Practice-based Evidence in Nutrition (PEN®) www.pennutrition.com
is the global resource for nutrition practice.
Welcome to the PEN® Evidence-based Practice Information Cycle Orientation tutorial developed by PEN® Global Team.

PEN® Orientation Materials

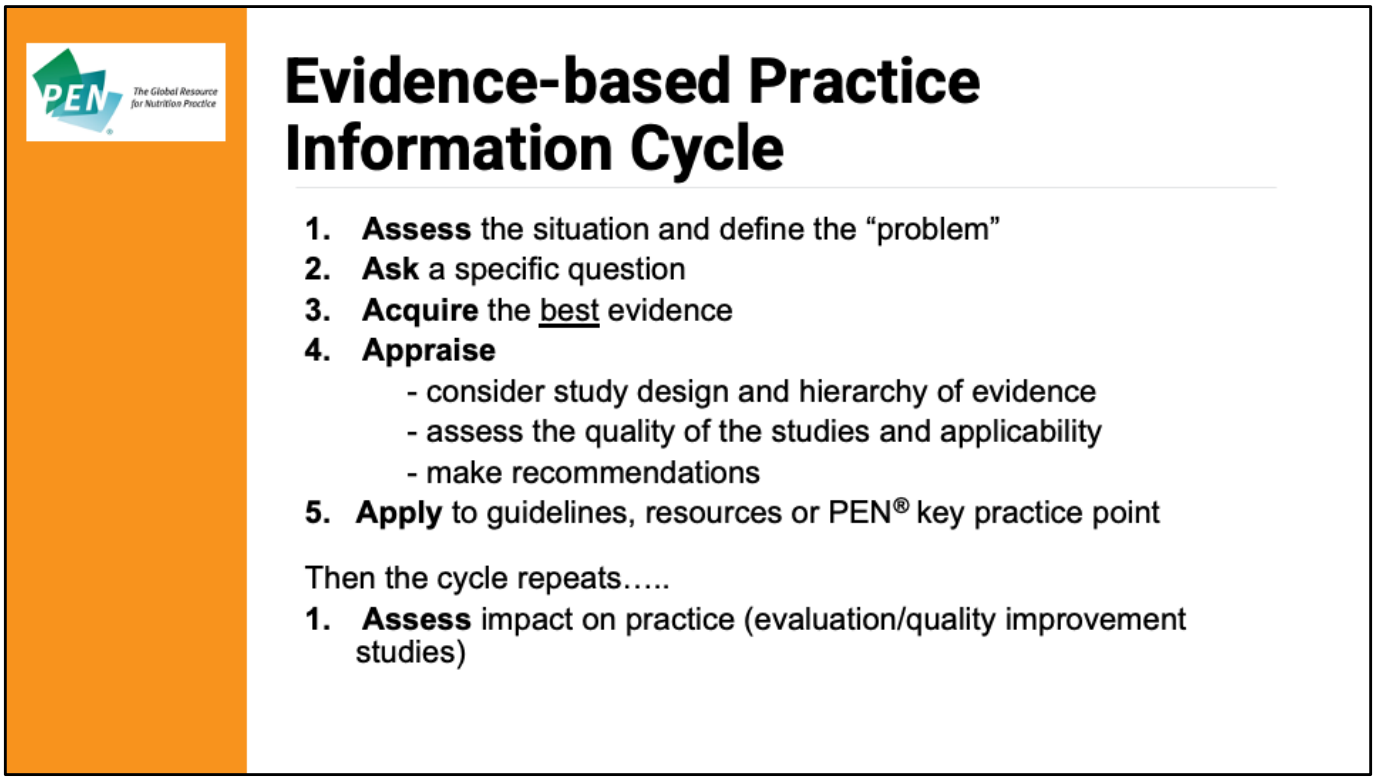
PEN® Tours

- PEN Dashboard Tour
- PEN Table of Contents Tour

PEN® Video Tutorials

- Introduction to PEN
- Getting to Know PEN Knowledge Pathways
- Using our PEN Tools and Resources
- Using the Practice Guidance Toolkit

If you are not very familiar with the structure of PEN® we recommend that you complete the PEN® Tours: https://www.pennutrition.com/tours.aspx and the PEN® Video Tutorials: https://www.pennutrition.com/videotutorials.aspx

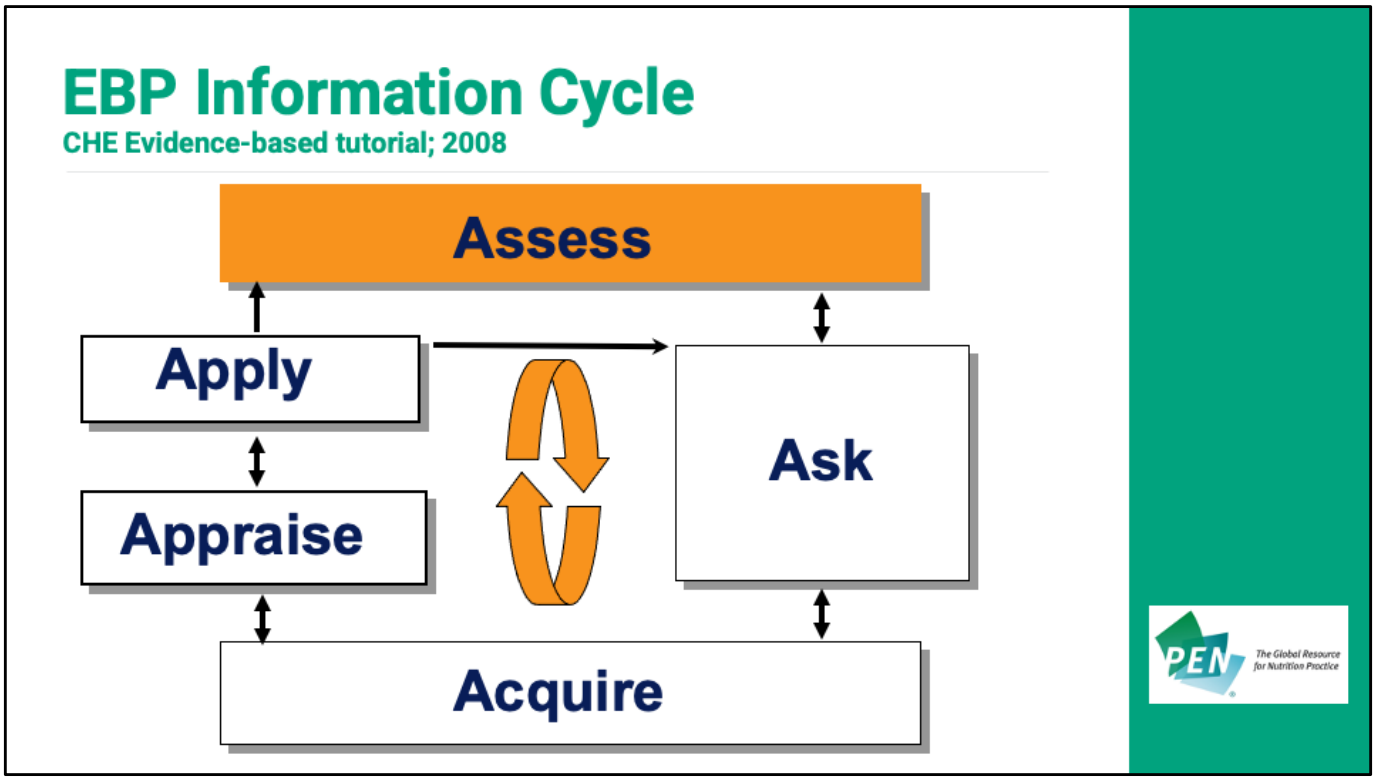


The framework we use for creating PEN® content is the Evidence-based Practice Information Cycle. It utilizes the 5 "A's"

- Assess
- Ask
- Acquire (note this says acquire the BEST evidence, NOT all the evidence (an important distinction)
- Appraise
- Apply

…and then the cycle repeats…

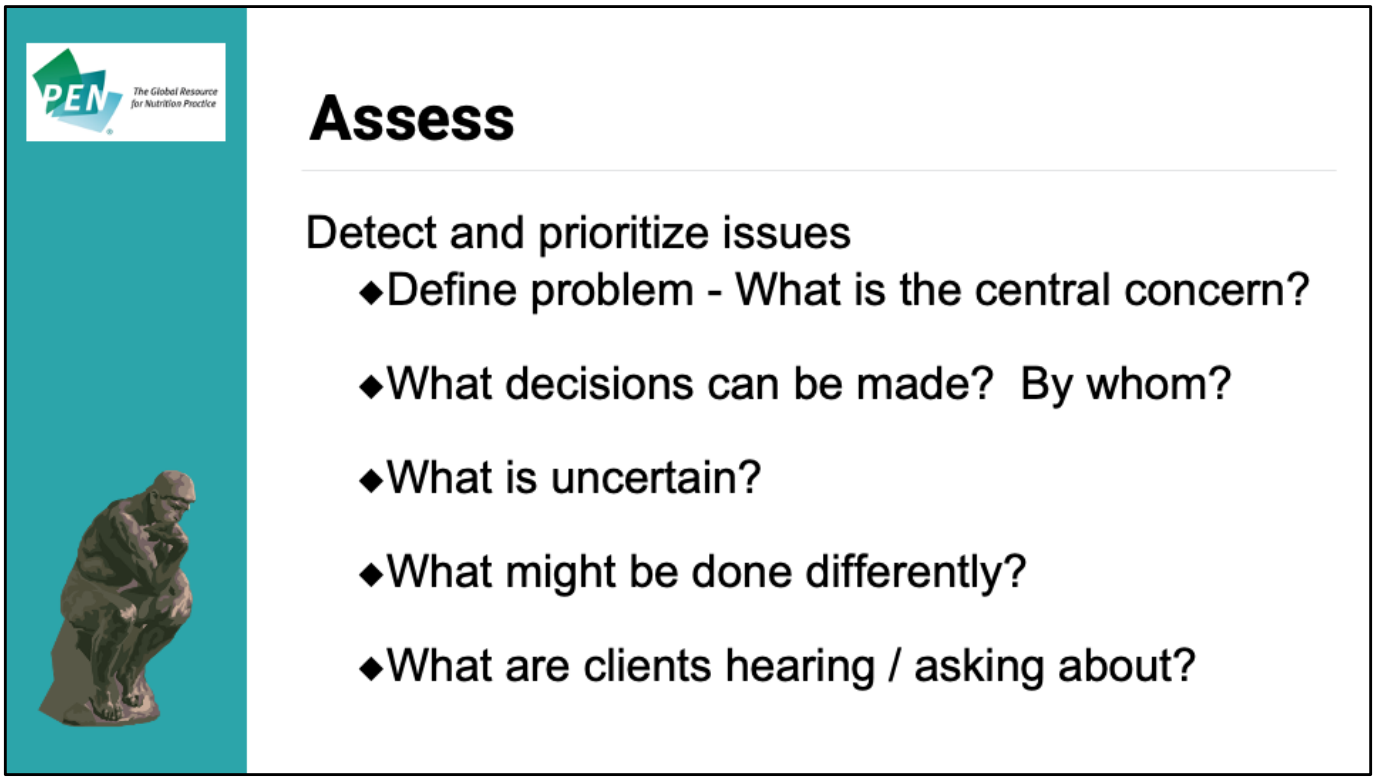
We're going to walk through each of the steps in some detail with you.



Assess is the starting point for Evidence-based Dietetic Practice

Evidence-based practice starts with a spirit of curiosity within a supportive dietetic culture.

Dietitians and health care practitioners can start by regularly asking questions about why they do what they do.



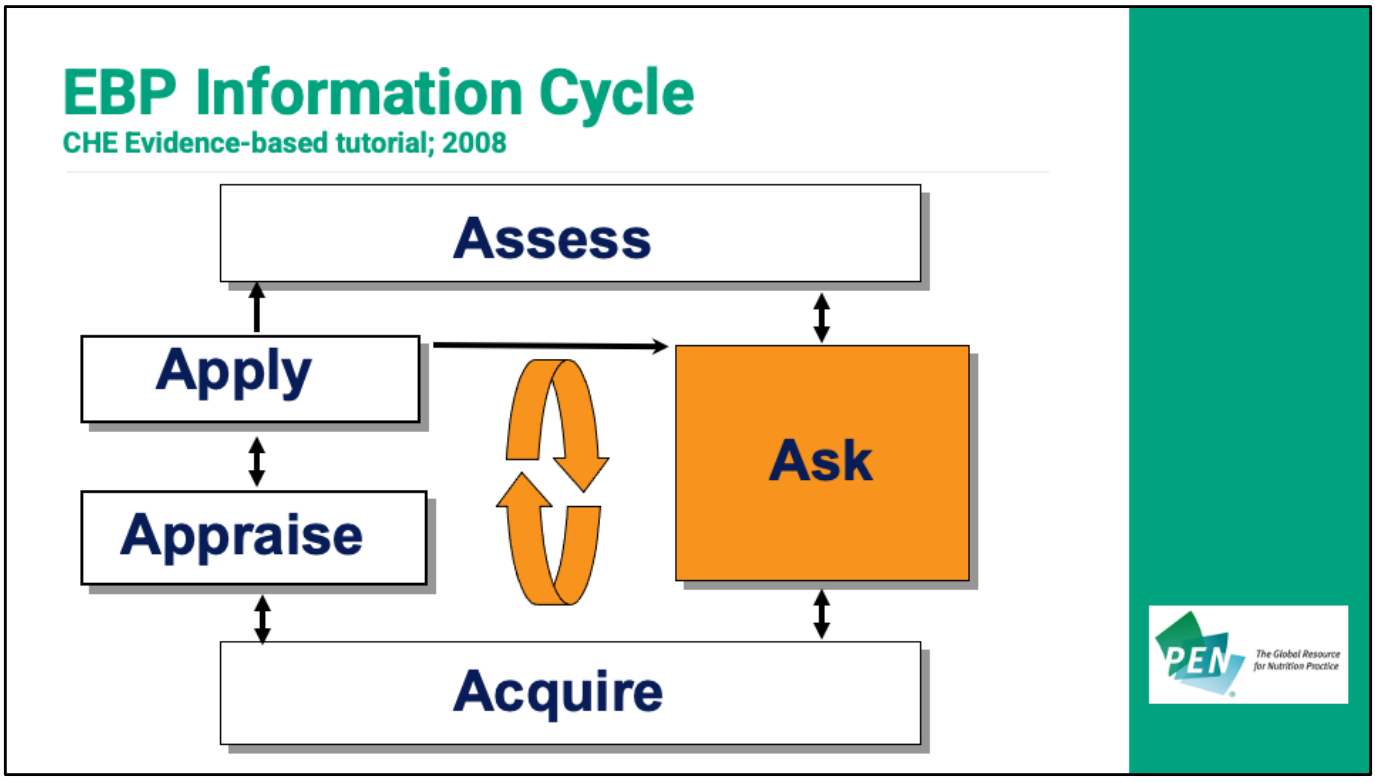
Developing what is sometimes called a Clinical Inquiry Approach calls for practitioners to adopt a mindset of informed skepticism.

Detect issues and prioritize issues – What is the central concern? Harm, prognosis , therapy, rehabilitation
- What decisions are made by whom?
- What is uncertain? urgent, fixable, frequent, doable, interesting

The evidence-based dietitian asks important and relevant questions.
What might be done differently? What choices would matter?
The focus here is finding and evaluating evidence that is: directly relevant to care, addresses knowledge gaps, is volatile.

Being driven by these questions, the informed skeptic goes to the literature and is able to find evidence to answer the questions**.**

The skills of finding the evidence replace the expectation that the individual clinician can be "all knowing". Expertise now lies in part on being able to find the evidence. We begin by creating a searchable question…



The next step in integrating evidence into practice is to convert information needs from practice into focused, structured, searchable questions.

With the volume of scientific literature today, the busy clinician doesn't have time to search through hundreds of articles to find an answer. The goal in asking clinical questions is to be able to find good quality, relevant research efficiently that will lead to sound evidence-based answers to resolve clinical problems and improve patient outcomes. One key to efficiency is asking a focused question.

Ask – frame the kinds of information you have identified in Step 1 or the ASSESS stage into searchable questions. Taking time to develop a "good" question will help you define what to look for and where to look.

Ask

Step 2 – Ask in PEN® Author's Guide

Types of Questions:

Background

- General knowledge, conditions, regulations etc
- Background document template

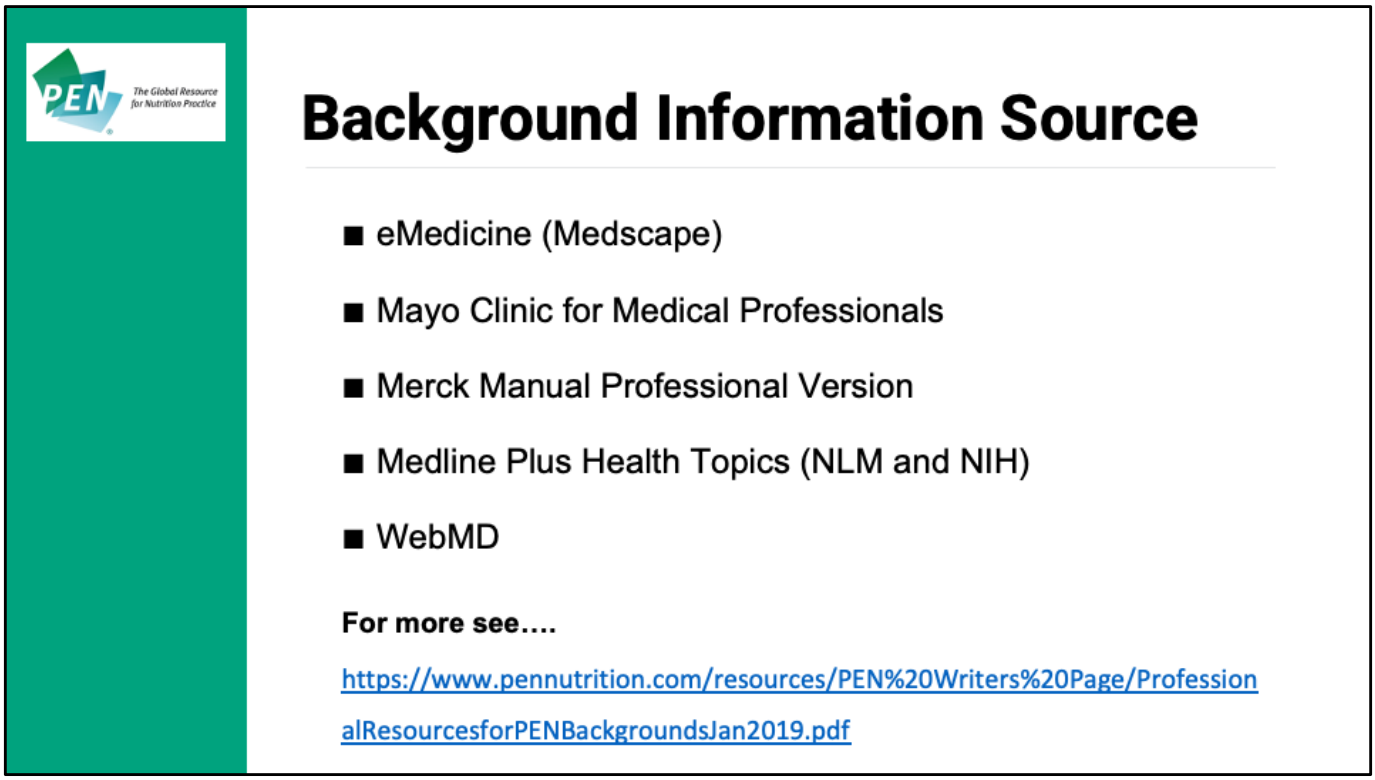
Foreground

- Specialized knowledge
- About choices / decision making
- PEN PICO question

There are two types of questions – *background* questions and *foreground* questions. ***Background*** questions are often of a general nature and relate to a condition for clinical topics or are about basic facts, descriptive stats or regulatory issues etc for non-clinical issues. Questions that pertain to a description of a disease, its etiology, prevalence, incidence, course etc. would be background questions. These are often questions asked by new learners. Answers can usually be found in various resources and textbooks, online sources such as the Merck Manual and MedlinePlus Encyclopedia and even narrative reviews and some original research studies depending on the topic. The PEN® Background documents, not surprisingly, house most of our Background questions. We did this deliberately to make it easier to find information… you don't have to wade through background to get to foreground questions… or vice versa

This training module and the "PEN® Asking the Question" module focus on developing Foreground questions

Foreground questions generally relate to more specialized knowledge which address issues of care, or decision making. Foreground questions usually ask about treatment, prevention, prognosis or diagnosis. These are questions more often asked by experts to address clinical or policy problems. We will be focusing on asking and finding answers to to *foreground* questions.



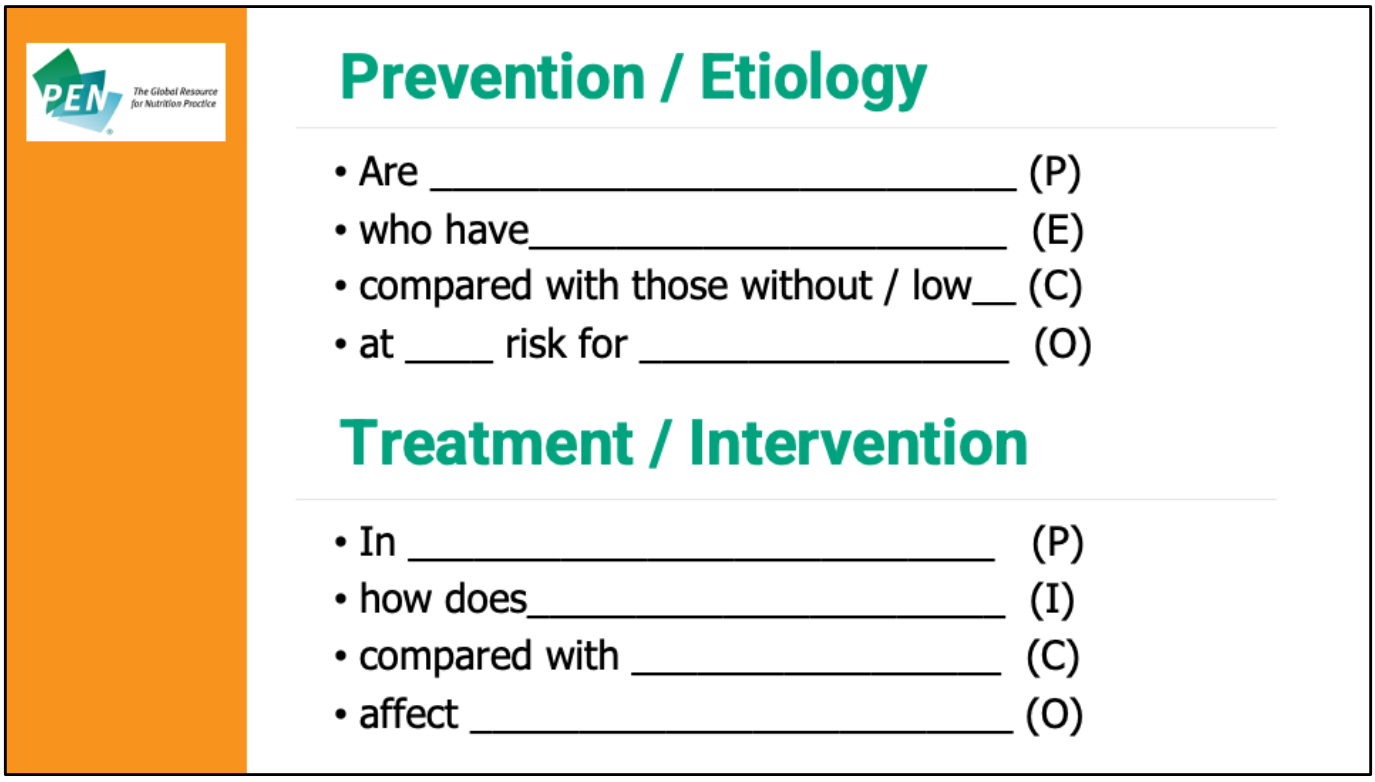
Here are some credible online sources to answer background questions.
■eMedicine (Medscape) http://emedicine.medscape.com/
■Mayo Clinic http://www.mayoclinic.org/
■Merck Manual Online http://www.merckmanuals.com/professional
■Medline Plus Health Topics (NLM and NIH)
http://www.nlm.nih.gov/medlineplus/healthtopics.html
■WebMD https://www.webmd.com/

A list of PEN Background Resources is available at: PEN Background Resources
https://www.pennutrition.com/resources/PEN%20Writers%20Page/ProfessionalResourcesforPENBackgroundsJan2019.pdf

PICO Questions

- Population – how would you define your population e.g. demographics, medical condition?
- Intervention or Exposure of interest – what are the intervention or prognostic factors?
- Comparison – is there an alternative or standard practice to compare to? What comparison is relevant? What is the control?
- Outcome – what do you hope to accomplish, improve or effect? What outcome is important to you and your patients/clients?

Use the PICO or PECO format to formulate a searchable question…
See PEN Author's Guide Step 2: Ask:
https://reso.pennutrition.com/dyncontent/Step2_Ask_Oct2021.pdf



Your question might have slightly different wording depending on whether your question relates to prevention or etiology of disease versus a treatment or intervention type question. Different types of questions are best answered by different types of studies and we'll talk more about that in a moment.

Ask

Types of inquiry in nutrition

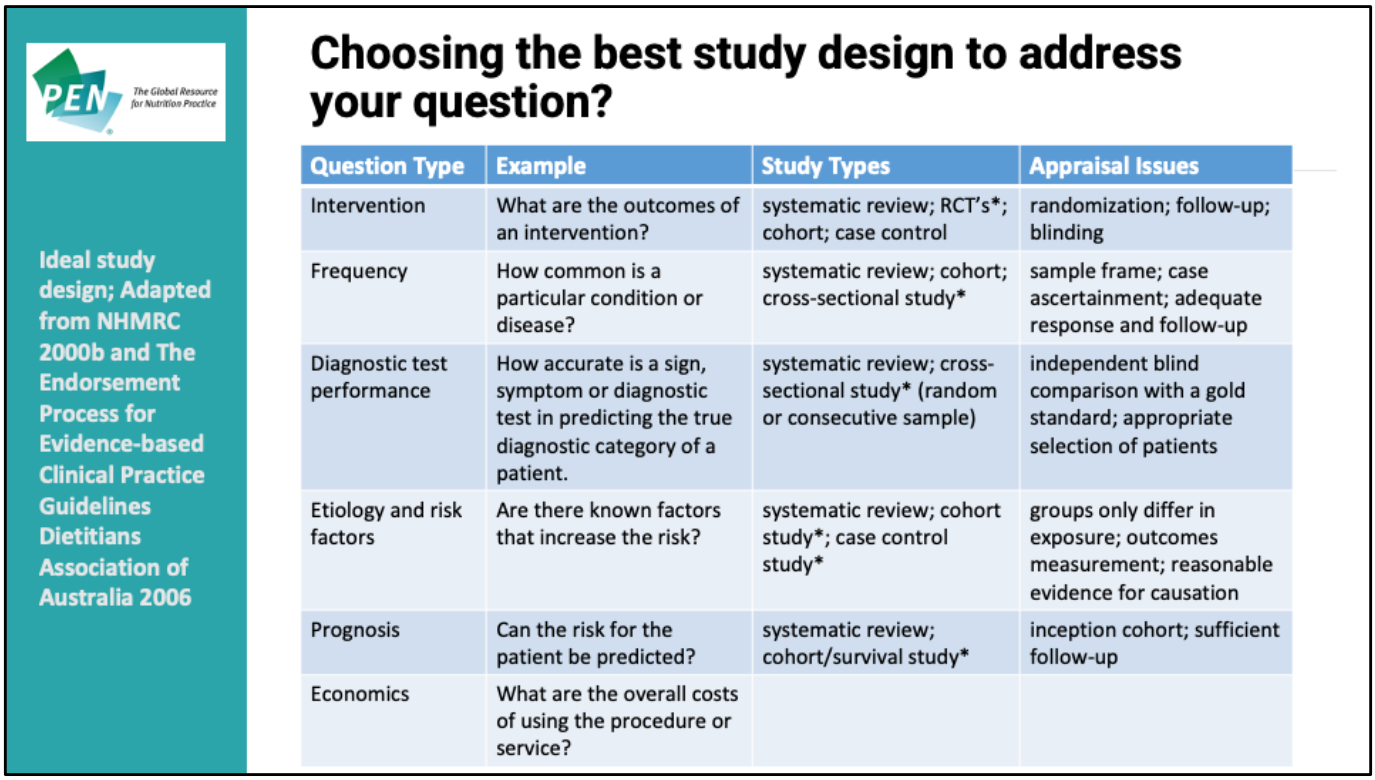
- Etiology
- Treatment / Intervention / Prevention
  - Efficacy
  - Harm

Most inquiries about nutrition evidence are regarding the etiology or the causes of diseases or about optimizing health via nutrition. Examples of etiology questions could include: does vitamin A deficiency cause night blindness?, is serum cholesterol associated with heart disease?

In nutrition, the majority of studies are observational, in which the investigators looked for associations between food or nutrient intakes and the occurrence of a disease, to describe the potential etiology of the disease. These studies usually describe the direction and strength of association of a particular exposure with a particular outcome. Examples of observational studies include cohort, cross-sectional, and case control studies.

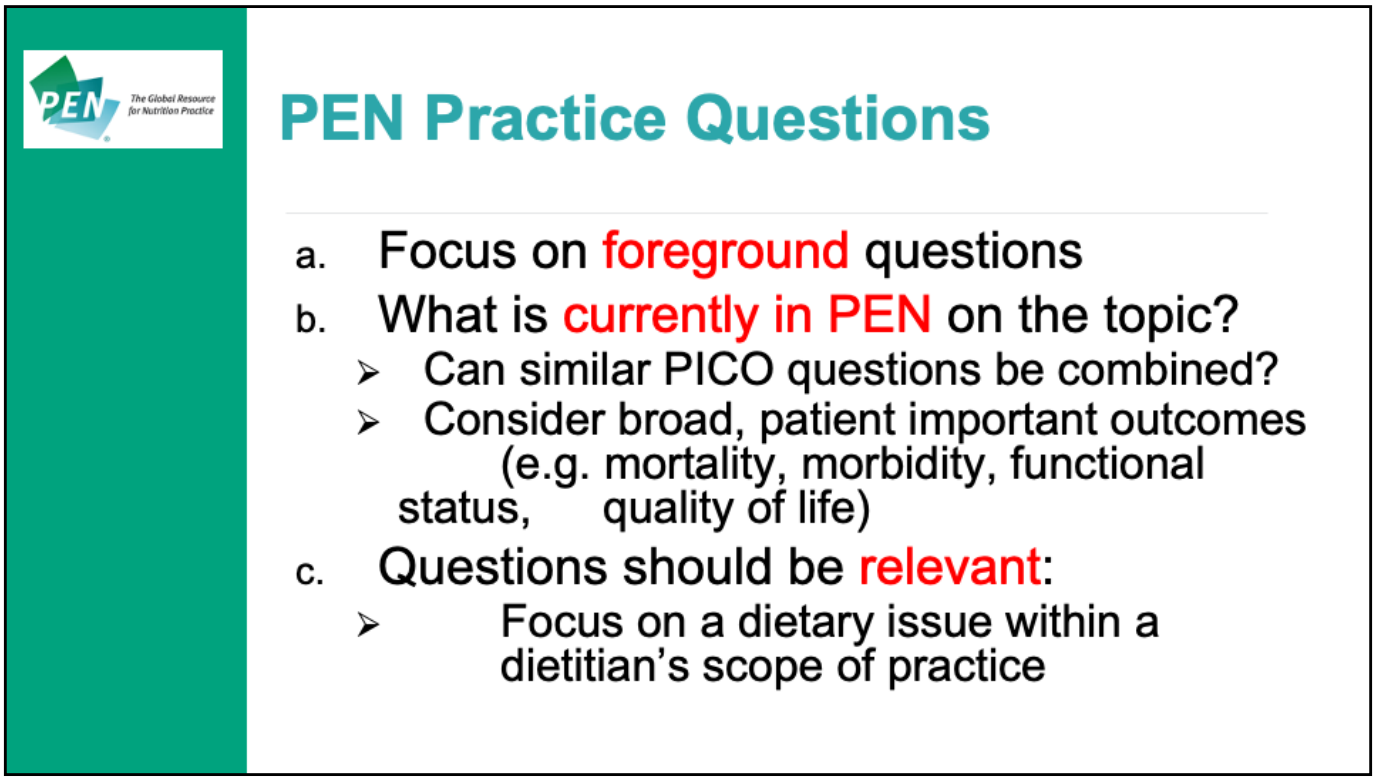
In comparison, some studies include an intervention, to test a particular treatment or prevention strategy for effectiveness and the potential to cause harm. The best of these intervention studies are randomized, referred to as randomized controlled trials, and they provide the most reliable form of evidence.

When we move to the appraisal section, you'll note that different types of studies (along with things like how consistent are the results from study to study) to determine what letter grade we give the evidence.

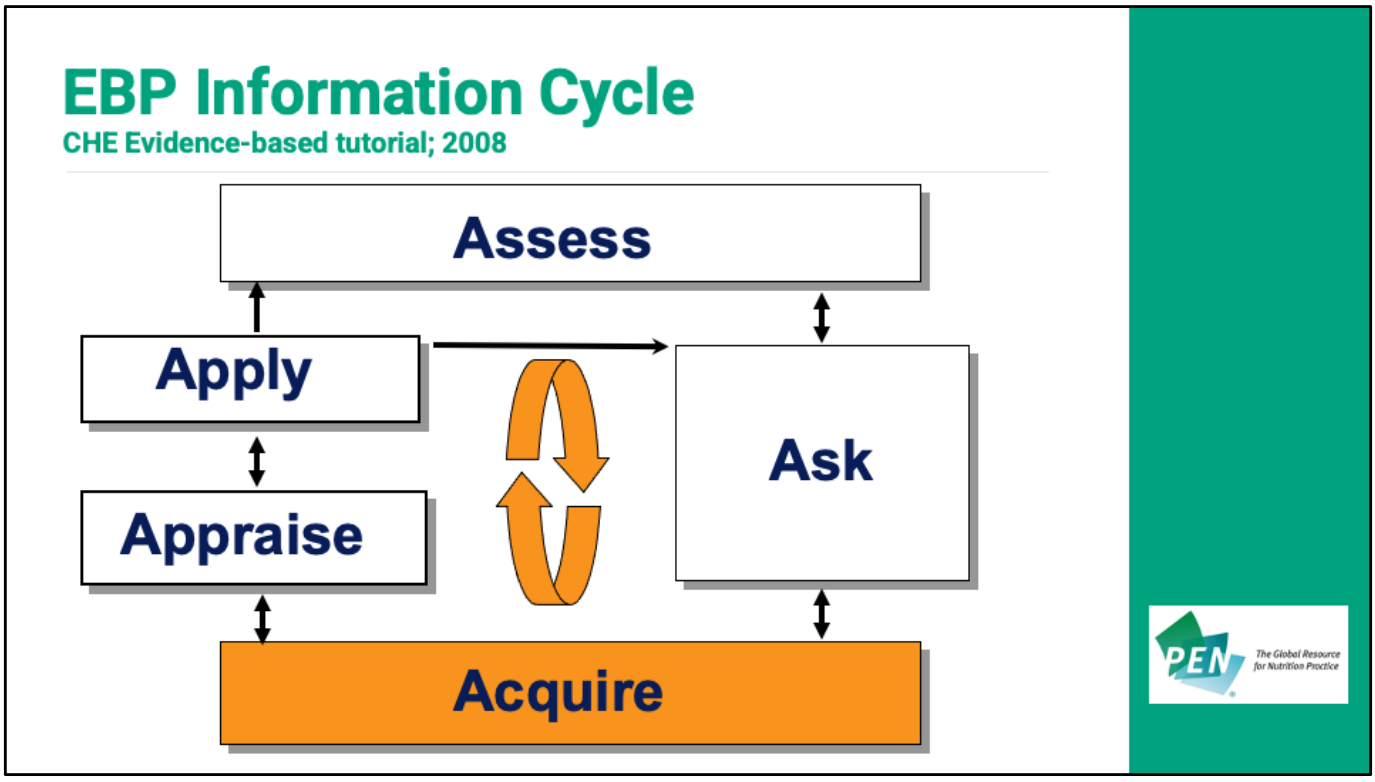


This chart indicates the ideal study design for various question types. It also suggests what might be some of the appraisal issues.

If you would like more details and practice on developing PICO questions work through the "PEN® Asking the Question" training module. If you are OK with developing PICO questions the next phase in the evidence-based practice information cycle is the Acquire phase.



For PEN Questions, the focus is on foreground questions.
Read rest of slide.



The goal in searching is ideally to find quality answers to your structured questions in a timely manner.
A number of sources are available that provide different types and levels or quality of evidence.
Remember earlier on, we said we are looking for **the BEST evidence**, usually not every shred of evidence on a particular topic.

To search efficiently, the first source that you search should be good pre-appraised or pre-filtered secondary sources that summarize the literature and give you a useful actionable plan based on the evidence. With these sources, the work of finding and critically appraising the literature has been done for you. Pre-filtered means that an individual or group of individuals with expertise in a particular area have reviewed and presented **the methodologically strongest data in the field.** We will spend a bit of time looking at credible examples of filtered literature in a moment.

Acquire

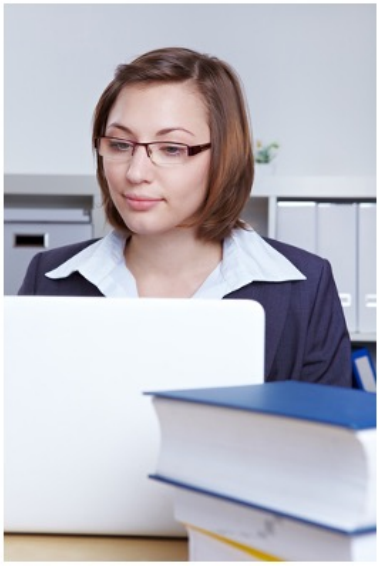
- What types of evidence exist?
- What levels of evidence exist?
- Where is evidence to be found?

So we need to discover
What types of evidence exist?
How good is the evidence?
Where or how do I find the relevant evidence?

Acquire

Searching for Evidence

See Step 3 – Acquire
in PEN® Authors Guide



The first step in acquiring is searching the literature. See Step 3- Acquire in PEN Author's Guide: https://reso.pennutrition.com/dyncontent/Step3_Acquire-May2022.pdf

A pdf of the Search Strategy worksheet is available at: https://www.pennutrition.com/resources/PEN%20Writers%20Page/Search%20Strategy_June2017_(rev%20Dec%202018).pdf
A training module for searching PubMed is available at: https://www.pennutrition.com/resources/PEN%20Writers%20Page/PENPubMedModule(Dec2018).pdf

PEN® Search Strategy

a. Define your topic (1 or 2 sentences in your own words, if possible, in the form of a well-built question – remember PICO)
b. Identify main concepts (come up with 2 to 4 keywords that define your topic, the keywords should all be separate terms that represent your main ideas)
c. Come up with as many synonyms for each main concept (first come up with the words you can think of, then use something like the MeSH dictionary to add to the list – **see PubMed module**)
d. Combine your terms using Boolean terms AND and OR
e. Identify any inclusion/exclusion criteria or limits (language, time period, types of study, etc…)
f. List other methods used to find information and record strategies used (reviewing references lists from key articles, searching the web for grey literature, other sources etc.)
g. Document your search strategy

Review the slide

Whether you are taking a filtered literature approach or looking for individual studies, you should also document your approach and the keywords you used.

Acquire – First Step

Hierarchical literature retrieval

Identifying best available evidence

A. Secondary sources
   i. Systematic review or guidelines based on systematic review
      - most recent and highest quality, most closely represents PICO
      - meta-analyses
   ii. Narrative review with a search strategy

B. Primary sources
   - High quality primary study more recent than the review

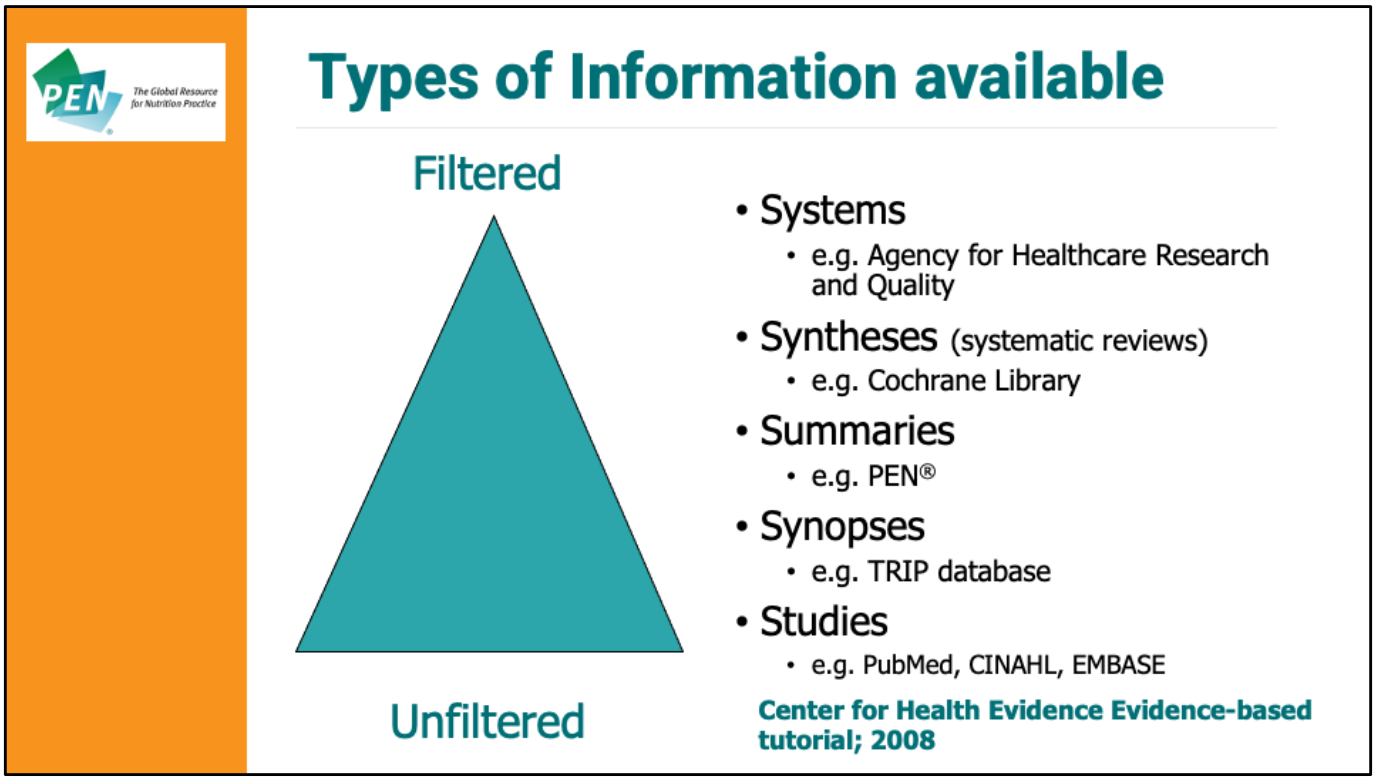
To search efficiently and find the best available evidence, the first search should be for good pre-appraised or pre-filtered secondary sources that summarize the literature and give you a useful actionable plan based on the evidence. With these sources, the work of finding and critically appraising the literature has been done for you. Pre-filtered means that an individual or group of individuals with expertise in a particular area have reviewed and presented the information that **was collected, appraised, and combined in the methodologically strongest way.**

<u>The Hierarchical literature approach:</u>

A. Secondary sources include: i). high quality systematic review (SR) or guidelines based on SR. (The quality of a systematic review can be assed as using AMSTAR 2 tool: https://amstar.ca/Amstar-2.php). If more than 1 SR is identified, pick only one if it addresses all important outcomes. Consider: most recent and highest quality or SR that most closely represents PICO. Meta-analyses are preferred over narrative summary of results.

ii). if no high quality secondary research, a recent narrative review can be used to summarize primary research. Such a review should include a search strategy and be balanced and objective.

B. Include high quality / impactful primary study(s) only if: it is more recent than the SR, it reports an important outcome not included in the SR or no review with a search strategy is available



In order to sort through the mountain of information in the literature, an accepted practice is to start with filtered literature. Classified as 5 'S's – Systems, Syntheses, Summaries, Synopses and Studies. The pyramid reflects the numbers usually found in these various types of literature and is not reflective of the quality of evidence. Starting at the top with the likely smallest number we have:

Systems link evidence to practice and can be found in practice guidelines.

Syntheses summarize results of many studies; use a systematic process for pooling evidence from multiple studies to synthesize the information into a systematic review or meta-analyses e.g. Cochrane library.

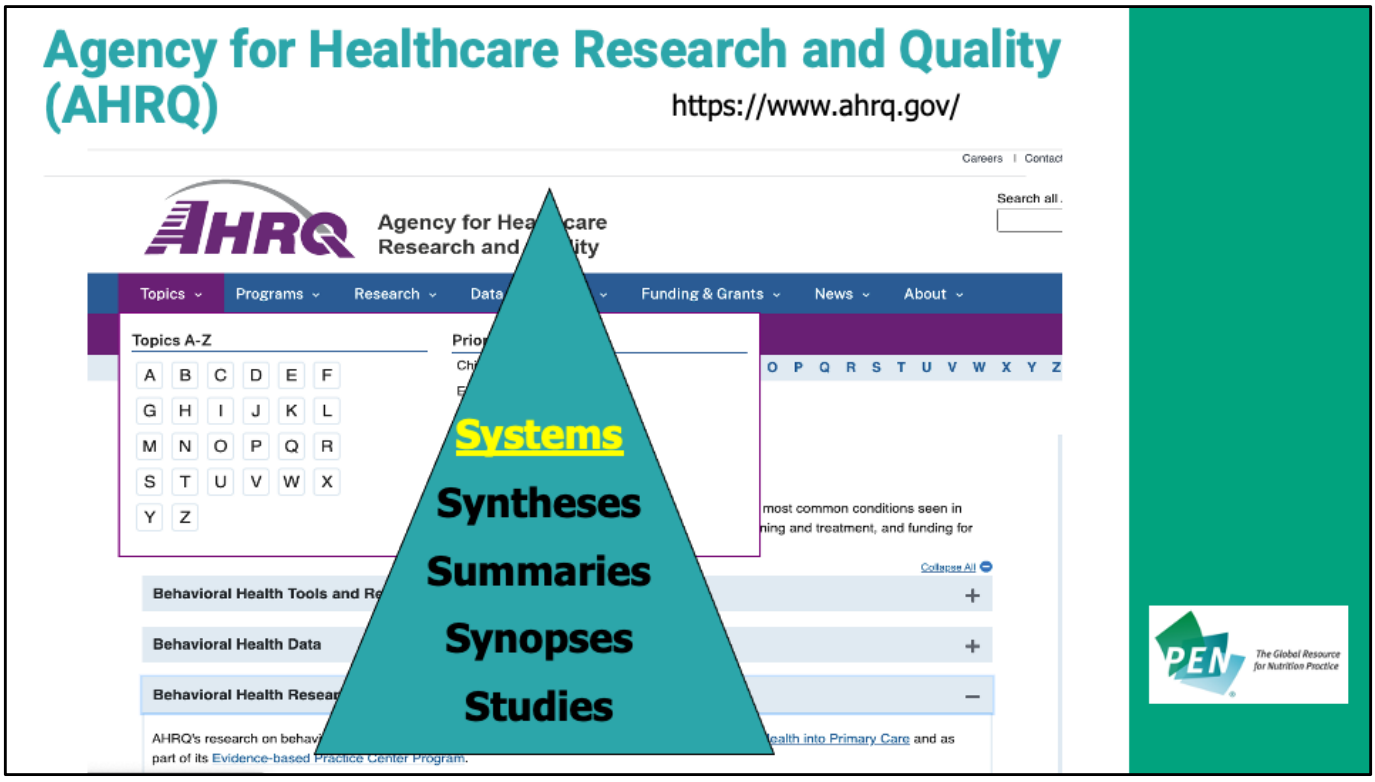
Summaries are regularly updated summaries of best evidence about clinical interventions; topics generated by clinicians and presented as clinical questions e.g. PEN®

Synopses summarize high quality articles into brief synopses. We do not use Synopses to write evidence statements but to find studies to review.

If evidence can still not be found (for example the clinical issue involves a rare condition or needs to be updated), then a search in the 'traditional literature' for individual Studies is necessary.

There are many advantages to using pre-filtered evidence, not the least of which that someone has already reviewed the literature and chosen only methodologies from the strongest studies to answer the research question. Even with filtered sources we still look at what has been published on the topic since the filtered source of information e.g. if a systematic review was published 6 months ago and their

literature search ended with a date a year prior to publication then we need to search the literature for the past 18 months to see what has been published since. Evidence statements in PEN® are usually composed of CPGs, systematic reviews and original research studies – some or all depending on the topic.
Let's look at accessing the sources of these 5 'S's in more detail.

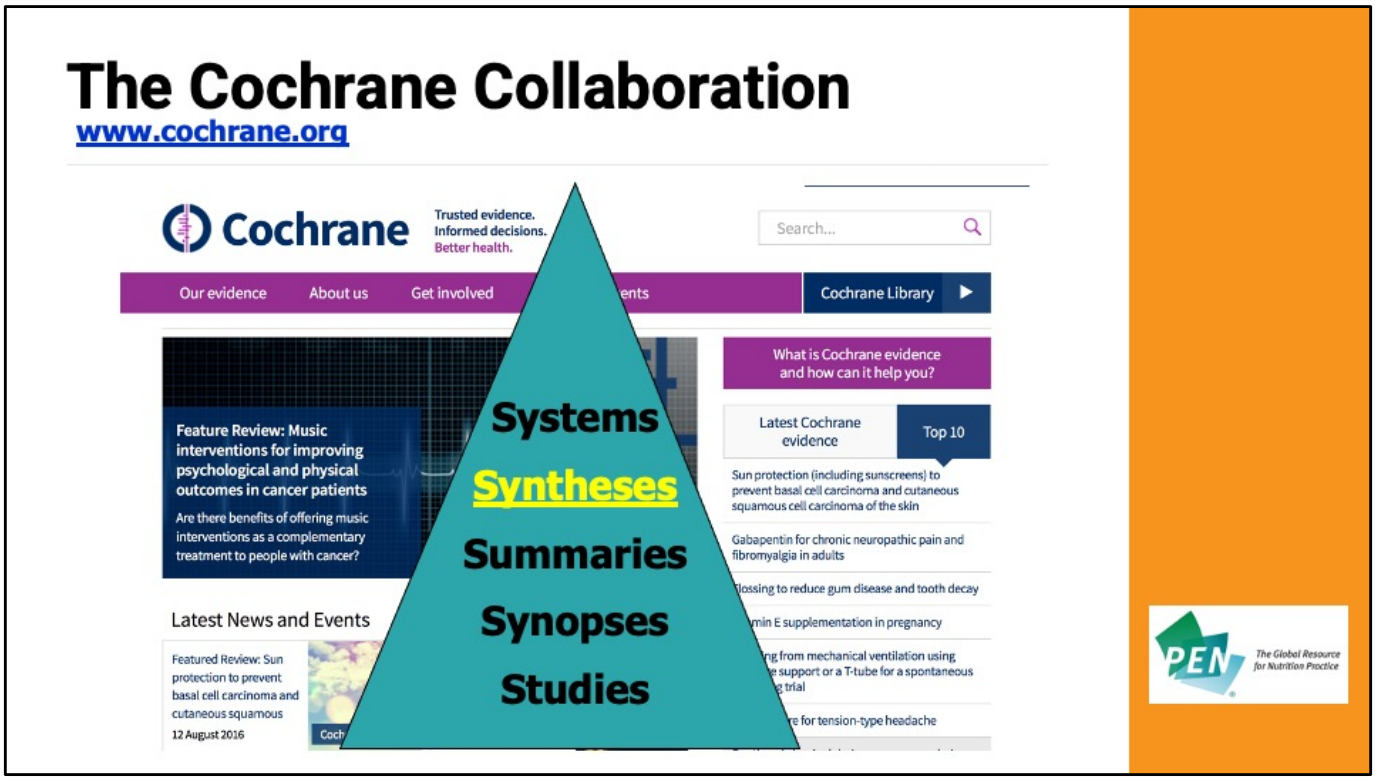


Agency for Healthcare Research and Quality https://www.ahrq.gov/ produced evidence within the US Dept of Health and Human Services.

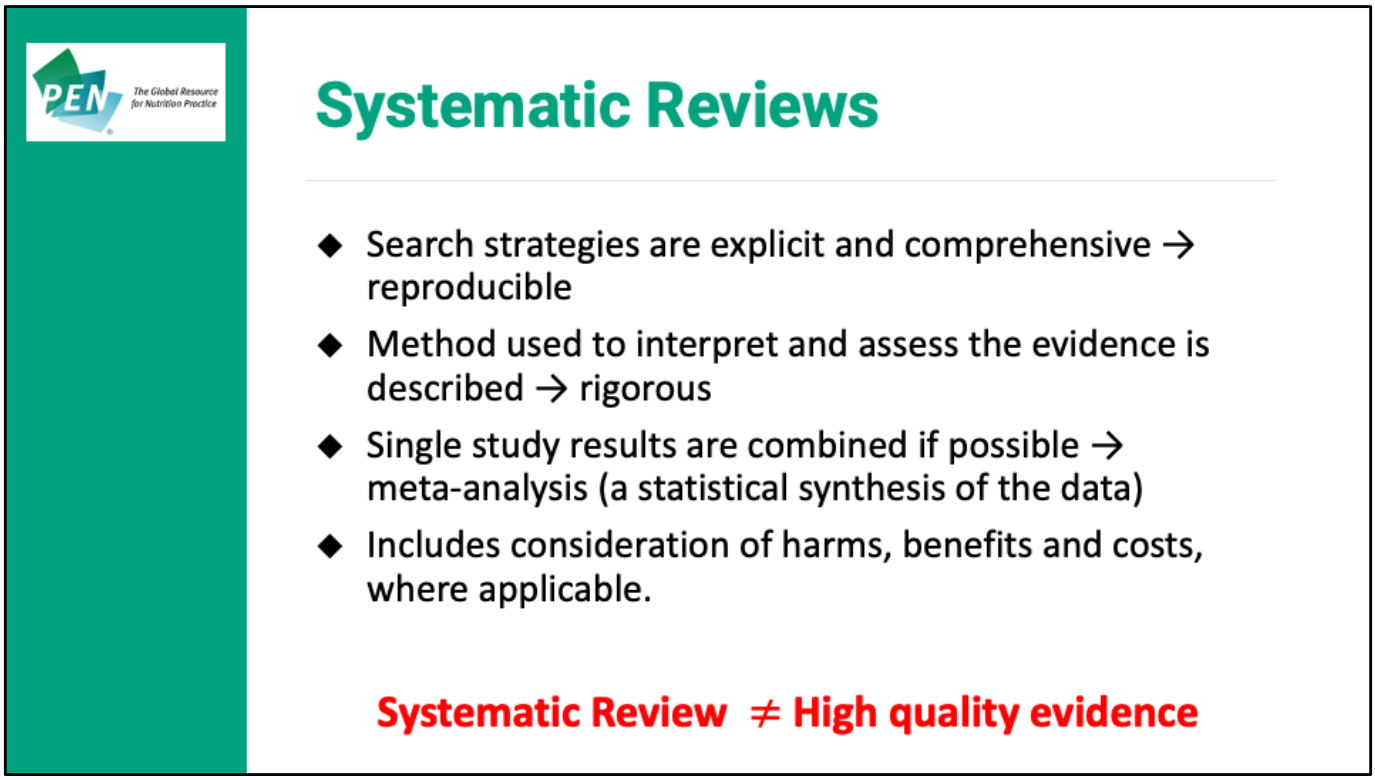
We also ask our PEN® writers to scan guidelines in all our partner countries… UK, AU, NZ and CDN
NICE, NHMRC, ESPEN etc.

Note: the quality of clinical guidelines need to be assessed just like is done for systematic reviews, meta-analyses and individual studies. CPG's are not necessarily better evidence than other sources of evidence. More on Clinical Practice Guidelines later.

Here you see the World Wide Cancer Research Fund International (http://www.wcrf.org/) and a link to their Continuous Update Project or CUPS… Ongoing work, adding to their systematic reviews… explicit with their search criteria and their grading system



Cochrane systematic reviews (http://www.cochrane.org/what-is-cochrane-evidence) are another example of syntheses, based on the best available information about healthcare interventions, usually limited to randomized controlled trials but case control and observation studies are reviewed as well, especially in public health topic reviews. They explore the evidence for and against the effectiveness and appropriateness of treatments (medications, surgery, education, etc) in specific circumstances. There are over 2200 reviews. Summaries / abstracts are available free - the complete reviews are published in The Cochrane Library which is available by subscription though some countries (notably the UK and Australia), and some workplaces, provide free access for certain sectors of their populations.



A systematic review is a rigorous systematic approach to review of primary studies on a topic.

Systematic review does not mean high quality evidence – the studies included in the review will determine the quality of evidence.

But especially when there are multiple SRs available, how to determine the best quality SR.

The search strategies are explicit and comprehensive - the databases searched, the dates included in the search and the selection criteria for studies are explicitly described (did the authors consider only RCTs? Study duration?). This means that anyone else conducting the review, would be able to replicate the review. Cochrane reviews include a detailed methods section that allows the reader to assess whether the review was done in such a way as to justify its conclusions – the type of clinical studies to be incorporated into a review is carefully considered, using predefined criteria; often only RCTs are used. Risk of bias is fully explored.

If the data collected in a review are of sufficient quality and similar enough, they are summarized statistically in a meta-analysis, which generally provides a better overall estimate of a clinical effect than the results from individual studies.

Systematic reviews also include a consideration of the harms or adverse effects associated with the treatment (or whether benefits outweigh harms) and

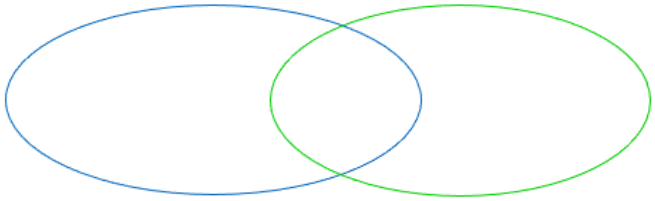
occasionally the costs of treatment where this can be determined.

Systematic Reviews and Meta-Analyses

- **Systematic Review**: A systematic summary of studies: applies strategies to limit bias in the gathering, critical appraisal, and synthesis of all relevant studies on a topic
- **Meta-analysis**: a statistical synthesis of the data of several studies with predetermined quality

Read the definitions of systematic reviews and meta-analysis.

Systematic Reviews and Meta-Analyses

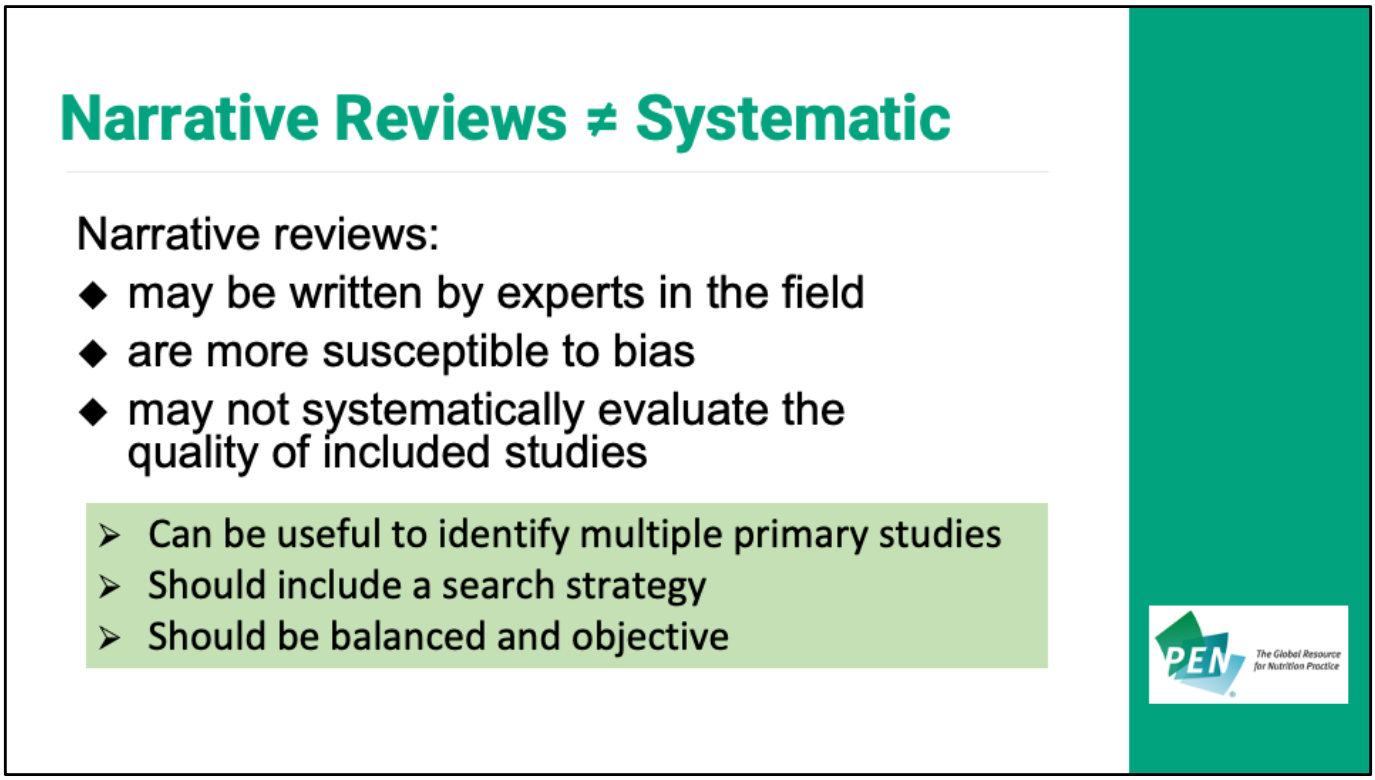


Systematic reviews may or may not have a meta-analysis as a component. It depends on the characteristics of the studies identified

Meta-analyses may or may not be based on a systematic review

There is generally a lot of overlap between systematic reviews and meta analyses. If conducting a PubMed search one should include both study types as Limits for searching.

These should not be confused with narrative reviews….

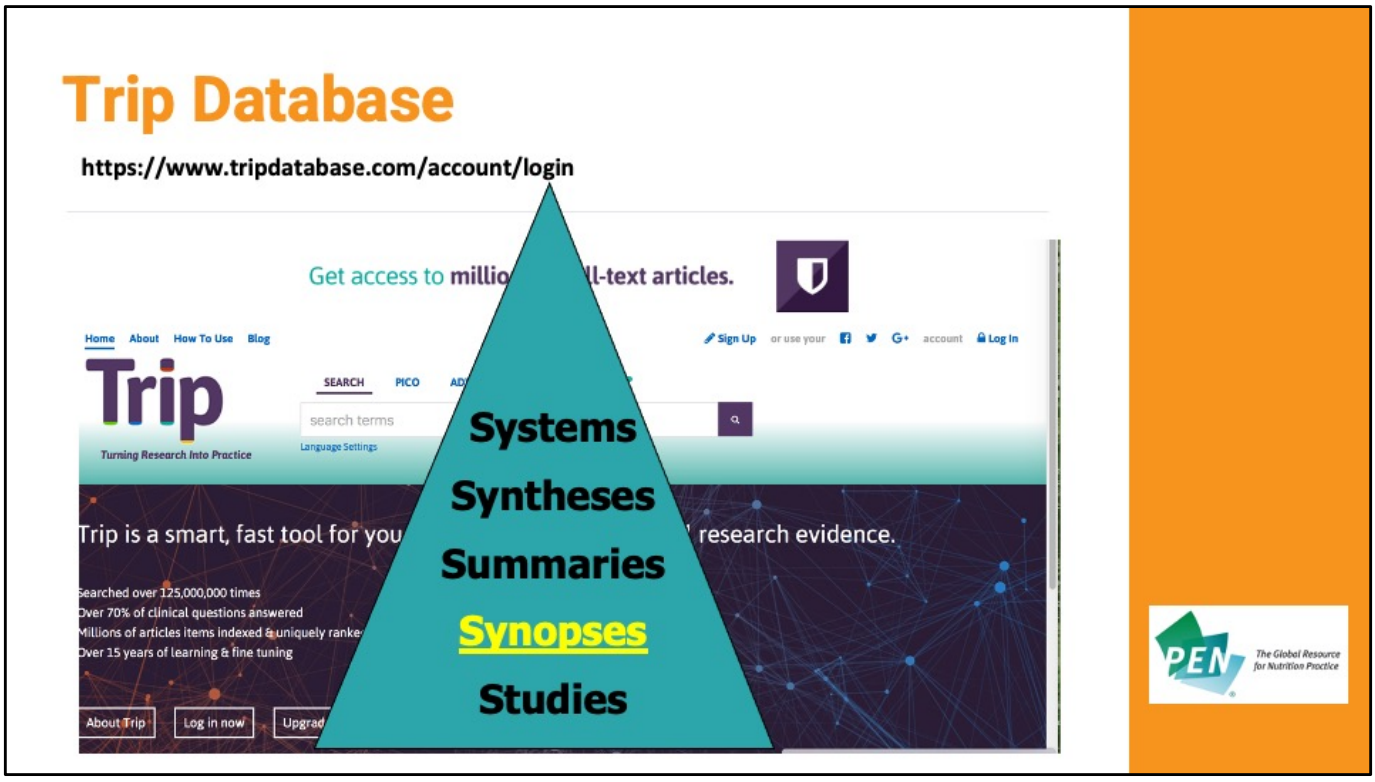


What distinguishes systematic reviews from traditional, narrative-type reviews?

Narrative reviews are definitely not the same as systematic reviews
More susceptible to bias – selectively citing studies
Read slide

PEN® itself is an example of a summary tool: http://www.pennutrition.com
It takes the best evidence and summarizes it into graded practice guidance.
Recall PEN®' has:

- Key practice points – including Evidence Syntheses and Practice guidance summaries
- Evidence summaries
- Practice Guidance Toolkits



The Trip Database - Taking Research into Practice (https://www.tripdatabase.com/account/login) has a free version and a subscription version. It is a database but can provide synopses of the evidence in response to keywords. They also identify guidelines, clinical trials, systematic reviews plus a great deal more. The TRIP database helps to find the literature but you still need to analyze, critique and summarize the studies, guidelines and systematics reviews. The Trip database can not be cited as a reference for evidence.

It is medically focused though so not all your nutrition questions are likely to be addressed in the detail you might like to see or need.

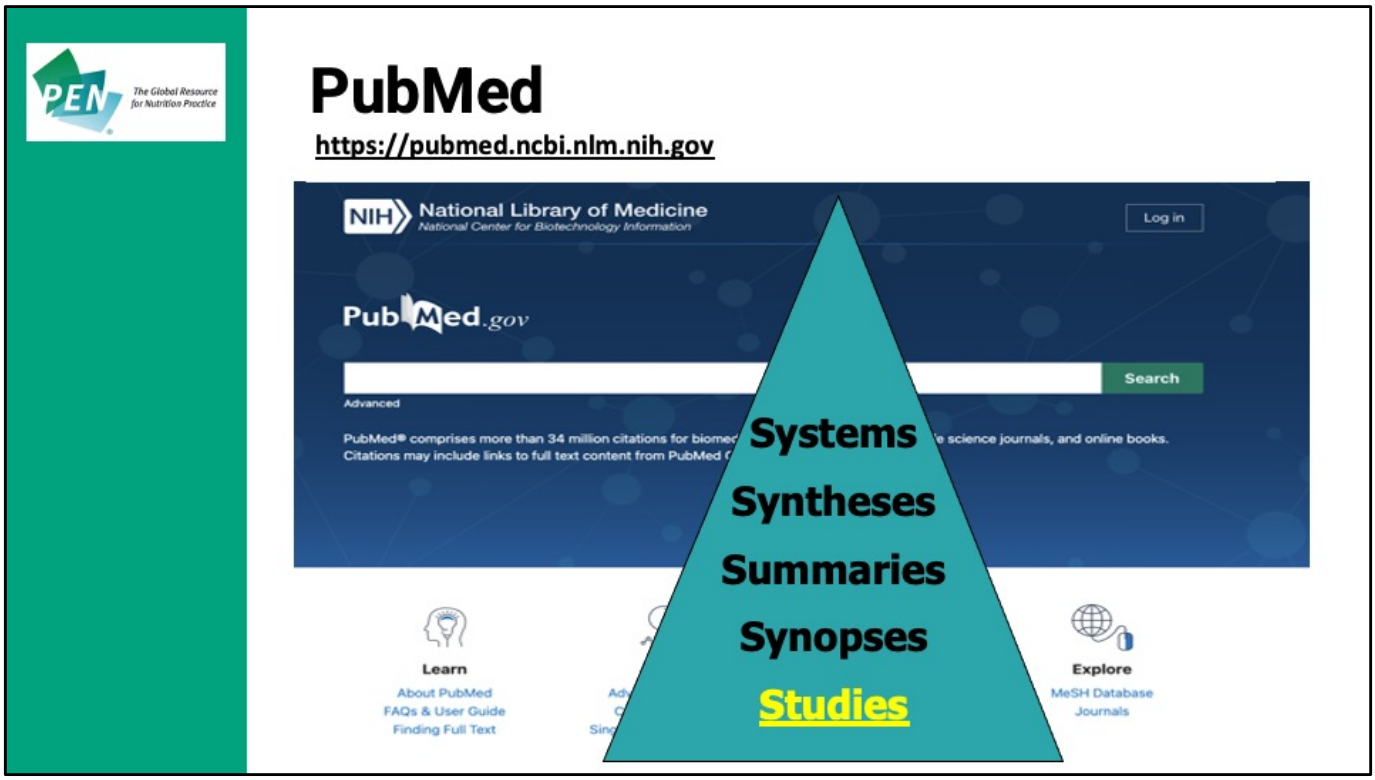
Primary studies

Consider when:

- Published more recent than review
- Patient-important outcome not included in the review
- No review available

PEN The Global Resource for Nutrition Practice

Read slide



Depending on the results of your search of pre-filtered literature you may find your answers without needing to do a traditional literature search or you may need to do a small search of the most recent literature. In some cases when there is no pre-filtered literature this may be the sole or primary type of searching. PubMed is a free tool for identifying studies and can also be used to access systematic reviews: https://pubmed.ncbi.nlm.nih.gov/

Literature Searching Summary

- Find the terms for your PICO variables to search
- Prepare a list of your MeSH terms and text words Look first for: Filtered literature (systematic reviews and clinical practice guidelines)
- After your search of the filtered literature, you likely will need to do some searching of primary studies (combine terms using Boolean connector “AND” or “OR”); use appropriate filters and don’t forget to check related citations
- In searching you may find other terms related to your topics that require you to do further searching
- Perhaps contact your local Librarian for a session on searching

If you have identified a systematic review that indicates the last search date of the review authors, you could filter your search of original research to only those studies published after that search date. Additionally, you may find additional studies that you missed in your original search by paying attention to the introduction and discussion of original research articles. Look to the article’s bibliography for the citations. Be systematic in your search strategies.

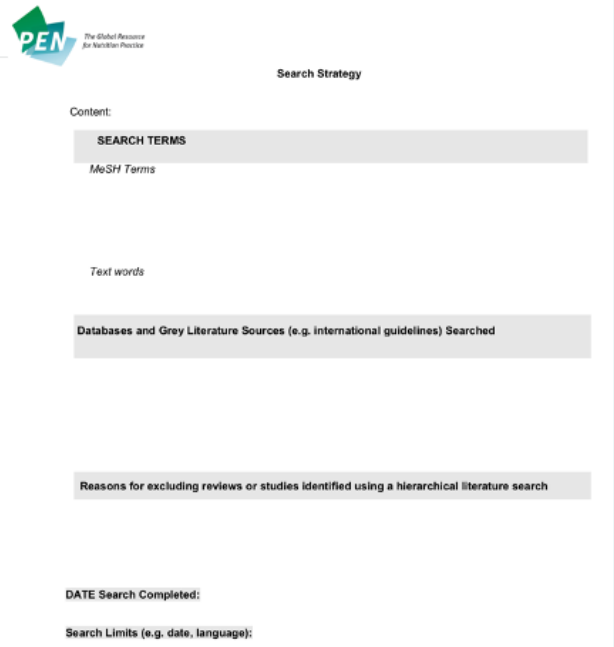
Remember defining your PICO question and searching are not always mutually exclusive. For example, in searching you may find in learning more about your topic that there are more appropriate search terms for locating the relevant literature and you may need to re-search.

If you would like more information on literature searching you can complete the “PEN® PubMed” training module.

Search Strategy

Document:

- Search Terms
- Databases Searched
- Reasons for excluding noteworthy studies
- Date search completed / Date range of Search



Search Strategy

Content:

SEARCH TERMS

MeSH Terms

Text words

Databases and Grey Literature Sources (e.g. international guidelines) Searched

Reasons for excluding reviews or studies identified using a hierarchical literature search

DATE Search Completed:

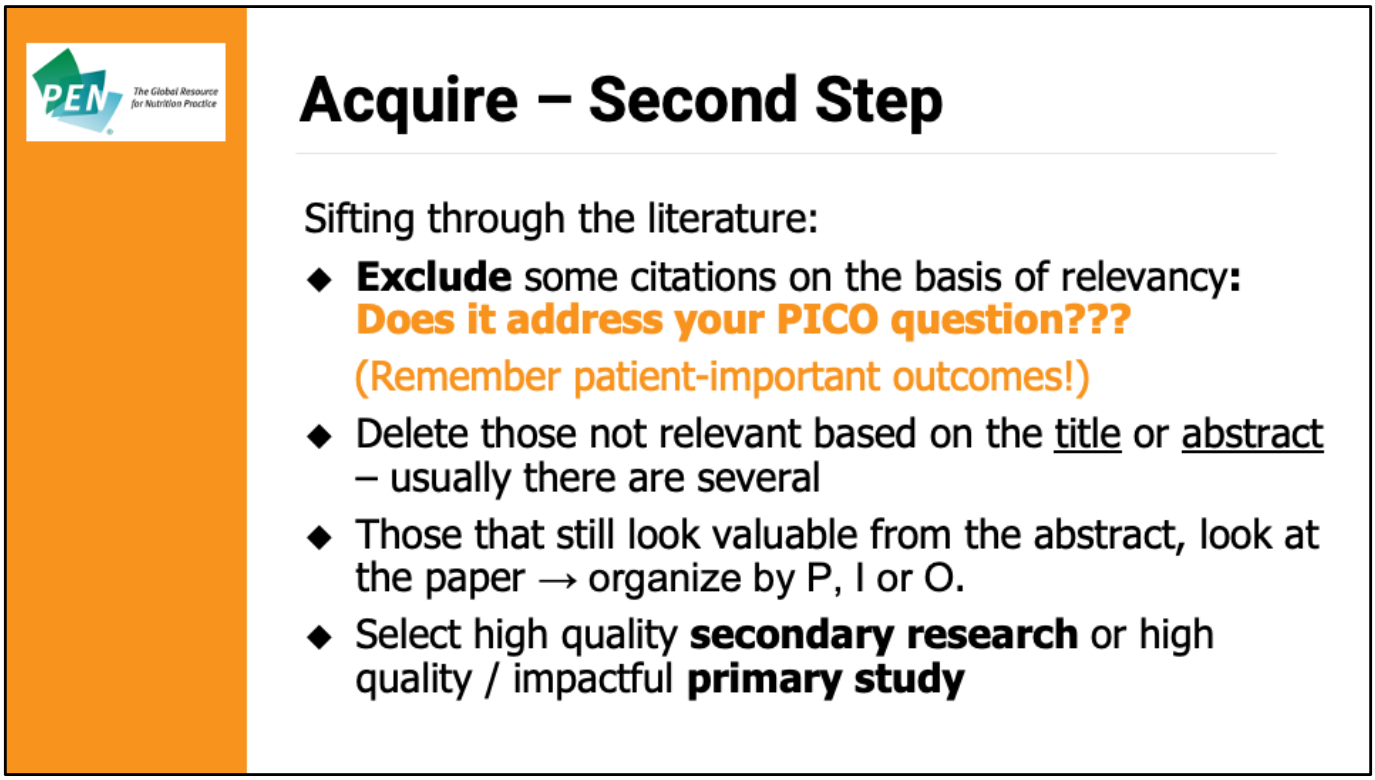
Search Limits (e.g. date, language):

Authors are asked to document their search strategy for each question, which will be sent to reviewers at the time of review.

The search strategy includes:

- Search Terms (MeSH terms and text words)
- Databases Searched
- Reasons for excluding particularly noteworthy or controversial studies / resources
- Date search completed / Date range of Search

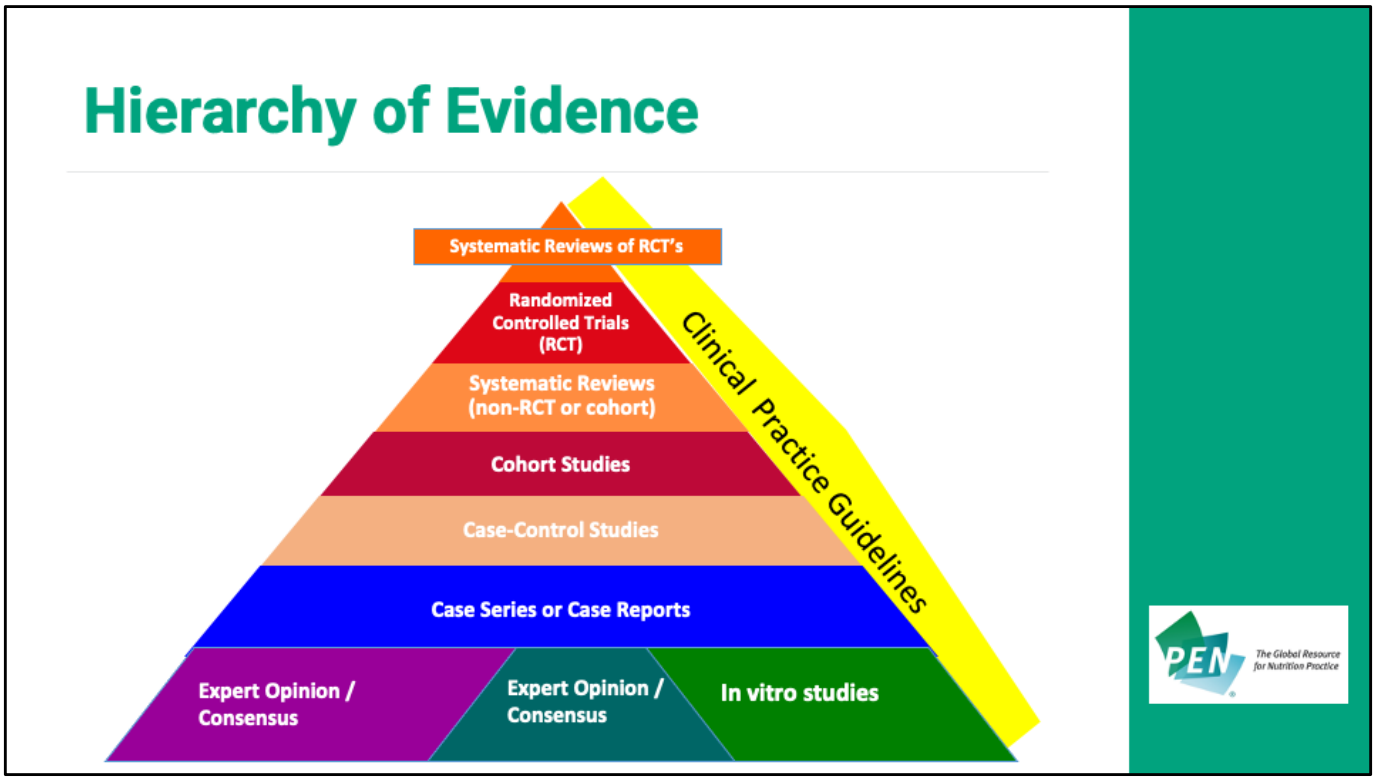
The search strategy document is available at: xxxxx



Not all relevant citations will be included in your evidence.
Remember,
If more than 1 systematic reiview is identified, pick only one if it addresses all important outcomes

Most recent, highest quality, closely represents the PICO

Once you have acquired the literature the second step is to sift through and see what is useful and what is not.



Hierarchy of Evidence: to help us understand that every study is not created equal and some are better quality evidence than others. Some types of studies are more appropriate depending on the question being asked.

In addition to the type or design of the study, the quality of the study (e.g. well designed, size, risk of bias…) is a key component in determining how it contributes to the graded evidence used in PEN®. **Slides 41 – 47** in this training module discuss the PEN® grading system and the PEN® Evidence Grading Checklist in some detail. Review the "Appraising the Literature" training module for more on assessing the quality of the study.

Depending on your quality assessment of the document then, generally the higher quality evidence in terms of design is from:

Higher quality: Systematic reviews – to be highest quality must be of RCTs, THEN RCTs THEN SRs of nonrandomized or cohort studies THEN Cohort studies THEN Case-control studies

Lower quality: Case series or Case reports - descriptions of a single or a series of cases of some illness

At the bottom are: Editorials, expert opinion – not actually evidence, but opinion

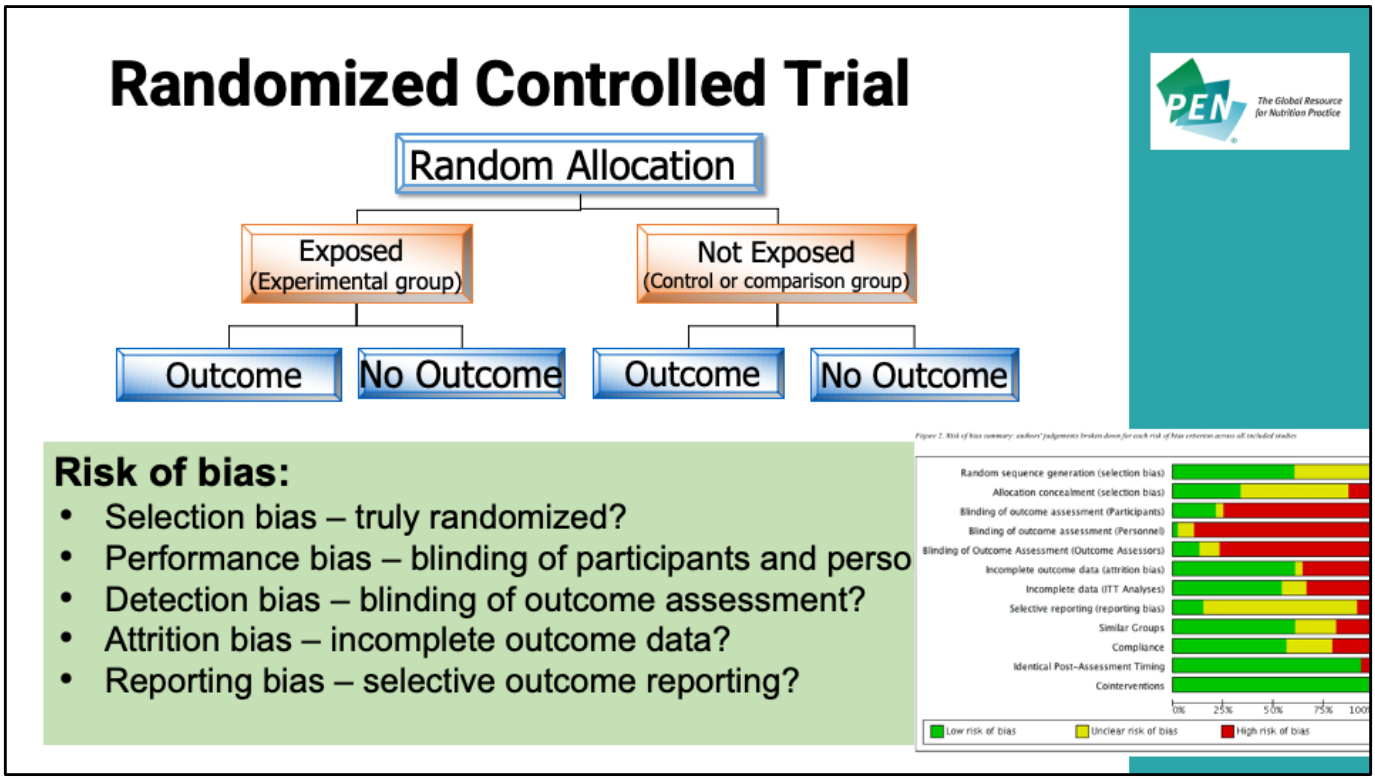
Animal research – studies conducted on animals cannot be applied directly to humans

In vitro - a biological process conducted in a laboratory container i.e. test tube or petri dish

Although there are some issues/questions where animal and in vitro studies are the most appropriate research design , the grade assigned to the resulting KPP would still be low.

As noted in PEN's grading checklist; clinical impact, generalizability and applicability also are considered in assigning Grades A, B, C and D.

Note: This is the current hierarchy of evidence but we are aware of continuing discussions taking place within groups such as Cochrane and GRADE on grading hierarchies. The PEN® team continues to monitor these discussions.

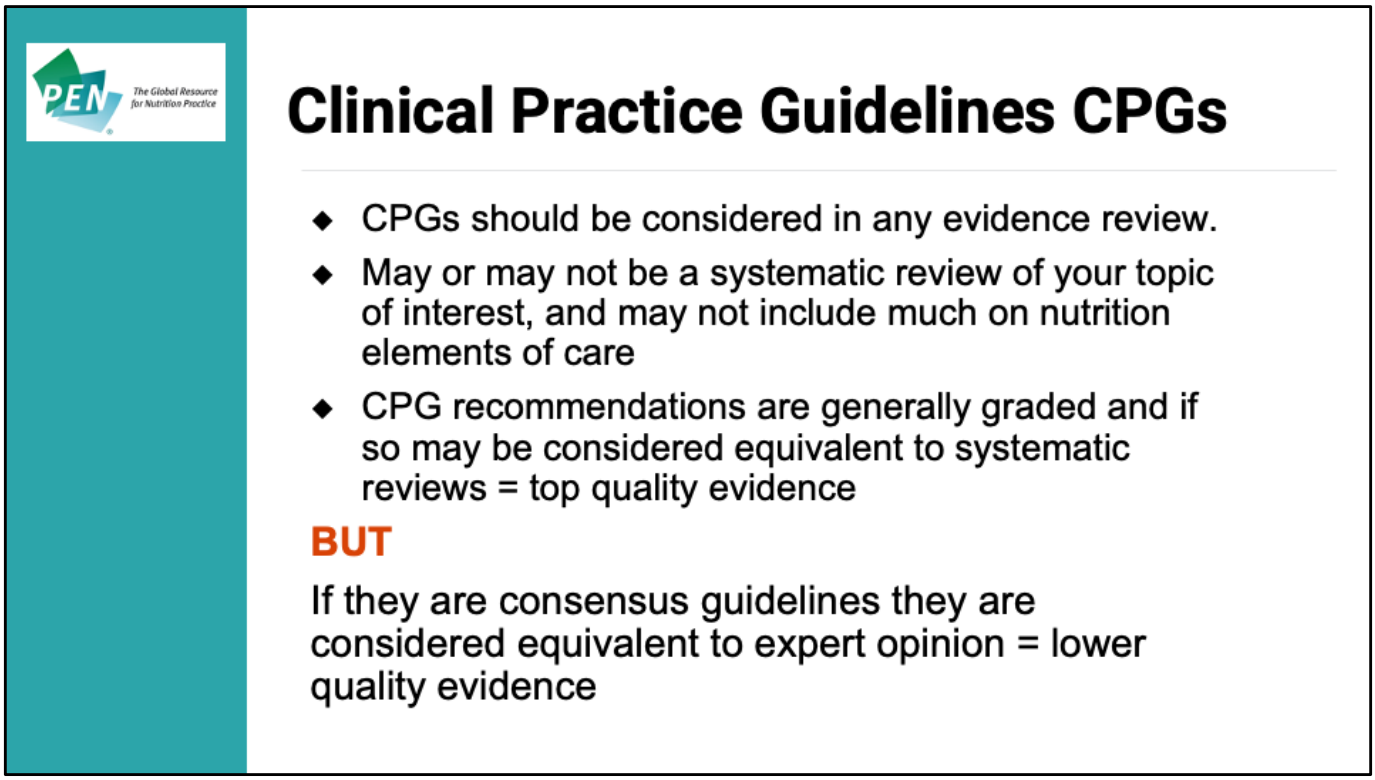


Randomized controlled trials (RCTs) are used to study the effectiveness of a treatment or therapy and can be used to determine causation.

RCTs are considered the strongest quantitative research design. They compare two or more groups where the participants are assigned to these groups through random allocation. This means that all of the participants have an equal chance of being in the experimental or comparison/control group. For any outcome, there are known and unknown factors that affect the outcome. Random allocation allows these factors to be evenly represented among the experimental and comparison/control groups. If random allocation works then both the experimental and control groups will be similar on all known and unknown factors, and thus any difference observed between the groups on the outcomes of interest, can be attributed to the intervention.

RCTs can suffer from weakness if:

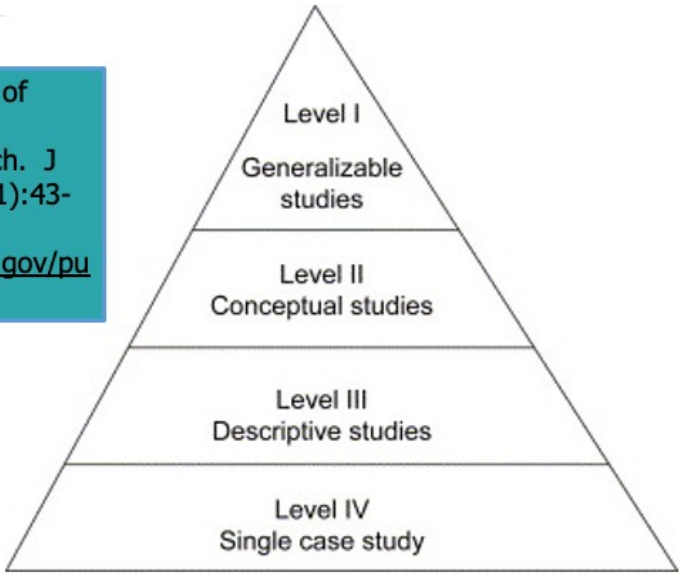
- It was not truly randomized
- Randomization process was not blinded (and could be altered, on purpose or not)
- It was not adequately blinded – subjects and investigators
- There was a high drop-out rate



Read slides… in the PEN® training module: "Appraising the Literature" we share some tools to evaluate CPGs…

Hierarchy of Qualitative Research

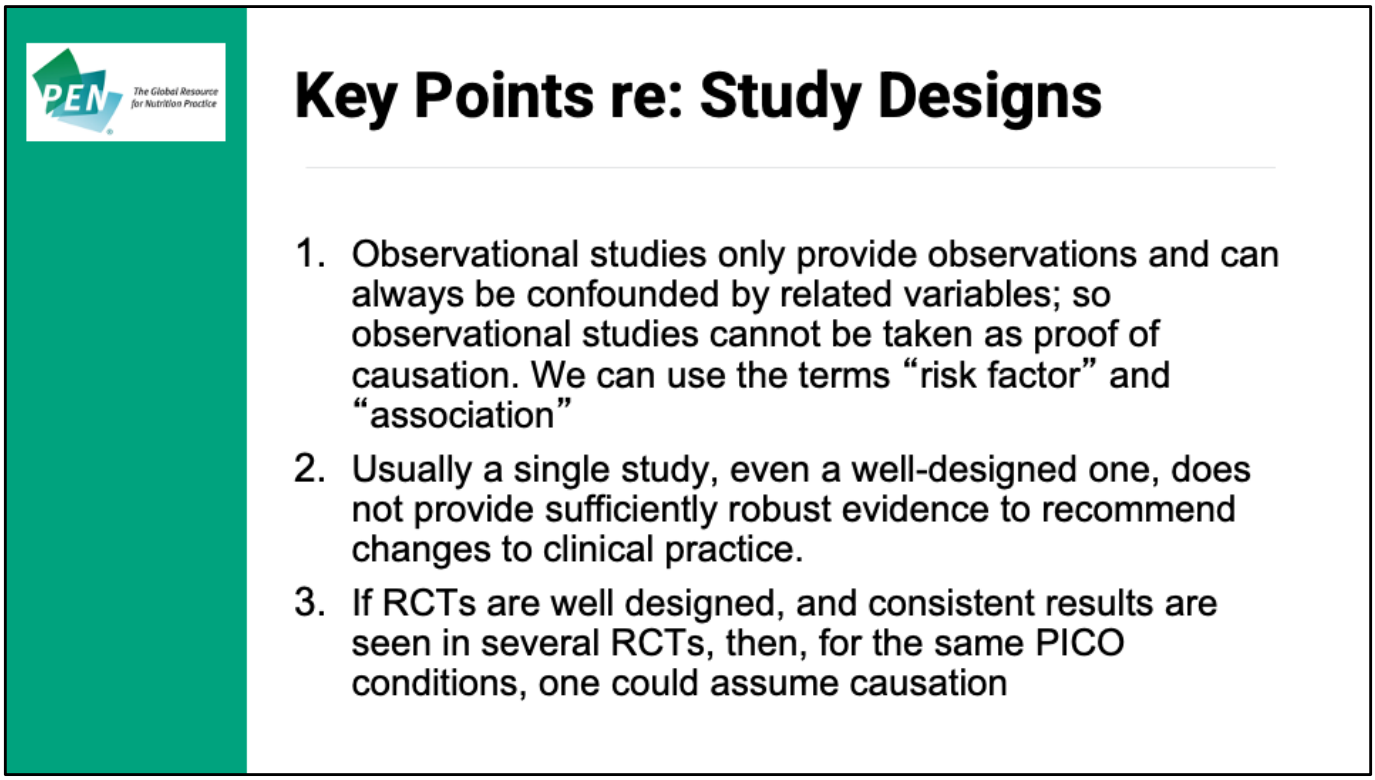
Daly J. et al. A hierarchy of evidence for assessing qualitative health research. J Clin Epidemiol. 2007;60(1):43-9. http://www.ncbi.nlm.nih.gov/pubmed/17161753



Here is a hierarchy for appraising qualitative evidence.

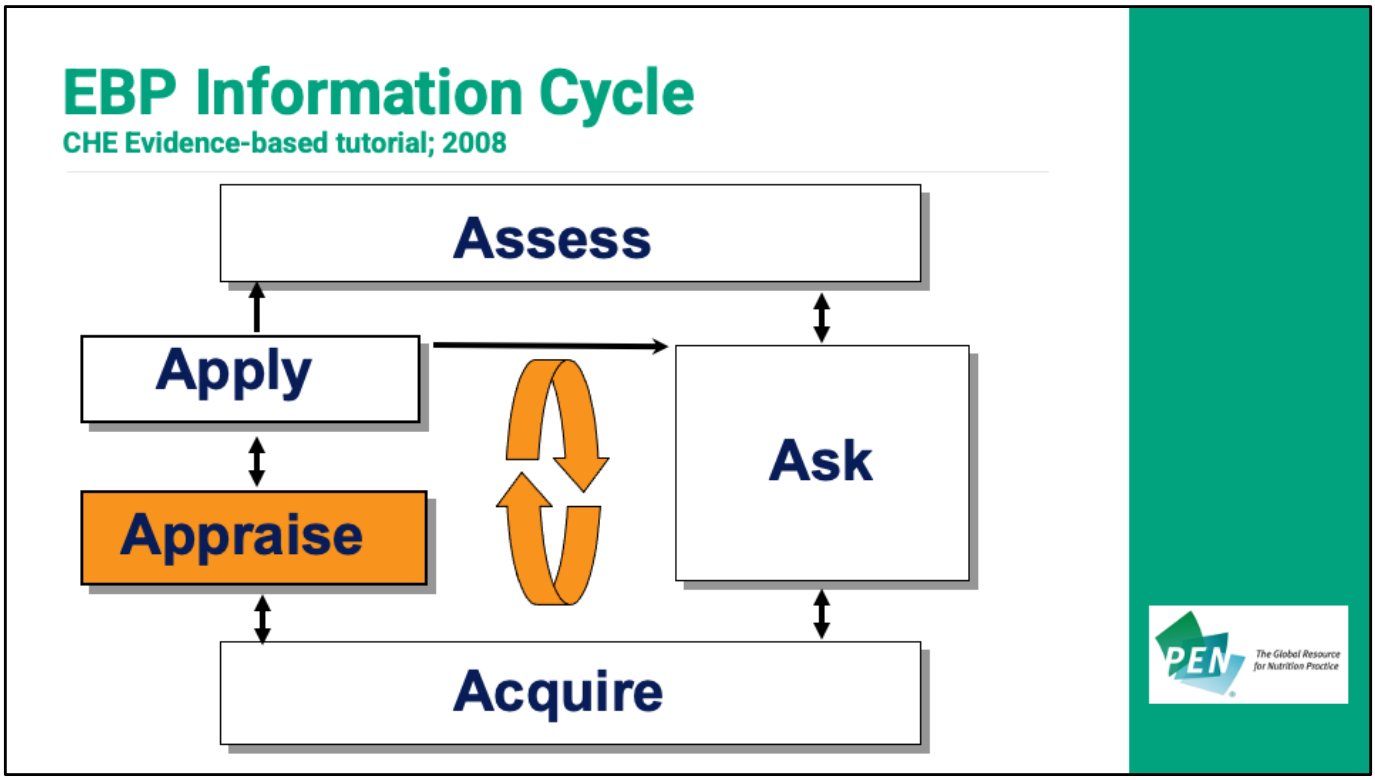
Qualitative studies use non-numerical information, and can provide valuable insight into how people experience states of health and illness or how things came about.

Generally qualitative studies are beyond the scope of this presentation. However, in case you are assessing qualitative evidence, here is a reference to a tool to assess their rigor. Abstract available at: http://www.ncbi.nlm.nih.gov/pubmed/17161753

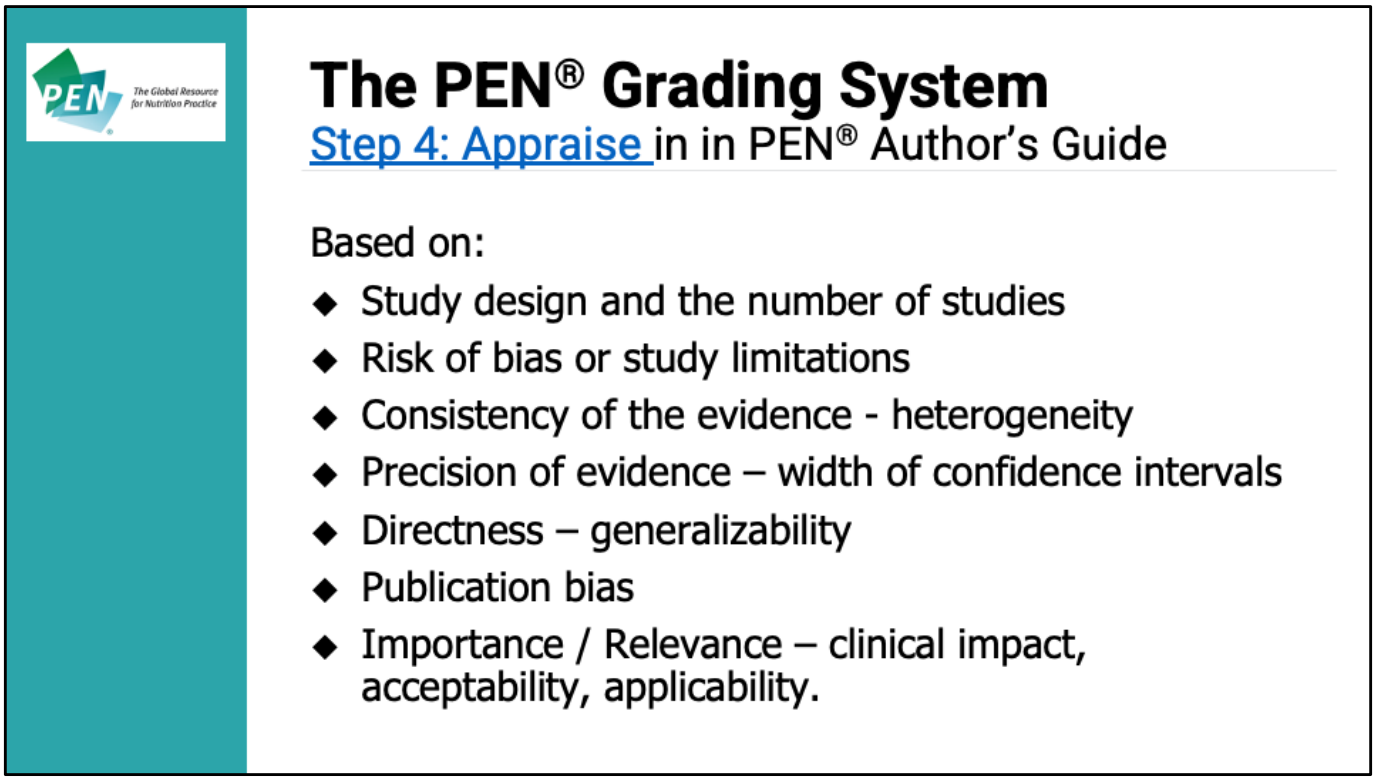


Read slide. If study design is new to you and you would like more information, complete the "PEN Quick Review of Study Designs" training module

Observational studies provide answers to questions regarding etiology of disease, or prognosis.



Critically appraising the evidence



Similar to other credible grading frameworks… the PEN® Grading system…read slide
PEN® Evidence Grading Checklist is posted on the PEN Authors and Reviewers Resources page as a PDF document:
https://reso.pennutrition.com/dyncontent/EvidenceGradingChecklist13Oct2021.pdf

Giving Evidence a Grade

PEN Evidence Grading Checklist

Grade (A):
The conclusion is supported by GOOD evidence.

Grade (B):
The conclusion is supported by FAIR evidence.

Grade (C):
The conclusion is supported by LIMITED evidence or expert opinion.

Grade (D):
A conclusion is either not possible or extremely limited because evidence is unavailable and/or of poor quality and/or is contradictory.

A number of information sources were used in developing a grading system for PEN. See references in Evidence Grading Checklist.

https://reso.pennutrition.com/dyncontent/EvidenceGradingChecklist13Oct2021.pdf

Grade A:

The conclusion is supported by GOOD evidence.

1. Quality or certainty of evidence

The results for a specific intervention/outcome are from high quality studies for answering the practice question as described in the bullet points below. Supporting studies might consist of:

Treatment/Intervention Studies

- good quality systematic review (SR) and meta-analysis (MA) of randomized controlled trials (RCTs) that meet most of the criteria in bullet points below
- two or more high quality randomized, controlled trials that meet most of the criteria in bullet points below.

Etiology/Prognosis Studies

- SR and MA of cohort studies or two or more independent well-done prospective cohort studies that meet most of the criteria described in bullet points below and where treatment/exposure effects are sufficiently large (e.g., 2-fold increase or decrease in one group compared to another), where a dose-response gradient is reported or when residual confounders would be likely to decrease the effect (e.g. sicker patients receive the exposure but still fare better).

Note: Evidence might also be in a position statement or practice guideline from a national body or organization reporting results of research studies based on the aforementioned types of research or assessed as high certainty of evidence using GRADE process.

	√
• Risk of bias or study limitations[i] - results are generally at low risk of bias with no apparent study limitations.	
• Inconsistency[ii] - results are generally consistent (low heterogeneity, e.g. I^2 < 40%).	
• Imprecision[iii] – effect estimates are generally precise if able to be determined, otherwise indicate not applicable (NA).	
• Indirectness[iv] – results are generalizable to the population being assessed.	
• Risk of publication bias or reporting bias[v] – not evident if assessed in MA, otherwise indicate not applicable (NA).	
2. Importance/Relevance[vi]	
• Clinical impact/balance between desirable and undesirable effects – the results are clinically important with a large gradient between benefits and risks.	
• Acceptability/values and preferences – most patients would value the outcomes as important and be willing to accept the intervention.	
• Applicability/costs – results are applicable to the practice setting and resource implications are justified.	

PEN The Global Resource for Nutrition Practice

This slide and the next 3 slides provide examples of evidence and other factors to consider in grading the evidence (this information is drawn from the PEN® Evidence Grading Checklist in PEN® Training Materials section of the website.

Grade B:

The conclusion is supported by FAIR evidence.

1. Quality or certainty of evidence

The results for a specific intervention/outcome are from studies of strong design with minor methodological concerns as described in the bullet points below or from studies with weaker designs for answering the practice question. Supporting studies might consist of:

Treatment/Intervention Studies

- systematic review (SR) of RCTs with some minor methodological issues as described in bullet points below.
- a single RCT with low risk of bias[i]
- two or more RCTs with a clinically significant conclusion and unclear risk of bias[i].

Etiology / Prognosis Studies

- SR of cohort studies or two or more well-done prospective cohort studies that meet most of the criteria in bullet points below.

Note: Evidence might also be in a position statement or practice guideline from a national body or organization reporting results of research studies based on the aforementioned types of research or assessed as moderate certainty of evidence using GRADE process.

	√
• Risk of bias or study limitations[i] – results may have unclear risk of bias with some study limitations.	
• Inconsistency[ii] – results may have minor inconsistencies at most (moderate heterogeneity e.g. I^2 30 to 60%).	
• Imprecision[iii] – effect estimates may have concerns about precision if able to be determined, otherwise indicate not applicable (NA).	
• Indirectness[iv] – there is minor doubt about generalizability to the population being assessed.	
• Risk of publication bias or reporting bias[v] – may be evident if assessed in MA, otherwise indicate not applicable (NA).	
2. Importance/Relevance[vi]	
• Clinical impact/balance between desirable and undesirable effects – there is minor doubt about the clinical importance of results with a moderate gradient between benefits and risks.	
• Acceptability/values and preferences – some patients would value the outcomes as important and likely be willing to accept the intervention.	
• Applicability/costs – results are generally applicable to the practice setting and resource implications may be justified.	

Grade C:

The conclusion is supported by LIMITED evidence.

1. Quality or certainty of evidence

The results for a specific intervention/outcome are from studies of weak design for answering the practice question or there is substantial uncertainty attached to the conclusion as described in most of the bullet points below. Supporting studies might consist of:

Treatment/Intervention Studies

- two or more RCTs with inconsistent results or high risk of bias
- non-randomized trial or trial that used historical controls
- systematic review (SR) of cohort or case-control studies (with homogeneity) or two or more well-done prospective cohort studies with consistent findings.

Etiology / Prognosis Studies

- SR of cohort and case-control studies (with heterogeneity) or two or more studies with some inconsistent results
- results from a single cohort study or two or more case-control studies, unconfirmed by other studies
- results from a number of high-quality cross-sectional studies, well described case reports or case series.

Note: Evidence might also be in a position statement or practice guideline from a national body or organization reporting results of research studies based on the aforementioned types of research or based on expert consensus or assessed as low or very low certainty of evidence using GRADE process.

	√
• Risk of bias or study limitations[i] - results are at a high risk of bias with obvious study limitations.	
• Inconsistency[ii] - results may be inconsistent (high heterogeneity e.g. I^2 >60%).	
• Imprecision[iii] – effect estimates may be imprecise if able to be determined, otherwise indicate not applicable (NA).	
• Indirectness[iv] – there may be substantial doubt about generalizability to the population being assessed or the outcome is a surrogate (e.g. markers such as blood tests).	
• Risk of publication bias or reporting bias[v] – may be evident if assessed in MA, otherwise indicate not applicable (NA).	
2. Importance/Relevance[vi]	
• Clinical impact/balance between desirable and undesirable effects – there is uncertainty about the clinical importance of the results with a small to moderate gradient between benefits and risks.	
• Acceptability/values and preferences – there is uncertainty about whether patients would value the outcomes as important and uncertainty about willingness to accept the intervention.	
• Costs/applicability – there is uncertainty about the applicability of the results to the practice setting and resource implications may be difficult to justify.	

Grade D:

A conclusion is not possible or extremely limited because evidence is unavailable and/or of poor quality and/or is contradictory

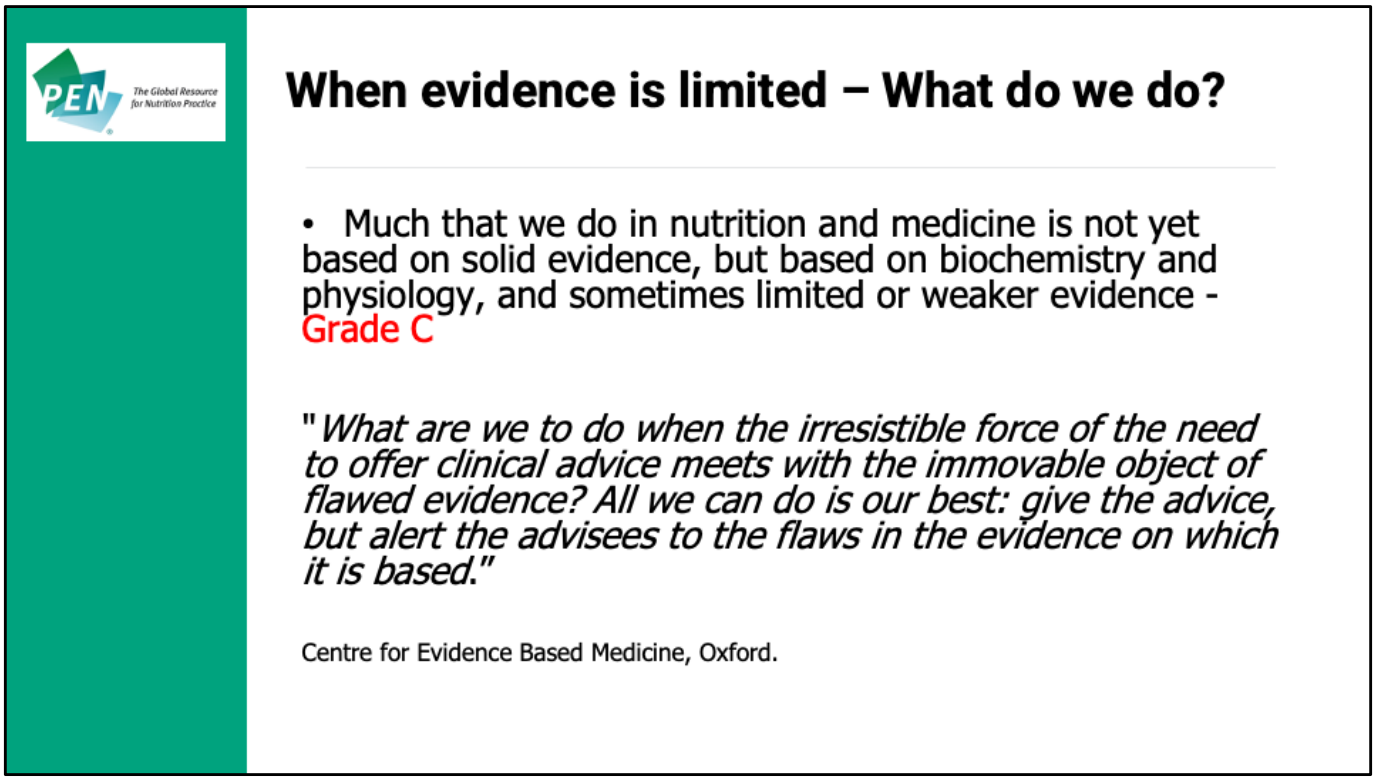
1. Quality or certainty of evidence

The results for a specific intervention/outcome are from a single study with major design flaws or from studies with contradictory results that meet all of the criteria in bullet points below such that conclusions can't be confidently drawn. Alternatively, evidence is lacking from either authoritative sources or research involving humans. Supporting studies might consist of:

- a very poorly designed and executed trial or intervention
- evidence from a single case report, case series, case-control study or ecological study unconfirmed by other studies
- anecdotal reports
- evidence from a small number of similar quality studies that report contradictory results (e.g. two cohort studies that report opposite associations)
- research in the *in vitro*, *ex vivo* or animal model.

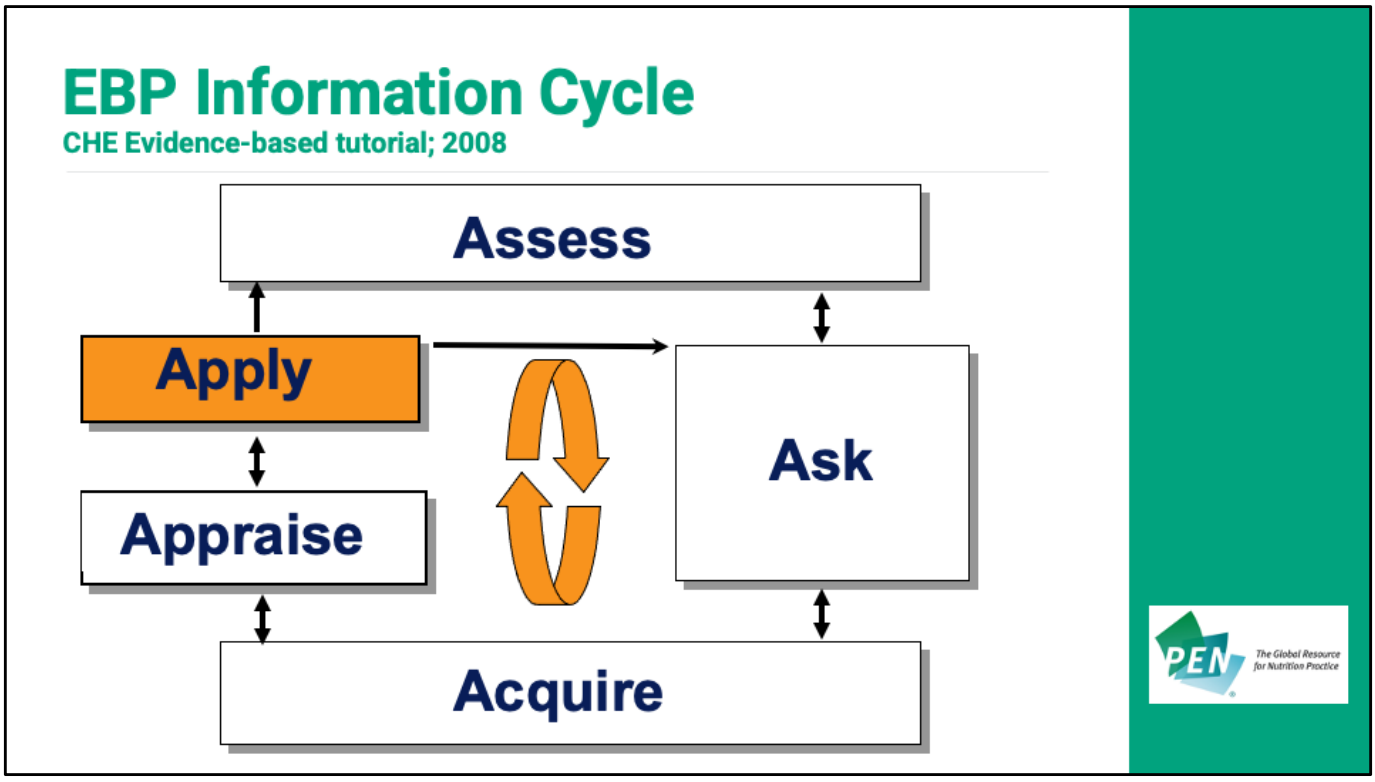
Note: Evidence might also be in a position statement or practice guideline from a national body or organization reporting results of research studies based on the aforementioned types of research or where no recommendation is able to be provided using GRADE process.

	√
• Risk of bias or study limitations[i] - results are at high risk of bias or with major study limitations.	
• Inconsistency[ii] - usually inconsistent	
• Imprecision[iii] – effect estimates are imprecise if able to be determined, otherwise indicate not applicable (NA).	
• Indirectness[iv] – not generalizable to the population being assessed, very limited generalizability or due to use of surrogate outcomes.	
• Risk of publication bias or reporting bias[v] – evident if assessed in MA, otherwise indicate not applicable (NA).	
2. **Importance/Relevance**[vi]	
• Clinical impact/balance between desirable and undesirable effects– the results are minimal or there is little to no gradient between benefits and risks.	
• Acceptability/values and preferences – many patients would not value the outcomes or be likely to be concerned about accepting the intervention.	
• Applicability/Costs – results are not applicable or have very limited applicability to the practice setting or have high resource implications.	

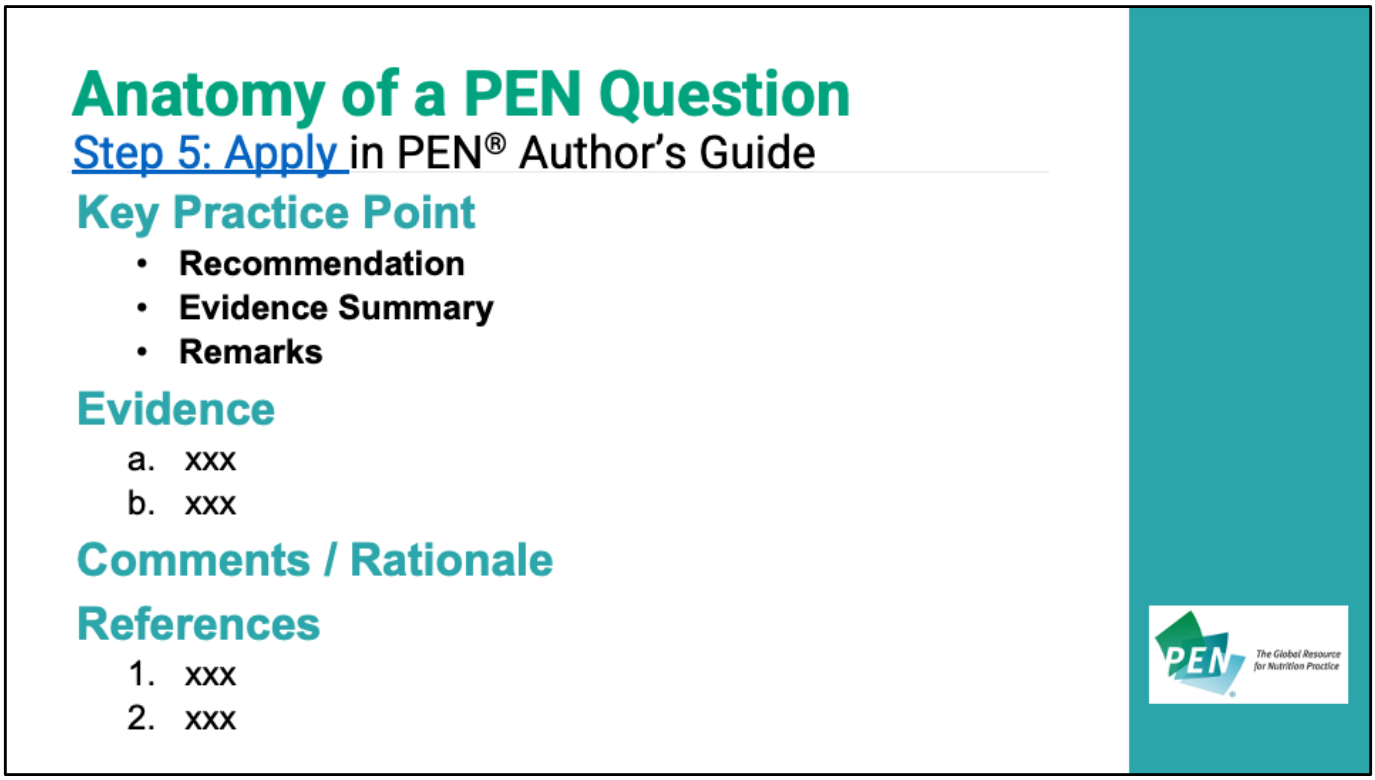


In other words, our job is to identify the level of evidence, whether it is high or low.

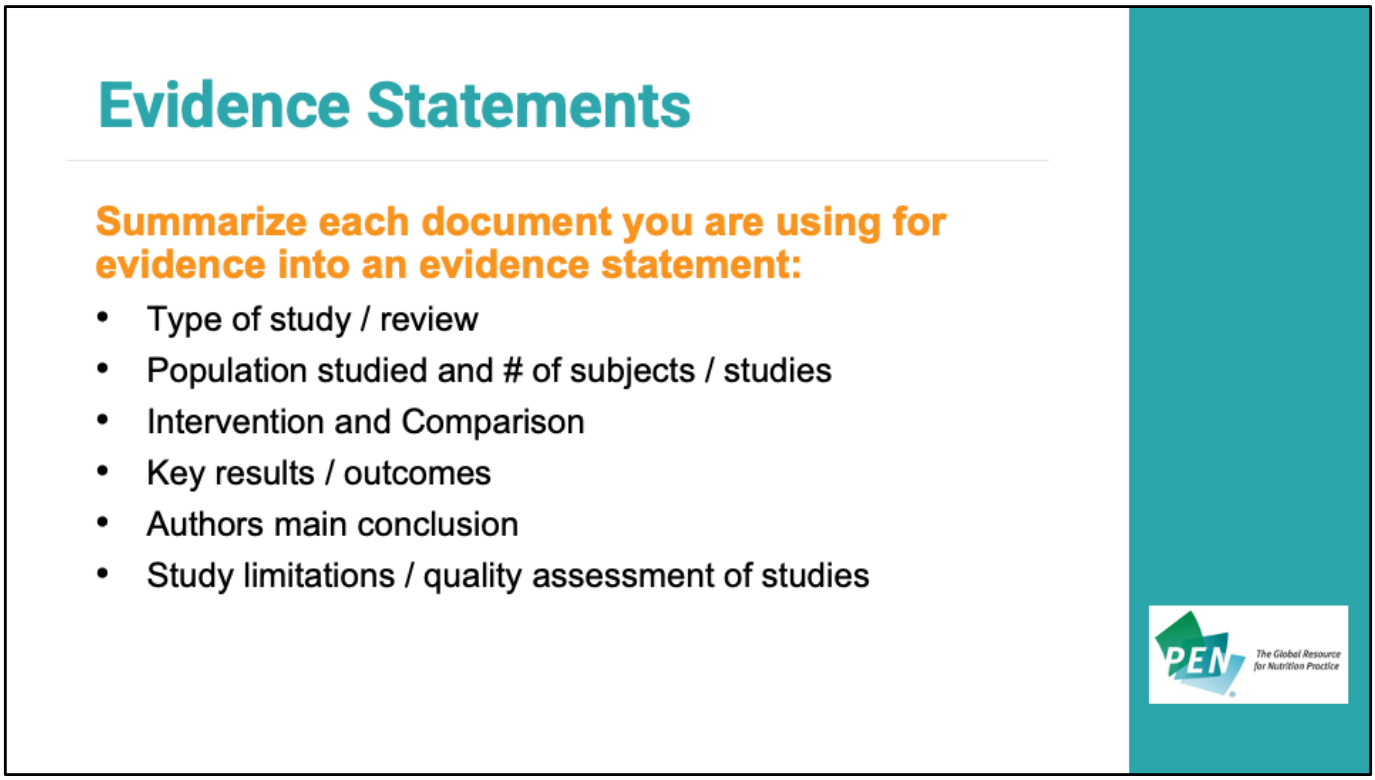
For more information on critically appraising the literature, we encourage you to view the "PEN® Appraising the Literature" training module which contains links to additional learning modules on appraisal as well as an additional guideline for appraising CPG's. It also walks you through an appraisal exercise.



Now the practical part – applying what you have found and developing the key practice point or practice recommendation. Applying the evidence you have found to answer your question is the basis of the PEN database and requires a number of steps that we are going to go through. This is the stage where the grade of evidence is assigned.



In writing the content for PEN, it is useful to look at an overview of the headings in a PEN question.



Keeping in mind these are suggested points of how would you might summarize the article into an evidence statement. The PEN® user should be able to have a snapshot of the article, why it has been used to support the key practice point and how it influences the grade of evidence for the key practice point.

The evidence statement should not be a re-gurgitation of the paper's abstract. In fact, so as not to be biased by how the author's summarized the study as they did in their abstract you may find it helpful when writing your evidence statements to not re-read the abstract until you are done extracting from the full paper.

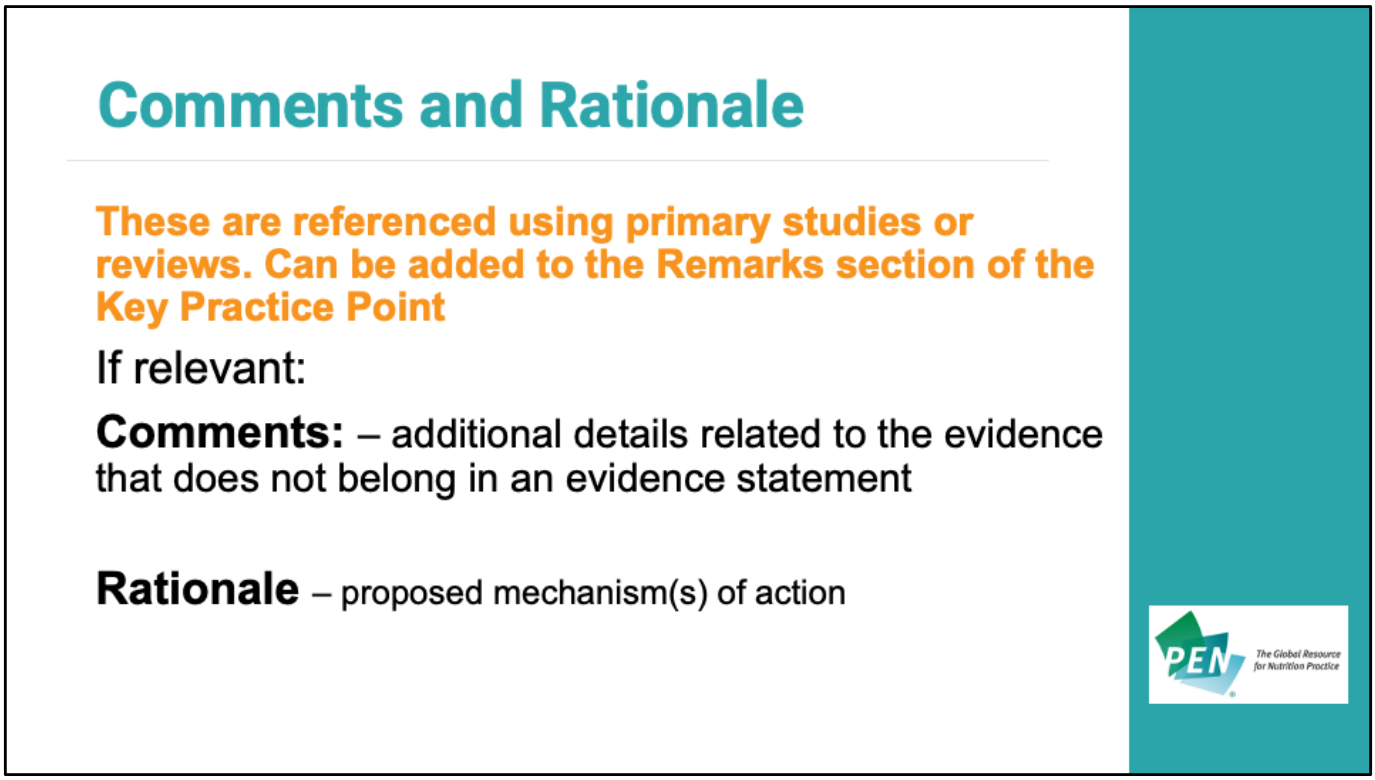
We want to be thorough but also concise. You will not always have to include inclusion/exclusion criteria in the evidence statement but should be evaluating these factors in your critical appraisal. Sometimes it can be concisely communicated in the description of the population. Likewise, the study methods do not need to be written in extreme detail but they should be evaluated in your critical appraisal for their limitations and appropriateness. Some aspects of methods and measures can be combined with the sentences describing the results. Additionally, you may find that there are results presented in the study that do not pertain to your practice question, these should not be included. Just include the findings that relate to your topic/question.

In addition to noting the study authors' main conclusions and admitted limitations, you should also note any limitations that you have identified in your critical appraisal of the study. To do this, re-insert the citation number to indicate that is the end of the information provided by the author and then make your statements regarding conclusions and limitations. See PEN® Authrs and Reviewers Guide: http://www.pennutrition.com/WriterGuide.aspx

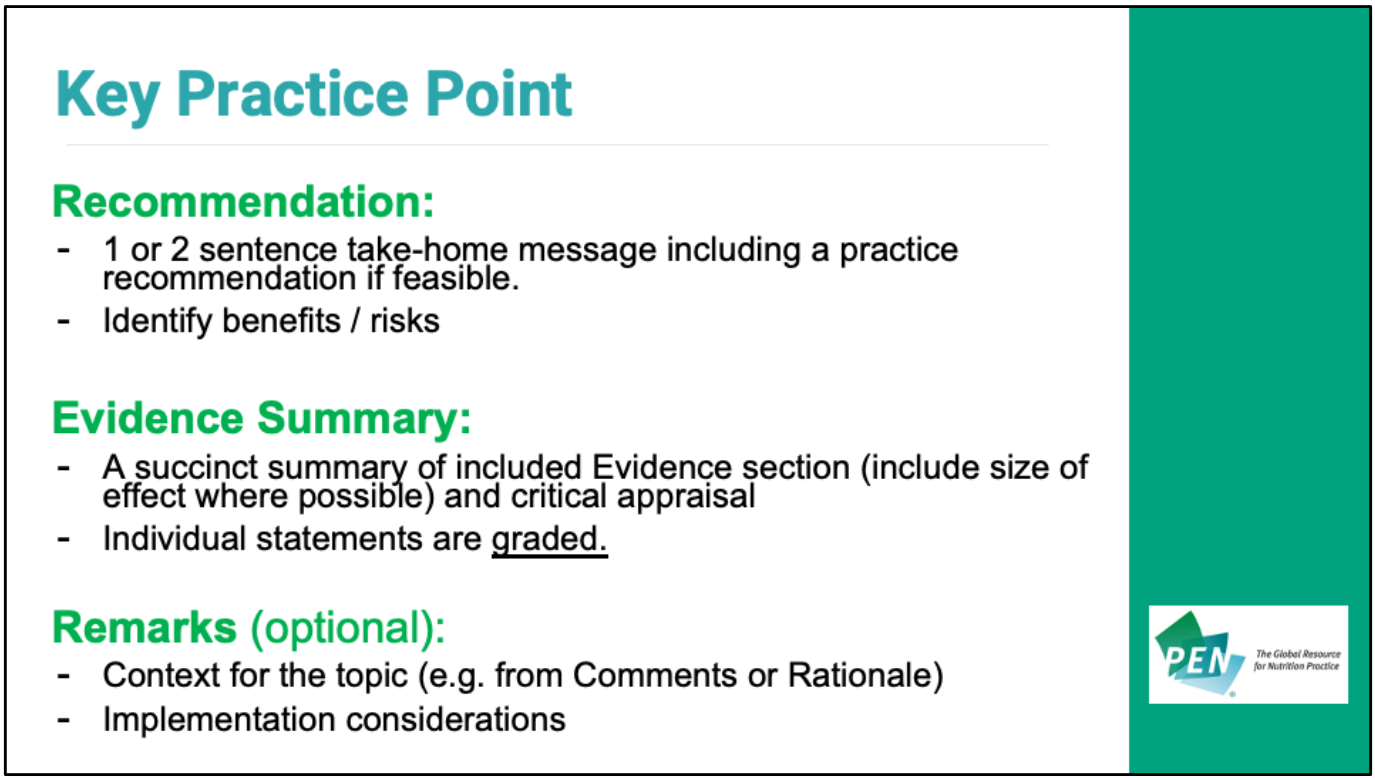
Evidence Statements (example)

A 2019 systematic review and meta-analysis (search to April 2017) investigated the effect of dietary isoflavones (naturally-occurring plant chemicals) or isoflavone foods (including soy) on the risk of breast cancer (1). A total of 16, moderate to high quality (assessed by the authors via Newcastle Ottawa Scale), prospective cohort studies (n=648,913), ranging from two to 14.1 years in length were included in the review. Studies were undertaken across a range of countries including the U.S. (n=5), Japan (n=4), U.K. (n=2), Netherlands (n=1), Sweden (n=1), France (n=1), China (n=1) and Singapore (n=1). For isoflavone intake, both high and moderate intake compared to low was not associated with an increased or decreased risk of developing breast cancer and this lack of association remained after further subgroup analysis. For intake of soy foods, a moderate intake compared to low was not associated with a difference in the risk of developing breast cancer. A high soy intake (six studies) compared with low was associated with a reduced risk of developing breast cancer (RR 0.87, 95%CI 0.76 to 1.00, *P*=0.048). The definition for high was not provided nor did it appear consistent between studies. The authors identified that the findings were limited by the differences of the included studies, particularly in regards to the methodology for measuring dietary exposure or intake. The authors concluded that a high intake of soy can reduce breast cancer risk.

Read slide



- Comments E,g, sources of chromium in foods, different valances of chromium – food versus chemical and industrial; length of trials and lack of clarity on safety
- Rationale: explains the proposed mechanism of action, reasoning behind the research hypothesis, explanations for theories



Taking all of the evidence into consideration develop a key practice point or practice recommendation that also succinctly summarizes the evidence used.

Read slide.

When relevant, it is important to consider risk versus benefits of a health decision with the client instead of feeling pressure to make the decision in the KPP and saying there is not enough evidence to say one should….. There are many examples in nutrition where the evidence is mixed or grey or incomplete.

So a KPP conclusion may sometimes be: “discuss risks and benefits with the client” versus “there is not enough strong evidence to recommend…..”

Key Practice Point - example

Recommendation

Commercial detoxification (detox) diets may be harmful and should not be recommended. There is no evidence to support the use of detox diets for weight loss, bowel health or to prevent colon cancer.

Evidence Summary

A 2015 narrative review noted that rigorous clinical research investigating commercial detox diets, including their effects on weight loss, has not been conducted and that the small amount of existing evidence has been primarily conducted in rodents or fish, is of very low quality and has significant methodological limitations. Risks associated with commercial detox diets include severe energy restriction, nutritional inadequacy, the potential overconsumption of supplements and the overuse of laxatives or diuretics. No benefits of commercial detox diets were described.

No clinical studies were found to support common detoxification diets (including macrobiotic, commercial cleanses or fasting) or herbal products to promote bowel health or prevent colon cancer in humans.

Grade of Evidence D

Remarks

Commercial detox diets are short-term diets (duration not defined) that try to eliminate "toxins" from the body and/or aid in weight loss through starvation or juice fasts and/or the use of laxatives, diuretics, vitamin or mineral supplements and "cleansing" foods.

See more examples in the Pregnancy Knowledge Pathway:
https://www.pennutrition.com/KnowledgePathway.aspx?kpid=3043

Other parts of a Knowledge Pathway

- **Practice Guidance Toolkit**
  - Overview including: key nutrition issues, nutrition assessment, intervention, monitoring / evaluation
  - Client handouts
- **Background**
- **Summary of Recommendations and Evidence**
  - Synthesizes Key Practice Points and Recommendations for each question
- **Related Tools and Resources**

For some of the country specific links our PEN resource managers have created collections – like you see in this example and therefore only one link is necessary. All guideline collections can be found in the PEN Menu: https://www.pennutrition.com/international_guidelines_collection.aspx

The International Healthy Eating Guideline Collection is available from: https://www.pennutrition.com/KnowledgePathway.aspx?kpid=3127&trid=19351&trcatid=27

PEN® Style Guide

PEN® Authors and Reviewers Resources – PEN Authors Tools

- PEN® Style Guide helps to provide consistency in PEN content with so many different authors and writing styles
- Using the PQ Template in the PEN Authors Templates section

See the PEN Style Guide: https://www.pennutrition.com/resources/PEN%20Writers%20Page/PENStyleGuideOctober2018.pdfhttp://www.pennutrition.com/authorsreviewersresources.aspx

Read slide

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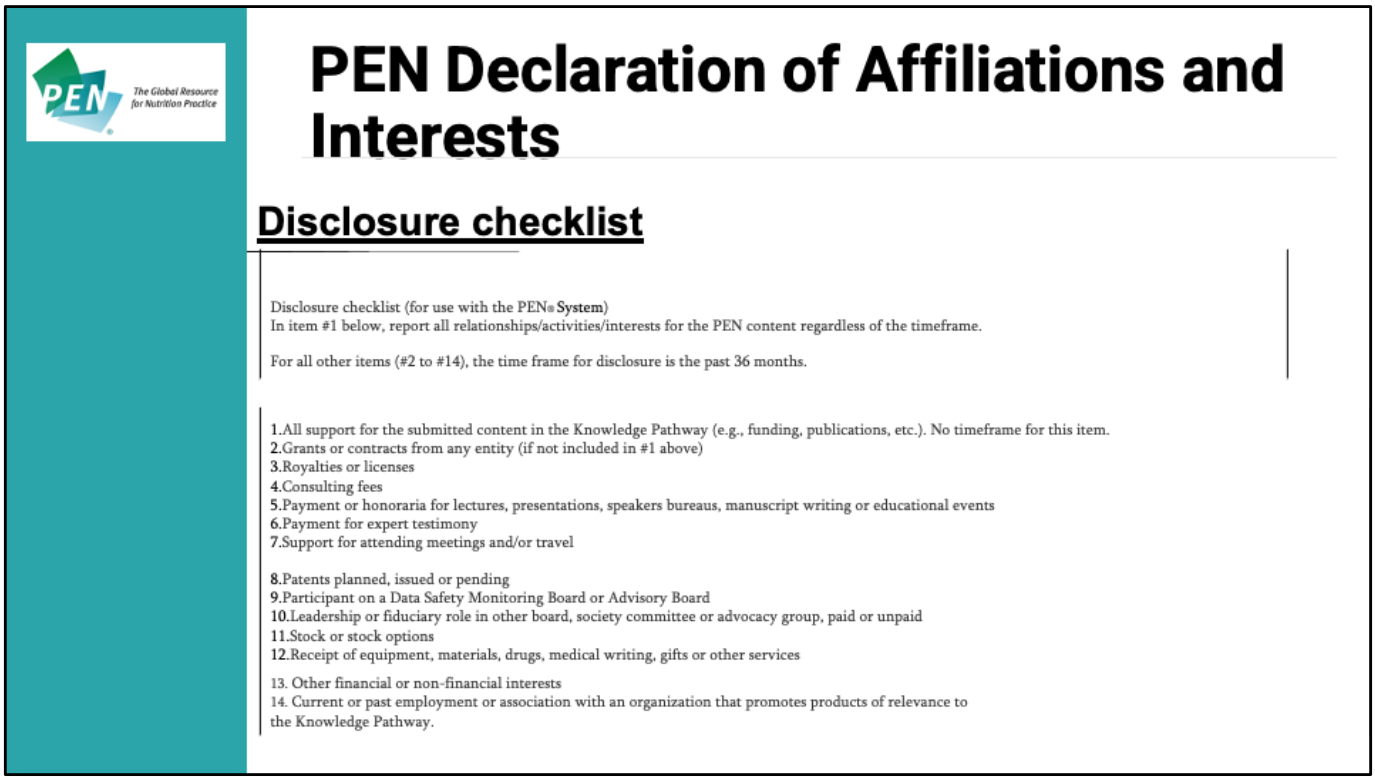
You will receive communications from “PEN Content” that have been sent via the PCMS:

- Asking you to change your password to access the system
- Inviting you to be an author of PEN content
- A link to your assignment and Dashboard

You will upload your content to the PCMS assignment when it is ready for review and sign all legal documents in the system.

A PCMS Guide for Authors can be found: https://reso.pennutrition.com/dyncontent/AuthorsGuidetoPENContentManagementSystem-PCMS(Feb232022).pdf



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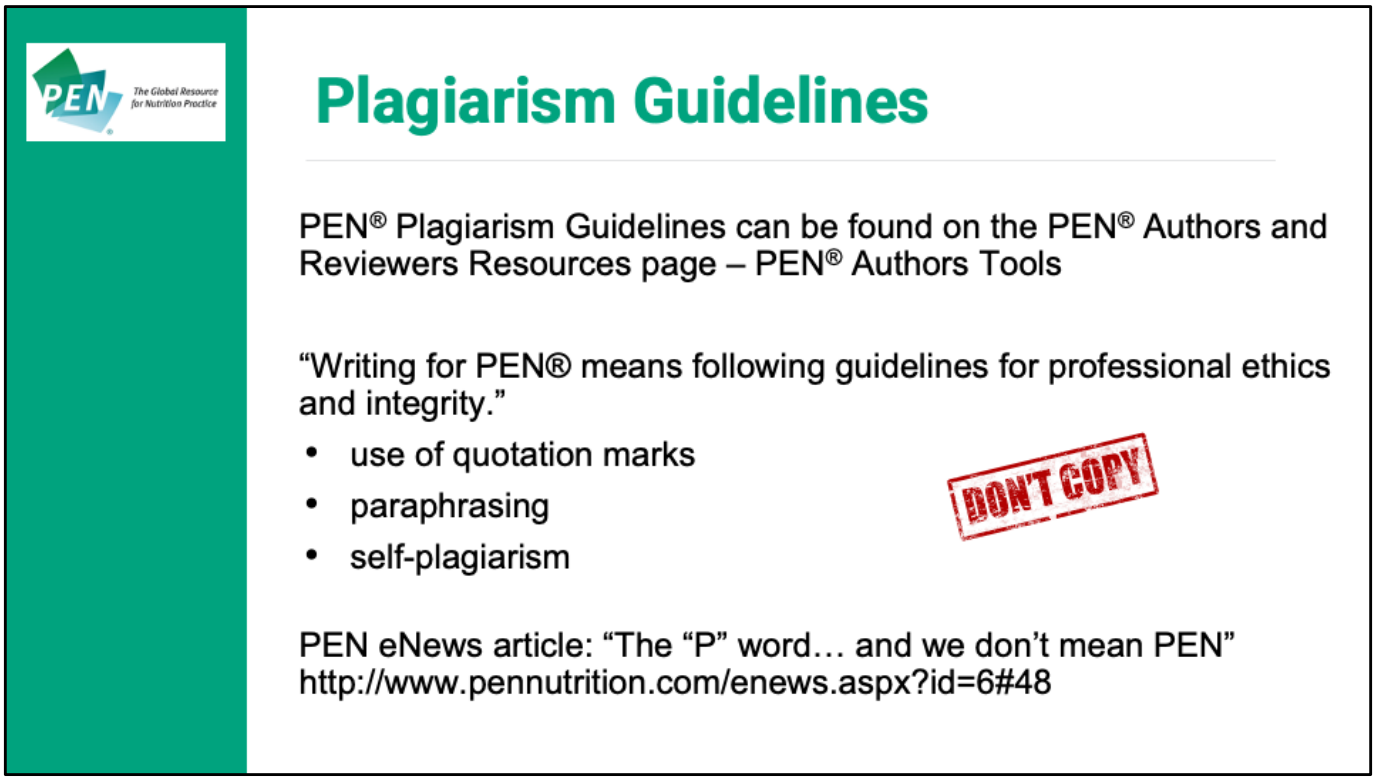
You can see the form on the PEN® website:
https://reso.pennutrition.com/dyncontent/PENDisclosureFormJuly2021.pdf



While it doesn't happen often, from time-to-time we do find some examples of plagiarism in PEN®. We do recognize that plagiarism can sometimes be un-intentional. To make sure you are well aware of all that may be deemed plagiarism and how to avoid it see the guidelines we have developed: http://www.pennutrition.com/resources/PEN_resources/PEN%20Writers%20Guide/PENPlagiarismGuidelines.pdf

To access the PEN eNews article: "The "P" word…. And we don't mean PEN" go to: http://www.pennutrition.com/enews.aspx?id=6#48

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PEN® Training Modules

The following other PEN® Training Modules are available:

- Asking the Question
- Appraising the Literature
- PubMed Module
- Quick Review of Study Designs

The other PEN® Author training modules can be accessed on the PEN® Authors and Reviewers Resources page:
http://www.pennutrition.com/authorsreviewersresources.aspx

Thank you for your time in reviewing this module!

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