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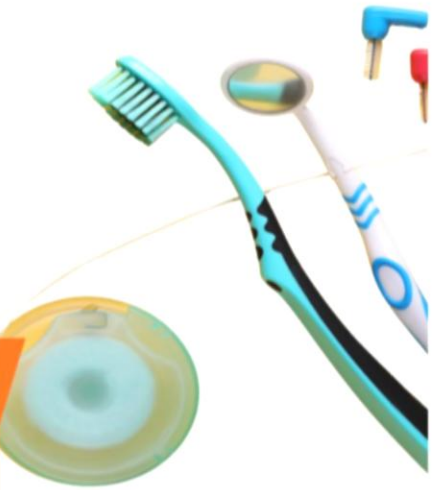
EVIDENCE BASED DENTISTRY



Written By :

Dr Pallavi Singh
Dr Shikha Sachan
Dr Smriti Tripathi

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www.fontfusionspublication.com
Contact - +917004837260

ABOUT THE PUBLISHER

Font Fusions Publication: Advancing Knowledge in Dental and Health Sciences. Font Fusions Publication is a dynamic platform committed to revolutionizing academic publishing in the fields of dental and health sciences. With a focus on open-access dissemination, the organization aims to provide researchers, clinicians, and academicians with avenues to share their work globally, fostering innovation and collaboration. Dr. Ritik Kashwani, a renowned expert in the field of dental and health sciences, leads Font Fusions Publication.

Oral Sphere Journal of Dental and Health Sciences of the flagship initiatives under Font Fusions Publication is the Oral Sphere Journal of Dental and Health Sciences. This peer-reviewed, open-access journal provides a comprehensive resource for contemporary research in dentistry and related health disciplines. The journal encompasses a broad range of topics, including digital dentistry, artificial intelligence in diagnostics, oral manifestations of systemic diseases, and advancements in therapeutic modalities. The journal's commitment to quality is evident in its rigorous editorial process and its inclusion in indexing platforms such as Crossref and Google Scholar (as of 2025), which enhances the visibility and impact of published research.

Books by Font Fusions Publication:

Advancements Across Oral Sphere: Innovations Shaping Modern Dentistry: Complementing the journal, Font Fusions Publication has also released a seminal book titled Advancements Across Oral Sphere: Innovations Shaping Modern Dentistry. Published on December 30, 2024, this book delves into cutting-edge developments in dental science and practice. Topics explored include digital dentistry, CAD/CAM technology, teledentistry, and the integration of artificial intelligence in clinical settings. The book aims to provide readers with insights into how these innovations are transforming patient care and clinical workflows. Authored by experts in the field, Advancements Across Oral Sphere serves as both a scholarly reference and a practical guide for professionals seeking to stay abreast of technological advancements in dentistry.

Innovations in Oral Sphere: Ahead of the Curve: It is a comprehensive exploration of the latest advancements in oral health, offering a forward-looking perspective on the future of dental care and oral sciences. This meticulously curated volume brings together contributions from esteemed professionals in the field, providing readers with a detailed and up-to-date account of transformative progress in oral health. The book explores cutting-edge technologies, interdisciplinary research, and a deeper understanding of the complex relationships between oral health and overall well-being. It encompasses a broad range of topics, including regenerative treatments, digital dentistry, innovative diagnostic tools, and minimally invasive procedures. Each chapter presents insights into how these innovations are shaping the future of dental care, emphasizing the importance of integrating discoveries with ethical practices and patient-centered care. What sets this book

apart is its forward-thinking approach. It not only examines the current state of oral health but also anticipates future developments, highlighting the growing importance of prevention, technology-driven solutions, and collaborative research in driving the future of oral health. This makes it an invaluable resource for students, practitioners, and researchers alike, serving as a guide to the ever-evolving world of oral health. Published by Font Fusions Publication Private Limited in May 2025, this book is priced at ₹270 and is available in India. It is printed and bound in Noida, India, and is available for purchase through Font Fusions Publication's website.

Cephalometrics for Orthognathic Surgery: Principles, Planning, and Precision: This essential text unravels the science and clinical relevance of cephalometry in orthognathic surgery. From foundational anatomical landmarks to advanced radiographic analyses, "Cephalometrics for Orthognathic Surgery" provides a structured and insightful approach to diagnosing dento-facial deformities and planning treatment.

Clinical Decision - Making & Case Management in Physiotherapy: This book provides a comprehensive guide to understanding the principles of clinical decision-making and the case management process in physiotherapy. It covers essential topics such as clinical reasoning models, including hypothetico-deductive, pattern recognition, and narrative reasoning, and emphasizes the importance of evidence-based practice. Key steps in clinical decision-making, from subjective and objective assessments to goal-setting, treatment planning, and outcome evaluation, are thoroughly explained. The book also explores case management, highlighting the role of physiotherapists in coordinating care, working with multidisciplinary teams, and ensuring patient-centered care across different stages, from acute to chronic conditions. Ethical and legal considerations, including informed consent, confidentiality, and professional boundaries, are discussed to help practitioners navigate complex clinical and ethical situations. Real-world case scenarios provide practical insights into applying these concepts in musculoskeletal, neurological, and geriatric care settings. Overall, the book serves as an invaluable resource for physiotherapists to enhance clinical decision-making and improve patient outcomes.

Commitment to Open Access and Global Collaboration: Font Fusions Publication's dedication to open access publishing ensures that knowledge is freely available to a global audience, breaking down barriers to information dissemination. By providing platforms like the Oral Sphere Journal and publishing comprehensive works such as Advancements Across Oral Sphere, the organization plays a pivotal role in advancing the fields of dental and health sciences. For researchers, clinicians, and academicians looking to contribute to or benefit from the latest developments in these fields, Font Fusions Publication offers valuable resources and opportunities for collaboration.

FOREWORD

Dentistry is both an art and a science. This book explores the integration of scientific research and clinical expertise to provide the highest quality dental care. It defines evidence-based dentistry (EBD) as the judicious use of the best available clinical evidence combined with the dentist's experience and the patient's needs. The text covers the history and evolution of EBD, emphasizing its importance in the modern dental practice and the changing role of the patient in the decision-making process.

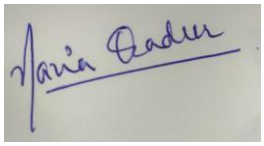
From understanding the foundational principles to the step-by-step process of evidence-based learning, this book guides dental professionals through the process of applying evidence in clinical practice. It highlights the shift from tradition-based to evidence-based care, offering practical insights into improving clinical decision-making, enhancing patient care, and staying current with the latest research. A must-read for dental practitioners aiming to bridge the gap between scientific research and everyday clinical decisions.

As the field of dentistry continues to evolve, the integration of evidence-based practices has become increasingly essential to the advancement of patient care. This book presents a comprehensive exploration of evidence-based dentistry (EBD), offering invaluable insights into its history, principles, and the critical role it plays in contemporary dental practices. Through this work, readers are guided through the process of blending clinical expertise with the best available evidence to enhance decision-making, improve patient outcomes, and adapt to the rapidly changing healthcare landscape.

The authors have meticulously examined the foundations of EBD, from its early development to its current application, making it an essential resource for both seasoned professionals and those new to the field. The text thoroughly covers the methods of integrating scientific research into clinical settings, emphasizing the importance of systematic reviews, critical appraisal of studies, and the judicious application of research findings.

This book is not merely an academic text; it is a call to action for dental professionals to embrace a culture of lifelong learning and evidence-based practice. As technology advances and patient expectations shift, the integration of robust clinical evidence into decision-making will be key to navigating the challenges and opportunities that lie ahead in dentistry.

Whether you are a student, clinician, or researcher, this book provides the tools and understanding necessary to engage with and contribute to the growing body of evidence that shapes dental practice. It is an indispensable guide for anyone committed to improving the quality of dental care through scientific evidence and clinical expertise.



Dr. Nazia Qadeer
Associate Professor, Department of Prosthodontics, Maharana Pratap Dental College, Kanpur, Uttar Pradesh, India

PREFACE

Dentistry, as both an art and a science, has continually evolved to meet the growing needs of patients, advancements in technology, and innovations in treatment approaches. This book aims to bridge the gap between scientific research and clinical practice, highlighting the importance of evidence-based dentistry (EBD) in shaping modern dental care. Over the past few decades, EBD has revolutionized the way dental professionals approach treatment, patient care, and clinical decision-making. By focusing on the integration of the best available clinical evidence, professional expertise, and patient preferences, EBD offers a framework that ensures both the effectiveness and safety of dental practices.

In this work, we explore the history, principles, and evolution of evidence-based dentistry, providing a comprehensive understanding of its essential role in modern clinical practice. The book is designed not only to inform but also to guide dental professionals at all stages of their careers, from students to seasoned practitioners, in adopting evidence-based practices into their daily routines. Through a detailed analysis of the processes involved in EBD—such as formulating clinical questions, searching for relevant evidence, critically appraising studies, and applying findings in practice this book serves as a practical guide to improving patient outcomes and advancing clinical decision-making.

As dentistry becomes increasingly intertwined with technology, the challenge lies in harnessing the vast amounts of data and evidence available to enhance clinical decisions. The rapid pace of research and the continuous flow of new evidence make it imperative for clinicians to stay informed and update their practices. This book offers tools and strategies for incorporating the latest research into everyday practice, ensuring that dental professionals can make informed, evidence-based decisions that directly benefit their patients.

The journey toward evidence-based practice requires a mindset shift a commitment to ongoing learning, critical thinking, and active engagement with scientific literature. By embracing the principles of EBD, dental professionals can not only stay current with the latest research but also contribute to the growing body of knowledge that shapes the future of dental care. This book is both a guide and a call to action, encouraging professionals to adopt evidence-based approaches that enhance both the science and the art of dentistry.

ACKLOWLEDGMENT

The completion of this book would not have been possible without the unwavering support and contributions of many individuals and organizations. It is with deep gratitude that I acknowledge the following:

First and foremost, I would like to express my heartfelt thanks to my co-authors, whose dedication, expertise, and commitment to evidence-based dentistry have made this work a reality. Their insights, thorough research, and collaborative spirit have been invaluable throughout the writing process.

I am deeply grateful to Font Fusions Publication for their professionalism and vision in bringing this book to life. Their commitment to advancing knowledge in dental and health sciences, particularly through open-access publishing, has allowed us to share this resource with a global audience. Special thanks go to Dr. Ritik Kashwani, whose leadership and support have been pivotal in the development of this book.

My sincere appreciation also extends to the academic institutions and dental professionals whose research and clinical experiences shaped the foundation of this book. Their work has provided both inspiration and guidance in crafting the comprehensive discussions on evidence-based practice presented here.

I would like to acknowledge the dental professionals and researchers who contributed to the ongoing conversations around evidence-based dentistry. Their insights have enriched the content of this book and helped clarify the complexities involved in integrating research with clinical care.

Lastly, I wish to thank my family and friends for their constant support, patience, and encouragement during the writing process. Their belief in me has been a source of motivation from start to finish.

To all those who have contributed to this book, whether through direct input, support, or inspiration, I extend my deepest gratitude. This work is a testament to the collective efforts of many, and I hope it serves as a meaningful resource for dental professionals committed to improving patient care through evidence-based practices.

INTRODUCTION

Dentistry is both an art and a science. It is a science because our fundamental understandings or building blocks of knowledge, if you will- are founded on the scientific process of research. This includes basic, applied, and clinical research. It is an art in that it draws on experience and personal observation, because science cannot account for the complexity of all variables in each situation. The synthesis of scientific understanding (evidence) and clinical observation (evidence) provides the basis for meaningful dental care.[1]

WHAT IS EVIDENCE –BASED DENTISTRY?

The foundation for evidence based practice was laid by **David Sackett** who has defined it as "integrating individual clinical expertise with the best available external clinical evidence from systematic research".[2]
The American Dental Association (ADA) defines evidence-based dentistry (EBD) as, "an approach to oral health care that requires the judicious integration of systematic assessments of clinically relevant scientific evidence, relating to the patient's oral and medical condition and history, with the dentist's clinical expertise and patient's treatment needs and preferences". [3]

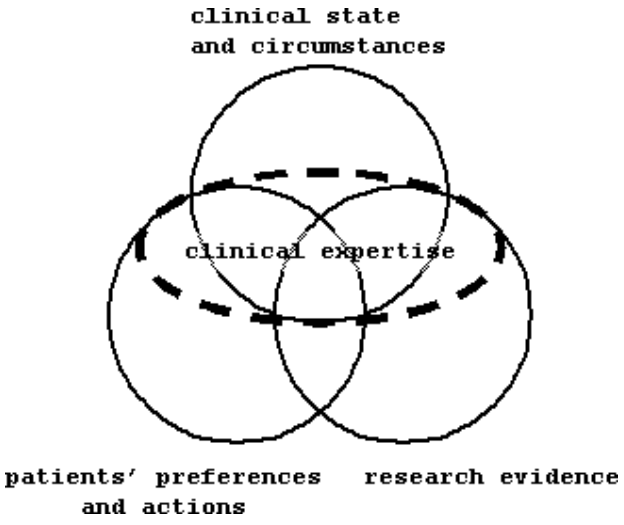


Figure 1: **Evidence – Based Dentistry**

Evidence based care is a technology that provides the best available current evidence on the basis of a proven and objectives set of principles.

The goal of evidence based health care is to identify the best available clinical evidence and combine this with clinical experience to meet the patient's needs. Like any scientific endeavor, the object is to find the best evidence that will facilitate good clinical decision making. [4]

History of evidence based learning:

Evidence-based dentistry, which is distinct from dentistry based on evidence, has permeated dental research and dental practice only in last few decades, as an offspring, as it were, of evidence-based health care in general and evidence-based medicine in particular.

The first coherent set of scientific position papers on evidence –based medicine dates back only three decades, published from McMaster University in the early 1970's. The actual theoretical concept of basing medical intervention upon evidence gathered by observations is indeed less than 200 years old and can be traced to Dr. Pierre Louis (medecine d'observation) in Paris and Dr. Maurizio Buffalini (Medicina basata sulle evidenze) in Florence in the mid-19th century. [5]

WHY IS EVIDENCE –BASED DENTISTRY REQUIRED?

The world in which we learn and practice dentistry is changing at an astonishing rate. Two phenomena the information explosion and the consumer movement, both of which are fortified by the extraordinary advance of the Internet are coming together to change the way all businesses, including health care, will function in the very near future.
The nature of the relationship between the patient and the clinician is changing. Patients are becoming partners in the decision-making process.
When many of us attended dental school, our primary sources of information were our teachers, textbooks and, occasionally, journal articles.
But the methods of delivery of information are changing. There is an increasing trend toward Web-based courses and instruction, as well as computer based interactive learning.[6]

There are two aspects to the clinical practice of dentistry. The surgical component includes all the manipulation of hard and soft tissue that is performed every day in dental practice. Examples are tooth preparation and restoration, scaling, orthodontics, and prosthesis fabrication. The other element involves decision making. The diagnosis of unlocalized dental pain, the prognosis for a periodontally compromised tooth, the choice of posterior restorative materials, and the risks/benefits assessment of third molar extractions are examples. Early in the career, decision making may be the most difficult aspect of clinical practice. There is an overwhelming array of choices with little or no structure on which to build an approach to solving the problems. As a practitioner gains experience, he or she acquires the advantage

having seen the results of previous decisions, good and bad, and can recall how a problem was dealt with previously.With experience, practitioners build up a mental library of circumstances that can be recognized when next encountered. This is practice by pattern recognition.Because of the infinite variety in the combinations of circumstances encountered every day, the choices made are commonly extensions of previous experiences. When no previous experience is available as a guide, a knowledge of basic biologic principles can guide decision making.Decision making in clinical practice thus is supported by pattern recognition when experience exists. When experience does not exist, the practitioner falls back on extensions from previous experiences or inferences from basic biologic principles. Continuing education guides and reinforces these strategies.

A comfort level develops, which is the confidence one gains with years in practice.Because the practice behaviors of dentists are highly divergent, there is clearly great variation in each practitioner's sample of knowledge and experience. Hence, the decisions reflect different biases and knowledge gaps among different clinicians. This consequence is the problem that evidence- based practice (EBP) is intended to address. The first step in EBP is to acknowledge that such gaps exist in one's personal knowledge and experience.[7]The principles of evidence-based dentistry finding the best information quickly when it is needed, assessing its quality and deciding whether it is relevant will help practitioner to use research evidence in making everday clinical decisions. [6,7]

STEPS INVOLVED IN EVIDENCE-BASED LEARNING PROCESS

Step-1:
Convert the need for information about prevention, diagnosis, prognosis, therapy etc, into an answerable question which relates specifically to the patient's requirements and the population of interest.

Step-2:
Track down the best evidence with which to answer that question.

Step-3:
Critically appraise the evidence for its validity (closeness to the truth), impact (size of the effect), and applicability (usefulness in clinical practice).

Step-4:
Integrate the critical appraisal with clinical expertise and with the patient's unique biology, values and circumstances.

Step-5:
Finally, evaluate performance in terms of effectiveness and efficiency by questioning the ability to complete steps1 -4 successfully, and seek ways to improve performance in future.[8]

TRADITION- BASED DENTAL CARE AND EVIDENCE –BASED DENTAL CARE

Tradition-based dental care and evidence-based dental care offer complementary paradigms for clinical decision-making. Tradition-based care emphasizes the primacy of knowledge, experience, and intuition in the exercise of good clinical judgment. Evidence-based care emphasizes the integration of good judgment with the best available evidence and the patient's values in the making of clinical decisions.[9]

A paradigm shift

Thomas Kuhn has described scientific paradigms as ways of looking at the world which define both the problems that can legitimately be addressed and the range of admissible evidence that may bear on their solution. When defects in an existing paradigm accumulate to the extent that the paradigm is no longer tenable, the paradigm is challenged and replaced by a new way of looking at the world.

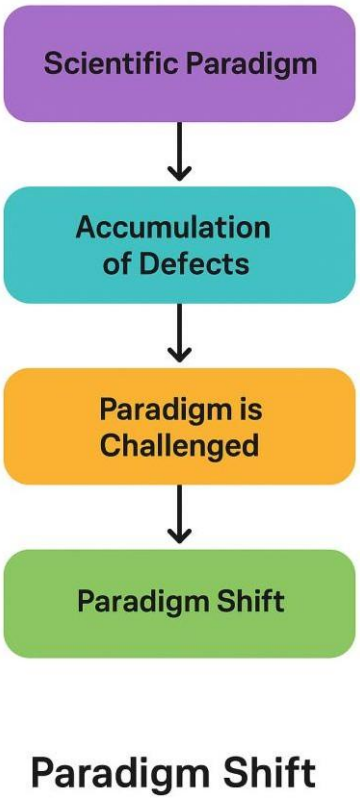


Figure 2: Thomas Kuhn paradigm shift

The former paradigm – The former paradigm was based on the following assumptions about the knowledge required to guide clinical practice:

i) Unsystematic observations from clinical experience are a valid way of building and maintaining one's knowledge about patient prognosis, the value of diagnostic tests, and the efficacy of treatment.

ii) The study and understanding of basic mechanisms of disease and pathophysiologic principles is a sufficient guide for clinical practice.

iii) A combination of thorough traditional medical or dental training and common sense is sufficient to allow one to evaluate new tests and treatment.

iv) Content expertise and clinical experience are a sufficient base from which to generate valid guidelines for clinical practice.

According to this paradigm clinicians have a number of options for sorting out clinical problems they face. They can reflect on their own clinical experience, reflect on the underlying biology, go to a textbook, or ask a local expert. The "Introduction" and "Discussion" sections of a paper could be considered an appropriate way of gaining the relevant information from a current journal.It

should be noted that this paradigm puts a high value on traditional scientific authority and adherence to standard approaches, and answers are frequently sought from direct contact with local experts, or reference to the writings of international experts.[10]

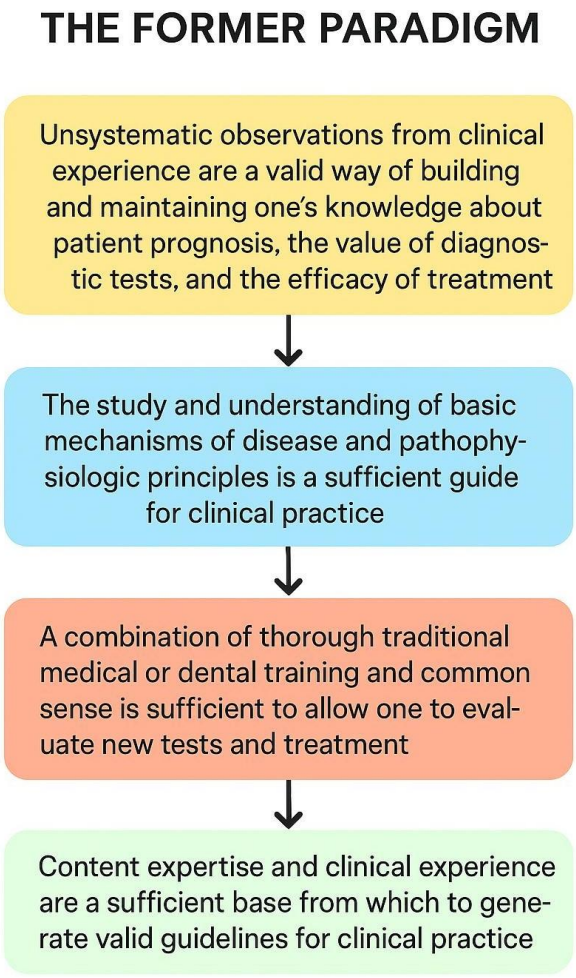


Figure 3: Traditional paradigm relies on experience, authority, basic science

The new paradigm

The assumptions of the new paradigm are as follows:

1) Clinical experience, and the development of clinical instincts (particularly with respect to diagnosis), are crucial and necessary parts of becoming a competent physician. Many aspects of clinical practice cannot, or will not, ever be adequately tested. Clinical experience, and

its lessons, are particularly important in these situations. At the same time, systematic attempts to record observations in a reproducible and unbiased fashion markedly increase the confidence one can have in knowledge about patient prognosis, the value of diagnostic tests, and the efficacy of treatment. In the absence of systematic observation one must be cautious in the interpretation of information derived from clinical experience and intuition, for it may at times be misleading.

2) The study and understanding of basic mechanisms of disease are necessary but insufficient guides for clinical practice. The rationales for diagnosis and treatment that follow from basic pathophysiologic principles may in fact be incorrect, leading to inaccurate predictions about the performance of diagnostic tests and the efficacy of treatments.

3) Understanding certain rules of evidence is necessary to correctly interpret literature on causation, prognosis, diagnostic tests, and treatment strategy.

It follows that clinicians should regularly consult the original literature (and read and be able to critically appraise the "Methods" and "Results" sections) in solving clinical problems and providing optimal patient care. It also follows that clinicians must be ready to accept and live with uncertainty, and to acknowledge that management decisions are often made in the face of relative ignorance of their true impact.[10]

The New Paradigm – Assumptions Guiding Clinical Practice

Aspect	*Key Assumptions of the New Paradigm*
Role of Clinical Experience	Clinical experience and instincts are essential, especially when evidence is limited; however, they must be interpreted cautiously.
Systematic Observation	Reproducible and unbiased recording of observations increases confidence in prognosis, diagnosis, and treatment efficacy.
Basic Science Knowledge	Understanding disease mechanisms is necessary but alone insufficient to guide clinical practice accurately.
Limits of Pathophysiology	Decisions based purely on pathophysiologic rationale may be misleading or incorrect.
Evidence Appraisal	Knowledge of rules of evidence is essential to correctly interpret research on causation, prognosis, diagnosis, and treatment.
Use of Literature	Clinicians should consult original research and critically appraise the Methods and Results sections.
Clinical Decision-Making	Acceptance of uncertainty is necessary; many decisions are made despite incomplete knowledge of outcomes.

Table 1: Evidence-based paradigm integrates experience, evidence, uncertainty, critical appraisal

Evidence-based care is a global movement in all the health science disciplines. It represents a philosophical shift in the approach to practice – a shift that emphasizes evidence over opinion and, at the same time, judgment over blind adherence to rules. This approach provides a bridge between research and everyday patient care.[11]

MODELS FOR CLINICAL DECISION MAKING

Model 1:

Model 1 or the experimental model is dynamic and provides direct feedback (for example, the restoration resolved the patient's pain and, therefore, was the appropriate treatment). On the other hand, this model's major drawbacks include its minimal scrutiny of the biases of the master clinician or educator and the absence of formal and independent mechanisms for considering clinical observations that do not agree with the master educator's opinions.

Model 2:

A second approach to clinical learning and decision-making builds on model-1 by adding one more important element. In addition to relying on experiences and expert opinions, dentists adhering to model 2 search for the best clinical scientif ic studies that might provide information that can assist in resolving clinical problem. Dentists who take this approach are expected to critically appraise the information provided in scientific studies and judge the validity of each study's conclusions.Model 2 may result in better decisions regarding clinical care and most importantly, provide clinicians with opportunities for lifelong learning. However, a major drawback of this model is that it requires nearly constant searching for evidence, an unrealistic expectation for most dentists.The recent appearance of two journals, Evidence- Based Dentistry and the Journal of Evidence- Based Dental Practice, is a major step forward. Both of these journals are devoted to critically appraising clinical studies and presenting information in a format that clinicians can use readily.

Model 3:

To resolve these problems, the evidence based dentistry process offers a third model. In this approach (model 3), the clinician locates and use system atic reviews of all the evidence that addresses a specific question.

The disadvantage of model 3 is that systematic reviews require expertise and time, and are currently limited in the scope of clinical question they address.The use of

only one model in regard to clinical decision making or life long learning is not advocated. However, model 1 by itself is insufficient to ensure that dentists consistently provide the best care to the public. An evidence- based practitioner should follow model 2 if there is enough good -quality clinical evidence or, ideally, model 3 if a systematic review of the evidence is available. [12]

ADVANTAGES OF EVIDENCE-BASED APPROACH

1 It improves the effective use *of research evidence in clinical practice*

The clinical problems solving approach to dentistry favours the early uptake of new and better treatments, or results in the early rejection of ineffective treatments.

2. It uses resources more effectively

Systematic reviews of materials, for example, may lead to the earlier adoption of the most effective ones. This in turn should lead to a reduction in replacement levels thereby saving resources.

3. It relies on evidence rather than authority for clinical decision making

Regular reviewing of the currently available evidence should develop us as practitioners so that we have the skills to evaluate evidence for ourselves based o n our own clinical practice and assessment of the evidence, rather than textbooks or authorities who may not be up to date. This appraisal of evidence is necessary to aid the approach to clinical decision making.

4. Monitor and develop clinical performance

Use of the skills outlined should enable us to monitor and develop our own clinical performance. This has been previously carried out by peer review. The success of this has resulted in clinical audit being introduced to general dental practice on an experimental basis. This provides an ideal opportunity for audit to be structured on an evidence based framework. The proposed clinical audit facilitators in dental practice could be key people in encouraging Evidence based dentistry which would improve the quality and focus of audit.

PROBLEMS OF INTRODUCING EVIDENCE BASED DENTISTRY

1. Amount of evidence

Currently over 2 million biomedical articles are published annually in some 20,000 journals. There are about 500 journals related to dentistry. Clearly not all of these articles are relevant to all areas of dental practice, nor can one hope to read more than a small minority.

2. Quality of evidence

Much of the ever increasing volume of evidence is produced to enhance career prospects rather than to increase knowledge. This can compromise quality. A number of publications that are widely read in dentistry are not subject to peer review and even when they are there is the tendency for publication bias. This bias may not be explicit but there is a tendency both by the researchers and editors to publish positive reviews. Negative trials can be equally valuable, and concerns have been raised that increasing sponsorship of medical trials by commercial concerns could result in non-publication of negative or unhelpful findings.

3. *Dissemination of evidence*

Unless good methods of dissemination are available even where there is good evidence it can take many years for a particular treatment to become the norm.

4. Practice based on authority rather than evidence

The use of techniques or therapies based on the views of authority rather than evidence may lead to the wrong treatment being performed. [13]

THE CLINICAL QUESTION

The process of creating an understanding of what constitutes worthwhile research is accomplished by providing a framework of questioning that reveals the level of uncertainty associated with the published evidence. The goal is to provide a process for continual learning that fosters maintenance of professional knowledge and skills in this age of expanding information.

The skills for practicing evidence-based care include: how to phrase clinical questions to allow effective and efficient searching, how to find useful articles, and what specific guidelines you can use to decide what to read. [14]

The first step in the quest for answers to clinical questions (and often the first stumbling block) is the formulation of a clear and focused question – one that is relevant and will help to carry out a quick and effective search. Most often, the original question is too broad. The first step consists of narrowing the question by deciding which elements are the most important to answer with a "hit and run search".[6]It may not always be easy to formulate good clinical questions. This is especially true when dealing with situations that are not routinely familiar. In such situations, we can consider that our questions take 1 of 2 forms; those that are "background" and those that are "foreground" in nature. Background clinical knowledge would include basic knowledge such as, "what is this disorder? "What causes it? "How does it present?"

Considering such background clinical knowledge, we might develop a foreground question such as "in patients with severe xerostomia, would a course of pilocarpine improve oral comfort and the quality of life (QOL) (over doing nothing) to be worth the potential side effects and cost?" Although foreground questions usually have 3 or 4 parts, background questions do not. These usually start with what, where, when, why, how and who, and end with a clinical entity, such as a health state or health intervention.

The reason for the different types of question is likely due to the level of experience the clinician has with the condition in question.

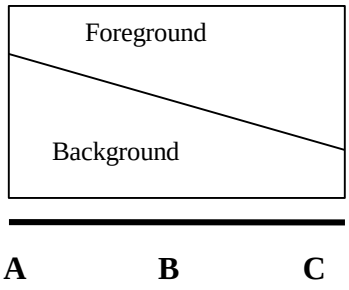


Figure 4: Foreground and Background Representation

In ***Figure 3*** the rectangle represents the universe of potentially relevant clinical knowledge, and the diagonal denotes the rough division between background and foreground knowledge. On the scale beneath are 3 levels of experience **"A"** is a learner with little clinical knowledge or experience, whose needs are largely of the background type portrayed by the vertical dimension of the rectangle. **"B"** has increased knowledge and experience, and the needs are more evenly divided. **"C"** has extensive knowledge and experience, and the majority of the knowledge needs would be foreground. In this diagram, please notice the diagonal is placed to show that clinicians are never too inexperienced to ask foreground questions, or too experienced to ask background questions. It is the condition of the patient that determines the knowledge needs. Clinicians may be at "C" for frequently

encountered problems, at "B" for occasional problems, and at "A" for new disorders or those outside their special area of interest.[14]

The practitioner must decide which questions to pursue in the limited time available. The first criterion in selecting which questions to pursue is to choose questions from the patient's perspective. The second criterion suggests that practitioners seek evidence on questions that assist in staying current and in preparing for the next occasion. Often in the pursuit of this information, however, the literature does not provide a definitive answer. To ration time effectively, the third criterion suggests choosing the questions that are most likely to yield a clear answer. Of course the searcher cannot know in advance whether the answer is available to be found. Common problems, however, are more likely to have a better body of literature than rare problems. Finally, of course, the searcher should choose interesting questions that spark the learning process.

Articulating the question makes it more likely that the practitioner's quest for scientific information will correspond with the patient's perception of what is important. Thus, there is better opportunity to include in the question issues that balance the potential for good with risk of harm. Similarly, the question should reflect the patient's wishes and priorities, concerns about costs, and cultural issues.

A carefully crafted question provides criteria against which found articles can be reviewed for closer inspection. As the titles and abstracts of articles are scanned, the searcher is asking, "Do I want to read this article in detail?" If the answer is no, the searcher wants that answer quickly, to be able to proceed to the next article. Having the criteria enunciated clearly in the question facilitates a quick judgment. Here again, the choice of outcome measures is often critical. Articles that address the same problems as those being researched using the same interventions but recording different outcomes are of general interest but are not necessarily relevant. Being able to ascertain quickly that the outcome reported is not the outcome of interest allows the searcher to move on the next article more quickly.

Another advantage of articulating a clearly defined question can be found in the communication between cooperating providers. In referring patients to specialists, general practitioners can focus the attention of the specialist and at the same time circumscribe the specialist's responsibility. It therefore is easier for the general practitioner to fulfill the duty to coordinate specialist services.

Finally, a significant benefit of taking the trouble to frame clinical questions is the opportunity to organize the questions for later reference. Lee et al suggest the development of critically appraised topics (CATS) that form a personal library of answers to clinical questions that have arisen. Of course, such a library needs to be updated from time to time, but it serves as a starting point for future searches and at the very least provides a compendium of accumulated best evidence on issues already encountered[7]

Once the clinical question has been phrased, the next step is to find the most current, best available evidence. Several options are available, which could include asking a colleague (or expert), checking text books and their references, looking through articles in journals, or searching through a bibliographic database.[14]

Colleagues:

This is usually the first option for most of us. Many healthcare professionals, not just dental team members, will remember learning to carry out various procedures 'on-the-job' i. e, from senior colleagues or from a peer who has had experience of the procedure.

An ***advantage*** of this source of evidence is that, chances are, one of our colleagues will have an answer, saving us spending time delving through books or papers. There is also the option of contacting a specialist in the field who can provide an expert opinion.

Disadvantages of this source are that although the definition of Evidence Based Dentistry acknowledges the value of expert knowledge and experience, these opinions are of the lowest level and should be considered only in relation to other types of evidence. Experts often disagree, may not be up-to-date in their knowledge of the particular issue you are raising, or may simply disagree with the current evidence, always sticking to their own preferred mode of treatment.

Books:

Books are a good source of comprehensive established information. The information is laid out in well-defined sections with an index of terms making them useful as quick references for basic back-ground information. The disadvantage is that, due the extended time it takes to research, script and publish a book (sometimes years), some of the information becomes out-of-date quickly. Books are unreliable as a major source of current information. [3]

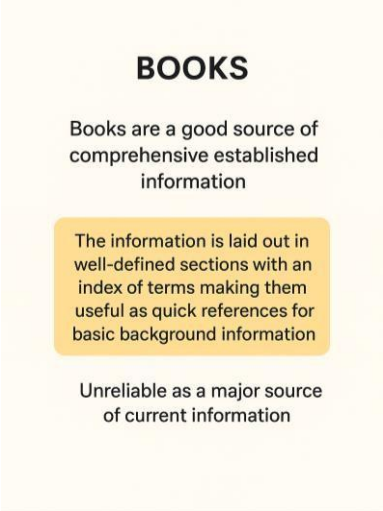


Figure 5: Advantages of book

Traditional reference sources:

Unless the clinician has access to a health sciences library,the use of traditional source materials such as **Index Medicus** or the **Index to Dental Literature** may be limited. Determining under which traditional headings in the ***Index to Dental Literature*** a particular topic is listed can also be time-consuming. Each volume of these indices generally covers the topics published in a single year, and searching through the array of these indices is often daunting. When reviewing these indices, the reader is urged to begin with the current year's index and to work backward in time, unless the exact publication date of an article on a particular subject is known. The exception for this technique might be a search for a treatment material or method that is antiquated or no longer practiced, such as the gold foil technique or the clinical use of a particular all-ceramic crown material that is no longer manufactured. For these historical searches, review articles might be useful initial sources for the topic of interest.

Peer-reviewed journal sources:

Figure 6: Peer-reviewed journal sources

Peer review generally implies that a submitted manuscript is blindly reviewed by one or more experts on the general topic of the manuscript, that suggestions for improving the manuscript are returned to the authors, and that, following revisions, the manuscript is again reviewed and copy-edited for clarity before being accepted for publication. Provided that the reviewers are skilled in the precepts of evidence based dentistry and apply those precepts when reviewing the manuscript, one can generally expect that most peer-reviewed articles are accurate. Subscribing to a periodical generally entitles the member to have access to the publisher's on-line journal source.

This on-line source gives the reader access to all published manuscripts from that journal, including all back issues that have been entered into the on-line source. One advantage of this technique is that it allows free access to the journal as long as the clinician subscribes to it; it also allows the clinician to discard old journal issues that may be consuming valuable space in the office or home.

The disadvantage of this search technique is that it allows a search for articles in only one particular journal, rather than providing a more comprehensive listing of all articles published on any given topic. This technique may prove too limiting when treatment decisions require a more comprehensive approach.[15]

Electronic databases:

Information on the Internet is often uncontrolled and unevaluated and may be inaccurate. It is imperative, therefore, that dentists understand the advantages and limitations of the Internet and are able to use it effectively to guide practice and assist their patients in their pursuit of oral health.

Because the quality of information is so variable on the Internet, some criteria have been suggested to assess Internet sites. These include the attributes and affiliations of the authors, the disclosure of funding sources, the regular updating of material, statements or (even better) linked citations leading to supporting evidence, endorsement by respected individuals or organizations, and common sense, coupled with your own experience and expertise. [16]

One of the easiest and most cost-effective methods to search the literature is through the use of the **PubMed** service from the federal government. This service can be accessed on the internet at ***http://www.ncbi.nlm.nih.gov/PubMed***.

The PubMed system was developed by the National Library of Medicine, located at the National Institutes of Health (NIH), and through the National Center for Biotechnology Information (NCBI). PubMed serves as an excellent search tool for accessing dental, medical, and biomedical literature citations and provides links to full-text journals at the web sites of participating publishers. Publishers participating in the PubMed service electronically submit their articles just before or at the time of publication. For the practicing clinician, PubMed provides free access to MEDLINE and Internet Grateful Med, the bibliographic databases that serve as an excellent source for obtaining current literature citations.[15]

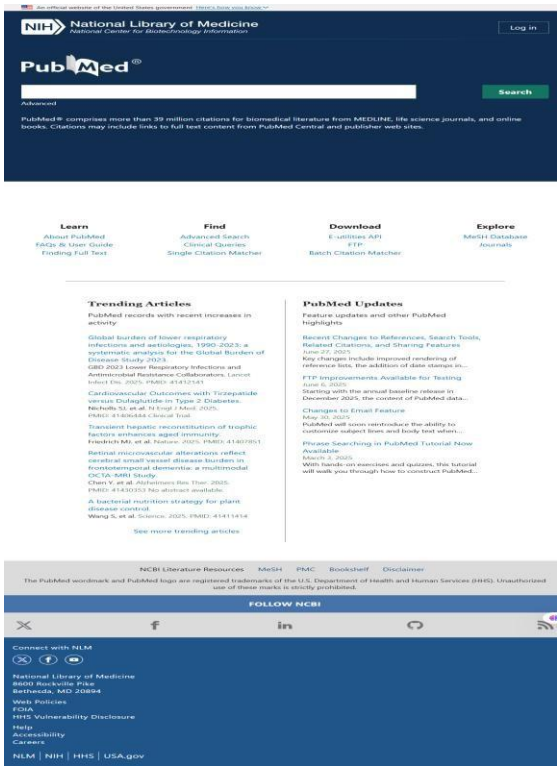


Figure 7: Pubmed Page

Medline

A number of excellent and highly specialized databases provide electronic access to medical and scientific literature. By far the most relevant and readily availabl e of these is MEDLINE. This multipurpose database, created and maintained by the United States National Library of Medicine (NLM) of the National Institutes of Health, is an index to the biomedical literature from 1966 onward, covering the disciplines of medicine, dentistry, nursing, veterinary medicine, health care services and the preclinical sciences.

Over 4,00,000 new references are added per year, at a rate of nearly 8,000 publications per week. Of the over 700 dental journals currently available worldwide, about 320 are indexed in MEDLINE.

MeSH (Medical Subject Headings) is a special vocabulary developed by the NLM to index each reference. The vocabulary contains main headings or index terms, each of which represents a single concept in the biomedical literature. Ne w terms are continuously added and outdated ones removed by subject specialists as new concepts emerge in the scientific literature. When a new citation (the MEDLINE term for information about an article, including its title, authors, source, institution, abstract and more) appears, trained NLM indexers choose the MeSH terms (usually 10 to 12) that best characterize the substance of the article. MeSH

terminology provides a consistent way to retrieve information and bypasses the problem of medical jargon and multiple synonyms for the same idea. Besides searching by subject, searching can be done by "text words", which are words or phrases in the title or abstract of the article. These are especially useful for new terminology (e.g.: new drugs or procedures). Text words should be used in combination with, rather than instead of, subject terms. The reason is that text words are "uncontrolled" vocubulary – that is, there is no guarantee that the word or phrase as used by the author is either relevant to or specific enough for your search.

A useful operation, called truncation, can also be employed when doing text word searches. A truncated term (or wild card, in search jargon) is the first part of a word followed by an asterisk. This feature allows all terms beginning with that part of the word to be searched. For example, "dent*" will find all terms that begin with the letters d-e-n-t, including "dental" "dentistry", "dentist" and so on. Both text words and subject terms can be combined using the Boolean operators AND, OR and NOT to control searches. AND is used when you want to retrieve papers that contain all of the concepts of interest. This feature reduces the number of hits and makes the search more precise. For example, "Head and neck neoplasms AND quality of life" will focus the search to papers in which these 2 concepts are key points. Adding AND radiation therapy "reduced the number of hits further. The operator OR, on the other hand, is used to broaden the search. If you are interested in non-surgical and non - drug therapy for TMD, you might use "AND temporomandibular dysfunction" with any other terms for therapy ("splint OR bruxism OR exercise OR stress reduction OR acupuncture OR occlusal adjustment" etc).

Terms can be excluded by using the term NOT – for example, "bone graft AND allograft NOT autograft" or in the TMD example, "temporomandibular dysfunction AND [therapy NOT drug therapy] AND [therapy NOT surgery]". Be sure to use uppercase letters for these Boolean operators. When looking for information in clinical settings, it is important to apply meaningful limits to reduce the number of irrelevant hits. Twenty-five to 30 titles are a reasonable number to review, although this will vary from person to person and will depend on the nature of the question at hand. In searching for answers to clinical questions, MEDLINE, because of its depth, breadth and continuous maintenance by the NLM, is the best source of evidence for health care.17 The Medline database is exactly the same, whichever company is selling it, but the commands differ according to the software. Vendors of Medline online and on CD ROM include Ovid Technologies (OVID) and Silver Platter Information (WinSPIRS). Some common problems in searching the scenarios have been drawn up using OVID software.

Problem: You are trying to find a known paper

Solution: Search the database by field suffix (title, author, journal, institution, etc) or by textwords **(Table 2).** First, get into the part of the database which covers the approximate year of the paper's publication. If you are already in the main Medline menu, select "database" (Alt-B). If you know the approximate title of the paper and perhaps the journal where it was published, you can use the title and journal search keys or (this is quicker) the.ti and .jn field suffixes. The box shows some other useful suffixes.

Table 2: Useful search field suffixes (OVID)

Syntax	Meaning	Example
.ab	Word in abstract	epilepsy.ab
.au	Author	smith-r.au
.jn	Journal	lancet.jn
.me	Single word, wherever it may appear as a MeSH term	ulcer.me
.ti	Word in title	epilepsy.ti
.tw	Word in title or abstract	epilepsy.tw
.ui	Unique identifier	91574637.ui
.yr	Year of publication	87.yr

Problem: You want to answer a specific question

Solution: Construct a focused (specific) search by combining two or more broad (sensitive) searches.

Problem: You want to get general information quickly about a well defined topic

Solution: Use subheadings and/ or the "limit set" options (Table 3 & 4) Subheadings are the fine tuning of the Medline indexing system; they classify articles on a particular MeSH topic into aetiology, prevention, therapy, and so on. The most useful ones are listed in the box. Try not to use subheadings unless you have unearthed an unmanageable set of articl es,

since an estimated 50% of articles in the Medline are inadequately or incorrectly classified by subheading.

Table 3: Useful subheadings (OVID)

Syntax	Meaning	Example
/ae	Adverse effects	**thalidomide/ae**
/co	Complications	**measels/co**
/ct	Contraindications (of drug)	**propranolol/ct**
/di	Diagnosis	**glioma/di**
/dt	Drug therapy	**depression/dt**
/ed	Education	**asthma/ed**
/ep	Epidemiology	**poliomyelitis/ep**
/hi	History	**mastectomy/hi**
/nu	Nursing	**cerebral palsy/nu**
/og	Organization/administration	**health service/og**
/pc	Prevention and control	**influenza/pc**
/px	Psychology	**diabetes/px**
/th	Therapy	**hypertension/th**
/tu	Therapeutic use (of drug)	**aspirin/tu**

The option "AIM journals" denotes all journals listed in the Abridged Index Medicus- that is, the "mainstream" medical journals. (Table 4)

Table 4

Useful "limit set" options	
AIM journals	Abstracts
Nursing journals	Local holdings
Dental journals	English language
Cancer journals	Male
Review articles	Human
Editorials	Publication year

Problem: Your search gives irrelevant articles

Solution: Refine your search as you go along in the light of interim results.Often, a search uncovers dozens of articles which are irrelevant to your question. The Boolean operator "not" can help here.Another way of getting rid of irrelevant articles is to narrow your textword search to adjacent words using the "adj" operator. For example, the term "home help" includes two very common words linked in a specific context. Link them as follows: 1 home adj help.tw

Problem: The search gives no articles, or too few

Solution: Firstly, don't overuse subheadings or the "limit set" options. Secondly, search under textwords as well as MeSH terms. Thirdly, learn about the "explode" command, and use it routinely.

The MeSH terms are like the branches of a tree with, for example, "asthma" subdividing into "asthma in children", "occupational asthma", and so on. Medline indexers are instructed to index items by using the most specific MeSH terms they can. If you just ask for articles on "asthma" you will miss all the articles indexed under "asthma in children" unless you "explode" the term using the following syntax : 1 exp asthma.

Problem: Limiting a set loses important articles but does not exclude those of low methodological quality

Solution: Apply an **EBQF** (evidence based quality filter).

These EBQFs (evidence based quality filters), which are listed below, are complex search strategies developed by some of the world's most experienced medical information experts. You can copy them into your personal computer and save them as strategies to be added to your subject searches.

Evidence based quality filters for everyday use:

a) Therapeutic interventions (What works?)
   1. exp clinical trials
   2. exp research design
   3. randomised controlled trial.pt.
   4. clinical trial.pt.
   5. (single or double or treble or triple).tw.
   6. (mask$ or blind$).tw.
   7. 5 and 6
   8. placebos/ or placebo.tw.
   9. 1 or 2 or 3 or 4 or 7 or 8

b) Aetiology (What causes it? What are the risk factors?)
   1. exp causality
   2. exp cohort studies
   3. exp risk
   4. 1 or 2 or 3
c) Diagnostic procedures
   1. exp "sensitivity and specificity"
   2. exp diagnostic errors
   3. exp mass screening
   4. 1 or 2 or 3
d) Epidemiology
   1. sn.xs

(This would find all articles indexed under any MeSH term with any of "statistics", "epidemiology", "ethnology", or "mortality" as subheadings.)

Problem: Medline hasn't helped

Solution: Explore other medical and paramedical databases.

***Shortcomings of Searching Medline*:**

Entry of articles onto the Medline database is open to human error, both from authors and editors who select key words for indexing, and from the librarians who group articles under subheadings and type in the abstracts. In addition, some sections of indexed journals are not available on Medline (for example, the News section of BMJ). According to one estimate, 40% of material which should be listed on Medline can, in reality, only be accessed by looking through all the journals again, by hand.[18]

The reasons for missed articles on searching MEDLINE are manifold. To understand the reasons for these limited returns, we should consider first how much information is actually available in the electronic record on which the search can be conducted.

Essentially, for the researcher, electronic searches chiefly rely on two things:

- the controlled vocabulary (in MEDLINE MeSH) terms assigned to the article by professional indexers; and
- Descriptors (text words) used by author/s in the title and abstract.

Where the detail of the study design is "lost" in the main body of the paper, this information will not be available in the electronic record and, further, is more likely to be missed by the indexers. Lack of detail in the title and abstract of t he paper will influence the results of a search, and as by no means all articles have abstracts, this limits the search potential even further.

Another limitation of electronic searching is that not all journals are indexed in MEDLINE and, in particular, non-English language references are underrepresented. There is good evidence that research findings showing statistically significant results are more likely to be published in English language journals. By excluding non-English language articles, the results of a systematic review are again susceptible to publication biases. [19]

THE COCHRANE COLLABORATION

The *history* of the Cochrane Collaboration dates back to the influential 1972 publication, *Effectiveness and Efficiency*, by the British physician/epidemiologist **Archie Cochrane**. In his essay, Cochrane emphasized the use of scientific evidence, rather than intuition, expert opinion, anecdotal experience or tradition in the evaluation of health care. In 1979, he wrote: it is surely a great criticism of our profession that we have not organized a critical summary, by specialty or sub-specialty, adapted periodically, of all relevant randomized controlled trials. In 1992, the British National Health Service created the Cochrane Centre, at Oxford, UK, named in honor of Archie Cochrane, to facilitate the preparation and maintenance of systematic reviews for all areas of health care. Tremendous international interest followed and by 1993, centres had been established in Denmark, Canada, the United States and Australia. There are now fifteen Cochrane Centres worldwide.

The main product of the Cochrane Collaboration is the **Cochrane Library**, an electronic library, issued quarterly, which contains databases of controlled trials and systematic reviews. The core work of the collaboration is done by the Collaborative Review Groups, which are formed by individuals who have a common interest in a health care problem and who work together through electronic means to prepare a systematic review on their chosen topic. [11]

The Cochrane Oral Health Group Trials Register:

A register of trials within dentistry exists in the form of the Cochrane Oral Healt h Group's Trials Register.

Cochrane Oral Health Group's (OHG) Trials Register was established in 1997. The purpose of the register is to provide an electronic resource to assist reviewe rs undertaking Cochrane systematic reviews on dental and oral health topics and to contribute to the Cochrane Central Database of Controlled Trials for the benefit of the increasing number of people across the world with access to *The Cochrane Library.*

The CENTRAL database is updated quarterly, chiefly from downloads from MEDLINE and EMBASE and from records submitted by Cochrane entities around the world covering all medical healthcare specialties.

Handsearching to Identify Trials:

Given the limitations of electronic searching, where comprehensive searching is paramount, then electronic searching must be supplemented by hand searching of key journals. Hand searching involves searching a journal page by page to identify all reports of controlled clinical trials, whether as full papers, abstracts, or correspondence.

A comprehensive search for all relevant trials combining electronic searching with hand searching of key journals is essential to the validity of systematic reviews. In recognizing the need for the potentially huge and tedious task of hand searching journals, the Cochrane Collaboration organized a worldwide hand searching program. The program is coordinated and managed by the New England Cochrane Center in the United States.

Collaborators from all around the world are hand searching health care journals and conference proceedings to contribute to the Cochrane worldwide hand searching program.

Cochrane Collaborative Review Groups are responsible for coordinating handsearching of journals related to the scope of their group, and the Oral Health Group coordinates and manages searches of the dental/oral health literature. Handsearching requires the searcher to read/scan a journal page by page to identify published and unpublished controlled clinical trials or information on trials such as abstracts and correspondence. The searcher then submits the information to the OHG Trials Search Coordinator. Any trials not previously identified are downloaded into the OHG Trials Register, which is in turn uploaded into the CENTRAL database in *The Cochrane Library*, thus enabling the results of the handsearcher's efforts to be accessible to anyone with access to the Cochrane Library across the world.[19]

OTHER INTERNET SOURCES

The best sites that have been found are those produced by academic centres, including university and hospital sites, government-sponsored and professional organization sites and the sites of several medical search engines.

Academic Centres:

Academic centre sites generally feature many useful resources. These include not only ways to find valid, up-to-date clinical information, including links to MEDLINE and the Cochrane Collaboration, but also tools to help you learn to

practise evidence-based care and to teach it to others. Many of these sites are linked to each other and to a number of other useful sites as well.

The Centre for Evidence-Based Dentistry (www.ihs.ox.ac.uk/cebd) is located at the Institute of Health Sciences, Oxford University, United Kingdom.

The School of Health and Related Research (ScHARR) at the University of Sheffield in the United Kingdom has a comprehensive document entitled *Netting the evidence: A ScHARR introduction to evidence to evidence based practice on the Internet* on their Web site (http://www.shef.ac.uk/-scharr/ir/netting).This document is an alphabetical complication of links to numerous multilingual and international resources.

The Health Information Research Unit at McMaster University (http/:hiru.hirunet.mcmaster.ca) in Hamilton, Ontario, has become internationally famous. This extensive, detailed site features many useful resources. It includes links to information and abstracts from the Cochrane Collaboration and the Canadian Cochrane Centre.

The library of the Ottawa General Hospital (www.ottawahospital.on.ca/professional/library) provides a large collection of links to resources for evidence –based health care.

The University of Toronto Centre for Evidence-based Medicine (www.library.utoronto.ca/medicine/ebm/) is based at Mount Sinai Hospital – part of the University Health Network. It has several useful features, including a large set of links to useful evidence-based medicine resources on the Internet (including journals, CDs, textbooks and Web sites), syllabi and a glossary of evidence –based terms.
Government –Sponsored and Professional Sites:

The best known sites in this category are the National Institute of Health (NIH) National Library of Medicine databases, particularly MEDLINE via PubMed (www.ncbi.nlm.nih.gov/) and NLM Gateway http://gateway.nlm.nih.gov).

Evidence-based Guidelines:

One of the most extensive collections of guidelines can be found in the National Guideline Clearinghouse (NGC). This database can be accessed through the Web site of the Agency for Healthcare Research and Quality (www.ahcpr.gov/clinic/cpgsix.htm) of the U.S. Department of Health and Human Services.

The Scottish Intercollegiate Guidelines Network (www.show.scot. nhs.uk/sign/) has published 43 guidelines.

Clinical Trials in Progress:

NIH Clinical Trials (http/:www.clinicaltrials.gov/) is a searchable site where you can do a broad search in a subject area to find clinical trials in progress or those recently closed to accrual.

Medical Search Engines:

There are several excellent medical search engines with remarkable search and retrieval capabilities for relevant health care information. Two particularly good sites are CliniWeb International and Medical Matrix.

ClinicWeb International (www.ohsu.edu/cliniweb/) is a multilingual index and table of contents to clinical information on the Web. It is produced and maintained by medical informatics specialists at the Oregon Health Sciences University. The focus of the site is clinical information relevant to health care education and practice consumer-oriented information is filtered out.

Medical Matrix (http://www.medmatrix.org/) is a commercial site for which free registration is required, but which has a clearly stated privacy policy. The site includes links to journals, symposia presentations, continuing education resources, textbooks, databases (such as MEDLINE), prescription assistance resources (such as searchable drug interaction databases), predetermined clinical searches and more.
Each Internet sites is ranked using a 5-star system, according to its usefulness for point-of-care application. [17]

Clinical practice guidelines:

Clinical practice guidelines have been defined as systematically developed statements to assist practitioners and patients in arriving at decisions on appropriate health care for specific clinical circumstances". They are not designed to replace clinical experience and knowledge but are recommendations to assist healthcare professionals in clinical practice. [3]

Different approaches have been used to develop guidelines, including expert opinion, group consensus and evidence based methods. Although experts may have a wealth of scientific knowledge, clinical experience and credibility, guidelines based on expert opinion are usually unstructured and informal, and are open to criticisms of bias and conflict of interest.

Guidelines derived from consensus meetings are more structured and formal. They represent the views of various stakeholders and may be useful for creating uniform practice policies, particularly in areas of controversy. However, the research considered may represent a biased sampling and the evidence is generally not available for scrutiny.

Evidence-based clinical practice guidelines (EB-CPGs) are structured and formal, and use rigorous, explicit and reproducible methods to assemble and evaluate the evidence. These guidelines are based on systematic reviews and incorporate values and preferences of patients and practitioners. The process of creating a well - developed EB-CPG includes external review and comment by those who will be using the guidelines – for example, a wide range of clinicians, as well as patients or their representatives.

The development of EB-CPGs in dentistry is in the beginning stages. [11]

The *disadvantage* of the guidelines is that they are general by their very nature, and may not be appropriate for every individual patient. This is where clinical experience and judgment becomes invaluable. [3]

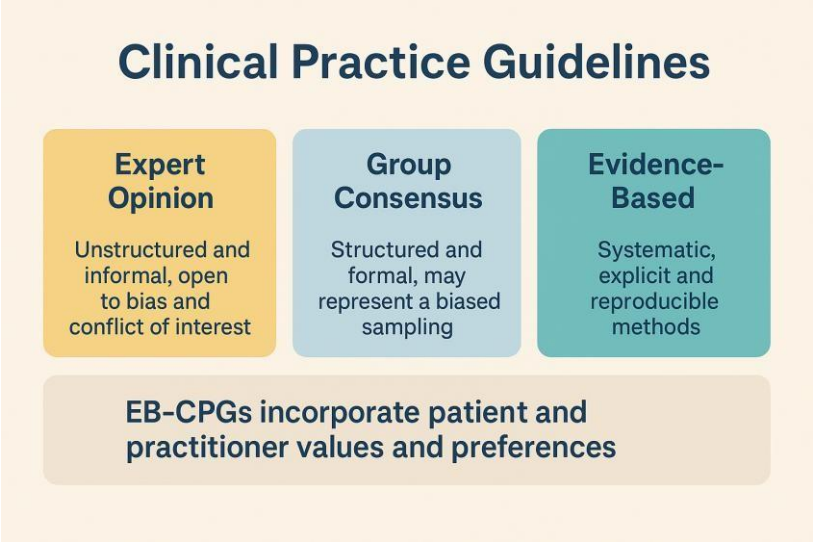


Figure 8: Clinical guidelines evolve from opinion to evidence-based practice

TYPE OF RESEARCH STUDIES

To evaluate research studies critically, clinicians must have a working knowledge of the principles of scientific research and an understanding of the various types of research studies. Briefly, there are two broad categories of research: **basic science** and **clinical research**. The principles that govern the validity of scientific research are common to both branches of scientific research. It is more

challenging to ensure that a study is free of bias with clinical research than with basic science or laboratory research, because in the laboratory the researcher has more control over the environment and other variables that may influence the results of the study**.**

All clinical research studies are encompassed under the broad heading of **epidemiologic studies**. Epidemiologic studies include studies that follow the natural course of disease or treatment effects as well as studies in which the investigators intervene in assigning a treatment for a particular condition or in using a preventive agent to decrease likelihood of disease. These studies can be categorized into two broad categories: ***Descriptive and Analytical studies***.

A. DESCRIPTIVE STUDIES :

Descriptive studies describe the general characteristics of the distribution of a disease, particularly in relation to person, place, and time. Descriptive studies commonly seen in dental literature are case reports and case series studies, which are detailed reports of an individual patient (case report) or a group of patients (case series) with a particular disease or who have received a particular treatment. An example of a case series study is one in which investigators report on patients treated in their practice with the particular implant system. This report may be a long term study in which investigators reports on variety of treatment outcomes. It is impossible to know what effect a particular treatment has on these outcomes without making a comparison with another treatment. This comparison is possible only with an analytical study design. [20]

Case reports and case series are often used to describe a condition (usually a rare disorder or a novel aspect of a less rare condition), a new treatment or innovation , or adverse effects of an intervention. They often provide a richness of information which cannot be conveyed in a trial. The description of cases may alert the world to important new problems and then allow hypothesis to be developed, leading to focused studies of stronger design. Case studies and case series are relegated to the lowest rungs of the evidence ladder, however, because isolated observations are collected in an uncontrolled, unsystematic manner and the information gained cannot be generalized to a larger population of patients. [21]

Cross-sectional surveys are another type of descriptive study that report the status of an individual with respect to the presence or absence of both exposure and disease assessed at one point in time. These studies are also limited in their ability to demonstrate definitively the benefits of a particular treatment or the significance of a particular exposure. For example, a study that examined 500 individuals, including a complete oral examination, a medical examination, and an interview regarding a variety of health, dietary, and sociodemographic factors, reports on the association between oral health and diet. The investigators report that individuals with good oral health also had a healthy diet, indicating that a

healthy diet contributes to adequate oral health. With a cross-sectional study it is impossible to conclude anything about causality. Adequate oral health might enable a person to consume more fruits and vegetables that constitute a healthy diet, a conclusion that is quite different from the conclusion that adequate diet results in good oral health. Essentially, in a cross-sectional study it is impossible to determine if A causes B or vice versa; this situation is analogous to the "chicken-and-egg" phenomenon. In summary, descriptive studies are often referred to as hypothesis-generating studies. They are often the first step in investigating a particular scientific question.

B. ANALYTIC STUDIES:

Analytic studies differ from descriptive studies in that they include an appropriate comparison group that permits the testing of epidemiologic hypotheses. Causality can be investigated with analytic studies. The two broad subcategories of analytic studies are intervention and observational studies.

Intervention studies or clinical trials are considered to be the "gold standard" for clinical research studies. Because the examiner assigns the exposure or treatment, it is often possible to blind both the subject and the examiner to the treatment assignment, creating a double-blinded study that minimizes bias of the study findings. Randomization to create similar study groups is possible only with clinical trials and therefore significantly increases the validity of these studies in comparison with other clinical research study designs. [20]

Randomized controlled trials (RCTs) cannot answer all clinical questions. There are situations where they may not be necessary, appropriate, ethical or feasible, or they simply may not have been done yet. In general, questions of therapy are best answered by RCTs, or even better, meta-analyses if available, whereas questions of diagnosis, prognosis and causation may be best addressed by observational (sometimes called "epidemiological") studies. [21]

An observational study is one in which the investigators do not intervene in any way, so they do not, for example, administer treatments or withhold factors which may influence the outcome of interest.[22]

In observational studies, investigators observe the natural course of events, noting which subjects are exposed or not exposed, which have had a particular treatment and which have not, and which have or have not developed the outcome. There are two subcategories of observational studies: Cohort studies and Case- control studies.[20]

Observational studies also can be cross-sectional or longitudinal. Longitudinal studies are those which require the individuals to be investigated over a period of time. [22]

1. Cohort studies:

A cohort study involves observing and monitoring a group of individuals over a period of time. Such studies come under a number of different guises, particularly in epidemiology, with names such as *cohort* studies, *longitudinal* studies and ***prospective*** studies, and although these studies may involve different definitions of the study population, the statistical analysis of each is essentially the same.

In a cohort study, the individuals in the sample from the relevant study population are first categorised according to the levels of the factor or factors of interest, perhaps a risk factor such as daily cigarette consumption so that each individual is classified as current smoker or non-smoker. This cohort of individuals is then monitored for a period of time and a change in status is noted. In an epidemiological study, the status may change, for example from 'without disease' to 'with disease', where the 'disease' might be oral cancer or the loss of at least one tooth. Such changes may be measured by the rate at which new cases of the disease occur in the study population. This rate is usually called the *incidence rate* of the disease. The observed incidence rates in the risk factor categories are then compared, usually by calculating their *ratio*, called a **relative risk**.[22]

A variation of a cohort study is a longitudinal study in which there is only one group. Included in the group (called ***inception cohort***) are people who have a positive screening test (for example, for a new genetic marker) or who have all been diagnosed with an early stage of a disease. They are then followed and evaluated on a repeated basis to assess the development of the disease (i.e., in the example of genetic marker), or the time frame for particular outcome measures, in the case of a chronic disease.[21]

Although a cohort study is time-consuming and costly, and is useful only for studying a common disease, it has the ***advantages*** that it can be used to study many disease outcomes as well as rare risk factors. [22] Cohort studies also have ***disadvantages***: they are inefficient for the study of rare diseases, they may be expensive and time consuming, and they have the potential for loss-to-follow-up bias that may affect the validity of the study.[20]

2. Case-control studies:

In a case-control study, sometimes called a ***case–referent***, ***retrospective*** or ***trohoc*** (cohort spelt backwards) study, a sample of cases, ie persons diagnosed as having the disease of interest, is compared with a group of comparable controls who do not have the disease. The cases and controls are separately categorized according to whether or not each has been exposed to the risk factor. Since it is impossible to estimate the relative risk directly in a case-control study (as the relative risk requires knowledge of disease rates rather than exposure rates), it is common to estimate the **odds ratio** instead. The odds ratio is the odds of disease in those exposed to the factor divided by the odds of disease in those not exposed to the factor. The odds ratio is a reasonable estimate of the relative risk of disease in

those who are and are not exposed to the factor provided the disease is rare and so its prevalence is low.

The ***disadvantages*** of a case-control study are that it is not possible to estimate the relative risk directly from the study (although if the prevalence of the disease is low, the odds ratio can be used as an estimate of the relative risk), that selection of the controls may be difficult and that it is possible to study only a single disease outcome in any one study.

However, case-control studies are relatively quick, easy and cheap to perform, and can be used to study many risk factors as well as rare diseases.

Sample surveys:

A sample survey is a particular form of cross-sectional observational study in which a sample of individuals is taken from a well defined population with the intention of using the observed characteristics in the sample as estimates of the corresponding characteristics in the population.[22]

EXPERIMENTAL STUDIES

An experimental study is one in which the investigator deliberately intervenes so that it is possible to observe the effect of the intervention on the response of interest, usually with a view to establishing whether a change in the response is attributable to the intervention. A clinical trial is an example of an experimental study.

If the study is experimental rather than observational then it must be designed in such a way that it gains the largest amount of information of the greatest reliability in an efficient manner. The objective, therefore, is to achieve an optimal balance between minimal sample size and maximum precision whilst eliminating sources of bias and identifying and controlling all sources of variation. This balance may be achieved by choosing the appropriate experimental design which takes into account the particular circumstances of the investigation.

One important distinguishing feature of any experimental design is whether the treatment comparisons are made *between* subjects (parallel group designs) or *within* subjects (matched designs or cross–over studies).

1. Parallel groups:

Parallel groups designs involve the basic observational units (typically, the subjects) being independently and randomly allocated to two or more treatment groups. The response is observed for every individual in the study and an aggregate measure (usually an arithmetic mean or median if the response is quantitave or a proportion if the response is qualitative) is calculated for each

treatment group. These summary measures are then compared appropriately so that the investigator can determine whether the responses differ significantly in the different treatment groups. The parallel group design therefore relies on comparisons which are made between groups of subjects. It should be noted that although generally desirable, it is not necessary to have an equal number of subjects in each group.

The randomized parallel groups design has the advantages that it is conceptually simple and the analysis is straightforward. In some circumstances, however, it may be appropriate to modify the simple parallel group design by employing a technique called blocking or stratification in addition to the simple randomization of subjects to treatments. This involves forming subgroups of individuals, the blocks or strata, such that the variation with respect to the vari able of interest within each stratum is smaller than the variation between the strata. Subsequent treatment comparisons are made between groups of subjects within each stratum, and the results properly combined to determine the overall treatment effect.

Stratification may also be employed because it is of interest to investigate whether the effect of treatment (say the difference in response in the two or more treatments groups) is the same for all strata of the study population.

The advantages of blocking or stratifying the study population before randomization are to enable interactions to be detected and estimated, to control the effect of known potential confounding factors and to improve precision. The **disadvantage** is that the statistical analysis is slightly more complicated.

2. Matched designs:

If the blocking described above is carried to extremes, then pairs of subjects (or triplets if there are three treatment categories) can be matched so that they are alike with respect to a number of potential confounding factors. For example, if it were decided to match for age and sex, the subjects in the study would be arranged in pairs so that the two individuals in each pair would be randomly allocated to different treatment/ intervention groups. The comparison between the two treatments is made within each matched pair and thus the treatment effect will be more precisely estimated than it would be with a parallel groups study within same number of subjects.

The advantage of a matched study compared with a parallel groups design is a gain in precision with same number of subjects, or equivalently, the same degree of precision of a parallel groups study can be achieved with a smaller total number of subjects.

The disadvantages of matching are that the study may become logistically difficult if too many matching factors are included and the inability to match some

subjects in the study. It may be difficult to investigate interactions in a matched study.

3. Cross- over trials:

The matched pairs study enables treatment comparisons to be made using similar experimental units. Rather than these experimental units being different subjects who have been matched appropriately, a similar type of study is one in which the subject acts as his/her own control with the subject being allocated both treatments, receiving them at different times. Such designs are called cross- over designs because the subject crosses over from one treatment to the other. The designs should involve randomising the order of administration of the treatments to each subject. The treatment comparison is then made within the subjects and, in the same way as a matched pairs study, increases the precision of the treatment effect for a given number of subjects.

Cross- over trials, although advantageous when compared to parallel groups designs in terms of precision or sample size, cannot be utilized for conditions which do not remain stable in the study period or which can be cured by the treatments being administered, when there is a carry –over effect from one treatment to another or when the response to treatment is prolonged. [22]

RANDOMIZED CONTROLLED TRIAL

The **clinical trial** is a planned experiment, strictly on human subjects, which is conducted with a view to investigating the efficacy of one or more treatments for a given condition. A well designed trial is one which, at the very least, is comparative in nature and incorporates randomization of patients to treatments; it is then called a **randomized controlled trial (RCT).** [23]

The first RCT was instituted in the early 1950s, evaluating streptomycin and bed rest compared with bed rest alone for tuberculosis. This research design has become the reference standard for comparative evaluations of therapies because of its prospective nature and the ability to control bias. [24]

Use of a 'control' treatment:

An essential feature of a clinical trial is that it is comparative in nature. This means that it is necessary to compare the results of a group of patients who are receiving the new treatment under investigation with another group of similar patients under some different treatment regime. This other treatment regime, the control treatment, may be an active treatment (*a* ***positive*** *control*) such as a

standard treatment that has been shown previously to be effective. Alternatively, if ethical considerations permit, the other treatment regime may be the absence of active treatment or else a dummy treatment, called a **placebo**, both of which are ***negative*** controls. A placebo is an inert substance which looks just like the active treatment. Its purpose is to separate the act of being treated from the real effect of the active treatment.

A clinical trial which includes a comparative group is called a **controlled clinical trial**. The reason for making the trial controlled is to ensure that, provided the composition of the treatment groups is similar, any conclusions drawn from the trial as to the effectiveness of the new treatment under consideration can be attributed solely to the administration of that and not to any other factors.

Randomization*:*

It may be that the clinician has a preconceived notion as to the effectiveness of the new treatment and this will influence the way in which the patients are allocated to various treatments, if given the freedom of choice. This might result in the more severely ill patients being allocated the standard treatment, or *vice – versa*, even if the clinician's intention is to be fair, and this in turn would result in a biased estimate of treatment effect. In order to avoid the possibility of this happening, the patients are randomly assigned treatments. This means that the method of determining which treatment each patient receives relies on chance rather than on personal judgment so that the potential for allocation bias is obviated. Random allocation i.e. randomization can be achieved by some mechanical method such as tossing a coin, but is more usually accomplished by using random number tables or computer generated random numbers. [23]

Different types of randomized controlled trial:

1. Randomized concurrent controlled trial:

In a randomized concurrent controlled trial (RCT) assignment of patients into study groups is a random allocation. Cohorts of individuals are either exposed or not exposed to the experiment maneuver and then both groups are followed for a specified time, assessing the outcome of interest. A concurrent control group allows both groups to be treated and measured in a standard blind fashion, thereby decreasing bias and increasing internal validity.

Depending on the question under investigation, there are often known or suspected variables that could have a large influence on outcome and might mask or interact with the experimental maneuver (smoking or diabetes in a periodontal therapy study). Before randomization, the subjects with these known variables are stratified, and a complicated randomization process (often requiring computer assistance) will attempt to place subjects with equal allocation of these known variables into each test group. Unknown variables that may influence outcome will also be equally placed in each test group by the randomization process. Because no pattern of allocation can be "perceived" by caregivers or the patients, bias in

delivering the maneuver and in data collection is reduced and internal validity is thus increased. Extraneous exposures and therapies, called co-interventions, that patients might become involved in during the test period, can also be controlled or monitored.

2. Quasi-randomized concurrent control trial:

The quasi-randomized concurrent control trial (QRCT) is similar to the RCT, but differs in that the subjects are not stratified as to known, confounding variables or are they randomly assigned to the test groups. Subjects are assigned using various quasi-random methods. Such as an-every-other subject assignment, every-other- day assignment, by odd-even birth dates, hospital numbers, and so forth.

Problems arise with this method because recruitment can be influenced. If a researcher believes that a subject would benefit from one of the therapies, the subject can be entered on that particular day. If a researcher believes that a subject would not benefit from a particular therapy, and his or her birth date or hospital number requires assignment to that therapy, the researcher or the practitioner might withdraw the subject from inclusion in the study. This "guiding" of allocation may be altruistic, but can offer considerable bias to the trial. This type of allocation is also difficult to keep blind from the caregivers and the subjects. Standardization of care and data collection can be compromised.

3. Randomized before and after study:

A before and after study allows investigators to offer 2 treatments to the same population of patients. Distribution of known and unknown patient variables are "inherently carried along with the patient" as he or she is given one therapy, and then given the other therapy. In this way, patients serve as their own control group. Critical design features include that the first therapy outcomes must be completely reversible (back to baseline) and "washed out of the patient's system" before delivery of the second therapy, and which therapy a subject receives first is through random assignment.

The difficulty of using this research design to answer a clinical question is that many dental maneuvers are not reversible. Drug trials are possible using a before and after study, allowing the drug effects and blood levels to return to baseline between therapies. The hygiene example is difficult to perform as a before and after study as the returning of the subjects to the baseline level of oral hygiene is difficult. Getting the first hygiene results to "wash-out of the patient's system" is problematic. Sometimes subjects are asked to discontinue all hygiene methods for several weeks before initiating the study and between therapies to establish a similar baseline.

Learning the first hygiene method might sensitize the patient to improved performance or learning the second hygiene method is a likely bias. The internal validity of the study related to treatment order bias is increased by the fact that

this possible influence of treatment order is balanced in both groups because all subjects received the maneuvers in a random sequence.

This type of trial is ideal for outcomes that occur in a relatively short period. In this way, co-interventions and differences that can occur in a patient as a result of elapsed time, namely, new comorbid conditions, lack of compliance, and so forth, can be minimized.[25]

***Advantages of Randomized controlled trial* :**

1. Allows rigorous evaluation of a single variable (effect of drug treatment versus placebo, for example) in a defined patient group
2. Prospective design (data are collected on events that happen after you decide to do the study)
3. Use hypotheticodeductive reasoning (seek to falsify, rather than confirm, in own hypothesis)
4. Potentially eradicates bias by comparing two otherwise identical groups
5. Allows for meta-analysis (combining the numerical results of several similar trials at a later date)

Disadvantages:

Expensive and time consuming; hence in practice:

- Many randomized controlled trials are either never done, are performed on too few patients, or undertaken for too short a period.
- Most are funded by large research bodies (university or government sponsored) or drug companies, who ultimately dictate the research agenda
- Surrogate end points often used in preference to clinical outcome measures may introduce "hidden bias", especially through:

1. Imperfect randomization
2. Failure to randomize all eligible patients (clinician only offers participation in the trial to patients he or she considers will respond well to the intervention)
3. Failure to blind assessors to randomization status of patients. [26]

***Ethical problems with randomized controlled trials* :**

The most serious objection to randomized controlled trials arises because of the ethical dilemma facing the researcher. There is a conflict between what might be termed *individual* and *collective* ethics. There is no easy solution to this ethical

dilemma. A balance has to be struck between concern for the individual and human experimentation for the advancement of science. At no stage should the former be sacrificed for the latter. To achieve a balance, it is important to employ safeguards for the individual patient and also to design and conduct the trial so that high scientific and organizational standards are attained throughout.

Guidelines for the ethical requirements of clinical research are outlined in the World Medical Association **Declaration of Helsinki**: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects which was adopted in Finland in 1964 and revised most recently in Edinburgh, Scotland in 2000. These guidelines provide a basis for 'protecting' the individual. Included in them is a requirement that **'informed consent'** is obtained from every patient (or legal guardian, if necessary) to be included in the trial. Informed consent implies that the patient is aware of and understands all the implications involved in the study which are known to the researchers, and is willing to accept these as a condition of his/her involvement in the study.[23]

INTEGRATIVE STUDIES

Basing important clinical decisions on single trials, especially when the result is a change in treatment policy, is risky. Because of the numbers of patients needed to detect small to moderate differences for clinically important outcome measures, definitive answers may not be found in single studies, unless they are well - designed "large simple trials". These "mega" trials, which usually involve many thousands of patients, have rarely been carried out in dentistry.

When the information from all relevant trials addressing the same question is combined using well-established, rigorous methodology, the result is a systematic review or overview. If the results of each trial were reported in such a way that they can be combined statistically by the researcher, the result is a quantitative systematic review or meta-analysis. Although systematic reviews are observational, retrospective research studies, they employ scientific methods to control bias and, in doing so, provide potent methods for synthesizing and summarizing data. In fact, systematic reviews are considered the highest level in the evidence hierarchy.[21]

Bias is a systematic error that distorts the true relationship between an event and its outcome. Bias will negatively affect the truth of the conclusions. In research, bias includes any systematic error in the design, conduct, or analysis of a study. Bias can occur at all stages of research, from the selection of the population, how treatment is provided, to how and when outcome measurements are made.

In health care research, bias can result in a mistaken estimate of a treatment's effect or an exposure's effect on the course of disease. These mistaken estimates

probably account for some of the conflicting conclusions observed in apparently similar studies. Mistaken estimates can lead to practitioners offering ineffective or even harmful treatments. It is the clinician's obligation to continue professional education by reviewing current literature. To optimize continued learning and patient care, clinicians should understand and scrutinize the various biases that can exist in research reports.[24]
Bias is present when the results from the study are systematically distorted and so are consistently above (or below) what they should be. Biases may arise in a number of ways. Typical *examples* are:

- ***Observer bias***- when one observer consistently over-reports (or under- reports) a variable. This may be resolved by training and calibration.
- ***Selection bias***- when the individuals in the study are not representative of the population of interest. This may be avoided by ensuring that a *random* method of selection is used rather than relying on purposive or judgment sampling, where investigators include in their sample those individuals who they believe are typical or representative of the population.
- ***Publication bias***- which is the tendency for journals to publish only 'significant' results.
- ***Recall bias***- when certain patients have a differential ability to remember details about their past.
- ***Allocation bias***- when the treatment groups in an experimental study are not comparable with respect to the variables influencing the response of interest. Random allocation (also called *randomisation*) of the treatment to the patients is a way of avoiding this bias.
- ***Assessment bias***- resulting from the manner in which the responses to treatment are assessed, often because of the subjective nature of those responses and the preconceived notions of those assessing the response. Making the trial 'blind' so that the study personnel and perhaps the patients are unaware of which treatment each patient receives is a way of overcoming assessment bias.[27]

One of the greatest biases of health care research arises from the methods of selecting the sample populations targeted for the research. If research subjects are inappropriately selected, no amount of stringent research methodology can counter the bias of sample population selection.
Bias control continues beyond design selection and population selection.

Specific methods of **bias control** should be implemented in the conduct and analysis of the investigation. These methods are applicable to all research designs:

1. Blind participants:

Blinding the investigators, examiners, and subjects to the intervention and the outcome is a significant controller of bias. Double blind methods are the ideal situations. Subjects and study personnel are blind to the treatment assignments and to any study events or information that might influence outcome assessments. Single blind methods blind either the examiner or the patient. When procedures are performed, the persons who examine subjects for outcomes or collect data from subjects should not be the same individuals who perform the procedures. Those who collect data should be blind to the hypotheses of the study.

2. Treat all subjects the same:

Specific methods for delivery of interventions, data collection and analyses should be determined before initiating an investigation. These protocols should assure that study participants in both treatment and control groups are treated and assessed equally. Doing so requires that the same follow up regimen, follow-up data, and tests be performed on all subjects.

Bias can result if patients with complications must alter follow-up regimens because the follow up examinations were not scheduled frequently enough. Subjects with less tolerance or with more complaints have potential for more frequent follow-up and have the potential of being evaluated differently. It is likely that more data will be gathered on these subjects. Pertinent data may be missed on subjects who return sporadically; their complications and improvements may need to be assessed by history taking rather than by examiner observation. The inequities in such data gathering should be recognized as potential biases.

3. Calibration and training of examiners:

Innumerable studies are available in the health care literature that specifically test the level of agreement among multiple examiners who are evaluating a clinical test, making a diagnosis, reading radiographs or measuring outcomes. Various indices of agreement have been formulated based on percentage, probabilities, correlation coefficients, the kappa statistics (κ) and others.

The κ **statistic** is preferred because it provides for an adjustment of agreement beyond chance and is appropriate for category scales and continuous data. It has been estimated that for many medical decisions clinical agreement is at a suboptimal level, with κ below 0.35. It has been proposed that κ less than 0.4 is poor agreement, κ 0f 0.40 to 0.75 is fair to good agreement, and κ above 0.75 to 1.00 is excellent agreement.

4. Accounting for all subjects:

It is disconcerting to an investigator to have subjects not complete a study. It is important to determine the characteristics of the subjects who left the study and to perform another analysis of the remaining subjects to determine if the two groups are still equivalent in the variables that might influence the treatment effect. In addition, one should determine if the dropouts are more common in one group than the other. Investigations are often undertaken to determine differences in treatment outcomes that are usually quite small. Often, the difference in outcomes between the therapies is only 10%. Loss of subjects will reduce the statistical ability to detect these small differences in outcome. Losing only 10% to 15% of subjects can render a study inconclusive.[24]

PUBLICATION BIAS IN HEALTHCARE RESEARCH

Bias can exist at all stages of the research process but an important, and often forgotten bias is whether research material becomes fully published within a readily accessible medium such as a journal.

Publication bias has been defined as the tendency on the part of investigators to submit, or the reviewers and editors, to accept manuscripts based on the direction or strength of the study findings. This definition concentrates on the fact that the strongest and most positive studies are most likely to be published. However, a better and broader definition of publication bias is that it is any influence that reduces the amount of good science appearing in the literature.

The most common method of assessment of publication bias is to review the publication rate of research originally presented at specialty conferences, and meetings. Although this provides baseline knowledge of the publication rates it is likely to underestimate the publication bias of all the research conducted in a particular speciality as the number of conferences and presenters is limited compared with the overall number of active researchers.

Time lag bias:

There is often an interval between presentation of research findings at a scientific meeting and publication of a full report. This may be due to final collation of results, delay in writing up, time taken for peer review and correction of reports, or simply journal's publication backlog. If such a time lag becomes 'excessive' it can produce another form of publication bias by delaying the appearance of relevant results and depleting the pool of available current research findings. This may also skew the significance of results, as trials with positive results are likely to be published before those with negative findings. Studies published late have the potential of being obsolete because they have been superseded by more recent publications. From the published literature it would seem that an acceptable time

limit is 30 months and after this the research publication could be considered delayed.

Publication language bias:

Language can also prove to be a barrier to the publication and collation of salient research findings. Papers submitted in English may be published more frequently than those of another language.

Egger et *al.,* looked at pairs of randomised controlled trial reports published in German and English. No differences were found between the German and English language papers with regard to design characteristics and quality of the reports. However, a greater proportion of the articles published in English (62%) reported significant differences with the outcome compared with those that had been published in German (35%). If only reports written in English are included in reviews and meta-analyses, then the inferences could be skewed by the predominance of positive results. It is recommended that all trial reports (irrespective of language) should be included in systematic reviews to increase the precision and reduce the number of systematic errors in future reviews.

Why is publication bias important?

1. Development of a biased pool of evidence
If there is a failure to publish current research or a delay in publication it is possible to develop a biased pool of evidence. Analysis of this evidence could then yield biased conclusions in systematic reviews and the point estimate of effect in meta-analyses.
2. Complete assessment of the evidence
Only when we have access to the full report do we have the potential to evaluate the research methodology and determine the usefulness of this research in rel ation to the whole body of evidence.
3. Publication as an ethical imperative
Despite negative findings, publication of 'good' research can prevent to duplication of effort, or provide a baseline methodology which can be adapted or improved.

Factors affecting publication bias*:*
A number if reasons have been cited for publication bias, including:

- Poor quality of research design
- Small sample size

- External funding
- Negative findings
- Failure of authors to submit manuscripts
- Rejection of manuscripts by journal editors

Conclusion:
Publication bias in medical specialities has been shown to influence the estimate of treatment effect. The level of publication bias and time lag to publication appear to be the same in dentistry as medicine. Systematic reviews of dental interventions are therefore just as likely to be affected by publication bias as medical ones.

HIERARCHY OF STUDIES

The quality of various research designs can be placed in a "***research design hierarchy***." The position of each research design within the hierarchy is a function of the strengths and weaknesses of features within each design. Many research designs are available in health care research, and there are ideal research designs to answer particular clinical questions. When the ideal design is used, the strength of the conclusions is great and this report exemplifies the "best available evidence" for making a treatment decision.

Understanding "strength of evidence" is at the heart of evidence-based health care. By using this hierarchial analysis of the research that comprises the relevant clinical literature, clinicians can ultimately determine a treatment plan based on the best-available evidence. This hierarchial analysis will also be relevant for study designs concerning the cause of disease, where exposure to a causal agent or event precedes the decision.

Consideration of the quality of any research requires an assessment of internal validity and lack of bias in the study.

Internal validity is defined as the correctness of the study results for the study population. It is influenced by how well the methods, outcome measurement, and data analyses are carried out in the study. A study's internal validity is threatened by bias and random variation. When selecting articles to offer best evidence, the question "Are the results valid" is answered by examining the control of bias and its effect on internal validity.

External validity, also called generalizability, relates to the ability to generalize the findings in the sample population to the general population. It is also a prime consideration for the practitioner asking the question, "Will the results of this study help me in caring for my patients?" External validity is what allows the observations from the study to hold true in other clinical settings. To be certain that a research report is relevant to the clinician, it requires that the report clearly define the patient population.

The higher the study design ranks in the research hierarchy, the better the study design minimizes bias and distributes random variation equally between the study groups. [25]

HIERARCHY OF STUDIES: EVIDENCE BASED VALUE

I. Studies with the highest level of evidence base
   A. Studies that review multiple, double blind, randomized design, clinical trials using clear, published selection and analytic approaches.
   B. Meta-analytic studies that combine multiple, double blind, randomized design clinical trials
   C. Multisite, randomised, small, well designed clinical trials

II. Studies with next level of evidence base
   A. One or more well designed, double-blind, randomized clinical trials.
   B. Experimental field studies in which subjects are randomly selected, sites are well matched, evaluators are well calibrated and experimental manipulations are carefully documented and systematic

III. Systematic, well–controlled, longitudinal studies with careful sampling
   A. One or more well-conducted cohort studies
   B. One or more well-conducted case-control studies

IV. Systematic, noncontrolled studies
   A. Surveys with random sampling (e.g. census)
   B. Cross-sectional studies with careful random selection and clear exclusion rules
   C. Longitudinal studies that control for attrition
   D. Field studies: descriptive and demographic studies
      i. With calibrated examiners
      ii. Careful sampling techniques
      iii. Natural experiments with random selection of sample

V. Dramatic uncontrolled field observations or experiments

VI. Expert committees, task forces, professional reports

VII. Studies with the lowest level of evidence base
   A. Case studies
   B. Editorials and articles in non-peer reviewed journals
   C. Opinion pieces

The strongest evidence is replication of the study findings. Independent replications provide clear evidence that the finding is not just a random event. The researcher demonstrates that the finding is not just an artifact of a single study but a consistent event.

Systematic reviews of research findings (meta-analysis) represent this improved level of evidence when the guidelines for study selection and statistical complication are followed. Systematic replication of findings using controlled studies provides evidence for the stability and validity of the reported phenomena. By combining randomized, selected studies (or the universe of available studies) from a pool of studies meeting explicit, predetermined, experimental design criteria, the researcher can counteract and eliminate bias that occurs in each individual study reviewed.

Randomized, controlled trials represent the next highest level of evidence. This level of evidence is supported by single (nonreplicated) experimental studies in which the experimental and control conditions are clearly specified and in which assignment to the experimental and control conditions is random.

Epidemiologic surveys in which the population is sampled systematically (random, stratified sampling) and the observers are calibrated serve as the next level of evidence.
Nonrandomized studies with controls such as case controlled studies and field studies form the next level of evidence. Studies using historical controls but using randomized sampling or selection serve as the next level. Cohort studies in which disease like assignments are made using correlational analysis are next in terms of evidence. Case reports and related anecdotal or descriptive evidence are next. Finally, the reports of expert committees and the opinion of experts form the lowest level of evidence.[29] **(Figure 9)**

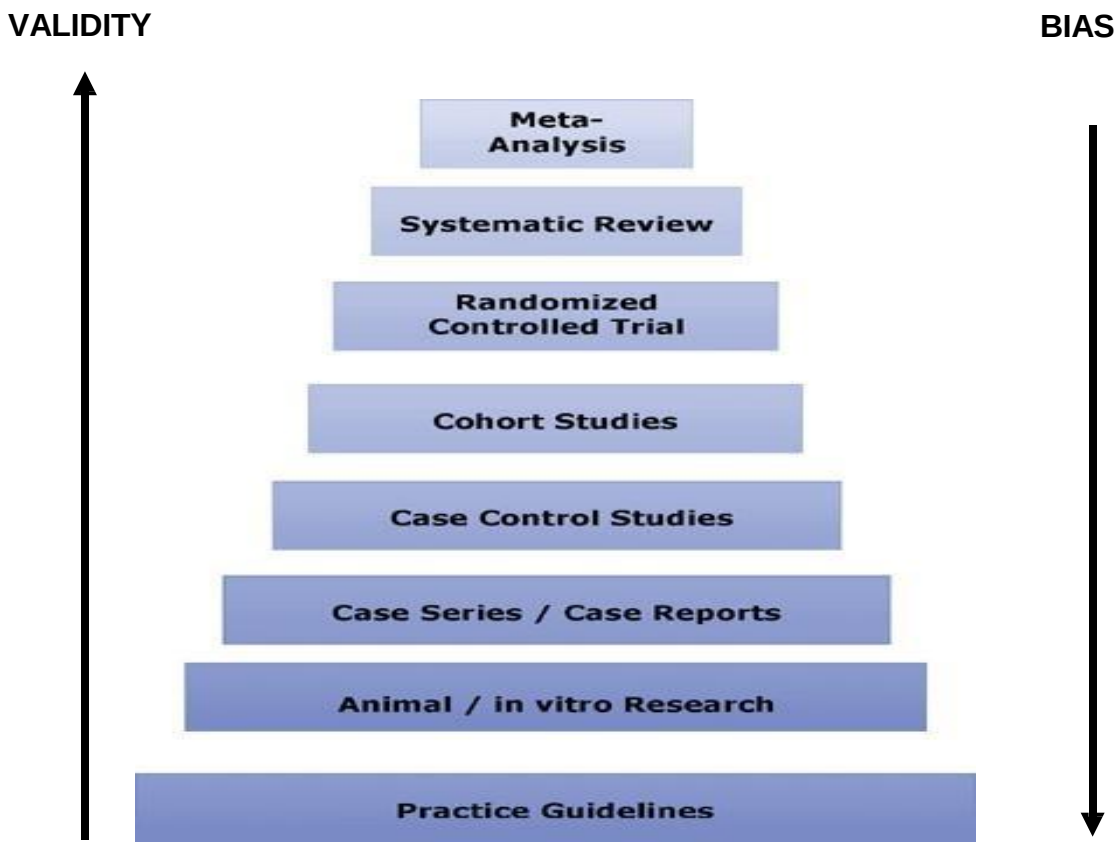


Figure 9: Evidence Hierarchy Pyramid

Systematic review is an overview of primary studies which contains an explicit statement of objectives, materials, and methods and has been conducted according to explicit and reproducible methodology.[30] When the results of primary studies are summarised but not statistically combined, the review may be called a **qualitative systematic review**. A quantitative systematic review, or **meta- analysis**, is a systematic review that uses statistical methods to combine the results of two or more studies. The term "**overview**" is sometimes used to denote a systematic review, whether quantitative or qualitative. Summaries of research that lack explicit descriptions of systematic methods are often called **narrative reviews**.

Differences between systematic and narrative reviews:

All reviews, narrative and systematic alike, are retrospective, observational research studies and are therefore subject to systematic and random error. Accordingly, the quality of a review- and thus its worth- depends on the extent to which scientific review methods have been used to minimize error and bias. This is the key feature that distinguishes traditional narrative reviews from systematic reviews (Table 5).

Table 5

Differences between narrative reviews and systematic reviews

FEATURE	NARRATIVE REVIEW	SYSTEMATIC REVIEW
Question	Often broad in focus	Often a focused clinical question
Sources and search	Not usually specified, potentially biased	Comprehensive sources and explicit strategy
Selection	Not usually specified, potentially biased	Criterion-based selection, uniformly applied
Appraisal	Variable	Rigorous critical appraisal
Synthesis	Often a qualitative summary	Usually evidence-based
Inferences	Sometimes evidence-based	Usually evidence-based

Most narrative review articles deal with a broad range of issues related to a given topic rather than addressing a particular issue in depth. For example, a narrative review on diabetes (such as that which might be found in a textbook chapter) might include sections on the physiology and pathophysiology of carbohydrate, lipid, and protein metabolism; the epidemiology of and prognosis associated with diabetes; diagnostic and screening approaches; and preventive, therapeutic, rehabilitative, and palliative interventions. Thus, narrative reviews may be most useful for obtaining a broad perspective on a topic; they are less often useful in furnishing quantitative answers to specific clinical questions.

Narrative reviews are appropriate for describing the history or development of a problem and its management. Narrative reviews may better describe cutting-edge developments if research is scant or preliminary or if studies are very limited by flawed design or execution. They may be particularly useful for discussing data in light of underlying theory and context. Narrative reviews can draw analogies and can conceptually integrate two independent fields of research, such as cancer and the acquired immunodeficiency syndrome.

However, the connection between clinical recommendations and evidence in narrative reviews is often tenuous, incomplete, or- worse still- based on a biased citation of studies. As a result, recommendations found in narrative reviews published in journals and textbooks often differ from recommendations found in systematic reviews. For example, narrative reviews may lag behind by more than a decade in endorsing a treatment of proven effectiveness, or they may continue to advocate a therapy long after it has been shown to be useless or harmful. Also, systematic reviews that incorporate quantitative techniques are more likely than narrative reviews to detect small but clinically meaningful treatment effects.[31]

The report of a systematic review is somewhat like that of a research paper; it contains a clear description of the aims, and the material and methods used by the reviewer. The alternative haphazard non-systematic review has no defined rules concerning the process of digesting the mass of information, and is open to abuse.[32]

Anatomy of a systematic review:

The specific features that illustrate the systematic approach and improve the chance of providing the best synthesized evidence are

- Preparation of a detailed research protocol that outlines the clinical question of interest
- Selection of criteria for inclusion of articles in the review
- Systematic search of relevant published and unpublished research
- Determination (by two reviewers) of articles that meet predefined inclusion criteria
- Critical appraisal of the quality of selected articles
- Extraction of outcome data from the selected articles
- Data combination (where appropriate) to synthesize and summarize the best evidence
- Report of findings relative to the knowledgebase and new questions raised by the findings [33]

F*ormulating questions and locating primary studies for inclusion in systematic reviews*:

A good systematic review is based on a well- formulated, answerable question. The question guides the review by defining which studies will be included, what the search strategy to identify the relevant primary studies should be, and which data need to be extracted from each study. Ask a poor question and you will get a poor review. A clear question also helps the reader rapidly assess whether the review is relevant to his or her own clinical practice.

Where Do Questions Come From?

Questions arise constantly in routine clinical practice, provided that clinicians a re prepared to admit their own level of uncertainty or lack of knowledge. The most relevant questions are often asked directly or indirectly by patients. Most clinica l encounters generate questions about diagnosis (“ What do I have, doctor?"), etiology ("Is it because I did X?”), prognosis (“How long do I have?"), or treatment or prevention (“Will Y do me any good?”).

Choosing an Important Question:

The number of possible questions for systematic reviews is limitless, but the time and resources with which to answer them are limited. Therefore, researchers who undertake systematic reviews must choose the most important questions. This is difficult because the importance of a question varies according to the perspective of the person asking it. For example, individual patients will probably regard questions about their conditions as the most important, regardless of how common or severe that condition is, whereas cardiologists will prefer questions about ischemic heart disease to those about migraine. Cancer and vascular disease are particularly important to persons in developed countries, whereas infectious diseases are more important to persons in developing countries. These differences highlight the need for each specialty to organize its own systematic reviews. Several factors should be considered when setting priorities for doing systematic reviews **(Table 7)**. [34]

Table 7: Factors to Consider When Determining the Importance of a Question as the basis for a Systematic Review

Disease or condition	**Intervention**	**Ability to Change Practice**	**Feasibility of Assessment**	**Other**
Effect on the patient or caregiver	Frequency of use or potential for use	Uncertainty of benefit or variation in practice	Availability of data	Interest and enthusiasm of reviewers
-Severity (mortality, morbidity, quality of life)				
-Duration				
-Financial cost (such as loss of earnings)				
Effect on society	Financial cost	Degree of established preferences	Financial cost	Degree of innovativeness
- Prevalence				
- Severity				
- Financial cost (such as lost production)		Timing (such as time since introduction of new practice or technology) Motivation to change		Topicality Ethical, social, and political considerations

Formulating the Question:

Having decided that a question is worth asking, the next step is to formulate it adequately. Clinical questions should have four basic components: the type of person involved, the type of exposure that the person experiences (be it a risk factor, prognostic factor, intervention, or diagnostic test), the type of control with which the exposure is being compared, and the outcomes to be addressed.

A clearly formulated question helps define the criteria that studies must meet to b e included in the review. These inclusion criteria can be divided into five categorie s, shown in **Table 8.** Each component must be carefully defined to strike a balance between making the definition too specific to be workable and making it too broad to be useful.

Table 8

Categories of Inclusion Criteria	*Subcategories*
Type of Person	**Disease or Condition**
	- Definition
	- Cause
	- Stage
	- Severity
	Personal Characteristics
	- Age
	- Sex
	- Symptoms
	Population or Setting
	- Community
	- Hospital (outpatient or inpatient)
Type of Exposure	- Definition
	- Intensity or dose
	- Timing
	- Duration
	- Method of delivery (group therapy or individual therapy, oral therapy or intravenous therapy)
Type of Control	- Absence of risk or prognostic factor (risk and prognostic reviews)
	- Gold standard test (diagnostic reviews)
	- Treatment controls (treatment and prevention reviews)
	- Active treatment or no treatment
	- Placebo control or open control
Type of Outcome	- Importance to patient
	- Clinically relevant or surrogate
	- Death, quality of life, disability, and symptoms or signs
	- Beneficial and harmful effects of interventions
	- Use of health care resources (economic evaluations)
	- Definitions
	- Timing of outcome assessment
Type of Study Design	- Experimental or observational
	- Randomized or nonrandomized controlled trials
	- Blinded or open trials
	- Confounded or unconfounded studies
	- In a comparison of treatment A versus no treatment, a trial of treatment A and treatment B versus no treatment is confounded by treatment B, whereas a trial of A and B versus B alone is not confounded.

How Broad Should the Inclusion Criteria Be?

The scope of the question and, hence, the inclusion criteria can be relatively broad or narrow. The choice of inclusion criteria depends on several factors. Questions must be clinically relevant: A broad question ("Has chemotherapy improved cancer survival?") will not help a clinician manage a patient with a particular tumor because of marked differences in the responses of different tumors. Inclusion criteria must also be clinically sensible.

If certain features of the patients or exposures are believed to significantly affect outcome, these features must be taken into account. Narrow inclusion criteria limit the amount of data in the review and thereby increase the risk for false-positive and false-negative results. A narrow question can be regarded as a subgroup of a broader question and can lead to the same problems generally found in subgroup analysis. Narrow inclusion criteria also preclude studying appropriate and clinically important subgroups in the context of a larger data set. Broad inclusion criteria increase the risk for finding heterogeneity (that is, significant variation in the results of different studies), thereby making analysis and interpretation of the results more difficult. If no heterogeneity is found even when broad inclusion criteria are used, the results are more generalizable. Heterogeneity among studies can be useful, however, because it allows the researcher to study what caused it and generate new hypotheses. Broad reviews can summarize large amounts of information in a single article; this may be more useful for readers but may require greater resources.

Although the inclusion criteria must be set before data collection begins, they should be flexible, provided that care is taken to avoid making changes that would be likely to introduce bias. Inclusion criteria should not be changed on the basis of the results of individual trials. It may, however, be reasonable to change the criteria if alternative, acceptable ways of defining the study population or intervention are discovered. Narrow criteria may also need to be broadened or broad criteria may need to be narrowed, depending on the amount of data found.[34]

***Checklist of data sources for a systematic review*:**

- *Medline database*
- *Cochrane controlled clinical trials register*
- *Other medical and paramedical databases*
- *Foreign language literature*
- *"Grey literature" (theses, internal reports, non-peer reviewed journals, pharmaceutical industry files)*

• *References (and references of references, etc) listed in primary sources*

• *Other unpublished sources known to experts in the field (seek by personal communication)*

• *Raw data from published trials (seek by personal communication)*

Assigning weight to trials in a systematic review:

Each trial should be evaluated in terms of its:

Methodological quality- the extent to which the design and conduct are likely to have prevented systematic errors (bias).

Precision- a measure of the likelihood of random errors (usually depicted as the width of the confidence interval around the result).

External validity- the extent to which the results are generalisable or applicable to a particular target population [30]

Searching for relevant articles:

A comprehensive search will probably yield many articles not useful for review. An article may be unsuitable because it does not directly relate to the question of interest or because a certain study design is methodologically too weak to provide valid information. The authors should clearly describe how the articles were chosen and, the method used applying methodologic criteria. Such criteria will not always produce studies that are valid, so a validity assessment is also necessary so that the review will be based on data that are as free from bias as possible. Guidelines for such assessment are available in dentistry for clinical questions that address diagnosis, prognosis, and treatment (Users' guides to dental literature). Such guidelines should be applied and reported in sufficient details to allow readers to assess the validity of the primary articles.

Even with the use of methodologic guidelines, assessments can be unreliable and biased. Such assessments can affect both the inclusion and validity assessment of the primary studies. As a safeguard, the primary studies should be assessed by at least two reviewers, each blind to the other's decision. The level of disagreement should be known, and the rules to reach consensus should be reported. To protect from the bias associated with a lack of blindness, the information regarding the institution and authors associated with the primary research can be removed before assessment for inclusion and validity.[33]

Obtaining data from randomized controlled trials for use in systematic review:

Complete identification of published and unpublished trials

The most important step in the conduct of any systematic review of randomised controlled trials is to identify and include all (or nearly all) of the relevant trials. This is needed whether the review is to be based on aggregate or individual patient data. Meta-analysis based on individual patient data always require direct contact with trialists (as do some review based on aggregate data), so these provide an additional means of identifying trials- enlisting the help and knowledge of those trialists.

Obtaining information on all randomised participants and excluding information on those who were not randomised.

All randomised patients should be included in the analysis in accordance with the treatment allocated at randomisation (an "intention to treat" analysis). In this way, the policy of using one treatment will be appropriately compared with the policy of using another. Many published papers will state that some patients have been judged ineligible and omitted from the analysis, and the people rerviewing the paper will be aware of the size of the problems this might cause. A more difficult problem arises if a publication contains no mention of randomised but ineligible patients, usually because the trialist considers these patients are no longer part of the trial. Occasionally, some non-randomised patients are included in a trial's published analysis- then it is important that these patients are excluded from the meta-anaysis. This can happen if a randomised trial was preceeded by a non- randomised run in phase, or if patients continue to be entered to one of the study's treatments after the randomisation has been closed. It can also happen if the randomisation is temporarily stopped during the trial.

Obtaining complete and unbiased information on all subgroups and outcomes studied

A trial that collects information on a variety of patient characteristics can have as many subgroup analysis as there are types of patients in the data. Constraints on space and other influences make it most likely that the analysis relating to the subgroups with the most striking results will be published. Thus, any subgroup analyses in a systematic review that uses only those subgroups available in published reports will be subject to both the effect of publication bias in the trials available for inclusion and an additional bias in the subgroups available for analysis. Similarly if a trial measures several outcome measures there will be a tendency for those showing the most striking results to be published. With regard to outcome measures, it may be possible to specify a uniform definition for a particular outcome and analyse this across all trials. It is worth remembering that whether or not a subgroup or outcome can be analysed will depend on its initial collection by the trialist (a decision that could not have been biased by the trial's

own results) and on the willingness of the trialist to supply data on that variable - a problem that can happen with any of the data or trials in the meta-analysis.

Obtaining complete follow up data

Whenever the results of a trial are published, those results become "frozen in time" and will usually remain so unless the trial is updated and published again, which happens rarely. The supply of information for a meta-analysis is another way in which the trial's results can be updated, both by providing additional follow up and by completing data that were missing at the time of publication.

How to obtain data that are as complete as possible:

Whether the information on the participants in the relevant randomised trials is collected as aggregate data or individual patient data, it must be collected from as many trials as possible. The data collection process may present the reviewer with several difficulties. Some trialists may be reluctant to supply their data, and there will often be practical difficulties in preparing data. It is important therefore to emphasise that any data supplied will be treated confidentially and will not be used for any additional purpose without the permission of the responsible trialist. In addition, any publications arising from the meta-analysis should be in the name of all the collaborators, and each trialist should have an opportunity to comment on the manuscript before publication. The trialists will also be the first people, other than the statistical secretariat, to see and discuss the overview results if these are presented first to a closed meeting of the collaborative group of all participating trialists. The process of data collection should be as simple and flexible as possible so as to help and encourage trialists to participate. In some instances, even if the initial request was for aggregate data it may be easier and preferable for the trialist to supply individual patient data so that the necessary tables can be prepared centrally.

***Benefits of using individual patient data rather than aggregate data*:**

1. Calculation of times to events

Perhaps the most substantial benefit is that it is not possible to calculate and analyse the times to specific events reliably without individual patient data. Such analysis might reveal prolongation of event free periods or differences in median survival for the treatments being compared. In addition, the time to event analyses contribute greater statistical power than is possible with the limited number of time points that would be available with aggregate data.

2. Checking and correcting data

The requirement for individual patient data can help to serve as a check on the use of fabricated data, either from a complete trial or part of a trial. Much more commonly, the central review of patient data will highlight problems with a

randomised trial that occurred through error rather than fraud, these mostly arise during the process of randomisation itself or in the follow up of patients in the treatment groups.For example, the individual patient data might reveal the exclusion of randomised participants or the inclusion of some who were not randomised. In either case the data on the missing patients could then be requested from the trialist, or the inclusion of additional non-randomised patients could be queried. Once all of the data are available, the appropriate intention to treat analysis can be performed.

3. Supply of additional patient data

If individual patient data are collected it is relatively easy for a trialist to supply additional follow up information or previously missing data on selected patients and for this to be incorporated in the meta-analysis, but if aggregate data were collected the trials would have to produce a new set of tables. [35]

A systematic review serves various purposes:

1. *It reduces a large amount of information to a manageable size. This information can be assimilated quickly by healthcare providers, researchers and policy makers. At the initial stage, the systematic review distinguishes between those studies that are essentially unsound and those that provide useful and scientifically worthwhile results in relation to the question of interest.*
2. *By combining the results from various studies which may have been conducted in slightly varying circumstances (e.g.using different definitions of disease or patient eligibility criteria), it may be possible to determine from the systematic review whether the results are consistent from study to study, and to generalise the results. Furthermore, a systematic review may offer the opportunity to explain any inconsistencies.*
3. *It is usually cheaper and quicker to conduct a systematic review than to embark on a new study.*
4. *It may reduce the delay between research discoveries and the implementation of new effective treatment strategies.*
5. *The systematic review combines information from individual studies so that its overall sample size is greater than that of any one study, and this leads to an increase in the power of the investigation. Thus, the systematic review has a greater chance of eliciting significant treatment effects, which is particularly helpful if the prevalence of the condition is low or if the effect of interest is small.*
6. *The systematic review has an increased sample size compared with any individual study so the estimates of the effects of interest are obtained with increased precision.*

A systematic review limits bias and improves the reliability and accuracy of recommendations because of its formalised and thorough method of investigation.[32]

META-ANALYSIS

What is meta-analysis? A useful definition was given by **Huque**: "A statistical analysis that combines or integrates the results of several independent clinical trials considered by the analyst to be 'combinable'. [36]

Meta-analysis applies scientific strategies that limit bias to the systematic identification and collection, critical appraisal, and synthesis of all relevant studies on a specific topic. It uses statistical methods to combine and summarize the results of several studies. Meta- analysis are therefore useful tools in decision-making and health technology assessment. Meta-analysis (also spelled *met-analysis* and *meta-analysis*) may be referred to in the literature under a number of synonyms, including *statistical overview*, *quantitative synthesis*, *combining*, *pooling*, and *weighted averaging*.[37]

Cumulative meta-analysis:

Cumulative meta-analysis is defined as the repeated performance of meta-analysis whenever a new trial becomes available for inclusion. Such cumulative meta- analysis can retrospectively identify the point in time when a treatment effect fir st reached conventional levels of significance.Another application of cumulative meta-analysis has been to correlate the accruing evidence with the recommendations made by experts in review articles and textbooks.

History of meta-analysis*:*

Efforts to pool results from separate studies are not new. In his account on the preventive effect of serum inoculations against enteric fever, statistician Karl Pearson, was in 1904 probably the first researcher reporting the use of formal techniques to combine data from different samples. The rationale put forward by Pearson for pooling studies is still one of the main reasons for undertaking meta-analysis today: "Many of the groups…are far too small to allow of any definite opinion being formed at all, having regard to the size of the probable error involved."The first meta-analysis assessing the effect of a therapeutic intervention was published in 1955; interestingly, the treatment being evaluated was the placebo. The development of more sophisticated statistical techniques, however, took place in the social sciences, in particular in education research, in the 1970s. The term meta- analysis was coined in 1976 by the psychologist Glass.[36]

In oral health care, the first meta-analysis indexed in the Medline database was published in 1989; it evaluated the effectiveness of tolonium chloride in oral cancer screening. This was followed shortly thereafter by a meta-analysis that investigated the effects of different fluoride delivery systems.[37]

Reasons *(advantages)* for performing meta-analysis*:*

Because of the small number of patients in many clinical trials, studies often do not have enough statistical power to assess the statistical relationships between interventions and

outcomes. Combination of the results of a number of small studies may increase the statistical power to detect small to moderate but significant effects. Meta-analysis may allow a single estimation of the effect of an intervention in the face of contradictory results from different studies assessing outcomes for the same intervention. The summarizing effects of meta-analysis provide a method for dealing with the explosion of information that has been seen in recent decades, thus providing a comprehensive overview of results in a given area of research. Through the rigorous process of identification of all existing data relevant to a particular topic, meta-analysis may be useful to quantify existing levels of data, thereby identifying areas in which questions have already been answered, and to identify data gaps in particular areas of research. Thus meta-analysis can assist in the planning of future research.

Some government guidelines recommend meta-analysis as the preferred method of summarizing evidence of effectiveness and safety of health technologies in the face of multiple study results. Clinicians, policy-makers, and consumers can all potentially benefit from an increased understanding and application of meta-analysis. The alternative to meta-analysis, the standard narrative review, is fraught with problems and is regarded as an inadequate quantitative method of summarizing the effects of intervention.[37]

Meta-analysis can also contribute considerations about the generalisability of study results. The findings of a particular study may be valid only for a population of patients with the same characteristics as those investigated in the trial. If many trials exist in different groups of patients, with similar results in the various trials, then it can be concluded that the effect of the intervention under study has some generality. By putting together all available data, meta-analyses are also better placed than individual trials to answer questions about whether an overall study result varies among subgroups- for example, among men and women, older and younger patients, or subjects with different degrees of severity of disease.

Meta-analysis thus not only consists of the combination of data but includes the epidemiological exploration and evaluation of results- the "epidemiology of results", whereby the findings of an original study replace the individual as the unit of analysis. New hypothesis that was not posed in the single studies can thus be tested in meta- analysis. Meta-analysis can also lead to the identification of the most promising or urgent research question, and may permit a more accurate calculation of the sample sizes needed in future studies.

The benefit of meta-analysis is that it renders an important part of the review process transparent. In traditional narrative reviews it is often not clear how the conclusions follow from the data examined.[36]

Steps involved in performing a meta-analysis:[37]

1. ***A priori definition of meta-analysis protocol-***

The meta-analysis must address a specific clinical question, which subsequently influences the type of studies that will be relevant and the type of data to be synthesized. The question(s) to be answered by the meta-analysis should be formulated in terms that address parameters of clinical significance, such as effectiveness and safety outcomes. It must specify the study identification and retrieval methods to be used, as well as criteria for study inclusion or exclusion from the meta-analysis. The reason(s) for inclusion or exclusion of study assessed must be explained. The methods by which decisions on inclusion or exclusion from the meta-analysis were made must be transparent, and the results must be reproducible. The protocol must specify the data to be abstracted from each source and the form the abstracted data must take- i.e., a standardized data extraction form must be developed. The protocol must specify the method of source quality rating. Any changes to the protocol after the commencement of the meta-analysis process should be reported and clearly justified.

2. *Study search and data identification-*

The main goal of the study search is to identify all appropriate and relevant data, published and unpublished, for possible inclusion in the meta-analysis. Sources available for searching include electronic databases such as Medline, Grateful Med, Embase, and Cancer-Lit. Each of these electronic databases differs from the others in content, time frame covered, and primary focus. Medline, for example, focuses mainly on clinical medicine journals published since 1964; Embase, on the other hand, indexes journals, conference proceedings, books and dissertations since 1974. Review articles, conference proceedings, symposia proceedings, industry reports, books, memoranda from expert consultations, and results of manual searching of literature lists of retrieved articles should be scanned for additional potential data sources. In cases in which language limitations have been applied to the search, the nature of these restrictions must be specified.

3. *Data extraction-*

Data extraction should be performed by 2 or more blinded extractors following a written protocol. Multiple extraction, in which 2 or more investigators abstract the data from each study independently and compare their results on completion, facilitates reproducibility of the data extraction process, identifies data entry errors, and identifies areas of ambiguity or confusion, which may be resolved through discussion at the completion of data extraction. The method of data extraction must be documented a priori, and extraction should be completed through use of a standardised data extraction form. Such a form is used to record and present the extracted data in a systematic way under the broad headings of a summary of trial characteristics, effectiveness parameters, clinical safety parameters, and laboratory safety parameters; it should also include the source quality rating score.

4. *Quality assessment of retrieved articles-*

Each data source should be assessed in terms of the quality of the data presented. Source quality rating should be performed through use of a validated standardised score that assesses the quality of study design, statistical analysis of the effectiveness and safety parameters, and presentation of the study results. The source quality rating score can be used to exclude studies with quality scores below a certain predefined value, or it can be used as a weighting factor in the analysis.

5. *Tests for heterogeneity-*

A group of studies is considered to be homogenous if all of them are attempting to estimate or observe the same true effect or if variability between the results of the different studies is due to random error only (intrastudy variability). Heterogeneity occurs when the true effect differs between studies and is therefore represented by a distribution of values rather than a single number. A statistical test for heterogeneity calculates the probability that differences between the observed results of the individual studies could have occurred by random variation alone. If that probability is below a certain level- e.g., if it is less than 0.05- then the studies are said to be heterogeneous. A statistical definition of significant heterogeneity (e.g., $P<.05$) should be specified a priori; an assessment of heterogeneity of the studies included in the meta-analysis should be then made through use of an appropriate statistical test, such as the chi-square test. Where significant heterogeneity is found to exist, the sources of heterogeneity should be identified and explained.

6. *Statistical combination of data-*

The statistical analysis of the data abstracted from the studies included in the meta-analysis should cover all the relevant and clinically useful measures of treatment effectiveness and safety and should be expressed in terms of a clinically meaningful outcome, such as odds ratio, relative risk, absolute probabilities, or number needed to treat (i.e., how many patients need to be treated to prevent one patient from experiencing an event). The type of statistical model used should reflect the nature of the trials analysed, and the use of a fixed-effects or random- effects model should be specified and justified. The fixed-effects method provides an estimate of single underlying effects, taking only intrastudy variability into account when calculating pooled values weighted by study size. It assumes that all studies are observing the same true effect and that variability is due to random error only. The random- effects model, which takes intrastudy variation into account, provides a more conservative estimate (usually with wider confidence intervals) and may be used when included studies are more heterogeneous in nature. The random-effects method assumes that the true effect differs between studies and is therefore represented by a distribution of values rather than by a

single number. The results should be expressed with confidence intervals and should include an analysis and statement of the significance level of the results obtained.

7. *Tests for publication bias-*

Publication bias arises whenever studies with positive and/or statistically significant results are more likely to be published than those with negative and/or nonsignificant results; it is brought about mainly by selective submission and acceptance/publication of papers. This may lead to an overestimation of the positive effects and an underestimation of the negative effects of interventions assessed.

8. *Sensitivity analysis-*

Sensitivity analysis should be performed to assess the robustness of the outcomes of the meta-analysis with respect to changes in the studies included. This can be performed in a number of ways, including assessment of the effect of sequential removal of trials identified as a cause of heterogeneity (outliers) and cumulative meta-analysis, in which the effects of adding studies sequentially to the meta- analysis on the basis of publication date, control group event rate, study size, size of differences between treatment and control, or study quality are assessed.

9. *Presentation of results-*

The results should include a structured summary or abstract. The key elements, including study design, number of patients starting and completing each included trial, form of treatment and treatment regime, and effectiveness and safety outcome measures of the individual studies included in and excluded from the meta-analysis, should be presented in tabulated form.

10. *Interpretation and discussion of the results-*

The results of the meta-analysis should be discussed in terms of current clinical practice. The strengths and weaknesses of both the individual studies included in the meta-analysis and the limitations of the meta-analysis itself should be acknowledged and discussed. The results of the meta-analysis and the power of these results should be discussed in the context of the results of the individual studies included and in comparison with other meta-analysis that have been performed.

When reading a meta-analysis and attempting to judge its quality, the reader can use the points listed a checklist of appropriate steps that should have been carried out by the study authors. The reader can use the minimum requirements for a good-quality meta-analysis listed in **Table 9,10** to further assist in judging the quality of a meta-analysis. If one or more steps have been omitted or if criteria have not been fulfilled, then the quality of the meta-analysis, and therefore the applicability of the results, conclusions, and recommendations drawn from it, may be called into question.

Table 9

Step	Description
1. A Priori Definition of Meta-Analysis Protocol	- Addresses specific question - Specifies study search procedure - Specifies inclusion/exclusion criteria
2. Study Search and Data Identification	- Multiple electronic database searching - Hand-searching - Reference list scanning - Consultation with experts
3. Data Extraction	- Extracted by more than 1 person following written protocol - Using standardized data extraction forms
4. Quality Assessment of Retrieved Articles	- Uses validated source quality rating score
5. Test for Heterogeneity	- Defines a priori significant level of heterogeneity - Uses relevant statistical test for heterogeneity (e.g., chi-square test) - Identifies/explains causes of significant heterogeneity - Uses random effects model if studies shown to be heterogeneous - Interprets results cautiously if studies heterogeneous
6. Statistical Combination of Data	- Justifies use of fixed or random effects model in presence/absence of heterogeneity - Calculates clinically relevant outcomes (e.g., odds ratio, relative risks, number needed to treat) - Calculates confidence intervals/measures of variance of outcomes
7. Tests for Publication Bias	- Funnel plots
8. Sensitivity Analysis	- Cumulative meta-analysis based on publication date, event rates, study size, effect size, study quality
9. Presentation of Results	- Includes tabulated summary of included/excluded trials - Tabulated and graphic presentation of results
10. Interpretation and Discussion of Results	- Interprets results in terms of current clinical practice - Discusses strengths and limitations - Discusses significance of results in comparison with individual included studies and other meta- analyses

Table 10:

Requirement	Description
Identification and Inclusion of All Relevant Studies/Data	- Exhaustive search for both published and unpublished data
Similar Treatments in Included Trials	- Are interventions comparable and results combinable? - Similar doses of drugs/intensities of interventions - Similar timing of administration of interventions
Comparable Patients in Included Trials	- Age - Gender - Disease duration - Disease severity - Coexisting illnesses - Concomitant medications influencing effectiveness and safety
Comparable Outcomes in Included Trials	- Studies assess same outcome measures of patient response - Outcomes must be measured by comparable methods
Similar Follow-up Lengths in Included Trials	- Decreasing effectiveness of interventions over time - Increasing dropouts because of ineffectiveness over time - Increasing percentage of patients experiencing side effects over time - Increasing dropouts because of side effects over time
Adequate Quality of Included Trials	- "Garbage in = garbage out"

Bias in meta- analysis:

The funnel plot test -

Funnel plots, plots of the trials' effect estimates against sample size, may be useful to assess the validity of meta-analysis. The funnel plot is based on the fact that precision in estimating the underlying treatment effect will increase as the sample size of the component studies increases. Results from smaller studies will scatter widely at the bottom of the graph, with the spread narrowing among larger studies. In the absence of bias, the plot will resemble a symmetrical inverted funnel. Conversely, if there is bias, funnel plots will often be skewed and asymmetrical.

***Sources of funnel plot asymmetry*:**

1. Selection bias
    a. Publication bias
    b. Location biases
        i. English language bias
        ii. Citation bias
        iii. Multiple publication bias

2. True heterogeneity
    a. Size of effect differs according to study size

    i. Intensity of intervention
    ii. Differences in underlying risk
3. Data irregularities
    a. Poor methodological design of small studies
    b. Inadequate analysis
    c. Fraud
4. Artefactual
    a. Choice of effect measure
5. Chance

Publication bias has long been associated with funnel plot asymmetry. Among published studies, however, the probability of identifying relevant trials for meta - analysis is also influenced by their results.

English language bias- the preferential publication of "negative" findings in journal published in languages other than English- makes the location and inclusion of such studies less likely.

As a consequence of *citation bias*, "negative" studies are quoted less frequently and are therefore more likely to be missed in the search of relevant trials. Results of "positive" are sometimes reported more than once, increasing the probability that they will be located for meta-analysis (multiple publication bias). These biases are likely to affect smaller studies to a greater degree than large trials.
Another source of asymmetry arises from differences in methodological qualities. Smaller studies are, on average, conducted and analysed with less methodological rigour than larger studies. Trials of lower quality also tend to show the larger effect.

The degree of asymmetry found in a funnel plot may depend on the statistic used to measure effect. Odd ratios overestimate the relative reduction, or increase, in risk if the event rate is high. This can lead to funnel plot asymmetry if the smaller trials were consistently conducted in patients with higher risk. Similarly, if even ts accrue at a constant rate, relative risks will move towards unity with increasing length of follow up. In large trials, follow up is often longer than in small studies. Finally, an asymmetrical funnel plot may arise by chance.

Very different mechanisms can thus lead to asymmetry in funnel plots, as summarised above. It is important to know, however, that this will always be associated with a biased overall estimate of effect when studies are combined in a meta-analysis. The more pronounced the asymmetry, the more likely it is that the amount of bias will be substantial. The exception to this rule arises when asymmetry is produced by chance alone.[38]

Disadvantages of meta-analysis:

In principle, a meta-analysis proffers the advantages of increased power, and increased precision of its estimates, when compared with a single study. In practice, the meta-analysis is open to criticism, essentially on four grounds:

1. Because journals rarely publish studies in which findings are non-significant, published research is biased in favour of significant results. A trial with a significant result is sometimes called a *positive* trial; a *negative* trial is one in which a clinically significant result is essentially ruled out. This publication bias leads to biased meta-analysis results unless the meta-analyst makes a serious attempt to identify and use the results in books, dissertations, unpublished papers presented at professional meetings or located in retrieval systems for unpublished papers (such as SIGLE produced by the European Association for Grey Literature), etc.
2. The studies included in the meta-analysis may differ in respect of features such as design, outcome measure, measuring technique, definition of variables and subjects, and duration of follow-up. Such clinical heterogeneity needs to be explored carefully as it may affect the overall conclusions and the clinical implications of the review. Generally, a meta-analysis of clinical trials is restricted to only those trials that are *randomised.* Additional requirements of blind or objective assessment of response, ideally with analysis by intention- to-treat and complete follow-up, are sometimes imposed. Such trials are less likely to lead to biased results than those which do not possess these attributes .
3. The studies included in the meta-analysis may vary in their quality, and it has been shown that a meta-analysis which comprises studies of high quality, as opposed to poor quality, tends to be less enthusiastic about an intervention. However, it can be argued that poorly designed or 'bad' studies should be included in the meta-analysis because of the inclusiveness of the method and the subjective nature of the considerations which might lead to their exclusion. The problem of including both 'good' and 'bad' studies can be handled empirically by conducting separate analyses for groups of studies of similar quality, and examining whether the results differ for poorly and well designed studies. Sometimes, the results from all the studies are combined by assigning weights to the studies according to their relative quality, but this approach can be criticised on grounds of the arbitrariness of the assignment.
4. The results included in the meta-analysis may not be independent. This situation arises when a multivariate study provides more than one test of significance relevant to the hypothesis that the meta-analysis is examining. Also, non-independence of the results may arise when the studies are conducted by the same investigator at different times, or by different investigators who have communicated with each other and modified their studies on the basis of earlier results. Furthermore, some trials are published more than once.[32]

Meta-analysis is a state-of-the-art method of summarizing the increasing amounts of the information that are generated from clinical research, but any meta -analysis shares the weakness of the original studies and also has a potential for bias because of the retrospective nature of the technique. Understanding the principles and methods involved in meta-analysis will help the dental practitioner to assess the value of meta-analysis encountered in the literature. When high-standard meta- analysis are used in clinical decision-making, an improvement in the quality of dental care may be anticipated.[37]

Conclusion:

Systematic reviews in the form of overviews or meta-analysis offer a solution for busy practitioners who have difficulty keeping abreast of current literature. Because systematic reviews can condense numerous studies into reliable and valid summaries of the best available evidence for a specific clinical problem, they offer significant benefit to busy clinicians.[33]

Systematic reviews can aid, but never replace, sound clinical reasoning. Clinicians reason about individual patients on the basis of analogy, experience, heuristics, and theory as well as research evidence. Awareness of a treatment's effectiveness does not confer knowledge about how to use that treatment in caring for individual patients. Evidence can lead to bad practice if it is applied in an uncritical or unfeeling way. Understanding the complex structure of medical decision making requires an appreciation of the ways in which knowledge, skills, values, and research evidence are integrated in each patient-clinician encounter.[31]

Twetman S et al[39] reported the findings concerning the caries preventive effect of **fluoride toothpastes** in non-selected populations of various ages with special emphasis on fluoride concentration and supervised versus non-supervised brushing.

Relevant literature was identified by searching the MEDLINE and Cochrane library databases using the following search terms: 'dental caries', 'fluoride toothpaste', 'fluoride dentifrice' and 'fluoride dental cream'.

It was decided not to include papers published prior to 1975 and the main reasons being: (i) the significant caries decline, making any generalization to the caries situation of today questionable and (ii) to sort out old toothpaste formulas and products no longer available or in use. Thus, a total of 77 papers were selected and ordered in full text. Data were extracted using a pilot-tested form and each article was assessed with a score A-C according to predetermined criteria for methodology and performance. Based on the evaluated literature, the level of

evidence was judged within the entire project group according to the protocol of the Swedish Council on Technology Assessment in Health Care (Table-11).
Out of the 77 papers that were critically assessed, 54 were included for evaluation of evidence.

Criteria for grading of assessed studies

Grade A:

All criteria below should be met:

Randomization by subject

Diagnostic reliability described

Baseline values described

Attrition explained, <10% per year

Blinded outcome assessment

Representative sample of population under study, results can be generalized.

Bias and confounders considered

Grade B:

All criteria below should be met:

Randomization by subject, school or class

Diagnostic reliability described

Baseline values described

Attrition explained, >10% per year

Blinded outcome assessment

Population under study defined, results cannot fully be generalized.

Bias and confounders considered

Grade C:

One or more of condition below should be met:

No or unclear randomisation

Diagnostic reliability not described

Baseline values not described

Attrition not explained or reported >10% per year

Non-blinded outcome assessment

Population under study not defined, results cannot be generalized.

Bias and confounders not considered

Table 11: Definition for level of evidence

Evidence level	Definition
1. Strong evidence	At least two studies assessed with level 'A'
2. Moderate evidence	One study with level 'A' and at least two with level 'B'
3. Limited evidence	At least two studies with level 'B'
4. Inconclusive evidence	Less than two studies with level 'B'

Effect compared with placebo:

The anti-caries effect of fluoride toothpaste in young permanent teeth was compared with placebo in 26 papers with an average prevented fraction of 24.9%.The mean number of saved DMFS/year was 0.58 (S ± 0.34). The number of saved tooth surfaces per year exhibited a statistically significant positive correlation with the baseline caries levels ($r = 0.542$, $P<0.01$). Seven of the included papers were assessed with score 'A'. There was thus strong evidence of a caries preventive effect of daily use of fluoride toothpaste compared to placebo in the young permanent dentition (evidence level 1).

Effect in the primary dentition:

Five studies concerning the caries preventive effect of fluoridated toothpaste in primary teeth were included in the evaluation. Rated with 'C', the results were clearly in favour of fluoride dentifrice in two of the three investigations. The findings from the available papers were suggestive and pointed in the same direction but only one was ranked with a 'B'. Thus, the evidence for caries prevention by fluoride toothpaste in the primary dentition was rated as inconclusive (evidence level 4).

Effect of supervised versus non-supervised tooth brushing:

Interventions dealing with supervised brushing displayed a higher preventive fraction than those with unsupervised interventions, both when compared to placebo (31.0 vs. 23.3%) and other fluoride-containing controls (12.0% vs. 3.9%). Four of the evaluated papers were assessed with grade 'A' and therefore we found strong evidence (evidence level 1) for the fact that supervised tooth brushing with fluoride containing toothpaste had a superior caries preventive effect over non supervised.

Influence of fluoride concentration:
Two questions were in focus regarding the possible dose-response relationship of fluoride in toothpaste. The first was whether or not toothpastes with a low fluoride content (<1,000 ppm) were as effective as standard dentifrices with 1,000 – 1,100 ppm and, secondly, whether those with higher fluoride were more effective. Four studies were considered for evaluation of the low fluoride issue in the young permanent dentition. Two C- rated papers displayed no significant differences between low fluoride and standard products, while two studies, scored 'A' and 'B', were in favour of the standard fluoride toothpastes. There was therefore limited evidence (level 3) for an anti-caries difference between low- fluoride and standard fluoride toothpastes in the young permanent dentition.

The evaluation of toothpastes with higher fluoride content was limited to comparisons between standard products and those containing 1,500 ppm. Nine papers were included in the evaluation. In seven of the papers, the results displayed a significantly higher caries reduction after the daily use of toothpaste with 1,500 ppm fluoride compared to standard formulations with a mean difference in prevented fraction of 9.7% (range 0 -22%). Six of the studies were rated grade 'A', and consequently we found strong evidence that toothpastes with 1,500 ppm of fluoride had a superior preventive effect compared with standard dentifrices with 1000 ppm F in the young permanent dentition when used daily (evidence level 1).

Mejare I et al [40] conducted a systematic review to find out caries – preventive effect of **fissure sealants**. The objectives of this study were to systematically determine the effectiveness of fissure sealants in preventing caries of occlusal surfaces of premolars and molars in the child /adolescent population and to examine factors potentially modifying the effect.

Relevant studies were identified by searching the Medline and Cochrane library databases (from 1966 to November 2001 with a later update in August 2003). The primary search strategy included the MeSH terms 'dental caries' and ‘pit and tissue sealants’. The term dental caries was also combined with the words 'sealant', 'sealants' and ‘sealing’. A total of 1250 records were identified. Filters were then used to allow the inclusion of only clinical trials, comparative studies, evaluatio n studies, cohort studies and retrospective studies. This search resulted in 390 records.
An article was read in full if at least one of the reviewers considered the study t o be potentially relevant according to the basic criteria for inclusion that has been set up in advance: randomised (RCT) and quasi randomised (split mouth) studies or controlled clinical trials (CCT). The outcome measure was caries increment (Δ DFT / Δ DFS or Δ dft / Δ dfs) and the follow up time at least 2 years. Another 13 articles were retrieved from the hand search. The grey literature was not included.

A total of 113 studies were assessed in detail. Thirteen of these studies met the inclusion criteria and formed the basis for evaluation of evidence of the caries – preventive effect of fissure sealants according to the criteria given in Table 12.

Table 12

Grade	Criteria
A (High value as evidence)	All criteria stated below should be met: - Randomization by children - Diagnostic reliability test made and described - Baseline DFT/DFS (dft/dfs) values described - Independent outcome assessment - Statistical analysis (difference between test and control group calculated) - Attrition reported, explained, not exceeding 10% per year - A representative sample of population under study; results can be generalized - Bias and possible confounders have been considered
B (Moderate value as evidence)	All criteria stated below should be met: - Randomization by children, school class, or tooth pair (split mouth) - Diagnostic reliability test made and described - Baseline DFT/DFS (dft/dfs) values described - Independent outcome assessment - Relative risk reduction or relative risk described - Attrition reported, not explained but not exceeding 10% per year - The population understanding defined, results cannot be generalized - Bias and possible confounders have been considered
C (Limited value as evidence)	One or more of the conditions stated below: - No or unclear randomization - Diagnostic reliability test not described - Baseline DFT/DFS (dft/dfs) values not described - No independent outcome assessment - Relative risk reduction or relative risk not described and cannot be calculated from the results - Attrition not reported or more than 10% per year - The population under study not defined - Potentially significant bias/confounders that could distort the results not considered

Definition of evidence level

- Strong evidence: At least 2 studies with high level of evidence (A) or good systematic review.
- Moderate evidence: One study with level (A) and at least 2 studies with moderate level of evidence (B)
- Limited evidence: At least 2 studies with level (B)
- Incomplete evidence: Less than 2 studies with level (B)

None of the studies was graded A, 2 were graded as B and 11 as C. The pooled estimate effect of resin based fissure sealing of 1st permanent molars showed that the relative risk of developing caries in fissure sealed teeth related to untreated control teeth was 0.67 (confidence intervals 0.55– 0.83) corresponding to relative risk reduction of 33%.

In conclusion, this review suggests limited evidence that resin based fissure sealing of 1st permanent molars has a caries preventive effect. There is incomplete evidence that fissure sealing of primary molars, premolars and permanent 2nd molars has a caries – preventive effect, or that fissure sealing is beneficial in child / adolescent populations at low risk of caries, and the same applies to populations at high risk of caries. Furthermore, there is incomplete evidence that fissure sealing with glass ionomer cements has a caries – preventive effect.

van Rijkom H.M. etal [41] performed a meta-analysis (I) to assess the overall caries-inhibiting effect of clinical fluoride gel treatment studies, based on explicit selection criteria, and (2) to explore factors potentially modifying the caries inhibiting effect of fluoride gel treatment, concerning the baseline caries prevalence of the target population, the general fluoride regimen, and application features.

Publications were screened which reported on the clinical effect of fluoride gel treatment in caries prevention. A literature search of clinical trials was conducted on the key words 'fluoride', 'gel', and '(dental) caries'. Articles were preselected which had been published between l965 and 1995 in the English and German language, and which had been catalogued in the MEDLINE database.To guarantee a meaningful analysis of the published research, additional inclusion and exclusion criteria were applied, to obtain comparability in dental and methodological respect.

Inclusion criteria were: (1) randomized clinical trials on study populations representative of the general population, receiving fluoride gel treatment versus no treatment or placebo treatment; (2) application to permanent teeth of children in the age range of 6-15 years at the start of the study; (3) availability of caries incidence data at surface level for all treatment groups, and (4) effect evaluation at the end of the application period.

Exclusion criteria were: (I) experimental treatment combining fluoride gel application with additional preventive measures (except the use of fluoride toothpaste) (2) dramatic (more than two-third) drop-out of participants during the study in one or more of the treatment groups and (3) publications on interim evaluation. 24 study results could be entered into meta-analysis.

The caries-inhibiting effect of fluoride gel application was expressed by the **prevented fraction (PF)** and the **'number needed to treat' (NNT)**. The PF is obtained by calculating the difference between the incidence of decayed, missing and filled surfaces (DMFS) in the control group (Ic) and the incidence in the experimental group (Ie) divided by the incidence of decayed, missing and filled surfaces in the control group. Thus PF =(Ic-Ie)/Ie, indicating the reduction of caries incidence by fluoride gel treatment relative to the incidence in the control group. In contrast to absolute reductions (Ic-Ie), the PF is assumed to be less sensitive to experimental circumstances such as the age range of the stud y population and the duration of the study. Presenting PFs also enables comparison with the results of the previous research, since most clinical studies and reviews on the fluoride gel application are evaluated by PFs.

The NNT is a measure for the efficiency of a preventive treatment, expressing the number of patients to be treated (with fluoride gel) in order to prevent 1 DMFS. The NNT = 1/(Ic. PF), and is, for a given PF, dependent on the caries incidence of the population and the follow-up years of the treatment. The NNT expresses the effectiveness of fluoride gel application according to the caries incidence of the target population, providing a detailed picture of treatment tailored to subgroups of patients. Moreover, the NNT can be used for cost/effect calculations.

From the articles analysed, several variables could be derived to study aspects tha t possibly influenced the caries-inhibiting effect of fluoride gel treatment, these being: (1) 'baseline caries prevalence', (2) 'general fluoride regimen', (3) 'gel application method', and (4) 'application frequency'.

(1) 'Baseline Caries Prevalence': Due to differences in mean ages of the study groups, the baseline caries prevalences are not well comparable.
(2) *'General Fluoride Regimen':* The general fluoride regimen was composed by combining data on the use of fluoride toothpaste and the consumption of fluoridated water.
(3) *'Gel Application Methods':* The gel application methods were classified according to (a) as either more than 1% fluoride or less the 1% fluoride, and (b) whether the gel was applied by tray or by brush.
(4) *'Application Frequencies':* The reported application frequencies were divided into five frequency intervals: (a) 1 time per year, (b) 2 times per year, (c) 4 -6 times per year, (d) once per 2-3 weeks, and (e) at least every day.

Regression analysis did not show any significant influence of 'application methods' (tray/brush), 'baseline caries prevalence', and 'general fluoride regimen' . Due to the large overlap in confidence intervals and taking into account the fact that no significant influences were found for the covariables, it may be assumed that all studies were equally effective so that one overall effect could be calcula ted by pooling the results. This overall caries-inhibiting effect (PF) is 22% (95% CI = 18-25%), which is calculated from samples involving a total of 8,263 children.

Marinho V.C.C. et al [42] performed a systematic review was to assess the effectiveness and safety of **fluoride gel**s in the prevention of dental caries in children and to examine formally the main factors that may influence their effectiveness including initial level of caries severity, background exposure to other fluoride sources, methods of application, and fluoride concentration.

Fluoride gels can be professionally or self applied under supervision, at a frequency from once to several times a year. Various fluoride compounds, concentrations, and methods of gel application have been used, with or without prior dental prophylaxis. Typically, acidulated phosphate fluoride (APF) gels in the concentration of 12,300 parts per million of fluoride (ppm F) arc professionally applied twice a year, In general operator-applied fluoride gels use trays and self-applied gels use either a tray or a toothbrush

Studies were included if participants were allocated randomly or quasirandomly to fluoride gel or placebo (for any method of gel application) or no treatment (for tray or cotton tips methods but not for brushing or flossing) for at least one year/school year and in which blind assessment of outcome was used or indicated. Participants had to be children aged sixteen or less at the start of the study.

The types of intervention included in this review are professionally or self -applied fluoride gels, using any fluoride agent, at any concentration, amount, or duration of application, and with any technique of application, provided the frequency of gel application was at least once a year. Studies in which the intervention consisted of any other caries preventive agent/procedure in addition to fluoride gel were excluded. The main outcome is caries increment as measured by the change in decayed, missing, and filled tooth surfaces (DMFS) in the permanent dentition. Caries incidence in deciduous teeth and specific side effects including tooth staining or discoloration, oral allergic reactions, and adverse symptoms such as nausea and vomiting were other outcomes considered relevant.

Authors attempted to identify all relevant studies irrespective of language, from 1965 to 2000, by employing a comprehensive search strategy. Authors searched several databases from data of inception to 2000, including MEDLINE, EMBASE, BIOSIS, SCISEARCH, LILACS/BBO, the Cochrane Central Register of

Controlled Trials (CENTRAL) (The Cochrane Library Issue 2, 2000), and the Cochrane Oral Health Group's Trials Register (May 2000). They also hand searched seven dental journals prospectively and the journal *Community Dentistry and Oral Epidemiology* from 1990 to January 2000, searched reference lists of articles, and contacted selected authors and manufacturers for unpublished studies.

A trial was excluded if random or quasirandom allocation was clearly not used or not stated and not indicated. A trial was also excluded if open outcome assessment was described or blind outcome assessment was not reported and unlikely (no description of an examination performed independently of previous results, of x - rays registered independently of clinical examination, of use of a placebo, and of examiners clearly not involved in giving treatment).

Twenty five trials were included, conducted between 1964 and 1996 (only five during 1980s and one in 1990s).

Effect of Fluoride Gel on Caries Increment:

Neither of the two trials reporting caries increment in deciduous tooth surfaces provided standard deviations or data from which these could be derived, and their results were therefore not pooled.

For all twenty-three trials combined, the D(M)FS prevented fraction pooled estimate was 0.28 (95 percent CI, 0.19 to 0.37; p<O.OOOI),suggesting a substantial benefit from the use of fluoride gel. Substantial heterogeneity in results could be observed graphically and statistically (Q = 135 on 22 degrees of freedom, p<O.OOO1).

Univariate meta-regression did not reveal any statistically significant associations between estimates of D(M)FS prevented fractions and the prespecified trial characteristics: baseline levels of caries, background exposure to other fluoride sources, background exposure to fluoridated water, background exposure to fluoride toothpaste, gel application mode (operator/self), gel application self - applied method (tray/brush), and fluoride concentration. There was an indication of greater benefit of fluoride gel with increasing frequency of application and wit h "total intensity of application" (frequency x concentration) with the prevented fraction.

Ismail A.I. et al [43] performed a systematic analysis of the dental literature and a meta-analysis to determine the strength of the association between **fluoride supplements and dental fluorosis**. A MEDLINE search was organized for all studies published, in English, between January 1966 and September 1997. The following key words were used to search for all documents written in the English literature: fluorosis, dental, fluoride, fluoride supplement or supplements, drop or drops, and tablet or tablets. A search for unpublished

studies was also carried out using contacts with researchers in the field. Two unpublished studies were located and one of them (which was subsequently published) was used in this review (permission was not obtained for the second paper).

The studies identified by the search were classified into two groups. The first group included cross-sectional/ case-control studies where information on use of fluoride supplements was obtained from self-administered questionnaires or interviews with parents. The second group included follow-up studies where data on fluoride use were available for a group of children and the investigators conducted an examination for presence of fluorosis at a later date. Ten cross- sectional/ case-control and four follow-up studies were located with enough data to allow for further quantitative analysis.

Results:

Qualitative review-Cross-sectional/case-control studies: all users of fluoride supplements

Children who used fluoride supplements during the first several years of life had a significant increase in the risk of developing dental fluorosis.Eight studies found statistically positive associations between the use of fluoride supplements and dental fluorosis. The OR of developing fluorosis in users of fluoride supplements during the first 8 years of life ranged from a low of 1.3 to a high of 10.7.

Follow-up studies: all users of fluoride supplements

The relative risk of developing fluorosis in children who used fluoride supplements during the first several years of life was highly significant. Children who started using fluoride supplements at the age of 6 months had 5.4 times higher incidence of dental fluorosis than children who did not use supplements at all. The use of fluoride supplements during the first year of life is associated wi th a statistically significant increase in risk of fluorosis. Children who used supplements starting at the age of 24 months had increased risk compared to non- users, but the RR was not statistically significant because of the small sample siz e.

Meta-analysis:

Cross –sectional/ case –control studies: all users of fluoride supplements

Overall, the meta-analyses found that the summary OR on average is between 2.1-2.3, indicating that children who use fluoride supplements.

Follow-up studies: all users of fluoride supplements

For the follow- up studies, the summary RR ranged between 1.3(2.6 -5.3) for the generalized variance method and 6.6 for the mantel- haenszel method. The DerSimonian-Laird method estimated that the summary RR was 3.5(2.3 -5.5). The

follow-up studies showed a strong association between any use of fluoride supplements and dental fluorosis because the determination of exposure to fluoride supplements was based on records or detailed interviews rather than recall by parents or self-administered questionnaires.

Appropriate use of fluoride supplements

When the meta-analysis were restricted to children who had regularly used fluoride supplements during at least first 6 years of life, the summary OR were between 2.4-2.6. For the follow- up studies, the DerSimonian- Laird method estimated a summary OR of 5.5(2.7-11.4), which is higher than the 3.5 reported in the previous analysis.

This analysis clearly shows that the use of fluoride supplements increases the risk of developing dental fluorosis. Though the severity of fluorosis in the large majority of children is very mild, dentists should inform the parents about the risks and benefits that are associated with the use of fluoride supplements. For many children, there may not be a need for an additional application of fluoride. For some children, the detrimental effect of a rampant caries attack outweighs the risk of developing dental fluorosis. For such children, an additional source of fluoride (in the form of drops and tablets that are chewed and swished in the mouth) may be beneficial.

van Rijkom H.M etal [44] perfomed a meta –analysis on published data on the **Caries-inhibiting effect of Chlorhexidine** Treatment. The objectives of this study were: (1) to assess an estimate of the caries-inhibiting effect of Chlorhexidine treatment more accurate than that provided by individual studies, and (2) to explore factors potentially modifying the effect of chlorhexidine in caries prevention, *i.e.*, the application method, application frequency, target population, the fluoride regime, tooth surfaces involved, and caries diagnosis.

A literature search was conducted on the key words "chlorhexidine" and "(dental) caries" in the MEDLINE database. A first selection on articles published between1975 and 1994 in English, French, or German resulted in 24 papers, which were all evaluated independently by two examiners. To provide for a systematic analysis of the past research, studies were selected on comparability for dental and methodological reasons. After an initial screening of the selected papers, these additional criteria were formulated: (1) chlorhexidine applied to permanent teeth from 11- to 15-year-old children; (2) studies performed in a clinical trial with randomly assigned treatment groups, including generally treated experimental groups as well as treatment focused on subjects in the experimental group with *Streptococcus mutans* >2.5 x 10^5ml saliva; (3) the availability of caries incidence data on surface level; (4) a treatment duration of at least one year; and (5) evaluation at the end of the treatment period.

Evaluation criteria:

The caries-inhibiting effect of chlorhexidine was expressed by the prevented fraction, calculated as the difference in number of new decayed and filled surfaces (DFS or DS) between the control group and the chlorhexidine group, divided by the number of new decayed and filled surfaces in the control group.

Covariables:

Several variables could be derived for the study of possible influences on the caries-inhibiting effect of chlorhexidine:

- "Application methods" consisted of topical gel application, rinsing, incorporation into toothpaste, and a combination of rinsing and toothpaste.
- "Application frequencies" were divided into intervals of (a) 90 to 180 days, (b) every 30 days, or (c) more frequently.
- "Caries risk" was recorded either as ‘nonselected' or as 'selected subjects with high caries risk', depending on the description in the relevant paper. (The latter was determined according to *Streptococcus mutans* levels or caries activity.
- The "fluoride regime" reflects the fluoride prophylaxis setting of each study, involving all participants of the individual studies in the control as well as the experimental groups. This variable was quantified and included in the analysis as an effect modifier. For analysis purposes, a distinction was made among: (1) those who used only fluoride toothpaste, (2) those who did additional rinsing with fluoride or had a fluoride application, and (3) those who had more frequent fluoride rinsing or fluoride rinsing in combination with fluoride application. In none of the papers was the use of fluoride tablets reported. Either the drinking water contained a negligible fluoride concentration or data were not available.
- Two "caries diagnostic" levels were distinguished: (1) dentinal caries, and (2) caries including enamel lesions. In one study, caries was scored radiographically, and in all other studies, it was scored clinically as well as radiographically.
- The factor “tooth surface” included “all tooth surfaces” or “approximal tooth surfaces”.

Results:

Multiple-regression analysis showed no significant influence on the prevented fractions for the variables "application method", "application frequency", "caries risk", "fluoride regime", "caries diagnosis", and "tooth surface", indicating

homogeneity of the studies. Three parameters were highly correlated: Multicollinearity was found among the variables "application method”,” application frequency", and caries diagnosis”, complicating the interpretation of the effect of each of these three variables separately.

The overall Caries-Inhibiting Effect of Chlorhexidine Treatment studies was 46% (95%CI =35%-57%).

Llodra J.C et al [45] performed a meta-analysis to analyze the effectiveness of **fissure sealants** In preventing dental caries.
Potential papers for analysis were located by a) search of the MEDLINE database from January 1975 to December 1990 (key word: pit and fissure sealant), b) a hand review of the references contained in MEDLINE articles, and c) a hand search of the abstracts published in 11 international journals known to publish data on the effectiveness of sealants resins. No attempt was made to identify unpublished studies.
A published study was included in the analysis if it satisfied all of the following criteria: a) it contained original data, b) the sealants were applied to permanent teeth, c) no other associated preventive measure had been used, d) the effectiveness of the sealant could be assessed, and e) the study was published in English, French or Spanish.

All articles were evaluated by two observers to minimize selection and data collection bias.

The search detected a total of 24 different studies reported in 34 articles. Overall effectiveness for autopolymerized fissure sealants when the results of these studies were pooled was 71.36% (95% CI = 69.69 -72.94), i.e., 71% of the caries in subjects treated with autopolymerized fissure sealant were avoided by the sealant. Overall effectiveness for light fissure sealants was 45.92% (95% CI = 43.50 - 48.24).

Sealants were found to be more effective in communities with fluoridation (82.69% vs. 71.28%).

Main conclusions of this study are: 1) fissure sealants are effective in preveting dental caries, 2) their effectiveness decreases with time, and periodic reapplicati on is advisable, 3) autopolymerizing sealants are more effective than U.V. light polymerizing sealants, 4) there appears to be a positive interaction between fluoride in the drinking water and the fissure sealants in preventing caries, 5) future studies should note whether the drinking water consumed by the study population is fluoridated or not, and 6) additional studies are needed to determine whether effectiveness is influenced by the operator.

Helfenstein U et al[46] analyzed a collection of studies designed to detect the caries preventive effects of **Duraphat (fluoride varnish)**. The authors concentrated on Duraphat and not on Fluor Protector because there have been fewer clinical trials than with Duraphat. In addition, many Fluor Protector studies have used the "split-mouth design". In these studies a fluoride leakage might influence control sites.

In order to find the papers concerned with the clinical effects of Duraphat the authors performed a systematic literature search by consulting the Index to Dental Literature from 1985 to 1991 (key words: topical, fluorides). In addition, the authors searched for studies in previous review articles.

In order to decide about the inclusion of a study in the MA, it had to meet certain methodological criteria: - The treatment agent had to be Duraphat. – The outcome measure had to be caries increment. – The study design had to be "follow-up". – The study design had to be "control vs. test group" and not "split mouth". – The control group must not have used Duraphat. – The study had to be performed on permanent teeth. – The study population had to consist of normal children (e.g. not diabetic). – Data had to be summarized in tabular form (and not only by means of a graphical display). – Sample sizes, mean values and standard deviations (or standard errors) had to be given for the treatment group and for the control group.

Searching systematically for papers as described above the authors found 30 studies. By applying the described strategy for study selection they obtained nine studies. One study was excluded even though it did pass their entry criteria: It applied to the "control group" an extremely intensive caries preventive treatment by a 3-weekly professional cleaning. Thus they finally obtained eight studies for meta-analysis.

The only significant explanatory variable was found to be study duration. It was found that caries reduction is negatively correlated with duration .

Manual versus powered toothbrushes – The Cochrane review

The Cochrane Oral Health Group is one of 49 Cochrane Collaboration research groups, with centers in 13 countries. It carries out systematic reviews of oral health – related studies.

On January 11, 2003, at the Forsyth Conference on Evidence Based Dentistry, The Cochrane Collaboration's Oral Health Group presented results of a new systematic review of electric tooth brushes.

The Cochrane Collaboration Oral Health Group developed and implemented search strategies to identify all relevant randomised controlled trials, irrespective of language. The following databases were searched by the group: The Cochrane

Oral Health Group's Trial Register, the Cochrane Central Register of Controlled trials, MEDLINE and the Cumulative Index to Nursing and Allied Health Literature. Manufacturers also were contacted for additional published and unpublished information. Trials were selected based on the following criteria: compared powered versus manual toothbrushes, used a randomised design, tested among the general public without disabilities, were at least 28 days in length and contained data regarding plaque and gingivitis. Trials were excluded if they compared only powered toothbrushes or only manual toothbrushes, were shorter than 28 days, or used a split mouth design.

The database search identified 354 trials, 139 of which were considered ineligible based on review of the title and abstracts. The researchers obtained the full text for 215 articles, 152 of which were considered ineligible. Of the remaining 63 articles, only 29 provided data that were useable for analysis.

The researchers grouped the clinical results from all six toothbrush categories according to trial time: short term (one month through three months) and long term (more than three months). The clinical results were also grouped according to outcome measure: plaque and gingivitis. Thus for each toothbrush category, there were four outcomes.

The results indicate that there was a wide range in plaque and gingivitis reduction among the powered toothbrushes. For plaque reduction, the average mean difference in the plaque index range from –0.2 to 1.2. A negative number indicates that, on average, the powered toothbrush was less effective than the manual toothbrush. Conversely, a positive number indicates that the powered was more effective than the manual toothbrush. The most effective powered toothbrush in terms of plaque reduction was the rotation-oscillation toothbrush. For this toothbrush, the mean difference of 1.2 converts to a plaque reduction of 7 percent.

For gingivitis reduction, the average mean difference in the gingivitis index ranged from –0.1 to 0.5. As with plaque reduction a negative number indicates that the manual toothbrush was more effective than the powered toothbrush, while a positive number indicates that the powered toothbrush was more effective. The most effective powered toothbrush for reducing gingivitis was the rotation- oscillation toothbrush. For this toothbrush, the mean difference of 0.5 converts to a gingivitis reduction of 17 percent.

Conclusions and clinical implications:
Some powered toothbrushes with a rotation oscillation action achieve a significant, but modest, reduction in plaque and gingivitis compared with manual toothbrushes.[47]

Bader JD et al[48] performed a systematic review of the periodic scientific literature to determine the strength of the evidence for the efficacy of professional caries preventive methods applied to high risk individuals, and the efficacy of professionally applied methods to arrest or reverse non-cavitated carious lesions.

To address above the two questions, a detailed search was conducted of the relevant English language literature from 1966 to October of 1999 using MEDLINE, EMBASE and the Cochrane controlled trials register. Reports in the gray literature, defined as theses, dissertations, product reports and unpublished studies were not pursued. Initial search of MEDLINE plus hand searching identified 1435 citations, with 43 additional citations identified through EMBASE.

Several inclusion and exclusion criteria were applied to the reports identified in the literature search. For both questions, studies were limited to in vivo designs involving human subjects, excluding in situ and in vitro studies. All studies without concurrent control groups were excluded (nil, placebo, or active). Because the question addressed only professional methods, only reports involving preventive or management interventions requiring professional application or prescription, or interventions likely to be undertaken only upon the recommendation of a dentist were included. Specifically excluded were dentifrice studies where dentifrice use was not a part of a larger intervention.

For the question involving the efficacy of preventive interventions in caries-active or high risk groups, studies where such classifications were not made on an individual basis were excluded.

For the question involving management of non-cavitated lesions, all studies where the lesions examined were identified as "initial", "incipient" or non-cavitated" were included. Studies where the lesion was not the unit of observation and analysis were excluded.

The inclusion and exclusion criteria were applied by examining titles, abstracts and, where necessary, full papers for the 1478 studies identified in the searches through dual independent reviews. 22 studies on the efficacy of caries preventive methods in caries-active / high-risk individuals were included. Five studies on the management of non-cavitated carious lesions were included. Two more studies were separately identified later, and added to the review.

The overall strength of the evidence for efficacy was based on the consistency of effects across studies, sample size, magnitude of effects and quality of the available studies. The categories for overall strength of the evidence were:

Good: Data are sufficient for evaluating efficacy. The sample size is substantial, the data are consistent and the findings indicate that the intervention is clearly superior to the placebo / usual care alternative.

Fair: Data are sufficient for evaluating efficacy. The sample size is adequate, but the data show some inconsistencies in outcomes between intervention and placebo / usual care groups such that efficacy is not clearly established.

Poor: Data are sufficient for evaluating efficacy. The sample size is sufficient, but the data show that the intervention is no more efficacious than placebo or usual care.

Insufficient: Data are insufficient for assessing the efficacy of the intervention, due to limited numbers of studies, limited sample sizes and / or poor quality.

Results:

Management of caries-active / high-risk individuals:

The interventions are shown in four groups, those based on fluorides, chlorhexidine, combinations involving chlorhexidine and fluoride or sealants and other agents.

1. Fluorides- Nine evaluations reported in seven studies examined the efficacy of fluorides for the prevention of carious lesions. All the studies involved children as subjects; one study examined effects on primary teeth. The percent reductions ranged from 7 to 30% among the eight interventions where comparisons were made to placebo or no treatment. However, only three of these reductions were statistically significant. Five of the interventions involved the use of fluoride varnish.

Of the other fluoride- based interventions, which included sodium, amine and ferric aluminum fluoride rinses and acidulated phosphate f luoride (APF) gel, only APF gel provided a statistically significant reduction in dental caries. The evidence for efficacy was judged to be *fair* for fluoride varnishes and *insufficient* for other fluoride based methods, based primarily on small numbers of s tudies of any type of intervention upon which to determine efficacy.

2. Chlorhexidine – Six studies reported seven evaluations of chlorhexidine gel, rinse and varnish preventive interventions. All of the studies were conducted among children, all evaluating efficacy on permanent teeth. Percent reductions ranged from –9 to 52%, although only two of the reductions, one gel and one rinse, were statistically significant. The evidence for efficacy was judged to be insufficient but suggestive of efficacy for all forms of chlorhexidine.

3. Combinations – Six studies reported seven interventions consisting of combined application of chlorhexidine and other preventive agents. Two of five chlorhexidine / fluoride rinses evaluated showed percent reductions of 34 and 43% with NNTs of 2.0 and 0.9, but only one of these results was statistically significant. The evidence for efficacy of any given combination treatment was

judged to be *insufficient,* due to limited evaluation of any one intervention and variability in outcomes, but evidence was generally suggestive of efficacy for combined treatment approaches.

4. Other agents – Six studies reported evaluations of other agents, including an antibiotic, occlusal sealants, an alum rinse, distribution of a high-risk protocol to treating dentists, and two studies of the effects of gum. Only two gum studies showed significant effects. The evidence was judged to be *insufficient* for any of these agents, none of which was represented by more than one study, although the evidence for the efficacy of gum-based interventions was found to be suggestive.

Prevention in radiotherapy patients:

Six studies reporting nine interventions were evaluated among patients receiving head and neck radiotherapy. These studies generally evaluated dail y fluoride or chlorhexidine interventions against alternative fluoride interventions in a limited number of subjects. The evidence for efficacy for both fluorides and chlorhexidine was judged to be *fair* among individuals receiving head and neck radiotherapy.

Prevention on orthodontically banded teeth:

Seven studies reporting 11 evaluations of preventive interventions were conducted on teeth with orthodontic bands. The studies were of two general types, short term studies where banded teeth were extracted after 4-5 weeks to measure depth of demineralization, and longer - term studies evaluating the number of lesions or the percent of sites that became demineralized. Overall, these studies suggest that a variety of preventive interventions may well reduce demineralization and hence carious lesions among individuals with orthodontically banded teeth. However, the evidence for efficacy was judged to be *insufficient* for any given method due to the small sample sizes, generally low quality scores and small number of studies per method.

Management of non-cavitated carious lesions:

Criteria for these studies required the presence of a non-cavitated smooth surface or pit and fissure lesion at baseline. Only seven studies, which described nine evaluations, were found, all on permanent teeth in children. The evidence for efficacy of any given method for arresting or reversing the progression of non-cavitated carious lesions was judged to be *insufficient* for any specific type of intervention due to the small number of studies and the lack of statistical testing in most studies.

Frencken JE et al[49] performed a meta-analysis to find out the effectiveness of single-surface ART restorations in the permanent dentition The literature search

was carried out on publications indexed in PubMed and MEDLINE up to 1 September 2003, with the following key words: restorations, survival, permanent (dentition), Atraumatic Restorative Treatment (ART), and amalgam. The search revealed 7 publications.

The inclusion criteria for the meta- analysis consisted of the following: randomized clinical trial, survival results after 1 -3 yrs, and sufficient power of the study. One publication had to be excluded because the power of the study was low. And in one publication, only survival results after 6 yrs were presented. These exclusions resulted in 5 studies being eligible for inclusion in the meta analysis. Three studies used a low viscosity glass ionomer. These 3 studies started in the late 1980s or early 1990s and were the first ones in which hand instruments and glass ionomers (ART) were compared with rotary instruments and amalgam (conventional approach). The remaining 2 studies started in 1995 and 1997 and used high viscosity glass ionomers produced for use with the ART approach. These newer materials have improved physical characteristics. Because of the use of different generations of glass ionomers and the accepted learning effect in the first 3 studies, the 5 studies were divided into 2 groups: 'early' and 'late' studies. Thus, homogeneity within the groups was secured.

Results:

In the early group of studies, single-surface amalgam restorations survived statistically significantly longer than single-surface ART restorations after 1, 2 and 3 yrs. In the late group of studies, there was no statistically significant difference between the 2 types of restorations. After 3 yrs, single-surface ART restorations in the late group of studies survived significantly longer than single surface amalgam restorations in the early group of studies.

Need for the users' guides*:*

Clinical information comes from two principal sources, the individual patient and research. To provide effective care, both types of information are needed. Information about the individual patient is elicited through a careful history, physical examination, and other investigations. The way in which clinicians obtain information from scientific research is less clear, but of no less importance to th e quality of care that patients receive.[50]
When you conduct a search, how do you quickly know which article(s) to read? Are there key features to look for which can guide you to the strongest evidence? By using **3 key questions** from the format of the Users' Guides, one can screen the titles and abstracts from a search to decide which are worthy of more careful study:

1. What are the results?

2. Are the results valid?

3. Will the results help me in caring for my patients?

Once these articles are identified, and if careful evaluation reveals that the results are of interest and possibly applicable to the question, then the research methods can be evaluated to determine whether they are valid or close to the truth.[14]

The Users' Guides are designed to help clinicians make decisions, and most clinical decisions are black and white; for example, we either start a treatment or we do not. It is understandable, therefore, that we seek black or white answers from the clinical literature. Unfortunately, evidence comes in shades of gray. Often, results may be valid, perhaps demonstrate an important effect, and might improve patient care.

The goal of the Users' Guides is to help clinicians sift through these shades of gray and make appropriate decisions, recognising the "level" of certainty (or strength of inference) underlying those decisions. The first key question- "Are the results of the study valid?"- and the last- "Will the results help me in caring for my patients?"- reflect the need to make a decision, despite the fact that the strength of the inferences that can be made based on a study spans a spectrum from strong to weak.

The importance of focused questions can be quickly assessed, and priority given to problems that are seen routinely and have practically important consequences. In general, those questions that are clearly related to a clinical decision about whether to use a therapeutic, preventive, or diagnostic interventions are the ones that warrant the most time. Focusing the question clarifies the target of the literature search and permits use of the appropriate guides for assessing validity in screening the titles and abstracts of the articles that are located.

Deciding if an article is likely to provide valid results:

The first question applied to any article tracked down in an effort to find an answer for a clinical problem concerns its closeness to the truth: are the results of this article valid? The **Table -13** presents two key guides to assess validity for primary studies (those that provide original data on a topic) and integrative studi es (those that summarize data from primary studies). For each type of integrative study, the first criterion has to do with whether the question is appropriately framed, and the second with whether the evidence was appropriately collected and summarized. The clinician can use these most important criteria to rapidly screen an abstract to determine whether it warrants the additional time required to read it in detail. These criteria can also be used to reduce the clinical literature to a manageable size when trying to keep up with new advances that are pertinent to one's practice.

Table 13: Guides or selecting articles that are most likely to providevalid results[50]

Therapy	**Primary studies** • Was the assignment of patients to treatments randomised? • Were all of the patients who entered the trial properly accounted for and attributed at its conclusion?
Diagnosis	• Was there an independent, blind comparison with a reference standard? • Did the patient sample include an appropriate spectrum of the sort of patients to whom the diagnostic test will be applied in clinical practice?
Harm	• Were there clearly identified comparison groups that were similar with respect to important determinants of outcome (other than the one of interest)? • Were outcomes and exposures measured in the same way in the groups being compared?
Prognosis	• Was there a representative patient sample at a well- defined point in the course of disease? • Was follow up sufficiently long and complete?
Overview	**Integrative studies** • Did the review address a clearly focused question? • Were the criteria used to select articles for inclusion appropriate?
Practice guidelines	• Were the options and outcomes clearly specified? • Did the guideline use an explicit process to identify, select, and combine evidence?
Decision analysis	• Did the analysis faithfully model a clinically important decision? • Was valid evidence used to develop the baseline probabilities and utilities?
Economic analysis	• Were two or more clearly described alternatives compared? • Were the expected consequences of each alternative based on valid evidence?

HOW TO EVALUATE AN ARTICLE ABOUT THERAPY?

Most of the patients fall into a practitioner's treatment routine, and practitioner base their therapy on procedures which they know best and with which they are comfortable. When dramatically new procedures become established, such as has happened with dental implant therapy, patients have a right- moral, ethical, and legal- to know the risks and benefits of any therapy that is recommended. When considering the merits of an information source, the reader or listener must clearly understand what the purpose of the study was and how the investigators sought to establish their premise, and the results of the study must be directed to this purpose statement. Even though the result of a study seems to offer evidence that indicates that the conclusions of the study were justified, the reader must ascertain whether the investigators used credible methods to arrive at conclusions. [51]

Readers' Guides for an Article about Therapy: [52]

1. Are the results of the study valid?

Primary guides:

- Was the assignment of patients to treatments randomized?
- Were all patients who entered the trial properly accounted for and attributed at its conclusion?
  - Was follow-up complete?
  - Were patients analyzed in the groups to which they were randomized?

Secondary guides:

- Were patients, health workers, and study personnel "blind" to treatment?
- Were the groups similar at the start of the trial?
- Aside from the experimental intervention, were the groups treated equally?

2. What were the results?

- How large was the treatment effect?
- How precise was the estimate of the treatment effect?

3. Will the results help me in caring for my patients?

- Can the results be applied to my patient care?
- Were all clinically important outcomes considered?
- Are the likely treatment benefits worth the potential harms and costs?

1. Are the Results of the Study Valid?

This question has to do with the validity or accuracy of the results and considers whether the treatment effect reported in the article represents the true direction and magnitude of the treatment effect. [53] Guyatt et al divided the assessment of validity into primary and secondary considerations or guides [51]-

Primary Guides:

Was the assignment of patients to treatment randomized ?

There are many methods by which subjects are selected and assigned to a study. The strongest evidence is gained by assigning participants by randomization - assuring that all who enter into investigation have an equal opportunity to be assigned to one of the study groups. If subjects are not randomized to treatment, there is serious potential for bias, which would invalidate the results. For example, it would be easy for the principal investigator to select those with a poorer prognosis to receive the secondary therapy or placebo, while those with an apparently better prognosis would receive the primary therapy.

Were all patients who entered the trial properly accounted for and attributed at its conclusion?

A rule of thumb is a dropout rate of greater than 20% compromises the validity of the study. There are many methods of dealing with dropouts. One method is to use the mean of the control group for the dropouts in the test group and the mean of the test group for the dropouts in control group. Another is to assume that all dropouts in the test group did poorly and all dropouts in the control group did well.

Although there is controversy among the epidemiologists over how to deal with dropouts, what is agreed on is that the method should be decided at the inception of the study, not after the data are collected. It is also the researchers' obligation to describe the method of dropout assessment for the reader. [51]

Was follow -up complete?

Every patient who entered the trial should be accounted for at its conclusion. If this is not done , or if substantial numbers of patients are reported as "lost to follow up," the validity of the study is open to question. The greater the number of subjects who are lost, the more the trial may be subject to bias because pat ients who are lost often have different prognoses from those who are retained , and may disappear because they suffer adverse outcomes (even death) or because they are doing well(and so did not return to the clinic to be assessed).

Were the patients analyzed in the groups to which they were randomized?

As in routine practice, patients in randomized trials sometimes forget to take their medicine or even refuse their treatment altogether. The reasons people don't take their medicine are often related to prognosis.

Excluding noncompliant patients from the analysis leaves behindthose who may be destined to have a better outcome and destroys the unbiased comparison provided by randomization. [53]

Secondary Guides :

Were patients, their clinicians, and the study personnel "blinded" to treatment?

Once the assignment is made, all evaluations of the groups' progress should be made without any observer knowledge as to which group is receiving which treatment. Only then can an unbiased assessment be made.

Every effort should be made to ensure that patients are blinded to their group assignment to preclude *participant bias* from occurring. Patients may have a preestablished preference or dislike for a given therapy, regimen, or material and may, purposely or inadvertenttly influence the results.

Were the groups similar at the start of the trial?

Cohort uniformity is essential in clinical studies. If there are age or gender variations, ethnic differences, or substantial variations in general health, these factors may influence the results. A cautious reseacher will assess the groups to which subjects were assigned to ascertain whether there might be factors that might have a bearing on the outcome.

Aside from the experimental intervention, were the groups treated equally?

When something is studied, the act of studying may alter that which is being studied. If an investigator recalls a "test group" more often than a control group, or if the "test group" receives additional adjunctive therapy (such as prophylaxis , antimicrobial therapy or a second drug given to counteract a side effect), the effect of the cointervention on the primary observation is unknown and affects the validity of the study. Every effort should be made to ensure that all groups receive equal treatment whenever possible.[51]

2. What were the results?

If the results are valid and the study likely yields an unbiased assessment of treatment effect,then the results are worth examining further. This second question considers the size and precision of the treatment's effect. The best estimate of that effect will be the study findings themselves; the precision of the estimate will be superior in larger studies.[53]

How large was the treatment effect?

Not all studies have results that are as easy to determine as life or death, cure or continued disease. Most investigations arrive at conclusions that require some cautious thought to determine the actual magnitude of the effect.

Readers must ascertain the degree of negative outcomes that invariably are the consequence of any therapy or treatment regime by establishing the risk involved (percentage experiencing negative effects in the study) and from that the ***absolute risk reduction* (ARR)** between the treatment group and the others in the study. Using X= negative outcomes in the control group, and Y= negative outcomes in the treatment group, the ARR= X-Y. Associated with absolute risk reduction is ***relative risk***, which is calculated by dividing the risk with therapy by the risk

without therapy (RR= Y/X). A common expression of efficacy is the ***relative risk reduction* (RRR)**. This evaluation is expressed as a percentage, and the larger the RRR, the more effective is the therapy (RRR= 1-(Y/X)x100).[51]
How Precise Was the Estimate of Treatment Effect?

*The true risk reduction can never be known; all we have is the estimate provided by rigorous controlled trials, and the best estimate of the true treatment effect is that observed in the trial. This estimate is called a "**point estimate**" in order to remind us that although the true value lies somewhere in its neighbourhood, it is unlikely to be precisely correct. Investigators tell us the neighbourhood within which the true effect likely lies by the statistical strategy of calculating confidence intervals (CIs).*
We usually (though arbitrarily) use the 95% CI, which can be simply interpreted as defining the range that includes the true RRR 95% of the time. You'll seldom find the true Relative Risk Reduction (RRR) toward the extremes of this interval, and you'll find the true RRR beyond these extremes only 5% of the time, a property of the CI that relates closely to the conventional level of "statistical significance" of P<.05.[52]

3. Will the results help me in caring for my patients?

This question has two parts. First ,are the results applicable to your patient?You should hesitate to institute the treatment either if your patient is too dissimilar from those in the trial, or if the outcome that has been improved isn't important to your patient. Second, if the results are applicable, what is the net impact of the treatment? The impact depends on both benefits and risks (side effects and toxic effects) of treatment and the consequences of withholding treatment. Thus , even an effective therapy might be withheld when a patient's prognosis is already good without treatment , especially when the treatment is accompanied by important side effects and toxic effects.[53]

Can the results be applied to my patient care?

The issue to *address* is *how confident you are that you can apply the results to a particular patient or patients in your practice. If the patient would have been enrolled in the study had she been there – that is, she meets all the inclusion criteria, and doesn't violate any of the exclusion criteria – there is little question that the results are applicable. If this is not the case, and she would not have been eligible for the study, judgement is required.* [52]

Were all clinically important outcomes considered?

Whereas a drug (therapy, material, regime) may be used for a benefit that is anticipated, other ramifications may be encountered. The use of base metal alloys as gold substitutes offered improved physical properties, but the question arose

whether allergies and tissue toxicity were correlated with their use. Secondary outcomes may only be observed in larger population samples and may not be immediately apparent in smaller trials.

If a study fails to mention secondary outcomes, it may only mean that the investigators did not have a large enough population to demonstrate such events or that the study ended too soon, not that such events do not arise.

Are the likely treatment benefits worth the potential harm and costs?

Although the primary effect of a drug or procedure may offer measurable benefit, it might also have side effects- obvious or covert- that negate or temper the advantages.

Risk-benefit analysis is essential to ascertain whether a therapy should be initiated, and the patient must be made aware of the negative aspects of a course of therapy and its potential benefits. A circumspect and intelligent analysis of all the aspects of any new therapy is an essential precursor to recommending or undertaking any course of therapy. [51]

How to Evaluate an article about Diagnostic Test?

Medical and dental therapy is provided in an effort to address a specific disease entity. The more specific the diagnosis of that disease, the more predictable the interventive therapy. Thus, precision and accuracy in diagnosis are of paramount importance to the patient and the clinician.

Choosing the appropriate diagnostic tests may provide a more accurate diagnosis earlier in the patient's episode of care and at a lower cost than if inappropriate tests are performed. Methods used to assist the clinician in the identification of the correct test will be of great benefit to all involved. Given the current state of Internet access, literature searches may be performed to determine sources of information on different tests that may yield conclusive answers. [54]

Table 14: Evaluating and applying the results of studies of diagnostic tests

Step	Guides/Questions
1. Are the results of the study valid?	**Primary guides:** - Was there an independent, blind comparison with a reference standard? - Did the patient sample include an appropriate spectrum of patients to whom the diagnostic test will be applied in clinical practice? **Secondary guides:** - Did the results of the test being evaluated influence the decision to perform the reference standard? - Were the methods for performing the test described in sufficient detail to permit replication?
2. What are the results?	- Are likelihood ratios for the test results presented or data necessary for their calculation provided?
3. Will the results help me in caring for my patients?	- Will the reproducibility of the test result and its interpretation be satisfactory in my setting? - Are the results applicable to my practice? - Will the results change my management? - Will patients be better off as a result of the test?

1. Are the results of the study valid?

To say the results are valid implies that the accuracy of the diagnostic test, as reported, is close enough to the truth to render the further examination of the study worthwhile. Firstly, you must determine if you can believe the results by considering how the authors assembled their patients and how they applied the test and an appropriate reference (or "gold" or "criterion") standard to the patients.

Primary guides:

Was there an independent, blind comparison with a reference standard?

The accuracy of a diagnostic test is best determined by comparing it with the truth. Accordingly, readers must assure themselves that an appropriate reference standard (such as biopsy, surgery, autopsy, or long term follow up) has been applied to every patient, along with the test under investigation. In reading articles about diagnostic tests, if you can't accept the reference standard, then the article is unlikely to provide valid results for your purposes. If you do accept the reference

standard, the next question is whether the test results and the reference standard were assessed independently of each other.
Did the patient sample include an appropriate spectrum of patients to whom the diagnostic test will be applied in clinical practice?

A diagnostic test is really useful only to the extent it distinguishes between target disorders or states that might otherwise be confused. Almost any test can distinguish healthy from the severely affected; this ability tells us nothing about the clinical utility of a test. The true pragmatic value of a test is therefore established only in a study that closely resembles clinical practice.

Secondary guides:

Did the results of the test being evaluated influence the decision to perform the reference standard?

The properties of a diagnostic test will be distorted if its result influences whether patient undergo confirmation by the reference standard. This situation, sometimes called **"verification bias"** or **"work-up bias"**.
Were the methods for performing the test described in sufficient detail to permit replication?

If the authors have concluded that you should use a diagnostic test, they must tell you how to use it. This description should cover all issues that are important in the preparation of the patient (diet, drugs to be avoided, precautions after the test), the performance of the test (technique, possibility of pain) and the analysis and interpretation of its resources.

2. What are the results of the study?

If you decide that the study results are valid, the next step is to determine the diagnostic test's accuracy. [56] The primary methods for determination of the diagnostic quality of a test are sensitivity, specificity, positive value, and likelihood ratios.[54]

Sensitivity and Specificity:

Sensitivity of a diagnostic test is the probability that a subject with the disease will be diagnosed positive, and *specificity* is the probability that a subject who is disease-free will be diagnosed negative. [57]

Table 15: Guides to calculating sensitivity, specificity, PPV, NPV, and accuracy

Test results	**Disease present**	**Disease absent**
Disease present	True-positive (a)	False-positive (b)
Disease absent	False-negative (c)	True-negative (d)

Sensitivity = a/(a + c).

Specificity = d/(b + d).

Positive predictive value (PPV) = a/(a + b).

Negative predictive value (NPV) = d/(c + d).

Accuracy = (a + d)/ (a + b + c + d).

Table 16: Calculation of sensitivity, specificity, PPV, and NPV for toludine blue staining

	Carcinoma	**Other than carcinoma**	**Total**
Positive stain	415 (a)	131 (b)	546 (a + b)
Negative stain	66 (c)	418 (d)	484 (c + d)
Total	481 (a + c)	549 (b + d)	1030

Sensitivity = a/ (a + c) = 415/ 481= 0.86 (86%)
Specificity = d/ (b + d) = 418/ 549 =0.79 (79%) PPV
= a/ (a + b) = 415/ 546 = 0.76
NPV = d/(c + d) =418/484 = 0.86

Using tables 16 and 17, toludine blue had a sensitivity (true positive/[true positive + false negative]) of 86% and a specificity (true negative/[false positive + true negative]) of 76% in determining the presence of squamous cell carcinoma in the oral cavity of patients enrolled in this study. Sensitivity is the proportion of patients with disease that were identified by the test. When sensitivity is high, there is a high true positive rate and a low rate of false negative. Hence, a n egative result to a highly sensitive test is a relatively reliable indicator that disease is absent. Specificity is the proportion of patients without disease who were

identified by the test. A high specificity means that there is a high number of true negative results and few false positive results. When a test with a high specificity results in a positive response, there is a good chance that disease is present because false positives are rare.

Although sensitivity and specificity values offer a simplified method of assessing the usefulness of a diagnostic test, they are not foolproof. These measures are useful when the prevalence of a disease, which can be defined as "the proportion of individuals in a population having a disease," is relatively high.

When disease prevalence is relatively low, sensitivity and specificity are less useful. However, 2 alternative measures, **"positive predictive value (PPV)"** and **"negative predictive value (NPV)"** may be more useful when disease prevalence is low. PPV (true positive/ [true positive + false positive]) and NPV (true negative/ [false negative + true negative]) are calculated using the horizontal rows in Table - 16 (PPV = a/ [a + b] and NPV = d/[c + d]). PPV can be interpreted to mean when a test result is positive, how often is the disease present; NPV can be interpreted to mean when a test is negative, how often is the disease absent. In the toludine study (Tables -17), the PPV is 0.76 and the NPV is 0.86.

To their advantage, positive and negative predictive values will change as disease prevalence varies, and therefore they are potentially more meaningful to the discrimination capacity of a test when a disease has low prevalence in the general population than when a disease has a high prevalence in the same population. However, the environment in which test results are obtained may diminish the usefulness of PPV's. For example, it appears that PPVs calculated from diagnostic tests administered in the private practice setting are less reliable than when calculated from tests administered in university hospitals. [54]

LIKELIHOOD RATIOS (LR):

Use of LRs offers the clinician a better method of determining whether a positive or negative finding from a diagnostic test is meaningful. In essence, an LR is a measure of how likely any one particular diagnostic finding is to occur in the presence or absence of a disease.

Table 17: Calculation of likelihood ratios for toludine blue staining

	Carcinoma	Other than carcinoma	Total
Positive stain	415 (a)	131 (b)	546 (a + b)
Negative stain	66 (c)	418 (d)	484 (c + d)
Doubtful stain	54 (e)	106 (f)	160 (e + f)
Total	535 (a + c + e)	655 (b + d + f)	1190

LR for a positive stain=(a/[a+c+e])/ (b/ [b+d+f]) = (415/535)/ (131/655)=3.88 LR for a negative stain=(c/[a+c+e])/(d/ [b+d+f]) = (66/535)/ (418/655) = 0.19 LR for a doubtful stain=(e/ [a+c+e])/ (f/[b+d+f]) = (54/535)/(106/655) = 0.62

Table 18: Guide to interpreting likelihood ratios

Likelihood ratios	Response
Greater than 10 or less than 0.1	Permit a conclusive shift in pretest probability to posttest probability.
Between 5 and 10 and between 0.1 and 0.2	Permit a moderate change in the pretest probability and the posttest probability.
Between 2 and 5 and between 0.5 and 0.2	Lend to only a small shift in probability
Between 2 and 0.5	Alter the pretest probability to minor (and probably unimportant) degree.

In regard to toludine blue (TB) study (Table -17), table- 18 presents the complete set of data (positive, negative and doubtful) presented by the authors. The LR for a positive test result is calculated by answering 2 questions. First, how likely is a positive toludine blue stain among lesions that are cancerous. Table-18 shows that of 535 cancerous lesions, 415 tested positive (415/535 = 0.775). Next, how likely is a positive toludine blue stain in lesions that are not malignant. Again, from Table-18, 655 lesions were nonmalignant, yet 131 tested positive (131/655 = 0.200). The ratio of these 2 likelihoods is the LR for a positive stain and is equal to 0.775 divided by 0.200 or 3.88.

One can calculate LRs for any level of a diagnostic test regardless of the number of level. In this case, there are two other levels of stain, namely, "negative" and "doubtful". Each calculation involves determining a ratio of the likeli hood of achieving the particular diagnostic test classification in lesions that are not cancerous.

When considering the LRs calculated for TB test, the LR for a positive finding is 3.88. Another way of interpreting this is to infer that a positive stain i s approximately 3.9 times more likely to occur in a cancerous lesion than it is likely to occur in a lesion that is noncancerous. The LR for a negative stain is 0.19 indicating that a negative stain is 5 times more likely to occur in a noncancerous lesion than it is likely to occur in a cancerous lesion. A negative stain is a better indicator of a noncancerous lesion than a positive stain is an indicator of a cancerous lesion. The LR for a doubtful stain is 0.62, which shows that a doubtful test result does not permit the clinician to alter the pretest probability of the presence of a cancerous lesion (Table- 19).

To fully appreciate the use of diagnostic tests and LRs, the clinician must understand the concept of pretest and posttest probabilities. This co ncept is known to dentists, but the terminology may not be readily recognized. The knowledge that a patient may have a certain malady is derived from making clinical assessment of signs and symptoms. The magnitude of the signs and symptoms, and the clinician's own experience level, formulate a "probability" that the malady exists. In many situations, the greater the probability of the malady, the more likely the clinician will order a diagnostic test to confirm, or exclude the malady. The pretest probability of various diseases is specific for each disease, specific for the signs and symptoms of that disease, and specific to the setting in which it is found.

When considering the use of TB as a diagnostic tool for oral cancer diagnosis, the pretest probability of a nonsmoking, nonalcohol-consuming young woman is significantly less than the pretest probability of the older, alcohol-consuming, male smoker. Our clinical experience and dental literature offers the clinical acumen to estimate pretest probabilities in the low-to-high range, and one may even be able to estimate a numeric probability. [54]

3. Will the results help me in caring for my patients?

The third step is to decide how to use this test, both for the individual patient and for your practice in general. Are the results of the study generalizable-i.e. can you apply them to this particular patient and to the kind of patients you see most often? How often are the test results likely to yield valuable information? Does the test provide additional information above and beyond the history and examination? Is it less expensive or more easily available than other diagnostic

tests for the same target disorder? Ultimately, are patients better off if the test is used? [56]

Will the reproducibility of the test result and its interpretation be satisfactory in my setting?

The value of any test depends on its ability to yield the same result when reapplied to stable patients. Poor reproducibility can result from problems with the test itself.

If the reproducibility of a test in the study setting is mediocre and disagreement between observers is common, and yet the test still discriminates well between those with and without the target condition, it is very useful. Under these circumstances, it is likely that test can be easily applied to your clinical setting. If reproducibility of a diagnostic test is very high and observer variation very low, either the test is simple and unambiguous or those interpreting it are highly skilled. If the latter applies, less skilled interpreters in your clinical setting may not do as well.

Will patients be better off as a result of the test?

The ultimate criterion for the usefulness of a diagnostic test is whether it adds information beyond that otherwise available, and whether this information leads to a change in management that is ultimately beneficial to the patient. [55]

Evaluating an article on harm

"Harm" from the patient's perspective can be defined as an encounter that results in a harmful or unwanted outcome. The encounter must always precede the outcome. Dentists also interview patients who may have experienced harmful exposures, leading to harmful events. Two classic clinical findings, "nursing- bottle caries" and "tetracycline staining" define the exposure and the harmful event in its clinical name. Life-style exposures or a patient characteristic/risk factor can result in a harmful outcome that must be countered by dental therapy.

Selection of the appropriate research design for studying a harmful outcome or adverse event is dependent on the research question and the feasibility of conducting the trial. Even though the appropriate design may have been used in the trial, it is important to determine whether the study was of a high quality related to gathering and assessing the comparison groups.[58]

In a study that identifies a harmful exposure, the choice of comparison groups has an enormous influence on the credibility of the results. Because the design of the

study determines the comparison group, a short description of different study designs is given below-

Randomized Controlled Trials – A randomized controlled trial (RCT) is a true experiment in which patients are assigned by a mechanism analogous to a coin flip, to either putative causal agent or some alternative experience (either another agent or no exposure at all). Investigators then follow the patients forward in tim e and assess whether they have experienced the outcome of interest. The great strength of RCT is that we can be confident that the study groups were similar not only with respect to determinants of outcome that we know about, but also those we do not know about.

Cohort Studies –When it is either not feasible or not ethical to randomly assign patients to be exposed or not exposed to a putative agent, investigators must find an alternative to RCT .In a cohort study, the investigator identifies exposed and non-exposed groups of patients and then follows them forward in time, monitoring the occurrence of outcomes.

Case –Control Studies – when the outcome of interest either is very rare or takes a long time to develop, cohort studies also may not be feasible. Investigators may use an alternative design in which they identify cases, patients who have already developed the outcome of interest (e.g. a disease, hospitalization, death). The investigators then choose controls, person who do not have outcome of interest, but who are otherwise similar to the cases with respect to important determinants of outcomes such as age, sex, and concurrent medical conditions. Investigators can then assess retrospectively the relative frequency of exposure to the putative harmful agent among the cases and controls. This observational design is called as case- control study.

Case Series and Case Reports- Case series and case reports do not provide any comparison group and they are therefore unable to satisfy the requirements of the first primary guide.[59]

1. Are the results of the study valid?

Primary guides:
Are there clearly identified comparison groups similar with respect to important determinants of outcome other than the one of interest?

The usual human comparison groups are (1) patients who have experienced the exposure but may or may not have the harmful outcome, compared with (2)

patients who have not experienced the harmful exposure but may or may not have the harmful outcome.

The clinical question that is being asked determines the study design that would give the strongest evidence. For instance, does the question involve a harmful side effect of a therapy, or does it involve the harmful outcome of a patient's lifestyle or risk factor that is not under the control of the clinician? In turn, the design of the study determines how the comparison groups are gathered.

Are the outcomes and exposures for both groups measured in the same way?

It is important that both groups are treated similarly in terms of method of discerning exposure history and method of measuring or grading the outcome. Subjects or interviewers with knowledge of the study hypothesis may bias study results and therefore should be blind to the study hypothesis or group assignments whenever possible.
Is follow-up sufficiently long and complete?

The investigators must have a sound hypothesis for the causal relationship of an intervention/exposure and an adverse event, to be assured that the patients have been followed for a long enough time. Studies that end before a sufficient number of subjects can achieve the outcome event will likely fail to demonstrate the appropriate causal relationship. When subjects are lost to follow-up before the outcome occurrence can be assessed, one must make a determination as to whether the subjects lost have influenced the final conclusions.

Secondary guides:

Is the temporal relationship of cause and effect correct, consistent, and reasonable?

The causal agent or exposure should precede the outcome. When determining cause and effect, it is imperative to understand not only the temporal relationship , but also understand that there may be exposures that frequently occur simultaneously or consecutively, followed by the outcome. The investigator maybe making observations on one exposure, when it is truly the other exposure that is causing the outcome.For example phenytoin therapy has been evaluated as a cause of gingival hyperplasia. Poor oral hygiene has also been implicated along with phenytoin as the cause of hyperplasia.

Is there a dose/response gradient?

The causal relationship is more convincing, if the risk of the outcome increases with an increase in dose of the harmful agent or increased time of exposure to the harmful agent. Likewise, decreased dose of the offending agent or decreased time of exposure should decrease the risk of outcome.

2. What are the results of the study?

How strong is the association between exposure and outcome?
For cohort, studies, one can determine the relative risk (RR) of the outcome of interest occurring in the exposed population, compared with the unexposed population.

For the calculations, use the incidence of the event in the exposed group divided by the incidence of the event in the unexposed group.

RR=(a/[a+b])/(c/[c+d])
For case-control studies, one calculates the exposure rate for those with the outcome of interest (cases) compared with subjects who do not have the outcome (controls) to produce an odds ratio. For very rare events the odds ratio closely approximates the relative risk. The odds ratio is determined by using the odds of a "case" having the event divided by the odds of the "control" having the event (see table-21).

Odds ratio = (a/c)/(b/d)

An RR of greater than 1 represents an increase in risk associated with exposure and a value less than 1 represents a reduction in risk.

When there is a small increase in RR or odds ratio and the study design may have been weak, ie, case-control study, clinicians should wait for stronger evidence before changing their clinical practice.

How precise is the estimate of the risk?

In addition to the relative risk, the estimate of the precision of the relative risk can be determined. This estimate is called the "confidence interval." Many clinicians have a better understanding of *P* values than they have of confidence intervals. The *P* value describes the risk of the false-positive conclusion that a treatment is efficacious when it is not. In other words, the *P* value tells how often these results

would have occurred by chance if the experimental treatment were really no different from the control.

Focusing on *P* values can have limitations in clinical decision making. Authorities have debated whether *P*<.05 represents an appropriate way of branding studies as simply "positive" or "negative".

Because of this concern, there is increasing interest in expressing study results with their associated confidence intervals (CIs). Use of a CI around the RR helps clinicians decide the range within which they can be confident of the RR estimate. Also somewhat arbitrarily, science invokes a 95% CI in clinical research.

3. **Will the results help me in caring for my patients?**
Are the results applicable to my practice?
After the clinician determines that the study is appropriate and that the associations of a cause and effect are strong, one should examine the population of the study and decide how it compares with his or her patient population. If you are satisfied that the populations and settings are similar, you may wish to change your clinical practice after asking yourself the next 2 questions.
Is the magnitude of the risk clinically relevant?

A clinician understands that adverse events usually described in reports can occur in both the nontreated and treated groups. The relative risk and odds ratio do not describe the frequency with which an adverse event occurs. They merely describes how often the adverse event occurs in an exposed group compared with an unexposed group. Clinicians can use harm data from an RCT or cohort study to assist in making a clinical judgement about the adverse event.

If my therapy causes harm, should I attempt to discontinue the therapy?

The clinician not only determines the magnitude of the adverse events of the exposure or therapy, but should also consider what benefits of therapy will be lost if the therapy is discontinued. To determine whether the therapy will do more harm than good, one can compare the adverse event outcomes of the therapy with the reduction of risk of the measured outcome in the therapy trial. [58]

How to evaluate an article about prognosis?

Every day we inform patients of the prognosis for a particular tooth or other clinical problems. But what are we really saying? For example, in offering an opinion about a tooth with reduced periodontal attachment, we (almost reflexively) consider various characteristics of the patient, such as age, oral hygiene status, bruxing habits, and occlusal loading. These characteristics serve as "prognostic factors." They need not actually cause the expected outcome, but

rather merely be associated with it strongly enough that the factors tend to predict the outcomes- good or bad. There are various kinds of prognostic factors: demographic (such as age, sex), disease specific (such as bleeding on probing), or comorbid (for example, radiated tissue, poorly controlled diabetes). Prognostic factors are usually distinguished from "risk factors" that are the characteristics associated with the development of the problem in the first place. Articles on prognosis then, look not only at the natural history of a given condition, but also at the clinical history.

The ideal way to test the effect of different prognostic factors would be to randomize patients to different factors. However, this may not be possible, or is unethical.

As a good alternative, the cohort study is a strong design to reveal the increased risk of a particular outcome being associated with a particular prognostic factor. Here, patients who have not yet had any of the potential outcomes are assigned into cohorts on the basis of the existing prognostic factors of interest. The investigators then follow the cohorts forward for a specific period, observing the subjects to determine whether the outcome of interest occurs. The frequency and/or timings of these outcome events for each cohort, yields information on each of the prognostic factors. The magnitude of the association is determined between each cohort's outcomes and each cohort's prognostic factors. We then have measured information on the prognosis of a disease process.

Another possible methodological design is the case-control study. In this design, the investigator gathers up "cases" (patients who have already had the outcome of interest) and "controls" (those who have not). The investigator selects patients for these groups that have characteristics as similar as possible, except for the possible prognostic/risk factors.[60]

1. Are the results of the study valid?

Primary guides:
Was there a representative and well-defined sample of patients at a similar point in the course of the disease?

In any article about the prognosis of a condition, the reader must be assured that the patients in the study really do have the condition of interest, and not some other process that could be confused with the condition of interest. The authors therefore should be very explicit in detailing the criteria by which patients were chosen for the study. Because the chosen patients are only a sample of all patients with the condition of interest, it is important that they be representative of the full range of people who have that condition. To establish this, the manner of recruiting the patients must be clearly reported. This description addresses possible biases that may cause the composition of the selected groups to favour 1 segment of the population. For example, patients chosen from speciality offices may have more severe problems, thereby making unfavourable outcomes more

likely compared with patients recruited through public advertising; a problem called "***referral filter bias***."

Outcome events may not occur at the same rate over time. It is important that all patients enter the study at the same point in their clinical course of the condition of interest. If subjects enter the study at different points in the clinical course of their disease, the recorded incidence of outcome events may be inaccurate.
Was follow-up sufficiently long and complete?

As noted previously, prognostic factors may precede an outcome by a long time, so it is necessary to follow the study patients for long enough for the outcome event to happen and be recorded. The length of follow-up therefore needs to be clearly outlined, in terms more specific than just the average length of observation for the group. The reader needs to know how many patients were actually followed for the full term of the study.

It is important to report the reasons for the loss of follow-up and show that these reasons are unrelated to the outcome, and that the "lost to follow-up" numbers are equally distributed in the 2 groups. Failure to report this information reduces the reader's confidence in the final study analyses.

Secondary Guides**:**
Were objective and unbiased outcome criteria used?

It is necessary to establish a clear definition of outcome events before the study starts to allow consistent recording of the study results. The definition may be simple e.g. the presence or absence of a tooth. Alternatively, the outcome may be more equivocal, such as the decision to remove the tooth. One dentist may declare the tooth salvageable where another would not. The important element is that, where any judgement is required to determine an outcome, the observer must be trained in the outcomes assessment and blind to the presence of the prognostic factors- or even the purpose of the study- wherever possible.

Similarly, where such judgements are made over more than 1 group of patients or more than 1 point in time, the measurement methods should be the same at each examination or observation.

Was there adjustment for important prognostic factors?

A useful way to learn about a suspected prognostic factor is to follow a cohort of patients who exhibit that factor. The incidence of outcomes in those people compared with the incidence in a control group will yield the relative risk (RR) of the outcome for that prognostic factor, compared with the control group. Indeed, several such groups can be followed, each with distinctive prognostic factors. However, for this arrangement to be valid, the group with the distinctive

prognostic factor must be the same in all other respects (that could have an effect on the outcome) as the control (or other comparison) groups.

2. What are the results?

How large is the risk of the outcome event(s) in a specified period?
This is a key question that patients often want answered. The reply can be expressed in 3 forms:

1. In absolute terms
2. In relative terms
3. Over time: The rate at which outcome events take place may not be constant over time, and neither of the above expressions reflect this. The survival curve provides a graphical representation of the incidence of outcome events over time. Starting at 100% (all subjects are free of events), the graph declines as each event occurs. Therefore, this requires that outcomes be clearly defined events, and the time of their occurrence must be recorded precisely.

How precise are the estimates of risk?

Because the 3 kinds of answers above are derived from samples of the population, they are necessarily estimates of the true risk of outcome for the population as a whole. How precise the estimates are will depend of course on the number of patients followed. Confidence intervals are an expression of that precision. The estimates can be quite precise for the shorter periods of follow-up, but will often decline as the periods grow longer. The length of time it takes to enroll the subjects, and the loss of some to follow-up will erode the number of subjects and thus the precision of the estimates of risk of the outcomes of interest will decrease.[60]

3. Will the results help me in caring for my patients?

Were the study patients similar to my own?

How well do the study results generalize to the patients in your practice?The authors should describe the study patients in enough detail to allow comparison with your patients. The article should list the patients' important clinical characteristics.The closer the match between the patient before you and those in the study, the more confident you can be in applying the study results to that patient.

Will the results lead directly to selecting or avoiding therapy?

Prognostic data often provide the basis for sensible decisions about therapy. Knowing the expected clinical course of your patient’s condition can help you judge whether treatment should be offered at all.

Are the results useful for reassuring or counselling patients?

A valid, precise, and generalizable result of uniformly good prognosis is very helpful to the clinician when reassuring a concerned patient or relative. [61]

HOW TO EVALUATE AN OVERVIEW

A comprehensive structured review of the published literature, that has an explicit and focused question, rules for inclusion of primary studies to present as evidenc e, an explanation of the strength of the evidence, and a summary of the collective findings from the primary studies is called an **overview.**

Overviews of the scientific literature are very useful to clinicians and researcher s who are responding to questions on the efficacy of patient therapy, or formulating a research project to address a basic science or transitional research question related to dentistry. An overview that addresses a well-defined question is more helpful to a reader than a haphazard or biased selection of the available citations.

Overviews must be read as critically as a primary research article. An overview uses specific methodologic criteria and should be viewed "as a study in itself." The fundamental difference between an overview and primary articles reporting the results of a study is the unit of analysis, not the scientific principles that apply.

Strategies for assessing an overview:

It is extremely important for the reader to follow a specific strategy when assessing an overview article. The basic elements of such a strategy should determine whether: (1) a clearly defined question was addressed, (2) specific search strategies were used, (3) preparation of the results was detailed, (4) the overall results of the overview were appropriate, and (5) the results can be applied to patient care.

The question in the overview must have 3 basic parts: (1) what is being reviewed (patient histories, elements of physical examination, diagnostic tests, treatment modalities, treatment outcomes), (2) in whom (the experimental population of interest), and (3) for what outcomes (consequences).

The overview should provide an explicit statement of the search strategies used by the author. Such strategies should include, but not necessarily be limited to, one or more bibliographic databases such as PUBMED, MEDLINE, or GREATFUL- MED, and include a statement of which key words were used and in what order they were used.

Differences in study results generally arise from sources: (1) different sorts of patients (with different oral environmental conditions or responsiveness to treatment), (2) different histories, ways of performing the diagnostic tests, or performing treatments (including the extent of therapy, lengths of the test periods , combinations of treatment, and compliance), (3) different outcomes (defined and measured in different ways and with different measurement systems and degrees of sensitivity), (4) different study methods (with different rigor and power), and
(5) the play of chance.

All 5 of these possible explanations should have been considered by the author in interpreting individual study results to ensure that it makes clinical sense to combine the studies. In addition, it is possible to test the extent to which differences among results of the individual studies are "significant " (greater than could be expected due to chance alone). The statistical analyses that are used to d o this are called tests of homogeneity. The more significant (closer to zero) the test, the less likely it is that the observed differences are due to chance alone.

Unfortunately, tests of homogeneity have limited power to detect differences. So, a nonsignificant test does not necessarily rule out important differences and large differences between study results still dictate some degree of caution in interpreting the overall findings.[62]

Investigators must make a host of decisions in preparing an overview, including determining the focus; identifying, selecting, and critically appraising the relevant studies (which we will call the "primary studies"); collecting and synthesizing (either quantitatively or nonquantitatively) the relevant information; and drawing conclusions. Avoiding errors in both meta-analyses and other overviews requires a systematic approach, and enabling users to assess the validity of an overview's results requires explicit reporting of the methods.

Table 19 - Systematic evaluation ensures valid, applicable overview conclusions

Step	Assessment Component	Key Points
1	Review Question	Clearly defined question addressed by the overview.
2	Question Structure	Includes what is reviewed, in whom, and for which outcomes.
3	Search Strategy	Explicit search methods stated (databases, keywords, order).
4	Study Selection	Relevant primary studies identified and critically appraised.
5	Data Preparation	Results collected and synthesized systematically.
6	Sources of Variation	Differences due to patients, interventions, outcomes, methods, or chance.
7	Interpretation	All sources of variation considered before combining studies.
8	Statistical Assessment	Tests of homogeneity used to assess variability beyond chance.
9	Caution in Results	Nonsignificant tests do not exclude important differences.
10	Transparency	Explicit reporting of methods enables validity assessment and reduces errors.

Table 20: Users' guides for how to use an overview [63]

1. Are the results of the study valid?

Primary guides:

- Did the overview address a focused clinical question?
- Were the criteria used to select articles for inclusion appropriate?

Secondary guides:

- Is it unlikely that important, relevant studies were missed?
- Was the validity of the included studies appraised?
- Were assessments of studies reproducible?
- Were the results similar from study to study?

2. *What are the results?*

- What are the overall results of the review?
- How precise were the results?

3. *Will the results help me in caring for my patients?*

- Can the results be applied to my patient care?
- Were all clinically important outcomes considered?
- Are the benefits worth the harms and costs?

1. Are the results of the overview valid?

Primary Guides:

D*id the overview address a focused clinical question?*

Unless an overview clearly states the question it addresses, you can only guess whether it is pertinent to your patient care. If the main question that an overview addresses is not clear from the title or abstract, it is probably a good idea to move on to the next article.
Many overviews address a number of questions. For example, a review article or a chapter from a textbook might include sections on the etiology, diagnosis, prognosis, treatment, and prevention of asthma. While such broad reviews can provide a useful introduction to an area, they usually offer limited support for their conclusions. Typically, you will find only a declarative statement followed by one or more citations. You must then study the references in order to judge the validity of the authors' conclusions.

Were the Criteria Used to Select Articles for Inclusion Appropriate?

To determine if the investigators reviewed the appropriate research, the reader needs to know the criteria they used to select research. These criteria should specify the patients, exposures, and outcomes of interest. They should also specify the methodologic standards used to select studies, and these standards should be similar to the primary validity criteria. Differences in the patients, exposures, and outcomes can lead to different results among overviews that appear to address the same clinical question. The clinician must be sure the criteria used to select the studies correspond to the clinical question that led her to the article in the first place.
If the authors state their inclusion criteria, it is less likely they will (as they want to do) preferentially cite studies that support their own prior conclusion. Bias in choosing articles to cite is a problem for both overviews and original reports of research.

Secondary Guides:

I*s it unlikely that important relevant studies were missed?*

It is important that authors conduct a thorough search for studies that meet their inclusion criteria. This should include the use of bibliographic databases, such as MEDLINE and EMBASE, checking the reference lists of the articles they retrieved, and personal contacts

with experts in the area. Unless the authors tell us what they did to locate relevant studies, it is difficult to know how likely it is that relevant studies were missed.

W*as the validity of the included studies appraised?*
Even if a review article includes only RCTs, it is important to know whether they were of good quality. Unfortunately, peer review does not guarantee the validity of published research.

There is no one correct way to assess validity. Some investigators may use long checklists to evaluate methodologic quality, while others focus on three or four key *aspects of the study. When considering whether to believe the results of an overview, you should check whether the authors examined criteria similar to those we have presented on deciding on the credibility of their primary studies.*

W*ere assessments of studies reproducible?*
Authors of review articles must decide which studies to include, how valid they are, and which data to extract from them. Each of these decisions requires judgement by the reviewers and each is subject to both mistakes (random errors) and bias (systematic errors). Having two or more people participate in each decision guards against errors, and if there is good agreement among the reviewers, the clinician can have more confidence in the results of the overview.

W*ere the results similar from study to study?*
Despite restrictive inclusion criteria, most systematic overviews document important differences in patients, exposures, outcome measures, and research methods from study to study. Readers must decide when these factors are so different that it no longer makes sense to combine the study results.

2. What are the results?

What are the overall results of the overview?

In overviews, investigators collect data from individual studies. These data must also be summarized, and increasingly, investigators are using quantitative methods to do so.
Simply comparing the number of positive studies with the number of negative studies is not an adequate way to summarize the results. With this sort of "vote counting," large and small studies are given equal weights, and (unlikely as it may seem) one investigator may interpret a study as positive, while another investigator interprets the same study as negative.
Typically, meta-analysts weight studies according to their size, with larger studies receiving more weight. Thus, the overall results represent a weighted average of the results of the individual studies.

You should look to the overall results of an overview the same way you look to the results of primary studies.

How precise were the results?

In the same way that it is possible to estimate the average effect across studies, it is possible to estimate a confidence interval (CI) around that estimate; ie, a range of values with a specified probability (typically 95%) of including the true effect.

3. Will the results help me in caring for my patients?
Can the results be applied to my patient care?

One of the advantages of an overview is that since it includes many studies, the results come from a very diverse range of patients. If the results are consistent across studies, they apply to this wide variety of patients. Even so, the clinician may still be left with doubts about the applicability of the results.For example, perhaps the patient is older than any of those included in the individual trials summarized by the overview. If studies using different members of a class of drug have been combined, one might question whether one of the drugs has a larger effect than the others.

Were all clinically important outcomes considered?

While it is a good idea to look for focused review articles because they are more likely to provide valid results, this does not mean that you should ignore outcomes that are not included in a review. Focused reviews of the evidence for individual outcomes are more likely to provide valid results, but a clinical decision requires considering all of them.

Are the benefits worth the harms and costs?

Finally, either explicitly or implicitly, when making a clinical decision the expected benefits must be weighted against the potential harms and costs.[63]

With regard to dentistry, these are indeed the best of times. We have available materials and techniques that visionaries could only dream of 25 years ago. We can predictably replace missing teeth with implant-supported prosthesis. We can regenerate tissue lost to disease and trauma. And yet, as our profession entered the 21st century, these are also the worst of times. As a profession, we have become so enamoured with our new technologies that we seem to have lost our collective common sense. We have many wonderful new materials and techniques, but do we have the wisdom to use them appropriately?

Due to rapid flux of materials, the idea has insidiously crept into our thinking process that clinical research data is not necessary in our decision -making process. Since nature abhors a vacuum, the void created by this lack of relevant clinical research has been filled with anecdotal information. Hence, the genesis of our newest source of information, the **nonrefereed dental "journal".** This new class of literature is based on the premise that the refereed literature is too slow and cumbersome. It is most often written with two overriding purposes: (1) to promote a product or device and (2) to promote the career of the author.

Three factors are primarily responsible for this trend. **First** is the lack of an evidence-based educational philosophy in dental education. Dental schools have traditionally placed a much greater emphasis on the mechanistic aspects of dentistry. An understanding and appreciation of the dental literature as a basis for clinical decision - making has never been the primary educational focus in dental schools.

The **second** factor is the market forces that have created the dental infomercial. The vast majority of the nonrefereed literature is sponsored by dental manufacturers. It is packaged to simulate traditional refereed journals and is not presented as the commercial advertising it truly is.

Third and certainly the most important factor is that many of us suffer from the late 20th-century malady of busyness. With all of the activities in our personal and professional lives, it is difficult for us to maintain our commitment to reading current literature. Since time is limited and the infomercial literature is more entertaining, we read it instead of refereed journals. However, it is the dentist, not the manufacturer, who makes the treatment decisions. Therefore, the ultimate responsibility for making these decisions, based on the best available evidence, lies with the dentist.[64]

The dental profession has received a great deal of criticism in the public press because of findings that enormous variations exist in treatment recommendations and health care practice. These variations have been attributed to (1) poor science underlying the clinical decisions, (2) poor quality of clinical care decisions and (3) variations in clinical skills. To counter these criticisms and to respond to the challenge of modern health care, **the dentist must combine evidence-based information with practical clinical experience** when engaging in the process of diagnosis, treatment planning and treatment. [29]

In an **evidence-based model of clinical practice,** a patient's consent for treatment requires full disclosure of scientifically validated information. In instances in which the evidence is lacking or weak, patients should be so informed. While Evidence - Based Dentistry (EBD) may seem to intrude on dentists' autonomy, the benefit of this practice model is that it protects dentists from legal liability by fully disclosing all information that has been critically reviewed by dentists and methodologists.[12]

EBD will increasingly have an impact on use and reimbursement. Within an evidence- based context, the rules of care delivery and how people get paid will change. Dental care delivery and reimbursement will become less and less based on the procedure and more and more based on the evidence. With evidence-based dentistry, the burden of proof will shift. The dentist or third party will need to justify a clinical decision with evidence. The power will no longer be located in hierarchy or seniority. Hierarchy and seniority will no longer be justification for authority. Evidence willl be the authority, not people. The dentist will be asked again and again to “put the statistics on the table”. If a treatment has solid justification, dentists will be faulted if they fail to provide it. This will also be the case for third parties, patients and unfortunately, lawyers.[4]

Barriers to using evidence-based methods in everyday practice include lack of appropriate skills for formulating clear questions, executing efficient electronic searches and evaluating the literature.

Often cited as a barrier to EBD is the lack of good clinical research in the form of well-designed, adequately powered randomized trials. The rigorous methodology demanded by systematic reviews for organizing and analyzing the literature in an area provides a valuable tool for identifying areas where the evidence is weak and where research is needed and feasible.

Perhaps the greatest impediments to the evidence-based movement are the fear and mistrust on the part of practitioners that the evidence will be misused by decision makers, particularly third-party funders and regulatory bodies, and that the individual autonomy of dentists, in caring for their patients, will be threatened. This is another compelling reason why the profession must embrace EBD and provide the leadership needed to protect the scientific integrity of the evidence. Practicing dentists must ensure, through direct involvement with the process, that guideline development methods are open and transparent and that the resulting guidelines are practical, useful and relevant.

Overcoming these barriers, exploiting the potential of information technology and applying sound scientific priniciples to everyday practice will allow dentists to meet the greatest challenge of practice- the provision of high quality, effective oral health care.[11]

Dental speciality groups are now beginning specifically to address the clinical applications of evidence-based methods in clinical care. Several forums are now in place to facilitate these (r)evolutionary changes:
The new journal Evidence-Based Dentistry brings oral health into the fold of a burgeoning field of medical speciality journals focused on evidence-based health care.
The Centre for Evidence-based Dentistry at Oxford University offers short-term intensive courses in Evidence-based Dentistry, a Critical Appraisal Skills Programme, and serves as the editorial centre for the journal Evidence-Based Dentistry.
The Harvard School of Dental Medicine's Office of Evidence-based Dentistry initiated a course "Evidence-based Dentistry" in its pre-doctoral dental curriculum, and offers a short-term, intensive graduate-level, clinical trials training program in Evidence-based Dentistry that includes an MPH degree in clinical effectiveness.[9]
The American Dental Association Commission on Accreditation requires , as part of the accreditation process of dental school curricula, that students develop the skills needed to manage scientific information will critical thinking. The requirement that students be able to locate, understand, and critically evaluate the dental literature provides some of the skill required to properly treat the patient in the clinical setting-in other words, the skill to understand, decipher, and apply evidence.[1]

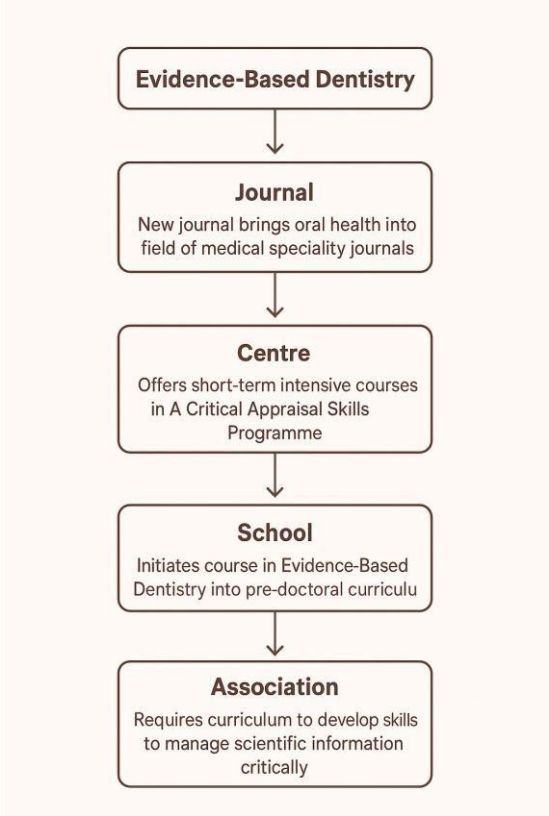


Figure 10: Evidence-based dentistry integrated through journals, education, and accreditation

Who will benefit from evidence- based dentistry:

In the current information era, knowledge is both a tool and a commodity that can be used to improve the decisions made by dentists every day. Information summarized within systematic reviews should assist dentists in making appropriate treatment decisions with patients. Evidence-based dentistry help dentists by providing simple and validated scientific summaries. Personal experience, because of its potential for bias, should no longer be the sole source of life long learning in dentistry. Furthermore, the lack of consistency in treatment decisions among dental and medical practices is problematic. Shifting from a reliance on the experimental model of decision making to an evidence based model would benefit all health care professions, as well as general public. [12]

- The ultimate beneficiaries of EBD are members of the **public**, who will reap the rewards of better care. The internet allows patients, as well as professionals, access to health care information. The public, however, does not have the tools to evaluate the data adequately and must rely on their educated dentists to help sort fact from fiction. Patients will be more educated, more involved in their treatment decisions, and more appreciative of quality care.

- **Dentists**, who will also benefit from EBD. Instead of conducting free product testing for dental product manufacturers, practitioners will have at their disposal more valid research on which to predicate their clinical decisions.

- **Researchers**, who will benefit by being called upon to do the clinical testing necessary before new products are placed on the market. [2]

Figure 11: Evidence-based dentistry benefits public, dentists, and researchers

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TERMS USED:

1. **Absolute risk-** observed or calculated probability of an event occurring in a population that is under study.
2. **Absolute risk difference-** the difference in the risk for disease or death between exposed and an unexposed population.
3. **Accuracy -** in measurement, a measure is accurate if it reflects the "true" state of the attribute being measured, without bias. In diagnostic tests, the proportion of test results that agree with the gold standard.
4. **Allocation -** assignment of a patient who meets the inclusion criteria of a study to the groups being followed, most often an experimental treatment group and a control (or usual treatment) group.
5. **Alpha error –** *see type* 1 *error* (the error that results if a true null hypothesis is rejected or if a difference is concluded when there is no difference.)
6. **Alternative hypothesis -** the opposite of the null hypothesis. It is the conclusion when the null hypothesis is rejected.
7. **Beta error -** *see typeII error* (the error that results if a false null hypothesis is not rejected or if a difference is not detected when there is a difference).
8. **Bias-** any systematic error that results in an incorrect estimate of the association between treatment or exposure and the result. The error related to the way the targeted and sampled populations differ; which threatens the validity of a study.
9. **Blind study-** an experimental study in which subjects do not know the treatment they are receiving; investigators may also be blind to the treatment subjects are receiving; see also *double-blind trial.*
10. **Case-control study -** an observational study that begins with patient cases who have the outcome or disease being investigated and control subjects who do not have the outcome or disease and then looks backward to identify possible precursors or risk factors.
11. **Case-series study -** a simple descriptive account of interesting or intriguing characteristics observed in a group of subjects.
12. **Categorical observation -** a variable whose values are categories (an example is type of anemia). See also *nominal scale.*
13. **Chance agreement -** a measure of the proportion of time in which 2 or more rates would agree in their measure or assessment of phenomena.
14. **Chi-square *(X^2)* test -** the statistical test used to test the null hypothesis that proportions are equal or, equivalently, that factors or characteristics are independent or not associated.

15. **Clinical significance -** in contrast to statistical significance, clinical significance is a difference between observations that is a tangible benefit to the patient. A comparison of groups could demonstrate a statistically significant difference without there being any tangible clinical difference perceived by the patient(s).
16. **Clinical trial -** an experimental study of a drug or procedure in which the subjects are humans.
17. **Coefficient of variation (CV) -** the standard deviation divided by the mean (generally multiplied by 100). It is used to obtain a measure of relative variation.
18. **Cohort -** a group of subjects who remain together in the same study over a period.
19. **Cohort study -** an observational study that begins with a set of subjects who have a risk factor (or have been exposed to an agent) and a second set of subjects who do not have the risk factor or exposure. Both sets are followed prospectively through time to learn how many in each set develop the outcome or consequences of interest.
20. **Co-intervention -** interventions, other than the treatment under study, that are applied differently to the treatment and control groups. Co-intervention is a serious problem when double blinding is absent or when the use of very effective nonstudy treatments is permitted.
21. **Concurrent controls -** control subjects assigned to a placebo or control condition during the same period of time that an experimental treatment or procedure is being evaluated.
22. **Confidence interval (CI) -** the interval computed from sample data that has given probability that the unknown parameter, such as the mean or proportion, is contained within the interval. Common confidence intervals are 90%, 95%, and 99%.
23. **Confidence limits -** the limit(s) of a confidence interval. These limits are computed from sample data and have a given probability that the unknown parameter is located between them.
24. **Confounding variable-** a variable more likely to be present in one group of subjects than in another that is related to the outcome of interests and thus potentially confuses, or "confounds," the results.
25. **Continuous scale -** a scale used to measure a numerical characteristic such as values that occur on a continuum (an example is age).
26. **Control group -** in a clinical trial, subjects assigned to the placebo or control condition; in a case-control study, subjects without the disease or outcome.
27. **Controlled trial-** a trial in which subjects are assigned to a control condition as well as to an experimental condition.
28. **Correlation coefficient-r -** (Pearson product moment) a measure of the linear relationship between 2 numerical measurements made on the same set of subjects. It ranges from -1 to +1, with zero indicating no relationship.
29. **Crossover study -** a clinical trial in which each group of subjects receives 2 or more treatments in different sequences.
30. **Cross-sectional study -** an observational study that examines a characteristic (or set of characteristics) in a set of subjects at one point in time; a "snap-shot" of a characteristic or condition of interest; also called survey or poll.

31. **Dependent variable -**a known variable, the value of which will affect the outcome of a study; also called a response or criterion variable.
32. **Descriptive statistics-** statistics such as the mean, the standard deviation, the proportion, and the rate used to describe attributes of a set of data.
33. **Dichotomous observation -** a nominal measure that has only 2 outcomes (examples are gender: male or female; survival: yes or no); also called binary.
34. **Discrete scale -** a scale used to measure a numerical characteristic that has integer values (an example is number of pregnancies).
35. **Distribution-** (population)-the frequency of occurrence for values of a characteristic or variable. Distributions may be based on empirical observations or may be theoretical probability distributions (e.g., normal, binomial, chi-square).
36. **Double-blind trial-** a clinical trial in which neither subjects nor the investigator(s) know which treatment subjects have received.
37. **Effect or effect size –** the magnitude of a difference or relationship. It is used for determining sample sizes and combining results across studies in meta-analysis.
38. **Effectiveness-** a measure of the benefit resulting from an intervention for a given health problem under usual conditions of clinical care for a particular group; this form of evaluation considers both the efficacy of an intervention and its acceptance by those to whom it is offered, answering the question, "Does the practice do more good than harm to people to whom it is offered?"
39. **Efficacy -** a measure of the benefit resulting from an intervention for a given health problem under the ideal conditions of an investigation; it answers the question, "Does the practice do more good than harm to people who fully comply with the recommendations?"
40. **Estimation -** act or process of using a sample of information from a population to draw conclusions about the parameters of that population.
41. **Event -** a single outcome (or set of outcomes) from an experiment.
42. **Experimental study -**a comparative study involving an intervention or manipulation. It is called a trial when human subjects are involved.
43. **False negative -** a test result that is negative in a person who has the disease.
44. **False positive -**a test result that is positive in a person who does not have the disease.
45. **Frequency distribution -** list of values that occurs, along with the frequency of occurrence, in a set of numerical observations. It may be set up as a frequency table or as a graph.
46. **Generalizability -** the extent to which the findings of a study from a sample of a population can be representative of, or inferred to, the total population (also called external validity).
47. **Gold standard -** in diagnostic testing, a procedure that always identifies the true condition-diseased or disease-free-of a patient.
48. **Historical cohort study -**a cohort study that uses existing records or historical data to determine the effect of a risk factor or exposure on a group of patients.
49. **Historical controls -** in clinical trials, previously collected observations on patients used as the control values against which the treatment is compared.

50. **Homogeneity -** the situation in which the standard deviation of the dependent (Y) variable is the same regardless of the value of the independent (X)variable; an assumption in ANOVA and regression.
51. **Hypothesis test -** an approach to statistical inference resulting in a decision to reject or not to reject the null hypothesis.
52. **Incidence -** a rate giving the proportion of people who develop a given disease or condition within a specified period.
53. **Independent events -** events whose occurrence or outcome has no effect on the probability of each other.
54. **Independent variable -** the explanatory or predictor variable in a study. It is sometimes called a factor in ANOVA.
55. **Inference (statistical) -**the process of drawing conclusions about a population using a sample of observations of the population.
56. **Interaction -** relationship between 2 independent variables that have a different effect on the dependent variable; i.e., the effect of one level of a factor A on the level of factor B.
57. **Interrater reliability -** the reliability between measurements made by two different persons (or raters).
58. **Interval scale -** a measurement scale that sorts and orders, like an ordinal scale, but there is a fixed unit of measurement associated with the scale.
59. **Intervention -** the maneuver used in an experimental study. It may be a drug or a procedure.
60. **Intrarater reliability -** the reliability between measurements made by the same person (or rater) at 2 different points in time.
61. **Kappa (K) -** a statistic used to measure; interrater or intrarater agreement for nominal measures.
62. **Level of significance -** the probability of incorrectly rejecting the null hypothesis after testing the hypothesis. Also see *alpha value* and *P value.*
63. **Likelihood ratio -** the ratio of true-positives to false positives in diagnostic testing.
64. **Longitudinal study -**a study that takes place over an extended period.
65. **Matching (or matched groups) -**the process of making 2 groups homogenous on possible confounding factors. It is sometimes done before randomization in clinical trials.
66. **Measurement error -** the amount by which a measurement is incorrect because of problems inherent in the measuring process; also called systematic error bias.
67. **Meta-analysis -** a method for combining the results from several independent studies of the same outcome so that an overall P value may be determined.
68. **Nominal scale -**the simplest scale of measurement. It is used for characteristics that have no numerical values (examples are race and gender).It is also called a categorical or qualitative scale.
69. **Nonrandomized trial -** a clinical trial in which subjects are assigned to treatments on other than a randomized basis. It is subjected to several biases.
70. **Null hypothesis-** the hypothesis being tested about a population. *Null* generally means "no difference" and thus refers to situations in which there is no difference (e.g., between the means in a treatment group and a control group).

71. **Number needed to treat (NNT) -** the number of patients who must be exposed to an intervention before the clinical outcome of interest can be expected to occur; for example, the number of patients needed to treat to prevent one adverse outcome.
72. **Numerical scale -** the highest level of measurement. It is used for characteristics that can be given numerical values; the difference between numbers have meaning (examples are height, weight, blood pressure level).It is also called an interval or ratio scale.
73. **Observational study -** a study that does not involve an intervention or manipulation. It is called case-control, cross-sectional, or cohort, depending on the design of the study.
74. **Odds -** the probability that an event will occur divided by the probability that the event will not occur; i.e., odds = P/ (I-P), where P is the probability.
75. **Odds ratio (OR) -** an estimate of the relative risk calculated in case-control studies. It is the odds that a patient was exposed to a given risk factor divided by the odds that a control was exposed to the risk factor.
76. **Ordinal scale -** used for characteristics that have an underlying order to their values; the numbers used are arbitrary (an example is plaque scores).
77. **Outcome** (in an experiment) - the result of an experiment or trial.
78. **Overview -** a structured review of the published literature, which has an explicit and focused question, rules for inclusion of primary studies to present as evidence, an explanation of the strength of the evidence, and a summary of the collective findings from the primary studies. When the data from the primary studies allow combining in rigorous statistical analysis, it is called a meta-analysis.
79. **Paired *t* test -** the statistical method for comparing the difference (or change) in a numerical variable observed for 2 paired (matched) groups. It also applies to before and after measurements made on the same group of subjects.
80. **Placebo -** a sham treatment or procedure. It is used to reduce bias in clinical studies.
81. **Population -** the entire collection of observations or subjects that have something In common and to which conclusions are inferred.
82. **Post-test odds -** (in diagnostic testing) - odds that a patient has a given disease or condition based on a diagnostic procedure. They are similar to the predictive value of a diagnostic test.
83. **Power -** the ability of a test statistic to detect a specified alternative hypothesis or difference of a specified size when the alternative hypothesis is true (i.e. $1 - \beta$ and β is the probability of a type II error).More loosely, it is the ability of a study to detect an actual effect or difference.
84. **Precision -** the range in which the best estimates of a true value approximate the true value. See *Confidence interval.*
85. **Predictive value of a negative test -** the proportion of time that a patient with a negative diagnostic test result does not have the disease being investigated.
86. **Predictive value of a positive test -** the proportion of time that a patient with a positive diagnostic test result had the disease being investigated.
87. **Pretest odds -** in diagnostic testing the odds a patient has a given disease or condition before a diagnostic procedure is performed and interpreted. They are similar to prior probabilities.

88. **Prevalence -** the proportion of people who have a given disease or condition at a specified point in time. It is not truly a rate, although it is often incorrectly called a prevalence rate.
89. **Probability -** the number of times an outcome occurs in the total number of trials. If *A* is the outcome, the probability of *A* is denoted as *P (A).*
90. **Prognostic factors -** demographic, disease-specific, or comorbid characteristics associated strongly enough with a condition's outcomes to predict accurately the eventual development of those outcomes. Compare with risk factors. Neither prognostic nor risk factors necessarily imply a cause-and-effect relationship.
91. **Prognosis -** the possible outcomes of a disease or condition and the likelihood that each one will occur.
92. **Proportion -** the number of observations with the characteristics of interest divided by the total number of observations. It is used to summarize counts.
93. **Prospective study -** a study designed before data are collected.
94. ***P* value -** the probability of observing a result as extreme as or more extreme than the one actually observed from chance alone (i.e., if the null hypothesis is true).
95. **Random assignment -** the use of random methods to assign different treatments to patients or vice versa.
96. **Random error or variation -** the variation in a sample that can be expected to occur by chance.
97. **Randomization -** the process of assigning subjects to different treatments (or vice versa) by using random numbers.
98. **Randomized clinical trial -** an experimental study in which subjects are randomly assigned to treatment groups.

ABOUT THE BOOK

Dentistry is both an art and a science. This book explores the integration of scientific research and clinical expertise to provide the highest quality dental care. It defines evidence-based dentistry (EBD) as the judicious use of the best available clinical evidence combined with the dentist's experience and the patient's needs. The text covers the history and evolution of EBD, emphasizing its importance in the modern dental practice and the changing role of the patient in the decision-making process. From understanding the foundational principles to the step-by-step process of evidence-based learning, this book guides dental professionals through the process of applying evidence in clinical practice. It highlights the shift from tradition-based to evidence-based care, offering practical insights into improving clinical decision-making, enhancing patient care, and staying current with the latest research. A must-read for dental practitioners aiming to bridge the gap between scientific research and everyday clinical decisions.

ABOUT THE EDITOR

Dr Pallavi Singh

Dr Pallavi Singh has been working in Saraswati Dental College, Lucknow from past 10 years and has organized many outreach activities, camps under her supervision. She is currently heading the Department of Public Health Dentistry. She has also facilitated many collaborations and MOU's of the Department increasing the reach of the institution manifolds. Delivered various lectures on subject related topic to students, faculty, as well as general population. She has an excellent academic record, with more than 60 papers in national & international journals with 6 book & 5 patents published on her name. She is a co-ordinator of various government organizations like Unnat Bharat Abhiyan, National Service Scheme representating the institute. She is also school innovation Evaluator appointed by Ministry of Education Innovation Cell. She is also active in dental public health related activities and is a member of various associations. She has also chaired various sessions at many conferences, CDE's and workshop. Had successfully completed the course on Global Tobacco Control: Learning from the Experts from John Hopkins Bloomberg School of Public Health.

Dr Shikha Sachan

Dr Shikha Sachan, a distinguished dental professional, earned her Bachelor of Dental Surgery (BDS) and Master of Dental Surgery (MDS) from Babu Banarsi Das College, Lucknow, India. Current serving as a Professor and Head in Department of Public Health Dentistry in Maharana Pratap Dental College and Hospital, kanpur. She has worked as a Junior Resident in king George Dental College, Lucknow India.Since then, she has been actively engaged in teaching the students.She is a renowned teacher with a teaching experience of more than 9 years. She is well known for her impressive style of teaching and is very popular among the student.She has done many publications in various journal.She is also a author of a book which has been published in 2024. She has organised more than 2500 dental camps in underserved communities, providing preventive care and oral health education. Also conducted community oral health surveys and contributed to data analysis for Public Health research and also collaborated with local NGOs, government health worked and dental teams to improve access dental care and also organised tobacco cessation counselling and awareness camps. Participated in National heath events like Worlds oral health day, No Tobacco day, Aids Day, Nutrition Month Programmes.

As a Public Health Dentist she is actively involved in the research, education, and strategic direction developed by health agencies to build a healthy community. As a public health dentist she is actively contributing to community oral health promotion through dental screening camps, School Outreach Programmes and Public Awareness campaigns. She has been focused on improving oral health outcomes among underserved population through accessible and preventive care.

Dr Smriti Tripathi

Dr Smriti Tripathi, a distinguished dental professional, earned her Bachelor of Dental Surgery (BDS) from Maharana Pratap Dental College and Hospital, Kanpur, India and MDS degree from Rama Dental College Hospital and Research Centre, Kanpur. Currently, serving as a Senior Lecturer in Department of Public Health Dentistry in Maharana Pratap Dental College and Hospital, kanpur.Since then, she has been actively engaged in teaching the students with a experience of more than 2 years.She has done publications and also a author of a book. She has organised various dental health checkup camps in various schools, institutions and rural & urban areas and also actively involved in Oral health research and training programmes. As a Public Health Dentist she is focused on promoting oral health and preventing oral diseases within communities and populations.She is a trained professionals with experience in community development programmes and basic health services, as a Public Health Dentist she is focused on promoting oral health and preventing oral diseases within communities and populations, along with their diagnosis and treatment.

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