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Sex/gender and additional equity characteristics of providers and patients in perioperative anesthesia trials: a cross-sectional analysis of the literature

Nicole Etherington[1], Michael Wu[2], Sylvain Boet[1,3]

[1]*Clinical Epidemiology Program, Ottawa Hospital Research Institute,* [2]*Faculty of Medicine, University of Ottawa,* [3]*Department of Anesthesiology and Pain Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, ON, Canada*

Review Article

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Corresponding author:
Sylvain Boet, M.D., Ph.D.
Department of Anesthesiology and Pain Medicine, The Ottawa Hospital, University of Ottawa & Clinical Epidemiology Program, The Ottawa Hospital, Research Institute, 501 Smyth Road, Ottawa, ON, K1H 8L6, Canada
Tel: +1-613-737-8899 ext. 78187
Fax: +1-613-737-8189
Email: sboet@toh.ca
ORCID: https://orcid.org/0000-0002-1679-818X

Sex and gender, among other equity-related characteristics, influence the process of care and patients' outcomes. Currently, the extent to which these characteristics are considered in the anesthesia literature remains unknown. This study assesses their incorporation in randomized controlled trials (RCTs) on anesthesia-related interventions, for both patients and healthcare providers. This is a cross-sectional analysis using an existing dataset derived from the anesthesia literature. The dataset originated from a scoping review searching MEDLINE, Embase, CINAHL, CENTRAL, and the Cochrane Database of Systematic reviews. RCTs investigating the effect of anesthesia-related interventions on mortality for adults undergoing surgery were included. Equity outcome measures were recorded for both patients and providers and assessed for inclusion in the study design, reporting of results, and analysis of intervention effects. Three-hundred sixty-one RCTs (n = 144,674) were included. Most RCTs (91%) reported patient sex/gender, with 58% of patients identified as male. There were 139 studies (39%), where 70% or more of the sample was male, compared to just 14 studies (4%), where 70% or more of the sample was female. Only 10 studies (3%) analyzed results by patient sex/gender, with one reporting a significant effect. There was substantial variation in how age was reported, although nearly all studies (98%) reported some measure of age. For healthcare providers, equity-related information was never available. Better consideration of sex/gender and additional health equity parameters for both patients and providers in RCTs is needed to improve evidence quality, and ultimately, patient care and outcome.

Keywords: Anesthesiology; Cross-sectional studies; Gender identity; Review; Sex; Social class.

Introduction

Clinical evidence based on randomized controlled trials (RCTs) often guides healthcare decisions in many countries around the world [1,2]. Although RCTs provide evidence on the impact of healthcare interventions, potential differences within and between population subgroups tend to be overlooked in the design, conduct, and analysis of RCTs [3–5]. For example, the Guidelines to the Practice of Clinical Hyperbaric Medicine and Provision of Hyperbaric Oxygen Treatment from the Canadian Undersea and Hyperbaric Medical Association recommend treating severe carbon monoxide (CO) poisoning with

hyperbaric oxygen therapy regardless of any health equity-related characteristics (e.g., sex, gender, education, and ethnicity) [6]. However, a recent study from Huijun et al. [7] recruited couples treated for CO poisoning and analyzed patient outcome according to sex and females' pre- or post-menopausal status. The authors demonstrated that 'sex is an important prognostic indicator in CO poisoning,' as severity of poisoning and subsequent outcome was worse for males relative to their female spouses. Thus, male patients may actually require a different course of treatment, highlighting the importance of considering health equity-related characteristics in optimizing patient care.

Without attention to health equity-related characteristics, the generalizability and applicability of RCT results can be reduced [3,5,8,9]. Continued implementation of some interventions based on previous RCT results can also generate further health inequities between groups [10]. Thus, consideration of health equity-related characteristics is important to optimize patient outcome, avoid research waste, advance health research and policy, and ultimately reduce population health inequities.

Health-related equity characteristics are increasingly being investigated in perioperative care [11–17]. These characteristics may be particularly relevant in anesthesia. Evidence suggests, for example, that patient sex impacts some aspects of care and outcomes. Specifically, patient sex and/or gender interacts with emergence and recovery from general anesthesia [18], postoperative complications [18], remifentanil dosing for laryngeal mask airway insertion [19], prescription of analgesics [20], and hypnotic and muscle relaxant effects of anesthetic drugs [21]. Though the impact of anesthesiologist sex and gender on practice and patient outcome is unknown, recent evidence suggest these factors influence surgical practice patterns, postoperative complications, and mortality [12,22,23]. There is limited work on additional equity characteristics, but some evidence suggests that racial-ethnic disparities exist in pain management and use of neuraxial anesthesia, and that both patient and provider factors are involved [12]. Based on these and other findings [24–27], it is necessary to assess the state of the anesthesia literature for incorporation of equity characteristics in RCTs. This can inform the design, analysis, and reporting of future RCTs as well as meta-analyses of existing trials.

If patient outcome after anesthesia care varies by sex and gender or any equity characteristic, then anesthesia trials must account for these variables in study design, reporting, and analysis. Similarly, if anesthesia practice varies by provider sex and/or gender and/or additional equity characteristics, interventions to improve practice must account for these factors. Currently, the extent to which sex, gender, and other health equity categories are considered in the anesthesia literature remains unknown. It is important to determine this information given the potential to improve patient outcomes, provider training, research, and knowledge translation.

This study aims to assess the extent to which sex/gender and other health equity variables are considered in the design, analysis, and reporting of RCTs investigating the impact of anesthesia-related interventions on adult surgical patient mortality. Health equity categories, including sex/gender, will be assessed for both patients and providers. We hypothesize that female patients are under-represented in anesthesia RCTs and that data are most often not reported or analyzed according to patient sex/gender. We also expect anesthesiologist sex/gender to be uncommonly reported and analyzed. Finally, we anticipate limited reporting and analysis of all additional health equity characteristics including age and ethnicity, for both patients and providers.

Materials and Methods

This study conducted a cross-sectional secondary analysis of the original data set of 369 RCTs from our previously completed scoping review of anesthesia-related interventions that impact surgical patient mortality [28]. Details can be found elsewhere [28], in supplementary data. In brief, RCTs were retrieved from the following electronic databases: MEDLINE, Embase, CINAHL, CENTRAL, and the Cochrane Database of Systematic Reviews. The original search strategy was developed by the research team with an information specialist and reviewed by another information specialist (PRESS) [29]. Language restrictions were not applied to the literature search; however, data were extracted only from studies published in English or French. All databases were searched from inception to March 2015.

RCTs were included in this data set if they involved an anesthesia-related intervention (i.e., an intervention during the perioperative period performed or organized by a healthcare provider trained in anesthesia) administered to an adult patient (older than 16 years old) and assessed mortality as an outcome. Mortality was selected as a criterion for inclusion based on its clinical importance and feasibility considerations. RCTs were not included if they focused only on comparing different surgical techniques or if they involved procedures using local anesthesia alone. Relevant studies and their data were previously identified and extracted in duplicate by pairs of independent reviewers for our aforementioned scoping review.

For the purposes of this study, an additional level of screening and data extraction was conducted by one reviewer and verified by a second reviewer using DistillerSR (Evidence Partners, Ottawa, Canada). Conflicts were resolved through consensus or in-

volvement of a third reviewer as needed. Eight studies were subsequently excluded due to patient sex/gender as an inclusion or exclusion criteria. These studies involved gynecologic procedures, mastectomies, orthopedic and cardiac surgeries performed on female patients only, and prostatectomies performed on male patients only. Thus, the final data set for this study included 361 RCTs (n = 144,674), that investigated anesthesia-related interventions impacting surgical patient mortality.

Ethical approval was not required for this study as all information was publicly available. This manuscript was prepared in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement [30].

We defined the population for this study as adult patients undergoing a surgical procedure with general anesthesia, and healthcare providers with training in anesthesia who are involved in RCTs investigating the impact of anesthesia-related interventions on surgical patient mortality.

Health equity variables were extracted according to the categories outlined by the PROGRESS-Plus framework that is the gold standard set out by the Cochrane Equity Methods Group [31]. Categories include: Place of residence, Race/ethnicity/culture/language, Occupation, Gender/sex, Religion, Education, Socioeconomic status, Social capital, as well as the 'Plus' categories of age, disability, and sexual orientation.

We assessed the design, reporting of results, and analysis of each RCT:

(1) Design: Consideration of PROGRESS-Plus categories in study design through sample representation of respective groups

(2) Reporting: Results disaggregated (i.e., reported separately) by PROGRESS-Plus categories

(3) Analysis: Differences in effect of intervention statistically tested by patient and provider PROGRESS-Plus categories

Equity outcome measures were recorded for both patients and providers.

For the race/ethnicity variable, participants were grouped into two categories, Caucasian and non-Caucasian, due to heterogeneity in the non-Caucasian groups reported by included studies.

Descriptive statistics and absolute values and percentages were used for both number of studies and participants.

DistillerSR (Evidence Partners, Canada) and Microsoft Excel (Microsoft Corp., United States) were used for extraction and analysis, respectively.

Results

Results are shown in Table 1. Full details of included studies are available in Supplemental Table 1. Seven studies (2%) did not incorporate any of the equity categories (865 patients [0.6%]). These studies are not included in Table 1.

Three hundred thirty studies (91%) considered patient sex/gender, with 83,784 (62%) patients identified as male and 51,925 (38%) identified as female. There were 139 studies (42%) where 70% or more of the sample was male compared to just 14 studies (4%) where 70% or more of the sample was female.

Three hundred fifty-two studies (98%) considered patient age (n = 146,682 [99%]). There was substantial variation in how age

Table 1. Analysis of Equity Outcomes in RCTs Investigating Anesthesia-related Interventions that Impact Mortality (n patients = 144,674, n studies = 361)

PROGRESS-Plus category	Sample design		Reporting of results (disaggregated)		Analysis	
	Patients; studies	Healthcare providers; studies	Patients; studies	Healthcare providers; studies	Patients; studies	Healthcare providers; studies
Sex/gender	135709 (91); 330 (91)*	NR	11538 (8); 12 (3)*	NR	11395 (8); 10 (3)*	NR
Age	146682 (99); 352 (98)*	NR	13933 (9); 22 (6)*	NR	13933 (9); 22 (6)*	NR
Race/ethnicity	22956 (15); 22 (6.1)*	NR	NR	NR	NR	NR
Occupation	343 (0.2); 1 (0.3)*	NR	NR	NR	NR	NR
Residence	2313 (1.6); 2 (0.6)*	NR	NR	NR	NR	NR
Language	NR	NR	NR	NR	NR	NR
Religion	NR	NR	NR	NR	NR	NR
Education	NR	NR	NR	NR	NR	NR
Socioeconomic status	NR	NR	NR	NR	NR	NR
Social capital	NR	NR	NR	NR	NR	NR
Disability	NR	NR	NR	NR	NR	NR
Sexual orientation	NR	NR	NR	NR	NR	NR

Values are presented as number of participants (%); number of studies (%). *It indicate categories with reported results. NR: not reported.

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was reported from overall population means and standard deviations to broad age ranges (e.g., under 65 years, over 65 years) to medians per control and intervention group.

Twenty-two studies (6.1%) considered patient race/ethnicity (n = 22,956 [15%]). Of these patients, 20,510 (89%) were Caucasian and 2,446 (11%) were non-Caucasian (Supplemental Table 2).

One study (0.3%, 343 patients [0.2%]) assigned patients a lifestyle score that took employment status into account, but did not indicate the distribution of patients per employment category [31].

Two studies (0.6%, 2,313 patients [1.7%]) look at residence or living situation. Hempenius et al. [32] included the categories alone-independent, with others-independent, protected housing-dependent, home for the elderly-dependent, and nursing home-dependent. Most patients (n = 125) lived independently, either alone (n = 59) or with others (n = 66). Carson et al. [33] considered whether patients lived in the United States (n = 1,222) or Canada (n = 794) as well as whether the patient lived in their own home or a retirement home (n = 1,778), nursing home (n = 214), and some other residence (n = 21).

Most studies (339 studies [94%], 134,589 patients [91%]) did not disaggregate results by any equity characteristic. The remaining 22 disaggregated results by sex/gender and/or age.

Twelve (3%) studies (11,538 patients [8%]) reported results separately by patient sex/gender (Supplemental Table 3). Twenty-two (6%) studies (13,933 patients [9%]) reported results separately by patient age (Supplemental Table 4). Of these studies, 9 also disaggregated results by sex/gender.

Ten studies (3%) tested for a significant difference in the effect of the intervention by patient sex/gender (n = 11,395 [8%]). One study (n = 762) involving cardiac surgery and a device-related intervention reported male sex increases the risk of mortality [33].

Of the 22 studies that presented results by age tested for significant differences, most studies (15 [68%]) reported no significant difference in the effect of the intervention by patient age, although 7 (32%) reported age to play a significant role, either increasing or decreasing risk of mortality.

Sex/gender, age, race/ethnicity, and any other equity category never appeared in any study for healthcare providers. This remains true for design, reporting, and analysis.

Discussion

This study examined the integration of health equity characteristics for both providers and patients in the design, analysis, and reporting of RCTs investigating the impact of anesthesia-related interventions on adult surgical patient mortality.

Although patients' sex/gender is generally included in the design of anesthesia RCTs, it is rarely considered in reporting of results and analysis. This is also true of age. Other patients' health equity characteristics are rarely included in the design, reporting of results, or analysis. Health equity characteristics of providers are never considered.

Reporting of patient sex/gender appears to be more common in the anesthesia literature than in surgery-specific clinical research, with only 2% of studies failing to provide any sex/gender-related data compared to nearly 20% in surgical studies [34]. This is certainly an encouraging practice, although more adequate incorporation into the study design should be promoted to permit sufficiently powered sub-group analyses. When sex/gender is not considered in trial design, it is impossible to ensure statistical power to any further analyses accounting for this factor. Not surprisingly, only 12 of the reviewed studies disaggregated results by patient sex/gender, 10 tested for significant differences, and only one reported a significant difference in mortality between male and female patients. Of course, we recognize that it is not always feasible to conduct sub-group analyses. However, even when studies are underpowered, or when sex/gender analyses may not be relevant, data should still be reported by sex/gender to facilitate future meta-analyses and to inform sample size calculations for future studies [35]. Reporting of this information can also improve the replicability of a study.

Overall, there was an over representation of male patients, with males comprising 70% or more of the sample in 139 (39%) of the included studies. This may be the result of most studies involving cardiac procedures, where trials have historically focused on male patients. However, the number of female patients undergoing cardiac surgery every year is increasing and heart disease remains a leading cause of death for women [36]. Further, in the last 20 years, the prevalence of myocardial infarctions has increased in midlife among women aged 35–54 years while simultaneously declining in men of the same age [37]. Heart disease and differences in its clinical presentation have traditionally been under-recognized in women, resulting in 'less aggressive treatment strategies and a lower representation of women in clinical trials' [37]. This is problematic, especially considering that women have poorer survival rates following many types of cardiac procedures [38]. Our findings underscore the need to recruit, report, and analyze according to sex/gender, particularly when assessing anesthesia interventions in cardiac surgery. With the majority of surgical procedures in the United States performed on female patients [39], it is critical to understand the implications of anesthesia-related interventions for both female and male patients, and how effects may differ between them. When data on male and female participants is aggregated, there is a risk of masking important sex/gen-

der differences and lead to adverse effects for patients in clinical practice [40]. For example, inadequate consideration of sex differences in pharmacokinetics and pharmacodynamics resulted in 10 drugs being withdrawn from the market, with eight posing greater health risks for women than for men [40,41]. Accordingly, trials investigating pharmaceutical interventions in anesthesia should consider these variables. Even if trials cannot analyze their data based on health-equity characteristics (e.g., because of small sample size), we believe that all trials should at least report their data based on health-equity characteristics. This way, future systematic reviews may be able to further explore the impact of health-equity characteristics on patient outcome in perioperative medicine.

Beyond sex/gender, few studies reported on additional health equity characteristics. One exception is age that was reported by all but one study. Like sex/gender, a much lower number of studies disaggregated and analyzed results by age. Though age was often included, it was reported in various ways. More standardized reporting of age (e.g., mean/SD or median/IQR for each group and participants overall) is needed as well as consideration of how it intersects with sex/gender given the importance of these two characteristics together for health. Again, standardized and disaggregated reporting would make future meta-analyses possible.

Race/ethnicity, another key health-related characteristic that can also interact with sex/gender and age, was reported in only 6% of the examined trials. Within these trials, nearly 90% of patients were Caucasian. Patients from other racial/ethnic groups were clearly under-represented, preventing understanding of the role patient race/ethnicity has in anesthesia-related interventions. Without this type of information, it is not possible to identify heterogeneity among patients, potentially augmenting the risks of particular interventions and certainly reducing the effectiveness of knowledge translation [42]. Research may wish to assess the role of race/ethnicity when considering the effectiveness of anesthesia interventions during metabolic and vitreoretinal procedures in particular, given recent findings of racial/ethnic differences in clinical presentation and outcomes [15,16].

Failure to examine differences in the effect of an intervention on clinical outcomes by sex/gender and additional health equity characteristics misses an opportunity to optimize patient care and may even pose significant risk to patient safety (e.g. different side effects, reactions to treatments, and biological and social factors influencing outcomes of a treatment). When equity characteristics remain absent from RCT analysis and interpretation, as found in reviews of other clinical trials [5,42], the external validity of the study remains limited [35]. When we wish to conclude patients are more or less likely to experience morbidity and/or mortality as a result of an intervention, it is important for results either to be appropriately generalizable to the broader patient population or to limit the results to a specific clearly defined sub-group based on certain equity characteristics. It is noteworthy, for example, that our study found pharmacotherapy trials and trials involving cardiac surgery to be based on mostly male and Caucasian samples, when some evidence suggests that these patient characteristics can be critical modifiers in these instances [21,43,44]. For example, female patients undergoing cardiac surgery often have different risk factors than male patients (e.g., older, higher body mass index), and higher hospital and early mortality has been found for those who undergo coronary artery bypass grafting [44]. This again emphasizes the need to study sex/gender and other equity characteristics when anesthesia interventions involve pharmacotherapy or cardiac surgery.

Because health equity characteristics are known determinants of health that can modify the relationship between healthcare interventions and outcomes of interest, their inclusion or exclusion in clinical trials also has implications for knowledge translation. We recognize that this type of data collection may not always be possible within the requirements of some Research Ethics Boards (REB) and this may have affected the ability of some of the included studies to collect adequate patient information. However, it is important for REBs to consider the benefits of collecting equity data in clinical trials, provided participant confidentiality is maintained. With emerging evidence that sex/gender and additional characteristics are relevant to how individuals respond to particular healthcare interventions, 'there is an ethical and scientific imperative to report to whom research results apply' [35]. When evidence is moved into practice, it must be determined whether it will improve outcomes for some or all patients. Part of advancing evidence-based practice in anesthesiology and other disciplines includes attention to the equitable representation of patients within the evidence base. If the evidence base exhibits sex/gender or any other type of bias, this limitation should be acknowledged in practice. For example, if women and non-Caucasians continue to be under-represented in anesthesia research, they may experience an increased likelihood of adverse events compared to male and Caucasian patients as a result of certain interventions. This has certainly been the case in other clinical areas such as infectious disease management [45]. Future anesthesia research can integrate these concerns into trial design and data analysis in order to enhance its value.

Integration of providers' equity-related parameters throughout all RCT elements (design, reporting, and analysis) appears to be non-existent. In the assessed anesthesia literature, no study reported provider sex/gender or any additional characteristic. Yet, these may be important in identifying differences in practice pat-

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terns and areas for improvement. For example, a recent study reports lower mortality and readmission rates for female internists compared to male internists [46]. Research also demonstrates that male physicians tend to undermanage female patients (e.g., less extensive investigation, providing less medication and at lower doses) but finds no difference in the treatment of male or female patients when the physician is a woman [47,48]. Sex/gender representation of anesthesia providers who deliver patient interventions in RCTs are currently unclear. Future research may examine if trends found among patients (e.g., more men than women; more Caucasians than non-Caucasians) are similar for providers. This may help to determine whether RCT findings are generalizable to all providers, or if patient intervention effectiveness varies by provider characteristic. Reporting of provider sex/gender, along with other equity characteristics, may help to determine representation of diverse provider groups in research trials. It would also allow future knowledge syntheses to assess the potential clinical effects of practice differences among various anesthetic provider groups.

Research has started to consider sex/gender for surgeons, finding implications for practice and patient outcome [12,22,23,49]. With an increasing number of women entering medical school every year, it is time for anesthesiology to do the same and to consider the implications of additional equity-related characteristics. For example, recent research suggests that when female anesthesiologists make an incorrect clinical decision, they are challenged more often than their male colleagues [50]. Sex/gender may therefore be important for interventions addressing leadership, communication, and overall teamwork in the operating room. Similarly, male and female anesthesia providers may benefit from different approaches to training, as demonstrated in surgery [49]. This may be especially needed if the sex/gender of anesthesia providers influences the patient outcome, similar to what emerging evidence shows for surgeons [12,23]. With the incorporation of equity-related parameters for anesthesia providers in research, knowledge translation interventions to improve practice may become optimally effective.

There are some limitations to generalizing the conclusions drawn from this review. It is not inclusive of all anesthesia-related papers and included only RCTs that assessed mortality as an outcome. In addition, because this review includes only studies published up until 2015, it may not reflect changes taking place within the literature in recent years. Other types of data sets may influence results. However, three recent studies of sex/gender reporting in medical research [5,42,51] found similar results to what we have reported here, suggesting our observed trends may apply to additional areas of anesthesia as well as other medical fields. Although it is possible that reporting of sex/gender and other equity characteristics has improved over the last decades, recent publication in the Lancet by Sugimoto et al. [42] suggests reporting has not significantly increased in recent years despite more attention being paid to sex/gender in research. For example, from 1980 to 2016, reporting of patient sex only increased by 8% in clinical medicine. In biomedical research, only 31% of papers published in 2016 reported the sex of patients [42]. Accordingly, while our data set represents a subset of the anesthesia literature, it is likely to still be representative of current reporting trends. Given that no equity measures were ever integrated for providers, it may also be reasonable to assume that these findings are consistent across anesthesia domains. It is possible that consideration of sex/gender and additional equity characteristics in anesthesia trials will improve over the next decade given evolving requirements of journals and funding agencies.

It should also be acknowledged that most studies in this dataset reported mortality as a secondary outcome. Still, this does not detract from the need to improve reporting of sex/gender and additional equity data regardless of the outcome assessed. Where it is not possible to analyze outcomes by certain equity parameters, reporting this data can still allow for future meta-analyses to evaluate potential differences.

A final possible limitation is that relevant studies may have not been included, despite conducting a rigorous and standardized search of the literature [28]. If mortality terms were not mentioned in the title or abstract of a study, they would not have been included due to the literature search and screening process. Nevertheless, as previously mentioned, this dataset is still likely to be representative of trends in the broader anesthesia literature.

There is a need for better integration of sex/gender and additional health equity parameters for both patients and providers in the design, reporting, and analysis of anesthesia RCTs in order to improve evidence quality and ultimately patient care and outcome.

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College, Hanover, NH, United States
Susan Bragg, MD, Department of Anesthesia, University of Toronto, Toronto, ON, Canada
Ian D. Carrigan, B.Sc., Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada
José De Wit, MD, Department of Anesthesia, University of Ottawa, Ottawa, ON, Canada
Sarah Larrigan, Biomedical Sciences, University of Ottawa, Ottawa, Ontario, Canada
Cassandra T. Mendonca, MD, Department of Anesthesia, University of Ottawa, Ottawa, ON, Canada
Isaac Miao, MD, Department of Anaesthesia, University of Ottawa, Ottawa, ON, Canada
Karim Mohamed, MD, Department of Anesthesia, University of Ottawa, Ottawa, ON, Canada
David Nicola, MD, B.Sc. (Hons.), Family Medicine, McGill University, Montreal, Quebec, Canada
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Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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Author Contributions

Nicole Etherington (Conceptualization; Formal analysis; Investigation; Writing – original draft)
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Sylvain Boet (Investigation; Supervision; Writing – review & editing)

Supplementary Materials

Supplementary Table 1. PROGRESS-Plus representation of patients in RCTs testing anesthesia-related interventions (n = 361)
Supplementary Table 2. Studies that report race/ethnicity
Supplementary Table 3. Studies that disaggregate by sex/gender
Supplementary Table 4. Studies that disaggregate by age

ORCID

Nicole Etherington, https://orcid.org/0000-0002-7933-4593
Michael Wu, https://orcid.org/0000-0003-0948-8500
Sylvain Boet, https://orcid.org/0000-0002-1679-818X

References

1. Burns PB, Rohrich RJ, Chung KC. The levels of evidence and their role in evidence-based medicine. Plast Reconstr Surg 2011; 128: 305-10.
2. Murad MH, Asi N, Alsawas M, Alahdab F. New evidence pyramid. Evid Based Med 2016; 21: 125-7.
3. Jull J, Whitehead M, Petticrew M, Kristjansson E, Gough D, Petkovic J, et al. When is a randomised controlled trial health equity relevant? Development and validation of a conceptual framework. BMJ Open 2017; 7: e015815.
4. Mbuagbaw L, Aves T, Shea B, Jull J, Welch V, Taljaard M, et al. Considerations and guidance in designing equity-relevant clinical trials. Int J Equity Health 2017; 16: 93.
5. Phillips SP, Hamberg K. Doubly blind: a systematic review of gender in randomised controlled trials. Glob Health Action 2016; 9: 29597.
6. DeLez K, Evans W, Wherrett C, Doherty P, Boisvert J, Bateman B, et al. Guidelines to the practice of clinical hyperbaric medicine and provision of hyperbaric oxygen treatment [Internet]. Canadian Undersea and Hyperbaric Medical Association: 2015 Jan 15 [cited 2019 Dec 16]. Available from https://cuhma.ca/application/files/2814/7978/0661/CUHMA_Standards_of_Practice_Guidelines_1st_Edition.pdf
7. Huijun H, Qiang S, Dazhi G, Yu Z, Yan L, Shuyi P, et al. Sex differences may affect the severity of poisoning and prognosis after carbon monoxide poisoning: a retrospective study. Undersea Hyperb Med 2016; 43: 207-15.
8. Berger JS, Melloni C, Wang TY, Dolor RJ, Frazier CG, Samad Z, et al. Reporting and representation of race/ethnicity in published randomized trials. Am Heart J 2009; 158: 742-7.
9. Clayton JA, Tannenbaum C. Reporting sex, gender, or both in clinical research? JAMA 2016; 316: 1863-4.
10. Lorenc T, Petticrew M, Welch V, Tugwell P. What types of interventions generate inequalities? Evidence from systematic reviews. J Epidemiol Community Health 2013; 67: 190-3.
11. Sun LY, Tu JV, Coutinho T, Turek M, Rubens FD, McDonnell L,

https://doi.org/10.4097/kja.19484

et al. Sex differences in outcomes of heart failure in an ambulatory, population-based cohort from 2009 to 2013. CMAJ 2018; 190: E848-54.
12. Wallis CJ, Ravi B, Coburn N, Nam RK, Detsky AS, Satkunasivam R. Comparison of postoperative outcomes among patients treated by male and female surgeons: a population based matched cohort study. BMJ 2017; 359: j4366.
13. Etherington N, Boet S. Why gender matters in the operating room: recommendations for a research agenda. Br J Anaesth 2018; 121: 997-9.
14. Hicks CW, Wang P, Bruhn WE, Abularrage CJ, Lum YW, Perler BA, et al. Race and socioeconomic differences associated with endovascular peripheral vascular interventions for newly diagnosed claudication. J Vasc Surg 2020; 72: 611-21.
15. Morton JM. Ethnic considerations for metabolic surgery. Diabetes Care 2016; 39: 949-53.
16. Gupta B, Neffendorf JE, Wong R, Laidlaw DA, Williamson TH. Ethnic variation in vitreoretinal surgery: differences in clinical presentation and outcome. Eur J Ophthalmol 2017; 27: 367-71.
17. Tsao MW, Delozier OM, Stiles ZE, Magnotti LJ, Behrman SW, Deneve JL, et al. The impact of race and socioeconomic status on the presentation, management and outcomes for gastric cancer patients: analysis from a metropolitan area in the southeast United States. J Surg Oncol 2020; 121: 494-502.
18. Myles PS, McLeod AD, Hunt JO, Fletcher H. Sex differences in speed of emergence and quality of recovery after anaesthesia: cohort study. BMJ 2001; 322: 710-1.
19. Joe HB, Kim JY, Kwak HJ, Oh SE, Lee SY, Park SY. Effect of sex differences in remifentanil requirements for the insertion of a laryngeal mask airway during propofol anesthesia: A prospective randomized trial. Medicine (Baltimore) 2016; 95: e5032.
20. Weisse CS, Sorum PC, Sanders KN, Syat BL. Do gender and race affect decisions about pain management? J Gen Intern Med 2001; 16: 211-7.
21. Adamus M, Gabrhelik T, Marek O. Influence of gender on the course of neuromuscular block following a single bolus dose of cisatracurium or rocuronium. Eur J Anaesthesiol 2008; 25: 589-95.
22. Meyerson SL, Sternbach JM, Zwischenberger JB, Bender EM. The Effect of Gender on Resident Autonomy in the Operating room. J Surg Educ 2017; 74: e111-8.
23. Sharoky CE, Sellers MM, Keele LJ, Wirtalla CJ, Karakousis GC, Morris JB, et al. Does Surgeon Sex Matter?: Practice Patterns and Outcomes of Female and Male Surgeons. Ann Surg 2018; 267: 1069-76.
24. Toledo P, Caballero JA. Racial and ethnic disparities in obstetrics and obstetric anesthesia in the United States. Curr Anesthesiol Rep 2013; 3: 292-9.
25. Fowler RA, Sabur N, Li P, Juurlink DN, Pinto R, Hladunewich MA, et al. Sex-and age-based differences in the delivery and outcomes of critical care. CMAJ 2007; 177: 1513-9.
26. Manderbacka K. Exploring gender and socioeconomic differences in treatment of coronary heart disease. Eur J Public Health 2005; 15: 634-9.
27. Curtis LH, Al-Khatib SM, Shea AM, Hammill BG, Hernandez AF, Schulman KA. Sex differences in the use of implantable cardioverter-defibrillators for primary and secondary prevention of sudden cardiac death. JAMA 2007; 298: 1517-24.
28. Boet S, Etherington N, Nicola D, Beck A, Bragg S, Carrigan ID, et al. Anesthesia interventions that alter perioperative mortality: a scoping review. Syst Rev 2018; 7: 218.
29. McGowan J, Sampson M, Salzwedel D, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Explanation and Elaboration [Internet]. Ottawa: CADT [updated 2016 Jan 21; cited 2019 Dec 16]. Available from https://www.cadth.ca/press-2015-guideline-explanation-and-elaboration.
30. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008; 61: 344-9.
31. Kollef MH, Skubas NJ, Sundt TM. A randomized clinical trial of continuous aspiration of subglottic secretions in cardiac surgery patients. Chest 1999; 116: 1339-46.
32. Hempenius L, Slaets JP, van Asselt D, de Bock GH, Wiggers T, van Leeuwen BL. Outcomes of a geriatric liaison intervention to prevent the development of postoperative delirium in frail elderly cancer patients: report on a multicentre, randomized, controlled trial. PLoS One 2013; 8: e64834.
33. Carson JL, Terrin ML, Noveck H, Sanders DW, Chaitman BR, Rhoads GG, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. N Engl J Med 2011; 365: 2453-62.
34. Fremes SE, Tamariz MG, Abramov D, Christakis GT, Sever JY, Sykora K, et al. Late results of the Warm Heart Trial: the influence of nonfatal cardiac events on late survival. Circulation 2000; 102: III339-45.
35. Mansukhani NA, Yoon DY, Teter KA, Stubbs VC, Helenowski IB, Woodruff TK, et al. Determining if sex bias exists in human surgical clinical research. JAMA Surg 2016; 151: 1022-30.
36. Mokhles MM, Siregar S, Versteegh MI, Noyez L, van Putte B, Vonk AB, et al. Male-female differences and survival in patients undergoing isolated mitral valve surgery: a nationwide cohort study in the Netherlands. Eur J Cardiothorac Surg 2016; 50: 482-7.

37. Maas AH, Appelman YE. Gender differences in coronary heart disease. Neth Heart J 2010; 18: 598-602.
38. Tran A, Ruel M, Chan V. Gender differences in outcomes following cardiac surgery: implications for managing patients with mitral valve disease. Curr Opin Cardiol 2015; 30: 151-4.
39. Elixhauser A, Andrews RM. Profile of inpatient operating room procedures in US hospitals in 2007. Arch Surg 2010; 145: 1201-8.
40. Franconi F, Campesi I. Sex and gender influences on pharmacological response: an overview. Expert Rev Clin Pharmacol 2014; 7: 469-85.
41. Franconi F, Brunelleschi S, Steardo L, Cuomo V. Gender differences in drug responses. Pharmacol Res 2007; 55: 81-95.
42. Sugimoto CR, Ahn YY, Smith E, Macaluso B, Larivière V. Factors affecting sex-related reporting in medical research: a cross-disciplinary bibliometric analysis. Lancet 2019; 393: 550-9.
43. Buchanan FF, Myles PS, Leslie K, Forbes A, Cicuttini F. Gender and recovery after general anesthesia combined with neuromuscular blocking drugs. Anesth Analg 2006; 102: 291-7.
44. Trienekens MP, Maas AH, Timman ST, Van Swieten HA, Noyez L. Sex differences in patient and procedural characteristics and early outcomes following cardiac surgery. J Cardiovasc Surg (Torino) 2015; 56: 817-23.
45. Fish EN. The X-files in immunity: sex-based differences predispose immune responses. Nat Rev Immunol 2008; 8: 737-44.
46. Tsugawa Y, Jena AB, Figueroa JF, Orav EJ, Blumenthal DM, Jha AK. Comparison of hospital mortality and readmission rates for medicare patients treated by male vs female physicians. JAMA Intern Med 2017; 177: 206-13.
47. Baumhäkel M, Müller U, Böhm M. Influence of gender of physicians and patients on guideline-recommended treatment of chronic heart failure in a cross-sectional study. Eur J Heart Fail 2009; 11: 299-303.
48. Ohlsson A, Lindahl B, Hanning M, Westerling R. Inequity of access to ACE inhibitors in Swedish heart failure patients: a register-based study. J Epidemiol Community Health 2016; 70: 97-103.
49. Ali A, Subhi Y, Ringsted C, Konge L. Gender differences in the acquisition of surgical skills: a systematic review. Surg Endosc 2015; 29: 3065-73.
50. Pattni N, Bould MD, Hayter MA, McLuckie D, Noble LM, Malavade A, et al. Gender, power and leadership: the effect of a superior's gender on respiratory therapists' ability to challenge leadership during a life-threatening emergency. Br J Anaesth 2017; 119: 697-702.
51. Leslie K, Edgley C, Lee AC, Sellar A, Sgroi J, Toh R. Reporting of sex and gender in human studies published in anaesthesia journals. Br J Anaesth 2018; 120: 1128-30.

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