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SHAM INVASIVE PROCEDURES IN BREAST SURGERY CLINICAL TRIALS: A LITERATURE REVIEW

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Introduction: Blinding is vital for randomized clinical trials to avoid bias and statistical errors. This can be more achievable for interventions requiring medication, but when discussing invasive procedures, finding a suitable placebo is complex and can cause ethical controversies.
Objectives: In this literature review, we will analyze in what scenarios sham procedures are used for breast surgery.
Methods: For this literature review, a computerized search was conducted in PubMed electronic database by using subject-specific headings and free-text words. The subject-specific search was based on the terms breast surgery, sham, placebo, and sham surgery. The electronic search was conducted until November 2022.
Results: A total of 35 articles from 2004 to 2022 were included in the original search, but only 10 studies were included in the analysis. The excluded studies did not evaluate breast surgery interventions or studied non-invasive procedures. The main limitation of this study is the indication for breast surgery. Most of these procedures are indicated for breast cancer or aesthetic reasons; therefore, studies using sham procedures would be unethical.
Discussion: The use of invasive sham procedures is limited in breast surgery. Pain management is currently the main area of focus for this methodology in breast cancer clinical trials given the ethical implications.

STATIN TREATMENT AND MUSCULAR SYMPTOMS: A LITERATURE REVIEW OF N-OF-1 TRIALS

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Introduction: Statins are widely prescribed medications for the prevention and treatment of cardiovascular disease in adults. A significant number of patients report adverse muscle symptoms (e.g., pain and stiffness) related to statins. Large randomized trials have shown that statin-related symptoms are mostly associated with a placebo effect; however, some patients still report intolerance.
Objectives: To clarify the effect of statins on muscle symptoms we aim to review the current literature on N-of-1 trials, which is a type of randomized, double-blind, multiple crossovers that evaluates treatment efficacy, safety profile, and tolerability at the individual level.
Methods: Publications of N-of-1 trials within the last 10 years assessing statin-related muscle symptoms were retrieved from the PubMed database using subject-specific headings and free-text words: N-of-1 trial, single case studies, cross-over studies, and statins.
Results: A total of 89 articles were included in the original search, but only 4 studies met the inclusion criteria. The excluded studies did not evaluate N-of-1 trials and statins. All N-of-1 trials reported no significant mean difference in muscle symptom scores between statins and placebo using visual analog scales. The main limitations of this study are the limited number of published studies, small sample size, and publication bias.
Discussion: A series of N-of-1 trials found no overall effect of statins on self-perceived muscle symptoms when compared to a placebo. These findings suggest that physicians should validate patients' concerns but also educate them about the potential nocebo effect before prescribing statins.

VALIDATION OF THE KIDNEY FAILURE RISK EQUATION (KFRE) IN MEXICAN DIABETIC POPULATION

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Introduction: Patients with CKD have a high risk of progression to kidney failure. Multiple factors influence the course of the disease and great efforts have been made to establish the temporality of kidney failure.
Objectives: This study assesses the 4-element KFRE formula as a method to predict the risk of kidney failure in the Mexican population with stage 3 to 5 diabetic nephropathy.
Methods: An observational study was conducted in a private hospital in Monterrey, México. Records of patients with a diagnosis

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of diabetes mellitus and stage 3 to 5 CKD were analyzed from January 2012 to August 2018. KFRE model was calculated and given follow-up after two years. The sensitivity, specificity, negative and positive predictive value between the KFRE, the GFR, and the prediction of progression of physicians were compared.
Results: After two years, 72.5% of the 102 patients remained in stage 3, stage 4 increased from 16.7 to 17.6%, and stage 5 from 1% to 9.8%, the latter requiring RRT. The best cut-off value for the KFRE was 5.855% with an AUC of 0.824 (95% CI); compared to GFR with an AUC of 0.48 (95% CI) and prediction of internists with AUC of 0.71 (95% CI).
Discussion: The KFRE model is a valid tool to apply to patients with diabetic nephropathy to assess which patient will progress to kidney failure in the next two years. This can aid decision-making in clinical practice and assist in the selection of tailored management and follow-up strategies.

ADHERENCE STRATEGY IN POST-STROKE PATIENTS – A SYSTEMATIC REVIEW

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Introduction: Patient adherence to therapy after stroke is challenging. A potential influence might be post-stroke depression, the most prevalent psychiatric comorbidity.
Objectives: This systematic review aims to summarize the available evidence addressing methods to improve adherence in post-stroke patients.
Methods: A systematic literature search on MEDLINE, LIVIVO, and Embase databases was performed for eligible randomized controlled trials (RCT) and observational studies that reported adherence strategies in post-stroke patients following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Literature search was limited to English and German languages and publication date before November 01.2022. Used combinations of search strings were ischemic stroke, cerebral infarction, cerebrovascular event, post-traumatic depression, depression, post-stroke, adherence, and compliance with the Boolean operators "AND" and "OR."
Results: We identified two RCTs, one prospective and one retrospective observational study. Individuals included were at least 16 years old. Among the strategies identified the use of antidepressants in combination with physiotherapy, care coordination and empathy nursing showed the most reliable approach for increasing treatment adherence whereas also motivational interviewing seems to be beneficial. Literature search revealed that few studies are investigating therapeutic strategies addressing adherence to treatment in post-stroke patients, which underscores the need for well-designed RCTs.
Discussion: A major limitation is the number of included studies. Furthermore, each of the studies reviewed had different reference points for measuring adherence, which limited comparability. A standardized study procedure for future studies is needed.

CLINICAL TRIAL QUALITY ASSESSMENT IN INTERVERTEBRAL DISC REGENERATION: INSIGHTS FROM PUBLICATION STATUS AND FUNDING SOURCES

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Introduction: Low back pain (LBP) is the main cause of disability worldwide and is primarily triggered by intervertebral disc degeneration (IDD). Although several treatment options exist, no therapeutic tool has demonstrated to halt the progressive course of IDD. Therefore, several clinical trials are being conducted to investigate different strategies to regenerate the intervertebral disc, with numerous studies not reaching completion nor being published.
Objectives: The aim of this study was to compare the publication status of clinical trials on novel regenerative treatments for IDD by funding source and to identify critical obstacles preventing their conclusion.
Methods: Prospective clinical trials investigating regenerative treatments for IDD and registered on ClinicalTrials.gov were included. Primary outcomes were publication status (published vs. unpublished) and investigational treatment funding (industry and private funding vs. university funding). Fisher's exact test was utilized to test the association for categorical variables between groups.
Results: 25 clinical trials were identified. Among these, only 6 (24%) have been published. The most common source of funding was university (52%), followed by industry (36%) and private companies (12%). Investigational treatments included intradiscal transplantation of autologous (56%) or allogeneic (12%) products alone or in combination with a carrier or delivery system (32%). In the latter case, these products were more likely utilized in industry or privately funded studies (p=0.0112). No significant difference was found in terms of funding regarding the publication status of included trials (p=0.9104).
Discussion: The results of this study showed that the majority of clinical trials investigating regenerative approaches for the treatment of IDD was never completed nor published. This is likely due to multiple factors, including difficult enrollment, high dropout rate, significant associated costs (Schol & Sakai, 2023) , and the tendency not to publish trials with negative results. Furthermore, retrieved data were often heterogeneous and not completely accurate. More accurate design and technical support from stakeholders and clinical research organizations (CROs) may likely increase the quality of future clinical trials in the field.

COMPUTER-AIDED UPPER GASTROINTESTINAL ENDOSCOPIC OUTCOMES IN BARRETT'S-RELATED DYSPLASIA DETECTION

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Introduction: Upper gastrointestinal endoscopy is the main screening tool for esophageal adenocarcinoma and its precursor lesions. While lower endoscopic quality benchmarks improve neoplasia detection rates, upper endoscopy has failed to establish clear evidence for improved survival rates attributed to screening. Proper screening is dependent on various endoscopic benchmarks including direct macroscopic mucosal visualization and histopathologic biopsies for early-stage dysplasia detection. Considering the risk for sampling error and inter-user variability, standardized validated tools have been proposed to facilitate dysplasia detection.
Objectives: The aim of this review is to summarize recent computer-aided endoscopic tools that facilitate esophageal dysplasia detection.

Methods: A PubMed systematic search using MeSH terms "Endoscopy, Gastrointestinal/methods", "Barrett Esophagus/diagnostic imaging", and "Artificial Intelligence" from January to November 2022. Articles that included computer-aided and esophageal dysplasia detection outcomes were included. Gray literature and articles with lower endoscopic outcomes were excluded.
Results: Overall, three articles (one randomized cross-over study, one review, and one prospective, clinical validation study) met the criteria. These articles included three computer-aided diagnostic (CAD) platforms for three different advanced endoscopic imaging tools. CAD platforms included improved dysplasia detection rates compared to the predefined expert endoscopist.
Discussion: Computer-aided diagnosis in esophageal dysplasia detection is a promising tool for future quality benchmarks; nevertheless, the variability of real-time versus post-hoc image analysis and multi-system image model training limits the external validity of tool implementation.

ADDRESSING CHRONIC PANCREATITIS PAIN IN CLINICAL TRIALS: OUTCOME ASSESSMENT VARIABILITY

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Introduction: Amid patients with chronic pancreatitis, pain constitutes the main factor disrupting quality of life. Efforts to mitigate its burden have not been satisfactory, hence, the advent of recent randomized clinical trials. Due to pain idiosyncrasy, extrapolation of promising new therapies could be obscured by variability in its assessment.
Objectives: It was aimed to review the differences in pain outcomes among clinical trials including adult patients with chronic pancreatitis.
Methods: The ClinicalTrials.gov database was used to retrieve articles, later filtered by screening and full-text review.
Results: A total of 52 references were collected. Of these, 55.7% utilized a single pain outcome descriptor, while the rest have at least 2 assessment tools. Instruments for evaluating pain were Visual Analogue Score (VAS) = 21, analgesic use = 19, Izbicki Score = 9, Numeric Rating Scales (NRS) = 8, the Brief Pain Inventory average (BPI-SF) or the COMPAT-SF pain severity score = 6. Less frequently used instruments included PROMIS Neuropathic and Nociceptive Pain Scale and Conditioned Pain Modulation score.
Discussion: The correlation between the type of treatment, prediction accuracy of different scales for treatment response and improvement on quality of life remain to be elucidated.

BLINDING IN NEUROSURGERY TRIALS: AN INHERENT METHODOLOGY CHALLENGE

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Introduction: The history of RCTs in neurosurgery is relatively young. Neurosurgery as a specialty did not start until the late 19th century. The first identified RCT in this field was a comparison between surgical and nonsurgical management of posterior communicating artery aneurysms published by McKissock et al. in 1960. Blinding is one of the hallmarks of methodological quality and failures in this process may increase the risk of bias, which can be a threat to the internal validity of a clinical trial. In surgical trials, using intervention with physical components makes blinding a complicated task.
Objectives: To review aspects related to the difficulties reported in the blinding process in the development of clinical trials in the neurosurgery field.
Methods: A literature search was performed in the PubMed database, using MeSH terms and terms contained in the title and abstract. A block with terms related to research methodology and another with terms related to neurosurgery were used. These blocks were crossed using the "and" connect, obtaining 9 articles. 3 of the 9 articles were considered eligible for this review.
Results: Recent assessments of neurosurgical trials with regard to the quality of reporting have noted that the overall quality tends to be low. The decision-making is often based on the lessons taught or personal experience and current practice is, at the very best, based on prospective observational series or use of multicenter, registry-based collection of prospective observational data. Blinding may be the methodological aspect with the most weaknesses. The described causes for this deficiency are: the interventional nature of neurosurgery; the significant variability in the surgical approach among neurosurgeons; and the expertise bias when the procedures are performed by highly expert surgeons and surgeons with less exposure to a similar procedure.
Discussion: Quality of blinding is one of the challenges faced by the researcher and the reader of clinical studies in neurosurgery. Not all neurosurgical questions can be answered through the conduct of an RCT, and given difficulties like these, alternative study design strategies must be considered in certain scenarios.

OUTCOMES IN TRIALS EVALUATING NEURAL STIMULATION AS A TREATMENT FOR FECAL INCONTINENCE: WHAT ARE AUTHORS CHOOSING?

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Introduction: Among the surgical alternatives in the management of fecal incontinence (FI), neural stimulation (NS) —sacral, pudendal, or tibial— has shown encouraging results in the last decade.
Objectives: The aim of this review is to identify trends in the choice of outcomes in trials evaluating NS in patients diagnosed with FI.
Methods: Using the ClinicalTrials.gov database, trials evaluating NS for the treatment of FI in adult patients were screened using the following keywords: "fecal incontinence", "surgery", "stimulation". Trials were excluded if other surgical or non-surgical treatment options were evaluated, if patients younger than 18 years were studied, or if patients being treated for urinary incontinence were included in the analysis.
Results: Eighteen trials meeting inclusion criteria were assessed. The most commonly utilized primary outcomes were patient reported clinical outcomes (57.9%), validated symptom severity scales (21.1%), quality of life (QoL) questionnaires (5.26%), surgical adverse events (5.26%), treatment costs (5.26%), and technical characteristics of the neurostimulator device (5.26%). The most common secondary outcomes were QoL (63.2%), validated symptom severity scales (47.4%), patient reported clinical outcomes (42.11%), manometric findings (31.6%), surgical adverse events (15.8%), and treatment costs (5.26%).
Discussion: Despite differences in methodology between trials evaluating NS in the management of FI, the choice of primary

and secondary outcomes appears to be sufficiently similar, allowing comparison between results reported by different studies. However, further research is warranted to determine homogeneity within the choice of available validated clinical scales in order to further promote comparability and reproducibility in the field.

KNOWLEDGE GAPS AND FUTURE DIRECTIONS OF MENDELIAN RANDOMIZATION STUDIES IN CARDIOLOGY: A SCOPING REVIEW

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Introduction: Confounders are an important source of bias for observational studies, and the results of these studies are often challenged by randomized clinical trials (1). And even when properly addressed, unmeasured confounders can greatly affect the study outcome, and are not solved even with advanced statistical methods (2). In addition, cardiovascular risk factors often have long-term effects, hard to characterize, and require significant resources to analyze. Mendelian randomization studies (MR) use a genetic variation to address how modifiable exposures influence outcomes, overcoming many of the classic in observational studies (3).
Objectives: No reviews have assessed the current tendencies and knowledge gaps of this design in cardiology. Categories in the field were defined using cardiology practice guidelines, each guideline theme representing a category.
Methods: Following this, a broad search strategy was implemented in PubMed, in which it revealed 254 articles. Of these, 135 were included in the analysis. The main exposure and outcomes were extracted from the articles.
Results: Atherosclerotic cardiovascular disease was the most studied area with 42 articles, followed by coronary artery disease (34), atrial fibrillation (27) and heart failure (14). Interestingly, hypertension had 7 MR, valvular heart disease only had 3 MR studies, and pulmonary embolism 1. No MR were found about pulmonary hypertension.
Discussion: Although it is common to search knowledge gaps by finding specific areas within a subject, widening our research scope can often reveal missed research areas. As MR become available to a broad scientific community, more studies are needed to evaluate and validate risk factors and outcomes for these diseases in Cardiology.

ADHERENCE ASSESSMENT OF DIETARY INTERVENTIONS FOR PEDIATRIC OBESITY IN THE UNITED STATES: A SCOPING REVIEW

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Introduction: In 2016, 340 million children were overweight. Recent studies showed an increasing prevalence of childhood obesity. To address this, it is considered that adequate nutrition and promotion of optimal eating behaviors since childhood can benefit current health status and predisposition to non-communicable diseases in adulthood. Sociocultural contexts, decision-making processes, perceptions and preferences, and environmental barriers play a critical role in dietary adherence. This review aims to explore how frequently adherence is assessed and reported in clinical trials testing nutritional interventions in children with obesity and which tools are used to assess adherence.
Objectives: This review aims to explore how frequently adherence is assessed and reported in clinical trials testing nutritional interventions in children with obesity and which tools are used to assess adherence.
Methods: A literature review was performed using the ClinicalTrials.gov database with the keywords, pediatric obesity, and diet therapy, also including the filters for the United States and children. Studies without related publications or evaluating different interventions were excluded. Adherence was considered as the degree to which study participants act in concordance with the study protocol or advice of the physician and it was inspected by looking at the term in each article.
Results: There were found a total of 41 clinical trials, with 43,9% of them being excluded after a preliminary review. Of the included articles 52,2% report an adherence assessment tool or adherence rate which is a low proportion considering that dietary intervention success highly depends on how adherent patients are.
Discussion: The proportion of studies reporting adherence assessment or adherence assessment tools is low considering that dietary intervention success highly depends on how adherent patients are. Furthermore, there is a high variability among the reported adherence assessment tools which highlights the need of a more unified system of assessment and reporting. ClinicalTrials.gov was the only database used for this study, perhaps excluding some relevant articles. After the preliminary revision, a high proportion of studies were excluded.