ABSTRACT

The new national guidelines for clinical research, the Ethical Guidelines for Medical and Biological Research Involving Human Subjects, were implemented in Japan in June 2021. The guidelines were developed by integrating two ethical guidelines: Ethical Guidelines for Medical and Health Research Involving Human Subjects and Ethical Guidelines for Human Genome/Gene Analysis Research. The Ethical Guidelines for Clinical Research were originally developed as three separate guidelines: Ethical Guidelines for Human Genome/Gene Analysis Research formulated in 2001, Ethical Guidelines for Epidemiological Research in 2002 and Ethical Guidelines for Clinical Research in 2003. They have undergone several amendments and integration in response to the government's policy changes, such as the protection of personal information, conflicts of interest and reliability of clinical research. The three major changes introduced in the New Integrated Guidelines in 2021 are centralized review, electromagnetic informed consent and research cooperating organization. These are expected to be used as tools to facilitate the conduct of research. This review discusses the regulations of academic clinical research in Japan, the history of ethical guidelines and the three major changes introduced in the New Integrated Guidelines.

ABSTRACT

Reflection is a complex concept in medical education research. No consensus exists on what reflection exactly entails; thus far, cross-comparing empirical findings has not resulted in definite evidence on how to foster reflection. The concept is as slippery as soap. This leaves the research field with the question, 'how can research approach the conceptual indeterminacy of reflection to produce knowledge?'. The authors conducted a critical narrative umbrella review of research on reflection in medical education. Forty-seven review studies on reflection research from 2000 onwards were reviewed. The authors used the foundational literature on reflection from Dewey and Schön as an analytical lens to identify and critically juxtapose common approaches in reflection research that tackle the conceptual complexity. Research on reflection must deal with the paradox that every conceptualization of reflection is either too sharp or too broad because it is entrenched in practice. The key to conceptualizing reflection lies in its use and purpose, which can be provided by in situ research of reflective practices.

ABSTRACT

Background: Medical degree programs use scholarly activities to support development of basic research skills, critical evaluation of medical information and promotion of medical research. The University of Sydney Doctor of Medicine Program includes a compulsory research project. Medical student projects are supervised by academic staff and affiliates, including biomedical science researchers and clinician-academics. This study investigated research supervisors' observations of the barriers to and enablers of successful medical student research projects.

Methods: Research supervisors (n = 130) completed an anonymous, online survey after the completion of the research project. Survey questions targeted the research supervisors' perceptions of barriers to successful completion of projects and sources of support for their supervision of the student project. Data were analysed by descriptive statistics and using manifest content analysis. Further quantitative investigation was made by cross-tabulation according to prior research supervision experience.

Results: Research supervisors reported that students needed both generic skills (75%) and research-based skills (71%) to successfully complete the project. The major barrier to successful research projects was the lack of protected time for research activities (61%). The assessment schedule with compulsory progress milestones enabled project completion (75%), and improved scientific presentation (90%) and writing (93%) skills. Supervisors requested further support for their students for statistics (75%), scientific writing (51%), and funding for projects (52%). Prior research supervision experience influenced the responses. Compared to novice supervisors, highly experienced supervisors were significantly more likely to want students to be allocated dedicated time for the project (P < 0.01) and reported higher rates of access to expert assistance in scientific writing, preparing ethics applications and research methodology. Novice supervisors reported higher rates of unexpected project delays and data acquisition problems (P < 0.05). Co-supervision was favoured by experienced supervisors but rejected by novice supervisors.

Conclusions: Both generic and research-related skills were important for medical student research project success. Overall, protected research time, financial and other academic support were identified as factors that would improve the research project program. Prior research supervision experience influences perceptions of program barriers and enablers. These findings will inform future support needs for projects and research supervisor training for the research supervision role.

Keywords: Medical research projects; Medical student projects; Research skills development; Research supervision practice; Research supervisors; Scholarly research; Student supervision; Student thesis.

4. *Vilalta A, Gutiérrez JA, Chaves S, Hernández M, Urbina S, Hompesch M. Adipose tissue measurement in clinical research for obesity, type 2 diabetes and NAFLD/NASH. Endocrinol Diabetes Metab. 2022 May;5(3):e00335. doi: 10.1002/edm2.335.*

ABSTRACT

Introduction: Excess body fat is linked to higher risks for metabolic syndrome, type 2 diabetes mellitus (T2DM), and cardiovascular disease (CV), among other health conditions. However, it is not only the level but also the distribution of body fat that contributes to increased disease risks. For example, an increased level of abdominal fat, or visceral adipose tissue (VAT), is associated with a higher risk of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH).

Methods: A review of the most relevant primary and secondary sources on body composition from the last 25 years was conducted. Relevant articles were identified using PUBMED and Google Scholar. Narrative synthesis was performed as statistical pooling was not possible due to the heterogeneous nature of the studies.

Results: The body mass index (BMI) is commonly used as a proxy measure of body fatness. However, BMI does not reflect the level and distribution of body fat. Other anthropometric methods such as waist circumference measurement and waist-hip ratio, as well as methodologies like hydro densitometry, bioelectrical impedance, and isotope dilution are also limited in their ability to determine body fat distribution. Imaging techniques to define body composition have greatly improved performance over traditional approaches. Ultrasound (US), computed tomography (CT), dual-energy X-ray absorptiometry (DXA), magnetic resonance imaging (MRI), are now commonly used in clinical research. Of these, MRI can provide the most accurate and high-resolution measure of body composition. In addition, MRI techniques are considered the best for the determination of fat at the organ level. On the other hand, imaging modalities require specialized, often expensive equipment and expert operation.

Conclusions: Anthropometric methods are suitable for rapid, high-volume screening of subjects but do not provide information on body fat distribution. Imaging techniques are more accurate but are expensive and do not lend themselves for high throughput. Therefore, successful trial strategies require a tiered approach in which subjects are first screened using anthropometric methods followed by more sophisticated modalities during the execution of the trial. This article provides a brief description of the most clinically relevant adipose tissue measurement techniques and discusses their value in obesity, diabetes, and NAFLD/NASH clinical research.

Keywords: NAFLD/NASH; adipose tissue distribution; diabetes; obesity.

5. *Cheng Li C, Foster AL, Han NHB, Trampuz A, Schuetz M. A bibliometric analysis of clinical research on fracture-related infection. Biomed Res Int. 2022 Apr 14;2022:8171831. doi: 10.1155/2022/8171831. eCollection 2022.*

ABSTRACT

Background: Infection following orthopaedic trauma surgery is increasingly recognized as one of the major research priorities with as primary goal, improving patient care. This increased interest has been anecdotally recognized through published research, research grants, and, finally, with the development of the fracture-related infection (FRI) consensus group. In 2017, the accepted consensus definition of FRI was published, which has been followed by consensus recommendations from both a surgical and medical perspective. A bibliometric analysis was performed to objectively describe the trends in published clinical research related to FRI.

Methods: The terms related to FRI were searched in the Web of Science database between 2000 and 2020. The characteristics of clinical research on FRI regarding the author, country, journal, institution, scientific output, top 100 most cited articles, and trend topics were analyzed using Bibliometrix and WPS Office.

Results: A total of 2597 records were eligible for inclusion in this bibliometric approach, with studies originating from 89 countries, including eight languages. The United States of America (USA) published the highest number of articles and citations. International collaborations were present between 72 countries, with the most active country being the USA. The most contributive institution was the University of California. The highest number of papers and citations were from the Injury-International Journal of the Care of the Injured and the Journal of Orthopaedic Trauma. The top 100 most cited articles were published in 27 different journals, with the number of citations ranging between 97 and 1004. The latest trend topics were related to the diagnosis of FRI.

Conclusion: The present bibliometric analysis shows the research characteristics and trends of FRI from multiple perspectives. The fact that there is an increasing number of studies being published on FRI shows the agreement among

scientists and clinicians that standardization with respect to this topic is very important.

6. Bandholm T, Thorborg K, Ardern CL Christensen R, Henriksen M. Writing up your clinical trial report for a scientific journal: the REPORT trial guide for effective and transparent research reporting without spin. Br J Sports Med. 2022 Jun;56(12):683-691. doi: 10.1136/bjsports-2021-105058.

ABSTRACT

The REPORT guide is a 'How to' guide to help you report your clinical research in an effective and transparent way. It is intended to supplement established first choice reporting tools, such as Consolidated Standards of Reporting Trials (CONSORT), by adding tacit knowledge (ie, learnt, informal or implicit knowledge) about reporting topics that we have struggled with as authors or see others struggle with as journal reviewers or editors. We focus on the randomised controlled trial, but the guide also applies to other study designs. Topics included in the REPORT guide cover reporting checklists, trial report structure, choice of title, writing style, trial registry and reporting consistency, spin or reporting bias, transparent data presentation (figures), open access considerations, data sharing and more. Preprint (open access): https://doi.org/10.31219/osf.io/qsxdz.

Keywords: education; methods; randomized controlled trial; research; sports medicine.

7. Jia Q, Chu H, Jin Z, Long H, Zhu B. High-throughput single-cell sequencing in cancer research. Signal Transduct Target Ther. 2022 May 3;7(1):145. doi: 10.1038/s41392-022-00990-4.

ABSTRACT

With advances in sequencing and instrument technology, bioinformatics analysis is being applied to batches of massive cells at single-cell resolution. High-throughput single-cell sequencing can be utilized for multi-omics characterization of tumor cells, stromal cells or infiltrated immune cells to evaluate tumor progression, responses to environmental perturbations, heterogeneous composition of the tumor microenvironment, and complex intercellular interactions between these factors. Particularly, single-cell sequencing of T cell receptors, alone or in combination with single-cell RNA sequencing, is useful in the fields of tumor immunology and immunotherapy. Clinical insights obtained from single-cell analysis are critically important for exploring the biomarkers of disease progression or antitumor treatment, as well as for guiding precise clinical decision-making for patients with malignant tumors. In this review, we summarize the clinical applications of single-cell sequencing in the fields of tumor cell evolution, tumor immunology, and tumor immunotherapy. Additionally, we analyze the tumor cell response to antitumor treatment, heterogeneity of the tumor microenvironment, and response or resistance to immune checkpoint immunotherapy. The limitations of single-cell analysis in cancer research are also discussed.

8. Mitra S, Sarker J, Mojumder A, Shibbir TB, Das R, Emran TB, et al. Genome editing and cancer: How far has research moved forward on CRISPR/Cas9? Biomed Pharmacother. 2022 Jun;150:113011. doi: 10.1016/j.biopha.2022.113011. Epub 2022 Apr 25.

ABSTRACT

Cancer accounted for almost ten million deaths worldwide in 2020. Metastasis, characterized by cancer cell invasion to other parts of the body, is the main cause of cancer morbidity and mortality. Therefore, understanding the molecular mechanisms of tumor formation and discovery of potential drug targets are of great importance. Gene editing techniques can be used to find novel drug targets and study molecular mechanisms. In this review, we describe how popular gene-editing methods such as CRISPR/Cas9, TALEN and ZFNs work, and, by comparing them, we demonstrate that CRISPR/Cas9 has superior efficiency and precision. We further provide an overview of the recent applications of CRISPR/Cas9 to cancer research, focusing on the most common cancers such as breast cancer, lung cancer, colorectal cancer, and prostate cancer. We describe how these applications will shape future research and treatment of cancer, and propose new ways to overcome current challenges.

Keywords: CRISPR/Cas9; Cancer; Genome editing; Molecular mechanisms; TALEN.

9. Hagenaars SC, Vangangelt KMH, Van Pelt GW, Karancsi Z, Tollenaar RAEM, Green, AR et al. Standardization of the tumor-stroma ratio scoring method for breast cancer research. Breast Cancer Res Treat. 2022 Jun;193(3):545-553. doi: 10.1007/s10549-022-06587-3.

ABSTRACT

Purpose: The tumor-stroma ratio (TSR) has repeatedly proven to be correlated with patient outcomes in breast cancer using large retrospective cohorts. However, studies validating the TSR often show variability in methodology, thereby hampering comparisons and uniform outcomes.

Method: This paper provides a detailed description of a simple and uniform TSR scoring method using Hematoxylin and Eosin (H&E)-stained core biopsies and resection tissue, specifically focused on breast cancer. Possible histological challenges that can be encountered during scoring including suggestions to overcome them are reported. Moreover, the procedure for TSR estimation in lymph nodes, scoring on digital images and the automatic assessment of the TSR using artificial intelligence are described.

Conclusion: Digitized scoring of tumor biopsies and resection material offers interesting future perspectives to determine patient prognosis and response to therapy. The fact that the TSR method is relatively easy, quick, and cheap, offers great potential for its implementation in routine diagnostics, but this requires high quality validation studies.

10. *Savage P, Cox B, Linden K, Coburn J, Shahmohammadi M, Menown I. Advances in Clinical Cardiology 2021: A Summary of Key Clinical Trials. Adv Ther. 2022 Jun;39(6):2398-2437. doi: 10.1007/s12325-022-02136-y.*

ABSTRACT

Introduction: Over the course of 2021, numerous key clinical trials with valuable contributions to clinical cardiology were published or presented at major international conferences. This review seeks to summarise these trials and reflect on their clinical context.

Methods: The authors reviewed clinical trials presented at major cardiology conferences during 2021 including the American College of Cardiology (ACC), European Association for Percutaneous Cardiovascular Interventions (EuroPCR), European Society of Cardiology (ESC), Transcatheter Cardiovascular Therapeutics (TCT), American Heart Association (AHA), European Heart Rhythm Association (EHRA), Society for Cardiovascular Angiography and Interventions (SCAI), TVT-The Heart Summit (TVT) and Cardiovascular Research Technologies (CRT). Trials with a broad relevance to the cardiology community and those with potential to change current practice were included.

Results: A total of 150 key cardiology clinical trials were identified for inclusion. Interventional cardiology data included trials evaluating the use of new generation novel stent technology and new intravascular physiology strategies such as quantitative flow ratio (QFR) to guide revascularisation in stable and unstable coronary artery disease. New trials in acute coronary syndromes focused on shock, out of hospital cardiac arrest (OOHCA), the impact of COVID-19 on ST-elevation myocardial infarction (STEMI) networks and optimal duration/type of antiplatelet treatment. Structural intervention trials included latest data on transcatheter aortic valve replacement (TAVR) and mitral, tricuspid and pulmonary valve interventions. Heart failure data included trials with sodium-glucose cotransporter 2 (SGLT2) inhibitors, sacubitril/valsartan and novel drugs such as mavacamten for hypertrophic cardiomyopathy (HCM). Prevention trials included new data on proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. In electrophysiology, new data regarding atrial fibrillation (AF) screening and new evidence for rhythm vs. rate control strategies were evaluated.

Conclusion: This article presents a summary of key clinical cardiology trials published and presented during the past year and should be of interest to both practising clinicians and researchers.

11. *Gupta AK, Leslie A, Hewitt JN, Kovoor JG, Ovenden CD, Edwards S, et al. Cardiac surgery on patients with COVID-19: a systematic review and meta-analysis. ANZ J Surg. 2022 May;92(5):1007-1014. doi: 10.1111/ans.17667.*

ABSTRACT

Introduction: The COVID-19 pandemic has had a significant impact on global surgery. In particular, deleterious effects of SARS-CoV-2 infection on the heart and cardiovascular system have been described. To inform surgical patients, we performed a systematic review and meta-analysis aiming to characterize outcomes of COVID-19 positive patients undergoing cardiac surgery.

Methods: The study protocol was registered with PROSPERO (CRD42021228533) and conformed with PRISMA 2020 and MOOSE guidelines. PubMed, Ovid MEDLINE and Web of Science were searched between 1 January 2019 to 24 February 2022 for studies reporting outcomes on COVID-19 positive patients undergoing cardiac surgery. Study screening, data extraction and risk of bias assessment were conducted in duplicate. Meta-analysis was conducted using a random-effects model where at least two studies had sufficient data for that variable.

Results: Searches identified 4223 articles of which 18 studies were included with a total 44 patients undergoing cardiac surgery. Within these studies, 12 (66.7%) reported populations undergoing coronary artery bypass graft (CABG) surgery, three (16.7%) aortic valve replacements (AVR) and three (16.7%) aortic dissection repairs. Overall mean postoperative length of ICU stay was 3.39 (95% confidence interval (CI): 0.38, 6.39) and mean postoperative length of hospital stay was 17.88 (95% CI: 14.57, 21.19).

Conclusion: This systematic review and meta-analysis investigated studies of limited quality which characterized cardiac surgery in COVID-19 positive patients and demonstrates that these patients have poor outcomes. Further issues to be explored are effects of COVID-19 on decision-making in cardiac surgery, and effects of COVID-19 on the cardiovascular system at a cellular level.