P values less than 0.05 to be significant. [b]SAE - Serious adverse events. [c]OAE - Other adverse events.

4.4.2. Adherence to trial registration deadline

Trials that were late to register did not differ from trials compliant with the registration deadline for all the data item reporting categories except for primary outcome reporting, which they misreported more often (Table 13).

Table 13. Association between adherence to the ClinicalTrials.gov registration deadline and discrepant trial data reporting between data registered on ClinicalTrials.gov and in the publication of the same trial.

Reporting category	Reporting consistency	Trials compliant with registration deadline (N=184)	Trials late to register (N=74)	p value [a]	Cramer's V
Results	consistent	130	49	0.484	0.044
	discrepant	54	25		
Outcome probability / dispersion measures	consistent	37	10	0.215	0.770
	discrepant	147	64		
SAE [b]	consistent	84	36	0.663	0.027
	discrepant	100	38		
OAE [c]	consistent	66	26	0.911	0.007
	discrepant	118	48		
Mortality	consistent	127	45	0.206	0.079
	discrepant	57	29		
Study size	consistent	170	63	0.075	0.111
	discrepant	14	11		
Study primary outcome(s)	consistent	151	52	**0.036**	0.130
	discrepant	33	22		
Study secondary	consistent	54	21	0.877	0.010

outcome	discrepant	130	53		
Selection criteria	consistent	50	12	0.062	0.116
	discrepant	134	62		
Study arm	consistent	177	70	0.565	0.036
	discrepant	7	4		
Enrollment date	consistent	55	21	0.809	0.015
	discrepant	129	53		

[a]We used chi-squared analysis and considered P values less than 0.05 to be significant. [b]SAE - Serious adverse events. [c]OAE - Other adverse events.

4.4.3. Publication in a journal following ICMJE recommendations

Whether the journal stated at the time of publication that it followed ICMJE recommendations was not a predictor for most data item categories, except for mortality reporting (Table 14).

Table 14. Association between publication in an ICMJE [a] - compliant journal and discrepant trial data reporting between data registered on ClinicalTrials.gov and in the publication of the same trial.

Reporting category	Reporting consistency	ICMJE journal (N=92)	Not an ICMJE journal (N=166)	p value [b]	Cramer's V
Results	consistent	65	114	0.741	0.021
	discrepant	27	52		
Outcome probability / dispersion measures	consistent	15	32	0.553	0.037
	discrepant	77	134		
SAE [c]	consistent	45	75	0.565	0.036
	discrepant	47	91		
OAE [d]	consistent	35	57	0.552	0.037
	discrepant	57	109		
Mortality	consistent	70	102	**0.017**	0.149
	discrepant	22	64		

Study size	consistent	87	146	0.085	0.107
	discrepant	5	20		
Study primary outcome(s)	consistent	76	127	0.252	0.071
	discrepant	16	39		
Study secondary outcome	consistent	29	46	0.518	0.040
	discrepant	63	120		
Selection criteria	consistent	24	38	0.565	0.036
	discrepant	68	128		
Study arm	consistent	90	157	0.216	0.077
	discrepant	2	9		
Enrollment date	consistent	28	48	0.798	0.016
	discrepant	64	118		
Registration deadline	compliant	68	116	0.493	0.043
	late	24	50		

[a]ICMJE – International Committee of Medical Journal Editors. [b]We used chi-squared analysis and considered P values less than 0.05 to be significant. [c]SAE - Serious adverse events. [d]OAE - Other adverse events.

4.4.4. Number of trial research centers

Data is presented in Table 15. Multi-center trials reported outcome probability or dispersion measures more consistently and adhered to the trial registration deadlines more frequently. They had higher frequencies of misreporting other adverse events.

Table 15. Association between the number of trial research sites and discrepant trial data reporting between data registered on ClinicalTrials.gov and in the publication of the same trial.

Reporting category	Reporting consistency	Single-center trials (N=214)	Multi-center trials (N=44)	p value [a]	Cramer's V
Results	consistent	150	29	0.583	0.027
	discrepant	64	15		
Outcome probability / dispersion measures	consistent	31	16	**0.001**	0.213
	discrepant	183	28		
SAE [b]	consistent	99	21	0.859	0.001
	discrepant	115	23		
OAE [c]	consistent	86	6	**0.001**	0.208
	discrepant	128	38		
Mortality	consistent	141	31	0.558	0.036
	discrepant	73	13		
Study size	consistent	194	39	0.680	0.022
	discrepant	20	5		
Study primary outcome(s)	consistent	168	35	0.878	0.010
	discrepant	46	9		
Study secondary outcome	consistent	58	17	0.125	0.096
	discrepant	156	27		
Selection criteria	consistent	53	9	0.542	0.043
	discrepant	161	35		
Study arm	consistent	205	42	0.919	0.004
	discrepant	9	2		
Enrollment date	consistent	62	14	0.706	0.017
	discrepant	152	30		
Registration deadline	compliant	147	37	**0.040**	0.128
	late	67	7		

[a]We used chi-squared analysis and considered P values less than 0.05 to be significant. [b]SAE - Serious adverse events. [c]OAE - Other adverse events.

4.4.5. Time periods

Comparisons between trials from 2009-2012 and 2017 periods are presented in Table 16, between trials from 2013-2016 and 2017-2020 periods in Table 17. The only data item with improved reporting over time was the all-cause mortality, in both comparisons.

Table 16. Association between trial completion date and discrepant trial data reporting between trial data on ClinicalTrials.gov and in publications of the same trial between the oldest and most recent trial group in our study.

Reporting category	Reporting consistency	RCTs[b] from 2009-2012 timeperiod (n=64)	RCTs from 2017-2020 timeperiod (n=62)	p value [a]	Cramer's V
Results	consistent	43	44	0.646	0.041
	discrepant	21	18		
Outcome probability / dispersion measures	consistent	17	10	0.154	0.127
	discrepant	47	52		
SAE [c]	consistent	23	26	0.490	0.062
	discrepant	41	36		
OAE [d]	consistent	15	24	0.064	0.165
	discrepant	49	38		
Mortality	consistent	19	60	**0.000**	0.694
	discrepant	45	2		
Study size	consistent	60	53	0.127	0.136
	discrepant	4	9		
Study primary outcome(s)	consistent	46	53	0.063	0.166
	discrepant	18	9		
Study secondary outcome(s)	consistent	15	23	0.095	0.149
	discrepant	49	39		
Selection criteria	consistent	13	19	0.183	0.119

	discrepant	51	43		
Study arm	consistent	64	59	0.075	0.159
	discrepant	0	3		
Enrollment date	consistent	17	24	0.146	0.130
	discrepant	47	38		
Registration deadline	compliant	44	44	0.786	0.024
	late	20	18		

[a] We used chi-squared analysis and considered P values less than 0.05 to be significant. [b] RCT- randomized controlled trial. [c] SAE - Serious adverse events. [d] OAE - Other adverse events.

Table 17. Association between trial completion date and discrepant trial data reporting between trial data on ClinicalTrials.gov and in publications of the same trial between the second most recent and the most recent trial group in our study.

Reporting category	Reporting consistency	RCTs from 2013-2016 timeperiod (n=132)	RCTs from 2017-2020 timeperiod (n=62)	p value [a]	Cramer's V
Results	consistent	92	44	0.857	0.013
	discrepant	40	18		
Outcome probability / dispersion measures	consistent	20	10	0.861	0.013
	discrepant	112	52		
SAE [c]	consistent	71	26	0.124	0.111
	discrepant	61	36		
OAE [d]	consistent	53	24	0.848	0.014
	discrepant	79	38		
Mortality	consistent	93	60	**0.000**	0.301
	discrepant	39	2		
Study size	consistent	120	53	0.257	0.081

	discrepant	12	9		
Study primary outcome(s)	consistent	104	53	0.268	0.079
	discrepant	28	9		
Study secondary outcome(s)	consistent	37	23	0.203	0.091
	discrepant	95	39		
Selection criteria	consistent	30	19	0.237	0.085
	discrepant	102	43		
Study arm	consistent	124	59	0.731	0.025
	discrepant	8	3		
Enrollment date	consistent	35	24	0.085	0.124
	discrepant	97	38		
Registration deadline	compliant	96	44	0.799	0.018
	late	36	18		

[a] We used chi-squared analysis and considered P values less than 0.05 to be significant. [b] RCT-randomized controlled trial. [c] SAE - Serious adverse events. [d] OAE - Other adverse events.

4.4.6. Publication in an anesthesiology journal

Trials published in anesthesiology journals reported adverse events with significantly more frequent discrepancies, both in SAE and OAE categories (see Table 18). Anesthesiology journals were more consistent in reporting outcome probability or dispersion measures.

Table 18. Association between publication in an anesthesiology journal and discrepant trial data reporting between data registered on ClinicalTrials.gov and in the publication of the same trial.

Reporting category	Reporting consistency	Anesthesiology journal (N=107)	Not an anesthesiology journal (N=151)	p value [b]	Cramer's V
Results	consistent	73	106	0.735	0.021
	discrepant	34	45		
Outcome probability /	consistent	29	18	**0.002**	0.194

dispersion measures	discrepant	78	133		
SAE [b]	consistent	40	80	**0.013**	0.154
	discrepant	67	71		
OAE [c]	consistent	28	64	**0.016**	0.180
	discrepant	78	87		
Mortality	consistent	66	106	0.153	0.089
	discrepant	41	45		
Study size	consistent	97	136	0.875	0.100
	discrepant	10	15		
Study primary outcome(s)	consistent	87	116	0.386	0.054
	discrepant	20	35		
Study secondary outcome	consistent	32	43	0.803	0.016
	discrepant	75	108		
Selection criteria	consistent	27	35	0.704	0.024
	discrepant	80	116		
Study arm	consistent	104	143	0.329	0.061
	discrepant	3	8		
Enrollment date	consistent	33	43	0.681	0.026
	discrepant	74	108		
Registration deadline	compliant	79	105	0.452	0.047
	late	28	46		

[a]We used chi-squared analysis and considered P values less than 0.05 to be significant. [b]SAE - Serious adverse events. [c]OAE - Other adverse events.

4.4.7. Publication in a journal indexed in JCR

Trials published in journals not indexed in JCR also reported adverse events with significantly more frequent discrepancies, both in SAE and OAE categories (see Table 19). They also had higher frequencies of study size reporting discrepancies.

Table 19. Association between publication in a journal indexed by JCR and discrepant trial data reporting between data registered on ClinicalTrials.gov and in the publication of the same trial.

Reporting category	Reporting consistency	Journal indexed by JCR (N=232)	Not a JCR-indexed journal (N=26)	p value [b]	Cramer's V
Results	consistent	165	14	0.070	0.113
	discrepant	67	12		
Outcome probability / dispersion measures	consistent	44	3	0.352	0.058
	discrepant	188	23		
SAE [b]	consistent	116	4	**0.001**	0.209
	discrepant	116	22		
OAE [c]	consistent	89	3	**0.023**	0.171
	discrepant	142	23		
Mortality	consistent	155	17	0.884	0.009
	discrepant	77	9		
Study size	consistent	213	20	**0.015**	0.151
	discrepant	19	6		
Study primary outcome(s)	consistent	184	19	0.462	0.046
	discrepant	48	7		
Study secondary outcome	consistent	69	6	0.478	0.044
	discrepant	163	20		
Selection criteria	consistent	53	9	0.183	0.083
	discrepant	179	17		
Study arm	consistent	222	25	0.912	0.007

	discrepant	10	1		
Enrollment date	consistent	70	6	0.452	0.047
	discrepant	162	20		
Registration deadline	compliant	169	15	0.105	0.101
	late	63	11		

[a]We used chi-squared analysis and considered P values less than 0.05 to be significant. [b]SAE - Serious adverse events. [c]OAE - Other adverse events.

4.5 Final Rule

Trials subject to the Final Rule in our study reported the all-cause mortality in a significantly more consistent manner (Table 20).

Table 20. Association of temporal applicability of the Final Rule to the trial and consistency of the all-cause mortality reporting in our study.

Reporting category	Reporting consistency	Trials preceding the Final Rule	Trials subject to the Final Rule	p value [a]	Cramer's V
Mortality	consistent	112	60	**0.000**	0.359
	discrepant	84	2		

[a] We used chi-squared analysis and considered P values less than 0.05 to be significant.

4.6 Testing the predictors for combined safety and results reporting consistency

The data for our binary logistic regression model are presented in Table 21. The logistic regression model was not statistically significant ($\chi 2 = 10.649$, $p = 0.059$). The model explained 7.1% of the variance in discrepancy presence (Nagelkerke R2). Trials completed before the Final Rule compliance deadline were 2.7 times more likely to misreport results, adverse events, or mortality data.

Table 21. Binary logistic regression analysis results for testing the chosen subgroups in our study for the presence of any discrepancy in the following data reporting categories: results, adverse events (both serious and other) and mortality.

Predictor	B[a]	Std. error	Df[b]	p-value	OR[c]	95% CI[d] for OR		VIF[e]
						Lower bound	Upper bound	
Timeperiod	0.989	0.372	1.0	0.008	2.688	1.297	5.569	1.006
Funding source	-0.384	0.585	1.0	0.511	0.681	0.216	2.143	1.383
ICMJE member	0.099	0.374	1.0	0.791	1.104	0.530	2.298	1.004
Multicenter trial	-0.742	0.707	1.0	0.294	0.476	0.119	1.903	1.341
Late to register	-0.271	0.413	1.0	0.511	0.763	0.340	1.712	1.053

Omnibus Tests of Model Coefficients		Hosmer and Lemeshow Test		Cox & Snell R Square	Nagelkerke R-Squared
χ^2	p-value	χ^2	p-value	0.040	0.071
10.649	0.059	4.675	0.586		

[a] B- estimated binary logistic regression coefficients for the models. [b] Df – Degrees of freedom. [c] OR – Odds ratio. [d] CI – Confidence interval. [e]VIF – Variance inflation factor.

4.7. Publication journal's impact factor as a predictor of study data and patient-centered elements reporting consistency

The IF of journals that published trials in our study was not a predictor of consistent reporting for any of the trial data categories that we investigated. The combined output of multiple univariable binary logistic regression analyses is presented in Table 22.

Table 22. Univariable binary logistic regression analysis results for testing the impact factor of publications in our study as a predictor of misreported trial data.

Data item with misreported data	B[a]	Std. error	p-value	OR[b]	95% CI[c] for OR	
					Lower bound	Upper bound
Results	-0.011	0.014	0.442	0.989	0.962	1.017
Outcome probability / dispersion measures	-0.004	0.010	0.649	0.996	0.977	1.015
SAE	0.010	0.010	0.348	1.010	0.989	1.031
OAE	-0.001	0.009	0.951	0.999	0.982	1.017
Mortality	0.004	0.009	0.664	1.004	0.986	1.022
Study size	-0.017	0.033	0.607	0.983	0.922	1.049
Primary outcome(s)	-0.030	0.029	0.302	0.971	0.917	1.027
Secondary outcome(s)	-0.023	0.012	0.069	0.978	0.954	1.002
Selection criteria	-0.016	0.010	0.111	0.984	0.964	1.004
Study arm	-0.004	0.026	0.892	0.996	0.947	1.049
Study enrollment date	0.091	0.048	0.058	1.095	0.997	1.204
Late for registration deadline	-0.002	0.011	0.817	0.998	0.977	1.019

Data item with misreported data	Constant OR	Omnibus Tests of Model Coefficients		Cox & Snell R Square	Nagelkerke R-Squared
		χ^2	p-value		
Results	0.436	0.782	0.376	0.003	0.005
Outcome probability / dispersion measures	4.415	0.191	0.662	0.001	0.001
SAE	0.935	1.040	0.308	0.004	0.006
OAE	1.613	0.004	0.951	0.000	0.000

Mortality	0.483	0.184	0.668	0.001	0.001
Study size	0.099	0.429	0.512	0.002	0.004
Primary outcome(s)	0.310	2.051	0.152	0.009	0.014
Secondary outcome(s)	2.778	4.709	0.030	0.020	0.029
Selection criteria	3.824	2.942	0.086	0.013	0.019
Study arm	0.046	0.021	0.885	0.000	0.000
Study enrollment date	1.449	8.254	0.004	0.035	0.049
Late for registration deadline	0.379	0.056	0.813	0.000	0.000

[a] B- estimated binary logistic regression coefficients for the models. [b] OR – Odds ratio. [c] CI – Confidence interval. There is a single degree of freedom for all analyses.

5. DISCUSSION

5.1. Results overview

Our study found that the reporting of patient-relevant data and study design elements across anesthesiology trial registry entries and their corresponding publications was not consistent. This corroborates findings from similar research in other clinical fields (58-60). Our study is novel for applying the methodology to describe instances of discrepant and misreported data in a large sample of anesthesiology RCTs, for investigating a broader range of data item categories, and for the choice of our subgroups. The overall consistency of reporting was arguably low for all reported data categories except for study arm and study size.

Our novel finding is that reporting of study design and patient-related data from anesthesiology trials failed to improve over time, except for all-cause mortality reporting, which appears to be effectively enforced by the Final Rule. This conclusion stands in contrast to a study by Mughal et al. in other fields of medicine, which found significant improvements in reporting across almost all data item categories since the enactment of the FDAAA legislation (61). The authors divided the trials into time windows similar to ours, so a question arises about possible differences in reporting practices in anesthesiology compared to other clinical fields.

Additionally, although the results data ranked among the more consistently reported data item categories in our cohort, approximately one-third of the trials had at least some misreporting of the essential data. Since results reporting as a category is vulnerable to publication bias favoring positive findings, additional research is needed to determine whether these discrepancies could be explained by publication bias.

Highly frequent inconsistencies in selection criteria reporting (76.4%) draw attention as an indicator of possible flawed research design and point of entry for research bias. Contrary to expectations, trials in our study that registered retroactively did not report selection criteria more consistently. This finding suggests that trialists may not engage in deliberate selective data reporting, but rather do not perceive the entire trial registration process as a serious procedure that produces a valid data source.

The opposite case in our study was found in sample size reporting, where retroactively registered trials were expected to report sample sizes more consistently overall, since they were registered at a point in time closer to, or even after, the study end. It is a paradox that trials in our study that met the

registration deadline reported sample sizes more consistently, with better reporting practices as the most probable explanation.

Other adverse events in our study were more frequently consistently reported in industry-funded and multi-center trials compared to their non-industry-funded and single-center counterparts. Perhaps industry funding or policies allow or motivate trialists to be more attentive to adverse event reporting, or industry policies. The nature of multi-center research could be compensating for multi-local study uniformity challenges by enacting stricter adherence to protocols, leading to better compliance with registration legislation.

This aligns with the results of a recent study by McCormick et al. (62), in which industry funding in a cohort investigating adverse event reporting in regional anesthesia trials correlated with greater consistency in safety reporting. Trials on regional anesthetics also accounted for a significant fraction of our selected cohort, whereas the important difference between our study designs is that they included non-ACTs. Accordingly, previous studies also found that industry-funded trials were more frequently prospectively registered (63,64).

Trials published in anesthesiology journals in our study had higher frequencies of adverse event misreporting, a novel finding that may indicate publication bias in the anesthesiology literature. This topic has been approached in the literature so far mainly from the perspective of the impact of PB on systematic reviews and meta-analyses, with calculated estimates that it was found in 50-80% of the reviews published in anesthesiology journals (65).

The impact factor of the publication journal was not a predictor of better reporting consistency in our study.

Whether the trial reported following ICMJE recommendations was also not characterized with better reporting quality, except for the all-cause mortality, an observation that is insightful regarding the ICMJE decision to discontinue maintaining the list (56).

The results of the present study can be generalized to other completed ClinicalTrials.gov trial records with similar data and results received after the FDAAA mandate. It should be emphasized that our cohort was selected among the trials that disclosed results designated as ACT by the FDA. The actual state of trial registration practices in real-world conditions may be even worse, since we already selected only trials that are compelled under US law to register and those that have already demonstrated a minimum level of legislative compliance by disclosing results. As already stated in the Introduction, at present, the number of non-US-based trials on the ClinicalTrials.gov registry has

surpassed the number of domestic trials, and a significant number of those trials are not subject to FDAAA.

5.2. Possible explanations for the existence of data misreporting

Although the existence of data discrepancies between registries and publications has been a known phenomenon for some time, the underlying causes of these discrepancies remain unknown and insufficiently researched.

From the authors' point of view, publication represents the pinnacle of trial conduct, so it is possible that some researchers may perceive the trial registration process just as an administrative requirement, a single step needed to ensure trial publication. If that is the case, they may not acknowledge the trial registry entry as an independent data source and may not be motivated to invest effort to update data after entry in a registry so that their manuscript may be eligible for publication in a journal that states completed trial registration as a requirement for publication. A study comparing more than 10,000 trials that were registered both in ClinicalTrials.gov and EUCTR found that 33.9 % of trials listed as “ongoing” on the EUCTR platform were designated as “completed” on ClinicalTrials.gov (66). This specific case leaves no room for intentional manipulation of trial status and suggests a certain level of general neglect of practices that are not strictly mandated. This could explain why many trialists did not report mortality or adverse events data in the respective fields before the Final Rule. The differences we observed could also be attributed to human-factor data entry errors, which are more likely if different research team members are assigned to input trial data in the the registered version and in the publication.

Also, there is a possibility that data modification could occur intentionally.

5.3. Implications of using the trial registries for meta-science and other forms of downstream data translation

As previously stated in the Introduction, the Cochrane Handbook encourages the use of clinical trial registration platforms as data sources in conducting meta-analyses. Discrepant results and key study elements raise further questions about which source is more reliable and closer to the study data. These questions are complex, and answers are elusive and multifaceted. From one viewpoint, clinical trial

registries are often promoted as a valuable data source assigned under the umbrella term “real world evidence” (RWE) (67) or “real world data” (RWD) (68). From the opposite viewpoint, although more susceptible to publication bias, publications guarantee a certain level of quality control through the peer-review process, while registries, as a rule, lack an independent entity to provide quality control, relying instead on the investigator’s transparency and motivation (69). Legislative measures promote the very existence of data disclosure; they lack the framework to enforce the high accuracy of study data.

The inconsistencies observed for both results and adverse event reporting in this study potentially hinder the use of ClinicalTrials.gov as a meta-research source. For example, a study examining 356,515 entries from the world’s largest implantable cardioverter defibrillator registry found that the number of reported complications was only one-third of those reported in publications (70). The presence of data in the wrong registry fields may also increase the potential for bias when automated data extraction or data mining is used to retrieve data, as described in a previous study (71). This is a topic that has grown in its importance since the point in time when we started our study, since the advent of large language models (LLMs) and rapid advances in the field of artificial intelligence (AI) have enabled the creation of research tools that were, until recently, difficult to develop. An RCT is currently investigating the accuracy and effectiveness of using AI tools to extract data for meta-analyses (72).

5.4. Potential measures to promote the quality and accuracy of clinical trial registries

The problem we examined is complex, and alleviation is likely possible only through the engagement of multiple stakeholders (73). These results emphasize the importance of peer reviewers and editorial staff comparing registration and publication at the journal level.

The potential use of clinical registries to assess the validity of trial data during the peer-review process is not a novel concept (74). Nevertheless, this prospect has been insufficiently studied in the broader medical research field and has never been studied in the field of anesthesiology. One study found that neither retroactive trial registration nor the presence of data discrepancies between the registry and the publication of the same trial significantly affected the likelihood of publication acceptance (75). The prominent article on the topic was published by Mathieu et al. (38). They found that only one-third of the reviewers used trial registries during the peer-review process. The rest of the participants stated inconvenience or lack of awareness of the importance of trial registration as reasons to ignore the use

of the registry as a tool. Furthermore, only 7.4% of them held the opinion that comparing the registry data with the manuscript should, in fact, be the peer-reviewer's responsibility.
Our finding that anesthesiology journals correlate with adverse events misreporting more frequently underscores the importance of implementing this prospect in the anesthesiology research field and warrants further research among anesthesiology journal peer reviewers. Using the registry source as a tool for validating the integrity and consistency of manuscript data and study design elements could be a worthwhile addition to the spectrum of practices used in the peer-review process, and should be adopted by peer reviewers and enforced by medical journal editors. If reporting inconsistencies would hinder the progression of the manuscript to publication, perhaps the authors would approach ensuring the validity of the registry-trial data more meticulously. To achieve the desired effect, peer reviewers should be trained in comparing registry-publication data, although the effectiveness of peer-reviewer training is a broad and complex topic (76,77).

Study reporting guidelines, such as those issued by the EQUATOR network, could be an efficient source of encouragement to perform a data consistency cross-check. Study sponsors could also be parties of interest that set expectations for reviewing study results in the registry. An example of a growing positive practice is the trend among journals to require the upload of raw data to open online repositories, thereby promoting transparency in trial data reporting (78).

It remains pertinent that registered trial data be evaluated for completeness to help prevent discrepancies in registries and subsequent publications.

5.5. Study limitations

There are some limitations to our study. A possible source of selection bias lies in our methodology's significant reliance on the ClinicalTrials.gov database and search algorithm. Our search is unable to detect trials that were in fact completed but whose status was not updated from "ongoing" to "completed" in the registry. This instance also applies to cases where authors did not disclose results. A previous study investigating this possibility determined that 29.5% of trials did not disclose results at a time point four years after completion, while those that did frequently delayed results disclosure for a year (79). Jones and colleagues found that some trials that were in fact completed maintain the trial

status designation in the registry as “ongoing” indefinitely to avoid the legislative compulsion for results disclosure (80).

Furthermore, during our trial selection process, we identified multiple RCTs that were mislabelled as anesthetic trials in the registry, even though they were conducted with non-anesthetic drugs. Although these were easy to exclude, we can also assume that the reverse scenario is possible, where trials actually conducted on anesthetic drugs were mislabelled as involving non-anesthetic drugs. This would make them invisible to our trial search process and would introduce a non-preventable source of potential selection bias. Another possible vector for selection bias is our method of publication search and retrieval, which was, in part, a manual process. Human error in data entry is also possible. Additionally, the wide variability in the time required for a trial to progress from completion to manuscript publication could leave insufficient time for our most recent trial entries in the selection process to achieve published status, making our most recent time window of trials vulnerable to selection bias as a subgroup.

As previously mentioned, it was not possible to determine the exact trial registration date if only the month and year were available on ClinicalTrials.gov, so we opted to “err on the safe side” and allowed a one-month leeway to avoid deeming a trial as late to register. However, the actual number of trials that were late to register could be higher than in our study. Holst and Carlisle found that 2% of trials in their 11,908 cohort retroactively manipulated study start date information in the registry so that their study could appear as prospectively registered afterwards (81). This could have affected our process of classification of trials according to adherence to the trial registration deadline. Similarly, our study was not designed to account for retroactive interventions in any registry data category.

Our subgroup analysis included testing for a wide spectrum of hypotheses; however, since we did not adjust for multiple comparisons in our analysis, it is possible that some statistically significant findings are in fact random occurrences.

It is important to note that, to conduct any inferential statistics in our study, we first had to translate a multitude of possible scenarios into a dichotomous categorical variable. While we granted an “amnesty” for certain minor misreporting cases, the fact remains that a certain amount of information is lost in the process. There is no system in existence for assigning value to severity to various types of reporting discrepancies, but we treat them all equally since minor inadequacies having the potential to translate into larger errors with downstream use and implementation of information.

Additionally, other factors we did not account for could have influenced the reporting of data in ClinicalTrials.gov after the final rule of the FDAAA.

Lastly, the omnibus test for the logistical regression model was not statistically significant, thus, caution should be exercised when interpreting the relationship between the outcome and predictor variables.

6. CONCLUSIONS

Our trial showed that anesthesiology RCTs have poor consistency of trial data between the ClinicalTrials.gov registry and associated publications. Retroactive trial registration is also a present issue. Anesthesiology journals exhibit publication bias, which is not mitigated by perceived journal quality. The quality of research practices in anesthesiology RCTs, therefore, leaves a significant room for improvement. The implementation of the FDAAA legislation successfully improved the quality of all-cause mortality reporting.

Researchers conducting meta-analyses could benefit from increased awareness of possible data discrepancies in clinical trial registries. All stakeholders in the medical journal ecosystem should strive to integrate a quality trial registration process as a vital prerequisite for the success of trial publication.

Ultimately, practicing anesthesiologists, as the end users of every trial publication, need to be informed about additional ways to evaluate data reporting quality. Our results could provide improved insight into the transparency of clinical trial reporting in anesthesiology and highlight sources of publication bias where certain trial data are altered. These practices can influence the composition of professional medical practice guidelines and clinicians' drug prescription decisions.

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8. SAŽETAK

Uvod / ciljevi: Kakvoća prikaza podataka kliničkih istraživanja iz područja anesteziologije je, do sada, bila nedovoljno istražena. Cilj ove studije je na kohorti sazdanoj od anesteziooloških istraživanja koja podliježu FDAAA legislativi ispitati dosljednost prikaza podataka vezanih za ustroj istraživanja, ishode, rezultate te neželjene događaje između dvaju izvora podataka: registracijske platforme *ClinicalTrials.gov* te pripadajućih publikacija.

Metode: U presječnom istraživanju uključili smo randomizirana klinička istraživanja provedena na 29 odabranih lijekova korištenih u anesteziologiji. Ispitali smo prikaz slijedećih kategorija podataka: rezultate i mjere ishoda, nuspojave, smrtnost, broj ispitanika uključenih u studiju, ishod studije, grane istraživanja, kriterije odabira ispitanika te datum uključivanja prvog ispitanika. Također smo ispitali i pridržavanje rokova za registriranje istraživanja pri *ClinicalTrials.gov* repozitoriju. Koristeći metodologiju opisnog istraživanja, prikazali smo pouzdanost prikaza podataka u repozitoriju i pripadajućoj publikaciji. Analizirali smo razlike u učestalosti nepodudarnosti ili neprimjerenog prikaza podataka među odabranim podskupinama.

Rezultati: Uključili smo 258 kliničkih istraživanja u periodu od 2009. do 2022. Udio retrospektivno registriranih istraživanja je bio 28,7%. Nepodudarnosti u prikazu rezultata su pronađene u 33,3% studija, a u prikazu teških nuspojava u 62,4%, odnosno 67,4% u prikazu lakših nuspojava. Primarni ishodi su prikazivani mnogo dosljednije nego sekundarni (77,5% naspram 27,9%). Kriteriji odabira (24%) i datum uključenja prvog ispitanika (29.5%) su bili najmanje dosljedno prikazane kategorije podataka. Jedina kategorija podataka čija se dosljednost prikazivanja poboljšala s vremenom je smrtnost. Anesteziološki časopisi i časopisi koji nisu indeksirani pri JCR su češće nepouzdano prijavljivali nuspojave. Čimbenik odjeka časopisa nije bio prediktor bolje dosljednosti prikaza podataka.

Conclusions: Podatci kliničkih istraživanja iz područja anesteziologije prikazuju se nepouzdano. Odgovorne osobe uključene u recenzentski postupak trebale bi razmotriti korištenje repozitorija registracije kliničkih istraživanja kao vrijednog oruđa za procijeniti integritet podataka. Također, nepodudarnosti između registrirane i publicirane inačice iste studije postavljaju pitanje o pouzdanosti obje inačice u svrhu prikupljanja podataka za meta-analize i donošenje odluka u kliničkoj medicini.

9. ABSTRACT

Background/Objectives: The trial registration process in anesthesiology, along with the consistency of reported data, has not been systematically investigated to date. Our study aims to describe the quality of data from anesthesiology RCTs submitted to ClinicalTrials.gov and to assess their consistency with the corresponding peer-reviewed publications. We examined the effects of the FDAAA legislation on anesthesiology drug trial reporting.

Methods: We designed a cross-sectional study selecting RCTs performed on anesthetic drugs. We investigated the quality of data reporting for specific items in the WHO dataset, including results and outcome probability measures, adverse events, all-cause mortality, study size, study outcome, study arm, selection criteria, and date of enrollment. Adherence to the ClinicalTrials.gov registration deadline was also evaluated. We used descriptive statistics to describe the data quality in both of our data sources, the registered version and publication of the same trial. We tested for differences in the frequency of data reporting discrepancies using chi-square analysis and logistic regression.

Results: 258 published trials from 2009 to 2022 were selected from the ClinicalTrials.gov database. We found that 28.7% of these were late to register. Discrepancies in reporting results occurred in 33.3% of the trials, serious adverse events in 62.4%, and other adverse events in 67.4%. Primary outcomes were reported much more consistently than secondary ones (77.5% vs 27.9%). The least consistently reported data items were selection criteria (24%) and enrollment date (29.5%). All-cause mortality was unique among the investigated data categories, being the only data item with improved reporting over time. Anesthesiology journals and non-JCR-indexed journals reported adverse events more often. Impact factor was not a predictor of better data reporting consistency.

Conclusions: Data reporting in anesthesiology trials is questionable in reliability. Whether trial registries or publications are more vulnerable to biased reporting is a question with no definitive answer. Nevertheless, we propose trial registries as an integral tool for validating trial data and the study design during the peer-review process. With trial registries recognized as valid sources of real-world data for secondary research, maintaining their reliability is increasingly important.

10. APPENDIX

Appendix 1. List of selected trials by NCT number:

NCT00997126 NCT02959996 NCT03838874 NCT02074709 NCT03001453 NCT02274870
NCT02777749 NCT02289079 NCT03149887 NCT03103100 NCT03663283 NCT02296099
NCT02222129 NCT04032327 NCT02444533 NCT01220024 NCT01272921 NCT01683071
NCT02480621 NCT03294109 NCT02111746 NCT02523599 NCT02189317 NCT02525133
NCT02052557 NCT02713490 NCT03359811 NCT02449915 NCT01829399 NCT02862912
NCT02223364 NCT02665273 NCT03269435 NCT03027661 NCT02891798 NCT03482973
NCT02525718 NCT03682302 NCT01709708 NCT01995045 NCT02100579 NCT03948386
NCT01701414 NCT03295721 NCT01586806 NCT02007096 NCT01286805 NCT02713230
NCT03272139 NCT02517905 NCT02011464 NCT01279447 NCT02519023 NCT02464176
NCT02462148 NCT01975285 NCT03007966 NCT01734161 NCT02506660 NCT01450007
NCT03151434 NCT02741713 NCT01616173 NCT02876055 NCT02509078 NCT02635542
NCT01219881 NCT01270620 NCT01310582 NCT01199237 NCT01277861 NCT03996148
NCT01368809 NCT01795495 NCT01188551 NCT03255824 NCT02168439 NCT01528891
NCT02004613 NCT03139279 NCT01344759 NCT02250703 NCT02653144 NCT01057381
NCT02546765 NCT02203019 NCT01739933 NCT03112993 NCT01158820 NCT02818569
NCT01449708 NCT02105415 NCT02643381 NCT02597478 NCT02459964 NCT01549002
NCT01846221 NCT01621230 NCT02683707 NCT02352922 NCT01832402 NCT01482091
NCT01244126 NCT02778880 NCT02349152 NCT01542645 NCT01515566 NCT02937506
NCT03307174 NCT02721017 NCT01114971 NCT02949271 NCT03373591 NCT02886286
NCT03110003 NCT02180893 NCT03448068 NCT03408483 NCT01826851 NCT02290873
NCT02532647 NCT02296892 NCT01145222 NCT01690988 NCT03472469 NCT02578862
NCT02397889 NCT02920528 NCT02452060 NCT02916927 NCT01558063 NCT01700829
NCT03621085 NCT02519595 NCT01387139 NCT03102736 NCT01538745 NCT04322968
NCT02489630 NCT03039543 NCT03001843 NCT01835262 NCT02306759 NCT02673372
NCT02487485 NCT03274453 NCT01507181 NCT00997321 NCT01591382 NCT01325493
NCT02360280 NCT02579928 NCT03909607 NCT01260662 NCT01880593 NCT02432456
NCT02539511 NCT02134951 NCT01790490 NCT03500289 NCT02596022 NCT02996591
NCT02139540 NCT03479216 NCT03801265 NCT01948908 NCT01641653 NCT03069677
NCT02096900 NCT03054844 NCT01830881 NCT03246724 NCT01999777 NCT02292082
NCT01335542 NCT01755234 NCT03241485 NCT01465191 NCT02912195 NCT01452789

NCT02009722 NCT01804075 NCT02530151 NCT03088826 NCT02848729 NCT02403830
NCT01539538 NCT01734551 NCT01878006 NCT02335294 NCT01242644 NCT02100748
NCT01136356 NCT02793947 NCT01871285 NCT02815709 NCT03196505 NCT02820324
NCT02222246 NCT02658149 NCT02570022 NCT02922985 NCT01444924 NCT03723447
NCT03176459 NCT03015532 NCT02354833 NCT01163214 NCT03154658 NCT02365961
NCT02242201 NCT02523235 NCT03704376 NCT02356588 NCT02475031 NCT03349034
NCT01759277 NCT02567968 NCT03502915 NCT03365011 NCT03283670 NCT01604785
NCT00997113 NCT01342510 NCT01557920 NCT02404610 NCT01222091 NCT03322657
NCT02260258 NCT03346070 NCT03346057 NCT03168308 NCT01479764 NCT03351608
NCT03063255 NCT02860507 NCT02861131 NCT03210376 NCT01480089 NCT03117140
NCT01898689 NCT01971645 NCT03746951 NCT02829944 NCT01782872 NCT02604550
NCT02662023 NCT02219438 NCT01824082 NCT02623361 NCT03549234 NCT01048658
NCT01660763 NCT01539642 NCT02909439 NCT03219294 NCT01958476 NCT0352150

11. CURRICULUM VITAE

IGOR VUKOVIĆ, M.D.

Anesthesiology, reanimatology and intensive care medicine specialist

WORK EXPERIENCE

- Attending physician 2023 – present
  General and Veteran Hospital "Hrvatski ponos" Knin
  Department of Anesthesiology, Reanimatology and Intensive Care Medicine

- Attending physician 2019 - 2023
  University hospital Split
  Department of Anesthesiology, Reanimatology and Intensive Care Medicine

- Resident physician 2014 - 2019
  University hospital Split
  Department of Anesthesiology, Reanimatology and Intensive Care Medicine

- Mobile emergency medicine doctor – team leader 2014
  Emergency Medical Service of the Lika-Senj County

- Teaching associate 2014
  University of Split School of Medicine
  Department of Pathophysiology

- Medical intern 2012 – 2013
  University hospital Split

EDUCATION

- Postgraduate school Translational Research in Biomedicine 2018 - present
  University of Split School of Medicine

- Medical Studies (integrated pregraduation and graduation program) 2006 - 2012
  University of Zagreb School of Medicine

- Classical Gymnasium "Don Frane Bulić" Split 2002-2006

FOREIGN LANGUAGE SKILLS

- English – proficient
- Italian – basic
- Russian – basic
- Greek - winner of state competition 2006
- Latin - finalist of state competition 2006

ACADEMIC PUBLICATIONS:

- Vuković I, Pranić S. Misreporting of Patient-Relevant and Study Design Elements in Anesthesiology Randomized Controlled Trials: An Observational Study. *Med. Sci.* 2025, 13(4):299
- Boric K, Jelicic Kadic A, Boric M, Zarandi-Nowroozi M, Jakus D, Cavar M, Dosenovic S, Jeric M, Batinic M, Vukovic I, Puljak L. Outcome domains and pain outcome measures in randomized controlled trials of interventions for postoperative pain in children and adolescents. Eur J Pain. 2019 Feb;23(2):389-396.
- Vukovic I, Bozic J, Markotic A, Ljubicic S, Ticinovic Kurir T. The missing link - likely pathogenetic role of GM3 and other gangliosides in the development of diabetic nephropathy. Kidney Blood Press Res. 2015;40(3):306-14.

HOBBIES AND INTERESTS

Registered chess competitor participating in Croatian League system 2002 - present

Founder of Chess Club "Student" Split