Session I: Planning Clinical Studies
—John J. Hefferren, Chairman

Types of Clinical Caries Studies: Epidemiological Surveys, Randomized Clinical Trials, and Demonstration Programs

J.W. STAMM

Professor and Chairman, Department of Community Dentistry, McGill University, Montreal, PQ, Canada

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Epidemiological studies of dental caries may generally be considered as implementing one of two research strategies. The first and perhaps the common type of investigation is the observational study, of which the cross-sectional survey is the most frequently employed. Also belonging in this category are cohort studies, which have had a small but important place in caries research. The second type of epidemiological study is the classical scientific experiment which, applied to the health field, is exemplified by the randomized clinical trial (RCT). As will be described below, there are major distinguishing characteristics between these two types of investigations. However, both classes of studies also share significant common features. Accordingly, this review will examine their key elements and respective applications in clinical investigations of dental caries. Demonstration programs, which usually are not considered as epidemiological research, will be considered toward the end of this paper.

When the survey or the clinical trial is employed in the study of dental caries, four distinct types of epidemiological objectives become apparent: (1) description of the caries status of the study population by presenting the distribution of dental decay among the population elements; (2) explanation of caries etiology by illuminating the determinants or risk factors associated with the disease; (3) predicting the relative occurrence and distribution of caries for a given population; and (4) controlling the extent of caries by suggesting and evaluating interventions which have the potential to prevent or treat the disease.[1]

Given these aims, well-designed dental surveys can almost always enhance scientific understanding of caries by improving on description, explanation, and/or prediction. What is often not fully appreciated is that true experimental methods such as the RCT are even better suited to attain these three objectives. As for the fourth aim, clinical trials have the unique additional property of providing a powerful approach to evaluating the effectiveness of a vast array of interventions developed for the elimination of dental decay.

Ignoring methodological considerations, the major distinction between the epidemiologic survey and the randomized clinical trial is their respective abilities to provide causal explanations. Specifically, while dental surveys permit the generation of hypotheses and the establishment of association models, scientific tradition has determined that only from properly conducted experiments can one infer cause-and-effect relationships. In practice, this means that randomized clinical trials are the gold standard in population-based clinical research.

Nevertheless, many circumstances arise in clinical research which preclude the application of experimental methods. For example, it may be impossible to randomize subjects, as in the case of the early water fluoridation studies.[2-4] Or, it may be unethical to randomize subjects with respect to a caries risk factor such as sucrose. It is for such situations that non-experimental, observational research designs may serve as respectable alternative investigative strategies.

The epidemiological caries survey.

The traditional epidemiological caries survey gathers one-shot, cross-sectional data which permit the analysis and reporting of disease prevalence. In fact, since 1938 rather less emphasis has been placed on caries prevalence, and most surveys focus almost exclusively on the decayed, missing, and filled (DMF) index as a more or less accurate measure of accumulated caries experience, at least for children and young adults.[5]

Objectives. — In general, the caries survey does not attain the description, explanation, and prediction objectives equally well. Specifically, a good survey almost always fulfills the first of these aims. Illustrative of this descriptive function are such investigations as the household survey of oral health in North Carolina[6], the recent dental caries survey of schoolchildren in the United States[7], and the survey of adult oral health in the United Kingdom[8]. The findings obtained from such surveys provide very useful descriptive analyses that may be applied to the development of more appropriate treatment strategies, the adoption of more suitable preventive programs, or the planning for future manpower configurations.

The dental survey is not nearly as well-suited to accomplish the second goal – namely, to provide explanations for the observed dental caries distribution. Two reasons account for this: First, the survey cannot incorporate sufficient information about the epidemiological triad of person, place, and time. Specifically, although the survey investigates caries according to person and place factors, it measures these simultaneously, and therefore, it is often unclear which factors preceded which to produce the disease. Second, in both their design and analysis, surveys can almost never isolate a potential caries risk factor to the degree necessary for establishing its role in causation. For example, consider the previously mentioned US survey of caries in schoolchildren. It is quite evident that the DMF level in the school-aged population is lower than was the case ten years ago. However, notice that the survey is quite limited in explaining why the caries index is lower. With regard to person and place, even the role played by water fluoridation is difficult to isolate, since residency histories are imprecise and foods processed with fluoridated water are sold in fluoride-deficient communities. With respect to time, it is difficult to rule out effects from fluoride dentifrices and other fluoride sources or changes in the application of examination criteria. Above all, declining caries levels have been observed in communities that have been on their present water fluoridation status for a considerable period of time, which further complicates estimating the true contribution of water fluoridation to the observed lower DMF values.

Finally, it is well-known that the standard results from dental surveys have not been strong predictors of future

caries experience at the level of the individual. For example, depending on the variables available and the time period involved, survey data have generally explained between 10 and 50% of the caries increment variance.

Inference and the factors that affect it. – Inferences from dental caries surveys are affected by a number of well-known considerations, including: (1) random selection, (2) sample size, (3) precision of measurement, (4) freedom from bias, and (5) proper statistical analysis. Random selection is the principle by which a sample is obtained from the larger target population in a manner that gives each member of the population a known probability of being chosen for the sample. It should be noted that it is not necessary for the selection probability to be equal for all members of the target population, and often there are persuasive design considerations for working with unequal sampling ratios. Perhaps the most crucial but also the most difficult aspect of random selection is the need to develop a formal, written sampling frame. Without such a step, the whole exercise of conducting a sample survey for dental caries becomes fraught with errors and severely compromises the inferences that may be drawn from the study, no matter how well its other phases are carried out. In general, during the early phases of planning the caries survey, it is good practice to consult with reputable survey experts or organizations about both the sampling design and the creation of the sampling frame.

The question of sample size and the matter of measurement precision are, respectively, the second and third considerations which bear on the inferences that may be drawn from the dental caries survey. While they are indeed widely different issues, both relate to the level of confidence that may be placed on either the parameter estimates or the analytical contrasts generated from the survey data. This derives from the fact that sample size operates on the denominator of both variance and standard error estimates, while measurement precision contributes to the size of their respective numerators. Methods for *a priori* determination of sample size are described in most textbooks on survey sampling.[9,10] Since there is only one major outcome variable being measured in a dental caries survey, and since there exists considerable prior knowledge as to expected means and standard deviations, the determination of sample size presents no particular problem. However, it should always be borne in mind that, if internal comparisons are planned from the survey results, sample size considerations should reflect the requirements of the subclass analyses. Whereas questions of sample size must be resolved in the early planning phase of the dental survey, the issue of measurement precision must be addressed both before and during field work. As part of the preparatory phase, it is very important to provide accurate descriptions and for the examiners to learn the caries diagnostic criteria to be employed during the project. Intensive training and calibration sessions are commonly employed for this purpose. Then, once the field work is under way, constant supervision must be exercised to reduce both inter- and intra-examiner variability to a minimum. In caries studies, the issue of measurement precision has been extensively addressed in a variety of reports which may be consulted for detailed discussions.[11-14]

Bias is the fourth consideration that may influence the quality of the inferences to be drawn from a caries survey. The principal sources of bias include non-coverage by the sampling frame, non-response by selected subjects, detection bias by the examiners, and susceptibility bias. Some of these may, on occasion, pose considerable problems. For example, it is not uncommon to find that dental surveys of the elderly include an excessive number of persons who live in community-operated homes or in geriatric institutions. The elderly who participate in "golden age" clubs tend also to be over-represented in such surveys. To the degree that the institutionalized elderly are less healthy than the ambulatory elderly who live in their own homes, a biased oral health picture may appear. This would be an illustration of non-coverage bias. Susceptibility bias is less commonly recognized in dental surveys. One example of this type of error relates to the tendency for the DMF index to be higher than expected in children who give evidence of routine and regular dental care. It may thus be believed that the level of dental caries in such children is higher than it really is. In essence, an intensive care system makes these children more susceptible to a higher average DMF value than caries incidence would dictate.[15,16]

The analysis invoked for a dental caries survey also influences the inferences that may be warranted. The major issue to highlight here is that when a dental survey is based on a particular sampling design, the statistical analysis should reflect the design effect.[17] This is perhaps one of the most common omissions in the analysis of dental surveys. In general, this will result in an under-exploitation of the information gathered, often at great expense and effort. Perhaps the other point to make about surveys is that all too often their analyses are limited to univariate methods, which in certain cases will be clearly misleading. Comparisons of dental caries in urban and rural subgroups is one such example. It seems obvious that, unless account is taken of the different educational, income, and fluoridation status inherent in urban and rural peoples, the often-reported differences in dental caries may be spuriously ascribed, at least in part, to residence location.[18]

The clinical trial.

A clinical trial may be defined as "a scientific research activity undertaken to define prospectively the effect and value of prophylactic/diagnostic/therapeutic agents, devices, regimens, procedures, etc., applied to human subjects".[19] In the dental caries field, the clinical trial is regarded as a fundamental method for population-based research.[20,21] Increasingly, clinical trials are gaining acceptance by the practicing dental profession, the dental academic community, and dental researchers in both industry and government. Clinical trials should be seen as a special type of cohort study in which the intervention or interventions are systematically introduced by the investigators so that any observed treatment effects are free from bias. Indeed, not only does the investigator control the assignment of treatment, he is also in a position to control a number of other factors, thereby permitting yet more accurate determination of the intervention's effect on the disease under study. In short, caries clinical trials represent a full application of the true scientific experiment.

Before describing some of the general features of clinical trials, it is useful to review briefly the frequently confusing nomenclature associated with them. First of all, the term "clinical trial" by itself has little meaning other than to refer collectively to the relatively large array of comparative clinical studies which seek to demonstrate the effectiveness or safety of a specific intervention. Next, the frequently encountered term "controlled clinical trial" is reserved for those studies which explicitly make provision for a control group of one sort or another. This should not be taken to mean that the control group has been necessarily established by random allocation. Examples of non-randomized

clinical trials occur when historical controls are employed or when natural experiments are investigated. Perhaps more common still is a third term, the "randomized clinical trial". This type of clinical investigation has had such a profound impact on health practice, and has found such a central place in epidemiological research, that a fuller elaboration of its features is indicated.

The randomized clinical trial. – As was already indicated, the randomized clinical trial is the most powerful method of conducting population-based clinical studies in the field of dentistry. Its introduction into clinical research is generally credited to Sir Austin Bradford Hill, who built on the principles of scientific experimentation developed by R.A. Fisher. The milestone investigation was the British Medical Research Council's 1948 study of the effect of streptomycin in the treatment of tuberculosis. The precise introduction of the RCT to dentistry is more difficult to determine. Certainly among the British dental researchers, Slack[22] and Naylor[23] were among the earliest to adopt the methodology of the RCT. In North America it appears that Chilton and Fertig can be credited with the first dental clinical trial, based on their 1958 report.[24]

Reduced to its simplest form, the distinguishing and unique feature of the RCT is that it includes, for prospective investigation, an experimental and a concurrent control group to which subjects who enter the study are allocated by a formal randomization procedure. The purpose of randomization is to ensure that at the outset of the study the experimental and control group are as alike as possible. During the actual conduct of the RCT, it is the role of the study protocol to maintain the comparability of the two groups on all factors other than the intervention being investigated. These features of the RCT, of course, extend to the case of multiple experimental and control groups.

Random allocation. – Randomization is most commonly attained by either simple random allocation or some form of stratified random allocation. For details concerning these techniques and indications for their use, good reference materials may be consulted.[25,26] While more exotic allocation procedures have been proposed, they are usually special-purpose designs that do not have much application to caries clinical trials. Since any scheme of formal random allocation is a fairly involved process, the advantages of randomization should be clearly known. First, randomization eliminates bias from the assignment of treatment once the study subject has agreed to enter the trial. In caries trials, for example, this would ensure that a potentially effective preventive is not disproportionately assigned, even subconsciously, to subjects most in need, or *vice versa.*

The second advantage is that randomization tends to balance the treatment groups with respect to prognostic factors or co-variates which may be related to dental caries outcomes. Significantly, this advantage holds whether such prognostic factors are known or unknown in advance. For example, stratified randomization will balance study groups with respect to age – a known prognostic variable for caries increments. It is clear, however, that this could also be accomplished *post hoc* by the use of co-variance analysis. But, in distinct contrast, co-variance cannot be employed at the analysis stage to balance or adjust study groups for antecedent fluoride tablet use, a variable on which it is almost impossible to obtain reliable information. However, in such circumstances randomization still remains effective. The applications of stratification and co-variance techniques for managing prognostic factors will be described by Kingman[27] and Grainger *et al.*[28] later in these proceedings.

The third advantage to randomization is that it provides the necessary theoretical basis for drawing inferences from the study results. In practice, this means that the investigator may apply the appropriate statistical tests to the data and, on the basis of these, may assign significance levels to the observed differences.

Blindness. – While randomization eliminates bias at the outset of a RCT, the employment of appropriate blinding techniques as part of the ongoing protocol is essential to maintain freedom from bias in generating the data. Two common methods are the single-blind and the double-blind designs, with the latter being preferred to the former in most cases. The need for and method of blinding should be carefully planned and monitored. In particular, since the double-blind procedure is complex and fragile, the investigators should ensure that the integrity of the procedure is maintained throughout the study. If not, the effort and expense devoted to employing the technique in the first place will be largely wasted.

Ethical issues. – Ethical concerns almost always arise when a RCT is contemplated. The issues are many and varied but inevitably include concerns about gaining subject participation, informed consent, adequacy of design, potential noxious effects of the agent being tested, and the possible withholding of beneficial treatment. There is no longer any justification for being unaware of the ethical issues encountered in clinical caries trials. The dental literature contains a number of good discussions of the topic.[29,30] Ethical considerations in the design of caries trials will be explored by Heifetz[31] later in the conference proceedings. With respect to the ethics issue and the RCT, a notion that must not be lost is that poorly informed dental practitioners may possess the potential to do much more harm to patients than will poorly informed patients be harmed by caries clinical trials. Since the very essence of the randomized clinical trial is to provide the dental profession with better therapeutic knowledge, the public has the most to gain by continuing to give its full support.

Sample size. – The question of adequate sample size for clinical caries trials is one that still receives too little attention, in spite of notable contributions to the literature by McClendon *et al.*[32] and Kingman[33]. The main and continuing problem is that too many clinical trials are undertaken without regard for the sample size requirements needed to reduce the Type II error to acceptable levels. Trials embarked upon with inadequate statistical power from the outset stand a good chance of generating indeterminate results and contributing little to the question being asked. This is particularly true of caries trials, since annual decay increments in children have fallen in recent years. In this situation, one is more likely to obtain a non-significant difference for a given sample size. In itself, this is nothing to worry about, since one of the important roles of clinical trials is to help the dental profession discard ineffective forms of therapy. Unfortunately, when a trial is undertaken which, upon completion, is found to have a 50% chance of missing a true 25% difference in caries increment, then the trial has not served any purpose at all if it obtained a statistically non-significant result.[34,35]

Explanatory and pragmatic attitudes in clinical trials. – Sixteen years ago, a seminal paper by Schwartz and Lellouch[36] questioned whether the randomized clinical trial as normally conceived represented a sufficient strategy to permit the optimal selection of therapeutic interventions for normal medical practice. The thesis advanced by these authors was that a rigid system of controls, the very strength of the RCT, mitigated against producing the types

of data necessary for deciding whether or not to implement an alternative therapeutic regimen. Schwartz and Lellouch argued that the requirements for internal validity by the RCT altered the definition of treatment and changed the manner of disease assessment from that used in conventional practice. Further, they suggested that subject selection, statistical management of withdrawal, and non-compliance, as well as the methods used for effecting study group comparisons, did not meet the needs for real-world decision-making. As part of their critique, they suggested that clinical trials have two purposes: one that is strictly scientific or explanatory, while the other would be pragmatic or decision-oriented.

In the clinical caries trial, some of the above considerations are obviously pertinent. For example, were the early trials of fissure sealants conducted in order to test their effect when used in the normal practice setting? Are clinical caries trials conducted in the public health setting properly analyzed when subjects lost during the trial are excluded from the analysis? Do results obtained from clinical trials of fluoride mouthrinses remain constant when applied on a much larger scale and over a longer time frame? Has the distinction between statistical and clinical significance been adequately addressed, particularly in the face of changes in the level of dental caries? These are extraordinarily difficult questions whose answers are far from simple. It is noteworthy that in North America the notion of the pragmatic clinical trial has not found wide acceptance, and, except for the paper by O'Mullane[37], few theoretical contributions have appeared in the dental caries literature.

Group randomization. – In the randomized clinical trial, individual subjects are allocated to the experimental and control groups. However, there are caries preventive measures for which it is possible to randomize groups but not individuals. Clinical trials of school water fluoridation or school-based dental health education programs are but two examples. Three reasons for relying on group randomization are: administrative convenience, therapeutic necessity, or the need to avoid between-subject contamination in the case of preventive programs that involve cognition on the part of study subjects. Frequently, all three considerations apply simultaneously. Group randomization poses some special problems for the investigator. First, both single- and double-blind protocols are almost impossible to maintain, but, with ingenuity, even such a dilemma may be overcome. For example, to control examiner bias in the Kingston-Newburgh water fluoridation trial, single-blind assessment of dental X-rays was carried out which confirmed that the overall findings of the unblinded clinical examiners were relatively unbiased. Second, sample sizes generally must be increased when group randomization is to be employed. Relatively simple procedures for determining sample size have been devised in the case where the size of the group to be randomized is small[38], or where it is large[39]. Good reviews of this subject have been provided in two recent works.[40,41]

Multi-center trials. – A multi-center trial is a collaborative effort involving more than one independent center for the enrollment and follow-up of study subjects. On the medical side, the relative number of multi-center trials has risen considerably during the past 15 years.[25] This trend may also be developing in dentistry for a number of reasons. First, multi-center caries trials may be one way of overcoming the increasing difficulty in recruiting study populations that are sufficiently large and meet specified criteria on prognostic variables, particularly minimum age-specific DMFS levels. Second, multi-center caries trials will almost always be more representative of the population for which one wants to draw inferences.[42] The third rationale is that multi-center trials enable investigators with similar interests to collaborate in solving common problems and sharing scientific knowledge of common interest. This will generally result in a more efficient diffusion of technical methodology and a faster and wider circulation of more recent results.

Multi-center trials also have potential disadvantages which must be confronted before such a project is undertaken. First, there will be a need for a substantial logistical organization. This means that appreciable resources will have to be devoted to ensure a quality undertaking. Fortunately, this consideration is appreciated by major funding agencies such as the National Institutes of Health.[43] Second, the multi-center trial runs a risk that one member of the group may not adhere to the aims and protocol as originally laid out. Third, unexpected data problems and analytical difficulties can arise which may well complicate the interpretation of the combined trial results.[44]

Special features of randomized caries trials. – In order to achieve better design for future caries trials, it is well to consider just a few of the special features of such studies. First, in the medical field, most RCT's to date have tested remedial therapies on patients with the disease. Such trials are usually short, often lasting for fewer than six months. In contrast, caries trials have been almost exclusively concerned with evaluating preventive therapies, and this only on the healthy tooth surfaces available in each participant. This has meant that, as for most preventive trials, the time interval for a caries trial is relatively lengthy, which makes the study quite expensive. Second – again unlike the medical field, where clinical trials are often called upon to test therapeutic interventions that are chemically quite different – in the caries field most of the trials conducted have focused on fluoride in one formulation or another. This means not only that the safety of most of these products is fairly well-established, but also that the investigator is often searching, in effect, for marginal differences. This has clear implications for sample size requirements in future trials.

Third, there is the question of how caries preventive outcomes should be conceptualized and analyzed. It is interesting to observe that virtually the whole medical literature on randomized clinical trials is built upon the notion of binary outcomes (*i.e.*, death, cancer, cardiovascular disease) for the subjects entering the study. The resultant data are then analyzed to provide ratios demonstrating reduced or elevated risk to the outcome under study. Whether this approach has practical implications for dental caries research is difficult to say at this point. However, it may well be that, with declining caries experience and the relatively large proportions of children who develop no new lesions during the period of a caries trial, the problem of optimal outcome measurement may become more urgent. The challenge is to find an approach that provides more analytical power other than the expensive and often inhibiting step of large increases to the minimum sample size requirements. This is one issue that will be addressed in part by Fleiss[45] and Varma[46] later in the proceedings.

A fourth special feature of caries trials is the problem of who decides whether a tooth surface has decayed or not, what kinds of criteria are being employed, and how reliably they are applied. Certainly it has become accepted practice in caries trials to expend considerable effort on calibrating the clinical examiners and to recommend the use of concurrent pair examinations for a certain percentage of sub-

jects. While such procedures are undoubtedly useful[14], they attack only part of the examiner reliability problem. In a recent publication, Ripa[47] reported that for a given examination cycle involving Long Island (New York) children, approximately 80% of the DMFS calls involved the F component. This implies that a considerable majority of diagnostic decisions were made by dentists who never underwent the calibration process. Under such circumstances, the question arises as to whether more should be done to involve local practicing dentists with certain elements of the caries trial. It also raises the question of whether the degree of reliability with which tooth decay is diagnosed for the caries trial as a whole is not in fact lower than that implied by reliability co-efficients applicable only to the clinical examiners formally attached to the trial. More will be said on this topic by Marthaler and Bell later in this conference.[48,14]

The non-randomized comparative study.

Throughout the discussion of surveys and clinical trials, the limitations of non-randomized studies have been raised. The central problem is that inferences from non-randomized studies are generally more suspect than those from RCT's. When randomization is not employed, comparisons between the treatment and comparison groups require the assumption that either the two groups are identical in all important variables except the treatment under study, or that one can adequately correct for all relevant differences. In the latter case, one must assume that all prognostic factors are known.[49]

Does this suggest that investigators should discard the idea of non-randomized trials altogether or, in reviewing the literature, should ignore the findings from non-randomized studies? Clearly, an affirmative answer to this question would be an extreme and conservative position. A reasonable alternative is to concede the need for non-randomized designs. In fact, there may be good reasons why non-randomized studies have to be contemplated. First, on occasion a non-randomized study is the only ethical way to conduct a caries trial. For example, in 1983 it would be considered unethical to conduct an analogue of the early Vipeholm study. Second, in certain instances, a non-randomized design is the only feasible way to conduct the research. Most conceivable studies of caries and water fluoridation would fall into this category. Third, it is usually true that non-randomized studies are cheaper, and they are often given extra consideration on this basis alone. Fourth, in relatively rare instances, a treatment is so obviously effective in a situation where no or few competing therapies exist that a RCT may simply not be necessary. This was certainly the case with the introduction of penicillin, for example. In spite of the above considerations, it remains that one should be very selective in the adoption and very stringent in the interpretation of non-randomized comparative studies.

Historical control groups. — In non-randomized trials, the most common alternative to the concurrent randomized control group is to employ historical controls as a basis for comparison. While this method is certainly preferable to using literature controls, investigators must appreciate that there are as many study circumstances where historical controls may serve reasonably well as there are situations where they perform extremely poorly. Examples of both can be found in the dental caries literature, and it therefore behooves clinical investigators to distinguish among these situations. Historical controls can be useful when the disease in question is not chronic; when there is no obvious time trend in disease incidence and prevalence; when the control treatment has been administered to groups of subjects in a period just prior to the study in question; when data on the disease status of the controls are adequate; and where the controls are sufficiently similar in terms of person and place to permit retrospective adjustment of the data prior to the analysis.[50] The type of dental study that meets most of the above criteria is illustrated by the classic investigations reporting the reduction in enamel mottling brought about by changing the drinking water supplies in Oakley, Idaho, and Andover, South Dakota.[51,52]

In general, historical controls are not desirable when one or more of the above conditions are appreciably violated. This appears to be the case in the Seagrove, North Carolina, school water fluoridation study, which uses historical controls for its analysis.[53] From the perspective of hypothesis testing, it is likely, as has been reported, that school water fluoridation has had a statistically significant effect on the dental caries experience of 6-17-year-old children. However, viewed from the standpoint of estimation, it is very doubtful that the 12-year caries reductions reported earlier this year can be scientifically explained solely or even largely in terms of the school water fluoridation intervention. Almost certainly there must have been other factors which contributed strongly to the observed decrease in caries during the 1968-1980 period. The secular decline in caries throughout the United States[7], and particularly in North Carolina[6], would alone lead to this suggestion. Precisely the same difficulty exists in the case of other studies appearing in the recent literature.[54]

Sacks *et al.* have compared the results from randomized clinical trials and historical control trials (HCT) where both studies investigated the same therapies.[55] On the basis of comparing 50 RCT's and 56 HCT's, the authors were able to demonstrate clearly that the HCT studies were far more likely than RCT's to show a significant difference in favor of the therapy. In fact, while the HCT's found the therapy effective in 79% of the trials, the RCT's found the therapy to be effective in only 20% of the studies undertaken. Interestingly, the reason for the relatively more frequent positive outcomes from the HCT's was not that their experimental groups performed better, but rather that their control groups performed worse than did the concurrent controls of the RCT's. It will be seen that this precisely describes the situation with the historical control dental caries trials cited above.

Demonstration programs. — Although the term "demonstration program" is sometimes used to describe a study that meets virtually all requirements of the randomized clinical trial, it is usually reserved for projects involving either non-randomized controls or no comparison groups at all. Therefore, demonstration programs form a very imprecise category of studies, one that eludes careful definition. In this view, a study such as the AFDH/Rand National Preventive Dentistry Demonstration Program[42] should be considered as a true randomized clinical trial, since it employs restricted stratified randomization of schools to assign the approximately 20,000 children into one of the six treatment regimens under study. As was indicated earlier, randomized group allocation is an acceptable procedure for RCT designs, provided that sample size requirements are properly determined. Similarly, studies that employ proper randomization, but use the "pragmatic"

approach by encouraging greater heterogeneity in study groups or testing of intact multi-component interventions, would still fall under the rubric of randomized clinical trial.

Demonstration programs had considerable currency during the 1970's; however, they have not yet been accepted as a proper dental epidemiological concept because of their inability to provide precise, reproducible answers to significant research questions in the dental care field. Nevertheless, there are a number of positive characteristics that ought to be cited on behalf of demonstration programs. First, a demonstration program can be legitimately used to establish whether an already-tested caries preventive, for example, is a practical measure (not practical and effective, however) in a private practice or public health setting. Second, because of their lack of scientific rigor, demonstration programs can be implemented rather quickly to capitalize on "hot" topics. This in turn can give such projects a rather higher profile than might otherwise be obtained. Third, because scientific rigor is not the prime criterion, the demonstration program can be placed into the hands of a larger number of investigators who, for example, might be strategically located throughout the country. This, too, may enhance the impact of such endeavors.

But as far as advancing knowledge or leading to better dental care decision-making is concerned, the following disadvantages are associated with demonstration programs. First, these types of projects are often a cover for poorly conceived and inadequately executed scientific work. Second, when the resultant findings are closely inspected, flaws in design may seriously undermine reported conclusions. Third, when the results from a number of demonstration programs are compared, the outcomes are occasionally so variable that no overall result emerges. As a consequence, for the investments made, little new knowledge is added, and uncertainties may be created instead. Fourth, while demonstration programs are frequently carried out to assess the cost-effectiveness of a particular therapeutic or preventive intervention, they generally under-utilize the technical expertise necessary to provide a proper analysis. The value of demonstration programs should be considered in light of these considerations.

Summary.

This has been a necessarily cursory overview of three types of clinical dental caries studies: the dental survey, the randomized clinical trial, and the non-randomized comparative study. Each of these studies may be used in its appropriate place, although only the survey and the randomized clinical trial are well-grounded in scientific theory. In general, the dental survey is well-suited to gathering basic cross-sectional data on dental caries, data that serve a variety of important practical and scientific interests in the dental care system. Clinical trials and non-randomized studies are applied in evaluating a variety of therapies for dental caries. Of the two, the randomized clinical trial is by far the more powerful. As a result, the clinical trial has found a central place in dentistry. The contributions that past and present clinical caries trials have made to dental health are quite evident to most observers. It is virtually inescapable that well-conducted clinical caries trials will make even more significant contributions to dental practice in the future, thereby further improving the oral health of all.

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