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- The patient (population or clinical problem of interest)
- The intervention (could be exposure, test or treatment)
- The comparison
- The outcome (ideally the one of interest to the patient)

ii. Searching the medical literature: for those studies that are most likely to give the best evidence.

iii. Finding the study: that will best be able to answer this question, determine the magnitude (effect size) and precision of the final results.
iv. Performing a critical appraisal of the study: to determine the validity of results. Looking for sources of bias that may represent a fatal flaw in the study.
v. Determining how the results will help in caring the patient (clinical application of the study)
vi. Evaluating the results in patient or population

Evidence Based Public Health (EBPH)

Jenicek, 1997 defined EBPH as the "conscientious, explicit, and judicious use of current best evidence in making decisions about the care of communities and populations in the domain of health protection, disease prevention, health maintenance and improvement (health promotion)."

A concise definition of EBPH is provided by Kohatsu – ""Evidence-based public health is the process of integrating science-based interventions with community preferences to improve the health of populations"

	medical treatments	
Time from intervention to outcome	- Shorter - Study on treatment of a medical condition (e.g. effectiveness of antibiotics for treatment of ARI) is likely to produce results in days or weeks, or even a surgical trials for cancer with endpoints of mortality within a few years	- Longer - Population based public health studies generally require a longer time period between intervention and outcome. - For example, a study on the effects of smoking cessation on lung cancer mortality
Professional training	- More formal, with certification and/or licensing	- Less formal, no standard certification
Decision making	- Individual - Decision making process is relatively homogenous	- Team - The higher level of heterogeneity means that multiple perspectives are involved in a more complicated decision-making process

Concept of "Evidence" in Public Health Practice

In the field of public health, evidence can be understood as some form of data- including epidemiologic data, results of program or policy evaluations, and qualitative data for uses in making judgments or decisions.

- Public health evidence is usually the result of complex cycle of observation, theory and experiment.
- The value or usefulness of evidence may vary by the type of stakeholder.
- Evidence can never be perfect and therefore the absence of excellent evidence does not make evidence-based decision making impossible; what is required is the best evidence available not the best evidence possible.

Action	Something should be done	This particular intervention should be implemented	How an intervention should be implemented

Level of scientific evidence

Category	How established	Data source examples
Evidence-based	Peer review via systematic review or narrative review	- Community guide - Cochrane reviews - Narrative review based on published literatures
Effective	Peer review	- Articles in the scientific literature - Research tested intervention programs - Technical reports with peer review
Promising	Written program evaluation without formal peer review	- State or federal government reports - Conference presentation
Emerging	Ongoing work, practice-based summaries, or evaluation works in progress	- Pilot studies - Projects funded by health foundation

According to Oxford Centre for Evidence based medicine, the levels of evidence include
1a. Systematic review of RCTs
1b. Individual RCT
2a. Systematic review of cohort studies
2b. Individual cohort study
2c. Outcomes research; ecological studies
3a. Systematic review of case-control studies
3b. Individual case study
4. Case series
5. Expert opinion without critical appraisal

- which an approach is based on, a variety of planning frameworks and behavioral science theories can be applied.
- As an example, ecological or systems models are increasingly used. Effective interventions are most grounded in health-behaviour theory.

iv. Community engagement occurs
- Community based public health approaches should involve community members in research and intervention projects and show progress in improving population health and addressing health disparities.
- Practitioners, academicians and community members collaboratively define issues of concern, develop strategies for intervention and evaluate the outcomes.

v. Sound evaluation principles are followed
- Too often in public health, programs and policies are implemented without much attention to systematic evaluation. In addition, even when programs are ineffective, they are sometimes continued because of historical or political considerations.
- Evaluation plans must be laid early in program development and should include both formative and outcome evaluation.
- This program evaluation should illustrate the use of both qualitative and quantitative data in framing an evaluation.

vi. Results are disseminated to others who need to know
- When a program or policy has been implemented, or when final results are known, others in public health can rely on findings to enhance their own use of evidence in decision making.
- Dissemination may occur to health professionals via the scientific literature, to the general public via the media, to policy makers through personal meetings, and to public health professionals via training courses.

- Over the past three decades, meta-analysis has been increasingly used to synthesize the findings of multiple research studies.
- Meta-analysis uses a quantitative approach to summarize evidence, in which results from separate studies are pooled to obtain a weighted average summary result.
- Its use has appeal because of its potential to pool a group of smaller studies, enhancing statistical power.
- It also may allow researchers to test subgroup effects (e.g., by gender or age group) that are sometimes difficult to assess in a single, smaller study.
- The key contribution of meta-analysis has been to provide a systematic, replicable, and objective method of integrating the findings of individual studies.

iv. Economic Evaluation

- Economic evaluation is an important component of evidence-based practice.
- It can provide information to help assess the relative value of alternative expenditures on public health programs and policies.
- In cost-benefit analysis, all of the costs and consequences of the decision options are valued in monetary terms.
- More often, the economic investment associated with an intervention is compared with the health impacts, such as cases of disease prevented or years of life saved. This technique, cost-effectiveness analysis (CEA), can suggest the relative value of alternative interventions (i.e., health return on dollars invested).
- CEA has become an increasingly important tool for researchers, practitioners, and policy makers. However, relevant data to support this type of analysis are not always available, especially for possible public policies designed to improve health.

v. Health Impact Assessment

- Health impact assessment (HIA) is a relatively new method that seeks to estimate the probable impact of a policy or intervention in non health sectors, such as agriculture, transportation, and economic development, on the health of the population.
- HIA has been gaining acceptance as a tool because of mounting evidence that social and physical environments are important determinants of health and health disparities in populations.
- It is now being used to help assess the potential effects of many policies and programs on health status and outcomes.

- This group has the additional responsibility of making policies on controversial public issues.
- Public health practitioners have the opportunity, even the obligation to carefully review the evidence for alternative ways to achieve the desired health goals.

iii. Stakeholders
- The third group of audience for EBPH is composed of stakeholders who will be affected by the intervention.
- This includes the public, especially those who vote, as well as interest groups formed to support or oppose specific policies, such as legality of abortion.

iv. Researchers
- The final user group is composed of researchers on population health issues, such as those who evaluate the impact of a specific policy or programs.
- They both develop and use evidence to answer research questions.

		studies.
4	Determining what is known through the scientific literature	- Adopting a systematic approach to identify, retrieve and evaluate relevant reports on scientific studies.
5	Developing and prioritizing program options	- The initial review of the scientific literature can sometimes highlight various intervention options. - Summaries of available evidence are often available in systematic reviews and practice guidelines.
6	Developing action plan and implementing interventions	- Setting goals and objectives - The course of action should describe how the goals and objectives will be achieved, what resources are required, and how responsibility for achieving objectives will be assigned
7	Evaluating the program or policy	- Assessing intermediate changes over time.

Challenges in implementation of evidence-based public health practice

i. Organizational culture

- Evidence based public health practice often relies on the evidence champions, who are willing to challenge the status quo and promote the new ways of decision making.
- For innovation, it is very important that organization support the changes.
- Rigid organization system is a barrier to the evidence based public heath, which make implementation of new programs and approaches difficult.
- Because old practices require less effort than working the new programs, new approaches may get opposed and threatened by colleagues and supervisors.

ii. Leadership

- Leaders of the public health system are important factors in determining the organizational culture and use of resources for evidence based approach.
- Attention of leadership toward science, quality and performance are important predictors of strong public health system.
- However in public health, leaders have to face challenges in choosing and implementing the evidence based new approaches

- Poor workforce training is common in public health sectors. Less than 20% of the workers in public health sectors have formal training in public health disciplines, and even lesser number have formal graduate training from a public health program.
- Principles of evidence based medicine are not uniformly taught in the public health sectors.

vi. Cultural and geographical differences
- There are large differences across the different countries in evidence based public health.
- Whereas evidence has been mostly developed in western world, use of evidence based approach to meet the public health problems is limited in developing countries.
- Even in developed world, results published in journal might not be true representative of all the populations of interest.

vii. Other challenges
- Lack of evidence on the effectiveness of certain public health interventions.
- Lack of time to gather information, analyze data and review the literature for evidence.

Relevance	• Is the evidence relevant to the problem being addressed?
Cost and benefits	• Is it affordable to implement this evidence? • What are the consequences of implementing this evidence? • What is the trade-offs?
Feasibility	• Is the evidence feasible to implement within the available time and money
Acceptability	• Is it consistent with community priorities, culture, values and the political situation?
Equitability	• Does it distribute resources fairly?
Sustainability	• Are the resources and incentives likely to support conditions to maintain the intervention?

1. How is the evidence generated?
   a. What is the philosophical basis for generating evidence?
   - Induction or deduction?
   - Empiricism or rationalism?
   - Reduction or holism?

   b. Technical/Methodological basis
   - Are these evidence generated by meta-analysis or systematic review?
   - Are these generated by experiments or observation?

Several such inquiries can be made for questions in each dimension listed in the above table so as to acquire pertinent answers that are imperative to effective implementation of evidence based public health practice.

and their associated forces or factors.

- For philosophy of public health, two chief objects are the patient's disease and health, along with the forces or factors responsible for causing them.
- What is/causes health? or What is/causes disease? are contentious questions for philosophers of public health.
- For philosophy of medicine, the most controversial debate centers around the presuppositions of reductionism and holism. Questions like "Can a disease be sufficiently reduced to its elemental components?" or "Is the patient more than simply the sum of physical parts?" drive discussion among philosophers of medicine.
- In addition, the debate between realism and antirealism has important traction within the field. This debate centers on questions like, "Are disease-causing entities real?" or "Are these entities socially constructed?"

Reductionism Vs Holism

Reductionism

- In science, the application of the reductionist paradigm consists of splitting reality into separate entities and studying their functioning.
- Origin of reductionism can be traced back to Rene Descartes (a French scholar of the sixteenth century) who viewed reality as the sum of components that could be divided into isolated entities, applying a mechanistic vision of the world. According to him, this decomposition and the resulting simplification would lead to the most appropriate explanation.
- In the broadest terms, reductionist approaches to disease look for fundamental mechanisms or processes that are the underlying causes of that disease.
- Rooted within this philosophy, the disease is believed to have a potential singular target for medical treatment. For infection, the target is the pathogen and for cancer, it is the tumor.
- In public health, reductionist approach has saved millions of lives through the development of drugs and the discovery of the role of vitamins, e.g., where vitamin deficiencies are prevalent.
- In recent years in light of large-scale genomic sequencing initiatives notably the Human Genome Project, there has been considerable emphasis on reducing diseases to the genetic or molecular level.

diets and/or overall quality of life rather than with only one specific nutrient, one food or food group.

While reductionism and holism are complementary, holistic approaches should be considered first before applying long and costly reductionist methods. Such an approach will avoid generalization from the specific according to a bottom-up approach. Public health practices targeting disease prevention have to first be viewed as holistic disciplines, and when necessary, more reductionist approaches could be efficiently implemented.

Characteristic	Reductionism	Holism
Principle	Behaviour of a biological system can be explained by the properties of its constituent parts	Biological systems possess emergent properties that are only possessed by the system as a whole and not by an isolated part of the system
Approach	One factor is singled out for attention and is given explanatory weight on its own	Many factors are simultaneously evaluated to assess the dynamics of the system
Model Characteristics	Linear, predictable, frequently deterministic	Non-linear, sensitive to initial conditions, probabilistic
Public health concept	Health is normalcy Health is risk reduction	Health is robustness Health is adaptation

Empiricism versus Rationalism

The dispute between rationalism and empiricism concerns the extent to which we are dependent upon sense experience in our effort to gain knowledge.

- Rationalists claim that there are significant ways in which our concepts and knowledge are gained independently of sense experience.
- Empiricists claim that sense experience is the ultimate source of all our concepts and knowledge.

Rationalism

- It is a philosophy of science which emphasizes the role that reason has to play in the generation of knowledge and discovery of truth.

- Experiences may trigger a process by which we bring this knowledge to consciousness, but the experiences do not provide us with the knowledge itself.

c) The innate concept thesis
- According to this thesis, we have some of the concepts we employ in a particular subject area as part of our rational nature and are not gained from experience. They are part of our rational nature.
- While sense experiences may trigger a process by which they are brought to consciousness, experience does not provide the concepts or determine the information they contain.

Empiricism
- In this method, knowledge is derived from experience and in particular from sensory experiences.
- As distinct from rationalism, empiricism denies the possibility of spontaneous ideas or a priori reasoning as a predecessor to the generation of evidence.
- In public health practice, it is not difficult to locate the place of empiricism as a means of generating relevant knowledge. E.g. use of empirically derived knowledge for public health practice.
- Evidence based public health practice is based within the philosophical doctrine of empiricism
- A key assumption of empiricism is that the knowledge gained from experience is received objectively by an unbiased human mind.
- Empiricists endorse the following claim for knowledge generation

a) The empiricism thesis
- The only source of knowledge or concepts we use is sensory experiences.
- Empiricism about a particular subject rejects the corresponding version of the Intuition/Deduction thesis and Innate Knowledge thesis.
- The Empiricism thesis does not entail that we have empirical knowledge. It entails that knowledge can only be gained, if at all, by experience.

these objects.

Antirealism

- Anti-realism, on the other hand, is the philosophical notion that observable objects and events are not actual objects and events as observed by a person but rather they are dependent upon the person observing them.
- In other words, these objects and events are mind-dependent—not mind-independent.
- Anti-realists deny the existence of objects and events apart from the mind cognizing them. Human minds construct these objects and events based on social or cultural values.

The debate between realism and anti-realism has important implications for philosophers of medicane and public health.

- For example, a contentious issue is whether disease entities or conditions for the expression of a disease are real or not.
- Realists argue that such entities or conditions are real and exist independent of medical researchers investigating them, while anti-realists deny their reality and existence.
- If we take the example of depression; According to realists, the neurotransmitter serotonin is a real entity that exists in a real brain— apart from clinical investigations or investigators. A low level of that transmitter is a real condition for the disease's expression. For anti-realists, however, serotonin is a laboratory or clinical construct based on experimental or clinical conditions. Changes in that construct lead to changes in understanding the disease.

Domains of Evidence Based Public Health Practice (Decision Making)

The conceptual model for Evidence Based Public Health Practice involves three interlinked domains (i.e. data strands) that must be integrated for deciding a course of public health actions.

i. Best available scientific evidence
ii. Client values, preferences and characteristics
iii. Resources including practitioner expertise

- The decision making is the central concept of the model and the action that ties the three domains together in EBPHP.

Fig: Domains/ elements of evidence based public health practice

i. Best available research evidence

- Evidence is comprised of research findings derived from the systematic collection of data through observation and experiment.
- What constitutes best research evidence depends upon the question needing to be addressed.
- For example, for questions about etiology or prognosis, the optimum research design is often a longitudinal cohort study. For questions concerning the efficacy and effectiveness of treatments, the research design least prone to bias or error is the RCT.
- Topping the evidence pyramid for a question about treatment is the systematic review, which synthesizes the findings from many treatment trials.
- Recently there have been renewed calls for contextualized research evidence that is directly relevant to the specific patient and practice context.
- The absence of excellent evidence does not make evidence based public health practice impossible; what is required is the best available not the best possible evidence.

ii. Client values, preferences and characteristics

- Except for single case studies, research evidence describes the average responses of individuals or groups.
- The core challenge addressed by EBPHP is how to apply the averaged data to an individual client.
- The evidence needs to be appraised in relation to the particular circumstances at hand. Client characteristics are one key set of contextualizing factors that need to be taken into account.
- Relevant client attributes includes health status, needs, history of treatment response, values and preferences.
- To decide whether available research evidence is truly relevant to the client, a judgment must be made about the comparability between the client and the study population.
- Client preferences are the lynch-pin of shared-decision making, but are also the least developed aspects of EBPHP model.
- The rationale for shared-decision making is to engage clients more fully in self-managing their own wellness and health care.

- EBPH process
- Communication and collaboration skills
- Engagement and intervention skills

UNIT 2: ADVANCES IN PUBLIC HEALTH SYSTEM RESEARCH

Community based participatory research

Community-based participatory research is a "collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings.
CBPR begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities."

When to use CBPR?
- CBPR is useful for emergent problems for which community partners are in search of solutions but evidence is lacking.
- CBPR can be used when specific issue emerges from the community and research partners are needed to rigorously assess the evidence and provide data.
- CBPR helps academics understand the community perspectives as they develop research questions and hypotheses together.

Characteristics/ Principles of the CBPR approach
i. It recognizes the community as a unit of identity,
ii. It builds on the strengths and resources of the community,
iii. It facilitates a collaborative and equitable partnership in all phases of research
iv. It promotes co-learning and capacity building among research partners,
v. It achieves a balance between research and action that mutually benefits all partners.
vi. It emphasizes the relevance of community-defined problems,
vii. It involves systems development using a cyclical and iterative process,
viii. It disseminates evidences to all partners and involves them in wider dissemination of results, and
ix. It involves long-term process and commitment to sustainability.

- Structural problems and social determinants of disease, such as poverty, unemployment, the stigmatization of persons living with HIV/AIDS, and lack of primary health care, can be addressed through CBPR approaches.

ii. Shared decision making
- Because of shared decision making, the community based participatory research process is able to use the strengths and insights that community and academic partners bring to framing health problems and developing solutions.

iii. Reciprocal transfer of expertise
- One of the benefits of CBPR is that they create space for co-learning, the reciprocal transfer of expertise and mutual ownership of research products between community and academic partners.
- The process of co-learning brings academic researchers and community members together and helps community participants to increase control and self-ownership of their health lives.

iv. Translation of evidence
- The CBPR approach increases the potential to translate evidence to develop, implement and disseminate effective public health interventions in diverse communities.

Weakness of CBPR
- It requires long time to form partnership
- The evidences generated from CBPR may not be generalized.
- Cost conflict may arise between partners on dissemination, strategies and decisions.
- CBPR may not be valued in academic environment.

behavior, and to study inter-organizational networks in public health systems.

Application of network analysis

i. To study existing public health networks (e.g. service referral networks)
ii. To apply a network theory to a health phenomenon (e.g. examining whether a contagion hypothesis explains patterns of STI transmission)
iii. To use a network approach for developing and implementing health interventions (e.g. using network characteristics to identify central actors to speed up diffusion of health information)

Network analysis method

i. Study design and data collection

- For network analysis design, data can be collected from individuals before the entire sample has been identified, recruited or interviewed.
- For many network studies, the entire network must be identified before the data collection starts. For example, in a study of peer relationships in a school, students in particular classroom s would be identified before starting to collect network data.
- In some cases, network identification may not have clearly defined boundaries. One useful network sampling approach is snowball sampling or respondent driven sampling.

ii. Data analysis

- Three broad approaches to analysis are generally used:
  a. Network visualization:
  - It allows researchers and audiences to view various graphical depiction of networks

  b. Descriptive analyses
  - Such analyses can reveal important details concerning the
    - Position of network actors
    - Properties of network sub-groups
    - Characteristics of a complete network

- Research on social network focuses more on how social structure and relationships act to promote or influence health and health behavior.
- E.g. influence of social support and social capital on morbidity and mortality.
- Descriptive studies of social support networks in various populations, such as chronically ill, depressed or elderly.

iii. Organizational network
- In organizational network analysis, the networks are comprised of agencies or organizations rather than individuals.
- E.g. network analysis of public and private agencies serving the mentally ill, organizations providing HIV/AIDS prevention and treatment services, etc.

Public health practice based research network
- Public health practice based research network is a program launched in 2008 by Robert Wood Johnson Foundation to expand delivery system research in public health setting
- Public health practice-based research networks (PBRNs) bring together public health agencies and academic researchers to study the organization, financing, and delivery of public health strategies in real-world practice settings, with the goal of producing actionable evidence that can be used to improve practice and policy.
- By 2014, there were 31 networks involving more than 1500 local public health agencies and more than 50 academic research units.
- Participating practitioners and researchers collaborate to identify pressing research questions of interest, design rigorous and relevant studies, execute research effectively, and translate findings rapidly into practice.
- As such, PBRNs represent vehicles for expanding the volume and quality of practice-based research needed for evidence-based decision-making in public health.

Advantages of network research
- By combining agencies it provides larger sample sizes, allows for comparative research across systems, is pragmatic, and results are readily translatable.
- As such, PH-PBRNs are considered critical new translational links that can expand the scientific knowledge needed to improve public health practice and population health.

- The mission of New Public Health is to maximize human health and well-being and to help redress societal and global inequities.

Applications of New Public Health

- While public health interventions cannot eliminate existing inequities in societies and globally, they can reduce the burdens of the poor and underserved through adoption of evidence-based public health interventions.
- The NPH incorporates a programmatic approach to health services with multiple parallel interventions to reduce the burden of disease and continue reduction in morbidity and mortality, and to improve quality of life.
- The NPH seeks to improve population health by application of cumulative evidence from published and other reports on epidemiology, nutrition, vaccines and many other related biological, physical and social sciences and technological developments.
- The New Public Health incorporates health policy, health promotion in addition to primary, secondary, and tertiary prevention and health systems management.

Global and National applications of Evidence Based Public Health

Public Health Interventions	Available Evidence	Application at Global Level	Application at National Level (Nepal)
IPV Vaccination	- There is precedent for type 2 wild polioviruses to be reintroduced into the population. - The introduction of at least one dose of IPV has an important supporting role in assuring complete global eradication of all polioviruses.	- More than 173 countries in the world have already introduced IPV and 21 countries have formally decided to introduce IPV by 2017.	- In 2014, Nepal introduced one dose of IPV in parallel with OPV to particularly bolster immunity to type 2 poliovirus.
Prophylactic HPV Vaccination	- Various clinical trial results show that HPV vaccines are safe and very effective in preventing cervical cancer.	- By 2013, HPV vaccine was a part of the National Immunization Program in more than 55 countries of the world.	- In Nepal, HPV vaccination was launched in Kaski and Chitwan in February 2016 as a demonstration program.
Iron and folic acid supplementation program for Anemia control	- A Cochrane review of daily iron supplementation to women during pregnancy reported a 70% reduction in anemia, a 67% reduction in iron deficiency anemia (IDA).	- WHO recommends daily iron supplementation during pregnancy as a part of the standard of care in populations at risk of iron deficiency.	- Government of Nepal provides free iron and folic acid to pregnant women after the first trimester (for 180 days) and post-partum mothers (for 45 days) as a part of Anemia control program
	Nepal's evidence: - Assessment from five districts showed that involvement of FCHVs can increase coverage and compliance of IFA tablets among pregnant women and postpartum women		- Intensification of Iron and Folic Acid Supplementation program expanded to 75 districts gradually
Maternal calcium supplementation	- Calcium supplementation during pregnancy in women at risk of low calcium intake reduces maternal hypertensive disorders and preterm birth. - A Cochrane review of various trials showed that calcium supplementation during pregnancy reduced the incidence of pre-eclampsia by 55% and preterm births by 24%.	- Based on evidences from two systematic reviews, WHO has recommended calcium supplementation as a part of the antenatal care for prevention of pre-eclampsia in pregnant women.	- In Nepal, a pilot program was recently implemented in Dailekh to ascertain the feasibility of distributing calcium during ANC services.

Vit-A supplementation in children	- Evidences for Cochrane review suggest that Vitamin A supplementation reduce all cause mortality by 24% and diarrhea related mortality by 28% in children aged 6-59 months.		- Vitamin A supplementation continues to be an effective intervention in children across the world including Nepal.
Zinc supplementation in children	- Zinc supplementation reduces the incidence of diarrhea and pneumonia. - The available evidences however do not support the use of Zinc in children less than six months of age.	- Implemented in many low income countries	- In Nepal, Zinc supplementation was piloted in five districts in 2005. Another pilot program (point of use water disinfection and zinc treatment, POUZN) was piloted in three districts in 2007 and scaled up to 30 districts in 2008.
CB-IMCI	- Nepal's Evidence - Control of Diarrhoeal Diseases (CDD) and the Acute Respiratory Infection (ARI) programs showed positive results at community settings		- CB-IMCI program was introduced in 1997 and scaled up nationwide in 2009
Community based neonatal care package	- Lancet series on Neonatal survival, 2007 showed that high coverage program of universal outreach and family-community care can result in more than 50% reductions in neonatal mortality	- Various community based packages with variable neonatal survival strategies have been introduced in different countries. E.g Bangladesh, Uganda, Tanzania, etc.	- Drawing on the results from Lancet Neonatal Survival Series, a community based newborn care package was developed by Nepal in 2009 and after successful pilot, it was scaled up to 39 districts by 2013.
Chlorhexidine Cord care	- There are high quality evidences from Cochrane and other systematic reviews that application chlorhexidine gels for skin or cord care are effective in preventing infections and improving newborn survival in low resource settings. - 23% Reduction in neonatal mortality when 7.1% chlorhexidine digluconate was used on the first day of life, as demonstrated by the clinical trials conducted in South Asia.	- Over 25 countries are now moving toward implementation of chlorhexidine for umbilical cord care	- Drawing on various international evidences as well as results of randomized trials conducted in Nepal, GON introduced Chlorhexidine "Navi" Care Program at all 75 districts. - The program was implemented in 49 districts in first phase between 2011 to 2014 and scaled up to all 75 districts in 2014.

ii. Delayed cord clamping
- A Cochrane review suggest that delayed cord clamping in full-term neonates lead to significant increase in newborn hemoglobin and higher serum ferritin concentration at 6 months of age.
- Another review of studies in preterm neonates concludes that delayed cord clamping is associated with 39% reduction in need for blood transfusion and a lower risk of complication after birth.
- Although promising evidence, these strategies have not yet been assessed for feasibility of implementation at scale in health systems.

Examples Non-evidence based public health practices

i. Deworming for improving nutritional indicators
- Although deworming is one of the strategies to improve nutrition in Nepal, evidences from Cochrane review suggest that mass treatment of all children in endemic areas with deworming tablets does not improve average nutritional status and hemoglobin.

ii. Post-partum vitamin A supplementation
- A Cochrane review showed that different doses of Vitamin A supplementation for postpartum women had no evidence on reduction of maternal and infant mortality and morbidity.
- This shows that the post-partum vitamin A supplementation, which is a national program of Nepal does not stand on evidence.

Global and national achievements in evidence based public health

i. Vaccine-Preventable Diseases
- Substantial achievements have been made globally as well as at national levels in the control of many vaccine-preventable diseases.
- The introduction of many vaccines has created a milestone in preventing and controlling many vaccine preventable diseases. Expanded immunization coverage is one of the most cost-effective and evidence based ways to advance global public health.
- In the decade of the 21st century (2001-2010), an estimated 2.5 million deaths were prevented each year among children aged <5 years through the use of measles, polio, and diphtheria-tetanus-pertusis (DPT) vaccines.

approximately 75% at-risk population in Sub-Saharan Africa was protected from malaria.
- In between 2000 and 2009, there was 21% decrease in estimated global malaria deaths.
- Nepal currently stands at pre-elimination phase for Malaria with a substantial reduction in malaria incidence and zero death rates. Nepal was close to achieve most of the malaria related MDG targets by 2015.

b. HIV/AIDS control
- The number of new HIV infections globally declined by 33% between 2001 and 2012. The numbers of AIDS deaths have also declined from 2.3 million in 2005 to 1.6 million in 2012. This achievement could be attributed to the introduction of evidence based public health interventions such as life-saving antiretroviral therapy, PMTCT strategies and other prevention approaches.
- In Nepal, with the application of these EBPH interventions, there has been 85% reduction in number of new HIV infections in the last decade between 2000 to 2015. The spread of HIV in Nepal has halted and begun to reverse

c. Tuberculosis control
- With the introduction of evidence based DOTS strategy and other TB prevention and control measures, the TB mortality in WHO South East Asian Region has decreased by more than 50% since 1990. The region has already achieved the global target of 50% reduction by 2015.
- The decline in prevalence of TB is observed in all member states with some reporting more than 50% decline.

d. Control of Neglected tropical diseases
- Following a evidence based chemotherapy (mass drug administration), increasing number of countries have started to eliminate lymphatic filariasis as a public health problem.
- The prevalence of lymphatic filariasis has significantly reduced in Nepal over the last decade and is in the phase of elimination.

iii. Tobacco control
- With the implementation of evidence-based, legally binding provisions of WHO's FCTC today about 4.7 billion people (63% of world's population) are covered by at least one comprehensive tobacco control measure.

b. Child health and nutrition

- Globally, with the introduction of evidence based interventions such as immunization, nutrition and IMCI activities, the under five mortality rate has decreased by 53% from and estimated rate of 91 deaths per 1000 live births to 43 deaths per 1000 live births in 2015.
- Although the impacts of CB-IMCI and CB-NCP approaches have not been well documented in Nepal, there has been a significant reduction in prevalence of pneumonia and diarrhea through these interventions.
- The combination of several evidence based public health interventions have led to the reduction of under-five mortality from 118 per 1000 live births to 39 per 100 live births in 2016. Similarly, IMR has been reduced from 78 per 1000 live births to 32 per 1000 live births in the same period.

Example of Knowledge representation

Suppose the language is arithmetic, then

- 'x', '≥' and 'y' are components (or symbols or words) of the language
- And syntax says that 'x≥y' is a valid sentence in the language, but '≥xy' is not
- The semantics say that 'x≥y' is false if y is bigger than x, and true otherwise

Components of good knowledge representation

For analysis purposes it is useful to be able to break any knowledge representation down into their four fundamental components:

1. The lexical part that determines which symbols or words are used in the representation's vocabulary.
2. The structural or syntactic part – that describes the constraints on how the symbols can be arranged, i.e. a grammar.
3. The semantic part – that establishes a way of associating real world meanings with the representations.
4. The procedural part – that specifies the access procedures that enables ways of creating and modifying representations and answering questions using them, i.e. how we generate and compute things with the representation.

Knowledge representation schemes

i. Network schemes
   - Semantic network
   - Conceptual graphs

ii. Structured schemes
   - Scripts
   - Frames

iii. Logical schemes
   - Predicate calculus
   - Propositional calculus

iv. Procedural schemes
   - IF..THEN..rules

- Retrieval is based on binary decision criteria (i.e. A document is predicted to be either relevant or not-relevant) without any notion of partial matching.
- Although Boolean expressions have precise semantics, frequently it is not simple to translate an information need into a Boolean expression.

Advantages
- Simple and easy method. Provides a good starting point for those new to the field.
- Supports exact query

ii. Vector space model
- This model recognizes that the use of binary weights is too limiting and proposes a framework in which partial matching is possible.
- This is accomplished by assigning non-binary weights to index terms in queries and in documents.
- Documents and queries are displayed as vectors in index-term space.
- Retrieval is based on whether the query vector and document vector are closed enough.

Advantages
- It's term weighting scheme improves retrieval performance
- Partial matching allows retrieval of documents that approximate the query conditions

Disadvantages
- Problems of polysemy and synonymy cannot be addressed
- Assumes that index terms are mutually independent.

iii. Probabilistic model
- The results retrieved by probabilistic information retrieval methods depend on estimations and probabilities.
- The first assumption is that terms are dispersed differently between relevant and non-relevant documents.
- A probabilistic method ranks documents and sorts them in decreasing order of probability of relevance to the information need once the probability is calculated

lexical matching that plague the classical vector model.
- It is a technique that projects queries and documents into space with latent semantic dimensions. It assumes that words that are close in meaning will occur in similar pieces of text
- Unlike Vector Space Model in which each term in the dataset is considered as a dimension in the feature space, Latent Semantic Indexing approximates the source space with fewer dimensions. To accomplish this decomposition of the original space, LSI uses matrix algebra technique termed Singular Value Decomposition or SVD.

Advantages
- Synonymy problem is solved
- LIS is capable of assuring decent results, much better than plain vector space model.
- Since it only involves decomposing term document matrix, it is faster, compared to other dimensionality reduction models.

Disadvantages
- Problems of polysemy remain unsolved
- A special algorithms for handling with large size matrices should be implemented
- LSI vectors require large storage

ii. Correlation method
- Concept: If a keyword is present in the document, correlated keywords should be taken into account as well. So, the concepts containing in the document aren't obscured by the choices of a specific vocabulary.
- In this method, correlation matrix is built based on the term-document matrix and Singular Value Decomposition (SVD) is used to reduce noises in the correlation of word.

Advantages
- This method is able to handle database with a very large number of documents and doesn't have to update the correlation matrix every time adding new documents.
- Number of documents are many times larger than number of keywords

		literature search

Major issues in information retrieval (Lexical problems)

Many languages can be difficult to understand because of ambiguities, leading to various possible interpretations of individual words.

1. Polysemy
- Many words used in information retrieval may have more than one meaning depending on the context it is used. This is called polysemy.
- Polysemy decreases the precision of the retrieval system.
- For example, using the word "Lead" may retrieve literatures containing information on chemical lead, a component of electrocardiogram or a verb indicating movement.
- Polysemy can create problems of word sense disambiguation: i.e. how to tell which sense is intended by a word in a given context

2. Homonymy
- Homonymy is also a form of lexical ambiguity which holds an importance in information retrieval.
- A homonym is a word that has the same pronunciation as another, but a different meaning, and in most cases a different spelling.
- Homonymy separates unrelated concepts. For example, if we have a query about 'AIDS' (the disease), and a retrieved document might also contains 'aids' in the sense of learning aid.
- Examples of homonymy: patience and patients, raise and rays, etc.
- Homonymy causes problems for natural language processing applications such as text to speech, speech recognition, information retrieval, etc.

3. Synonymy
- Many words have one or more synonyms, which are different words representing the same thing.
- Synonymy decreases the amount of information retrieved.
- Some examples in health care include the synonyms "high" and "elevated" as well as "cancer" and carcinoma".

Following are some of the techniques used in information retrieval using Natural Language Processing

i. Query expansion

- Query expansion comprises finding synonyms of the query terms using thesaurus.
- The original query term along with additional synonym terms are then used for judging the relevance of the documents.
- Therefore query expansion improves the recall of the information retrieval system.

ii. Word sense disambiguation

- Natural language processing involves many phases of which the significant one is word sense disambiguation.
- A word can have different meaning depending on the context it is used. This is called polysemy.
- Word sense disambiguation involves techniques of identifying a suitable meaning of words and sentences in a particular context by applying computational procedures.
- It is an Artificial Intelligence problem that needs resolution for ambiguity of words. .
- Some of the techniques used in word sense disambiguation include knowledge based approaches, learning based approaches and hybrid approaches.

iii. Phrase extraction (Word-N-Grams)

- Instead of using words, combination of words (phrases) is more useful in determining the underlying semantic meaning.
- Document representation using Bag-of-Phrases model also called a word-N-grams have worked better than the bag of words model.

iv. Conceptual retrieval

Collaborative Information Seeking

- Collaborative information seeking (CIS) is the study of the systems and practices that enable individuals to collaborate during the seeking, searching, and retrieval of information.
- Such projects often involve information searching or information retrieval (IR), information gathering, and information sharing.

ii. Sharing of knowledge
- This allows searchers to influence each other's activities as they interact with the retrieval system in pursuit of their information need

UNIT 4: SYSTEMATIC REVIEW PROCESS

Systematic Review

A systematic review may be defined as a review addressing a specific research question (on treatment, diagnosis, prognosis or etiology) using explicit methodology of collecting, selecting and appraising studies and, whenever appropriate, synthesizing their results quantitatively.

- When applied properly, systematic review can help the decision-making process in different ways
  - Identifying treatments that are not effective;
  - Summarizing the likely magnitude of benefits of effective treatments;
  - Identifying unanticipated risks of apparently effective treatments;
  - Identifying gaps of knowledge;
  - Auditing the quality of existing randomized controlled trials.

Advantages of systematic review
- Reduces bias
- Resolves controversy between conflicting findings
- Provides reliable basis for decision making

Process of systematic review
1. Formulate the review question
- The first stage in systematic review involves defining the review question, forming hypotheses and developing a review title.
- According to the PICO framework, the question should define the Population(s), Intervention(s), Comparator(s) and Outcome(s)

- Although Boolean searching (e.g. AND, OR, NOT) and proximity operators (e.g. NEAR, NEXT) are usually available, every database interface has its own search syntax (e.g. different truncation and wildcards) and a different thesaurus for indexing (e.g. MeSH for MEDLINE and EMTREE for EMBASE).
- The key in developing an optimal search strategy is to balance sensitivity (retrieving a high proportion of relevant studies) with specificity (retrieving a low proportion of irrelevant studies).
- Searches generally include several relevant electronic databases (Medline, HINARI, CENTRAL, etc.) but can also include checking article reference lists, hand-searching key journals/ grey-literature, and personal communication with experts or key researchers in the field.

4. Selecting studies
- Once a comprehensive list of abstracts has been retrieved and reviewed, any studies appearing to meet inclusion criteria would then be obtained and reviewed in full.
- This process of review is generally done by at least two reviewers to establish inter-rater reliability.
- The authors should keep a log of all reviewed studies with reasons for inclusion or exclusion.
- In some cases it may be necessary to contact study authors to obtain missing information needed for data pooling (e.g., means, standard deviations).

5. Extracting data
- It can be helpful to create and use a standardized data extraction form or table to organize the information extracted from each reviewed study (e.g., authors, publication year, number of participants, age range, study design, outcomes, included/excluded, outcomes and findings).

6. Assessing study quality/ critical appraisal
- There has been a movement in recent years to better assess the quality of each study included in systematic reviews.
- The risk-of-bias tool is preferably used method for assessing the quality of RCT. A different tool may be needed if non–randomized controlled trials are included.

7. Analyzing data and interpreting results

Sources of Literature Search

i. Bibliographic Databases

- Searches of health-related bibliographic databases are generally the easiest and least time-consuming way to identify an initial set of relevant reports of studies.
- Some bibliographic databases, such as MEDLINE and EMBASE, include abstracts for the majority of recent records.
- A key advantage of these databases is that they can be searched electronically both for free text terms/keywords in the title or abstract and by using the standardized indexing terms, or controlled vocabulary, assigned to each record.
- There are number of international initiatives to provide free or low cost online access to databases (and full-tect journals) over the internet.
- Some of the popular bibliographic database in the social, behavioural and health sciences include:
  - Cochrane central register of controlled trials (CENTRAL)
  - MEDLINE
  - Health InterNetwork Access to Research Initiative (HINARI)
  - The Cochrane Library
  - EMBASE
  - PsycINFO

ii. Journals and other non-bibliographic database sources

- Journals and other non-bibliographic database sources includes

a. Full text journals available electronically

- The full text of an increasing number of journals is available electronically on a subscription basis or free of charge on the internet.
- In addition to providing a convenient method for retrieving the full article of already identified records, full-text journals can also be searched electronically, depending on the search interface, in a similar way to the way database records can be searched in a bibliographic database.

- British Library Inside
- Index of conference proceedings
- ISI Proceedings

c. Other reviews and reference lists

- Many systematic reviews may be found in The Campbell Library as well as Cochrane Library, which includes the Database of Systematic Reviews as well as The Database of Abstracts of Reviews of Effects (DARE).

d. Web-searching

- Using general internet search engines such as Google to identify potential studies may be a good secondary resource as these may be used to retrieve current (both published and unpublished) studies.
- Also organizational websites (including for research institutes and universities) may be searched for their studies and trial records.
- Search engines that have large up-to-date databases include the following
  - Google (includes Google Scholar)
  - All the Web
  - Bing
  - Yahoo search

iii. Unpublished and ongoing studies

- Some completed studies are never published. Finding out about unpublished studies, and including them in a systematic review when eligible and appropriate, is important for minimizing bias.
- Colleagues can be important source of information about unpublished studies.
- Another approach of finding unpublished studies is to send a comprehensive list of relevant articles along with the inclusion criteria for the review to the first author of reports of included studies, asking if they know of any additional studies (published or unpublished) that might be relevant.
- In order to identify ongoing trial and studies, few initiatives have been made. For example,
  - International Clinical Trials Registry Platform Search Portal – launched by WHO
  - International Standard Randomised Controlled Trial Number Register

- The time period that the researcher is interested in
- Whether data from unpublished studies are to be included
- The study designs that will be included

Sensitivity versus Precision

- Searches for systematic reviews aim to be too extensive in order to ensure that as many as possible of the necessary and relevant studies are included in the review.
- It is, however, necessary to strike a balance between striving for comprehensiveness and maintaining relevance when developing a search strategy.
- Increasing the comprehensiveness (or sensitivity) of a search will reduce its precision and will retrieve more non-relevant articles.

Sensitivity is defined as the number of relevant reports identified divided by the total number of relevant reports in existence.
Precision is defined as the number of relevant reports identified divided by the total number of reports identified.

- Developing a search strategy is an iterative process in which the terms that are initially used may be modified based on what has already been retrieved.
- There are diminishing returns for search efforts; after a certain stage, each additional unit of time invested in searching returns fewer references that are relevant to the review.
- Consequently there comes a point where the rewards of further searching may not be worth the effort required to identify the additional references.
- The decision as to how much to invest in the search process depends on the question a review addresses and the resources that are available.
- It should be noted, however, that article abstracts identified through a literature search can be 'scan-read' very quickly to ascertain potential relevance.
- At a conservatively estimated reading rate of two abstracts per minute, the results of a database search can be 'scan-read' at the rate of 120 per hour (or approximately 1000 over an 8-hour period), so the high yield and low precision associated with systematic review searching is not as daunting as it might at first appear in comparison with the total time to be invested in the review.

trials).
- CENTRAL however, aims to contain only reports with study designs possibly relevant for inclusion in systematic review. So searches of CENTRAL should not use a trials 'filter'.

Controlled Vocabulary and Free Text Terms

- MEDLINE, EMBASE and many other databases can be searched using standardized subject terms assigned by indexers.
- Standardized subject terms (as part of controlled vocabulary) are useful because they provide a way of retrieving articles that may use different words to describe the same concept and because they can provide information beyond that which is simply contained in the words of the title and abstract.
- One of the way to begin to identify controlled vocabulary terms for a particular database is to retrieve articles from that database the meet the inclusion criteria for the review, and to note common text words and the subject terms the indexers have applied to the articles, which can then be used for a full search.
- Having identifies a key article; additional relevant articles can be located for example by using 'Related Articles' option in PubMed.
- Additional controlled vocabulary terms should be identified using the search tools provided with the database such as MeSH database option in PubMed.
- Many database thesauri offer the facility to 'explode' subject terms to include more specific terms automatically in the search.
- For example, a MEDLINE search using the MeSH term BRAIN INJURIES, if exploded, will automatically search not only for the term BRAIN INJURIES but also for the more specific term SHAKEN BABY SYNDROME.
- It is important the MeSH terms are 'exploded' wherever appropriate, in order not to miss relevant articles.
- Free text terms are usually necessary to retrieve older records as because indexing terms related to study design poorly available for articles prior to 1990s.
- In order to identify as many relevant records as possible searches should comprise a combination of subject terms selected from the controlled vocabulary or thesaurus ('exploded' where appropriate) with a wide range of free-text terms.

- Example: Searching for mental health OR eating disorders find articles that contain at least one of these search terms

b. AND
- Set of terms should be developed for the population, intervention and outcome. These three set of terms can be joined together with the 'AND' operator.
- Joining the terms with 'AND' operator retrieves the set of articles that addresses both the population or condition of interest and the intervention to be evaluated.
- Searching for mental health AND eating disorders finds articles that mention both of these topics.
- The limitation of this approach is that if the article does not contain at least one term from each of the three sets, it would not be identified.

c. NOT
- NOT reduces the number of results by excluding a search term.
- Searching for for mental health NOT eating disorders find articles that mentions mental health but removes any articles that mention eating disorders.

ii. Using proximity operators (NEAR, WITHIN and ADJ)
- Some database suppliers allow the searcher to use proximity operators (e.g. NEAR, ADJ, WITHIN) which specifies the relationship of two concepts within a field.
- For example, by using the 'ADJ' operator, two search terms adjacent to each other can be searched.
- In addition, some search software allows specifying that the words should be within a specific number of words of each other.
- The 'NEAR' operator in Cochrane Library will find the search terms within six words of each other.
- This results in higher sensitivity than simple phrase searching but greater precision than use of the 'AND' operator.
- The availability and commands of proximity operators will vary depending on the supplier of the database.

iii. Dealing with synonyms, related terms, variant spellings and truncation
- When designing a search strategy, in order to be as comprehensive as possible, it is necessary to include a wide range of free-text terms for each of the concepts selected. For example:

iv. Language and Date Restrictions

- The identification and translation of, or at least data extraction from, trials reported in languages other than English can substantially add to the costs of a review and the time taken to complete it.
- Whenever possible review authors should attempt to identify and assess for eligibility, all relevant reports irrespective of language of publication.
- Ideally no language restrictions should be included in the search strategy in order to minimize bias.
- The application of a Date restriction will depend on the research question being addressed. For example, if it is known that relevant studies could only have been reported during a specific time period, for example if the intervention was only available after a certain time point (e.g. web-based learning in schools would not be addressed prior to the mid-1990's).

v. Using search filters vs limiting commands

- Search filters are search strategies that are designed to retrieve specific types of records, such as those of a particular methodological design.
- Search filters are used extensively in the medical and health sciences. For example, the RCT filter developed by Cochrance for Medline has been well tested and may be used as it is.
- Additionally, some databases allow limiting search to methodological design (e.g. empirical study) or document type (e.g. research reports). This is commonly performed by using the limit command

Updating Searches

- When a Cochrane review is updates, the search process will have to be reviewed.
- Those databases that were previously searched and are considered relevant for the update will need to be searched again.
- The previous search strategies will need to be updated to reflect issues such as:
  - Changes in indexing such as the addition or removal of controlled vocabulary terms
  - Changes in search syntax
  - Comments or criticisms of the previous search strategies
- If any of the databases originally searched are not to be searched for the update this should be explained and justified.

of, studies.

- The choice of which software to use is likely to be influenced by what is available and thus supported at the review author's institution.
- Of the packages listed above, Reference Manager is generally considered to be very efficient for identifying duplicate references but it does not support the wider range of character sets allowing references to be entered correctly in languages other than English, whereas EndNote does.
- Bibliographic software also facilitates storage of information about the methods and process of a search.
- In addition to full record citation, the following fields should be considered for downloading from databases, when available
  - Abstract
  - Accession number
  - Affiliation/address
  - Article identifier/ Digital Object Identifier (DOI)
  - Index terms/thesaurus terms/keywords, etc.

Meta-analysis	Narrative synthesis	Deal with heterogenecity (eg. subgroup analyses)

Purpose of meta-analysis

i. To increase power
- Power is the chance of detecting a real effect as statistically significant if it exists.
- Many individual studies are too small to detect small effects, but when several are combined there is a higher chance of detecting an effect.

ii. To improve precision
- The estimation of an intervention effect can be improved when it is based on more information.

iii. To answer questions not posed by the individual studies
- Primary studies often involve a specific type of patient and explicitly defined interventions. A selection of studies in which these characteristics differ can allow investigation of the consistency of effect and, if relevant, allow reasons for differences in effect estimates to be investigated.

iv. To settle controversies arising from apparently conflicting studies or to generate new hypotheses.
- Statistical analysis of findings allows the degree of conflict to be formally assessed, and reasons for different results to be explored and quantified.

Process of meta-analysis

Meta-analysis is typically a two-stage process.
- In the first stage, a summary statistic is calculated for each study, to describe the observed intervention effect.
- In the second stage, a summary (pooled) intervention effect estimate is calculated as a weighted average of the intervention effects estimated in the individual studies.

a. Meta-analysis of dichotomous outcomes

- There are four widely used methods for meta-analysis of dichotomous outcomes
  - Fixed effect methods: Mantel-Haenszel method, Peto method and Inverse variance methods
  - Random effect method: DerSimonian and Laird method
- All these methods are available as analysis options in RevMan
- The Peto method can only pool odds ratios whilst the other three methods can pool odds ratios, risk ratios and risk differences.

b. Meta-analysis of continuous outcomes

- Two methods of analysis are available in RevMan for meta-analysis of continuous data: the inverse variance fixed effect method and the inverse variance random effects method.
- The outcomes should have a normal distribution in each intervention arm in each study for meta-analysis of continuous data.

c. Combining dichotomous and continuous outcomes

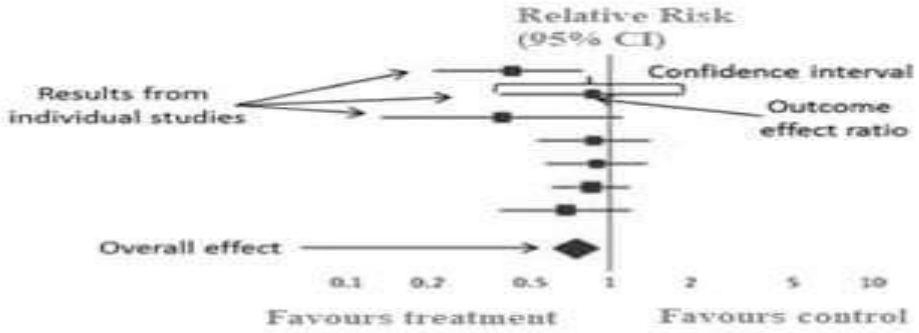
- Occasionally authors encounter a situation where data for the same outcome are presented in some studies as dichotomous data and in other studies as continuous data.
- There are statistical approaches available which will re-express odds ratios as standardized mean differences (and vice versa), allowing dichotomous and continuous data to be pooled together.
- Once standardized mean differences (or log odds ratios) and their standard errors have been computed for all studies in the meta-analysis, they can be combined using the generic inverse-variance method in RevMan.

d. Meta-analysis of ordinal outcomes

- Ordinal data are most commonly meta-analyzed as dichotomous data or continuous data depending on the way that the study author performed the original analyses
- Occasionally it is possible to analyze the data using proportional odds models. This model uses the proportional odds ratio as the measure of intervention effect.
- These estimates may be meta-analyzed using the generic inverse-variance method in RevMan.

interval, where the dimension of the square reflects the weight of each study.

- A solid vertical line usually corresponds to no effect of treatment. The summary point estimate is usually represented with a diamond at the bottom of the graph with the horizontal extremities indicating the confidence interval. This graphic solution gives an immediate overview of the results.



Addressing Reporting Biases

- It has been recognized that only a proportion of research projects reach publication in an indexed journal and thus become easily identifiable for systematic reviews.
- Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results.
- Statistically significant, 'positive' results that indicate that an intervention works are more likely to be published, more likely to be published rapidly, more likely to be published in English, more likely to be published in high impact journals and more likely to be cited by others.
- The contribution made to the totality of the evidence in systematic reviews by studies with non-significant results is as important as that from studies with statistically significant results.

	publication bias	included in a meta-analysis. - The inclusion of duplicated data may lead to overestimation of intervention effects.
4	Location bias	- The publication of research findings in journals with different ease of access or levels of indexing in standard databases
5	Citation bias	- The citation or non-citation of research findings, depending on the nature and direction of the results. - If positive studies are more likely cited, they may be more likely to be located and thus more likely to be included in a systematic review, thus biasing the finding.
6	Language bias	- The publication of research findings in a particular language. - Most of the studies are usually published in English and thus bias could be introduced when reviews are exclusively based on English language reports.
7	Outcome reporting bias	- The selective reporting of some outcomes but not others, depending on the nature and direction of the results. - The choice of outcomes that are reported can be influenced by the results, potentially making published results misleading.

Detecting reporting bias

i. Funnel plot

- A funnel plot is a simple scatter plot of the intervention effect estimates from individual studies against some measure of each study's size or precision.
- The name 'funnel plot' arises from the fact that precision of the estimated intervention effect increases as the size of the study increases
- Effect estimates from small studies will therefore scatter more widely at the bottom of the graph, with the spread narrowing among larger studies.
- If there is no publication bias the funnel plot will be symmetrical (inverted).

Measures to avoid reporting bias

i. Including unpublished studies in systematic review

- Publication bias clearly is a major threat to the validity of any type of review, but particularly of unsystematic, narrative reviews.
- Obtaining and including data from unpublished trials appears to be one obvious way of avoiding this problem.

- If the confidence interval is relatively narrow, the effect size is known precisely. If the interval is wider the uncertainty is greater.
- Intervals that are very wide indicate that we have little knowledge about the effect, and that further information is needed.
- A 95% confidence interval is often interpreted as indicating a range within which we can be 95% certain that the true effect lies.

b. Interpreting p-values and statistical significance
- A p value that is very small indicates that the observed effect is very unlikely to have arisen purely by chance and therefore provided evidence against null hypothesis.
- P value if often interpreted by examining whether it is smaller than particular threshold values. In particular, p values less than 0.05 are often reported as statistically significant and interpreted as being small enough to justify the rejection of null hypothesis.
- RevMan provides two p values. One relates to the summary effect in a meta-analysis and is from a Z test of null hypothesis that there is no effect. The other relates to heterogeneity between studies and is from a chi-squared test of null hypothesis that there is no heterogeneity.
- While making interpretations, a larger P value (e.g. greater than 0.05) may be often be misinterpreted as evidence that "the intervention has no effect" while the correct interpretation is that "there is not strong evidence that the intervention has an effect"

ii. Interpreting results from dichotomous outcomes
- There are several measures for comparing dichotomous outcomes in two group. Meta-analyses are usually undertaken using risk ratios (RR), odds ratio (OR) or risk difference.

a. Interpreting risk ratio
- Relative risk reduction is a convenient way interpreting a risk ratio in the form of percentage reduction in risk.
- For example: a risk ratio of 0.75 can be interpreted as a relative reduction in risk by 25%.

b. Interpreting risk difference
- The risk difference is often referred to as the absolute risk reduction (ARR), and may be presented as a percentage (for example, 1%), as a decimal (for example, 0.01), or as counts (for example, 10 out of 1000)

a. Interpreting SMDs using thumb rule

- As per the rule of thumb for interpreting SMDs (effect sizes), 0.2 represents a small effect, 0.5 a moderate effect and 0.8 a large effect.
- Variations may exist such as <0.4 as small, 0.4 to 0.7 as moderate and >0.7 as large.

b. Interpreting SMDs by transformation to odds ratio

- SMDs may be transformed to a log odds ratio which is an approximation of true result. The log odds ratio can be estimated as $(\pi/\sqrt{3}) \times$ SMD.
- The resulting odds ratio can then be combined with an assumed control group risk to obtain an absolute risk reduction.

Drawing conclusions

- When making conclusions, the authors should not mistake in concluding 'no evidence of an effect' for an 'evidence of no effect'. When there is inconclusive evidence, it is wrong to claim that it shows that an intervention has 'no effect' or is 'no different' from the control intervention.
- Author's conclusions from Cochrane and systematic reviews are usually divided into implications for practice and implications for research.

a. Implications for practice

- Drawing conclusions about the practical usefulness of an intervention entails making trade-offs, either implicitly or explicitly, between the estimated benefits, harms and the estimated costs.
- Making such trade-offs and making recommendations for action goes beyond a systematic review and requires additional information. Authors of systematic review should not make recommendations.
- The authors may lay out actions that healthcare professionals and patients could take, after describing the quality of evidence and the balance of benefits and harms.
- Other factors that might influence a decision should also be highlighted, including any known factors that would be expected to modify the effects of the intervention.

b. Implications for research

- Review conclusions should help people make well-informed decisions about future healthcare research.

- Intervention reviews assess the benefits and harms of interventions used in healthcare and health policy.
- Diagnostic test accuracy reviews assess how well a diagnostic test performs in diagnosing and detecting a particular disease.
- Methodology reviews address issues relevant to how systematic reviews and clinical trials are conducted and reported.
- Qualitative reviews synthesize qualitative evidence to address questions on aspects other than effectiveness.
- Prognosis reviews address the probable course or future outcome(s) of people with a health problem.

The step below outlines the general process involved in Cochrane Collaboration review

i. Developing Cochrane protocol

ii. Defining the review question and developing criteria for including studies
- Defining questions and eligibility criteria
- Defining types of participants
- Defining types of interventions
- Defining types of outcomes
- Defining types of study
- Defining the scope of review questions

iii. Searching for studies
- Designing search strategies
- Managing references
- Documenting and reporting the search process

iv. Selecting studies and collecting data
- Selecting studies
- Extracting data from reports
- Extracting study results and converting to the desired format
- Managing data

- A Cochrane recommended 'risk of bias tool' can be used to assess the risk of bias in included studies. This is a domain-based evaluation in which critical assessments are made separately for different domains

Sources of bias in studies and it's relevant domains

Sources of bias	Description	Relevant domains in "Risk of bias" tool
Selection bias	Systematic differences between baseline characteristics of the groups that are compared. E.g. Selection of participants with differential age characteristics	• Random sequence generation • Allocation sequence concealment
Performance bias	Systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest. E.g. participant who are aware that they are not receiving any treatment (intervention) may seek other forms of care	• Blinding of participants, personnel and outcome assessors. • Other potential threats to validity.
Attrition bias	Systematic difference in loss to follow up (or withdrawals) between two groups	• Incomplete outcome data. • Blinding of participants, personnel and outcome assessors
Detection bias	Systematic differences between groups in how outcomes are determined. E.g. If the researcher is aware of intervention/ research, the outcome might be assessed with bias	• Blinding of participants, personnel and outcome assessors. • Other potential threats to validity.
Reporting bias	Systematic differences between reported and unreported findings E.g. Only publishing favorable outcomes, leaving readers with incomplete and skewed understanding of the results	• Selective outcome reporting

	• Ensures that patients enroll into a study without knowing which group they will be assigned to. • If the researcher knows the next patient will be allocated to intervention, he/she may try to help a certain patient whom he thinks will benefit more from intervention.	opaque envelopes • Date of birth • Case record number	• Sequentially numbered drug containers of identical appearance • Sequentially numbered, opaque, sealed envelopes.
Blinding of participants, personnel & outcome assessors	• Masking of participants & assessor from knowledge about which intervention was received. • Ensures control group receive similar amount of attention, ancillary treatment and investigations • Avoids performance and detection bias	• No blinding or incomplete blinding, and outcome likely to be influenced • Blinding done, but likely that the blinding could have been broken	• No blinding or incomplete blinding, but outcome unlikely to be influenced • Blinding done, and unlikely that the blinding could have been broken
Incomplete Outcome Data	• Unavailability of complete outcome data for review o Attrition: Loss to follow up, withdrawals o Exclusions: Available data not included in analysis and report • Can lead to attrition bias	• Reasons for missing data related to outcome • Imbalance in numbers or reasons for missing data across groups • Proportion of missing outcomes or plausible effect size (difference in mean or standardized diff. in means) enough to have a clinically relevant effect • Inappropriate use of imputation	• No missing outcome data • Reasons for missing data not related to outcome • Missing data balanced across groups and reasons are similar • Proportion of missing outcomes or plausible effect size (difference in mean or standardized diff. in means) not enough to have a clinically relevant effect

UNIT 5: WRITING SCIENTIFIC REPORTS, GUIDELINES AND ARTICLES

Concept of Scientific Writing

Scientific writing is a technical writing by a scientist with audience of peers or other scientists.

- Scientific writing can take many forms from a paper in an academic journal to an article in a scientific magazine.
- Scientific papers are typically published as journal articles, which are usually reviewed by peers prior to publication; and / or conference proceedings

Characteristics of scientific writing

i. Evidence based
- Scientific reports are based on evidences and avoid making assumptions.
- It presents how and where data were collected and supports its conclusions with valid evidences.

ii. Clear and Simple
- Scientific writing avoids unnecessary details, uses direct language, avoiding vague or complicated sentences.
- Technical terms and jargon are used only when they are necessary for accuracy.

iii. Structured logically
- Ideas and processes in scientific articles are expressed in a logical order.
- The texts are divided into sections with clear headings. A scientific research publication normally follows an IMRaD structure (Introduction, Methods, Results and Discussion).

iv. Accurate
- Scientific papers reports accurate facts and figures.
- It avoids vague and ambiguous language such as about, approximately, almost.

Title and Abstract

- Choosing a title can be one of the most challenging aspects of scientific manuscript writing.
- Abstracts of various manuscripts are freely available online, and the readers rely on these to search relevant literature.
- A concise and standalone abstract serves as a resume for the manuscript and helps the readers decide whether it is relevant to their work.
- Abstract should be written according to the journal's guidelines, but it is preferable to restrict the word limit to less than 250 words.
- No reference should be cited in the abstract part of the manuscript.
- The abstract includes:
    - Background and aims which should convey the need for the study
    - Materials and methods should briefly describe the settings, design, parameters to be observed and statistical analysis
    - Results should be brief with emphasis on significant findings
    - Conclusions should be short and strong.

Components of a scientific Manuscript

A manuscript is usually divided into four parts: an introduction, methods, results and discussion, also referred to as the IMRaD format.

1. Introduction

- It is the section where the author states the purpose or rationale for carrying out the research.
- Information about the background of the problem (what is known) and its current state (what is unknown) is included in the introduction.
- Authors have to highlight the gaps in the literature that the study is going to fill and state the relevance of research question.
- Research hypothesis and study outcomes (primary and secondary) are integral parts of introduction. This creates a strong background on which the aims and objectives of the study are built.
- Important statements need to be backed by pertinent references, but too many references should be avoided as they dilute the novelty of the study.
- There are no maximum word limits for introduction, but it is preferable to restrict it to <10%–15% of total word count of the paper.

- Results confirm or reject the hypothesis which was built initially during planning of the study, but they do not prove anything.
- It is better to write the result section after figures and tables are constructed and including them in the outline.
- The observations should be presented in the order listed in the methods, preferably from general to specific.
- All the findings whether significant or not should be stated without bias or interpretation.
- The results determine whether the original research question has been answered and it forms the base for direction for future studies.

4. Discussion
- In this section, the results are discussed but not repeated or summarized.
- One should begin with a summary of the main findings or by answering the research question in the first paragraph itself.
- This is followed by a literary comparison with other studies and implications in clinical practice or research.
- When comparing with other studies, the most recent articles from the highest impact journals must be selected.
- In case of contrasting results, scientific and clinical explanation must be provided if possible with a valid reference.
- The strengths and limitations of the study should be acknowledged, and means for improvement should be suggested along with future direction for such studies.
- The discussion section should end after appropriately mentioning the conclusions in brief.
- Conclusion part should contain the key message that has been discussed in the manuscript. It should be brief, succinct and should not mention anything which has not been discussed earlier in the text.

Scientific Paper Reading and Evaluation

Purpose of reading/reviewing a scientific paper

- For general background: Overview, history, controversies, syntheses
- To find descriptive statistics: trends, rates, or risk distributions
- To find evidence of associations, risk factors, or causes
- To find evidence of effectiveness (diagnostic, therapy, program evaluation, effects of policy)
- To find other articles, bibliographic information

The purpose should guide how the article is to be read

Purpose	Parts of paper to read
General background	Abstract; Introduction, discussion
Data	Tables and possibly, results
Evidence	Abstract (superficial) or whole article (careful, critical evaluation)
Methodology	Methods, results and discussion
Bibliographic information	Discussion, References

		- Did the authors state the objectives of the study precisely and clearly? - Did the authors state specific hypotheses?
Methods	Study design	- Are the study design and methods defined?
	Selection of participants	- Are the size and key characteristics of the sample described? - Is the sampling method appropriate? - Were the participants suitable for informing research? - How representative was the sample? - Was bias introduced in the determination of study groups?
	Measurements	- Were the measurements accurate, valid? - Was the intervention well described and applied appropriately, equitably and effectively? - Were important confounders measured?
	Analysis	- Was confounding adjusted for? - What did statistical tests indicate? - Do the selected statistical tests appear appropriate?
Results	Results	- Did the authors describe the characteristics of their subjects and compare the comparison groups? - Were the associations or findings biologically – not just statistically significant? - Did the results address the objectives or hypotheses?
Discussion	Discussion	- Context: How do these findings fit into what is known? - Limitations: Are the authors appropriately thoughtful in describing limitation? - Do the authors' conclusions and implications follow from the findings?

Key considerations to be made:

- Strengths and limitations of the paper should be provided with specific example.
- The critique should be justified by giving rationale and possible suggestions.
- Objectivity is must in critiquing a scientific paper.

Importance of citation and referencing

i. Provides credit and attribution:
- Data citations provide scholarly credit and normative and legal attribution to all contributors of the data.
- By citing the work of a particular scholar, the author acknowledges and respects the intellectual property rights of that researcher.

ii. Assures legitimacy of data
- When any products are cited in the article, it helps to ensure whether data have been taken from the legitimate sources and are valid.
- Referencing is a way to provide evidence to support the assertions and claims provided in the scientific article.
- Referencing provides the reader with an indication of the quality and authority of the material that has been cited.

iii. Avoids plagiarism
- Plagiarism occurs when one author deliberately uses another's work without permission, credit, or acknowledgement.
- Citation and referencing is the best ways to credit the work of others and avoid the charges of plagiarism.

iv. Ensures scientific rigor
- Referencing ensures the extent to which the author(s) have been thorough and careful in their scientific work.
- Extensive referencing is a hallmark of a widely read and well-informed scientific paper.
- The arguments backed up by well referenced scientific papers adds more credibility and scientific rigor to the author's work

v. Easy retrieval of relevant articles
- Appropriate referencing of cited articles allows the reader to refer back to any external scientific papers that the author(s) have stated or discussed in their article.

	permission and acknowledgment of the original source.	quotation marks are put around the copied text.
Substantial Copying	This can include research materials, processes, tables, or equipment	"Substantial" can be defined as both quantity and quality of what was copied. If the research work captures the essence of another's work, it should be cited.
Paraphrasing	Reproducing someone else's ideas while not copying word for word, without permission and acknowledgment of the original source	Paraphrasing is only acceptable if the source is properly referenced without changing the meaning intended by the source.
Text-recycling	Reproducing portions of an author's own work in a paper, and resubmitting it for publication as an entirely new paper.	

Ways to Avoid Plagiarism

i. Paraphrasing
- This paraphrase is a patchwork composed of pieces in the original author's language and pieces in the author's words, all rearranged into a new pattern, but with none of the borrowed pieces in quotation marks.
- While paraphrasing, the verbatim should not be copied for more than two words in a row from the text being referred.
- If more than two words are used together, then the researcher will have to use quotation marks.

ii. Citing
- Citing is one of the effective ways to avoid plagiarism. Citing the works that one is borrowing ideas from for a paper is critical.

- Reusing one's own work from previous papers into new one can lead to self-plagiarism.
- Therefore, if one needs to use the points or ideas from previous paper to build on an another paper, he/she must cite themselves just as citing the work of others.

vi. Referencing
- One of the most important ways to avoid plagiarism is including a reference page or page of works cited at the end of the research paper.
- This page must meet the appropriate document formatting guidelines (Vancouver, Harvard, APA, etc.).
- This information is very specific and includes the author(s), date of publication, title, and source.

Anti-plagiarism strategies for research paper

1. Awareness strategies
- Understanding why researchers plagiarize and addressing the causes through proper awareness is the best way to avoid plagiarism now as well in the future.
- Many plagiarisms may occur simply because the researchers, especially young learners (students) do not know what plagiarism actually is.
- While some may think that copying from others is merely an acceptable practice of recycling, some others may take the thrill of rule breaking.
- Therefore making researchers (students) aware of plagiarism and sensitizing the about the criticality of plagiarism could be tremendously useful.

i. Discussing the benefits of citing sources
- Many students perceive that whenever they cite a source, they are weakening their writing.
- Research guides and faculties may help students understand that citing a source, whether paraphrased or quoted will reveal that they have synthesized the findings into their own argument.
- Discussing the benefits of appropriate quoting and citations might create their interests in maintaining a respect for intellectual property and proper attribution of ideas and words.

- Forbidding students to perform research on common topics for which there are already a substantial number of papers written on them, could be helpful.
- The students may be provided with list of specific topic and asked to choose among them. These topics could be changed from term to term.
- Providing unique topics or rarely researched topics, there are poor chances for students to plagiarize.

iii. Requiring process steps for the paper
- A research guide may set a series of due dates throughout the term for the various steps of the research paper process: topic or problem, research material, outline, research draft, final annotated bibliography, final draft, etc.
- The rough draft provides a quick glance on whether whole sections are appearing without citations and if the work is original. At the draft stage, the supervisor has the opportunity to educate the researcher further and discuss how proper citation works.

iv. Making requirements for annotated bibliography
- Asking to prepare an annotated bibliography can create tensions for researchers who have copied a paper for someone else.
- Annotation should include a brief summary of the source, where it was located, and an evaluation about the usefulness of the source (why it was a credible source for the paper?).
- Because many papers do not include annotated bibliographies, the researchers are bound to work on their original papers.

v. Making requirements for up to date references
- If the university/ institute makes requirement for latest literatures (e.g. less than 10 years old), this will automatically eliminate thousands of online papers for inclusion.

3. Strategies for detection of plagiarism
- Detecting plagiarism can provide a courtroom proof of plagiarism. Finding clues can help profitably while discussing with the researcher.

iii. Using Plagiarism detector
- Software that detects plagiarism may also used if the plagiarism is suspected to be critical.
- A number of commercial softwares are available for plagiarism detection such as Turnitin, Plagiarism finder, plagium, dupli checker, iThenticate, etc.

Types and Styles of referencing

APA

- APA style is an author-date citation style. It was developed mainly for use in psychology, but has also been adopted by other disciplines.
- There are two major components to the APA author-date style
  - In-text author-date citation at the appropriate place within the text of the document
  - Detailed reference list at the end of the document

Fundamental guidelines

i. In-text citation
- The in-text citation consists of author surname (s) followed by the year of publication.
- For direct quotes, page or paragraph numbers should be included (e.g. Miller, 2008, p.45).
- If quoting or citing a source which has been cited within another document, the original source should be mentioned together with the secondary reference details (for e.g. Miller, 2008 as cited in Smith, 2016). Only the secondary source should be included in the reference list.
- If the citation is at the end of a sentence, the full stop is placed after the reference.
- For citations in bracket with two authors, the'&' symbol can be used (e.g. Miller & Jones, 2010).

ii. Creating list of references
- The references should be listed in alphabetical order by author surname/family name according to the first listed author.
- Where there are two articles with the same authors and date, the references are ordered alphabetically by article title and a letter suffix is added to the year of publication (e.g. 2003a, 2003b...)
- The names of organization should be provided in full.

Disadvantages of APA style

- When large numbers of articles must be cited at particular points in the text, the long strings of citations within parentheses may be highly irritating to readers as a gross interruption of the text.
- The rules for sequence of citations, punctuation within citations and alphabetization of reference list are more complex than rules for citing by number.

Harvard Style (Parenthetical Referencing)

- The Harvard referencing system is a brief citation to a source and is given in parentheses within the text of an article, and full citations collected in alphabetical order under "List of References," heading at the end.
- This style is also known as the "author-date" style.
- There are many varieties of Harvard referencing system and the styles used may differ from place to place.
- Harvard is very similar to APA.

Fundamental guidelines and features of Harvard system

i. In-text citation

- The identification of references within the text of the article/ report are identified by "author date" style.
- The name can be a part of a sentence and the date only given in brackets or sometimes both the name and date are put in brackets depending on how the citation is used within the wording of the paragraph.
  Eg. Fischer (2011) remarks on.....
  .....has been remarked on (Fischer 2011)
- When the article is cited in the document for the first time, the names of all authors are given. Every time this article is cited after the first reference only the first name of first author is used followed by 'et al'. e.g. Fischer, et al (2012)
- Works published by the same author(s) in the same year are assigned the letters of the alphabet in ascending order. E.g. John et al. (2014a, 2014b)

ii. Creating list of references

- Reference list should appear at the end of your article/report with the entries listed alphabetically by author's name (in-text citation) regardless of the order that they were given in the text.

citations within parentheses may be highly irritating to readers as a gross interruption of the text.
- The rules for sequence of citations, punctuation within citations and alphabetization of reference list are more complex than rules for citing by number.

Vancouver Style
- The Vancouver reference style is the one that is commonly used in the medical field and when publishing in medical journals.
- Vancouver is a "numbered" style where number is assigned to each reference as it is used.

Fundamental guidelines and features of Vancouver system

i. In-text citation
- The identification of references within the text of the article are identified by Arabic numerals in superscript or bracket.
- A number is assigned to each reference as it is cited.
- A number must be used even if an author was named in the sentence
  eg. Smith[12] argued that.....
- The original number assigned to a reference is re-used every time the reference is cited in text, regardless of the previous position in text.
- When multiple references are cited at a given place in a text, a hyphen is used to join the first and last numbers that are inclusive, eg. [6-8]
- Commas are used to separate non-inclusive numbers e.g. [2,3,4,5,7,9] is abbreviated to [2-5,7,9].

ii. Creating list of references
- Reference list should appear at the end of your article/report with the entries listed numerically and in the same order that they were given in the text.
- Book and journal titles are not placed in italics or quotation marks.
- Only first words of the article title and words that normally begin with a capital letter are capitalized.
- The name of the author should be given with the surname first, followed by the initial(s). The authors are listed in the order in which they appear on the title page. Where there are more than six authors, only the first six should be listed, followed by "et al".

Endnote is a commercial reference management software package, used to manage bibliographies and references when writing scientific papers and articles.

- It can either be installed in personal computer (Endnote Desktop) or internet based (Endnote Web) version can be used.
- Endnote can help construct reference libraries in four different ways
  - Filters can be created in electronically linked library to search for references.
  - By means of linked files defined in Endnote, searches can be made directly inside the program.
  - Any PDF file or a folder containing PDF files can be transferred into a program (import function). Thus, metadata can be extracted from PDF files, and masthead of the reference can be read.
  - Internet domain names can be constructed manually

Key features

- Works offline
- Cite While You Write (CYYW) module in the Endnote program ensures integration between Endnote and MS Word. This helps to place references according to the writing rules of the selected journal and list of references can be arranged.
- It can share data with other reference management software
- It can hold unlimited number of records per library or folder
- Endnote uses the language setting from the computer's operating system

Advantages

- Endnote can automatically format the citation into any of over 2,000 different styles.
- Most bibliographic databases allow users to export references to their Endnote libraries. So users do not have to manually enter the citation information.
- It is possible to save a single image, document, excel spreadsheet or other file type to each reference in an Endnote library.

Limitations

- Commercial software (not free of charge)
- A method for exporting citations varies from database to database and must be learned on a case-by-case basis.

Advantages
- Most bibliographic databases allow users to export references to reference manager. So users do not have to manually enter the citation information.
- It is possible to save a single image, document, excel spreadsheet or other file type to each reference in a reference manager.

Disadvantages
- No longer available in the market. The producer stopped developing Reference Manager in 2008.
- Uses English language only

Refworks

Refworks is a web-based commercial reference management software.
Refworks is distributed through Cambridge Scientific Abstracts and as a result, many of the CSA databases work seamlessly with the program.
Use of other personal file management programs can use Refworks in conjunction with their software.

Key features
- Format: Web-based application
- Ability to create references manually using a variety of template.
- A master list of authors, keywords and journals
- A built-in search engine for searching databases like PubMed and online catalogs
- Ability to import from remote databases
- Ability to format in-text citations and references from a manuscript
- A word processor integration utility called Write-N-Cite enables users to insert references from their Refworks accounts into MS Word documents.

Advantages
- Because it is web-based, users can assess the program remotely from anywhere with an internet connection.
- Installation of software or upgrade is not necessary
- It is very easy to learn and teach. The simplicity of the interface makes it an useful program for students and busy clinicians
- Institutional licenses allow universities to subscribe to Refworks on behalf of all their students, faculty and staff.

- Compatible with PubMed, Google scholar and dozens of other database and library sources assessable by internet browser

Advantages
- Free. An open source program
- Fast and easy: one click saves a citation
- Personal library can be accessed from anywhere via the internet.
- Works the same for every web page and every database, without requiring log-ins
- PDF's, images and/or snapshots of webpages automatically attach to citations.

Disadvantages
- Works only with firefox browser
- Because of the way Zotero gets its data, some data can be 'glitchy' and my need to be corrected manually.
- Not as robust for data management as other options (e.g. no search and replace, no duplicate entry check)