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Examine The Design, Execution, And Analysis Of Clinical Research In Restorative Dentistry

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ABSTRACT

Background: The pyramid of evidence is usually cited when discussing evidence-based medicine or dentistry (EBM/EBD), with randomised controlled(efficacy) trials and their syntheses (in the form of systematic reviews and meta-analyses) being the strongest category of evidence. Thus, confounding bias is potentially avoided, similar to a randomised controlled experiment.

Aim's & Objectives: Clinical research should be a significant factor in dentists' decisions on dental materials. Design, execution, analysis, and reporting of studies have an effect on their usefulness. We evaluate issues with current studies and highlight potential areas for improvement.

Methods & Materials: On the basis of systematically and non-systematically gathered data, we illustrate where and why present clinical dentistry studies produce suboptimal outcomes. Taking cues from the field of general health, we propose future directions for clinical dental material research.

Results: Randomized controlled (efficacy) trials continue to be a cornerstone of dental material science because they eliminate selection bias and, if well-designed and done, offer excellent internal validity. In light of their expense and low external validity, alternatives such as practice-based or pragmatic controlled trials or observational research might supplement the existing body of knowledge. Prior to implementation, researchers should focus on study comparators and setting (answering questions pertinent to clinical dentistry) and pay close attention to statistical power, taking into account the study objective (superiority or non-inferiority trial), the anticipated event rate, and attrition. In the absence of a core result set, patients and other stakeholders should be consulted in the selection of study outcomes. Studies ought to be pre-registered, and reporting must follow to guidelines. Statistical analysis should account for potential clustering.

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Significance: Numerous clinical research in dental material science are underpowered, with little validity and practical use for making daily decisions. In order to improve dental treatment, dental researchers should replicate efforts in other medical professions to make clinical trials more valid and useful.

Keywords: execution, analysis , restorative , Longevity

INTRODUCTION

Randomized controlled trials

When addressing evidence-based medicine or dentistry (EBM/EBD), the pyramid of evidence is commonly referenced, with randomised controlled (efficacy) trials and their syntheses (in the form of system-atic reviews and meta-analyses) being the strongest sort of evidence. Theoretically, as in a randomised controlled experiment, confounding bias is eliminated [1]. Confounding fallacy – The conventional pyramid of evidence (a) is based on efficacy and meta-efficacy research as the strongest type of evidence. For translation into the real world, however, this is merely the foundation, as other factors are more significant (b). Thus, the question "does it work?" serves simply as a springboard for more inquiries concerning applicability and practicability (c) [1]. consists of patients chosen to receive one comparator being consistently distinct from those chosen to receive another comparator [2]. For instance, when comparing the performance of glass ionomer cement restorations to that of composite in non-randomized trials, where placement of the restoration type is decided by the patient (considering aesthetics, price, or longevity) and the dentist (considering indication, applicability, and income), it is possible that such bias is present [3].

A randomised trial must always evaluate treatments amenable to randomization, which makes randomised designs difficult to apply if randomization is unacceptable to patients (Zelen's design could be used in such a situation [4]) or ethically impossible (for example, assuming that one would need to restrict patients' access to therapies that are believed to be superior due to randomization). In any case, randomised trials are often conducted in a highly controlled environment, providing optimal circumstances for the administration of the intervention to typically highly selected patient populations. The latter is more accurate given that only a subset of patients will accept enrollment in a randomised trial, while other patients may decline to participate [5].

Comparing different materials in the same mouth, often known as a split-mouth design, is one technique to increase the power of a trial. When two (or more) teeth may be randomly assigned to receive one material or another, it is possible to compare the materials within the same patient (intra-individual comparisons). This has significant statistical advantages, as the noise(variance) created by patients differing in a number of unmeasured characteristics is reduced (within the same patient, only minor noise exists, for instance between different sites). However, these designs should not be mistaken with placing the same material on multiple teeth of the same patient: While this may appear to be a simple method for increasing sample sizes, itis in fact not trivial and requires specific statistical handling during sample size estimation and analysis, as the

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multiple teeth are not, in fact, independent from one another (as multiple patients typically are), but instead frequently exhibit correlated behaviour. In general, these characteristics must be considered during sample size determination, as they have a significant impact on trial power. The difficulty of sample selection and size persists throughout the follow-up of randomised trials, with drop-outs frequently being non-random and linked to either patient characteristics or the intervention (we will discuss options ofhow to overcome the latter problem later on). This dropout should be accounted for correspondingly, as will be detailed below. When assessing the "sustainability" of an intervention, in the case of restorative dentistry, the survival of dental restorations, the problems in follow-up are also of great importance. It has been noted that the median follow-up period for dental restoration material trials was only two years [6]. Observing restorations for only two years typically generates few "events," i.e. restoration failures, as restoration failures typically occur later on. Moreover, follow-up durations influence the type of failure observed; a meta-analysis revealed that restoration failures in the first year are primarily endodontic complications, whereas secondary caries appeared predominantly after several years of clinical treatment [8]. As the measurement of events is the basis for comparing interventions (restoration materials), many short-term trials can merely state that materials are performing similarly (recording no or only one or two events in each group) - which may be an incorrect conclusion when taking into account the lifespan that is relevant for dental restorations [6,9]. The testing of brand-new materials, which carry a risk of unanticipated catastrophic failures, is one exception where trial times may be proactively curtailed. Note, however, that such failures would be recorded and communicated to the principalinvestigator, who would be responsible for deciding whether to discontinue the study and stop recruiting additional patients, despite the fact that larger sample sizes and longer trial periods were previously intended.

In addition, the preparation of randomised trials is arduous and expensive, particularly if the inclusion criteria are stringent, so limiting the pool from which patients can be recruited and increasing the recruitment efforts. Costs are also expensive if follow-up visits are arranged with a high frequency and if a large number of (complex) parameters are captured during these visits. As mentioned previously, randomised trials typically take years to conduct (from registrationover ethics approval over recruitment, treatment and follow-up). This is problematic in a highly inventive sector such as restorative dentistry, where comparisons are required in shorter cycles, and where, due to the enormous number of accessible materials, hundreds of trials must be undertaken annually to provide an adequate data foundation for strong comparisons. Lastly, and most importantly from the standpoint of enhancing general dental practise, trials should advise dental practitioners regarding which therapy works best in their hands, in their practise; that is, in real-world scenarios, not in laboratory settings. The question of whether a therapy works under ideal conditions – which is what the majority of randomised controlled (efficacy) trials measure- is merely a springboard for asking the more pertinent questions regarding effectiveness in daily life, the applicability of a restorative intervention, and clinicians' and patients' acceptance of it [10,11]. Efficacy trials comparematerials (under ideal conditions). Typically, alternative designs examine elements beyond the theoretical performance of the material, such as handling or efficiency, or compare various restorative processes.

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Pragmatic trials

An alternative practice-based design, also known as a pragmatic-controlled trial, analyses several practises that make distinct decisions for identical dental issues. For instance, when a patient with a larger filling and a fractured cusp presents to thepractice with a broken cusp, one practitioner may decide to make a crown or indirect restoration (treatment A), whilst another practitioner may want to make a direct restoration (treatment B). Treatment A or B will not be assigned at random, but rather based on the preferences and selections of both dentists (and patients). By performing risk assessment and allocating patients to high, intermediate, and low risk groups for oral diseases and conditions such as caries and bruxism, respectively, using the best prognostic and preferably validated criteria [14], a certain level of control over the effect of different baseline risks on outcome is maintained. These studies are primarily prospective observational (see below). 1.4. Studies of retrospective observation Prospective or retrospective observational studies of two or more interventions (materials) may be conducted. Retrospective observational studies are more prevalent, with the study building on preexisting data that was typically collected in a routine (non-research) context (like a dental practice). Such studies are not planned, and only post-implementation evaluations are conducted. As mentioned in the introduction, such investigations are theoretically highly susceptible to confounding bias. In addition, routine data are frequently underreported (incomplete information on confounders, as well as on interventions and outcomes) [15]. Decisions are not uniform and can be influenced by factors other than the condition (clinician skill, patient preferences, or healthcare culture, for example). It is typically impossible to provide a comprehensive explanation for specific judgements. In many studies in such settings, it is not possible to ascertain precisely why restorations were replaced or teeth were extracted, as there are typically no defined decision criteria and explanations are not recorded in full [16–20]. However, when a practitioner changes a technique or material from one period to another for the same indication, it is conceivable to compare the outcomes of the materials and approaches because the bulk of confounding variables remain the same [21]. In addition, clinical dentistry is subject to precisely these factors: context, preferences, and routine. Thus, routine data from observational studies have a high external validity (they are likely to be applicable to general dentistry) but a low internal validity (they are susceptible to a number of biases) [22]. The fundamental question is whether the data obtained from such research are system-atically distorted, i.e., whether the outcomes are system-atically distinct from those of randomised controlled trials. A recent Cochrane review included 14 meta-analyses on this topic (none from the dental setting) and found no significant difference between observational studies and randomised trials, with some studies indicating higher, others indicating lower, and the majority indicating similar effects found in both study types [23]. In contrast, a more recent study discovered that observational studies utilising routine data typically reveal greater treatment effects than subsequent randomised trials [22].

To undertake any assessment and adjustment, however, the baseline characteristics of patients must be known, which, as previously said, is not always the case, at least in retrospective research [16]. A recent systematic evaluation of patient characteristics and risk variables in clinical studies reached the conclusion that manystudies lacked information addressing these aspects. The authors stated that examination of patient factors and other variables should be

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incorporated into clinical research investigating restoration survival, as some of these factors were demonstrated to influence restoration failure independent of material type.[17]

During analysis, researchers must additionally account for drop-outs, or missing data. Rarely are these missing completely at random; only in this instance is an available case analysis appropriate, in which lost patients are either not entered at all or treated as censored [6]. It is extremely unlikely that dropouts occur at random: For instance, patients with unfavourable outcomes (being discouraged or in urgent need of care, seeking it elsewhere) or positive outcomes (perceiving no need to re-attend) may drop out of a trial disproportionately, frequently having a considerable impact on the ending of a study [18,19]. If sufficient data are available to determine whether dropouts were associated with particular (known) criteria (age, gender, etc.), then it may be possible to adjust the results accordingly. Frequently, it will be impossible to completely address the underlying causes and variables that account for the missing data. In this instance, researchers should conduct a range of analyses to account for this, such as treating all drop-outs as failures or assuming that all drop-outs in one group were due to failure but none in the other (best and worst case scenarios)[20]. This helps to determine the potential impact of student dropouts (andattrition bias). A particular concern is the loss of patients from split-mouth trials; in this case, both the test and control groups are lost in a balanced manner. This increases the likelihood that data are absent at random. Nonetheless, it is recommended to examine the impact of attrition as indicated. It is discussed elsewhere [21] how to evaluate attrition bias and how to treat it effectively. Due to the fact that attrition can have a major impact on overall results and conclusions, there is no acceptable rule for dropout. Instead, dropout should be thoroughly investigated and individually addressed for each study. 3.3. Compilation of trial data Last, the available evidence from individual research must be collated and integrated to determine whether the whole body of data is homogeneous and consistent or confusing and difficult to interpret. Usual research methods include systematic reviews and meta-analysis. Several aspects are present here. First, researchers should adhere to established reporting standards such as PRISMA [12] and register their review before doing it (safeguarding themselves against selective reporting, outcome switching or search sequencet weaking). Note that justifiable variations from any protocol are not a problem; they only need to be specified in the study report. Second, reviewers should carefully assess all comparables pertinent to an issue and should not impose unwarranted limitations on their inclusion criteria. On the other side, incorporating a large number of comparators may indicate that a large number of outcomes have been employed. In this regard, COS may potentially make a difference by facilitating a more efficient and transparent assessment and comparison of trial findings. In the field of dental restoration materials, two additional factors emerge: the sheer volume of comparisons and the regularity with which new studies are published.[23] The latter should be addressed by updating reviews on a frequent basis; this is now only typical in Cochrane reviews. It is difficult for reviewers and meta-analysts to synthesise these comparators into groups [17] due to the vast number of comparators. Pairwise meta-analysis frequently disregards a huge number of trials since only a small number of comparators (composite versus amalgam, for example) are evaluated. Network meta-analysis may be able to circumvent these limitations [16]. Nonetheless, the results of network meta-analysis are susceptible to distortion if the network is sparsely filled, with certain connections being created by only one or a small number of trials (which would have a

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significant impact on the ranking of the derived materials) [18]. Also, if trials comparing interventions A and B are methodologically distinct from those comparing B and C, this will lead to incorrect findings regarding the performance of A versus C. Network meta-analysts should determine if transitivity, i.e. the true comparability of all groups entered in a network meta-analysis, is given [24-26], for example by comparing important parameters affecting a material's performance (such as the patient population, its caries risk, age, the setting, the experience of operators, and many others) [20-22].

CONCLUSIONS

Randomized controlled trials continue to be a cornerstone of dental material research because they eliminate selection bias and, if well-designed and conducted, offer a high level of internal validity. Alternatives such as practice-based or pragmatic controlled trials or observational studies can supplement the evidence base and may be appropriate for addressing specific questions unrelated to the performance of a material (like applicability). In any event, clinical investigations should strive to follow-up treatments for adequate time periods, as the majority of significant failures in restorative dentistry occur late, not quickly after restoration placement. Trials should be adequately powered, and power should be considered beforehand, taking into account what is being demonstrated (superiority, non-inferiority). There is a need for core outcome sets in restorative dentistry, which may boost therelevance of measured outcomes for all stakeholders, not only dental researchers, lower the danger of selective reporting, and enhance synthesis by improving trial comparability. Researchers should also document patient-related confounding factors in addition to material-related variables. Studies must be pre-registered, and reporting must adhere to requirements. Statistical analysis should account for potential clustering. Numerous clinical studies have poor validity and utility for making daily healthcare decisions. In order to improve dental treatment, dental researchers should replicate efforts made in other medical professions to make clinical trials more valid and useful.

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